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Volume 18
Number 5
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See prescribing summary on page A13

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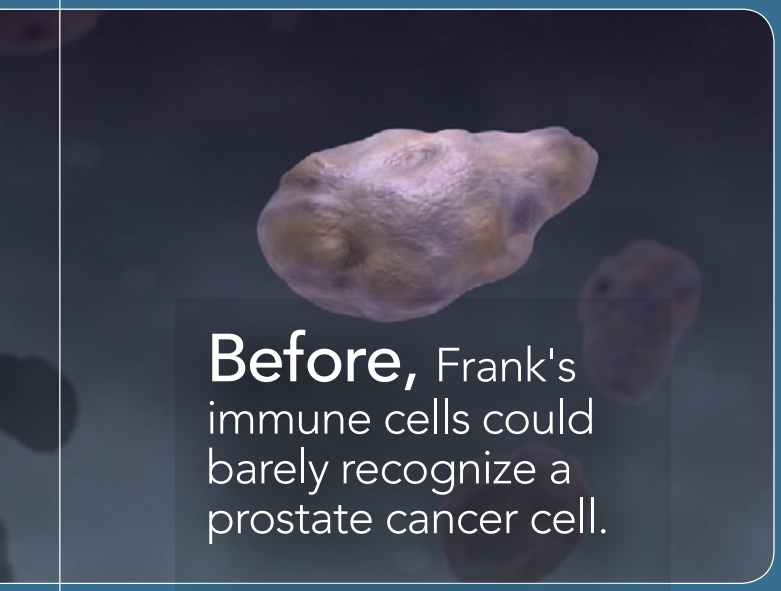
Contents

Volume 18, Number 5, October 2011

In asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer



PROVENGE is the first in a new class of therapy

that is designed to activate a patient's own antigen-presenting cells to stimulate an immune response against prostate cancer.

- **Extends median survival beyond 2 years—**25.8 months compared with 21.7 months for patients in the control* group (*P*=.032)
- **Reduction in risk of death—22.5%** (HR=0.775, 95% CI: 0.614, 0.979)
- **Therapy completed in 3 cycles—**3 infusions, at approximately 2-week intervals†
- **Most common adverse events are primarily mild or moderate—** chills, fatigue, fever, back pain, nausea, joint ache, and headache

*Control was nonactivated, autologous, peripheral blood mononuclear cells.
†The dosing interval ranged from 1 to 15 weeks in controlled clinical trials.

INDICATION: PROVENGE® (sipuleucel-T) is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer.

IMPORTANT SAFETY INFORMATION: PROVENGE is intended solely for autologous use and is not routinely tested for transmissible infectious diseases.

In controlled clinical trials, serious adverse events reported in the PROVENGE group include acute infusion reactions (occurring within 1 day of infusion) and cerebrovascular events. Severe (Grade 3) acute infusion reactions were reported in 3.5% of patients in the PROVENGE group. Reactions included chills, fever, fatigue, asthenia, dyspnea, hypoxia, bronchospasm, dizziness, headache, hypertension, muscle ache, nausea, and vomiting. No Grade 4 or 5 acute infusion reactions were reported in patients in the PROVENGE group.

The most common adverse events (incidence ≥15%) reported in the PROVENGE group are chills, fatigue, fever, back pain, nausea, joint ache, and headache.

Please see Brief Summary of full Prescribing Information on the adjacent page.

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PROVENGE®
(sipuleucel-T)
Stimulate a Response

PROVENGE® (sipuleucel-T)
Suspension for Intravenous Infusion **Rx Only**

BRIEF SUMMARY – See full Prescribing Information for complete product information

INDICATIONS AND USAGE: PROVENGE® (sipuleucel-T) is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer.

DOSAGE AND ADMINISTRATION

- **For Autologous Use Only.**
- The recommended course of therapy for PROVENGE is 3 complete doses, given at approximately 2-week intervals.
- Premedicate patients with oral acetaminophen and an antihistamine such as diphenhydramine.
- Before infusion, confirm that the patient's identity matches the patient identifiers on the infusion bag.
- **Do Not Initiate Infusion of Expired Product.**
- Infuse PROVENGE intravenously over a period of approximately 60 minutes. **Do Not Use a Cell Filter.**
- Interrupt or slow infusion as necessary for acute infusion reactions, depending on the severity of the reaction.

(See Dosage and Administration [2] of full Prescribing Information.)

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

- **PROVENGE is intended solely for autologous use.**
- **Acute infusion reactions** (reported within 1 day of infusion) included, but were not limited to, fever, chills, respiratory events (dyspnea, hypoxia, and bronchospasm), nausea, vomiting, fatigue, hypertension, and tachycardia. In controlled clinical trials, 71.2% of patients in the PROVENGE group developed an acute infusion reaction.

  In controlled clinical trials, severe (Grade 3) acute infusion reactions were reported in 3.5% of patients in the PROVENGE group. Reactions included chills, fever, fatigue, asthenia, dyspnea, hypoxia, bronchospasm, dizziness, headache, hypertension, muscle ache, nausea, and vomiting. The incidence of severe events was greater following the second infusion (2.1% vs 0.8% following the first infusion), and decreased to 1.3% following the third infusion. Some (1.2%) patients in the PROVENGE group were hospitalized within 1 day of infusion for management of acute infusion reactions. No Grade 4 or 5 acute infusion reactions were reported in patients in the PROVENGE group.

  Closely monitor patients with cardiac or pulmonary conditions. In the event of an acute infusion reaction, the infusion rate may be decreased, or the infusion stopped, depending on the severity of the reaction. Appropriate medical therapy should be administered as needed.
- **Handling Precautions for Control of Infectious Disease.** PROVENGE is **not** routinely tested for transmissible infectious diseases. Therefore, patient leukapheresis material and PROVENGE may carry the risk of transmitting infectious diseases to health care professionals handling the product. Universal precautions should be followed.
- **Concomitant Chemotherapy or Immunosuppressive Therapy.** Use of either chemotherapy or immunosuppressive agents (such as systemic corticosteroids) given concurrently with the leukapheresis procedure or PROVENGE has not been studied. PROVENGE is designed to stimulate the immune system, and concurrent use of immunosuppressive agents may alter the efficacy and/or safety of PROVENGE. Therefore, patients should be carefully evaluated to determine whether it is medically appropriate to reduce or discontinue immunosuppressive agents prior to treatment with PROVENGE.
- **Product Safety Testing.** PROVENGE is released for infusion based on the microbial and sterility results from several tests: microbial contamination determination by Gram stain, endotoxin content, and in-process sterility with a 2-day incubation to determine absence of microbial growth. The final (7-day incubation) sterility test results are not available at the time of infusion. If the sterility results become positive for microbial contamination after PROVENGE has been approved for infusion, Dendreon will notify the treating physician. Dendreon will attempt to identify the microorganism, perform antibiotic sensitivity testing on recovered microorganisms, and communicate the results to the treating physician. Dendreon may request additional information from the physician in order to determine the source of contamination.

(See Warnings and Precautions [5] of full Prescribing Information.)

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety evaluation of PROVENGE is based on 601 prostate cancer patients in the PROVENGE group who underwent at least 1 leukapheresis procedure in four randomized, controlled clinical trials. The control was non-activated autologousperipheral blood mononuclear cells.

The most common adverse events, reported in patients in the PROVENGE group at a rate ≥15%, were chills, fatigue, fever, back pain, nausea, joint ache, and headache. Severe (Grade 3) and life-threatening (Grade 4) adverse events were reported in 23.6% and 4.0% of patients in the PROVENGE group compared with 25.1% and 3.3% of patients in the control group. Fatal (Grade 5) adverse events were reported in 3.3% of patients in the PROVENGE group compared with 3.6% of patients in the control group.

Serious adverse events were reported in 24.0% of patients in the PROVENGE group and 25.1% of patients in the control group. Serious adverse events in the PROVENGE group included acute infusion reactions *(see Warnings and Precautions)*, cerebrovascular events, and single case reports of eosinophilia, rhabdomyolysis, myasthenia gravis, myositis, and tumor flare.

PROVENGE was discontinued in 1.5% of patients in Study 1 (PROVENGE group n=341; Control group n=171) due to adverse events. Some patients who required central venous catheters for treatment with PROVENGE developed infections, including sepsis. A small number of these patients discontinued treatment as a result. Monitoring for infectious sequelae in patients with central venous catheters is recommended.

Each dose of PROVENGE requires a standard leukapheresis procedure approximately 3 days prior to the infusion. Adverse events that were reported ≤1 day following a leukapheresis procedure in ≥5% of patients in controlled clinical trials included citrate toxicity (14.2%), oral paresthesia (12.6%), paresthesia (11.4%), and fatigue (8.3%).

Table 1 provides the frequency and severity of adverse events reported in ≥5% of patients in the PROVENGE group of randomized, controlled trials of men with prostate cancer. The population included 485 patients with metastatic castrate resistant prostate cancer and 116 patients with non-metastatic androgen dependent prostate cancer who were scheduled to receive 3 infusions of PROVENGE at approximately 2-week intervals. The population was age 40 to 91 years (median 70 years), and 90.6% of patients were Caucasian.

Table 1 Incidence of Adverse Events Occurring in ≥5% of Patients Randomized to PROVENGE

	PROVENGE (N = 601)		Control* (N = 303)	
	All Grades n (%)	Grade 3-5 n (%)	All Grades n (%)	Grade 3-5 n (%)
Any Adverse Event	**591 (98.3)**	**186 (30.9)**	**291 (96.0)**	**97 (32.0)**
Chills	319 (53.1)	13 (2.2)	33 (10.9)	0 (0.0)
Fatigue	247 (41.1)	6 (1.0)	105 (34.7)	4 (1.3)
Fever	188 (31.3)	6 (1.0)	29 (9.6)	3 (1.0)
Back pain	178 (29.6)	18 (3.0)	87 (28.7)	9 (3.0)
Nausea	129 (21.5)	3 (0.5)	45 (14.9)	0 (0.0)
Joint ache	118 (19.6)	11 (1.8)	62 (20.5)	5 (1.7)
Headache	109 (18.1)	4 (0.7)	20 (6.6)	0 (0.0)
Citrate toxicity	89 (14.8)	0 (0.0)	43 (14.2)	0 (0.0)
Paresthesia	85 (14.1)	1 (0.2)	43 (14.2)	0 (0.0)
Vomiting	80 (13.3)	2 (0.3)	23 (7.6)	0 (0.0)
Anemia	75 (12.5)	11 (1.8)	34 (11.2)	7 (2.3)
Constipation	74 (12.3)	1 (0.2)	40 (13.2)	3 (1.0)
Pain	74 (12.3)	7 (1.2)	20 (6.6)	3 (1.0)
Paresthesia oral	74 (12.3)	0 (0.0)	43 (14.2)	0 (0.0)
Pain in extremity	73 (12.1)	5 (0.8)	40 (13.2)	1 (0.3)
Dizziness	71 (11.8)	2 (0.3)	34 (11.2)	0 (0.0)
Muscle ache	71 (11.8)	3 (0.5)	17 (5.6)	0 (0.0)
Asthenia	65 (10.8)	6 (1.0)	20 (6.6)	2 (0.7)
Diarrhea	60 (10.0)	1 (0.2)	34 (11.2)	3 (1.0)
Influenza-like illness	58 (9.7)	0 (0.0)	11 (3.6)	0 (0.0)
Musculoskeletal pain	54 (9.0)	3 (0.5)	31 (10.2)	3 (1.0)
Dyspnea	52 (8.7)	11 (1.8)	14 (4.6)	3 (1.0)
Edema peripheral	50 (8.3)	1 (0.2)	31 (10.2)	1 (0.3)
Hot flush	49 (8.2)	2 (0.3)	29 (9.6)	1 (0.3)
Hematuria	46 (7.7)	6 (1.0)	18 (5.9)	3 (1.0)
Muscle spasms	46 (7.7)	2 (0.3)	17 (5.6)	0 (0.0)

(Table 1 continued on next page.)

Table 1 Incidence of Adverse Events Occurring in ≥5% of Patients Randomized to PROVENGE

	PROVENGE (N = 601)		Control* (N = 303)	
	All Grades n (%)	Grade 3-5 n (%)	All Grades n (%)	Grade 3-5 n (%)
Hypertension	45 (7.5)	3 (0.5)	14 (4.6)	0 (0.0)
Anorexia	39 (6.5)	1 (0.2)	33 (10.9)	3 (1.0)
Bone pain	38 (6.3)	4 (0.7)	22 (7.3)	3 (1.0)
Upper respiratory tract infection	38 (6.3)	0 (0.0)	18 (5.9)	0 (0.0)
Insomnia	37 (6.2)	0 (0.0)	22 (7.3)	1 (0.3)
Musculoskeletal chest pain	36 (6.0)	2 (0.3)	23 (7.6)	2 (0.7)
Cough	35 (5.8)	0 (0.0)	17 (5.6)	0 (0.0)
Neck pain	34 (5.7)	3 (0.5)	14 (4.6)	2 (0.7)
Weight decreased	34 (5.7)	2 (0.3)	24 (7.9)	1 (0.3)
Urinary tract infection	33 (5.5)	1 (0.2)	18 (5.9)	2 (0.7)
Rash	31 (5.2)	0 (0.0)	10 (3.3)	0 (0.0)
Sweating	30 (5.0)	1 (0.2)	3 (1.0)	0 (0.0)
Tremor	30 (5.0)	0 (0.0)	9 (3.0)	0 (0.0)

*Control was non-activated autologous peripheral blood mononuclear cells.

Cerebrovascular Events. In controlled clinical trials, cerebrovascular events, including hemorrhagic and ischemic strokes, were reported in 3.5% of patients in the PROVENGE group compared with 2.6% of patients in the control group.

(See Adverse Reactions [6] of full Prescribing Information.)

To report SUSPECTED ADVERSE REACTIONS, contact Dendreon Corporation at 1-877-336-3736 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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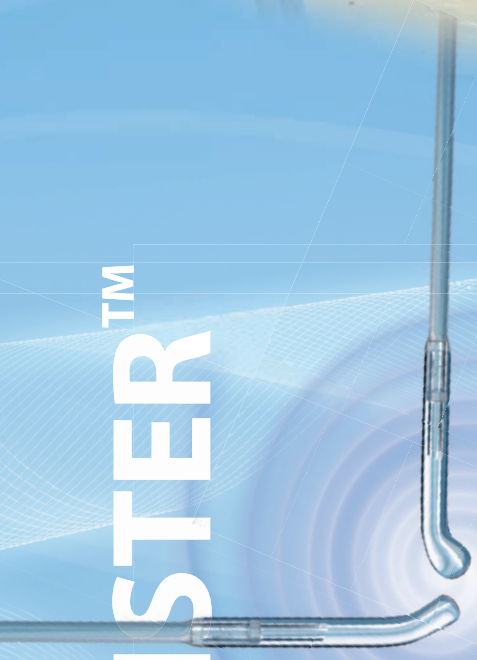

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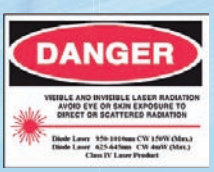

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EDITORIAL

How Many Clicks Does It Take To Get To The Middle Of An EHR?

The electronic health record (EHR) is the current darling of health care reform, the "must have" item for all health care providers. Advertisements boldly announce that the EHR "...allows doctors to spend more face time with patients than on paperwork".

In the ancient history of the paper chart (circa 2008), I would sit face to face with a patient and scan the chart. Flipping through the chart would remind me of key elements in their history. Today I speak to them indirectly over my shoulder while I stare at the computer screen clicking my way through screen after screen searching for that key page, ultimately spending less face time with the patient.

What seems to be paramount in the new world of the EHR is to collect information. Some of this is to achieve the nirvana of "meaningful use". According to one EHR web site "...simply collecting information without addressing the human experience creates disconnection instead of connection; often leading to dissatisfaction by both the patient and provider." I'll click to that.

HIPAA (Health Insurance Portability and Accountability Act) creates another challenge to the efficiency of the EHR. While the need for security of the system is readily apparent, sites require that the EHR system logs out after a relatively few minutes of inactivity. On a typical 25 visit outpatient day (I admit an embarrassingly low number compared to our primary care colleagues) I have to log back in dozens of times. This repetitive activity sometimes makes me feel like I am developing OCD. A thumb swipe or proximity tag system would do much for the EHR functionality allowing instant "re-access" to the EHR. Somewhere in cyberspace I am convinced that there is some arbitrary "regulation" making this logical efficiency unthinkable. Forcing EHR users to manually type and click into the system seems to have become the de-facto norm.

According to EMRconsultant.com, over 600 different EHR vendors exists with each having its own proprietary methods of maintaining data, making efficient communications across EHR systems a challenge to the goal of improving health care communication. Sadly, there exists a government proven and robust nationwide EHR system that can handle vast amounts of data. The Veterans Administration EHR system has stood the test of time. The lack of billing capability has been cited as a reason for not widely distributing the system.

Government incentives are motivating many to rapidly adopt the EHR. Perhaps too rapidly, before the bugs and inefficiencies in these new systems are worked out and the goal of enhanced productivity, cost reductions and improved patient care and safety can be achieved. The official message is that the government is not "forcing" doctors to adopt the EHR, but if doctors do not implement EHRs in their practices, Medicare will deduct 1% of payments in 2015 with the "penalty" increasing to 5% in 2019. Is there really a choice?

One highly touted feature of the EHR was to reduce prescribing errors. A recent study has demonstrated that we are not there yet with the error rate between written and electronically sent prescriptions identical at about 10%. Considering it takes about a dozen clicks to e-prescribe I can see why this might be.

Once fully implemented, the EHR will hopefully be more than the electronic file cabinet of information that it is today. We still have to rely on volumes of paper charts in storage that frequently need to be retrieved from their secret mountain location and scanned into the EHR, an unrecognized cost of transitioning to an EHR beyond the hardware and software. It will take years to fully transition away from the paper chart and work out all of the bugs in a system of this magnitude and importance. The EHR will ultimately serve the health care needs of the future if we can all survive the challenges of the implementation process.

For Mr. Owl, it took only three licks to get to the center of the Tootsie Pop. I wish I could be so lucky.

Leonard G. Gomella, MD
Thomas Jefferson University, Philadelphia PA
Editor-in-Chief

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LEGENDS IN UROLOGY

Arthur Smith, MD
The Arthur Smith Institute of Urology
Chairman Emeritus
Department of Urology
Long Island Medical Center
New Hyde Park, New York, USA

At the American Urological Association (AUA) meeting this year, I was honored to receive the Lifetime Achievement Award and a flattering invitation to contribute to this "Legends in Urology" series. I listened to the accolades from the President of the AUA, as he enumerated how I had developed a subspecialty of urology, formed an international society and founded a journal, and many thoughts flashed through my mind. I could not help thinking that I had been at the right place at the right time to embrace the opportunities to achieve those goals. Moreover, I was fortunate to inter-relate with an outstanding group of colleagues. Collectively, we stimulated each other to develop new techniques and instruments that to a large extent displaced the techniques and instruments with which we were trained.

Early years in the new field

I emigrated from South Africa to the United States in 1977 and was appointed to the staff of the Veterans Administration (as it was then called) Hospital in Minneapolis. One of my first patients had an obstruction of one ureter from cancer of the prostate gland. I elected to re-implant his ureter. A few days postoperatively, he developed a leak from his anastomotic site. Unfortunately, this persisted, and I decided to stent the anastomosis. I could not advance the stent in the usual retrograde manner because of the position of the uretero-cystostomy, so I conceived a plan to pull the stent through the ureter. This involved performing a percutaneous nephrostomy, advancing a catheter down the ureter, grasping the end of that catheter cystoscopically, and then attaching a series of catheters that would allow me to place a Gibbons' stent in the optimal position. This worked very effectively, and in order to explain the technique at our complications conference, I asked the VA Hospital artist to draw a series of pictures to depict the steps in the procedure. The pictures were outstanding and I published them. That was the first paper in endourology, although we did not know it at the time.

This concept of advancing a catheter down the ureter from a percutaneous nephrostomy intrigued me, and I started applying it to other situations. For example, if one attached a stone basket to the catheter, one could capture a stone or even multiple stones because it was guaranteed that the basket could always be moved around appropriately in the ureter. In those days, we did not have ureteroscopes. Other applications were facilitating a ureteral meatotomy and extracting stones from the ureter in a patient with an ileal conduit. The nephrostomy tract became a highway to the interior of the kidney.

Endourology becomes a new Specialty

While I was at the VA Hospital, I was fortunate to work with a very talented radiologist, Dr. Bob Miller, a pioneer of another new specialty, interventional radiology. He could always position a catheter exactly where I wanted it to be located. The hospital had several paraplegic and quadraplegic patients who had indwelling nephrostomy tubes that often became dislodged or occluded. A logical solution was the insertion of circle-tube nephrostomies. This involved making a second nephrostomy puncture, inserting a guide-wire and then retrieving its end through the original nephrostomy site. With Bob's assistance, we were able to grasp the end of the guide-wire with a stone basket, and thereafter, we merely dilated the tract and inserted the circle tube.

The next application of the nephrostomy tract was the attempt to dissolve stones by chemolysis. The installation of acetylcysteine together with sodium bicarbonate was highly effective for ridding patients of cystine stones.

I then used Renacidin to dissolve struvite stones. This was certainly less dramatic because it took a long time, but in those days, the veterans were happy to stay in the hospital and have three good meals a day. It took about 3-4 weeks of continuous irrigation to dissolve a stone.....not very cost effective!

While I was at the VA Hospital, I collaborated with an outstanding resident, Dr. Ralph Clayman, and that collaboration continues to this day, even as he has ascended to the position of medical school dean. At the time, he would allow me to work on only some of the stone patients; he hid the other patients from me because he wanted to do open surgery on them!! He later changed direction, becoming one of the leading developers and exponents of minimally invasive urology.

A name for the new specialty

The VA Hospital was associated with the University of Minnesota Medical School, and at that time the chairman of the urology department was Dr. Elwin E. Fraley. He suggested that we use a descriptive term to embrace this developing field of urology. I selected the name "ENDO-UROLOGY" from the various names that he proposed, as I felt that this quite accurately described the procedures that we were performing. I then defined "Endo-Urology" as "closed manipulation of the genito-urinary tract". This resulted in a poster presentation at the 1978 AUA meeting entitled "Endourology," which my residents privately retitled "End-of-Urology." Their humor was aimed at what they saw as a progressive decrease in the numbers of open surgery procedures!

New adventures at the University of Minnesota

I transferred from the VA Hospital to the University of Minnesota Hospital, where I worked closely with Drs. Willie Castaneda and Kurt Amplatz. The former is the Editor-in-Chief of the leading text in interventional radiology and co-author of my first book on Endo-Urology. Subsequently, I published *Smith's Textbook of Endourology*, and the third edition will be out shortly.

It soon became routine for us to insert a nephrostomy tube in anyone who presented with obstruction of the upper tract, which avoided the bleeding complications and morbidity associated with operating on uremic patients. When I presented these data at a meeting of the Minnesota Urological Society, these concepts were not well-received and the consensus seemed to be that I was apprehensive about operating!!

Kurt Amplatz had an excellent technician in his laboratory, and if one wanted a particular instrument, he would create it by the next day. We thought it would be a good idea to dilate a nephrostomy tract rapidly and then remove a stone or flush it out. The first Amplatz dilators were cylinders with a flush end, but we found that if the kidney was irrigated with those Amplatz sheaths, the pelvic mucosa adhered to the end of the sheath and from then on, the sheaths were cut obliquely to allow irrigation. However, irrigation in itself was a bad idea because it could give rise to gram-negative septicemia. I thought the concept of rapid dilation of the nephrostomy tract was a monumental break-through, but the paper we submitted was rejected by several journals.

Move to the East

In 1982, I became the Chairman of the Urology Department at Long Island Jewish Medical Center in New York and shortly thereafter edited an issue of the *Urologic Clinics of North America* which was devoted to endourology. In the same year, John Wickham organized the 1st World Congress of Endourology in London. Ralph Clayman had recently returned to the University of Minnesota as a faculty member, having done a fellowship in Texas, and he organized the 1st Hands-on Course in Endourology. He came up with the concept of using a pig kidney to teach participants to perform nephrostomies, dilate the tracts, and remove stones. These two efforts launched an era of courses both at the University of Minnesota and Long Island Jewish Medical Center, which drew large numbers of urologists who were eager to learn these procedures.

Subsequently, Drs. Joe Segura, Ralph Clayman, Gopal Badlani, and I formed the "Endourology Society" and held the first World Congress of Endourology in New York City. The financial responsibility of hosting this meeting

was onerous, and we were worried that if it did not attract the requisite attendance or company support, we would have to suffer the losses. Fortunately, Gopal Badlani was able to make it economically viable, and this allowed us to expand the role of the Society. We established fellowships with definite requirements, held annual World Congresses, and, as societies are prone to do, produced a journal.

The journal was definitely not our idea. When Mary Ann Liebert, the highly successful medical and scientific publisher, asked me to start an endo-urology journal for the Society, I tried to demur, because, as I said to her, there were already too many journals. As I soon discovered, Mary Ann does not understand the word "no". I then said that I would edit the journal only if Ralph Clayman, who I knew agreed with me that the world did not need another urology journal, was the coeditor. He too said "no" to Mary Ann, and we thought that we had surely killed the project, but clearly we had underestimated her determination. A few days later, Ralph called to inform me that she had called him again and we were now coeditors of the *Journal of Endourology!*

Our "unnecessary" journal started out as a quarterly, but there soon were so many excellent submissions that Liebert increased the frequency of publication, first to six times a year and now monthly, and each issue is fat with invaluable material. The journal is distributed to thousands of urologists, and most residents in Canada, the USA, Europe, and now many parts of Asia and South America get a free copy. Its website posts videos so that subscribers can view an operative procedure on the Internet at home or even in the operating room. Some issues devoted entirely to techniques have been mailed with CD-ROMs on which those techniques are illustrated with videos. The titles and abstracts of all the papers are translated into 10 languages, making it a truly international journal. This has become necessary, as many countries have formed endourology societies that are affiliated with the original society.

The Society now is stronger than ever, with Steve Nakada as secretary, John Denstedt as Treasurer, and Ralph Clayman as President. We all hope it will continue to evolve successfully. It already has given rise to several sections or subsocieties, many of which have separate meetings. These include the Society for Urology and Engineering, The Robotic Group, The Focal Therapy Group, and Videourology. I was fortunate to be President of the Society for 25 years, with Joe Segura as Vice-President, Gopal Badlani as Treasurer, and Ralph Clayman as Secretary.

I have always believed it is my duty, as part of training the next generation, to stimulate my residents and fellows to publish, because publishing makes one aware of what has been done previously and encourages one to think deeply about one's own findings and what it means. For this reason, I have usually made them the first author in most of the 550 papers and chapters that I have published, as well as in the 150 videos. Five years ago, Lou Kavoussi was appointed Chairman. Not only did he encourage me to continue to work full-time in the department, but he named the department "The Arthur Smith Institute of Urology" and I will always be indebted to him.

As I look back at the development and continuing evolution of endo-urology, I have come to realize that what made it possible was that the thinking of the founders of the endo-urology society meshed so well. We looked at a clinical problem and asked "Do you suppose.....?" "What if.....?" and "Could we.....?" and kept working at it until we had good answers. We also benefited immeasurably from the creativity of many people we never met: the brilliant engineers who created the high-resolution imaging equipment, the increasingly capable endoscopes, and the many devices: catheters, stone baskets, guide-wires, and stents. Often, so prolific were the ideas that an instrument would become obsolete soon after it was produced, as someone came up with a better idea. As a result of this wide collaboration, our specialty was transformed. All these developments have vastly improved the care of patients with urological problems. And that, not the applause and awards (welcome and satisfying as they are), was always the goal of our work.

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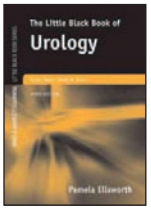
BOOK REVIEW

The Little Black Book of Urology, 3rd Edition

Pamela Ellsworth, MD



ISBN: 1449620035, 274 pages
Publisher: Jones and Bartlett Publishers, Inc.
Rating: ★★★ (three stars out of five)

Description

This is the third edition of a brief and general overview of major urologic disease processes in adults and children using a genitourinary organ-based approach.

Purpose

The purpose is to cover common urologic conditions encountered in general medical and urology practices. The book provides a good overview of pathophysiology, diagnosis, and treatment of these conditions.

Audience

This is a valuable quick reference for both general practitioners and urologists (especially those in training). In particular, the book is well suited for general practitioners, as it provides a urologist's view and thought process behind the work up and treatment of patients with a variety of urologic conditions. Those already specializing in the field of urology, residents or students in training, may find this book useful as a quick guide to management of patients on the hospital wards or in the office.

Features

The first seven chapters deal with common urologic diseases in the adult patient while the remaining six concern the pediatric patient population. The chapters are subdivided into an organ system approach. Each disease process is named and presented in a systematic method. The cause, epidemiology, pathophysiology, symptoms/signs, differential diagnosis, laboratory/radiologic findings, and treatment options are given for each disease condition. Additional references are embedded in the text to provide further in-depth analysis if desired. The book is clear and concise. The tables are well done and appropriately supplement the text. I was pleased with the attention to the references, which should serve readers well who want to investigate further. There are a few limitations that bear mentioning. First, at times the number of references embedded in the text seems overwhelming. Perhaps placing these at the end of a section or chapter may serve readers better. Second, the paucity of figures, images, and color art is apparent, especially for radiologic or physical exam findings, which would help readers' understanding of many topics. Finally, an electronic version of the book that would allow for on-demand access via a mobile device would be useful for clinicians or students in need of a quick reference who do not wish to carry a book in their coat pocket.

Assessment

This book offers enough detail for clinicians/students to gain a good understanding of urologic conditions. The tables and references supplement the text well. Additional figures or artwork would give readers a better visual understanding in certain sections. Overall, this will be an excellent resource for those interested in a quick reference on a multitude of common urologic diseases..

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REVIEW

Immunotherapy in the treatment of advanced prostate cancer

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DJAVAN B, NELSON K, KAZZAZI A, BRUHN A, SADRI H, GOMEZ-PINILLOS A, FERRARI AC. Immunotherapy in the treatment of advanced prostate cancer. The Canadian Journal of Urology. 2011;18(5):5865-5874.

Prostate cancer is a complex disease, and treatment selection is informed by numerous variables depending on the stage of disease. Moreover, patient expectations and the impact of treatment-related adverse events may influence treatment choices. Available treatment options over the course of the disease have included surgery, radiation therapy, hormonal therapy, immunotherapy, and chemotherapy. This complexity requires an understanding of a wide range of treatment options and the support of a multidisciplinary team that involves urologists, radiation oncologists, diagnostic radiologists, pathologists, and medical oncologists. Collaboration among these physicians allows for a comprehensive treatment strategy that addresses the individual needs of the patient throughout the course of his disease.

Prior to 2004, treatment options for metastatic castrate-resistant prostate cancer (CRPC) were limited to therapies for palliation of pain and reduction of skeletal-related events. Over the past 7 years, four therapeutic options—three within the last 2 years—that provide a survival benefit in this setting have been approved. These therapies have diverse mechanisms, perhaps reflecting the complex nature of advanced prostate cancer. Among them is sipuleucel-T, the first autologous immunotherapy approved for any cancer. This review will discuss the rapidly changing treatment environment for metastatic CRPC and the increased exploration of immunotherapeutic approaches to advanced prostate cancer.

Key Words: immunotherapy, metastatic castrate-resistant prostate cancer, advanced prostate cancer, sipuleucel-T, abiraterone, docetaxel, cabazitaxel, PSA-TRICOM, ipilimumab, autologous cellular immunotherapy, active immunotherapy, GVAX

Disease state overview

Prostate cancer is the most commonly diagnosed malignancy, excluding skin cancer, and the second leading cause of death from cancer among men in the United States.[1] As a result of the introduction of widespread prostate-specific antigen (PSA) screening approximately 20 years ago, prostate cancer is now diagnosed predominantly as local/regional disease, Figure 1.[1] This change is also reflected in the dramatic stage migration that has occurred, both in the United States and Europe,[2,3] such that about 84% of cases of prostate cancer in the United States are low or intermediate risk at diagnosis.[2]

The 10 year survival rate for low risk, clinically localized disease is approximately 95% with definitive treatment (surgery or radiation therapy).[4,5] However, nearly one-third of the subset of men with intermediate to high risk disease who receive definitive treatment will develop progressive disease that requires additional therapy.[6] A subgroup of these men experience local recurrence that can be treated with adjuvant or salvage radiation therapy following a radical prostatectomy or with cryotherapy if they have received radiation therapy.[7-10]

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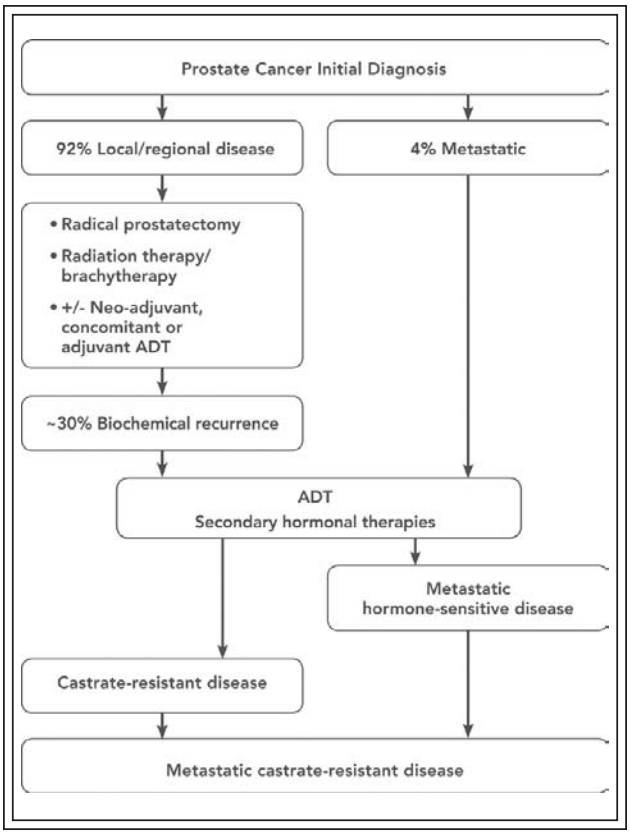

Figure 1. Prostate cancer disease progression.

A considerable body of evidence has been developed defining clinical parameters that can serve as guides for physicians in determining treatment for patients with biochemical recurrence after definitive therapies.[11-15] These parameters include Gleason score, time to biochemical recurrence, tumor stage, and PSA doubling time (PSADT). PSADT after local therapy has been validated to be the most predictive marker of survival[12-14] and is currently used in clinical trials to select patients with biochemical failure for new treatment modalities as well as to define the need to initiate androgen deprivation therapy (ADT).

ADT has been the cornerstone of treatment for men whose disease progresses after all forms of definitive therapy have been exhausted and for those men who present with de novo metastatic disease.[16,17] Although ADT is highly effective in reducing tumor burden and PSA levels, its use in patients with rising PSA has been controversial given the effects associated with long term use, including reduced quality of life, increased risk of incident diabetes and cardiovascular disease, metabolic syndrome, and fractures.[18-20] ADT is used in the following settings: as neoadjuvant and adjuvant therapy with primary radiation therapy for high risk disease, where it offers a survival advantage over radiation alone; in locally advanced disease not amenable to definitive local therapy, where it has been shown to increase time to progression; in the case of lymph node metastases, after radical prostatectomy; and for the palliation of symptomatic metastases.[17,21,22]

Although the median duration of response is approximately 10 years,[23,24] nearly all men receiving ADT will eventually develop progressive disease. Some men will respond to secondary hormonal manipulations, including addition or withdrawal of antiandrogens, adrenal androgen inhibitors such as ketoconazole, or estrogens; however, their disease will inevitably progress to castration resistant prostate cancer (CRPC).[16]

Unlike early prostate cancer, CRPC is an aggressive disease. Progression to overtly metastatic disease is relatively rapid among men with progressive nonmetastatic CRPC, with median bone-metastasis-free survival of 25 months to 30 months.[25,26] Men with metastatic CRPC have had a poor prognosis, with median survival of only 16 to 20 months,[27-29] although patients treated with docetaxel and/or other active treatments now available for this disease may live significantly longer. Optimizing survival may require the use of multiple lines of therapy, elevating the importance of tolerability when introducing new therapies. The goal is to maintain quality of life while simultaneously increasing survival.

Treatment of metastatic CRPC

Prior to 2004, treatment options such as mitoxantrone provided palliation of pain for patients with metastatic CRPC, but did not extend survival.[30,31] Two landmark trials, SWOG-9916 and TAX327, were the first studies to demonstrate a survival benefit for patients with metastatic CRPC.[27,28] In SWOG-9916, docetaxel (Taxotere: sanofi-aventis) in combination with estramustine was compared with mitoxantrone plus prednisone. An improvement in survival of 1.9 months (17.5 months versus 15.6 months, p = .002) was observed, along with improvements in progression-free survival (PFS) and objective response rates (ORR).[27] In this trial, progression was defined as tumor progression, PSA progression, or death.

In TAX327, patients with metastatic CRPC received two different schedules of docetaxel plus prednisone compared with mitoxantrone plus prednisone, Table 1.[28] An overall survival benefit from docetaxel every 3 weeks was seen (18.9 months versus 16.5 months), but no significant survival difference was seen with weekly

docetaxel. Pain control and PSA-ORR were also higher with docetaxel. Common toxicities included nausea, vomiting, diarrhea, and sensory neuropathy, as well as Grade 3/4 neutropenia in 32% of patients. Although these studies disproved the notion that metastatic CRPC was refractory to chemotherapy, the survival benefit was modest and came at the expense of considerable toxicity. Often, physicians will not recommend chemotherapy for men with metastatic CRPC until they develop symptomatic pain.[32]

In 2010, another chemotherapeutic agent, cabazitaxel (Jevtana: sanofi-aventis), was approved after having demonstrated a survival advantage in the postdocetaxel setting. Like docetaxel, cabazitaxel is a cytotoxic agent that inhibits microtubule activity, but cabazitaxel was shown to have activity in docetaxel-resistant preclinical models. The phase III TROPIC trial compared cabazitaxel plus prednisone with mitoxantrone plus prednisone in patients who had progressed after first-line docetaxel therapy, Table 1.[33] There was a 2.4 month improvement in median overall survival with cabazitaxel (15.1 months versus 12.7 months). Grade 3/4 adverse events included febrile neutropenia and diarrhea, as well as neutropenia in 81.7% of patients. In addition, more deaths from neutropenia and its consequences and cardiac causes occurred in the cabazitaxel group than in the mitoxantrone comparator group, leading to the recommendation for careful monitoring of blood counts, especially in the elderly and in patients with underlying cardiac disease.[34]

In 2011, abiraterone (Zytiga: Centocor Ortho Biotech), an additional option shown to have a survival benefit in the postdocetaxel setting, was approved. Abiraterone is a potent inhibitor of the

TABLE 1. **Current therapeutic options for treatment of metastatic CRPC**

Therapy	Approval	Pivotal trial name	Pivotal trial design	Outcomes	
				Primary	Secondary
Docetaxel	2004	TAX327[28]	Docetaxel plus prednisone every 3 weeks vs. mitoxantrone plus prednisone in metastatic CRPC	OS: 18.9 months vs. 16.5 months in the control group; HR 0.76 (95% CI 0.62 to 0.94) p = .009	PSA response: 45% vs. 32 p < .001 Pain response: 22% vs. 13% p = .009
Sipuleucel-T	2010	IMPACT[39]	Sipuleucel-T vs. control in asymptomatic or minimally symptomatic metastatic CRPC	OS: 25.8 months vs. 21.7 months in the control group; HR 0.77 (95% CI 0.61 to 0.97) p = .03	TTP 3.7 months vs. 3.6 months HR 0.95 (95% CI 0.77 to 1.17) p = .063
Cabazitaxel	2010	TROPIC[33]	Cabazitaxel plus prednisone vs. mitoxantrone plus prednisone in metastatic CRPC following docetaxel therapy	OS: 15.1 months vs. 12.7 months in the control group; HR 0.70 (95% CI 0.59 to 0.83) p < .0001	PFS 2.8 months vs. 1.4 months HR 0.74 (95% CI 0.64 to 0.86) p < .0001
Abiraterone	2011	COU-AA-301[36]	Abiraterone plus prednisone vs. placebo plus prednisone in metastatic CRPC following docetaxel therapy	OS: 14.8 months vs. 10.9 months in the placebo group; HR 0.65 (95% CI 0.54 to 0.77) p < .001	TTPSAP 10.2 months vs. 6.6 months p < .001 PFS 5.6 months vs 3.6 months p < .001 PSA response rate 29% vs. 6% p < .001

OS = overall survival; TTP = time to progression; TTPSAP = time to PSA progression; PFS = progression-free survival

androgen biosynthesis enzyme CYP17, which has been shown to dramatically reduce both adrenal and intratumoral androgen production.[35] In the phase III trial COU-AA-301 in men with metastatic CRPC that had progressed with docetaxel therapy, a survival benefit of 3.9 months in favor of abiraterone plus prednisone compared with prednisone alone was shown (14.8 months versus 10.9 months, $p < .001$); Table 1.[36] Secondary endpoints, including time to PSA progression, PFS, and PSA response rate, also showed a benefit with abiraterone. In this trial, PFS was a composite endpoint that included a 25% increase in PSA over the patient's baseline/nadir and protocol-defined radiographic progression as well as symptomatic or clinical progression. Adverse events were mainly related to mineralcorticoid excess, including hypokalemia (17%) and fluid retention (31%); Grade 3/4 hypokalemia and hypertension were infrequent. Abiraterone is given with prednisone (5 mg BID) to help mitigate adverse effects; however, the effects of long term use of prednisone in this population have not been studied.

Immunotherapy presents a new approach to the treatment of advanced prostate cancer. Although the clinical benefits of passive immunotherapy using monoclonal antibodies are established in other cancers, it has not been shown to be an effective approach in prostate cancer.[37] The approval of sipuleucel-T (Provenge: Dendreon) in 2010 marks the first active immunotherapy ever to demonstrate significant clinical benefit in any solid tumor in a large, controlled, randomized phase III clinical trial, Table 1. Sipuleucel-T is indicated for patients with asymptomatic or minimally symptomatic metastatic CRPC—a patient population that typically has not been offered docetaxel-based chemotherapy until their disease progresses to the onset of symptoms.[38]

Autologous cellular immunotherapy in prostate cancer

Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. Sipuleucel-T consists of autologous

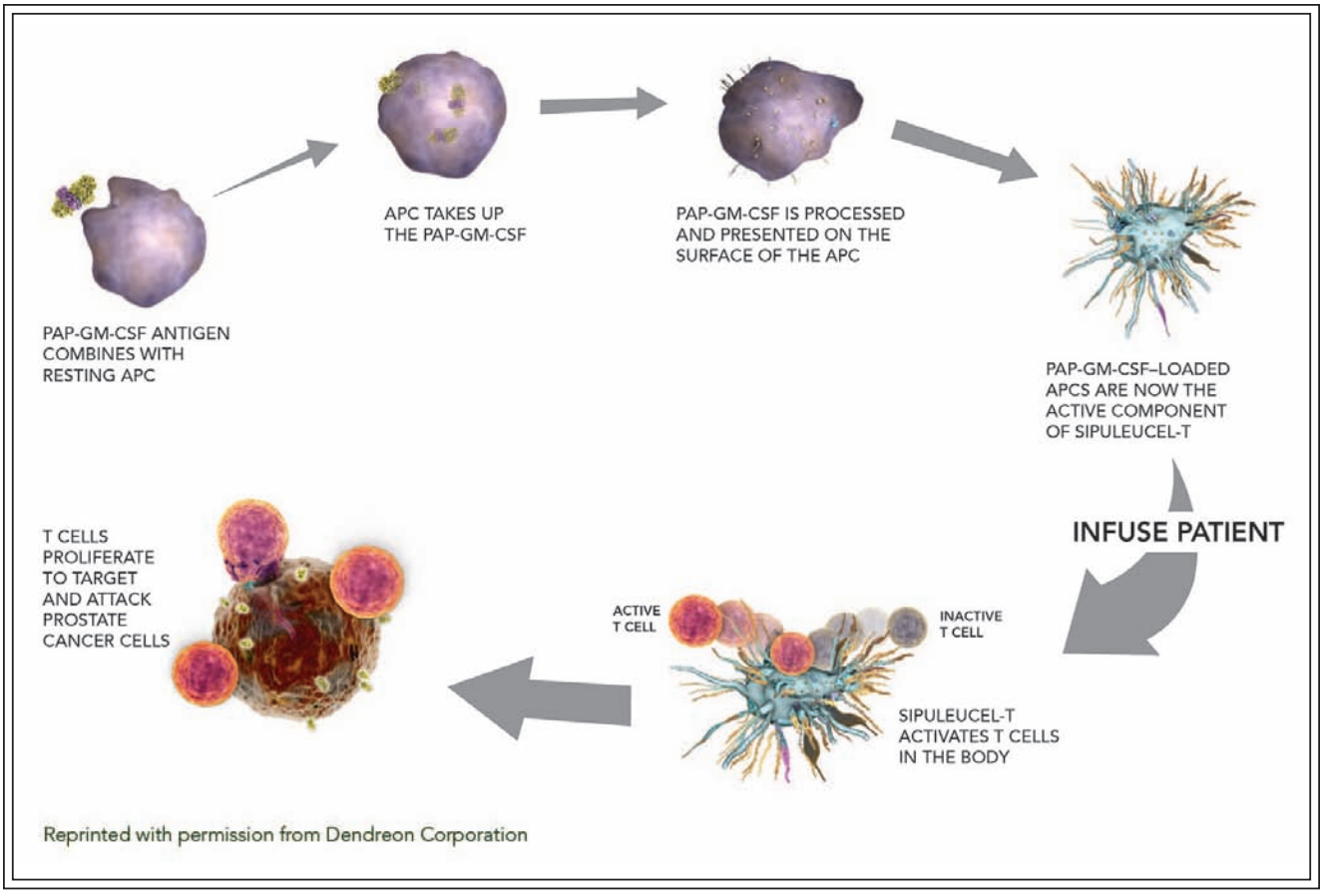

Figure 2. Sipuleucel-T proposed mechanism of action.

peripheral blood mononuclear cells, including antigen-presenting cells (APCs), that are activated ex vivo by culture with a recombinant protein consisting of prostatic acid phosphatase (PAP), an antigen expressed in more than 95% of prostate tumors, linked to granulocyte-macrophage colony-stimulating factor (GM-CSF), an immune cell activator, Figure 2.[39,40]

During ex vivo culture with the PAP-GM-CSF antigen, APCs take up and process the recombinant antigen into small peptides that are then displayed on the APC surface. These antigen-loaded APCs have the ability to initiate an adaptive immune response by activating antigen-specific T cells.[41] In the pivotal trial of sipuleucel-T, immune responses were assessed in a subset of patients.[39] In the sipuleucel-T group, antibody and T-cell responses against the immunizing antigen were observed in 66.2% and 73.0% of patients, respectively, compared with 2.9% and 12.1% of patients in the control group. Patients in the sipuleucel-T group who had an antibody titer > 400 against the immunizing antigen at any time after baseline lived longer than those who had an antibody titer ≤ 400 ($p < .001$).

Sipuleucel-T was initially evaluated in two phase III clinical trials involving men with metastatic CRPC and no cancer-related pain.[42,43] At the time these trials were developed, there were no approved therapies for men with metastatic CRPC. The primary endpoint in both trials was time to progression (TTP). Disease progression was defined as radiographic evidence of progressive disease, or new cancer-related pain associated with a radiographic anatomical correlation, or other clinical events consistent with progression.

In trial D9901, 127 patients were randomized, 82 patients in the sipuleucel-T group and 45 patients in the control group. Median TTP was 11.7 weeks in the sipuleucel-T group compared with 10.0 weeks in the control group ($p = .052$).[42] Although this trial did not meet its primary endpoint, a planned survival analysis demonstrated a significant survival benefit for treatment with sipuleucel-T (median survival 25.9 weeks versus 21.4 weeks in the control group [$p = .010$]).[42,43] The second trial, D9902A, also showed no benefit in terms of TTP.[43]

Based on the findings from these two trials, a larger trial, IMPACT (Immunotherapy for Prostate Adenocarcinoma Treatment), was initiated and overall survival was reported as the primary endpoint, Table 1. The IMPACT trial randomized 512 men with asymptomatic or minimally symptomatic (not needing opioids for cancer-related pain) metastatic CRPC to the sipuleucel-T group (n = 341) or the control group (n = 171).[39]

The median survival was 25.8 months in the sipuleucel-T group compared with 21.7 months in the control group (HR = 0.78 (95% CI 0.61, 0.98 [$p = .03$])), and the 36 month survival probability was 31.7% versus 23% in the control group.[39] As observed in the previous trials, TTP was not significantly different in the two groups. In the IMPACT trial, TTP was defined as radiographic evidence of progressive disease. On determination of objective disease progression, patients were treated at the discretion of their physicians, including docetaxel-based therapy (57.2% of patients in the sipuleucel-T group). Sensitivity analyses adjusting for the use and timing of docetaxel in the IMPACT trial and in an analysis of all three phase III trials of sipuleucel-T showed a consistent treatment effect for sipuleucel-T, confirming that the survival benefit is independent of the effects of subsequent docetaxel therapy.[39,44]

Adverse events were mild to moderate in 65.2% of patients.[39] Adverse events that were more frequently reported in the sipuleucel-T group included chills, fever, and headache. These data were the basis for the approval of sipuleucel-T for men with asymptomatic or minimally symptomatic metastatic CRPC.

The survival benefit of 4.1 months in the IMPACT trial and 4.5 months in the D9901 trial may underrepresent the survival benefit of therapy with sipuleucel-T. On determination of objective disease progression, patients in the control arm had the option of receiving 3 infusions of an autologous immunotherapy made from cells cryopreserved at the time of control generation (APC8015F).[39,42,43] In an integrated analysis, 66.3% (165/249) received APC8015F. APC8015F-treated patients had improved postprogression survival compared with untreated controls (HR = 0.52 (95% CI 0.37, 0.73 [$p = .0001$])).[45] Thus, postprogression treatment with APC8015F may have extended survival in the control group, potentially reducing the magnitude of the survival difference observed between the sipuleucel-T group and the control group.

Sequencing available treatment options

With the rapidly changing treatment landscape for metastatic CRPC, it is important to integrate these new therapeutic options to ensure that patients have the opportunity to take advantage of agents providing a survival benefit. For men with metastatic CRPC, the course of their disease may have extended over 10 to 15 years,[4,5] and they may have received multiple therapies, including surgery, radiation therapy, and various hormonal therapies. Given that most of these men are older and dealing with medical comorbidities

and the toxicities associated with the long term use of ADT, their ability to tolerate additional treatment for metastatic CRPC might be compromised.

Sipuleucel-T expands treatment options by providing a significant clinical benefit for men with asymptomatic or minimally symptomatic metastatic CRPC. Patients with metastatic CRPC who benefit most are those who do not need opioids or steroids for cancer-related pain and who have a good performance status, with life expectancy greater than 6 months. The goal is to provide maximum time to achieve an immune response before moving on to subsequent therapies. Docetaxel-based chemotherapy is considered the best option for men with metastasis who develop symptoms such as pain, and therefore have a more clinically advanced stage of the disease.[38] However, patients with asymptomatic or minimally symptomatic disease who had prior exposure to chemotherapy also benefited from sipuleucel-T despite more clinically advanced disease.[39]

Intriguing emerging data suggest that subsequent therapies may combine with the induced immune response from active immunotherapies, resulting in a combination that is more effective than either treatment alone.[46,47] Analyses of studies of other active immunotherapies have found that patients who received an active immunotherapy did better than expected on subsequent chemotherapy.[48,49] Whether sipuleucel-T induces an immune response that augments subsequent therapies awaits further studies.

Other immunotherapies in development for the treatment of advanced prostate cancer

The approval of sipuleucel-T seems to have invigorated efforts to leverage the immune system against cancer. Three agents in development are GVAX (BioSante, United States), ipilimumab (Yervoy: Bristol-Myers Squibb, United States), and PSA-TRICOM (Prostvac: Bavarian Nordic ImmunoTherapeutics, United States).

GVAX is a granulocyte-macrophage colony-stimulating factor (GM-CSF)–secreting, allogeneic cellular immunotherapy based on two prostate cancer cell lines that were genetically modified with the gene that encodes human GM-CSF and then irradiated to prevent cell division. Treatment with GVAX involves injection of whole tumor cells to provoke an immune response to prostate cancer. The rationale for this therapy is that the multiple antigens expressed by the tumor cells coupled with GM-CSF to induce growth, maturation, and recruitment of dendritic cells to process and present the antigens would increase the likelihood of a robust immune response to the diverse antigens in cancer cells in advanced disease.[50,51]

Two phase I/II trials of GVAX in men with asymptomatic metastatic CRPC showed promising clinical activity and provided a foundation for two phase III trials, one of GVAX versus docetaxel plus prednisone in men with asymptomatic metastatic CRPC and the other of GVAX plus docetaxel versus docetaxel plus prednisone in men with symptomatic metastatic CRPC, Table 2.[51-55] The first trial was prematurely terminated for lack of efficacy based on an interim analysis.[52] The second trial was also prematurely terminated, but in this case due to an excess of deaths in the treatment arm.[54] Only recently has clinical development of GVAX been reinitiated.

Ipilimumab is a fully human monoclonal antibody that binds to cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4). CTLA-4 is a molecule expressed by T cells after they have been activated. The binding of these T cells to APCs through CTLA-4 is a mechanism to down-regulate T-cell activation. Ipilimumab, by blocking this interaction, is thought to prolong and enhance T–cell-mediated immune activity—releasing the brake on the immune system.[55]

Ipilimumab has been studied most extensively in metastatic melanoma where it was shown to provide improved overall survival compared with an active control.[56] Early work in metastatic CRPC demonstrated PSA-modulating effects.[57] In a phase II study, patients with nonmetastatic disease treated with androgen ablation and ipilimumab were more likely to have undetectable PSA levels at 3 months (55% compared with 38% with androgen ablation alone).[58] Ipilimumab is currently being evaluated in two phase III clinical trials with overall survival as the primary endpoint, Table 2.[59,60] The first trial compares ipilimumab with placebo in men with asymptomatic or minimally symptomatic metastatic CRPC, and the second compares ipilimumab with placebo following radiotherapy in men with metastatic CRPC who have received prior docetaxel therapy.

PSA-TRICOM is a prostate cancer vaccine regimen that consists of a primary vaccination with a recombinant vaccinia virus vector followed by several booster vaccinations with a recombinant fowlpox virus vector. Both vectors contain transgenes for human PSA and 3 T-cell costimulatory molecules. PSA-TRICOM was designed to enhance and sustain an antitumor immune response. The vaccines are given subcutaneously where they infect APCs and generate proteins on the surface of the APCs. Interaction of these APCs with T cells initiates an immune response targeted to prostate cancer.[61]

TABLE 2. **Immunotherapies in development in metastatic CRPC**

Immunotherapy	Clinical development	Trial design	Results
GVAX	Phase III	GVAX vs. docetaxel plus prednisone in asymptomatic metastatic CRPC	Prematurely terminated for lack of efficacy
	Phase III	GVAX plus docetaxel vs. docetaxel plus prednisone in symptomatic metastatic CRPC	Prematurely terminated due to survival advantage in the control group: 12.2 months in the treatment group vs. 14.1 months in the control group
Ipilimumab	Phase III	Ipilimumab vs. placebo in asymptomatic or minimally symptomatic metastatic CRPC	Ongoing
	Phase III	Ipilimumab vs. placebo following radiotherapy in metastatic CRPC post-docetaxel	Ongoing
PSA-TRICOM	Phase II	PSA-TRICOM vs. control in minimally symptomatic CRPC	Primary endpoint PFS: 3.8 months vs. 3.7 months in the control group At 3 years, OS 25.1 months vs. 16.6 months; HR 0.56 (95% CI, 0.37 to 0.85)

In a randomized phase II trial of PSA-TRICOM in men with minimally symptomatic (not requiring narcotics for cancer-related pain) metastatic CRPC, an overall survival benefit of 8.5 months (25.1 months in the PSA-TRICOM group compared with 16.6 months in the placebo group) was seen at 3 years post-study, Table 2. Overall survival, however, was not the primary endpoint in this trial. Similar to the initial phase III trials of sipuleucel-T, the primary endpoint was PFS, and no difference between the two groups was found.[62]

Discussion

Sipuleucel-T represents the first active immunotherapy approach to the treatment of prostate cancer and solid tumors in general. The survival benefit paired with a lack of effect on disease progression is perplexing for many. This discordance between survival and disease progression also has been observed with PSA-TRICOM and ipilimumab. The randomized phase II trial of PSA-TRICOM in men with metastatic CRPC showed a significant survival advantage with similar PFS in the two groups.[62] In metastatic melanoma, ipilimumab demonstrated a survival benefit without any improvement in median PFS compared with an active control.[56]

Thus, a survival benefit without an impact on PFS may be a feature of immunotherapies. This phenomenon may reflect the time it takes to generate an immune response. Unlike cytotoxic therapies, which have their greatest effects soon after initiation of therapy, immunotherapies engage the immune system to generate a response—a process that may take months. Madan et al[63] proposed a model in which immunotherapy induces an active antitumor immune response that produces a continued cumulative slowing pressure on tumor growth rate rather than an immediate or dramatic change in tumor burden. These changes may lead to substantially longer overall survival. Whether conventional response measures can adequately capture clinical benefit for immunotherapies remains to be proven.

The relatively short duration of therapy and the absence of an effect on disease progression present a dilemma for physicians seeking to understand how to sequence therapies. Since patients are maintained on ADT during therapy with sipuleucel-T, secondary hormonal manipulations may be a strategy for managing PSA. Changes in symptoms or dramatic

changes in PSA or PSA velocity serve as indicators to perform repeat imaging to determine if objective disease progression has occurred and whether or not to introduce subsequent therapies. The decision to recommend additional therapeutic options should be based on clinical judgment; however, delaying therapies such as chemotherapy or corticosteroids for as long as possible will minimize the negative impact of their immunosuppressive effects on the induced immune response.[64]

Efforts to identify markers of response are ongoing. A recent report on the effect of sipuleucel-T on time to disease-related pain in patients with asymptomatic metastatic CRPC indicated 12 month pain-free estimates at 39.3% for sipuleucel-T compared with 18.9% for control.[65] There was a trend toward a delay in time to disease-related pain beginning 6 months after randomization, which is consistent with a potentially delayed antitumor effect of immunotherapy.

Current data demonstrate that sipuleucel-T is a viable treatment option for men with asymptomatic or minimally symptomatic metastatic CRPC. Research related to optimal timing of immunosuppressive agents following treatment with sipuleucel-T as well as ongoing research in earlier stages of disease and in combination with other new treatment options will help realize the full potential of immunotherapy in the treatment of prostate cancer.

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References

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: The impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin* 2011;61(4):212-236.
2. Cooperburg MR, Lubeck DP, Mehta SS, CapSURE. Time trends in clinical risk stratification for prostate cancer: implications for outcomes (data from CaPSURE). *J Urol* 2003;170(6 Pt 2):S21-S25.
3. Djavan B, Ravery V, Rocco B et al. European study of radical prostatectomy: time trends in Europe, 1993-2005. *BJU Int* 2007; 100(suppl 2):22-25.
4. Stephenson AJ, Kattan MW, Eastham JA et al. Prostate cancer–specific mortality after radical prostatectomy for patients treated in the prostate-specific antigen era. *J Clin Oncol* 2009;27(26): 4300-4305.
5. Alicikus ZA, Yamada Y, Zhang Z et al. Ten-year outcomes of high-dose, intensity-modulated radiotherapy for localized prostate cancer. *Cancer* 2011;117(7):1429-1437.
6. Djavan B, Moul JW, Zlotta A, Remzi M, Ravery V. PSA progression following radical prostatectomy and radiation therapy: new standards in the new millennium. *Eur Urol* 2003;43(1):12-27.
7. Peschel RE, Robnett TJ, Hesse D et al. PSA based review of adjuvant and salvage radiation therapy vs. observation in postoperative prostate cancer patients. *Int J Cancer* 2000;90(1):29-36.
8. vander Kooy MJ, Pisansky TM, Cha SS, Blute ML. Irradiation for locally recurrent carcinoma of the prostate following radical prostatectomy. *Urology* 1997;49(1):65-70.
9. Siddiqui SA, Mynderse LA, Zincke H et al. Treatment of prostate cancer local recurrence after radical retropubic prostatectomy with 17-gauge interstitial transperineal cryoablation: initial experience. *Urology* 2007;70(1):80-85.
10. Donnelly BJ, Saliken JC, Ernst DS et al. Role of transrectal ultrasound guided salvage cryosurgery for recurrent prostate carcinoma after radiotherapy. *Prostate Cancer Prostatic Dis* 2005; 8(3):235-242.
11. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 1999;281(17):1591-1597.
12. D'Amico AV, Moul J, Carroll PR, Sun L, Lubeck D, Chen M-H. Prostate specific antigen doubling time as a surrogate end point for prostate cancer specific mortality following radical prostatectomy or radiation therapy. *J Urol* 2004;172(5 Pt 2): S42-S47.
13. Freedland SJ, Humphreys EB, Mangold LA et al. Risk of prostate cancer–specific mortality following biochemical recurrence after radical prostatectomy. *JAMA* 2005;294(4):433-439.
14. Antonarakis ES, Chen Y, Elsamanoudi SI et al. Long-term overall survival and metastasis-free survival for men with prostate-specific antigen-recurrent prostate cancer after prostatectomy: analysis of the Center for Prostate Disease Research National Database. *BJU Int* 2011;108(3):378-385. doi: 10.1111/j.1464-410X. 2010.09878.x. Epub 2010 Nov 23.
15. Kazzazi A, Djavan B. Current status of pelvic lymph node dissection in prostate cancer: the New York PLND nomogram. *Can J Urol* 2011;18(2):5585-5591.
16. Perlmutter MA, Lepor H. Androgen deprivation therapy in the treatment of advanced prostate cancer. *Rev Urol* 2007;9(suppl 1): S3-S8.
17. The Medical Research Council Prostate Cancer Working Party Investigators Group. Immediate versus deferred treatment for advanced prostatic cancer: initial results of the Medical Research Council Trial. *Br J Urol* 1997;79(2):235-246.
18. Braga-Basaria M, Dobs AS, Muller DC et al. Metabolic syndrome in men with prostate cancer undergoing long-term androgen-deprivation therapy. *J Clin Oncol* 2006;24(24):3979-3983.
19. Shahinian VB, Kuo Y-F, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* 2005; 352(2):154-164.
20. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. *J Clin Oncol* 2006;24(27):4448-4456.
21. Bolla M. Adjuvant hormonal treatment with radiotherapy for locally advanced prostate cancer. *Eur Urol* 1999:35(suppl 1): 23-25.
22. Messing EM, Manola MJ, Sarosdy M, Wilding G, Crawford ED, Trump D. Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer. *N Engl J Med* 1999;341(24):1781-1788.

23. Goodman A. Intermittent androgen suppression called new standard of care for men with PSA recurrence. *The ASCO POST* Web site. www.ascopost.com/articles/march-15-2011/intermittent-androgen-suppression-called-new-standard-of-care-for-men-with-psa-recurrence/. Accessed July 9, 2011.
24. Bianco FJ, Dotan ZA, Kattan MW et al. Duration of response to androgen deprivation therapy and survival after subsequent biochemical relapse in men initially treated with radical prostatectomy. *J Clin Oncol* 2004:22(suppl; abstract 4552).
25. Smith MR, Cook R, Lee K-A, Nelson JB. Disease and host characteristics as predictors of time to first bone metastasis and death in men with progressive castration-resistant nonmetastatic prostate cancer. *Cancer* 2011;117(10):2077-2085.
26. Smith MR, Kabbinivar F, Saad F et al. Natural history of rising serum prostate-specific antigen in men with castrate nonmetastatic prostate cancer. *J Clin Oncol* 2005;23(13):2918-2925.
27. Petrylak DP, Tangen CM, Hussain MH et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med* 2004:351(15):1513-1520.
28. Tannock IF, de Wit R, Berry WR et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 2004;351(15):1502-1512.
29. Carducci MA, Saad F, Abrahamsson P-A et al. A phase 3 randomized controlled trial of the efficacy and safety of atrasentan in men with metastatic hormone-refractory prostate cancer. *Cancer* 2007;110(9):1959-1966.
30. Tannock IF, Osoba D, Stockler MR et al. Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points. *J Clin Oncol* 1996;14(6):1756-1764.
31. Kantoff PW, Halabi S, Conaway M et al. Hydrocortisone with or without mitoxantrone in men with hormone-refractory prostate cancer: results of the cancer and leukemia group B 9182 study. *J Clin Oncol* 1999;17(8):2506-2513.
32. Pienta KJ, Smith DC. Advances in prostate cancer chemotherapy: a new era begins. *CA Cancer J Clin* 2005;55(5):300-318.
33. de Bono JS, Oudard S, Ozguroglu M et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castrate-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet* 2010;376(9747):1147-1154.
34. Ruch JM, Hussain MH. Evolving therapeutic paradigms for advanced prostate cancer. *Oncology (Williston Park)* 2011;25(6):496-504, 508.
35. Attard G, Reid AH, Olmos D, de Bono JS. Antitumor activity with CYP17 blockade indicates that castration-resistant prostate cancer frequently remains hormone driven. *Cancer Res* 2009;69(12):4937-4940.
36. de Bono JS, Logothetis CJ, Molina A et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011;364(21):1995-2005.
37. Weiner LM, Dhodapkar MV, Ferrone S. Monoclonal antibodies for cancer immunotherapy. *Lancet* 2009(9668);373:1033-1040.
38. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. V.3.2011. National Comprehensive Cancer Network Web site. www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed May 23, 2011.
39. Kantoff PW, Higano CS, Shore ND et al; for the IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med* 2010;363(5):411-422.
40. Goldstein NS. Immunophenotypic characterization of 225 prostate adenocarcinomas with intermediate or high Gleason scores. *Am J Clin Pathol* 2002;117(3):471-477.
41. Treating and preventing cancer with vaccines. National Cancer Institute Web site. http://www.cancer.gov/clinicaltrials/education/cancervaccines/page1/. Accessed October 26, 2009.
42. Small EJ, Schellhammer PF, Higano CS et al. Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. *J Clin Oncol* 2006;24(19):3089-3094.
43. Higano CS, Schellhammer PF, Small EJ et al. Integrated data from 2 randomized, double-blind, placebo-controlled phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* 2009;115(16):3670-3679.
44. Petrylak DP, Dawson NA, Gardner T et al. Persistence of immunotherapy survival effects of sipuleucel-T and relationship to postrandomization docetaxel use in phase III studies. *J Clin Oncol* 2010;28:15s(suppl; abstract 4551).
45. Gomella LG, Nabhan C, Whitmore JB, Frohlich MW, George DJ. Post-progression treatment with APC8015F may have prolonged survival of subjects in the control arm of sipuleucel-T phase III studies. *J Clin Oncol* 2011;29(suppl; abstract 4534.)
46. Schlom J, Arlen PM, Gulley JL. Cancer vaccines: moving beyond current paradigms. *Clin Cancer Res* 2007;13(13):3776-3782.
47. Gulley JL, Madan RA, Arlen PM. Enhancing efficacy of therapeutic vaccines by combination with other modalities. *Vaccine* 2007;25(suppl 2):B39-B96.
48. Gribben JG, Ryan DP, Boyajian R et al. Unexpected association between induction of immunity to the universal tumor antigen CYP1B1 and response to next therapy. *Clin Cancer Res* 2005;11(12):4430-4436.
49. Antonia SJ, Mirza N, Fricke I et al. Combination of p53 cancer vaccine with chemotherapy in patients with extensive stage small cell lung cancer. *Clin Cancer Res* 2006;12(3 Pt 1):878-887.
50. Simons JW, Carducci MA, Mikhak et al. Phase I/II trial of an allogeneic cellular immunotherapy in hormone-naïve prostate cancer. *Clin Cancer Res* 2006;12(11 Pt 1):3394-4301.
51. Small EJ, Sacks N, Nemunaitis J et al. Granulocyte macrophage colony-stimulating factor-secreting allogeneic cellular immunotherapy for hormone-refractory prostate cancer. *Clin Cancer Res* 2007;13(13):3883-3891.
52. Higano CS, Corman JM, Smith DC et al. Phase 1/2 dose-escalation study of a GM-CSF-secreting, allogeneic, cellular immunotherapy for metastatic hormone-refractory prostate cancer. *Cancer* 2008;113(5):975-984.
53. Higano C, Saad F, Somer B et al. A phase III trial of GVAX immunotherapy for prostate cancer versus docetaxel plus prednisone in asymptomatic, castration-resistant prostate cancer (CRPC). Presented at: 2009 Genitourinary Cancers Symposium; February 26-28, 2009; Orlando, Florida. Abstract LBA150.
54. Small E, Demkow T, Gerritsen WR et al. A phase III trial of GVAX immunotherapy for prostate cancer in combination with docetaxel versus docetaxel plus prednisone in symptomatic, castration-resistant prostate cancer (CRPC). Presented at: 2009 Genitourinary Cancers Symposium; February 26-28, 2009; Orlando, Florida. Abstract 7.
55. Murillo O, Arina A, Tirapu I et al. Potentiation of therapeutic immune responses against malignancies with monoclonal antibodies. *Clin Cancer Res* 2003;9(15):5454-5464.
56. Hodi FS, O'Day SJ, McDermott DF et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010;363(8):711-723.
57. Small EJ, Tchekmedyian NS, Rini BI et al. A pilot trial of CTLA-4 blockade with human anti-CTLA-4 in patients with hormone-refractory prostate cancer. *Clin Cancer Res* 2007;13(6):1810-1815.
58. Tollefson MK, Karnes RJ, Thompson RH et al. A randomized phase II study of ipilimumab with androgen ablation compared with androgen ablation alone in patients with advanced prostate cancer. Presented at: 2010 Genitourinary Cancers Symposium; March 5-7, 2010; San Francisco, CA. Abstract 168.
59. Phase 3 study of immunotherapy to treat advanced prostate cancer. ClinicalTrials.gov Web site. http://clinicaltrials.gov/ct2/show/NCT01057810?id=NCT01057810 &rank=1. Updated July 6, 2011. Accessed July 18, 2011.

60. Study of immunotherapy to treat advanced prostate cancer. ClinicalTrials.gov Web site. http://clinicaltrials.gov/ct2/show/NCT00861614?id=NCT00861614&rank=1. Updated July 7, 2011. Accessed July 18, 2011.
61. Eder JP, Kantoff PW, Roper K et al. A phase I trial of a recombinant vaccinia virus expressing prostate-specific antigen in advanced prostate cancer. *Clin Cancer Res* 2000;6(5):1632-1638.
62. Kantoff PW, Schuetz TJ, Blumenstein BA et al. Overall survival analysis of a phase II randomized controlled trial of a poxviral-based PSA-targeted immunotherapy in metastatic castration-resistant prostate cancer. *J Clin Oncol* 2010;28(7):1099-1105.
63. Madan RA, Gulley JL, Fojo T, Dahut WL. Therapeutic cancer vaccines in prostate cancer: the paradox of improved survival without changes in time to progression. *Oncologist* 2010;15(9): 969-975.
64. Cheever MA, Higano CS. PROVENGE (sipuleucel-T) in prostate cancer: the first FDA-approved therapeutic cancer vaccine. *Clin Cancer Res* 2011:17(11):3520-3526.
65. Small EJ, Higano CS, Kantoff PW et al. Time to disease-related pain after sipuleucel-T in asymptomatic patients with metastatic castrate-resistant prostate cancer (mCRPC): results from three randomized phase III trials. *J Clin Oncol* 2011:29(suppl; abstract 4661).

REVIEW

Screening for prostate cancer: the current evidence and guidelines controversy

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Introduction: *Prostate cancer presents a global public health dilemma. While screening with prostate specific antigen (PSA) has led to more men diagnosed with prostate cancer than in previous years, the potential for negative effects from over-diagnosis and treatment cannot be ignored.*

Materials and methods: *We reviewed Medline for recent articles that discuss clinical trials, evidence based recommendations and guidelines from major medical organizations in the United States and worldwide concerning prostate cancer screening.*

Results: *Results from the European Randomized Screening for Prostate Cancer (ERSPC), the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, and Göteborg Swedish trials regarding prostate screening are controversial with the ERSPC and Göteborg showing a reduction in prostate cancer mortality and the PLCO trial showing no benefit. Recommendations from the American Urological Association (AUA), Japanese Urological Association (JUA), and National Comprehensive Cancer Network (NCCN) have recommended that all men obtain a baseline PSA beginning at age 40. The American Cancer Society (ACS) stratifies screening recommendations based on age and risk, but states that screening should take place only after an informed discussion between provider and patient. The United States Preventative Health Service Task Force (USPSTF) states that evidence is insufficient to assess the risks and benefits of prostate cancer screening in men younger than 75 years. Other major international health organizations offer a similar reserved approach or recommend against screening for prostate cancer. Most groups indicate that screening to determine who should undergo prostate biopsy typically includes both a serum PSA and digital rectal examination, with the latest ACS publications noting that the rectal exam is optional. A common theme from all groups is that an informed discussion with the patients is strongly recommended and that screening does increase the number of men diagnosed with non-metastatic, early disease*

Conclusions: *Prostate cancer screening guidelines vary widely between countries and between different medical organizations within individual countries including the United States. Further, the evidence for and against prostate cancer screening remains highly controversial. Longitudinal follow up of completed screening trials is ongoing and may yield additional findings as the time course of prostate cancer outcomes can be protracted. The literature controversy suggests that no standard of care exists for prostate cancer screening today. Until there is agreement in guidelines between major professional organizations who have weighed in on this topic, patients and physicians should be encouraged to consider engaging in shared and informed decision process concerning screening for prostate cancer.*

Key Words: cancer screening guidelines, prostate cancer screening, PSA screening

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Introduction

Prostate cancer currently represents a significant burden to men's health. In 2011, an estimated 240,890 new cases of prostate cancer will be diagnosed in the United States which accounts for 25% of newly

diagnosed cancers.[1] Approximately 32,050 men died in 2010 due to prostate cancer with 33,320 expected to die in 2011, trailing only lung cancer as a cause of cancer death in men.[2] Presently, an estimated 1 in 6 men in the United States will be diagnosed with this disease in their lifetime.[2] Global statistics for prostate cancer generally mirror those found in the United States. In 2008, approximately 900,000 men were diagnosed with prostate cancer worldwide, with the highest rates primarily in developed countries of Europe, North and South America, and Oceanic nations.[3]

In spite of its high incidence and prevalence, the progression of prostate cancer in most men is relatively slow. Most tumors remain organ confined allowing for potentially life-saving treatments to be instituted in such cases.[4] In fact, the number of cancer-related deaths has decreased by approximately 35% over a 10 year span from 1997 to 2007.[5,6] Although improved cancer therapies, earlier use of hormonal therapy, and lifestyle changes can all partially explain this phenomenon, the temporal association with the advent of large scale population screening with the prostate specific antigen (PSA) blood test is evident and has probably had substantial impact on temporal changes in incidence and mortality rates.[7-10] However, the death rate has remained relatively constant over the last several years, suggesting a need for improvements in our strategies to detect prostate cancer at an earlier and potentially more curable state.

PSA, a glycoprotein secreted by prostate epithelial cells, was first introduced in the 1980s as a serum marker for monitoring disease status after definitive treatment in men with prostate cancer.[11] Prior to this development, the digital rectal examination (DRE) was the primary tool employed by physicians for detection of prostate cancer. In conjunction with DRE, PSA has since become a widely used clinical tool to help identify men with prostate cancer.[12,13] However, PSA does not diagnose prostate cancer with 100% certainty, as its serum value can be elevated in both benign and malignant conditions of the prostate and not all men with prostate cancer will have high PSA levels. Despite this fact, the use of PSA has evolved to become the main serum marker utilized in prostate cancer screening protocols.[14] An elevated PSA level or an abnormal rectal exam are the most common indications for a prostate biopsy. In this article, we review the current prostate cancer screening literature published by various national and international societies, and report on the present Level 1 evidence examining the effects of prostate cancer screening.

Prostate cancer screening

The primary goal of prostate cancer screening is the early detection of men with clinically significant cancers resulting in a reduction of overall morbidity and mortality associated with this disease. Screening may allow for diagnosis of more localized cancers, resulting in improved cancer specific mortality with appropriate treatment. However, earlier detection can also result in over-diagnosis of clinically indolent cancers, resulting in over-treatment and untoward treatment-related side effects, which impact quality of life as well as produce unnecessary costs and burdens to our healthcare system. The potential for introducing lead or length-time bias cloud the picture. These conundrums lead to the current confusion and disagreement among urologic and public health societies regarding which patients should be offered screening for prostate cancer.

United States screening guidelines

The current prostate cancer screening recommendations from several United States national health organizations are not uniform. The American Cancer Society (ACS), National Comprehensive Cancer Network (NCCN), United States Preventive Services Task Force (USPSTF), and American Urological Association (AUA) all have differing opinions regarding this complex problem, Table 1.[15-20]

The ACS stratifies screening recommendations based on age and risk, and recommend that screening should take place only after an informed discussion has taken place between the healthcare provider and patient regarding the benefits and harms associated with testing. More specifically, the discussion regarding screening should begin in men age 50 with life expectancy over 10 years, in men age 45 who are at high risk (e.g. African-American men or those with a first degree relative diagnosed at age < 65 years), or men age 40 with the highest risk (e.g. several first degree relatives diagnosed with prostate cancer).[15,16] After discussion, men who wish to be screened should be offered a PSA with or without a DRE.

The NCCN provides a set of sequential recommendations, or trigger points, regarding prostate cancer screening.[17] Similar to the ACS guidelines, a thorough discussion between physician and patient regarding the risks and benefits of screening is recommended. Guidelines also recommend that a complete history and physical with questions regarding general health, medical comorbidities, family history, race, social history, and any prior history of prostate cancer testing or treatment should be conducted prior

TABLE 1. **United States prostate cancer major organization screening recommendations as of May 2011[15-20]**

Organization	Recommendation
U.S. Preventative Services Task Force (USPSTF)	1. Current evidence insufficient to recommend screening 2. No screening in any man > 75 years of age 3. Informed discussion held with patient if he wishes to be screened
American Cancer Society (ACS) American College of Physicians (similar to the ACS)	1. Not in favor of routine screening 2. After informed discussion held for those who wish to be screened: • Screen all men with PSA, with or without DRE, at 50 years of age with > 10 years life expectancy • Screen men at 45 years of age with high risk[a] • Screen men at 40 years of age with highest risk[b] • No screening in any man > 75 years of age
National Comprehensive Cancer Network (NCCN)	1. Baseline DRE and PSA at 40 years of age[c] 2. Repeat screening at 45 years of age if PSA < 1.0 ng/mL 3. Annual screening at 50 years of age 4. Informed discussion with all patients
American Urological Association	1. Baseline DRE and PSA at 40 years of age 2. Screening stopped at age 75, but may be continued if the patient has a life expectancy of 10 years or more 3. Informed discussion with all patients

[a]defined as those who are African-American or have a 1st degree relative diagnosed with prostate cancer at < 65 years of age
[b]defined as those who have several 1st degree relatives diagnosed with prostate cancer at < 65 years of age
[c]category 2B recommendation as defined by the NCCN: based on lower level evidence and there is non-uniform NCCN consensus (but no major disagreement)

to any screening. It is expected that this process will eventually lead to a decision regarding screening that is patient specific. The NCCN stresses that their practice guidelines are not an attempt to provide support for national screening protocols but to merely provide a framework for patients and physicians who choose to undergo screening for prostate cancer.

The USPSTF states that the current evidence is insufficient to assess the risks and benefits of prostate cancer screening in men younger than 75 years.[18,19] Inadequate data are available to determine if treatment of prostate cancer detected by screening improves health-related outcomes compared with treatment after clinical detection alone. The USPSTF recommends against screening any man older than 75 years of age stating that the harms outweigh the benefits in this scenario.[19] Furthermore, the USPSTF takes the position that a PSA test should not be ordered by the physician until a full discussion regarding the potential risks and benefits are discussed with the patient. It is important to note, that these guidelines were published prior to recently published large randomized trials regarding prostate cancer screening.

The AUA presented a PSA best practice statement in an update in 2009.[20] Similar to previous guidelines, a statement regarding individualized care and a discussion of the risks and benefits between patient and physician is recommended. Analogous to the ACS, the AUA stresses early detection in men starting at 50 years of age and younger in those at higher risk. Men who wish to be screened must have both a PSA and a DRE. Additionally, the AUA promotes obtaining a baseline PSA value in all men at 40 years of age.[20] Although the AUA acknowledges that the prevalence of prostate cancer in this age group was low and that there is risk of over-diagnosis and treatment, they presented several arguments for their decision. First, age adjusted mortality for prostate cancer in men ages 55 to 64 is approximately 18 per 100,000 males and if time from diagnosis to death is on average 15 to 20 years then younger men who will die from the disease may have benefited from earlier diagnosis.[21,22] Second, cancer detected in men less than 50 years of age often represents lower stage disease and offers a higher success rate for curative therapies.[23-25] Finally, PSA in a 40 year old is more specific as there are fewer opportunities to misinterpret its result due to confounders (e.g. BPH) that can potentially raise its value.[26] The AUA discourages screening in those men with less than

TABLE 2. **International prostate cancer screening recommendations as of May 2011**[27-30]

Organization	Recommendation
European Association of Urology U.K. National Health Services New Zealand National Health Committee	1. Against national screening due to risk of over-treatment 2. Men should be evaluated on case by case basis and discuss all risks and benefits with their physician
Japanese Urological Association	1. Baseline PSA, with or without DRE, at 40 years of age 2. Annual PSA at 50 years of age 3. No upper age limit cut-off for PSA testing

10 year life expectancy. Similar to the statements made by the NCCN the AUA maintains that their recommendations should be used as a resource for both physicians and patients and do not represent a fixed set of guidelines for prostate cancer screening.

International screening guidelines

Variation in international prostate cancer screening guidelines reflects the situation found in the United States. The European Association of Urology (EAU), United Kingdom National Health Services (UK NHS), New Zealand National Health Committee (NHC), and Japanese Urological Association (JUA) differ in opinion regarding the role of PSA and DRE for national screening of prostate cancer, Table 2.[27-30]

The EAU position statement published in May of 2009 states that the current available evidence argues against recommending national screening for prostate cancer because of significant risk of over-treatment.[27] This position is based on concern that screening would lead to over-diagnosis of prostate cancer and subsequent treatment related comorbidities that outweigh the benefits obtained from early detection. Lack of support for screening is also influenced by the low specificity among current screening algorithms and the inability of screening tests to selectively diagnose those with high risk or aggressive disease. In lieu of national screening, it is recommended that men who wish to consider screening should be evaluated on a case by case basis.

The UK NHS and the New Zealand NHC present a similar guideline statement as the EAU – there is currently insufficient evidence at this time to recommend national screening protocols for prostate cancer.[28,29] United Kingdom and New Zealand guidelines also state that after a discussion is held regarding all risks and benefits of prostate cancer testing and treatment, individualized screening programs are suggested for physicians and patients in these countries.

In contrast to the stance taken by the above organizations, the JUA makes a firm recommendation in favor of prostate cancer screening in guidelines published in 2010.[30,31] The JUA recommends that men should obtain a PSA, with or without a DRE, starting at 50 years of age and those with a positive family history should have one at 40 years of age. The JUA also states that every man should have a baseline PSA checked at 40 years of age regardless of risk.[30]

Current evidence

The guidelines provided by the above health organizations have been largely formulated around the evidence from several large randomized trials with regards to the impact of prostate cancer screening using PSA and DRE. Among the first was a Canadian trial which was first reported in 1999 in the journal The Prostate.[10] The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Screening for Prostate Cancer (ERSPC) were both large multi-institutional trials that published their initial reports simultaneously in March of 2009 in The New England Journal of Medicine.[7,8] The results from these two large studies have been the most quoted by health organizations when making arguments for or against national prostate cancer screening programs. Less discussed, but equally important, is a study from Göteborg Sweden published in 2010 that has added further evidence to the growing debate.[9]

Quebec prostate cancer trial

One of the first randomized controlled trials in favor of prostate cancer screening originated from Quebec Canada in the late 90s.[10] A total of 46,193 men aged 45 to 80 years were randomized to no screening or screening with PSA and DRE at their first initial visit and PSA only thereafter. A PSA level of 3 ng/mL was used as a trigger for further work up (e.g. transrectal ultrasound guided biopsy). The patient groups were

randomized to a 2:1 ratio in favor of screening to compensate for possible low numbers due to a lack of awareness of prostate cancer in their target population. Cancer specific mortality was the primary endpoint. The study reported 137 deaths among 38,056 non-screened men and only 5 deaths among 8,137 screened individuals. The follow up period for this study was 7 years. An odds ratio of 3.25 (p value < 0.01) in support of prostate cancer screening was given. Unfortunately, the results of this article have been criticized due to several methodological problems.[32] Those men not screened for prostate cancer had on average a 3 year lead time to develop the disease over those that were screened. Additionally, the analysis of the data as an observational study instead of a randomized control trial, introduced several biases that ultimately over-estimated the effects of screening. Cross over from patients who were not invited for screening but were then screened further muddled the data. As such, this study has largely fallen out of favor as a reference for those that support prostate cancer screening.

Prostate, lung, colorectal, and ovarian (PLCO) cancer screening trial

The PLCO trial was a United States based multi-institutional randomized controlled trial of 76,693 men, Table 3.[8] This elegantly designed trial reported information on prostate cancer incidence, cancer specific mortality, all-cause mortality, and cancer staging and is one of few with high compliance rates and total patient accrual. Patient characteristics between the screened and non-screened men were virtually identical. Men in the screening group received an annual PSA for 6 years and a DRE for 4 years. A total of 7 years of follow up was provided (from the years 1993 to 2001). The reported incidence of prostate cancer per 10,000 person-years in the screening group was 116 compared to 95 in the control group (rate ratio 1.11 95% CI [1.16 to 1.39]). The cancer specific mortality per 10,000 person-years was 2.0 in the screened group and 1.7 in the unscreened population (rate ratio 1.13; 95% CI [0.75 to 1.70]). The percentage of those diagnosed with low stage I or II cancers were also similar regardless of the group. Based on these results, neither prostate cancer incidence nor mortality demonstrated difference due to screening.

Although the PLCO has several methodological strengths, several key points warrant further discussion. First, although the trial appears to be equally randomized between study groups, approximately 44% of patients in the control group had at least one PSA test prior to entry and by the 6th year 52% of the control population had been screened. This suggests that the controls may contain men who are not only less likely to have prostate

TABLE 3. **Recent randomized control trials regarding prostate cancer screening[7-9]**

Trial	Methods and materials	Summary of results	Study strengths or weaknesses
ERSPC	• 182,000 men aged 50-74 years • 7 European countries • PSA every 4 years vs. no PSA • 82% in screened group with ≥ one PSA	• 8.8 years of follow up • Relative risk reduction of 20% • 41% reduction in incidence of metastatic disease • Adjusted rate ratio for death from prostate cancer 0.8 • NNS = 1410 and NNT = 48	• Different PSA cut-offs to trigger biopsy • Short follow up time: if data extrapolated out to just 12 years then NNT = 503 and NNT = 18
PLCO	• 76,693 men • 10 U.S. institutions • Annual PSA for 6 years and DRE every 4 years vs. usual care • 86% compliance in screened group	• 7 years of follow up • Incidence of prostate cancer 116 per 10,000 person years in screened group vs. 95 in controls • No difference in risk of death between groups	• Not true randomization: 52% of control group had a PSA and 44% of men prior to randomization had PSA • PSA cut-off of 4 ng/mL used to trigger further workup • Short follow up time
Göteborg	• 20,000 Swedish men • PSA every 2 years vs. no screening • 76% first time compliance rate	• 14 years median follow up • 58% increased diagnosis of prostate cancer and 44% fewer prostate cancer deaths in screened arm • NNS = 293 and NNT = 12	• Younger patient population • Shorter interval of screening • Lower rate of contamination • Long duration of follow up than ERSPC (14 yrs vs 9 yrs) • Subset of ERSPC study

cancer but also less likely to have higher-stage or life-threatening disease. Studies have closely examined the rate of contamination in the control arm of the PLCO trial demonstrating rates of routine PSA screening of 33% at year 0 to 46% at study year 5 while rates of any PSA testing at year 5 was as high as 55%.[33] Comparing this study scenario to one with no contamination and perfect compliance, the methodological parameters of the PLCO trial will tend to show relative risk outcomes which demonstrate no difference between arms and thus the ability to show significant mortality benefit between arms is made more difficult. Additionally, as a portion of patients initially enrolled already had an established baseline PSA, some cancers detectable on initial screening may have been already removed from the randomized population. Second, a PSA level of 4 ng/mL was used to trigger further work up. Generally, lower cut-off values may lead to detection of more cancers especially those that have lower stage and are associated with better cancer specific survival data. Third, the follow up time of 7 years, although long for contemporary prostate cancer screening literature, is not sufficient, given the long natural history of prostate cancer. Ten to 15 year follow up results will yield additional information about prostate cancer specific mortality rates.

A re-analysis of PLCO with consideration of existing comorbidities revealed a significant decrease in the risk of prostate cancer specific mortality (22 versus 38 deaths; adjusted hazard ratio [AHR] 0.56; 95% CI [0.33 to 0.95]; p value = 0.03) in men with no or minimal comorbidity randomly assigned to intervention versus usual care. The additional number needed to treat (NNT) to prevent one prostate cancer death at 10 years was five. This reanalysis suggests that the selective use of PSA screening for men in good health appears to reduce the risk of prostate cancer mortality with minimal over treatment.[34]

European randomized study of prostate cancer

The ERSPC was a European based multi-institutional randomized control trial initiated in the 1990s which accrued 182,000 men between the ages of 50 to 74, Table 3.[7] Median follow up time was 9 years in duration. The screening group received a PSA test every 4 years and demonstrated a cumulative prostate cancer incidence of 8.2% versus 4.8% in the control group. The rate ratio for cancer specific mortality in the screened population was 0.80 (95% CI [0.65 to 0.98]) with an absolute risk difference of 0.71 prostate cancer deaths per 1000 men. A 20% corresponding relative risk reduction in mortality was determined with the number needed to screen (NNS) at 1410 men and NNT at 48 men to prevent one prostate cancer related death demonstrating a moderate advantage for screening. However, a 41% reduction of metastatic cancers were detected in the screening group in addition to the identification of a higher percentage of patients with low risk disease – Gleason scores 6 and 7 of 72.2% and 27.8% respectively in the screened group versus 54.8% and 45.2% in the controls.

Additional analysis of the ERSPC data may further improve the mortality reduction and screening benefit found in the study. First, reports have estimated that after adjustment for non-compliance in the screening population and contamination in the control arm the mortality benefit found in the ERSPC population can be as high as 30% – increasing the initial benefit by half.[35] Second, similar to the PLCO trial, the relatively short median follow up time of 9 years likely underestimates the survival benefit in those who were screened for prostate cancer. In fact, the NNS and NNT decrease to 503 and 18 respectively when data is extrapolated out to a modest 12 years of follow up.[36] Third, data was gathered cumulatively from several European nations and the PSA cut-off value that triggered further work up was non-uniform among study centers. While most institutions used a value of 3 ng/mL as a point for biopsy referral, others used higher values and incorporated factors such as DRE and PSA kinetics to determine if further work up was necessary.

Like all screening trials, the results of the ERSPC study should be examined with certain caveats. Risk of over-diagnosis was estimated by some to approach 50% while the benefits of screening were restricted to the core age group of 55 to 69 years at the time of randomization. While demonstrating a mortality benefit associated with screening, the ERSPC also revealed a high likelihood of over-diagnosis and over-treatment. Some have argued that unequal treatment decisions in both arms of the study may have impacted mortality results. Close analysis shows that control arm patients with high risk prostate cancer were more likely to receive radiotherapy (OR 1.43, p = 0.047), expectant management (OR 2.92, p = 0.007), or hormonal therapy (OR 1.11, p = 0.02) instead of radical prostatectomy. However, the trial arm had only a minor role in the treatment choice when compared to other variables demonstrating that differences in treatment between arms is unlikely to play a major role in interpreting mortality results in the ERSPC trial.[37]

Göteborg Sweden trial

The results of a randomized control trial from Göteborg Sweden that appeared in Lancet Oncology in August of 2010 have been far less publicized than its two predecessors; the ERSPC and PLCO, Table 3.[9] A total of 20,000 men aged 50-64 years were randomized in a 1:1 ratio to screening with PSA every 2 years versus no screening. The primary endpoint was cancer specific

mortality analyzed using an intent-to-screen modality with a follow up time of 14 years. There was a 76% first time compliance rate among those offered screening resulting in a total of 1138 men diagnosed with prostate cancer with a cumulative incidence of 12.7%. In the matched controls 718 men were diagnosed with prostate cancer at an incidence of 8.2% with a calculated hazard ratio of 1.64 (95% CI [1.50-1.80]). Those patients screened with PSA were also diagnosed more frequently with both lower stage disease and lower incidence of metastases. The rate ratio for death was 0.56 for those screened versus non-screened. Additionally, compared to the results reported by the ERSPC study the NNS and NNT were a modest 293 and 12 respectively in the Swedish trial.

The Göteborg study demonstrated better outcomes with screening compared to both the larger ERSPC and PLCO trials. Interestingly, data from the cohort of patients in this study were part of the results reported in the larger ERSPC trial. Components of the Göteborg trial design including: younger patient population (median 56 years of age compared to > 60 years in ERSPC/PLCO), shorter interval of screening (every 2 years compared to 4 years of the ERSPC), lower rate of PSA testing prior to entry (approximately 3% compared to 44% in the PLCO), lower rate of contamination in the control group, and longer duration of follow up from randomization (median 14 years) all contribute to the findings showing benefit to prostate cancer screening. The 44% relative risk reduction in death demonstrated from this study may be the strongest evidence that screening for prostate cancer with PSA can be effective in lowering cancer specific mortality.

Discussion

Despite the publication of the results of several long-awaited randomized trials, the controversy surrounding prostate cancer screening continues. Various groups have different guidelines regarding screening with the majority favoring individualized programs after discussion between physician and patient. This non-uniform view between health organizations is problematic as it provides a mixed message to the general patient population and healthcare provider alike.

The interpretation of the current Level 1 evidence based on PSA testing is also varied. Concerns over statistical analysis issues, contamination of control groups, insufficient follow up time, differing levels of PSA triggering work up, and inappropriate screening intervals have led to the wide range of findings in these randomized control trials. Nonetheless, screening program data from the ERSPC and Göteborg compare favorably to those of breast and colon cancer, where routine screening is widely recommended. In 2009, meta-analysis of breast cancer data showed NNS with mammography of 377 for women aged 60 to 69 years and 1339 for women aged 50 to 59 years after 11 to 20 years of follow up.[38,39] For colorectal cancer screening with fecal occult blood test the NNS after 10 years of follow up was 1173 while the number for flexible sigmoidoscopy was 489 at a median follow up of 11 years.[40,41] In this regard, testing with PSA is at minimum comparable to mammograms and fecal occult blood tests or sigmoidoscopy.

The use of serum PSA as a primary diagnostic tool in the current screening trials may not possess high enough specificity and sensitivity for prostate cancer diagnosis but it appears to be arguably one of the best screening markers available.[42] In a man at age 50 with a PSA < 1.5 ng/mL his risk of developing prostate cancer in the next 7-8 years is < 5%. With a PSA level of 2.5 ng/mL the risk increases to greater than 20% and at a PSA of 4.0 ng/mL the risk approaches 40%. There is a trend towards a PSA determination at a younger age in an attempt to identify those men who harbor aggressive disease and are destined to suffer consequences if left undiagnosed until later in life. Organizations such as the AUA recommend annual screening with a DRE and serum PSA test starting at age 40 for all men with a life expectancy of more than 10 years.

Consideration to using the on line prostate cancer risk assessment tools when involved in joint decision making may be useful.[43,44] This nomogram (http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp) is based on the Prostate Cancer Prevention Trial (PCPT) and may help in the decision to undergo prostate biopsy. [43]

Screening efforts in the future will need to focus more on determining who harbors aggressive life threatening cancer and who has indolent cancer. Novel markers such as urinary PCA3 or single-nucleotide polymorphisms (SNPs) may help identify those with higher risk cancers when compared to PSA alone.[45-47] Advanced imaging modalities such as contrast enhanced ultrasound for targeted biopsies of the prostate and improved MRI techniques may also aid in differentiating indolent from aggressive disease detected by PSA.[48-50] In the interim, selective use of PSA testing in healthy men appears to reduce the risk of prostate cancer specific mortality. The risk of over-treatment can be lessened by either selective or an active surveillance approach with the potential for deferred treatment in certain men.[51] For completeness in this discussion, the Tyrol Prostate Cancer Demonstration Project was a population comparison between a screened and unscreened region of Austria.[52] In the Tyrol region where treatment and screening were widespread, there was a reduction in

prostate cancer mortality rates significantly greater than the reduction in the rest of Austria. While a "positive" study in support of screening it cannot be considered as a Level 1 evidence randomized trial.

The data from the recently randomized control trials needs to be followed up in future published articles as the potential benefits of prostate cancer screening may take an extended period of time to be recognized as significant. A large UK based trial known as ProtecT (Prostate testing for cancer and Treatment) will provide additional data on screening in the coming years.[53] Recommendations and guidelines will evolve as new data is presented.

Conclusion

The benefits of screening are clear and in general supported by the major professional organizations in the United States: earlier diagnosis of cancer, discovery of more localized disease, and reduction in initial diagnosis of metastases. The improvement in prostate cancer specific mortality is supported by several studies, but not supported by others. These benefits must be weighed against the current limitations: potential downsides of over-diagnosis and over-treatment of clinically insignificant cancers.

This controversy in the literature suggests that no "standard of care" exists for prostate cancer screening at the present time. Healthcare providers and patients should continue to have conversations regarding the heterogeneous nature of PSA testing. To further reduce morbidity and mortality from prostate cancer, newer approaches for screening, early detection, and prevention are needed.[54] If a decision is made to screen and the patient is ultimately diagnosed with prostate cancer, patients should seek expert advice from those who are able to provide objective information on all treatment options. Those options for localized disease should include a discussion of active surveillance if appropriate, before deciding on any definitive treatment. □

References

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer Statistics, 2011: The impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin* 2011 Jun 17. (epub ahead of print).
2. Ries LA, Melbert D, Krapcho M et al. SEER Cancer Statistics Review, 1975-2005, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2005/, based on November 2007 SEER data submission, posted to the SEER web site, 2008.
3. Center M, Siegel R, Ahmedin J. American Cancer Society. Global Cancer Facts & Figures 2nd Edition. Atlanta: American Cancer Society; 2011.
4. Galper SL, Chen MH, Catalona WJ et al. Evidence to support a continued stage migration and decrease in prostate cancer specific mortality. *J Urol* 2006;175(3 Pt 1):907-912.
5. Potosky AL, Feuer EJ, Levin DL. Impact of screening on incidence and mortality of prostate cancer in the United States. *Epidemiol Rev* 2001;23:181-186.
6. *Renal & Urology News*, Dec 2007, Vol 6, No 12.
7. Schroder FH, Hugosson J, Roobol MJ et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med* 2009;360(13):1320-1328.
8. Andriole GL, Grubb RL, Buys SS et al. Mortality results from a randomized prostate cancer screening trial. *N Engl J Med* 2009; 360(13):1310-1319.
9. Hugosson J, Carlsson S, Aus G et al. Mortality results from the Göteborg randomized population based prostate-cancer screening trial. *Lancet Oncol* 2010;11(8):725-732.
10. Labrie F, Candas B, Dupont A et al. Screening decreases prostate cancer death: first analysis of the 1988 Quebec Prospective Randomized Controlled Trial. *The Prostate* 1999;38(2):83-91.
11. Stamey TA, Yang N, Hay AR et al. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. *N Engl J Med* 1987;317(15):909-916.
12. Catalona WJ, Smith DS, Ratliff TL et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *N Engl J Med* 1991;324(17):1156-1161.
13. Woolf SH. Screening for prostate cancer with prostate-specific antigen: An examination of the evidence. *N Engl J Med* 1995; 333(21):1401-1405.
14. Dvajan B, Eckersberger E, Finkelstein J et al. Prostate cancer screening and PSA. *Prim Care: Clin Office Pract* 2010;37(3):441-449.
15. Brawley OW, Gansler T. Introducing the 2010 American Cancer Society Prostate Cancer Screening Guideline. *CA Cancer J Clin* 2010; 60(2):68-69.
16. Smith RA, Cokkinides V, Brooks D et al. Cancer screening in the United States, 2011: A review of current American Cancer Society guidelines and issues in cancer screening. *CA Cancer J Clin* 2011; 61(1):8-30.
17. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Prostate Cancer Early Detection. Version.2.2010. Available at: www.nccn.org
18. Lin K, Lipsitz R, Miller T et al. Benefits and harms of prostate-specific antigen screening for prostate cancer: an evidence update for the U.S. Preventative Services Task Force. *Ann Intern Med* 2008;149(3):192-199.
19. U.S. Preventive Services Task Force. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008;149(3):185-191.
20. Greene KL, Albertsen PC, Babaian RJ et al. Prostate specific antigen best practice statement: 2009 update. *J Urol* 2009;182(5):2232-2241.
21. Johansson JE, Andren O, Andersson SO et al. Natural history of early, localized prostate cancer. *JAMA* 2004;291(22):2713-2719.
22. Horan AH, McGehee M. Mean time to cancer-specific death of apparently clinically localized prostate cancer: policy implications for threshold ages in prostate-specific antigen screening and ablative therapy. *BJU Int* 2000;85(9):1063-1066.
23. Carter HB, Epstein JI, Partin AW. Influence of age and prostate-specific antigen on the chance of curable prostate cancer among men with non-palpable disease. *Urology* 1999;53(1):126-130.
24. Smith CV, Bauer JJ, Connelly RR et al. Prostate cancer in men age 50 years or younger: a review of the Department of Defense Center for Prostate Disease Research multicenter prostate cancer database. *J Urol* 2000;164(6):1964-1967.
25. Khan MA, Han M, Partin AW et al. Long-term cancer control of radical prostatectomy in men younger than 50 years of age: update 2003. *Urology* 2003;62(1):86-91.
26. Morgan TO, Jacobsen SJ, McCarthy WF et al. Age-specific reference ranges for prostate-specific antigen in black men. *N Engl J Med* 1996;335(5):304-310.

27. Abrahamsson P, Artibani W, Chapple CR, Wirth M. European Association of Urology position statement on screening for prostate cancer. *Eur Urol 2009;*56(2):270-271.
28. Logan R, Fougere G, Hague K et al. Prostate Cancer Screening in New Zealand. New Zealand National Health Committee. Publication available at: http://www.nhc.health.govt.nz/moh.nsf/indexcm/nhc-prostate-cancer-screening?Open.
29. Burford DC, Austoker KM. Prostate cancer risk management programme information for primary care; PSA testing in asymptomatic men. Evidence document. NHS Cancer Screening Programmes, 2010. Available at: http://www.cancerscreening.nhs.uk/prostate/pcrmp02.pdf
30. Committee for Establishment of the Guidelines on Screening for Prostate Cancer; Japanese Urological Association. Updated Japanese Urological Association Guidelines on prostate-specific antigen-based screening for prostate cancer in 2010. *Int J Urol* 2010;17(10):830-838.
31. Suzuki H, Flanigan RC, Okuyama A. Prostate specific antigen (PSA)-based screening. *Int J Urol* 2008;15(9):757-762.
32. Boer R, Schroder FH. Quebec randomized controlled trial on prostate cancer screening shows no evidence for mortality reduction – Letter to the Editor. *Prostate* 1999;40(2):130-131.
33. Pinsky PF, Black A, Kramer BS et al. Assessing contamination and compliance in the prostate component of the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. *Clin Trials* 2010;7(4):303-311.
34. Crawford ED, Grubb R, Black A et al. Comorbidity and mortality results from a randomized prostate cancer screening trial. *J Clin Oncol* 2011;29(4):355-361.
35. Roobol MJ, Kerkhof M, Schroder FH et al. Prostate cancer mortality reduction by prostate specific antigen-based screening adjusted for nonattendance and contamination in the European Randomised Study of Screening for Prostate Cancer (ERSPC). *Eur Urol* 2009;56(4):584-591.
36. Loeb S, Vonesh E, Metter J et al. What is the true number needed to screen and treat to save a life with prostate-specific antigen testing? *J Clin Oncol* 201129(4):464-467.
37. Wolters T, Roobol MJ, Steyerberg EW et al. The effect of study arm on prostate cancer treatment in a large screening trial (ERSPC). *Int J Cancer* 2010;126(10):2387-2393.
38. Gotzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database Syst Rev* 2009;4:CD001877.
39. Nelson HD, Tyne K, Naik A et al. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Ann Intern Med* 2009;151(10):727-737.
40. Towler B, Irwig L, Glasziou P et al. A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, hemoccult. *BMJ* 1998;317(7158):559-565.
41. Atkin WS, Edwards R, Kralj-Hans I et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet* 2010;375(9726):1624-1633.
42. Aus G, Damber JE, Khatami A et al. Individualized screening interval for prostate cancer based on prostate-specific antigen level: results of a prospective, randomized, population-based study. *Arch Intern Med* 2005;165(16):1857-1861.
43. Thompson IM, Ankerst DP, Chi C et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. *J Natl Cancer Inst* 2006;98(8):529-534.
44. Myers RE. Prostate Cancer Screening. Psycho-Oncology, 2nd edition. Hallard JC, Breitbart WS, Jacobsen PB, et al. NY: Oxford University Press. 2010. pp. 98-102.
45. Marks LS, Fradet Y, Deras IL et al. PCA3 molecular urine assay for prostate cancer in men undergoing repeat biopsy. *J Urol* 2007;69(3):532-535.
46. Roobol MJ, Schroder FH, van Leeuwen P et al. Performance of the PCA3 gene and PSA in prescreened men: exploring the value of PCA3 for a first-line diagnostic test. *Eur Urol* 2010;58(4):475-481.
47. Sun J, Kader AK, Hus F et al. Inherited genetic markers discovered to date are able to identify a significant number of men at considerably elevated risk for prostate cancer. *Prostate* 2011;71(4):421-430.
48. Bonekamp D, Jacobs MA, El-khaouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. *Radiographics* 2011;31(3):677-703.
49. Nelson ED, Slotoroff CB, Gomella LG et al. Targeted biopsy of the prostate: the impact of color Doppler imaging and elastography on prostate cancer detection and Gleason score. *Urology* 2007;70(6):1136-1140.
50. Trabulsi EJ, Sackett D, Gomella LG et al. Enhanced transrectal ultrasound modalities in the diagnosis of prostate cancer. *Urology* 2010;76(5):1025-1033.
51. Tosoian JJ, Trock BJ, Landis P et al. Active surveillance program for prostate cancer: an update of the johns Hopkins experience. *J Clin Oncol* 2011;29(16):2185-2190.
52. Bartsch G, Horninger W, Klocker H et al. Prostate Cancer Demonstration Project: early detection, treatment, outcome, incidence and mortality. *BJU Int* 2008;101(7):809-816.
53. Rosario DJ, Lane JA, Metcalfe C et al. Contribution of a single repeat PSA test to prostate cancer risk assessment: experience from the ProtecT study. *Eur Urol* 2008;53(4):777-784.
54. Esserman L, Shieh Y, Thompson I. Rethinking screening for breast cancer and prostate cancer. JAMA 2009;302(15):1685-1692.

Editor's Note

At the time of publication of the October issue of the *Canadian Journal of Urology (CJU)*, the US Preventative Services Task Force was preparing to publish an article in *Annals of Internal Medicine* recommending that healthy men no longer receive PSA testing to screen for prostate cancer (Cancer Letter, Vol 37, No 37 Oct. 7, 2011).Their conclusions were based in large part on the screening trials reviewed in this article and will cite PSA screening as having a "D" level of evidence rating. The "D" rating means that "there is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits." There is no doubt that this recommendation to abandon PSA based screening will continue to fuel the evidence and guidelines controversy discussed in this paper.

Leonard G. Gomella, MD

Markers of accessory sex glands function in men with varicocele, relationship with seminal parameters

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VIVAS-ACEVEDO G, LOZANO-HERNANDEZ R, CAMEJO MI. Markers of accessory sex glands function in men with varicocele, relationship with seminal parameters. The Canadian Journal of Urology. 2011;18(5):5884-5889.

Introduction: *Varicocele has been associated with decreased semen quality, not much is known about the effect of varicocele on the accessory sex glands function. The purpose of this study was to evaluate the relationship among varicocele, seminal parameters and biochemical markers of accessory sex glands: neutral alpha glucosidase (NAG, epididymis), fructose (seminal vesicles), prostatic acid phosphatase (PAP) and zinc (prostate).*

Materials and methods: *A clinical study was performed in 190 men with varicocele and 100 men normozoospermic as control group. Semen analysis, hypoosmotic swelling test (HOST), polymorphonuclear (PMN), fructose, zinc, PAP and NAG were determinate. Differences were evaluated by, t test, ANOVA and a Pearson's coefficient correlation.*

Results: *Varicocele group showed a decrease in sperm motility, normal morphology, HOST and vitality. No differences were observed in fructose, PAP and zinc levels between control and varicocele group. The NAG was significantly decreased in varicocele group. A positive correlation was observed between both fructose and PAP with semen volume, sperm concentration, PMN, and zinc levels. Additionally, a decrease of NAG was correlated with a decrease of normal sperm morphology, motility, vitality and HOST.*

Conclusions: *Varicocele does not alter fructose secretion by seminal vesicles and PAP and zinc by prostate. Varicocele is associated with a decrease of NAG activity in seminal fluid, suggesting epididymal dysfunction possibly associated with a detrimental in sperm quality.*

Key Words: fructose, neutral alpha glucosidase (NAG), prostatic acid phosphatase (PAP), sperm, varicocele, zinc

Introduction

The accessory sex glands play an important role in the acquisition of sperm fertilization potential. It has been reported that sperm motility may be influenced by the components of seminal plasma.[1,2] The semen is constituted by the contribution of the testicular-epididymal fluid (< 10%), prostatic (20%-40%); seminal vesicles (50%-80%) and urethral and bulbourethral glands (< 10%).[3] Each gland contributes with different molecules in the ejaculation: carnitine, neutral alpha glucosidase and glycerophosphocholine from epididymis, citrate, zinc and prostatic acid phosphatase from prostate and fructose and prostaglandins from seminal vesicles.[4]

Varicocele has been associated with decreased sperm quality.[5-7] However there is little information

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about the effect of varicocele on the function and secretion of the accessory sex glands[8,9] and the possible relationship with the biochemical markers composition of semen and seminal parameters.

The purpose of this study was to explore the relationship among varicocele and biochemical markers of accessory sex glands secretion, by measure of fructose levels (seminal vesicles), epididimal neutral alpha glucosidase (NAG), prostatic acid phosphatase (PAP) activity and zinc (prostate) and the effect on the seminal parameters.

Material and methods

Patients

Every analysis has been performed after obtaining institutional board approval and each one of the patients gave their express consent. A clinical cross-sectional analysis has been conducted in patients on infertility evaluation at a diagnostic centre (Centro Diagnóstico de Infertilidad y Enfermedades Genéticas, Mérida), from January 2007 to May 2009.

Men with current or former urogenital-diseases, patients positive to anti-C trachomatis antibodies (EIA kit Monovalent IgA ImmunoComb II ORGENIC, Israel), men with azoospermia or hypogonadism were excluded.

A total of 190 consecutive patients with varicocele were included in the study (grade I: 42; grade II: 66; grade III: 23; bilateral: 59). Varicocele was clinically classified as grade I (palpable with Valsalva manoeuvre), grade II (palpable without Valsalva manoeuvre), grade III (visible through the scrotal skin) or bilateral (some grade of varicocele in both testes). The diagnostic of varicocele was confirmed by Doppler ecography. Additionally, 100 of normozoospermic men without varicocele were selected as control group. All patients were evaluated by two male infertility specialists (medical record, physical examination and criteria of inclusion-exclusion) and a semen analysis was performed.

Semen analysis

Semen samples were collected by masturbation after 3 to 5 days of ejaculatory abstinence. After semen liquefaction, seminal analysis was performed according to WHO criteria.[10] Normal values were: total sperm (rapid and slow progressives; a + b) motility (≥ 50%), sperm concentration ≥ 20 x 10^6 per mL, and normal sperm forms of ≥ 30%.

The hypoosmotic swelling test (HOST) has been performed by mixing 0.1 mL of semen with 1.0 mL of a hypo-osmotic solution prepared as follow: 7.3 g of sodium citrate and 13.5 g of fructose and 1000 mL of distilled water.[11] The mixture has been incubated for 60 minutes at 37°C, the semen samples were examined under phase contrast microscope at 400x. Two hundred spermatozoa were evaluated.

Leukocytes, polymorphonuclear granulocyte neutrophils (PMN), were counted by the method Endtz[12] modified by Politch et al.[13] Briefly, 0.0375% H_2O_2 was added to 4 mL benzidine stock solution (0.0125% w/v benzidine, Sigma Aldricht, in 50% ethanol). Twenty microlitres of ejaculate was mixed with 20 mL fresh benzidine–H_2O_2 solution. After 5 min of incubation, 160 mL of PBS was added and peroxidase-positive (round, brown stained) and peroxidase-negative (unstained) cells were counted in a Mackler chamber using a phase-contrast microscope.

Biochemical analysis

Concentration of seminal fructose has been measure according Mann method colorimetric test,[14,15] using acid resorcinol; 50 µl of deproteinized seminal plasma was mixed with 1.0 mL of acid resorcinol to give a color reaction. Prostatic acid phosphatase activity has been analyzed by means of hydrolysis of p-nitrophenyl phosphate. Seminal plasma was diluted 1:10.000 in distilled water and p-nitrophenyl phosphate has been used as substrate. Colorimetric measurement has been made at 480 nm.[16]

Seminal zinc concentration has been measured by colorimetric method described by Johnsen & Eliasson, modified for Cooper et al.[17] The compound 2-(5-bromo-2-pyridylazo)-5-(N-propyl-N-sulphopropylamino)-phenol (5-Br-PAPS) binds with zinc, producing a change in a colour, which absorbs light at a wavelength range of 560 nm.

The neutral alpha glucosidase has been measured in all samples of seminal plasma according to the photometric method described by Guérin et al.[18] Seminal plasma contains both a neutral α-glucosidase isoenzyme, which originates in the epididymis, and an acid isoenzyme provided by the prostate. The latter can be selectively inhibited by sodium dodecyl sulfate (SDS) to allow measurement of the neutral α-glucosidase, which reflects epididymal function. Accounting for non-glucosidase-related substrate breakdown, by using the inhibitor castanospermine, makes the assay more sensitive. The substrate (paranitrophenyl α-D-glucopyranoside) is hydrolysed specifically by a-NAG into paranitrophenyl, during 2 h of incubation at 37°C, pH 6.8. The quantity of paranitrophenyl is measured by spectrophotometer at a wavelength of 405 nm. One international unit (U) of glucosidase activity is defined as the production of 1 µmol product (p-nitrophenyl) per minute at 37°C, pH 6.8.

TABLE 1. **Seminal parameters in control and varicocele group**

	Control (n = 100)	Varicocele (n = 190)	p value
Semen volume (mL)	3.7 ± 1.0	3.6 ± 1.7	ns
Sperm x 10^6/mL	63.9 ± 41.1	71.5 ± 48.5	ns
Motility a + b (%)	68.7 ± 10.2	53.2 ± 20.0	0.0001
Normal morphology (%)	37.1 ± 6.6	31.8 ± 9.7	0.0001
HOST (%)	67.7 ± 2.8	50.4 ± 15.8	0.0001
Vitality (%)	80.8 ± 4.8	66.3 ± 16.1	0.0001
PMN/ejaculate	1.8 ± 0.9	3.7 ± 3.0	0.0001

Statistical analyses

Statistical analysis has been performed using SPSS 10.0 statistical software for Windows (SPSS, Chicago, IL, USA). Basic descriptive statistics (mean ± SD) were calculated to varicocele groups (grades I, II, III and bilateral) and control group. Differences between varicocele total group and control group were determined by t-test. Differences between varicocele (different grades) and control group were determined by analysis of variance (ANOVA) and LSD *pos hoc* comparison for normally distributed values. Pearson´s coefficient correlation has been performed, p values below 0.05 were considered statistically significant.

Results

The average age of the control group was 32.3 ± 7.1 years while in the varicocele group was 28.4 ± 9.4 ($p < 0.05$). Because age may affect the results of the seminal parameters, we performed an ANOVA using age as a covariate. Table 1 shows the seminal parameters in control group and varicocele group. There were no significant differences in the sperm concentration/mL between varicocele total group (grade I+II+III+bilateral) and control group. However, the percentages of following seminal parameters were statistically higher ($p < 0.0001$) in the control group than in the varicocele group: motility a + b, normal morphology, hypoosmotic swelling test and sperm vitality. The concentration of polymorphonuclear (PMN)/ejaculate was increased in varicocele group in comparison with control group.

Table 2 shows the fructose levels, prostatic acid phosphatase activity, zinc levels and neutral alpha glucosidase activity in semen in control group, total varicocele group and varicocele subgroups: grade I, II, III, and bilateral. There was no significant statistical difference between control and varicocele total group in seminal levels of: fructose, PAP and zinc. On the other hand, the activity of the epididymis marker, the neutral alpha glucosidase (NAG), was diminished in patients with varicocele. The ANOVA post hoc analysis (LSD) showed that NAG mU/ejaculate was decreased in all the grades of varicocele.

TABLE 2. **Markers of accessory sex glands in control and varicocele groups**

	Control (n = 100)	Varicocele total group (n = 190)	p value	Varicocele grade I (n = 42)	Varicocele grade II (n = 66)	Varicocele grade III (n = 23)	Varicocele bilateral (n = 59)
Semen volume (mL)	3.7 ± 1.0	3.6 ± 1.7	ns	3.5 ± 1.7	3.5 ± 1.6	3.7 ± 2.0	3.7 ± 1.7
Fructose (mg/ejaculate)	967.8 ± 311.7	1026.4 ± 673.9	ns	1085.8 ± 735.0	944.3 ±575.9	1130.4 ± 919.2	1035.5 ± 625.7
Prostatic acid phosphatase (U/ejaculate)	2360.5 ± 807.9	2531.3 ± 1655.4	ns	2650.3 ± 1503.1	2424.4 ± 18.5	2772.3 ± 1997.2	2472.3 ± 1455.2
Zinc (µmol/ ejaculate)	10.5 ± 8.1	11.8 ± 7.5	ns	10.8 ± 6.7	12.5 ± 7.6	8.9 ± 9.5	13.0 ± 6.8
Neutral alpha glucosidase (mU/ejaculate)	33.0 ± 8.5	15.8 ± 7.7[a]	< 0.0001	16.0 ± 7.0[a]	14.6 ± 6.7[a]	16.3 ± 7.4[a]	16.9 ± 9.3[a]

Values are expressed as mean ± SD
[a]as compared to control group

TABLE 3. **Correlation coefficients between markers of accessory sex glands and sperm parameters in total group of men evaluated (n = 290)**

	Correlation	r Pearson
↑ Fructose (mg/ejaculate)	↑ volume	0.77
	↑ Sperm concentration/ejaculate	0.26
	↑ PMN/ejaculate	0.42
	↑ PAP (U/ejaculate)	0.44
	↑ Zinc (µmol/ejaculate)	0.41
↑ PAP (U/ejaculate)	↑ volume	0.65
	↑ Sperm concentration/ejaculate	0.31
	↑ PMN/ejaculate	0.37
	↑ Zinc (µmol/ejaculate)	0.41
↑ Zinc (µmol/ejaculate)	↑ volume	0.62
	↑ Sperm concentration/ejaculate	0.40
	↑ Motility a + b	0.12
	↑ PMN/ejaculate	0.37
↑ NAG (mU/ejaculate)	↑ Normal morphology	0.14
	↑ Motility a + b	0.23
	↑ Vitality	0.26
	↑ HOST	0.32
	↓ PMN/ejaculate	-0.19

All correlations were statistically significant ($p < 0.05$).
PAP = prostatic acid phosphatase activity; NAG = neutral alpha glucosidase; PMN = polymorphonuclear granulocyte neutrophils; HOST = hypoosmotic swelling test

Table 3 shows the correlation studies between fructose, PAP, zinc, NAG in seminal plasma and sperm parameters in total group of men evaluated (control + varicocele). A positive correlation was observed between both fructose and PAP with the following variables: volume, sperm concentration, PMN, and zinc. Additionally zinc concentration was positively correlated with semen volume, sperm concentration, progressive motility and polymorphonuclear cells and was negatively associated with sperm vitality. On the other hand, NAG was positively correlated with: normal sperm morphology, progressively motility, sperm vitality and hypoosmotic swelling test.

Discussion

In the present study, the markers of epididymal, prostate and seminal vesicles were associated with seminal parameters in normozoospermic men and patients with varicocele, to determinate if varicocele could affect secretion of accessory sex glands. No differences were observed in fructose, PAP and zinc levels between normozoospermic men and patients with varicocele. Similar to our study, Andò et al[8] showed no differences in the concentrations of fructose, however, they found a decrease in PAP and zinc concentration in patients with varicocele; the difference may be explained because in the present study we used modified techniques for zinc and PAP, while they employed the original techniques. Additionally, a recent publication by our group[19] found no significant difference in the concentration of Zn, in another group of men with varicocele or normospermic, by using the equipment "Total Reflection X-Ray Fluorescence".

In the present investigation the percentage of spermatozoa with normal morphology, motility, vitality, and HOST was reduced in patients with varicocele. A previous investigation from our laboratory,[7] showed a detailed analysis of the relationship between degrees of varicocele and seminal parameters, reporting that the percentage of sperm with normal morphology was the unique parameter, that changed between varicocele grades, decreasing in men with varicocele grade III, while other parameters are not affected in relation to the degrees of varicocele, indicating that seminal parameters are affected by the presence or absence of varicocele, regardless of grade.

The activity of NAG was significantly decreased in varicocele total group, similar results were found in a previous study,[9] however, this is the first study which

shows that NAG activity decreased in all grades of varicocele, could be possible that varicocele presence, regardless the grade, affects epididymal functions. NAG is secreted by the epididymal epithelium, mostly in the corpus and cauda.[20] Experimental varicocele in rat produces detrimental effects of the epididymal epithelium with apparition of deformed sperm and macrophages into the epididymal lumen and, also a significant reduction of the NAG activity in the caput, corpus and cauda of epididymis.[21] Previous studies reported a positive association between NAG and sperm motility, as in this study,[9,22] while another study does not show correlation.[23]

The epididymis performs an important role in the maturation of spermatozoa,[24] if the varicocele affects epididymis function, sperm quality could be impaired. Epididymis is located within the scrotum, sharing the same conditions of the testis with varicocele, such as a high reactive oxygen species levels and low total antioxidant capacity, compared with the healthy subjects.[25,26] These conditions could produce failure in the sperm maturation, manifested as poor motility, morphology and sperm membrane quality. Importantly, in this study the concentration of NAG was positively correlated with an increase in normal morphology, motility a + b, vitality and HOST, variables that can be modified by sperm storage in the epididymis.

The HOST evaluates the functional integrity of the sperm membrane: under hypo-osmotic conditions spermatozoa "swell' due to the influx of water and the expansion of the membranes. Jeyendran et al[11] reported a good correlation between the percentage of spermatozoa in a semen sample that were capable of undergoing swelling and the percentage of denuded hamster oocytes that were penetrated by capacitated spermatozoa from the same semen sample. Moreover, a recent publication[27] reported that HOST identifies individual spermatozoa with a minimal DNA fragmentation. Additionally a study reported that a decrease in neutral alpha-glucosidase correlated with an increase in the percentage of DNA fragmentation,[28] these results suggested that HOST, NAG and DNA fragmentation could be associated.

In the present research we conducted correlation coefficients studies between markers of accessory sex glands and sperm parameters in total group of men evaluated, in order to determine whether the concentrations of these markers are related to semen quality and may be linked to the findings for varicocele. It has long been suggested that both prostatic and vesicular fluid affect sperm motility. An investigation reports a negative correlation between number of motile spermatozoa and fructose concentration (mg/mL),[15] while another study shows the opposite [4] and another, similar as our study, found no association.[29] Previous studies reported that a marker of prostatic origin, such as prostate-specific antigen, showed a significant positive association with percentage of sperm progressive motility.[1,30,31] In the present study an increase in zinc concentration was associated with an increase of sperm motility and sperm count, which agrees with previous studies.[18,32] On the other hand, we found an increase of PMN in varicocele group as compared with control group; a similar result has been reported recently.[26] However, future studies are necessary to elucidate the origin of PMN in semen.

In relation to the seminal volume and markers of accessory glands, the results indicate that fructose, zinc and PAP were positively correlated with semen volume, it could be explained by the substantial contribution of volume, to final ejaculate, by the seminal vesicles and prostate. However, NAG was not correlated with semen volume, possibly because the epididymis contributes little to the ejaculate volume.

Finally, it is necessary for future research to investigate the process that could explain the decreasing of epididymal NAG activity during varicocele. Additionally, it would be important to assess whether the varicocelectomy leads to an improvement in epididymal NAG activity. In conclusion, varicocele does not alter fructose secretion by seminal vesicles and PAP and zinc by prostate. Varicocele is associated with a decrease of NAG activity in seminal fluid, suggesting epididymal dysfunction possibly associated with a detrimental in sperm quality. □

References

1. Elzanaty S, Richthoff J, Malm J, Giwercman A. The impact of epididymal and accessory sex gland function on sperm motility. *Hum Reprod* 2002;17(11):2904-2911.
2. Zöpfgen A, Priem F, Sudhoff F et al. Relationship between semen quality and the seminal plasma components carnitine, neutral alpha glucosidase, fructose, citrate and granulocyte elastase in infertile men compared with a normal population. *Hum Reprod* 2000;15(4):840-845.
3. Ndovi TT, Parsons T, Choi L, Caffo B, Rohde C, Hendrix CW. A new method to estimate quantitatively seminal vesicle and prostate gland contributions to ejaculate. *Br J Clin Pharmacol* 2007; 63(4):404-420.

4. Said L, Galeraud-Denis I, Carreau S, Saâd A. Relationship between semen quality and seminal plasma components: neutral alpha glucosidase, fructose and citrate in infertile men compared with a normospermic population of Tunisian men. *Andrologia* 2009;41(3):150-156.
5. Andrade-Rocha FT. Significance of sperm characteristics in the evaluation of adolescents, adults and older men with varicocele. *J Postgrad Med* 2007;53(1):8-13.
6. Agarwal A, Deepinder F, Cocuzza M, Agarwal R, Short RA, Sabanegh E, Marmar JL. Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach. *Urology* 2007;70(3):532-538.
7. Vivas-Acevedo G, Lozano JR, Camejo MI. Effect of varicocele grade and age on seminal parameters. *Urol Int* 2010;85(2):194-199.
8. Andò S, Carpino A, Buffone M, Maggiolini M, Giacchetto C, Seidita. Fructose, prostatic acid phosphatase and zinc levels in the seminal plasma of varicoceles. *Int J Fertil* 1990;35(4): 249-252.
9. Roaiah MM, Mostafa T, Salem D, El-Nashar AR, Kamel II, El-Kashlan MS. Alpha-1,4-Glucosidase activity in infertile oligoasthenozoospermic men with and without varicocele. *Andrologia* 2007;39(1):28-32.
10. World Health Organization. WHO Laboratory Manual for the Examination of Human Semen and Sperm–Cervical Mucus Interaction, 3rd ed. Cambridge: Cambridge University Press, 1992.
11. Jeyendran RS, VanderVen HH, Perez, Pelaez M, Crabo BG, Zaneveld LJ. Development of an assay to assess the functional integrity of the human sperm membrane and its relationship to other semen characteristics. *J Reprod Fertil* 1984;70(1):219-228.
12. Endtz AW. A rapid staining method for differentiating granulocytes from germinal cells in Papanicolau-stained semen. *Acta Cytol* 1974;18(1):2-7.
13. Politch JA, Wolff H, Hill JA, Anderson DJ. Comparison of methods to enumerate white blood cells in semen. *Fertil Steril* 1993; 60(2):372-375.
14. Mann T. Biochemistry of Semen and of the Male Reproductive Tract Methuen, London; Wiley, New York, 1964.
15. Lewis-Jones DI, Aird IA, Biljan MM, Kingsland CR. Effects of sperm activity on zinc and fructose concentrations in seminal plasma. *Hum Reprod* 1996;11(11):2465-2467.
16. Andolz P, Bielsa MA. Semen humano. Manual y Atlas. 1ra ed. Madrid: Editorial Garsi SA;1995.
17. Cooper TG, Jockenhövel F, Nieschlag E. Variations in semen parameters from fathers. *Hum Reprod* 1991;6(6):859-866.
18. Guerin JF, Ali HB, Rollet J, Souchier C, Czyba JC. Alpha-glucosidase as a specific epididymal enzyme marker: its validity for the etiologic diagnosis of azoospermia. *J Androl* 1986;7(3): 156-162.
19. Camejo MI, Abdala L, Vivas-Acevedo G, Lozano-Hernández R, Angeli-Greaves M, Greaves ED. Selenium, copper and zinc in seminal plasma of men with varicocele, relationship with seminal parameters. *Biol Trace Elem Res* 2011, Jan 15. [Epub ahead of print]
20. Cooper TG, Weidner W, Nieschlag E. The influence of inflammation of the human male genital tract on secretion of the seminal markers alpha-glucosidase, glycerophosphocholine, carnitine, fructose and citric acid. *Int J Androl* 1990;13(5):329-336
21. Zhang QY, Qiu SD, Ma XN, Yu HM, Wu YW. Effect of experimental varicocele on structure and function of epididymis in adolescent rats. *Asian J Androl* 2003;5(2):108-112.
22. Mahmoud AM, Geslevich J, Kint J et al. Seminal plasma alpha-glucosidase activity and male infertility. *Hum Reprod* 1998; 13(3):591-595.
23. Levrant S, Watanabe M, Land S, Sauer R, Jeyendran RS. The relevance of neutral alpha-glucosidase activity in andrology. *Syst Biol Reprod Med* 2009;55(2):116.
24. Cornwall GA. New insights into epididymal biology and function. *Hum Reprod Update* 2009;15(2):213-227.
25. Pasqualotto FF, Sundaram A, Sharma RK, Borges E Jr, Pasqualotto EB, Agarwal A. Semen quality and oxidative stress scores in fertile and infertile patients with varicocele. *Fertil Steril* 2008;89(3):602-607.
26. Blumer CG, Fariello RM, Restelli AE, Spaine DM, Bertolla RP, Cedenho AP. Sperm nuclear DNA fragmentation and mitochondrial activity in men with varicocele. *Fertil Steril* 2008; 90(5):1716-1722.
27. Stanger JD, Vo L, Yovich JL, Almahbobi G. Hypo-osmotic swelling test identifies individual spermatozoa with minimal DNA fragmentation. *Reprod Biomed Online* 2010;21(4):474-484.
28. Watanabe M, Roussev R, Ahlering P, Sauer R, Coulam C, Jeyendran RS. Correlation between neutral alpha-glucosidase activity and sperm DNA fragmentation. *Andrologia* 2009;41(5):316-318.
29. Andrade-Rocha FT. Seminal fructose levels in male infertility: relationship with sperm characteristics. *Int Urol Nephrol* 1999; 31(1):107-111.
30. Elzanaty S. Association between age and epididymal and accessory sex gland function and their relation to sperm motility. *Arch Androl* 2007;53(3):149-156.
31. Carpino A, Sisci D, Aquila S et al. Adnexal gland secretion markers in unexplained asthenozoospermia. *Arch Androl* 1994; 32(1):37-43.
32. Mankad M, Sathawara NG, Doshi H, Saiyed HN, Kumar S. Seminal plasma zinc concentration and alpha-glucosidase activity with respect to semen quality. *Biol Trace Elem Res* 2006; 110(2):97-106.

Maximizing intravesical therapy options: is there an advantage to the administration of perioperative mitomycin C prior to an induction course of BCG?

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BADALATO GM, HRUBY G, RAZMJOO M, MCKIERNAN JM. Maximizing intravesical therapy options: is there an advantage to the administration of perioperative mitomycin C prior to an induction course of BCG? The Canadian Journal of Urology. 2011;18(5):5890-5895.

Introduction: *This study sought to evaluate cancer-specific outcomes among patients who received perioperative mitomycin C (MMC) prior to induction BCG versus those who received induction BCG alone.*

Materials and methods: *Between January 2000 and August 2010, 260 patients were identified who underwent a course of induction BCG with or without concomitant perioperative MMC. Specifically, patients who received 40 mg MMC following transurethral resection of all visible tumor followed by an induction course of BCG were compared to a similar cohort of patients who received induction BCG alone. The primary endpoints were overall and recurrence-free survival (RFS).*

Results: *A total of 212 patients were identified who received induction BCG alone, and 48 who received perioperative MMC with induction BCG. The aggregate patient cohort was comprised of those with non-muscle invasive disease (NMI), and there was no difference between groupings with respect to common demographic and pathologic variables. Over a median follow up of 34.5 months, there was no difference in overall survival between cohorts. RFS was superior among patients who received combined therapy (5 year survival: 37.5% versus 56.3%, p = 0.023). Nevertheless, the regimen of intravesical therapy did not reach significance as an independent predictor (HR 0.61, p = 0.055, CI 0.36-1.01).*

Conclusion: *Although the combination therapy group demonstrated a significant RFS advantage, the intravesical therapy regimen did not independently modulate this benefit. Further investigation is warranted to determine if immediate MMC prior to a course of induction BCG confers a benefit to RFS. Nevertheless, this pilot investigation sets an important precedent on the management of NMI bladder cancer, nonwithstanding the absence of contemporary large scale, randomized trials.*

Key Words: BCG, mitomycin C, combination intravesical therapy, recurrence-free survival

Introduction

The practice of using multiple antineoplastic drugs in combined regimens has not been applied consistently in the use of intravesical agents for the treatment of transitional cell cancer (TCC) of the bladder. The immunotherapeutic BCG and the chemotherapeutic mitomycin C (MMC) are hypothesized to have a potentially synergistic effect in combination. In fact, in vitro models using combination therapy with bladder cancer cells demonstrated enhanced antineoplastic activity compared to treatment with chemotherapy or BCG alone.[1] Furthermore, clinical data, mostly from northern Europe, has addressed concurrent therapy with mitomycin and BCG, attributing two roles to mitomycin: that of an anitprolifierative action and of a tissue-scarring or surface-modifying attribute that enables BCG to attach more efficiently to urothelium.[2-8] Three small studies have since focused on the import of these findings as it pertains to non-muscle invasive (NMI) bladder cancer, demonstrating low recurrence rates utilizing varying protocols for the administration of epirubicin and BCG chemoimmunoprophylaxis.[9-11]

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Based on these precedents, this investigation sought to determine whether a clinical benefit might be rendered among patients with TCC of the bladder who received a single dose of MMC prior to the initiation of a BCG regimen. Specifically, this study sought to evaluate cancer-specific outcomes among patients who received perioperative MMC prior to induction BCG versus those who received induction BCG alone.

Materials and methods

Patients were retrospectively identified from the Institutional Review Board-approved Urologic Oncology Database. Tumors were staged according to the 6th edition of the TNM system of the American Joint Cancer Committee/Union Internationale Contre le Cancer Staging Manual.[12] Between January 2000 and August 2010, 267 patients were identified who underwent a course of induction BCG with or without concomitant perioperative MMC. In particular, patients who received 40 mg MMC following transurethral resection of all visible tumor followed by an induction course of BCG were compared to a similar cohort of patients who received induction BCG alone. The induction course of BCG was administered according to SWOG protocol, and this therapy did not necessarily include subsequent maintenance treatments. Patients with tumors in the upper urinary tract were excluded.

Patients were then stratified by the intravesical treatment regimen received, namely combination or monotherapy, and both univariate and multivariate analytic models were created. Kaplan-Meier curves were extrapolated to evaluate primary endpoints of overall and recurrence-free survival for each cohort, and the groups were in turn compared using the log-rank test. Statistical analysis was done using SAS version 9.1, with $p < 0.05$ considered significant.

Results

A total of 212 patients were identified who received induction BCG alone, and 48 who received perioperative

TABLE 1. **A comparison of demographic and pathologic variables amongst combination and monotherapy groups**

	Induction BCG alone	**Perioperative MMC + induction BCG**	**p value**
Total cohort	212	48	
Clinical data			
Age, yr, mean (SD)	69.6 + 11.5	69.64 +11.3	0.931
Gender (%)			0.684
Male	152/212 (71.7)	33/48 (68.7)	
Female	60/212 (28.3)	15/48 (31.2)	
Race (%)			0.464
Caucasian	165 (77.8)	42 (87.5)	
African American	14 (6.6)	2 (4.2)	
Hispanic	19 (9.0)	3 (6.2)	
Other	14 (6.6)	1 (2.1)	
Pathological data			
Stage at initial biopsy (%)			0.043
Ta	80 (37.7)	24 (50.0)	
Tis[a]	38 (17.9)	2 (4.2)	
T1	94 (44.3)	22 (45.8)	
CIS (%)[b]	61/212 (28.8)	12/48 (25.0)	0.599
LVI (%)	4/212 (1.9)	2/48 (4.2)	0.342
High grade (%)	148/212 (69.8)	38/48 (79.1)	0.195

[a]denotes patients with stage Tis only.
[b]denotes patients with concurrent CIS, exclusive of those with Tis as a stage.
BCG = Bacillus Calmette-Guerin; MMC = mitomycin C; SD = standard deviation
CIS = carcinoma in situ; LVI = lymphovascular invasion

TABLE 2. **Univariate and multivariate cox regression analyses predicting recurrence-free survival in patients treated with induction BCG alone versus those treated with induction BCG and MMC**

	Univariate analysis			Multivariate analysis		
Variable	**HR**	**p value**	**95% CI**	**HR**	**p value**	**95% CI**
Age	1.01	0.144	1.00-1.03			
Race						
African American	1.10	0.788	0.54-2.27			
Hispanic	0.89	0.724	0.46-1.70			
Other	1.05	0.894	0.49-2.27			
Male sex	1.19	0.373	0.81-1.73			
Initial stage						
Ta	1.00	referent		referent		
Tis	1.22	0.425	0.74-2.01	1.52	0.214	0.79-2.93
T1	0.91	0.624	0.62-1.33	0.94	0.749	0.63-1.39
CIS	0.88	0.521	0.59-1.30	0.71	0.205	0.42-1.21
LVI	0.72	0.578	0.23-2.27	0.88	0.836	0.28-2.83
High grade	0.84	0.344	0.58-1.21	0.89	0.586	0.60-1.33
Receipt of MMC	0.58	0.030	0.35-0.95	0.61	0.055	0.36-1.01

HR = hazard ratio; MMC = mitomycin C; CIS = carcinoma in situ; LVI = lymphovascular invasion

MMC in conjunction with induction BCG. The mean follow up was 43.6 ± 38.1 months (median 35) in the BCG group and 33.0 ± 21.3 months (median 32.5) (p = 0.0583) in the MMC/BCG cohort. Approximately 78/212 (36.8%) and 23/48 (47.9%) patients in the BCG alone and BCG/MMC groups, respectively, went on to receive maintenance BCG (p = 0.214). A large proportion of patients in both cohorts had T1 disease in a similar distribution (BCG: 94 (44.3%) versus BCG/MMC: 22 (45.8%)); however, the groupings were disparate (p = 0.043) with respect to the frequency of Ta (BCG: 80 (37.7%) versus BCG/MMC 24 (50.0%)) and Tis disease (BCG: 38 (17.9%) versus BCG/MMC: 2 (4.2%)), Table 1. There was no statistical difference between groups with respect to demographic variables of age (p = 0.931), gender (p = 0.684), or race (= 0.464); similarly, no difference in pathological variables of concomitant CIS (p = 0.599), the presence of lymphovascular invasion (LVI) (p = 0.342), and the detection of high grade disease (p = 0.195) was noted between cohorts, Table 1.

Although log-rank analysis did not substantiate a difference between cohorts with respect to overall survival, recurrence-free survival was superior in patients who received combined intravesical therapy, Figure 1. In fact, the 5 year recurrence free survival among the BCG alone group was 37.5% as compared to 56.3% in the combination therapy grouping (p = 0.023). This association was confirmed in a univariable cox regression model predicting recurrence-free survival (HR 0.58, p = 0.030, CI 0.35-0.95), Table 2. However, in a multivariable model, controlling for initial biopsy stage and the presence of CIS, LVI, and high grade disease, receipt of MMC was no longer predictive of recurrence-free survival by a narrow margin (HR 0.61, p = 0.055, CI 0.36-1.01), Table 2.

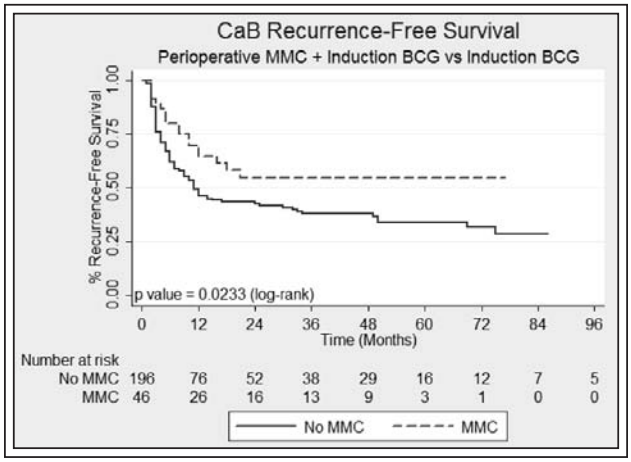

Figure 1. Recurrence-free survival among both cohorts; there is a significant survival advantage favoring those patients who received combination therapy (p = 0.0233).

Discussion

The present study demonstrates that patients receiving immediate MMC prior to an induction course of BCG sustain a favorable recurrence-free survival, albeit further work is required to determine if the course of intravesical therapy independently modulates this outcome. Although the efficacy of combining these two agents has been examined in prior work, to our knowledge, this is the largest contemporary report to evaluate outcomes associated with a single perioperative dose of mitomycin prior to BCG induction, a scheme of administration which is common in clinical practice.

Historically, three prospective randomized trials have been borne out in recent years that compare BCG monotherapy to combination with intravesical chemotherapy; these trials have generally included high risk NMI bladder cancer patients with no specific attention to the role of carcinoma-in-situ (CIS). Cai et al, much in the vein of the current study, evaluated the impact of one immediate epirubicin instillation preceding the administration of BCG.[13] The comparative regimes resulted in a 57.5% recurrence-free rate in the combined group, as opposed to 50.6% in the BCG-alone group, a differential that was not statistically significant ($p = 0.82$). In another study, the regular administration of electromotive MMC in combination with BCG resulted in not only a lower recurrence rate (41.9% versus 57.9%, $p = 0.0012$), but also a significantly lower disease-specific mortality within the combination group (5.6% versus 16.2%, $p = 0.01$).[14] The degree to which the electromotive delivery of MMC contributed to this remarkable differential among cohorts cannot be extrapolated from the data. The final study included a total of 56 Ta-T1 tumors of unknown grade, whereby patients received immediate MMC at the time of TUR in addition to four weekly courses of this agent.[15] Patients relegated to the BCG alone arm were exempt from immediate instillation, and received only BCG weekly for 6 weeks. Subjects in both cohorts went on to receive BCG monthly for 1 year. The combination group sustained a significantly longer time to first recurrence, substantiating multiple prior reports on the efficacy of alternating therapy by the Finnbladder Group.[5]

As a recent complement to the aforementioned collection of prospective trials, EORTC 30993 features the results of a randomized phase II trial involving combined therapy in patients with NMI disease along with CIS, be it primary, secondary, or concurrent. These patients received six weekly instillations of MMC followed by six weekly instillations of BCG or a total of 9 weekly instillations of BCG with an intervening rest period. Complete response and disease-free rates were similar to those receiving BCG alone, however, establishing that sequential intravesical chemotherapy and BCG had no role for the treatment of CIS. Of note the timing and protocol of administration in the EORTC trial was different than the regimen detailed in this investigation, so the cancer-specific results cannot be directly extrapolated to the cohort of patients described herein. Nevertheless, the role of CIS was accounted for in the current study, and, as evidenced by the findings of EORTC 30993, this feature should be an important consideration not only in clinical management, but also in the critique and formulation of related investigations moving forward.[16]

In addition to its relevancy to multiple antecedent studies, the results of the current investigation were substantiated by findings reported in abstract form by Kader in a prospective protocol with a similar program of intravesical treatment; although, the latter study involved a smaller cohort of patients with NMI disease.[17] In this study of 128 patients followed over a mean of 26 months, 63% of the patients receiving MMC were recurrence-free at last follow up, as compared to 45% in the BCG monotherapy group. Furthermore, an analysis of the side effect profile revealed an even distribution amongst groups, with 30% of patients in each group reporting an adverse event, the majority of which constituted lower urinary tract symptoms. This report thus corroborates the findings discussed herein with respect to the sequence and timing of medication administration. Furthermore, given the prospective design of the Kader study, insight into the side effect profile was afforded, which was equivalent among both cohorts, for each program of therapy.

Although the results described in this report and in the aforementioned abstract are promising, many questions involving the molecular mechanisms behind these clinical observations remain poorly defined. A basis for these explanations involves the premise that MMC must be administered immediately following tumor resection in order to reduce the risk of tumor reimplantation following transurethral resection. In accordance with this recommendation, data from a randomized trial has cited that one instillation of MMC alone immediately following resection reduced the risk of tumor recurrence by approximately 34%.[18-21] Moreover, as it pertains to the literature on combination therapy, several of the studies involving combination therapy feature the administration of BCG prior to MMC, thus allowing for the hypothesis that BCG-induced inflammation might "prime" bladder urothelium for the delivery and action of MMC. Whether the effect of MMC is additive or synergistic with BCG in this scenario remains unknown. However, BCG is postulated to initially provoke a

cytokine and T-cell mediated response against tumor;[22] with the administration of MMC, the active metabolites of this agent then add to the antineoplastic effects by cross-linking DNA to all tissue layers of the bladder affected by superficial bladder cancer.[23,24] While these explanations make mechanistic sense, they seemingly do not apply to the sequence of administration described in this study, whereby MMC is given prior to BCG. Also, these postulates seem to hinge on the concept of multiple administrations of BCG and MMC, and may not fully account for the presumed durable impact of immediate, one-time administration of MMC following transurethral resection. Thus, whether the benefit from immediate MMC and induction BCG is derived from the sequential, independent action of these agents or through a complementary mechanism, perhaps involving urothelial surface modification, remains indeterminate.[2-8]

Furthermore, in addition to speculating on the molecular mechanisms underpinning these clinical observations, consideration might also be given to the limitations of this study. First, the retrospective nature of this analysis restricts the ability to standardize cohorts as might have been afforded via prospective randomization. For instance, although the groups were matched with respect to many important demographic and pathologic characteristics, a disproportionate number of patients with Tis were included in the monotherapy cohort (17.9% versus 4.2%); and, this disparity might have contributed to the fact receipt of MMC did not reach significance on multivariable analysis. A randomized controlled-trial would thus afford the ideal medium to ensure that clinically more aggressive appearing tumors were not discriminately being assigned to one therapy in particular. In conjunction with this, a larger cohort would ensure that the study was powered sufficiently to substantiate the differences in outcome between combined versus monotherapy, as alluded to herein. In this way, this investigation might serve as a precursor or pilot study for larger-scale investigations on this clinically relevant issue. Furthermore, quality of life and side effect information was not available for consideration at the time this retrospective review was performed, and, in addition to therapeutic efficacy, these considerations remain important considerations before combination therapy can be implemented. Side effect profiling for combination therapy is particularly important in order to determine how this program modulates the frequency of known adverse effects associated with BCG and mitomycin C individually;[21,25-27] furthermore, it must be established if these adverse events occur in a summative fashion in the setting of combined therapy and whether tolerability will be affected as a consequence.

Despite these limitations, however, this study adds a valuable contribution to the growing body of literature on combination intravesical algorithms in the management of TCC of the bladder. Future investigations stand to determine if perioperative MMC prior to induction BCG may increase recurrence-free survival.

Conclusion

The administration of perioperative MMC prior to an induction course of BCG did not confer an overall survival advantage. Although the combination therapy group demonstrated a significant recurrence-free survival advantage, the intravesical therapy regimen did not independently modulate this benefit. Further investigation is warranted to determine if immediate MMC prior to a course of induction BCG confers a benefit to recurrence-free survival. Given the clinical relevance of these conclusions, the findings discussed herein may serve as pilot data to guide such a larger-scale, randomized-controlled trial. □

References

1. Rajala P, Kaasinen E, Rintala E et al. Cytostatic effect of different strains of Bacillus Calmette-Guerin on human bladder cancer cells in vitro alone and in combination with mitomycin C and interferon-alpha. *Urol Res* 1992;20(3):215-217.
2. Kaasinen E, Rintala E, Hellstrom P et al. Factors explaining recurrence in patients undergoing chemoimmunotherapy regimens for frequently recurring superficial bladder carcinoma. *Eur Urol* 2002;42(2):167-174.
3. Kaasinen E, Rintala E, Pere AK et al. Weekly mitomycin C followed by monthly bacillus Calmette-Guerin or alternating monthly interferon-alpha2B and bacillus Calmette-Guerin for prophylaxis of recurrent papillary superficial bladder carcinoma. *J Urol* 2000;164(1):47-52.
4. Kaasinen E, Wijkstrom H, Malmstrom PU et al. Alternating mitomycin C and BCG instillations versus BCG alone in treatment of carcinoma in situ of the urinary bladder: a nordic study. *Eur Urol* 2003;43(6):637-645.
5. Rintala E, Jauhiainen K, Kaasinen E, Nurmi M, Alfthan O. Alternating mitomycin C and bacillus Calmette-Guerin instillation prophylaxis for recurrent papillary (stages Ta to T1) superficial bladder cancer. Finnbladder Group. *J Urol* 1996;156(1):56-59; discussion 59-60.
6. Rintala E, Jauhiainen K, Rajala P, Ruutu M, Kaasinen E, Alfthan O. Alternating mitomycin C and bacillus Calmette-Guerin instillation therapy for carcinoma in situ of the bladder. The Finnbladder Group. *J Urol* 1995;154(6):2050-2053.
7. Van der Meijden AP, Hall RR, Macaluso MP, Pawinsky A, Sylvester R, Van Glabbeke M. Marker tumour responses to the sequential combination of intravesical therapy with mitomycin-C and BCG-RIVM in multiple superficial bladder tumours. Report from the European Organisation for Research and Treatment on Cancer-Genitourinary Group (EORTC 30897). *Eur Urol* 1996;29(2): 199-203.

8. Witjes JA, Caris CT, Mungan NA, Debruyne FM, Witjes WP. Results of a randomized phase III trial of sequential intravesical therapy with mitomycin C and bacillus Calmette-Guerin versus mitomycin C alone in patients with superficial bladder cancer. *J Urol* 1998;160(5):1668-1671;discussion 1671-1672.
9. Bono AV, Lovisolo JA, Saredi G. Transurethral resection and sequential chemo-immunoprophylaxis in primary T1G3 bladder cancer. *Eur Urol* 2000;37(4):478-483.
10. Erol A, Ozgur S, Basar M, Cetin S. Trial with bacillus Calmette-Guerin and epirubicin combination in the prophylaxis of superficial bladder cancer. *Urol Int* 1994;52(2):69-72.
11. Uekado Y, Hirano A, Shinka T, Ohkawa T. The effects of intravesical chemoimmunotherapy with epirubicin and bacillus Calmette-Guerin for prophylaxis of recurrence of superficial bladder cancer: a preliminary report. *Cancer Chemother Pharmacol* 1994;35(Suppl): S65-S68.
12. Greene FL, Page DL, Fleming ID et al. AJCC Cancer Staging Manual, 6th Edition. New York, Springer, 2002.
13. Cai T, Nesi G, Tinacci G et al. Can early single dose instillation of epirubicin improve bacillus Calmette-Guerin efficacy in patients with nonmuscle invasive high risk bladder cancer? Results from a prospective, randomized, double-blind controlled study. *J Urol* 2008;180(1):110-115.
14. Di Stasi SM, Giannantoni A, Giurioli A et al. Sequential BCG and electromotive mitomycin versus BCG alone for high-risk superficial bladder cancer: a randomised controlled trial. *Lancet Oncol* 2006; 7(1):43-51.
15. El Mohsen M, Shelbaia A, El Ghobashy S et al. Sequential chemoimmunotherapy using Mitomycin followed by bacillus Calmette-Guerin versus single agent immunotherapy (BCG) for recurrent superficial bladder tumors. *UroToday Int J* 2010:3.
16. Oosterlinck W, Kirkali Z, Sylvester R et al. Sequential intravesical chemoimmunotherapy with mitomycin C and Bacillus Calmette-Guerin and with Bacillus Calmette-Guerin alone in patients with carcinoma in situ of the urinary bladder: results of an EORTC genito-urinary group randomized phase 2 trial (30993). *Eur Urol* 2011;59(3):438-446.
17. Kader OAE. Immediate mitomycin C instillation followed by usual BCG course versus usual BCG alone for superficial transitional cell carcinoma of the bladder (4 years experience), AUA Abstract #1473. Fakous, Egypt, 2010.
18. Solsona E, Iborra I, Ricos JV, Monros JL, Casanova J, Dumont R. Effectiveness of a single immediate mitomycin C instillation in patients with low risk superficial bladder cancer: short and long-term followup. *J Urol* 1999;161(4):1120-1123.
19. Tolley DA, Parmar MK, Grigor KM et al. The effect of intravesical mitomycin C on recurrence of newly diagnosed superficial bladder cancer: a further report with 7 years of follow up. *J Urol* 1996;155(4): 1233-1238.
20. Shelley MD, Mason MD, Kynaston H: Intravesical therapy for superficial bladder cancer: a systematic review of randomised trials and meta-analyses. *Cancer Treat Rev* 2010;36(3):195-205.
21. Shapiro O, Jones K, Wang C, Landas S, Haas GP. Risk of post-operative intravesical mitomycin C instillation following transurethral bladder tumor resection. *Can J Urol* 2006;13(6):3317-3320.
22. Alexandroff AB, Jackson AM, O'Donnell MA, James K. BCG immunotherapy of bladder cancer: 20 years on. *Lancet* 1999; 353(9165):1689-1694.
23. Di Stasi SM, Giannantoni A, Massoud R, et al: Electromotive versus passive diffusion of mitomycin C into human bladder wall: concentration-depth profiles studies. *Cancer Res* 1999;59(19): 4912-4918.
24. Chen F, Zhang G, Iwamoto Y, See WA. BCG directly induces cell cycle arrest in human transitional carcinoma cell lines as a consequence of integrin cross-linking. *BMC Urol* 2005;5:8.
25. Caso J, Qin D, Sexton WJ. Eosinophilic cystitis following immediate post-resection intravesical instillation of mitomycin-C. *Can J Urol* 2010;17(3):5223-5225.
26. Sylvester RJ. Bacillus Calmette-Guerin treatment of non-muscle invasive bladder cancer. *Int J Urol* 2011;18(2):113-120.
27. Bolenz C, Cao Y, Arancibia MF, Trojan L, Alken P, Michel MS. Intravesical mitomycin C for superficial transitional cell carcinoma. *Expert Rev Anticancer Ther* 2006;6(8):1273-1282.

MINIMALLY INVASIVE AND ROBOTIC SURGERY

Preoperative predictors of surgical approach for partial nephrectomy

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RAMAN JD, SMITH B, MESSER J, ROHNER TJ, HARPSTER LE, REESE CT. Preoperative predictors of surgical approach for partial nephrectomy. The Canadian Journal of Urology. 2011;18(5):5896-5902.

Introduction: *To evaluate preoperative parameters of patients undergoing partial nephrectomy to determine variables that impact selection of operative approach.*

Materials and methods: *The charts of 229 consecutive patients undergoing partial nephrectomy were reviewed. Clinical data points and associated axial imaging were evaluated to determine factors which contributed to selection of an open (versus laparoscopic) operation.*

Results: *A total of 140 men and 89 women with a mean age of 57 years, body mass index (BMI) of 31, and glomerular filtration rate (GFR) of 82 mL/min/1.73 m^2 were included. Twenty-three percent of patients had prior abdominal surgery and 7% had a history of contralateral renal cell carcinoma (RCC). The mean tumor size was 3.4 cm (range, 0.7-11) with 23% of lesions being endophytic, 38% involving the collecting system, and 29% being hilar. Thirty-four patients (15%) had multifocal lesions. Overall, 130 patients underwent an open partial nephrectomy (OPN) and 99 a laparoscopic partial nephrectomy (LPN). On univariate analysis, preoperative GFR (p = 0.05), a history of contralateral RCC surgery (p = 0.02), tumor size (p = 0.04), renal sinus/collecting system involvement (p = 0.001), renal hilar location (p = 0.001), tumor multifocality (p = 0.004), surgeon laparoscopic case volume of < 25 cases (p = 0.03), and lack of fellowship laparoscopic training (p = 0.02) all were associated with an open surgical approach. In a logistic regression model incorporating these eight variables, only renal hilar location (OR 2.63, 95% CI 1.17-5.88, p = 0.02) remained significantly associated with OPN.*

Conclusions: *Many parameters including increasing BMI, preoperative GFR, prior abdominal surgery, endophytic tumor location, and renal sinus/collecting system involvement do not necessarily preclude a minimally invasive partial nephrectomy. In our experience, renal hilar tumors were over 2.5 fold more likely to be managed by OPN owing to the complexity of resection.*

Key Words: nephron sparing surgery, partial nephrectomy, open surgery, minimally invasive surgery

Introduction

Renal cell carcinoma (RCC) is the 3rd most common genitourinary malignancy accounting for almost 61,000 new cases and over 13,000 cancer related deaths in 2011.[1] Population based studies have implicated that the incidence of RCC has increased 3%-4% yearly since the 1970s.[2] Owing to the increased use of non-invasive abdominal cross-sectional imaging, this trend has been associated with detection of a greater proportion of incidental small renal masses (SRMs).[3,4] While surgical extirpation remains the gold standard for localized RCC, it is apparent that radical nephrectomy represents significant overtreatment for many of these SRMs. Nephron-sparing surgery confers equivalent oncologic and superior renal function outcomes when compared to radical nephrectomy for patients with renal tumors smaller than 4 cm.[5,6] Recent series have further highlighted that such benefits persist even when considering larger localized renal tumors up to 7 cm.[7]

Over the past decade, laparoscopic partial nephrectomy (LPN) has assumed a greater role in the management of SRMs. Contemporary series implicate that for experienced surgeons, LPN provides comparable oncologic and renal function outcomes to open partial nephrectomy (OPN).[8] Furthermore, LPN has been associated with lower narcotic requirements,

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improved cosmesis, earlier resumption of diet, lower cost, and decreased hospital length of stay.[9] However, LPN is a challenging operative procedure with a technique that continue to evolve and a steep learning curve necessary to minimize ischemia times and associated complications.[10,11]

The dissemination of laparoscopy into surgical training[12] has contributed to an increasing number of urologists who may be comfortable with a minimally invasive approach with respect to partial nephrectomy for SRMs. Therefore, it is valuable for such surgeons to be aware of preoperative factors that can potentially contribute to selection of OPN versus LPN. Such considerations would not only facilitate appropriate patient counseling prior to surgery, but may also minimize the likelihood of intraoperative or postoperative complications during LPN. Within our institution, there exists a collaborative relationship among open and minimally invasive surgeons such that all radiographic films are reviewed prior to partial nephrectomy to determine optimal treatment approach. To date, however, selection of a particular modality for partial nephrectomy was loosely based on a compilation of patient, tumor, and surgeon-related variables. We therefore attempt to objectify this process and aid other urologists by presenting our experience with preoperative clinical and radiographic factors that contributed to the selection of an open versus laparoscopic approach for partial nephrectomy.

Materials and methods

Study population

Institutional review board (IRB) approval was obtained to review medical charts and radiographic studies of patients who underwent surgical intervention for an enhancing renal mass between January 2003 and April 2009. Of 715 identified cases, 397 underwent a radical nephrectomy, 258 a partial nephrectomy, and 60 thermal ablation (cryoablation or RFA). We specifically began analysis in 2003 as this represented a time point 18 months (and 15 cases) after the introduction of LPN at our institution. We, therefore, believed that collecting data at this point would obviate some inherent case selection bias associated with introduction of a novel procedure (LPN). OPN was accomplished either by a flank extraperitoneal approach or a transbdominal approach at the discretion of the operative surgeon. Patients younger than 18 years of age, those with a functional or anatomic solitary kidney, patients undergoing bilateral synchronous nephron-sparing surgery, and those without available cross-sectional imaging for review were excluded from analysis. With such criteria, we identified 229 patients who underwent an OPN (n = 130) or LPN (n = 99) that constituted our study cohort.

Clinical variables

Clinical data points included patient age, gender, race, body mass index (BMI), estimated glomerular filtration rate (eGFR), comorbid conditions, history of contralateral RCC surgery (thermal ablation, partial or radical nephrectomy), prior abdominal surgery, and year of surgery. The abbreviated Modification of Diet in Renal Disease Study (MDRD) formula, a function of serum creatinine and demographic variables, was used to assess preoperative eGFR: GFR (in mL/minute/1.73 m^2) = 186 x [serum creatinine $(mg/dL)^{-0.154}$] x $(age^{-0.203})$ x (0.742, if female) x (1.21, if African-American).[13] Comorbidities included diabetes, hypertension, as well as an aggregate of conditions as represented by the Charlson-Romano (CR) index.

Radiographic data

All preoperative computed tomography (CT) or magnetic resonance imaging (MRI) was reviewed by two authors. Variables of interest included tumor size (maximum diameter in cm), laterality, polar location (upper, interpolar, or lower), focality (uni- versus, multi-), depth of tumor, anterior versus posterior location, involvement of the renal sinus/collecting system, or abutment of the renal hilum. Depth of tumor was classified as follows: 1) Exophytic: ≥ 60% extension of tumor off the natural surface of the kidney; 2) Mesophytic: tumor extends 40% to 60% off the kidney; 3) Endophytic: ≤ 40% of the lesion extending off the kidney. Abutment of the renal hilum was defined by tumors adjacent to the main renal artery or vein or the first segmental branch from the either of these vascular structures.

Surgeon data

Our partial nephrectomy databases were also reviewed for surgeon-specific variables that may be determinants for surgical approach. Included in this group were number of years in practice, annual surgical volume, annual number of renal surgery cases, fellowship training in laparoscopy, and total number of laparoscopy cases performed (< or > 25 cases). The referral system at our hospital results in equal distribution amongst all new kidney cancer cases (unless specified by the patient and/or referring physician) amongst the four urologists included in this study. Interestingly, our two highest volume renal cancer surgeons readily incorporate both open and laparoscopic approaches into their practice.

Pathologic data

All specimens were reviewed by institutional pathologists. Staging was according to the American Joint Committee on Cancer (AJCC) and tumors were graded using Fuhrman criteria.[14] Positive surgical margins were defined as tumor cells touching the inked margin of the final specimen.

Statistical analysis

Univariate analysis was initially performed to determine which clinical, surgeon-specific, and radiographic variables were associated with a particular type of partial nephrectomy. Continuous and categorical variables were analyzed using the Mann-Whitney U and Pearson chi-square tests, respectively. For the chi-square test, odds ratios with 95% confidence intervals were used to quantify the magnitude and direction of any significant associations. Exact tests were employed when presented with small cell counts. The variables determined to have significant association on univariate analysis were incorporated into a logistic regression model. A process of backwards elimination was used which started with the full model including all variables. The variable with the largest p value greater than 0.15 was eliminated from the model at each step, and all variables eliminated from the model at the previous steps were added back and retained if their p value was less than 0.10.

Results

Clinical variables

Overall, 130 patients (57%) underwent an OPN, while 99 (43%) had a LPN. Table 1 highlights clinical and demographic characteristics of this surgical cohort stratified by surgical approach. A total of 140 men and 89 women with a mean age of 57 years and BMI of 31 were included in this study. 15 patients (7%) had a prior history of contralateral RCC therapy, and approximately 25% of this patient cohort had at least one prior abdominal operation. Mean preoperative estimated GFR for this group was 81.6 mL/min/1.73 m^2 with chronic kidney disease (CKD) stage distribution being CKD I (eGFR > 90) 38%, CKD II (eGFR 60-89) 45%, CKD III (eGFR 30-59) 16%, and CKD IV (eGFR 15-29) 1%. When stratified by year of surgery, the percentage of laparoscopically managed renal tumors increased from 23% (2003 and 2005) to 52% (2006 to 2009). On univariate analysis of preoperative clinical variables, a history of contralateral RCC surgery (p = 0.02) and baseline eGFR (p = 0.05) was associated with an open (versus laparoscopic) partial nephrectomy. Conversely, patient age, gender, race, BMI, comorbid conditions, prior abdominal surgery, year of surgery, and individual CKD stages (p = 0.13) all were not associated with a particular surgical approach.

Radiographic variables

Table 2 demonstrates imaging and pathologic characteristics of renal tumors managed by partial nephrectomy. The mean tumor size was 3.4 cm (range, 0.7 to 11) with a relatively equal distribution across the upper, middle, and lower poles of the kidney. Thirty-four patients (15%) had multifocal renal tumors, and 60% of tumors were located on the anterior surface of the kidney. Overall, 23% of tumors were endophytic, 38% involved the renal sinus/collecting system, and 29% were classified as renal hilar lesions. On univariate analysis of radiographic variables, tumor size (p = 0.04), multifocality (p = 0.004), renal sinus/collecting system involvement (p = 0.001), and renal hilar location (p = 0.001) were all associated with an open approach for partial nephrectomy. Tumor depth (p = 0.08), polar location (p = 0.15), and anterior (versus posterior) distribution (p = 0.53) however, were not associated with a particular surgical approach.

Surgeon variables

Amongst our four urologists managing kidney cancer, two had a cumulative laparoscopic case volume of at least 25 cases. One of these two urologists also had formal fellowship training in laparoscopy and endourology. The mean annual case volume for all four surgeons ranged between 680 and 870 cases, while the specific number of renal surgery cases ranged between 15 and 45 cases annually. On univariate analysis, lack of fellowship training in laparoscopy (p = 0.02) and cumulative laparoscopic case volume < 25 cases (p = 0.03) were associated with OPN, while annual case volume (p = 0.44), annual number of renal surgery cases (p = 0.19), and number of years in practice (p = 0.73) were not associated with specific approach.

Pathology

Over 80% of renal tumors were histologically confirmed RCC with a similar distribution between open and laparoscopic cases. Of the RCC lesions, over 75% were pT1a tumors, 15% were pT1b tumors, and 10% were staged ≥ pT2. An open surgical approach was associated with more advanced pathology (p = 0.03). Positive surgical margins occurred in six cases (2.6%) with no difference between surgical approach (2.3% open versus 3.0% laparoscopic, p = 0.73).

Predictors for method of partial nephrectomy

Logistic regression methodology was used to create a model based upon the preoperative clinical, surgeon-related, and radiographic variables that were found to be significantly associated with the type of partial nephrectomy on univariate analysis. The variables

TABLE 1. **Clinical and demographic characteristics of this surgical cohort stratified by surgical approach**

Variable	All patients (n = 229)	Open (n = 130)	Laparoscopic (n = 99)	p value
Age (mean)	57.1	57.4	56.8	0.78
[median; range]	(59); 21-93	(59); 21-93	(58) 21-82	
Gender (no., %)				
Male	140 (61.1%)	81 (62.3%)	59 (59.6%)	0.68
Female	89 (38.9%)	49 (37.7%)	40 (40.4%)	
Race (no., %)				
Caucasian	213 (93)	122 (94)	91 (92)	0.54
African American	6 (3)	3 (2)	3 (3)	
Hispanic	7 (3)	4 (3)	3 (3)	
Asian	1 (1)	1 (1)	0 (0)	
Other	2 (1)	0 (0)	2 (2)	
BMI (mean)	30.5	30.3	30.8	0.56
[median; range]	(30); 21-50	(30); 21-50	(30); 22-45	
CR index (mean)	2.5	2.6	2.3	0.17
[median); range]	(2); 0-10	(2); 0-8	(2); 0-10	
HTN (no., %)				
No	90 (39)	47 (36)	43 (43)	0.26
Yes	139 (61)	83 (64)	56 (57)	
Diabetes (no., %)				
No	184 (80)	101 (78)	83 (84)	0.25
Yes	45 (20)	29 (22)	16 (16)	
Hx contralateral RCC surgery (no., %)				
No	214 (93)	116 (90)	98 (99)	0.02
Yes	15 (7)	14 (10)	1 (1)	
Prior abdominal surgery (no., %)				
No	175 (77)	96 (74)	79 (79)	0.34
Yes	54 (23)	34 (26)	20 (21)	
Preop Cr (mean)	1.05	1.12	0.97	0.02
[median; range]	(0.9); 0.4-9.9	(0.98); 0.4-9.9	(0.9); 0.5-3.44	
Preop GFR (mean)	81.6	78.4	85.7	0.05
[(median); range]	(81.0); 20-171	(79); 30-170	(85.5); 20-171	
Year of surgery				
2003-2005	70	54	16	
2006-2009	159	76	83	0.08

incorporate into the model included: preoperative GFR, prior contralateral RCC therapy, tumor size, tumor focality, renal sinus/collecting system involvement, abutment of the renal hilar vasculature, fellowship training in laparoscopy, and cumulative laparoscopic case volume.

In the regression model incorporating these eight variables, only renal hilar location (odds ratio [OR] 2.63, 95% CI 1.17-5.88, p = 0.02) remained significantly associated with open nephron sparing surgery.

Discussion

The concept of renal preservation has increasingly emerged as a central tenet in the management of renal cortical neoplasms.[15] Contemporary data has implicated a link between CKD and cardiovascular events, risk of hospitalization, and all cause mortality.[16] These associations coupled with evidence that patients undergoing radical nephrectomy are more likely develop CKD emphasizes that nephron sparing

TABLE 2. **Imaging and pathology data for renal tumors managed by partial nephrectomy**

Variable	All patients (n = 229)	Open (n = 130)	Laparoscopic (n = 99)	p value
Imaging data				
Size cm (mean)	3.4	3.6	3.0	0.04
[median; range]	(3.0); 0.7-11	(3.1); 1.2-11	(2.7) 0.7-10.1	
Location (no., %)				
Upper	71 (31)	48 (37)	25 (25)	0.15
Middle	67 (30)	38 (30)	29 (29)	
Lower	89 (39)	44 (34)	45 (45)	
Multifocal (no., %)				
No	195 (85)	103 (79)	92 (93)	0.004
Yes	34 (15)	27 (21)	7 (7)	
Anterior (no., %)				
No	92 (40)	55 (42)	37 (37)	0.53
Yes	137 (60)	75 (58)	62 (63)	
Tumor depth (no., %)				
Endophytic	53 (23)	38 (29)	17 (17)	0.08
Mesophytic	88 (38)	53 (41)	36 (36)	
Exophytic	88 (38)	39 (30)	46 (46)	
Renal sinus/collecting system (no., %)				
No	142 (62)	68 (52)	74 (75)	0.001
Yes	87 (38)	62 (48)	25 (25)	
Hilar (no., %)				
No	163 (71)	79 (61)	84 (85)	0.001
Yes	66 (29)	51 (39)	15 (15)	
Final pathologic data				
Histology (no., %)				
RCC	191 (83)	109 (84)	82 (83)	0.88
Clear cell	141 (62)	80 (62)	61 (62)	
Papillary	41 (18)	25 (19)	16 (16)	
Chromophobe	9 (4)	4 (3)	5 (5)	
Benign	38 (17)	21 (16)	17 (17)	
Stage (no., %)*				
pT1a	148 (77)	80 (73)	68 (83)	0.03
pT1b	26 (14)	16 (15)	10 (12)	
pT2	7 (4)	6 (6)	1 (1)	
pT3a	9 (5)	6 (6)	3 (4)	
pT3b	1 (1)	1 (1)	0 (0)	
Fuhrman grade (mean)	1.9	1.9	1.8	0.45
[median; range]	(2.0); 1-4	(2.0); 1-4	(2.0); 1-4	

*distribution for 191 patients with pathologically confirmed RCC

surgery should be considered in the management of RCC, specifically as it relates to small renal masses.[6,17,18] While urologists increasingly are embracing the principle of kidney sparing surgery for SRMs, the surgical approach and means to achieve this goal remains a debate. In particular, an impetus in the surgical community is incorporation of minimally invasive techniques to manage diseases. With respect to nephron sparing surgery, several retrospective studies have implicated lower narcotic requirements, improved cosmesis, earlier resumption of diet, and shorter hospital duration for patients managed by LPN

compared to OPN.[9,19] Such benefits, however, often need to be balanced against a higher complication profile for LPN even in the hands of expert minimally invasive surgeons.[11]

A concern amongst many "open" and "minimally invasive" surgeons is that each group is married to a particular approach without adapting operative strategy to patient and lesion characteristics. This dichotomy between surgical disciplines, however, is increasingly blurred for urologists completing contemporary urologic residency and fellowship training.[12] Such trainees are amply versed in partial nephrectomy techniques with the growth of laparoscopy and robotics facilitating an increased utilization of such modalities to manage more complex renal masses.[11,20,21] With such a surgical armamentarium, an important consideration is appropriate selection of operative approach for nephron sparing surgery that maintains oncologic outcomes while minimizing surgical morbidity.

In this study of 229 renal lesions managed by partial nephrectomy, we sought to identify preoperative clinical, surgeon-related, and imaging characteristics that contributed to management by either an open or laparoscopic approach. With respect to clinical variables, we observed that prior contralateral RCC surgery ($p = 0.02$) and preoperative estimated GFR ($p = 0.05$) were more likely to be associated with an open surgical approach. Interestingly, several other variables that historically would have been indications for OPN (i.e. higher BMI and prior abdominal surgery) were not associated with a particular treatment modality. Reviewing associated radiographic imaging highlighted that tumor size ($p = 0.04$), multifocality ($p = 0.004$), renal sinus/collecting system involvement ($p = 0.001$), and abutment to the renal hilar vasculature ($p = 0.001$) all were associated with OPN. When considering surgeon-specific variables, we observed that a fewer cumulative laparoscopic cases ($p = 0.03$) and lack of fellowship training in laparoscopy ($p = 0.02$) were associated with an open approach. When incorporating these variables in a logistic regression model, however, only renal hilar location independently was associated with OPN with a 2.6 fold greater likelihood of being managed by an open versus laparoscopic approach. Furthermore, review of the overall positive margin rate of 2.6% with similar outcomes for OPN and LPN underscores that the quality of the operation was not compromised when selecting treatment approach.

Accepting that nephron sparing surgery should be considered for all SRMs, we believe that our findings provide urologists managing renal tumors a means to objectify the decision making process for partial nephrectomy approach. In our experience, preoperative clinical variables contributed minimally to surgical technique, while radiographic data had significant bearing on operative approach. Other groups have recently made similar observations. In 2009, Kutikov and Uzzo introduced the concept of the R.E.N.A.L nephrometry score as a means to more accurately characterize salient radiographic anatomy of renal masses.[22] This same group subsequently evaluated patterns of surgical treatment for renal masses as a function of the tumor's Nephrometry score.[23] Here, they observed that a large tumor size predicted OPN versus minimally invasive surgery (MIS)-PN, while a difficult location (as defined by polar lines) demonstrated the smallest predictive ability. Additionally, a lower "N" score (nearness to sinus/urothelium) was most predictive of MIS-PN versus OPN. Hayn and colleagues further applied the R.E.N.A.L. nephrometry score retrospectively to patients with renal tumors managed by LPN and observed that a higher score was associated with an increased estimated blood loss, warm ischemia time, and length hospital stay.[24] They, therefore, concluded that such considerations may be helpful in counseling patients and may stratify tumors based on the technical difficulty of performing LPN. While our study does not utilize a scoring system, the observations are similar and further underscores that certain tumor characteristics may encourage use of an open versus minimally invasive approach for partial nephrectomy.

We feel that the approach to a renal mass should start with consideration of whether the lesion can be managed by nephron sparing surgery. Thereafter, the urologist should examine whether nephron sparing surgery can be accomplished safely by minimally invasive techniques. Using variables that we have defined in this study or in the context of a nephrometry score would aid in objectifying the decision for surgical approach for partial nephrectomy. Such an approach allows optimum sparing of the renal unit while tailoring therapy to minimize surgical morbidity. We acknowledge several limitations. Firstly, the retrospective nature of the study fails to account for patient specific variables that may have contributed to treatment choice beyond what we measured. Secondly, our study does not calculate nephrometry scores, which may better objectively quantify the complexity of a renal lesion. However, in that system, different lesions may be classified similarly due to the aggregate nature of the scoring system. Additionally, hilar location (which was highly predictive for OPN in our

study) lacks a true score in the described R.E.N.A.L. model. Thirdly, the collaborative approach of our group to review films to determine optimal treatment approach (open versus laparoscopic) may not be generally applicable. Indeed, in our study, surgeon-specific factors were not associated with treatment approach on multivariate analysis potentially due to this internal referral system. Finally, our analysis included cases prior to the introduction of robotic assisted partial nephrectomy. Indeed, such technology has been increasingly incorporated for SRMs and may likely increase the complexity of lesions that can be approached via minimally invasive surgery.

Conclusions

An increasing volume of renal lesions can be managed by nephron sparing surgery. Many parameters including increasing BMI, preoperative GFR, prior abdominal surgery, endophytic tumor location, and renal sinus/collecting system involvement do not necessarily preclude a minimally invasive partial nephrectomy. In our experience, renal hilar tumors were over 2.5 fold more likely to be managed by open partial nephrectomy likely owing to the complexity of resection. □

References

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *Ca Cancer J Clin* 2011;61(4):212-236.
2. Chow WH, Devesa SS, Warren JL, Fraumeni JF. Rising incidence of renal cell cancer in the United States. *JAMA* 1999;281(17): 1628-1631.
3. Hock LM, Lynch J, Balaji KC. Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data. *J Urol* 2002;167(1):57-60.
4. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. *J Natl Cancer Inst* 2006;98(18):1331-1334.
5. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. *J Urol* 2000;163(2):442-445.
6. Huang WC, Levey AS, Serio AM et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol* 2006;7(9):735-740.
7. Thompson RH, Siddiqui S, Lohse CM, Leibovich BC, Russo P, Blute ML. Partial versus radical nephrectomy for 4 to 7 cm renal cortical tumors. *J Urol* 2009;182(6):2601-2606.
8. Marszalek M, Meixl H, Polajnar M, Rauchenwald M, Jeschke K, Madersbacher S. Laparoscopic and open partial nephrectomy: a matched-pair comparison of 200 patients. *Eur Urol* 2009; 55(5):1171-1178.
9. Schiff JD, Palese M, Vaughan ED Jr, Sosa RE, Coll D, Del Pizzo JJ. Laparoscopic vs open partial nephrectomy in consecutive patients: the Cornell experience. *BJU Int* 2005;96(6):811-814.
10. Porpiglia F, Volpe A, Billia M, Scarpa RM. Laparoscopic versus open partial nephrectomy: analysis of the current literature. *Eur Urol* 2008;53(4):732-742;discussion 742-743.
11. Gill IS, Kavoussi LR, Lane BR et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. *J Urol* 2007;178(1):41-46.
12. Duchene DA, Moinzadeh A, Gill IS, Clayman RV, Winfield HN. Survey of residency training in laparoscopic and robotic surgery. *J Urol* 2006;176(5):2158-2166;discussion 2167.
13. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;130(6):461-470.
14. Kidney. In 6th Edition of the AJCC cancer staging manual. New York: Springer Press; 323-329.
15. Boorjian SA, Uzzo RG. The evolving management of small renal masses. *Curr Oncol Rep* 2009;11(3):211-217.
16. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351(13):1296-1305.
17. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clin Proc* 2000;75(12):1236-1242.
18. Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial nephrectomy versus radical nephrectomy in patients with small renal tumors--is there a difference in mortality and cardiovascular outcomes? *J Urol* 2009;181(1):55-61;discussion 61-62.
19. Beasley KA, Al Omar M, Shaikh A et al. Laparoscopic versus open partial nephrectomy. *Urology* 2004;64(3):458-461.
20. Benway BM, Bhayani SB, Rogers CG et al. Robot-assisted partial nephrectomy: an international experience. *Eur Urol* 2010; 57(5):815-820.
21. Scoll BJ, Uzzo RG, Chen DY et al. Robot-assisted partial nephrectomy: a large single-institutional experience. *Urology* 2010;75(6):1328-1334.
22. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol* 2009;182(3):844-853.
23. Canter, D. Kutikov A, Manley B et al. Objectifying surgical decision-making for the enhancing renal mass. *J Urol* 2010;183(4, supplement):e203.
24. Hayn M, Schwaab T, Underwood W, Kim H. Application of R.E.N.A.L. nephrometry score to laparoscopic partial nephrectomy. *J Urol* 2010;183(4, supplement):e245.

Thermal ablation of small renal masses: intermediate outcomes from a Canadian center

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Introduction: *Cryoablation (CA) and radio frequency ablation (RFA) are nephron sparing procedures that destroy renal tissue in situ rather than by surgical removal. Both thermal ablative techniques are advocated in select patient population with a small renal mass and multiple comorbidities which may preclude major surgery. Unfortunately long term oncologic outcomes of these procedures are unknown.*

Materials and methods: *We report oncologic outcomes following CA and RFA in patients with small renal masses, from a single center, during a 48 month follow up period. Thirty patients underwent thermal ablation of a small renal mass, 7 with RFA and 23 with CA.*

Results: *Median tumor size on preoperative CT was 2.6 cm ± 0.87 cm. Four patients experienced a loco-regional treatment failure and underwent subsequent radical nephrectomy. Two patients were diagnosed with metastatic renal cell cancer in the follow up period. Six patients died during the follow up period, five from unrelated cause and one from metastatic RCC (overall survival 80%, RCC-specific survival 96%).*

Conclusions: *This study demonstrates low RCC recurrence rates and in combination with previously published reports supports the effectiveness of thermal ablation therapy as primary therapeutic option in a very specific patient population.*

Key Words: nephron sparing procedures, renal cell cancer, cryoablation, radiofrequency ablation

Introduction

Small renal mass can be defined as a contrast enhancing mass equal to or less than 4 cm in the greatest dimension, on abdominal imaging.[1] Small renal masses constitute 48%-68% of all renal tumors and approximately 38% of all surgically removed renal tumors.[2,3] Up to 80% of small renal masses are found to be malignant and 20% benign.[4]

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Cryoablation (CA) and radio frequency ablation (RFA) are nephron sparing procedures that destroy renal tissue in situ rather than by surgical removal. Both techniques are advocated in select patient population with a small renal mass and multiple comorbidities which may preclude major surgery.

Both techniques offer decreased morbidity, shorter period of hospitalization, convalescence and renal function preservation.[5] In contrast to laparoscopic or open partial nephrectomy, neither of the techniques requires clamping of the renal vessels nor advanced laparoscopic skills required for suturing and renal reconstruction.[6] Both techniques are associated with low morbidity. This is an additional advantage when considering the treatment of patients with small renal mass who are older, and may have coexisting medical morbidities.

Unfortunately long term oncologic outcomes for these procedures are unknown. We report oncologic outcomes following cryoablation and radiofrequency ablation in patients with small renal masses, from a single center, during a 4 year follow up period.

Materials and methods

We performed a retrospective chart review of patients who had CA and RFA at our institution, during the 2003-2009 year period. Institutional ethics approval was obtained (UWO HSREB 1150E). The indication for CA or RFA was a stage T1 renal cancer less or equal to 4 cm in the greatest diameter that enhanced on preoperative abdominal CT scan. Biopsy was performed prior to ablation in all cases except for patients who were on anticoagulant medications, in which case the biopsy was performed immediately pre-treatment, when the anticoagulation was reversed.

Twenty-three renal masses were found to be posterior on the renal surface and accessible with percutaneous approach. Of the 23 masses all were smaller than 4 cm. Fourteen masses were found to be ≥ 50% exophytic, 6 masses ≤ 50% exophytic and 3 masses were found to be completely endophytic. Of the 23 masses 16 were found to be ≥ 7 mm away from the renal hilum/sinus, 7 were found to be within 4 mm-7 mm from the renal hilum/sinus. Of the 23 masses, eight were found to be located completely within upper or lower pole of the kidney, in relation to the polar line. Eleven tumors were found to cross the polar line and four were found to be ≥ 50% across the polar line or to cross the axillary line of the kidney.

Laparoscopic CA was performed in seven patients by a single surgeon, as previously described in the literature (Galil Medical, 4.8 mm cryoprobe).[7] All seven patients had anterior tumors, judged to be inaccessible by percutaneous approach. All other CA and RFA cases were performed percutaneously, by a single interventional radiologist, with the urologist's input. Two freeze-thaw cycles were performed in each CA case, with 3-5 probes. The RFA was performed with two heating cycles using the RITA250 generator (RITA Medical Systems, Inc., Mountain View, CA), with final RFA ablation of the needle tract.

Patients records were reviewed for patient age, existing comorbidities, type of thermoablative therapy used, pre and operative hemoglobin, pre and postoperative serum creatinine. All patients had a negative metastatic work up. Tumor specific information was obtained including tumor size on the initial CT scan, initial tumor enhancement, results of pre CT-guided tumor biopsy, tumor size, enhancement on the follow up CT scans and results of post treatment renal mass biopsy. At our institution the patient follow up was CT contrast study of the abdomen and pelvis at 3, 6, 12, 24, 36 and 48 months post treatment. All patients received renal function adjusted contrast and had renal function protective measures implemented, such as adequate hydration. Post treatment renal biopsy was performed at 6 months following the treatment, in all patients available for follow up. Treatment outcome was recorded as no recurrence if there was no mass enhancement on post treatment imaging or if the mass involuted or disappeared and a negative post treatment biopsy. Recurrence post treatment was defined as contrast enhancement of the mass, increase in size or a positive post treatment biopsy.

Data was analyzed using GraphPad Prism 4 software (GraphPad, San Diego, CA, USA). Data were analyzed using Analysis of Variance (ANOVA) with Dunnett's Multiple Comparison post test (> 2 groups). Significance was assessed at $p < 0.05$.

TABLE 1. **Patient characteristics**

Patient age (range, mean)	49-82 (67.6 ± 11.8)
ECOG status	
0	4
1	8
2	9
3	8
4	1
Mean tumor size (largest diameter)	2.71 ± 0.9
Mean preoperative creatinine (μmol/L)	115.6 ± 49.4 (75-315)
Mean postoperative creatinine (μmol/L)	114.9 ± 49.9 (67-301)
Mean preoperative Hb (mmol/L)	138.3 ± 21.4 (81-182)
Mean postoperative Hb (mmol/L)	127.1 ± 20.2 (80-173)
Treatment modality	
RFA	7
Cryoablation	
Laparoscopic	7
Percutaneous	23
Number of cryotherapy probes used	
1	7
2	8
3	9
4	5
6	1

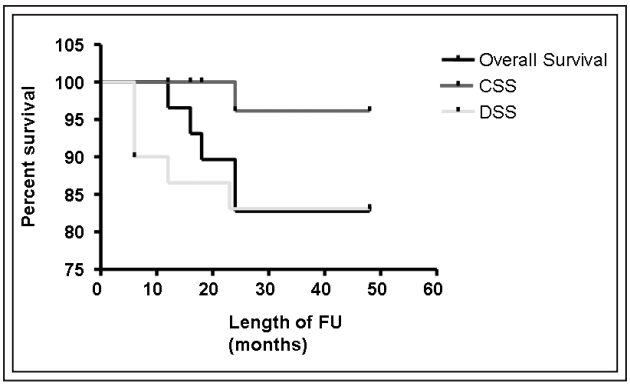

Figure 1. Kaplan-Meier survival curves after thermal ablation of small renal mass in 30 patients.

Results

Thirty patients underwent thermal ablation of the small renal mass, Figure 1. Choice of treatment modality (RFA versus CA) was non-randomized and based on availability of resources at our center. We performed 7 RFAs and 23 CA in the specified time period. The patient age range was 49-84 years. Median ECOG score was 2. Mean tumor size on preoperative CT was 2.6 cm ± 0.87 cm. The average length of follow up was 48 months. Patient's demographic information and tumor characteristics on imaging are in Table1.

Seven patients were treated laparoscopically, as the tumors were found to be on the anterior renal surface and inaccessible percutaneously. Four had a nephrometry score of 4a (1+1+1+a+1) and three had a score of 5a (1+2+1+a+1).

Twenty-four out of 30 patients had a pretreatment biopsy diagnosed as RCC. Results of image guided renal mass biopsies can be seen in Table 2.

Twenty patients were available for postoperative renal mass biopsy. Two patients were diagnosed with post treatment persistent malignancy on post treatment renal mass biopsy, four had a final pathology report as "suspicious for malignacy". Post treatment renal mass biopsy results are presented in Table 3.

Four patients experienced a loco-regional treatment failure and underwent subsequent radical nephrectomy. Three patients had clear cell RCC on final surgical pathology, one papillary RCC. The RCC recurrence occurred 6-23 months post thermal ablative therapy. Two patients were diagnosed with metastatic renal cell cancer in the follow up period. One patient developed metastatic disease to the brain and had undergone radiation therapy. This patient is alive with the disease. Overall outcomes of CA and RFA are represented in Table 4.

We examined the pre-treatment imaging of the four patients who recurred to further describe their lesion using the nephrometric system. The first patient had a nephrometry score of 7p (1+2+2+p+2) and was found to have a persistent tumor enhancement at 6 months post CA. He had a negative post cryoablation biopsy, final post nephrectomy pathology report demonstrating pT3aN0Mo clear cell RCC. The second patient had a nephrometry score of 7p (2+1+1+p+3) and was diagnosed with a recurrence at 6 months post RFA. He recurred along the RFA tract in addition to kidney. His final post nephrectomy pathology report demonstrated pT4NxM1 clear cell RCC, with brain and lung metastases. The third patient had a score of 7p (1+2+1+p+3) and was found to recur at 6

TABLE 2. **Pretreatment renal mass biopsy results**

Non diagnostic	4
Neoplasia, not specified	6
Clear cell RCC	7
Papillary RCC	5
Chromophobe RCC	7
Angiomyolipoma	1
Oncocytoma	1
Not performed	4

TABLE 3. **Post treatment renal mass biopsy results**

Negative for malignancy	12
Non-diagnostic	10
Suspicious for malignancy	4
RCC	2

TABLE 4. **Outcomes of renal mass ablation treatment**

	Biopsy + RCC/ neoplasia
Number of patients	20
Number of recurrences (%)	6 (20%)
Loco-regional	4 (13%)
Metastatic	2 (6.7%)
Number of cancer deaths (%)	1 (3.3%)
% 5 year survival	
Overall	24/30 (80%)
Disease specific	24/25 (96%)
Disease free	20/25 (80%)

months post CA. His post nephrectomy pathology report demonstrated pT3b clear cell RCC. The fourth patient had a nephrometry score of 5p (1+2+1+p+1) and experienced a recurrence at 23 months post CA. His post nephrectomy pathology report demonstrated pT1aN0M0 papillary RCC.

Six patients died during our follow up, five from unrelated cause and one from metastatic RCC (overall survival 80%, RCC specific survival 96%). In the non-RCC group causes of mortality were: cardiac arrest in the recovery room immediately following the CA (one); complications following aortic valve replacement surgery (one); non-metastatic hip fracture and death from acute pneumonia while recovering following the orthopedic surgery (one); de novo pancreatic cancer (one); de novo squamous cell lung cancer (one).

Discussion

Thermal ablative therapy is currently considered as a legitimate treatment option for a patient with a small renal mass and medical comorbidities. Indications for use of thermal ablation are a renal tumor ≤ 4 cm occurring in the elderly patient, patient who is considered high risk for surgery due to medical comorbidities, patient with severe renal dysfunction, surgically scarred abdomen, a small renal mass in a post partial nephrectomy remnant or the request of an informed younger patient.[5] Thermal ablative therapy relies on insertion of needle applicators within the renal mass and subsequent generation of temperatures which are cytocidal.[8] The initial needle insertion can be performed either laparoscopically or percutaneously, with percutaneous approach associated with decreased morbidity.

Twenty patients in this series (67%) underwent postoperative needle biopsy at 6 months post treatment, four patients refused or were unable to undergo it. RCC was found in two patients and four had a final pathology report as "suspicious for malignancy". Two patients with a positive biopsy also had a persistent contrast enhancement on postoperative CT scan. Of the four patients who underwent a post thermal ablation nephrectomy, only two had a positive biopsy. The remaining two patients with suspicious biopsy had a complete involution of the renal mass and remain disease free at present. The indication for nephrectomy in the first patient was an enlarging renal mass. In the second patient the indication for surgery an enhancing mass along percutaneous tract. In 10 cases, the post thermal ablation biopsy was not diagnostic. Taken together, these data confirm that needle biopsy of the ablated tumor is not a fail-safe diagnostic modality and cannot be used for follow up alone. Furthermore, it underscores the necessity of regimented and dedicated long term radiologic monitoring. A recent study[7] argued that biopsy of the lesion must be performed and we have used this strategy in the cases discussed.

In this series, abdominal contrast-enhanced CT was used for follow up in all cases. In 20 patients, CT scan demonstrated an absence of contrast enhancement and gradual decrease in the renal mass. In four patients, persistent enhancement was demonstrated and subsequent nephrectomy performed. Two patients were followed with MRI or renal US due to pre-existing poor renal function.

In this series, we experienced a single peri-operative mortality (3%). This occurred in a 79-year-old female with a history of coronary artery disease and a previous 5 vessel coronary artery bypass. The indication for CA was a biopsy proven RCC that was initially observed but continued to enlarge radiographically. This patient underwent a successful CA and developed massive myocardial infarction in the recovery room. Additionally, we experienced one case of limited retroperitoneal bleed following RFA (3%). These results are similar to previously published reports, which demonstrated 1% cardiac complication rate, 1%-5% hemorrhage rate and 10% overall complication rate.[7] We did not experience any ureteral injuries or strictures in this series.

Early comparisons of the two thermal modalities were in favor of CA.[9,10] However, more contemporary series[11-15] suggest improved outcomes with RFA. In our series, we had four tumor recurrences, one of whom occurred in a patient treated with RFA, three in patients treated with CA. These results do not suggest a difference in recurrence between the two modalities and we cannot make definitive conclusions from this series due to the non-randomized nature of the study.

At present, there is a relative paucity of data on long term effectiveness of thermal ablation therapy. Reflecting this fact, our patient population was highly selected to include older patients with coexisting morbidities, who were found to be poor surgical candidates. We report 80% overall survival in our patient group and 96% disease specific survival during our follow up. These data are similar to recently published outcomes, demonstrating 84% overall and 92% disease specific 5 year survival.[7,13,15] These data are inferior in comparison to contemporary series describing surgical management of T1 RCC, but still demonstrated low RCC recurrence rates. In combination with previously published reports, this report supports the effectiveness of thermal ablation therapy as primary therapeutic option in a very specific patient population. □

References

1. Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. *Cancer* 2004;100(4):738-745.
2. Nguyen MM, Gill IS, Ellison LM. The evolving presentation of renal carcinoma in the United States: trends from the Surveillance, Epidemiology, and End Results Program. *J Urol* 2006;176(6 Pt 1): 2397-2400.
3. Lee CT, Katz J, Shi W, Thaler HT, Reuter VE, Russo P. Surgical management of renal tumors 4 cm or less in a contemporary cohort. *J Urol* 2000;163(3):730-736.
4. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol* 2003;170(6 Pt 1):2217-2220.
5. Gill IS Aron M, Gervais DA, Jewett MA. Clinical practice. Small Renal Mass. *N Engl J Med* 2010;362(7):624-634.
6. Gill IS, Desai MM, Kaouk JH et al. Laparoscopic partial nephrectomy for renal tumor: duplicating open surgical techniques. *J Urol* 2002;167(2 Pt 1):469-477.
7. Aron M, Kamoi K, Remer E, Berger A, Desai, Gill I. Laparoscopic renal cryoablation: 8-year, single surgeon outcomes. *J Urol* 2010; 183(3):889-895.
8. Silverman SG, Israel GM, Herts BR, Richie JP. Management of the incidental renal mass. *Radiology* 2008;249(1):16-31.
9. Matlaga BR, Zagoria RJ, Woodruff RD, Torti FM, Hall MC. Phase II trial of radiofrequency ablation of renal cancer: evaluation of the kill zone. *J Urol* 2002;168(6):2401-2405.
10. Rendon RA, Kachura JR, Sweet JM, et al. The uncertainty of radiofrequency treatment of renal cell carcinoma: Findings at immediate and delayed nephrectomy. *J Urol* 2002;167(4): 1587-1592.
11. Hwang JJ, Walther MM, Pautler SE et al. Radio frequency ablation of small renal tumors: intermediate results. *J Urol* 2004; 171(5):1814-1818.
12. Zagoria RJ, Hawkins AD, Clark PE et al. Percutaneous CT-guided radiofrequency ablation of renal neoplasms: Factors influencing success. *AJR Am J Roentgenol* 2004;183(1):201-207.
13. Tracy CR, Raman JD, Donnally C, Trimmer CK et al. Durable oncologic outcomes after radiofrequency ablation: experience from treating 243 small renal masses over 7.5 years. *Cancer* 2010; 116(13):3135-3142.
14. Pirasteh A, Snyder L, Boncher N et al. Cryoablation vs. Radiofrequency ablation for small renal masses. *Acad Radiol* 2011;18(1):97-100.
15. Remzi M, Javadli E, Ozsoy M. Management of small renal masses: a review. *World J Urol* 2010;28(3):275-281.

Aggressive angiomyxoma presenting as urinary retention in a male: a case report and literature review

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KORRECT GS, KESLER MV, STRUP SE. Aggressive angiomyxoma presenting as urinary retention in a male: a case report and literature review. The Canadian Journal of Urology. 2011;18(5):5908-5910.

We present a case of pelvic aggressive angiomyxoma presenting as urinary retention in a male. A 46-year-old male presented with urinary retention and was found on computed tomography (CT) scan of the pelvis to have a large pelvic tumor. A transrectal ultrasound guided needle biopsy of the tumor and prostate revealed a myxoid tumor; low volume, low grade prostate cancer was also detected. The patient underwent radical prostatectomy and excision of the pelvic tumor which was diagnosed as aggressive angiomyxoma (AAM). The patient was free of recurrence after 1 year of follow up.

AAM is a benign myxoid tumor seen very rarely in males. Treatment consists of surgical excision with negative margins. Tumors variably express estrogen and progesterone receptors. Immunohistochemistry should be used to exclude other benign and malignant tumors. Patients should be followed with axial imaging as recurrence is common.

Key Words: aggressive angiomyxoma, male, myxoid tumor, mesenchymal tumor

Introduction

Aggressive angiomyxoma (AAM) is a rare, benign, locally infiltrative myxoid tumor most commonly arising in the pelvic and genital soft tissues of adult females.[1] It has a 6-fold higher incidence in females, and has a high rate of recurrence, even after complete extirpation.[2] There have been fewer than 50 cases of AAM reported in males, usually presenting as scrotal masses or mimicking groin hernias. This tumor rarely metastasizes and often expresses hormone receptors.[3]

Case report

We report the case of an otherwise healthy 46-year-old Caucasian male who initially presented to an area emergency department in acute urinary retention. A computed tomography (CT) scan of the abdomen and pelvis without contrast revealed a distended urinary bladder and an 11 cm well demarcated soft tissue structure posterior to, and anteriorly displacing the urinary bladder, Figure 1. A Foley catheter was placed, and a urologic referral was made.

The patient reported sporadic, brief episodes of slowing of stream over the past year. Digital rectal examination (DRE) of the left lobe of the prostate was partially obscured by a soft structure. Cystoscopy was unremarkable, and a transrectal ultrasound (TRUS) revealed what appeared to be a cystic structure arising from the left seminal vesicle. This structure was evaluated and biopsied using TRUS; a sextant biopsy of the prostate was also performed secondary to abnormal DRE.

The biopsy of the pelvic mass was interpreted as fibromuscular soft tissue with myxoid change. The patient was also found to have a small volume Gleason 6 (3 + 3) adenocarcinoma of the prostate on the right. The patient underwent excision of the pelvic mass and radical prostatectomy. The lesion was firm in nature and appeared to arise deep within the pelvis,

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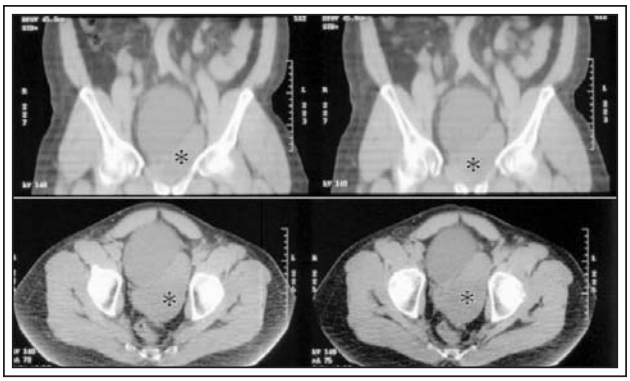

Figure 1. CT scan showing mass posterior and lateral to urinary bladder (asterisks).

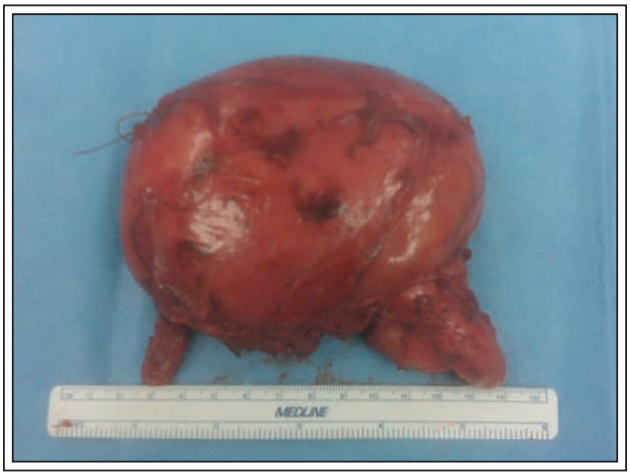

Figure 2. Gross specimen measuring 11 cm in greatest dimension.

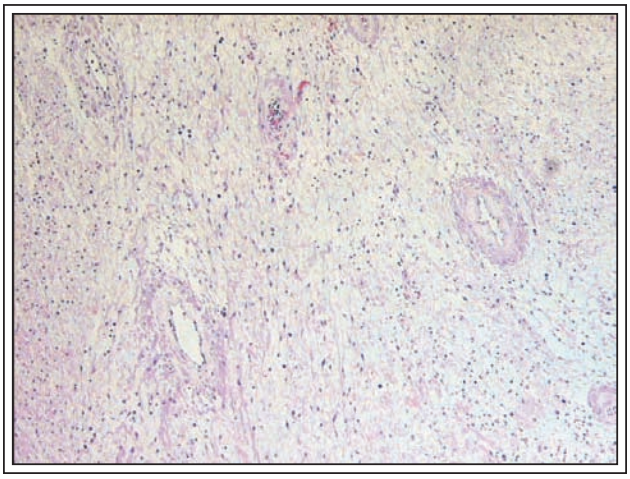

Figure 3. Photomicrograph of aggressive angiomyxoma showing myxoid stroma and numerous thick-walled vessels. (200x, H&E)

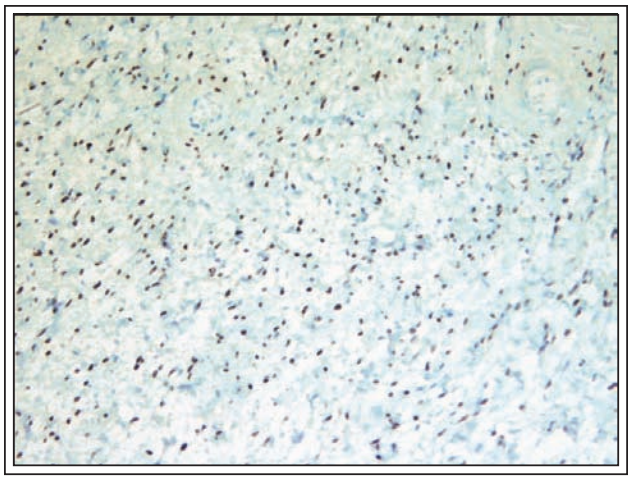

Figure 4. Photomicrograph of aggressive angiomyxoma with immunohistochemical stain showing estrogen receptor positivity (blue). (400x)

lateral to the prostate and the dorsal venous complex. The specimen measured 11 cm x 9.5 cm x 3.6 cm and weighed 300 grams, Figure 2.

The pelvic mass, diagnosed as aggressive angiomyxoma, was described by the reviewing pathologist as a low grade mesynchymal tumor with numerous mast cells, a myxoid stroma and abundant blood vessels, Figure 3. On immunohistochemical analysis, the tissue was found to stain positive for smooth muscle actin (SMA), estrogen receptors (ER), and progesterone receptors (PR), Figures 4 and 5. It stained negative for desmin and S-100 protein. The final prostate specimen revealed T2cNxMx Gleason 6 (3 + 3) adenocarcinoma.

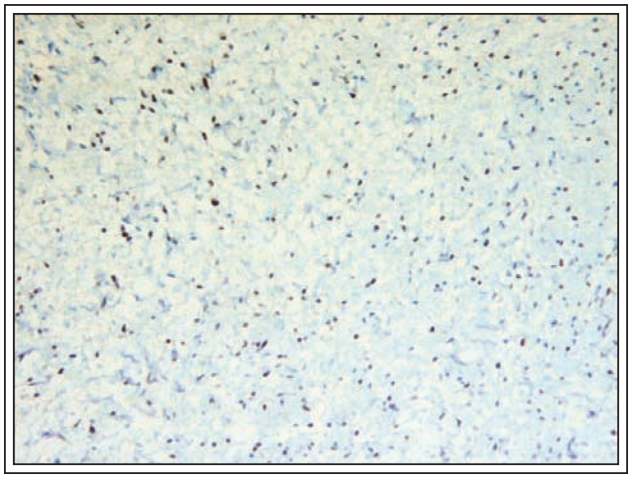

Figure 5. Photomicrograph of aggressive angiomyxoma with immunohistochemical stain showing progesterone receptor positivity (light blue). (400x)

Discussion

Since first being described in 1983 by Steeper and Rosai there have been approximately 250 published cases of AAM, the majority of patients being adult females.[4,5] Fewer than 50 cases have been reported in males, usually arising in the scrotum, pelvic wall, spermatic cord, perineal region, and intrapelvic organs.[1,2] The mean age of presentation in men is 46 years, with a range of 1 to 82 years.[6] CT scan shows a clearly delineated mass with moderate enhancement, and magnetic resonance imaging (MRI) reveals a characteristic swirling pattern in approximately 83% of cases.[7]

AAMs are typically large, most are between 2 cm and 17 cm in greatest dimension, however there have been reports of even larger lesions.[3] Gross inspection typically reveals a soft, smooth, gelatinous, gray-white tissue with occasional firm fibrous areas.[3] Microscopically, these tumors are bland with a hypocellular myxoid stroma.[3] Tumor cells are stellate or spindled in appearance with rare nuclear pleomorphism and mitotic figures.[3,8] Abundant blood vessels of varying size and type are frequently present and there is often a chronic inflammatory background within the stroma.[3]

Immunohistochemical (IHC) features play a key role in the diagnosis of AAM. Tumors usually stain positive for vimentin, variably for muscle specific actin and α-smooth muscle actin, and negative for desmin, S-100 protein, and CD34.[6] Greater than 90% of tumors in females are ER and PR postive. The rate of ER/PR positivity in men is unclear; in a series of four tumors, one stained positive for ER, and three for PR.[9] IHC evaluation should be used to distinguish AAM from other benign (including intramuscular myxoma, neurofibroma with myoid change, and angiomyofibromyxoma) and malignant (myxoid liposarcoma, myxoid malignant fibrohistiocytoma, and embryonal rhabdomyosarcoma) tumors.[6]

Local recurrence is common (36% to 72%), and occurs in the first 3 years in greater than 70% of cases.[6] It has been reported in a retrospective study of 106 cases that completeness of extirpation may not be significantly associated with recurrence rate in female patients, though wide complete excision with tumor free margins is recommended.[10] Metastasis is very rare with two reported cases in females, both culminating in patient death.[11]

Surgical excision has been the standard method of treatment, however there have been reports of use of radiotherapy, and angioembolization.[10] There is one reported case of complete resolution of an AAM recurrence using gonadotropin-releasing hormone agonist (GnRH) monotherapy in a female.[12] The role of long term hormonal therapy for treatment of AAM in males remains unclear.[6,12] There is no consensus regarding duration and nature of follow up, however most advocate the use of history, physical examination and an imaging modality, usually MRI.[5]

Conclusion

Aggressive angiomyxoma is a benign myxoid tumor seen infrequently in men. It usually arises in the pelvic and genital soft tissues and is treated by surgical excision. Local recurrence is common, and metastasis is rare. The role of GnRH treatment in men is unclear. There is no standard follow up regimen for this tumor in men, though it should include an axial imaging modality.

This case was reported secondary to the rarity of the tumor, the unique mode of presentation, and the presence of the coexisting condition of prostate cancer. Currently the patient is doing well, with no evidence of prostate cancer recurrence (serum PSA < 0.05 ng/mL). He is potent and voiding freely with improving post-prosatatectomy urinary incontinence. There is no clinical evidence of AAM recurrence. □

References

1. Malik A, Singh KJ, Mehta A. Aggressive angiomyxoma of the spermatic cord: A rare entity. *Indian J Urol* 2009;25(1):137-139.
2. Chihara Y, Fujimoto K, Takada S et al. Aggressive angiomyxoma in the scrotum expressing androgen and progesterone receptors. *Int J Urol* 2003;10(12):672-675.
3. Kidric DM, MacLennan GT. Aggressive angiomyxoma of the male genital region. *J Urol* 2008;180(4):1506.
4. Steeper TA, Rosai J. Aggressive angiomyxoma of the female pelvis and perineum. Report of 9 cases of a distinctive type of gynecologic soft tissue neoplasm. *Am J Surg Pathol* 1983;7(5):463-475.
5. Haldar K, Martinek IE, Kehoe S. Aggressive angiomyxoma: a case series and literature review. *Eur J Surg Oncol* 2010;36(4):335-339.
6. Minagawa T, Matsushita K, Shimada R et al. Aggressive angiomyxoma mimicking inguinal hernia in a man. *Int J Clin Oncol* 2009;14(4):365-368.
7. Outwater EK, Marchetto BE, Wagner BJ et al. Aggressive angiomyxoma: findings on CT and MR imaging. *Am J Roentgenol* 1999;172(2):310-313.
8. Hastak MS, Raghuvanshi SR, Sahu S et al. Aggressive angiomyxoma in men. *J Assoc Physicians India* 2008;56:373-375.
9. Idrees MT, Hoch BL, Wang BY et al. Aggressive angiomyxoma of male genital region. Report of 4 cases with immunohistochemical evaluation including hormone receptor status. *Ann Diagn Pathol* 2006;10(4):197-204.
10. Chan IM, Hon E, Ngai SW, Ng TY, Wong LC. Aggressive angiomyxoma in females: is radical resection the only option? *Acta Obstet Gynecol Scand* 2000;79(3):216-220.
11. Blandamura S, Cruz J, Faure Vergara L et al. Aggressive angiomyxoma: A second case of metastasis with patient's death. *Hum Pathol* 2003;34(10):1072-1074.
12. Fine BA, Gershenson DM. Primary medical management of recurrent aggressive angiomyxoma of the vulva with a gonadtropin-releasing hormone agonist. *Gynecol Oncol* 2001;81(1):120-122.

Bilateral renal malakoplakia with acute renal failure: a case report and literature review

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RICHTER LA, ISAACSON M, VERGHESE M, KRISHNAN J. Bilateral renal malakoplakia with acute renal failure: a case report and literature review. The Canadian Journal of Urology. 2011;18(5):5911-5913.

Malakoplakia involving the genitourinary tract is a rare inflammatory disorder that presents a diagnostic challenge. Renal parenchymal involvement is particularly uncommon. We report a case of bilateral renal malakoplakia that presented with acute renal failure and simulated xanthogranulomatous pyelonephritis (XGP). The etiology, clinical course, and management of malakoplakia are reviewed, emphasizing the distinct characteristics of the disease that lead to its accurate diagnosis.

Key Words: malakoplakia, xanthogranulomatous pyelonephritis, renal failure

Case report

A 71-year-old female with a history of hypertension and alcoholism was transferred to our hospital for management of new onset renal failure. The patient had been in stable health until 4 days prior, when she presented to an outside hospital with fatigue, dysuria and diarrhea. A careful history elicited an unintentional 30 pound weight loss over the past year. She denied any bony pain or hematuria.

The patient's medical history was significant for controlled hypertension and a remote history of alcoholism. Her only prior surgery was an abdominal hysterectomy and bilateral oopherectomy for fibroids performed over 15 years ago. Physical exam revealed a thin woman in no acute distress. Abdomen was soft, nontender, with a well- healed lower midline abdominal scar. Admission labs revealed acute renal failure with a creatinine of 6.1. She had a leukocytosis of 20,000.

In response to patient's leukocytosis, urine and blood cultures had been drawn at the outside hospital, both of which were positive for E.coli. Based on these culture results, the patient was started on ciprofloxacin for urosepsis. Despite antibiotic therapy, she remained persistently febrile with an elevated WBC, even after completing her ciprofloxacin course. Additional antibiotic treatment with Vancomycin and Aztreonam was started, with no clinical improvement.

Persistent fevers unresponsive to antibiotic therapy prompted a CT scan of the abdomen and pelvis. The CT scan revealed diffuse heterogeneous enlargement of both kidneys as well as multiple renal masses. No retroperitoneal adenopathy was noted. The bilateral enlarged appearance was suspicious for an infiltrative process such as lymphoma, leukemia or metastatic disease. A CT of the chest and a nuclear medicine scan ruled out any evidence of lung or skeletal metastases respectively.

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Our next step was a CT guided core biopsy of one of the renal masses in hopes of obtaining tissue diagnosis. Pathology results revealed foamy histiocytes and a polymorphous population of lymphocytes, with a final read of xanthogranulomatous pyelonephritis (XGP). As suspected by prior radiologic workup, there was no evidence of malignancy.

The patient's acute renal failure was initially treated with conservative measures. When creatinine did not show improvement she started hemodialysis. At the time of patient's tissue diagnosis with XGP, the patient had been dialysis dependent for over 1 month.

In this patient with an overall septic course despite lengthy antibiotic treatment, persistent renal failure, and a tissue diagnosis of xanthogranulomatous pyelonephritis, the decision was made to undergo bilateral nephrectomy.

Open bilateral nephrectomy was uneventful. Postoperatively, patient's leukocytosis gradually declined from her admission baseline of 20,000 to 9,000. Concurrently, the patient defervesced. Final pathologic diagnosis of the surgical specimen was bilateral renal malakoplakia, as evidenced by Michaelis-Gutman bodies.

Discussion

Malakoplakia is a rare inflammatory disorder originally described by Michaelis and Gutman in 1902. The urinary tract is the organ system most often affected by this rare disorder. Within the urinary system, invasion most commonly involves the bladder mucosa. Renal parenchymal malakoplakia is considered relatively rare, with only 14 published cases of bilateral involvement over the past 20 years.[1]

Clinical presentation of renal malakoplakia involves urinary tract infection, pyelonephritis, and kidney enlargement. It tends to occur at middle age, typically in patients with chronic urinary tract infections. Additionally, almost half of affected patients have systemic disorders that impair immune function.[2]

The pathophysiology of the disease is thought to be due to inadequate intracellular destruction of phagocytosed bacteria. Low intracellular levels of cyclic guanosine monophosphate seem to be the cause of this impaired destruction of bacterial debris.[2] Microscopically, concretions composed of partially digested and mineralized bacterial fragments can be seen within the cytoplasm of macrophages. These concretions, containing calcium phosphate and iron salts from bacterial breakdown, are called Michaelis-Gutmann (M-G) bodies.[3] Histologically, plaques containing large macrophages with concretions and occasional multinucleate giant cells can often be seen, Figure 1. The diagnosis of malakoplakia, is dependent on the demonstration of these pathognomonic M-G bodies.[4] In the presented case, the renal biopsy was misdiagnosed as XPG. However, pathology of the final surgical specimen revealed the presence of M-G bodies within the renal parenchyma, diagnostic of malakoplakia.

The clinical presentation of XGP has many similarities to that of renal malakoplakia, and they may be easily confused. Both occur in the setting of chronic infection and obstruction, and both have urine cultures almost invariably positive for E.coli.[3] Malakoplakia is even considered by some to exist in a diagnostic spectrum that includes XGP. Although the characteristic imaging of XGP is of a staghorn calculus within enlarged kidneys, the diagnosis of XGP versus malakoplakia cannot be made solely on radiologic findings. Histologically, both disease processes involve collections of macrophages in the setting of infection, but it is the histologic presence of M-G bodies that distinguishes malakoplakia from XGP. To date, there is no consensus for the pathologic classification of XGP. However, the microscopic progression of XGP been broadly grouped into three forms: nonspecific tubulointerstitial nephritis with rare foamy macrophages, followed by megalocytic tubulointerstitial nephritis with increased foamy macrophages, and finally xanthogranulomatous pyelonephritis as the final phase with foamy macrophages devoid of intracellular inclusions on light-microscopy.[4] Given the clinical similarities between the two diagnoses, it is easy to see why the core biopsy result, read as XGP, seemed plausible for our patient.

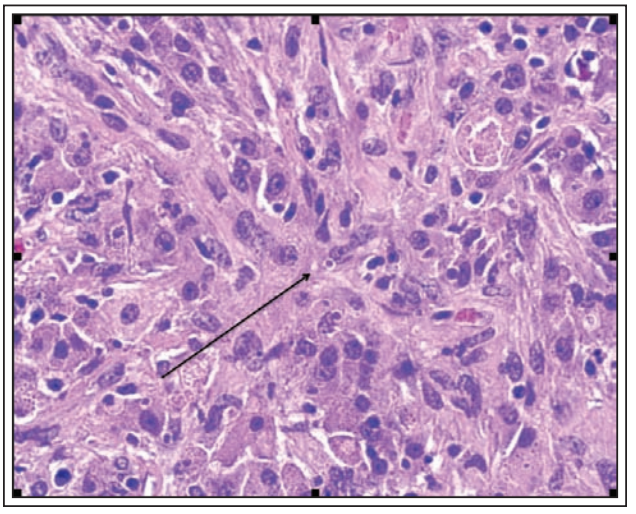

Figure 1. Presence of multiple Michaelis-Gutmann bodies in the renal surgical specimen (PAS stain, original magnification, x 100).

Other diagnoses that were appropriately considered based on the presenting triad of acute renal failure, fever and leukocytosis included acute interstitial nephritis (often as result of an allergic reaction to a drug), autoimmune disease, or an infiltrative process. Urinary tract obstruction with infection, particularly secondary to stone disease, involves a similar presentation, but would likely be seen with flank pain or nausea.

What is intriguing about this case, is not only the bilateral parenchymal involvement, but also that the course of renal deterioration was so rapid, and seemingly, so irreversible. When described in the literature in the 1970's, bilateral renal malakoplakia was understood to be a "progressive and destructive disease...and shown to be uniformly fatal".[5] Although no longer viewed as universally fatal, one of the consequences of bilateral renal malakoplakia is the progressive deterioration of kidney function, typically to the point of dialysis dependence. The recommendation for antibiotic treatment of the disease began in the 1970's. At this time, although antibiotics sterilized the urine, they had not been shown to alter the course of the disease.[5] More recent case reports, however, have shown preservation of function, and even reversal of acute renal failure, with antibiotic treatment. Flouroquinolones, because of their intracellular penetration, are the antibiotics of choice in clearing bacteria and halting interstitial damage. Patients treated with antibiotics promptly may be able to delay dialysis dependence for several years. In Tam et al's review of cases involving bilateral renal parenchymal malakoplakia only 6 of the 25 patients had significant impairment of renal function. Of these 6, only 3 ultimately required hemodialysis.[6] The patients who require dialysis have sustained such severe kidney damage prior to antibiotic treatment that despite destruction of bacteria, irreversible injury to the interstitium has already occurred. It is the prompt treatment of renal malakoplakia with antibiotics that is important for preservation of renal function.

An important question to consider is whether our surgical plan would have changed had the core biopsy results returned as renal parenchymal malakoplakia, rather than XGP. At the time of renal biopsy our patient had already been dialysis dependent for 1 month. She had a persistently elevated WBC and continued to be febrile despite IV antibiotic therapy. Her renal injury by the time of IV antibiotic treatment was already irreversible. In retrospect, despite an incorrect diagnosis by core biopsy, our surgical management would not likely have changed, because the patient's clinical status was already severely compromised.

Malakoplakia, as an infectious process, is a disease that targets the immunocompromised. In fact, over half of the patients affected by malakoplakia have systemic disorders that impair immune function.[2] Review of the literature revealed that alcoholism affected a large number of patients affected by bilateral renal malakoplakia with acute renal failure requiring dialysis. Our patient also had a history significant for alcoholism. Presumably, alcoholism interferes with the infection response, thereby allowing the development and progression of renal parenchymal malakoplakia.

Our understanding of renal malakoplakia has been a slow evolution since Michaelis-Gutman bodies were first reported in 1902. Renal parenchymal malakoplakia should be on the differential for patients presenting with chronic urinary tract infection, acute renal failure, and enlarged kidneys by imaging. The clinical and radiologic presentation of XGP and renal malakoplakia are quite similar, and may easily be confused. As learned in this case, as it is a spectrum disease, a diagnosis of renal parenchymal malakoplakia should be entertained in cases where XGP is considered. As malakoplakia is a histologic diagnosis, a timely renal biopsy improves chances of early antibiotic treatment and gives the best chances for preservation of renal function. □

References

1. Hong JJ, Liao PL, Lin JL et al. Bilateral renal parenchymal malakoplakia presenting as haemolitic-uraemic syndrome. *Nephrol Dial Transplant* 1999;14(9):2206-2209.
2. Rames RA, Bissada NK. Extensive pelvic malakoplakia: diagnosis and management. J Urol 1995;154(2Pt 1):523-524.
3. Tolkoff-Rubin NE, Cotran RS, Rubin RH. Urinary Tract Infection, Pyelonephritis, and Reflux Nephropathy. In: Brenner BM and Levine SA, eds. Brenner & Rector's The Kidney. 8th ed. Philadelphia, PA: Saunders Elsevier; 2004:1230-1231.
4. Albitar S, Genin R, Fen-Chong M et al. The febrile patient presenting with acute renal failure and enlarged kidneys- another mode of presentation of malakoplakia. *Nephrol Dial Transplant* 1997; 12(8):1724-1726.
5. Ho KL, Rassek Z, Nam SH. Bilateral renal malakoplakia. *Urology* 1979;13(3):321-323.
6. Tam VK, Kung WH, Li R, Chan KW. Renal parenchymal malakoplakia: a rare cause of ARF with a review of recent literature. *Amer J Kidney Dis* 2003;41(6):e13-e17.
7. Scully, RE, Mark EJ, McNeely WF, Ebeling SH, Ellender SM, Peters CC. Case records of the Massachusetts General Hospital: Case 31-2000. *N Engl J Med* 2000;343(15):1105-1108.
8. Bowers JH, Cathey WJ. Malakoplakia of the kidney with renal failure. *Am J Clin Pathol* 1971;55(6):765.

Incidentally discovered capillary hemangioma of the prostate

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RISTAU BT, TOMASZEWSKI JJ, PARWANI AV, OST MC. Incidentally discovered capillary hemangioma of the prostate. The Canadian Journal of Urology. 2011;18(5):5914-5915.

We present the case of a 69-year-old male with incidentally discovered capillary hemangiomas at radical prostatectomy. Hemangiomas of genitourinary origin are extremely rare, typically benign vascular tumors. This finding represents the first reported hemangioma within a radical prostatectomy specimen..

Key Words: capillary hemangioma, prostate cancer, radical prostatectomy

Introduction

Hemangiomas are vascular tumors comprised of a benign endothelial proliferation. They are most commonly found during infancy as cutaneous, hepatic, or gastrointestinal lesions.[1] Their presence within the genitourinary system is rare. We report a case of a 69-year-old male who underwent radical prostatectomy for elevated PSA and biopsy-proven adenocarcinoma of the prostate. Pathology revealed capillary hemagiomas within the radical prostatectomy specimen.

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Case report

We present the case of an otherwise healthy 69-year-old male who presented with an elevated PSA of 7.6 ng/mL on routine screening. He denied hematuria and significant genitourinary symptoms. Prostate biopsy revealed Gleason 3 + 3 = 6 prostate adenocarcinoma in 1/12 cores, and the patient underwent an uncomplicated open radical retropubic prostatectomy. Microscopic examination of the prostatectomy specimen revealed Gleason 3 + 4 = 7 prostate adenocarcinoma, 0/7 positive lymph nodes, and capillary hemangiomas, Figure 1. At 8 years of follow up, his PSA remains undetectable.

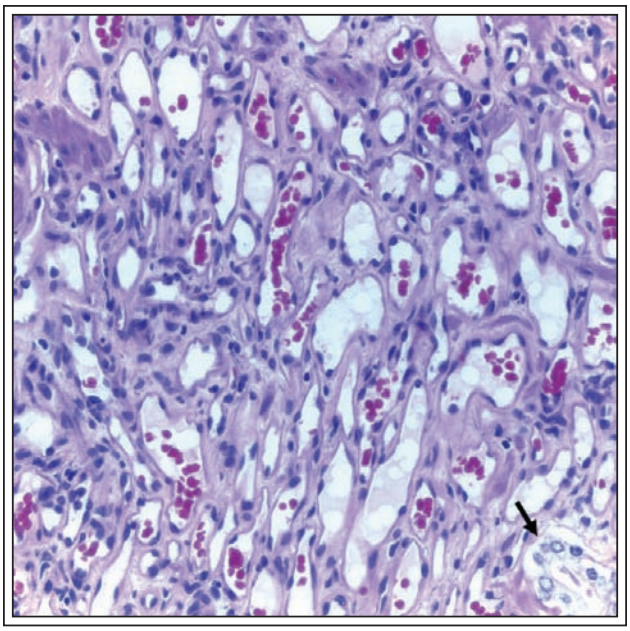

Figure 1. Capillary hemangioma, incidentally discovered during histological evaluation of the prostate. The section shows multiple intertwining small capillary-sized vessels lined by endothelium with relatively flat or plump nuclei. The proliferating vessels were adjacent to a focus of prostatic adenocarcinoma, Gleason score 3 + 4 = 7. Note one neoplastic prostatic gland at the bottom left edge of the image (arrow).

Discussion

Hemangiomas are typically benign vascular tumors encountered very rarely in the lower genitourinary tract. They have been described in the posterior urethra in conjunction with hematuria and hematospermia.[2,3] There are reports within the pediatric population of bladder hemangiomas as a rare cause of gross hematuria.[4-6] Although capillary hemangiomas generally represent benign neoplasms, their rarity within the prostate precludes further comment on clinical significance. Theoretically, they could present problems at prostate biopsy with excessive hemorrhage, though this has not been reported. To our knowledge, this represents the first reported case of capillary hemangioma discovered incidentally at radical prostatectomy. □

References

1. Holland KE, Drolet BA. Infantile hemangioma. *Pediatr Clin North Am* 2010;57(5):1069-1083.
2. Saito S. Posterior urethral hemangioma: one of the unknown causes of hematuria and/or hematospermia. *Urology* 2008;71(1):168.e11-e14.
3. de León JP, Arce J, Gausa L, Villavicencio H. Hemangioma of the prostatic urethra: holmium laser treatment. *Urol Int* 2008;80(1):108-110.
4. Ashley RA, Figueroa TE. Gross hematuria in a 3-year-old girl caused by a large isolated bladder hemangioma. *Urology* 2010;76(4):952-954.
5. Wiygul JB, Palmer L. Isolated hemangioma causing gross painless hematuria in an adolescent male. *Urology* 2010;76:463-464.
6. Ikeda T, Shimamoto K, Tanji N et al. Cavernous hemangioma of the urinary bladder in an 8-year-old child. *Int J Urol* 2004;11(6):429-431.

RESIDENT'S CORNER

Urethral foreign body insertion for secondary gain in the incarcerated population

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MASTROMICHALIS M, SACKMAN D, TYCAST JF, CHEHVAL MJ. Urethral foreign body insertion for secondary gain in the incarcerated population. The Canadian Journal of Urology. 2011;18(5):5916-5917.

Not uncommonly, hostile prison environments can lead desperate prisoners to place foreign materials into natural orifices in an effort to gain transfer to an outside healthcare facility. In this article, we present a case series of urethral foreign body insertion of varying burdens and durations requiring transfer to our facility for surgical management. Endoscopic retrieval was the initial management in each case; one case required conversion to open cystotomy for complete removal due the orientation, amount of inserted foreign body, and erosion into the proximal urethral and bladder urothelium.

Key Words: urethra, foreign body, endoscopy, prison, incarceration, secondary gain

Introduction

Self-insertion of urethral foreign body for secondary gain in the prison population is a rarely described phenomenon that can present a surgical challenge to the urologist. In hostile prison environments, prisoners can become desperate in an effort to avoid violence and assault, and in an effort to gain transfer to a healthcare facility, may attempt to swallow or place foreign body into natural orifices such as the urethra. The incarcerated have an understanding that foreign body concealed in natural orifices can easily exceed the correctional facilities' medical and surgical capabilities; prisoners utilize this knowledge to gain a temporary transfer out of prison. To the authors' knowledge, this case series is the second report of urethral foreign body insertion in the incarcerated population in an effort to garner outside medical attention.[1]

Case report

Patient A was transferred to the emergency department in acute urinary retention with blood per urethra and bilateral flank pain. Upon history, the patient confirmed the insertion of three ink pen refills into his urethra 5 months ago and an additional three refills the week prior to his presentation. He reported a strong desire for transfer after multiple cross-cultural altercations over the prior month. Abdominal and pelvic roentgenograms were obtained in the emergency department and revealed multiple radioopaque foreign body in the bladder and proximal urethra and admission serum creatinine was 3.2 mg/dL. The patient was taken immediately to the operating room after a brief discussion with psychiatric medicine. Endoscopic management of the foreign bodies was attempted but due to orientation of the ink refills and erosion into urethral and bladder mucosa, open cystotomy was required for the complete foreign body burden removal, Figure 1. The patient was discharged to the correctional facility on postoperative day number two with an indwelling Foley catheter; the patient successfully voided on postoperative day five at the correctional facility.

The second case is Patient A returning to the emergency department 6 months after his initial intervention with five pen-ink refills per urethra that were all placed within the previous week. The patient was spontaneously voiding blood tinged urine and denied any other symptoms. Given the short duration of placement and no prolonged interval between pen refill insertions, erosion was not an issue. Psychiatric medicine was again notified that the patient had returned, and the patient was taken immediately to the operating room. This case was managed endoscopically with a 22-Fr cystoscope and a 30 degree lens utilizing cystoscopic graspers and a Segura basket. The patient was returned to the facility later that evening without Foley catheter.

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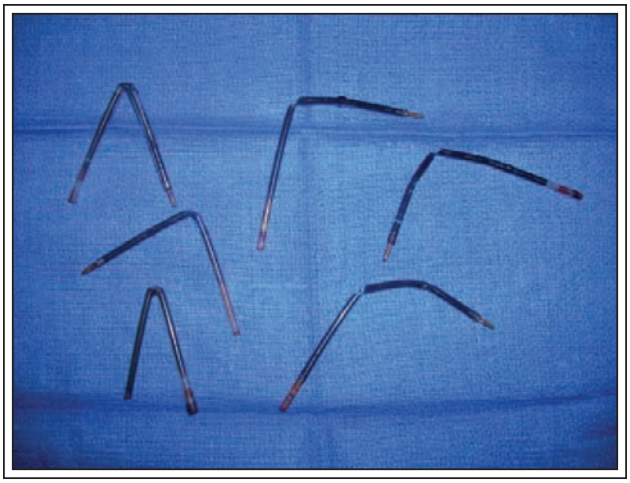

Figure 1. A total of six ink pen refills were retrieved from Patient A's lower urinary tract. Note the V-shaped bend required to advance the objects proximally.

The third case is Patient B who was transferred to the emergency department after ingesting cafeteria utensils and inserting several objects per urethra 3 days prior to transfer after obtaining the idea from Patient A in the prison recreation yard. He reported several episodes of assault and desired transfer out of the correctional facility for nausea, hematuria and stranguria. Three "spork" utensils were ingested and three ink pen refills and two pieces of milk carton cardboard were inserted per urethra; all objects were endoscopically retrieved utilizing a cystoscopic grasper and a Segura basket. Gastroenterology gastroscopically retrieved the entire alimentary foreign body burden, Figure 2.

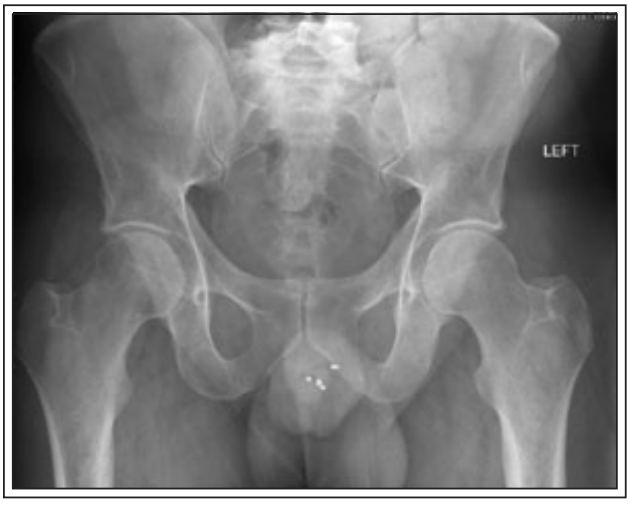

Figure 2. Patient B's pelvic roentgenogram demonstrating a lower urinary tract foreign body burden.

Discussion

The insertion of foreign body into the lower urinary tract for secondary gain (i.e., transfer to a healthcare facility) is a rare phenomenon that can be an unexpected surgical challenge with psychiatric implications. These patients can present with a wide range of signs; the most popular include urinary retention and gross hematuria, but systemic manifestations such as fevers, uremia, or sepsis can occur; the most effective management for removal is determined by the length of time to presentation from insertion, the number and size of the foreign body burden, radiographic orientation and endoscopic mobility of the object.*2-6* In most circumstances, endoscopic management is a reasonable initial intervention with the understanding that conversion to laparoscopic or open surgery can be necessary in cases of larger burdens of prolonged duration; cystotomy is not uncommonly required for complete object removal particularly when an endoscopic approach cannot completely clear the foreign body burden or visualization of the entire lower urinary tract is compromised.[2]

The communication of successful transfers out of correctional facilities leading another prisoner to emulate this act is consistent with the socially contagious nature of urethral foreign body insertion as described in the index case of urethral foreign bodies in the incarcerated population.[1] News of successful furloughs from incarceration travels quickly, and it appears a select few will risk temporary or even permanent consequences to the genitalia or the lower urinary tract for a break from a hostile prison environment. These patients need not only prompt surgical intervention, but also a psychiatric medicine evaluation and long term treatment; changes to prisoner privileges and restricting access to repeatedly inserted foreign bodies should be considered. □

References

1. Rada RT, James W. Urethral insertion of foreign bodies. A report of contagious self-mutilation in a maximum-security hospital. *Arch Gen Psychiatry* 1982;39(4):423-429
2. van Ophoven A, deKernion JB. Clinical management of foreign bodies of the genitourinary tract. *J Urol* 2000;164(2):274-287.
3. Trehan RK, Haroon A, Memon S, Turner D. Successful removal of a telephone cable, a foreign body through the urethra into the bladder: a case report. *J Med Case Reports* 2007;1:153.
4. Stravodimos KG, Koritsiadis G, Koutalellis G. Electrical wire as a foreign body in a male urethra: a case report. *J Med Case Reports* 2009;3:49.
5. Rahman NU, Elliott SP, McAninch JW. Self-inflicted male urethral foreign body insertion: endoscopic management and complications. *BJU Int* 2004;94(7):1051-1053.
6. Brison D, Lamba S, Jafary A, Bhalla R, Baker SR. Case report: urinary retention secondary to a foreign body in the male urethra. *Emerg Radiol* 2006;13(3):143-145.
7. Sukkarieh T, Smaldone M, Shah B. Multiple foreign bodies in the anterior and posterior urethra. *Int Braz J Urol* 2004;30(3):219-220.

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GreenLight 180W XPS photovaporization of the prostate: how I do it

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ZORN KC, LIBERMAN D. Greenlight 180W XPS photovaporization of the prostate: how I do it. The Canadian Journal of Urology. 2011;18(5):5918-5926.

Transurethral resection of the prostate (TURP) is the most common surgical intervention for benign prostatic hyperplasia (BPH), largely due to lower urinary tract symptoms refractory to medical therapy. TURP remains the gold standard for men with prostates sized 30g-80g, while open prostatectomy has been the preferred option for men with glands larger than 80g-100 g and those with other lower urinary tract anomalies such as large bladder stones or bladder diverticula. Unfortunately, these procedures have complications including bleeding (often requiring transfusion in 7%-13% of cases), electrolyte abnormalities (2% TURP syndrome), erectile dysfunction (6%-10%), and retrograde ejaculation (50%-75%). The overall incidence of a second intervention (repeat TURP, urethrotomy and bladder neck incision) has been reported in 12% and 15% of men at 5 and 10 years following TURP. Alternative therapies have been developed with the aim of reducing the level of complications while maintaining efficacy. These include microwave therapy, transurethral needle ablation, and a range of laser procedures (Holmium, Diode, Thulium and 532nm-Greenlight).

Photoselective vaporization of the prostate (PVP), initially launched as a 60W prototype, was ultimately introduced to the urology community as a 80W system (American Medical Systems, Minnetonka, Minnesota, USA), has been the predominant device used in clinical trials. This 1st generation used an Nd:YAG laser beam passed through a potassium-titanyl-phosphate (KTP) crystal, halving the wavelength (to 532nm), doubling the laser's frequency, and resulting in a green light. Outcomes have demonstrated a reduced frequency and severity of clinical complications, however it was limited to smaller prostate sizes. In 2006, the 120W lithium triborate laser (LBO), also known as the GreenLight HPS (High Performance System) laser was introduced. This laser utilizes a diode pumped Nd:YAG laser light that is emitted through an LBO instead of a KTP crystal, resulting in a higher-powered 532 nm wavelength green light laser while still using the same 70-degree deflecting, side firing, silica fiber delivery system. The HPS offered an 88% more collimated beam and smaller spot size, resulting in much higher irradiance or power density in its 2 predecessors (60W and 80W) with a beam divergence of 8 versus 15 degrees. The primary aim for this upgrade was to reduce lasing time and improve clinical outcomes while demonstrating the same degree of safety for patients. Limitations of the 120W system included treatment of large prostates greater than 80g-100g and increased cost related to fiber devitrification and fracture. In 2011, the 180W-Greenlight XPS system was introduced, not only with increased power setting to vaporize tissue quicker but significant fiber-design changes. Internal cooling, metal-tip cap protection and FiberLife (temperature sensing feedback), better preserve the integrity of the fiber generally producing a 1-fiber per case expectation. Initial personal experience with XPS has provided comparable outcomes related to morbidity, but with the opportunity to perform a more complete and rapid procedure. Published clinical data with the XPS is unfortunately lacking.

The objective of this report is to detail our approach and technique for GreenLight XPS drawing on personal experience with both enucleation and vaporization techniques with various laser technologies along with having performed over 500 GreenLight HPS and 100 XPS procedures. In this regard, recommendations for training are also made, which relate to existing users of the 80W and 120W GreenLight laser as well as to new laser users.

Key Words: BPH, photovaporization, prostate

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Introduction

Photoselective vaporization of the prostate (PVP) using the 532nm GreenLight laser (American Medical Systems, Minnetonka, MN, USA) has shown over its evolution to

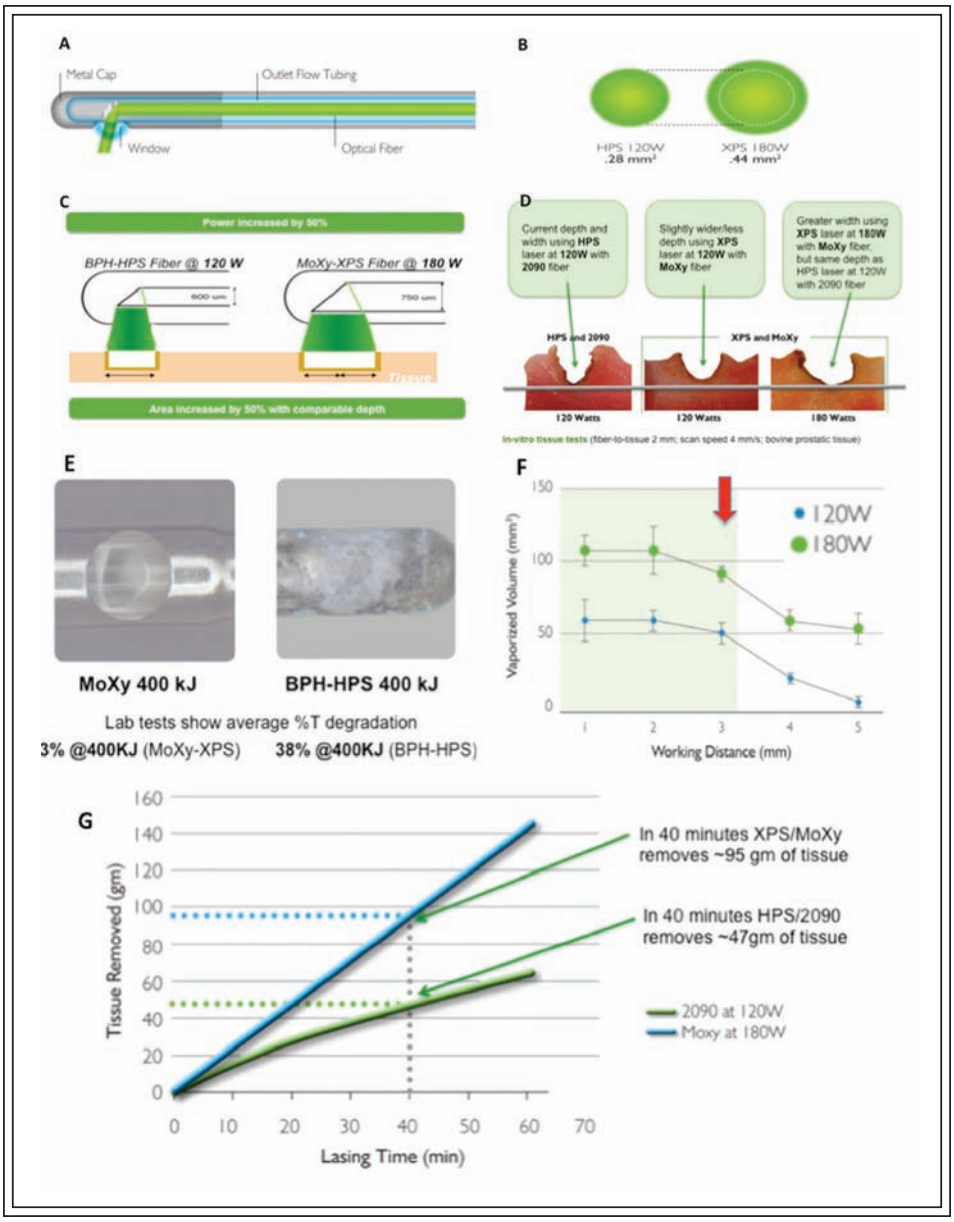

Figure 1. **A)** MoXy fiber construct demonstrating the novel steel-tipped protective cap and fiber cooling. What is not shown is the feedback mechanism to tissue sensing which alerts the surgeon to potential fiber overheating by pulsing during treatment. **B)** Demonstration of the difference in surface area of the collimated beam between the former HPS 120W system and XPS 180W system. **C)** Despite the increase in 50% power, the increase of 50% of the surface area allows similar depth of treatment thereby increasing treatment efficiency while minimizing increase in complication (capsular perforation or thermal tissue injury). **D)** In-vitro testing of the HPS and former fiber (2090) quartz tip fiber at full 120W power compared to the XPS/MoXy fiber fired equally at 120W and full 180W power. Note the same depth of tissue interaction however greater tissue vaporization even at equivalent 120W power. **E)** Post treatment examination demonstrates the preserved glass integrity by the metal cap on the MoXy fiber (left) compared to the former 2090 fiber which contacts tissue during treatment leading to devitrification. **F)** Graphic summary of laser-tissue interaction with varying distances. Note that the optimal distance is less than 2 mm from the prostate surface with significant drop off occurring after 3 mm. **G)** In-vitro model demonstration of the time-saving efficiency afforded by the XPS/MoXy system. Note the drop off curve (green) of the HPS which loses efficiency as the treatment progresses (due to the natural degradation of the silica fiber). The XPS remains relatively linear and is able to treat nearly double the tissue volume at 40 minutes of laser therapy compared to HPS-GL.
Courtesy of: American Medical Systems, Inc., Minnetonka, Minnesota USA. www.AmericanMedicalSystems.com

be equivalent to transurethral resection of the prostate (TURP), specifically for small to medium sized glands.[1-13] Benefits of this modality include reduced complications, shorter hospitalization and catheterization as well as the ability to treat patients who are anticoagulated and with coagulopathies.[14,15]

Since described by Malek et al using the potassium-titanyl-phosphate 80W system,[16-17] there have been two significant upgrades in the laser device, namely the increased power with the use of lithium triborate, offered by the 120W HPS (2006) and the 180W XPS (2010) systems. Such increase in power output and improvement in laser

beam collimation allow for more time-efficient tissue treatment. The second upgrade has been the new XPS-specific, MoXy liquid-cooled, steel-caped fiber provides significant improved speed and efficiency during vaporization by reducing tissue debris devitrification, Figure 1a. It is this principle of quartz-cap degradation on former fibers that significantly reduced power delivery throughout procedure. To achieve the proven safety profile of the GreenLight HPS system and improve the rate of vaporization, the power of the XPS/MoXy system was increased by 50% while simultaneously increasing the area of the laser beam by 50% (0.28 mm^2 versus 0.44 mm^2), Figure 1b, 1c, 1d. The benefit of the joint XPS system and MoXy fibre is a wider tissue vaporization effect without sacrificing the depth of vaporization and coagulation (< 2 mm). Compared to first and second generation systems, the latest XPS model significantly increases the speed of tissue removal (twice the speed of HPS) and durability of fiber longevity (often 1 fiber per case), Figure 1e, 1f, 1g.

Unfortunately, for the novice urologist embarking on GreenLight PVP, there has been a battery of published techniques using GreenLight for the treatment of benign prostatic hyperplasia (BPH).[6] However, the ultimate outcome of any technique is thoroughness of prostatic tissue vaporization down to the surgical capsule. Herein, we present our approach that focuses on early identification of anatomic landmarks and systematic energy delivery.

Pre-op assessment of GreenLight XPS candidates

A thorough history and physical examination is essential to evaluate PVP candidates as suggested by both the American Urological Association (AUA) and Canadian Urological Association (CUA) BPH-guidelines. Use of the American Urological Association Symptom Index (AUA-SI) is an excellent, validated, quantitative assessment tool to evaluate symptoms and bother. A quantitative assessment of bother (as defined in the QoL question) is recommended to grade the severity of lower urinary tract symptoms (LUTS) and to understand the degree of bother caused by those symptoms. A focused physical examination should be performed to assess the suprapubic area for bladder distension, and motor and sensory function of the perineum and lower limbs. A digital rectal exam (DRE) should be performed to evaluate anal sphincter tone and the prostate gland with regard to approximate size, consistency, shape and abnormalities suggestive of prostate cancer. The DRE estimation of prostate volume has been shown to be inaccurate when compared to transrectal ultrasound (TRUS) and it for that reason, I recommend prostate sizing prior to intervention, Figure 2a. Not only does it properly optimize operative time planning, it also assists the anesthesia team with medication dosing, particularly with spinal anesthetics. Furthermore, prior to all interventions, urine flowmetry and post-void residual volumes are obtained to confirm bladder outlet obstruction. Flexible cystoscopy is also carried out to assess for the presence of any urethral pathology (stricture), prostatic length, lobe asymmetry or medial lobe presence and the condition of the bladder (trabeculation, diverticula, tumor or stones), Figure 2b. Serum prostate-specific antigen (PSA), urinalysis and urine culture are also obtained on all men prior to surgery.

Dedicated urodynamic study would only be suggested in a male patient with significant overactive bladder symptoms and neuropathic conditions (diabetes, disc herniation or upper neurological defects). A cystometrogram (CMG) would also help in the preoperative counseling of men with significant urinary retention (> 1 L) to assess detrusor contractility.

Informed consent is obtained with surgical risks discussed, which include:[18-25] prolonged hematuria (> 2 weeks) (15%), irritative voiding symptoms (20%), urinary retention (5%) requiring replacement of Foley catheter, urinary incontinence (1%), retrograde ejaculation (> 70%), urinary track infection (3%) as well as the rare possible injury of the bladder and ureteral orifices.

Set up and equipment

Unless medically indicated (anticoagulated male, significant medical comorbidity), GreenLight XPS procedures are carried out at our institution as same-day, outpatient surgery. General anesthesia with laryngeal mask or a spinal anesthesia with a short acting medication (chlorpromazine) is preferred since it favors successful catheter removal 4-6 hours following surgery.

Before procedure initiation, we suggest that the surgeon verify all equipment is set up (camera attached to working sheath, white balance, light cord and irrigation tube positioned) and back-table material (catheter placed over stylet and syringe with 30 cc NS) ready before initial cystoscopy, Figure 2c. That way, there will be less unnecessary scope movement within the patient, thereby reducing unwanted bleeding. We utilize a Storz 24Fr laser resectoscope and assess the condition of metallic edges as part of our checklist. Room temperature 3 L normal saline bags are hung through a Y-tube adapter 60 cm-80 cm above patient height. Furthermore, the MoXy fiber is cooled via a dedicated 1 L bag of saline. The patient is prepped with a disinfectant solution (chlorhexidine 4%) and put into the dorsal lithotomy. Preoperative antibiotics

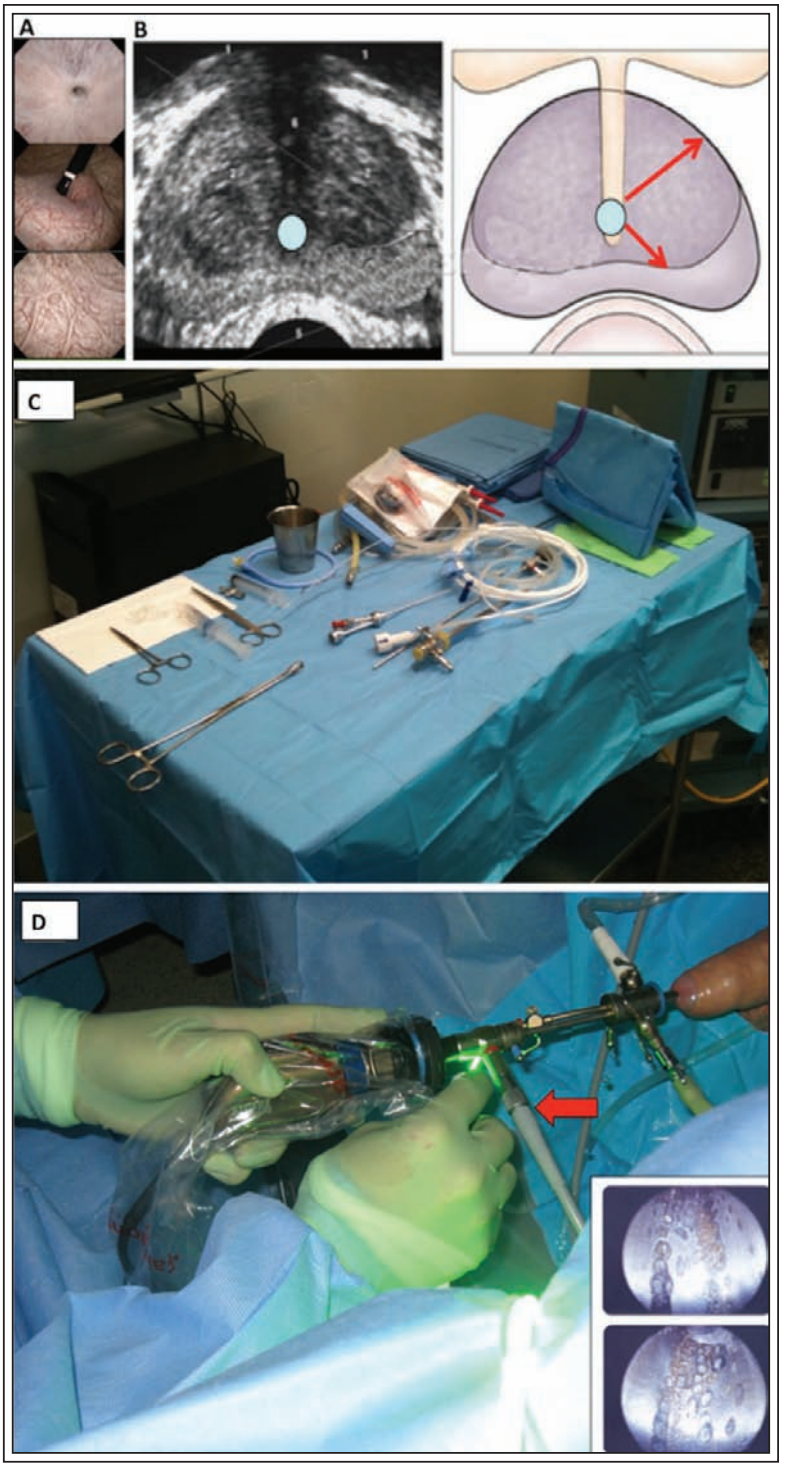

Figure 2. A) Cystoscopic evaluation prior to laser management to assess for the presence of urethral stricture, bladder stones, median lobe or the presence of intravesical intrusion as well as assess the condition of the bladder from chronic obstruction. **B)** Importance of the transrectal ultrasound (TRUS) prior to surgical intervention. Not only does it help accurately size the gland and demonstrate the presence of a median lobe, it can directly help plan the surgical time. I personally prefer to do my own TRUS imaging to also assess the various distances from the urethra to the capsule at 5- and 1-o'clock positions to prepare for surgery. **C)** Basic operative set up which include the cystoscope, 24F Storz laser-dedicated continuous flow sheath, irrigation tubing, MoXy fiber and end-of-procedure Foley 20F 2-way catheter, metal sylet and 30 cc NS filled syringe. **D)** Importance of recognizing the anterior beak of the laser metal sheath. Compared to the standard TURP where there is an angled-flush ceramic edge, the laser sheet includes a 2 cm beak which protrudes beyond the site of the the cystoscope lens tip. During treatment, when treating the prostate area between 9- and 3-o'clock positions (anterior), it is essential to rotate the outer sheath via the 30° lens to move the metal beak out of the way of the laser. Other options include working at a greater distance from the lens. It will not take more than a few seconds to create a full-thickness hole through the metal. Coupled to basic laser recommendations, this demonstration of laser power should convince all surgeons to wear their protective eyewear.

and if indicated, subcutaneous heparin are administered. We also suggest for those starting on their learning curve to digitally record initial cases for self-evaluation and teaching purposes.

Surgical mechanics of TURP versus GreenLight XPS

Compared to standard TURP, which is dominantly a one-handed procedure, GreenLight PVP demands a greater deal of two-hand involvement.[17-25] More specifically, the non-dominant hand stabilizes sheath at verumontanum, the dominant hand extends the loop to the bladder neck and within 2-3 seconds, supinates the wrist to excise a strip of tissue. Depth of loop penetration is not visually guided and is controlled with the non-dominant hand and gauged by surgeon experience. With GreenLight XPS, there is more dependence on two-hand coordination to achieve optimal results. As such, for the new user,

GreenLight XPS poses a mechanically more complex and different approached procedure. Rather than remaining stationary at the verumontanum, the non-dominant hand, which holds the camera, is withdrawn *simultaneously* as the MoXy fiber is pulled back during vaporization. This ensures a safe working distance with the laser energy so as not to damage the metal sheath or camera lens. The non-dominant hand is also responsible for maintaining optimal treatment distance (1 mm-3 mm) from the tissue. As such, the non-dominant hand is much more dynamic throughout the procedure; as is the dominant surgeon hand. Compared to the TURP, which the mechanics is in the turn of the wrist, the GreenLight XPS technique involves the coordination of movements at the wrist, elbow and shoulder.

Factors influencing vaporization efficiency

Working distance

The rate of efficiency of laser treatment declines after 3 mm, and so I try to work 1 MoXy fiber cap (width = 1.8 mm) away from the prostate surface, Figure 1f.

Energy settings

When treating the prostatic urethral mucosal surface, which is highly vascular, initial setting should be 80W for vaporization and 30W for coagulation. Once the mucosa has been treated and the adenoma is exposed with a larger working space, the vapor setting is increased by increments of 10W up to 120W and for larger glands (> 80 g) and more fibrous tissue, increased to 180W.

Sweep speed and angle

Based on bovine models, a sweep speed of 0.5 to 1.0 sweeps/second has been demonstrated to be more efficient and remove significantly more tissue than faster sweep speeds.[19] Therefore, in our clinical practice we conform to the above mentioned sweep speed during prostate resection (2 seconds per each 30-degree rotation or 4 mm sweep per second). Compared to conventional TURP, the surgeon must show patience and not sweep at faster rates. Ex-vivo analysis has showed that larger sweeping angles generated wider but more superficial vaporization defects, leading to smaller vaporized volumes. Specifically, vaporization volumes with angles of 0, 15, or 30 degrees were significantly greater than those with rotational angles of 45, 60, and 90 degrees.[20]

Greenlight XPS procedure description, Figure 3

STEP 1: Getting started and landmark demarcation

Careful, atraumatic, camerascopic introduction of the working sheath is essential to avoid unnecessary mucosal bleeding, particularly at the bladder neck and median lobe. The bladder should be inspected for tumors as well as identification of the orifices especially in the case of high bladder necks. In cases with large median lobes, I will avoid excessive torqueing and occasionally defer identification of ureteral orifices until the bladder neck has been debulked. Careless bleeding will slow down tissue treatment and hamper visual acuity.

I routinely mark the limits of dissection from the 3- to 9-'clock locations at both bladder neck and apex using the 30W coagulation setting. This maneuver limits bleeding and allows for a visual guide to avoid migration of treatment beyond the verumontanum. I also leave the last 1 cm just behind the verumontanum untreated and manage this just prior to case completion with lowered energy setting.

Planning the initial incision depends on the size and dimensions of the gland. High bladder necks and particularly, kissing lateral lobes often require debulking to allow for adequate working space. For small sized glands (< 60 g), an initial treatment groove down to the capsule is made at 5 o'clock from the bladder neck to the verumontanum at 80W power. This initial incision, which I feel is extremely valuable, serves as a depth reference throughout the procedure. For larger glands (> 60 g) or those men with median lobes, a second grooved-incision is created at the 7 o'clock positions prior to clearing the floor.

STEP 2: Prostate floor tissue treatment

Once the initial grooves are made, the floor is then treated at either 120W or 180W. The key during this surgical segment is to treat tissue with the laser fiber cap in contact with the capsule however rotating the cap and delivering energy horizontally along-side the capsular fibers. We feel that this helps reduce the unlikely chances of capsular perforation and more clinically-relevant, urinary irritative symptoms. Occasionally, fibrous and avascular tissue can be encountered which does not vaporize well. In such instances, the tissue can be enucleated from beneath along the capsule and released into the bladder for later removal. The surgeon should be cognizant of the width of the tissue strip to allow facile removal.

STEP 3: Lateral lobe treatment

Once the floor and median lobe have been treated (5- to 7- o'clock zone), I generally turn my attention first (being a right-handed surgeon) to the patient's left lateral lobe. With the working sheath rotated by tilting the light cord and therefore the 30-degree cystoscope lens to a 9-o'clock position in my hands

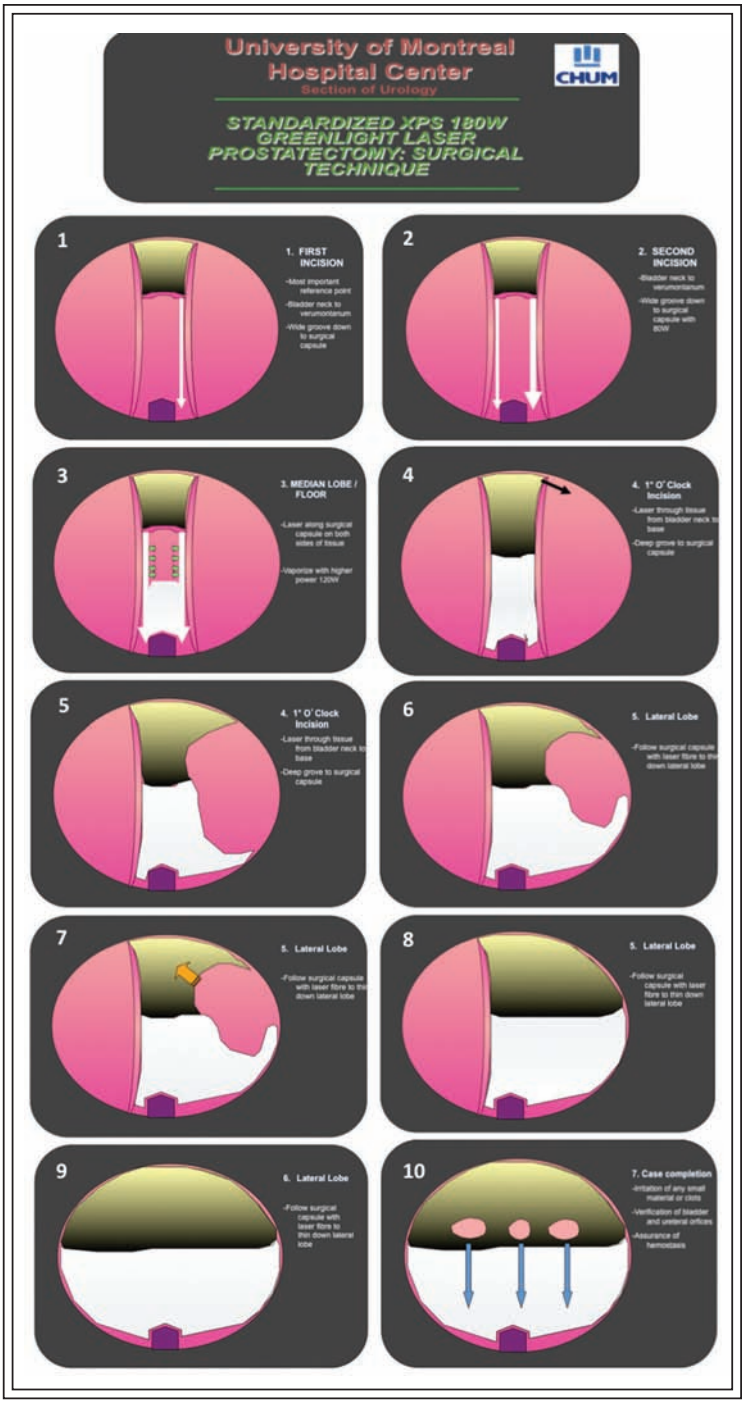

Figure 3. University of Montreal standardized approach to GreenLight XPS photovaporization of the prostate. **1)** After careful cystoscopic inspection of the bladder and prostatic urethral, initial working space is created. The limits of treatment are demarcated using 30W hemostasis of the bladder neck and prostatic apex 5 mm-10 mm proximal to the verumontanum. Thereafter, an initial incision is created at the 5-o'clock position down to the surgical capsule. Slow sweep speeds (4 mm/sec) are encouraged at 1 fiber cap distance from the mucosa. Vaporization begins at 80W power. **2)** Particularly for median lobes and larger prostates, a second incision grove is made at the 7-o'clock position down to the surgical capsule (transverse fibers). **3)** Adenoma is treated laterally at 120W with the laser fiber placed in the groove and aimed horizontally. Thermal energy is thereby minimized toward the capsule to reduce postoperative irritative symptoms. **4)** Once the floor has been completed from bladder neck to apex, the patients left lobe is treated. **5)** The scope is rotated to direct the laser beam to the 1-o'clock location and created a releasing incision groove. Special attention should be made when pulling the fiber back so as not to injure the sphincter. Pre-marking the limit with hemostasis setting is recommended. This will allow the bulk of the lateral lobe to fall into the working space and **6)** allow treatment from the 1- and 5-o'clock directions from a capsule position centripetally. **7)** Power is usually increased to 180W setting to easily vaporize the more difficult and less vascular stromal adenoma. Again, the laser is aimed more into the tissue along the defined the capsule to reduce the risk of perforation and unnecessary/unwanted bleeding. **8)** Once complete, the attention is directed to the patient's right lateral lobe, repeating the maneuvers 5-8 with an initial 11-o'clock incision grove to the capsule. **9)** Once complete, the prostatic fossa is viewed from the verumontanum with the inflow irrigation stopped. The apical tissue is treated with low-power 80W setting for any remaining obstructive tissue. **10)** Hemostasis is then checked with the bladder emptied 50% and any tissue pieces or clots removed. The bladder is then re-filled and the 20F 2-way catheter is gently placed and then filled with 30 cc in its balloon.

(thereby avoiding direct laser firing at the metal beak), another groove is treated at the patient's 1-o'clock prostate tissue, Figure 2d. This is taken down repetitively to the capsule to allow the bulk of the left lobe to drop into the urethral canal. The surgeon can then treat the pedicle of tissue from the 5- and 1-o'clock positions by side firing again at the tissue from the level of the capsule. I find the 180W power setting shows its

great advantage during lateral lobe treatment. Formerly with the HPS 120W system, I would incise long pillars of tissue and free them into the bladder to optimize OR time however with the higher power setting, the GreenLight XPS obviates the need for tissue enucleation. Once complete, the high-release grooved incision is made at the 11-o'clock area to drop the patient's right lobe and thereafter treat with systematic vaporization.

STEP 4: Managing bleeding

Occasionally, arterial bleeding is encountered during tissue vaporization, which significantly obscures vision. I will usually shorten my working distance with the laser fiber to optimize water flow and use the beak of the sheet to compress the bleeding vessel. Once visualized, the aiming beam of the laser is aimed and the vessel is circumscribed using the 30W coagulation setting. For instances where proximal tissue obscures the location of the vessel, tissue vaporization can be performed to expose the bleeding area. Vaporization over the bleeding area with a larger working area and faster sweep speed can also be attempted to coagulate the bleeder.

In the instance where the above measures are not satisfactory for hemostasis, I will use a Bugbee electrode to control the vessel in an end-on manner. Another option is to suspend laser surgery and place a 20F catheter with 30 mL in the balloon and provide 5 minutes of manual traction prior to resuming the procedure.

STEP 5: Apical treatment

Careful attention should be taken to the apex. The power should be lowered to 80W to avoid thermal sphincteric trauma. I will occasionally try to leave a small flap of apical tissue just above the verumontanum for younger men who desire antegrade ejaculation and older gentlemen (> 70) for risk of stress urinary incontinence.

STEP 6: Assurance of tissue treatment, hemostasis and case completion

Upon procedure completion, I will first empty 50% of the bladder and replace the scope back into the sheath with the water flow reduced to a minimum. Aside from small venous oozing areas commonly along the bladder neck floor and mucosal edges at the apex, which are easily coagulated with the 30W TruCoag setting, arterial pumpers are sought and treated. If the transitional zone tissue has been adequately treated, the cavity will remain a large defect. I again like to assess the bladder wall, ureteral orifices and identify any tissue pieces which can be removed. The bladder is then filled before passing the 2-way 20F urinary catheter over a stylet guide. Thirty milliliters of saline are instilled to fill the balloon. I generally rinse the bladder again with the saline irrigation to remove tissue pieces or any small clots which could obstruct the catheter.

In the occasional instances where the outflow is bloody, Foley traction can be provided for 5 minutes while irrigating the bladder. For men who were treated while in an anticoagulated state (ie. Coumadin for a metallic heart valve), I will place a 22F 3-way catheter and plug the inflow port in the event continuous flow is required. These men are kept at least overnight for observation.

Postoperative management

After transfer to the recovery room, the patient is hydrated through an intravenous and encouraged to drink fluids. Six hours following the procedure, the patient is evaluated for a trial of void (TOV). Factors that affect attempting TOV include the color of urine, time of the day, type of anesthesia and status of the bladder. The bladder is filled with 300 mL of saline and a bladder scan residual volume is obtained prior to discharge. Discharge medications include a fluoroquinolone (Ciprofloxacin) for 7 days and a stool softener to avoid constipation. Men are encouraged to avoid narcotics for discomfort. Patients are advised to avoid any strenuous activity, Vasalva-like maneuvers (heavy lifting > 20 lbs) including sexual activity for 2-3 weeks, especially those who resume anticoagulation. If anticoagulation medication was stopped before the procedure, it would be restarted following recommendations from the internist. If anticoagulants were not stopped, the high risk patient would be observed in hospital for 24-48 hours.

Follow up

A scheduled appointment is organized 1 month after hospital discharge. In our experience 20%-30% of patients will report irritative urinary symptoms (frequency, terminal dysuria), which tends to be self-limited. It is our practice to start men with severe symptoms on an antimuscarinic agent and anti-inflammatories for 1-3 months and schedule a close follow up in clinic to re-evaluate their symptoms.

At 3 months a PSA, urinary flow rate and AUA-SI questionnaire (IPSS) is obtained to evaluate resolution of bladder outlet obstruction. A drop of at least 50%-70% in preoperative PSA should be expected following the intervention to verify the degree of adenoma removal.[20] Given my interest in the clinical outcomes of such patients, follow up visits are also scheduled at 6 and 12 months followed by yearly assessments to assess the durability of GreenLight XPS.

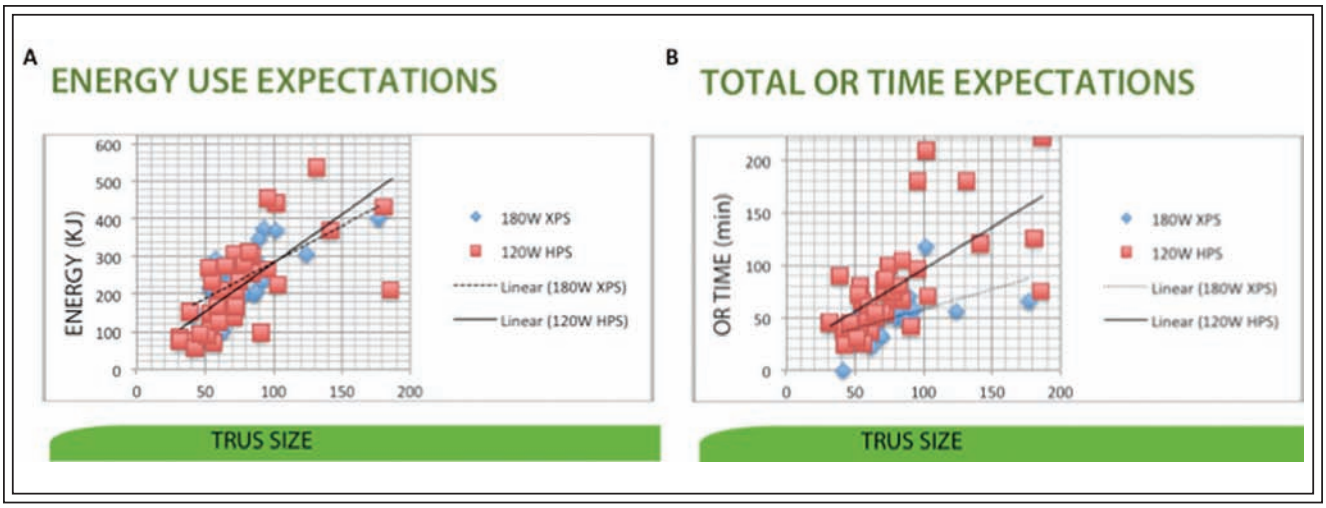

Figure 4. Personal experience of initial 100 GreenLight XPS cases compared to previous HPS system perioperative outcomes. **A)** Graphic demonstration of energy usage depending on TRUS prostate size. Note the relatively linear curve and similarity between the HPS and XPS systems of kJ used per gram of TRUS prostate measurement. **B)** Graphic demonstration of total surgical time (start of urethral introduction of scope to Foley placement) depending on TRUS prostate size. Note the separation and divergence of both curves favoring the GreenLight XPS, particularly as the TRUS size increases.

Training recommendations

Until the GreenLight simulator along with universal physician laser-credentialing pathways exists, the training recommendations with the GreenLight XPS are dependent on whether the surgeon is an experienced or inexperienced user. For the experienced GreenLight user (one who has completed 30 cases) mentoring and proctoring should take place on at least one occasion. Coupled to the online training module, this will ensure the hands-on review new XPS features (increased power options (120-180W), TruCoag and FiberLife features) and equipment set up (internal fiber cooling).

The inexperienced PVP user who is a trained urologist should undertake a formal training course, complete the online new-users on-line training module, watch several (5-10) live procedures performed by an experienced surgeon, and be subsequently proctored for a minimum of five cases, although this number may vary depending on proctor's discretion. Any supplemental, ongoing training should be conducted with the aid of the proctor. During the first 20 independent cases, the learning objectives should solidify the knowledge of prostatic anatomy, laser-tissue interaction (sweep speed, power setting and distance from tissue), standardized approach to the procedure and management of bleeding and complications.

Keys to success

Initial GreenLight XPS cases should be well selected and be properly screened with cystoscopy and TRUS. Uncomplicated men (no anticoagulation) with prostates sized less than 60 cc by ultrasonography, no median lobe are to be done at first. Personal experience suggests that it is poor patient selection (underestimating prostate volume only with DRE, presence of an unseen median lobe) that results in difficult working situations (little working space, bleeding) that drives surgeons back to their comfort zone being TURP. Another inexpensive tool that aids in surgeon education is the digital video recorder. There is tremendous value in self critique and peer evaluation.

Conclusion

Since performing my first GreenLight XPS laser PVP procedure in April 2011, I have been able to treat over 100 men thus far ranging from 43 g to 229 g. It is my experience that the XPS system along with durability of the MoXy fiber, afford the urologist an effective treatment option for BPH however with shorter length of stay in hospital, less postoperative catheter time and the elimination of TURP syndrome electrolyte anomalies, OR time constrains and need for transfusion. From a cost perspective (approximately 800$ CAD per fiber), we routinely only use 1 fiber per

case. I have had no fiber failure during treatment thus far with the MoXy fiber. With the GreenLight XPS system, I am able to complete 6-8 cases per surgical day and have impressively been able to treat larger glands with significantly quicker operative times, Figure 4, without compromise of outcomes or increased complication. We are currently analyzing our first 100 XPS system patients and will be publishing our data shortly.

Disclosure

Dr. Kevin C. Zorn - American Medical System (AMS) – consultant, proctor; Dr. Daniel Liberman - none □

References

1. Malek RS, Kang HW, Peng YS, Stinson D, Beck MT, Koullick E. Photoselective vaporization prostatectomy: experience with a novel 180 W 532 nm lithium triborate laser and fiber delivery system in living dogs. *J Urol* 2011;185(2):712-718.
2. Bachmann A, Schürch L, Ruszat et al. Photoselective vaporization (PVP) versus transurethral resection of the prostate (TURP): a prospective bi-centre study of perioperative morbidity and early functional outcome. *Eur Urol* 2005;48(6):965-971.
3. Bachmann A, Ruszat R, Wyler S et al. Photoselective vaporization of the prostate: the basel experience after 108 procedures. *Eur Urol* 2005;47(6):798-804.
4. Volkan T, Ihsan TA, Yilmaz O et al. Short term outcomes of high power (80 W) potassium-titanyl-phosphate laser vaporization of the prostate. *Eur Urol* 2005;48(4):608-613.
5. Tugcu V, Tasci AI, Sahin S, Zorluoglu F. Comparison of photoselective vaporization of the prostate and transurethral resection of the prostate: a prospective nonrandomized bicenter trial with 2-year follow-up. *J Endourol* 2008;22(7): 1519-1525.
6. Muir G, Sancha FG, Bachmann A et al. Techniques and training with GreenLight HPS 120-W laser therapy of the prostate: position paper. *Eur Urol Suppl* 2008;7(4):370-377.
7. Choi B, Tabatabaei S, Bachmann A et al. GreenLight HPS 120-W laser for benign prostatic hyperplasia: comparative complications and technical recommendations. *Eur Urol Suppl* 2008;7(4):384-392.
8. Kang HW, Jebens D, Malek RS, Mitchell G, Koullick E. Laser vaporization of bovine prostate: a quantitative comparison of potassium-titanyl-phosphate and lithium triborate lasers. *J Urol* 2008;180(6):2675-2680.
9. Malek RS, Kang HW, Coad JE, Koullick E. Greenlight photoselective 120-watt 532-nm lithium triborate laser vaporization prostatectomy in living canines. *J Endourol* 2009; 23(5):837-845.
10. Ruszat R, Seitz M, Wyler SF et al. Prospective single-centre comparison of 120-W diode-pumped solid-state high-intensity system laser vaporization of the prostate and 200-W high-intensive diode-laser ablation of the prostate for treating benign prostatic hyperplasia. *BJU Int* 2009;104(6):820-825.
11. Ruszat R, Wyler SF, Seitz M et al. Comparison of potassium-titanyl-phosphate laser vaporization of the prostate and transurethral resection of the prostate: update of a prospective non-randomized two-centre study. *BJU Int* 2008;102(10):1432-1438; discussion 1438-1439.
12. Ruszat R, Wyler S, Forster T et al. Safety and effectiveness of photoselective vaporization of the prostate (PVP) in patients on ongoing oral anticoagulation. *Eur Urol* 2007;51(4):1031-1038; discussion 1038-1041.
13. Ruszat R, Wyler S, Seifert HH et al. Photoselective vaporization of the prostate: experience with prostate adenomas > 80 cm^3. *Urologe A* 2006;45(7):858-864.
14. Ruszat R, Seitz M, Wyler SF et al. GreenLight laser vaporization of the prostate: single-center experience and long-term results after 500 procedures. *Eur Urol* 2008;54(4):893-901.
15. Te AE, Malloy TR, Stein BS et al. Photoselective vaporization of the prostate for the treatment of benign prostatic hyperplasia: 12-month results from the first United States multicenter prospective trial. *J Urol* 2004;172(4 Pt 1):1404-1408.
16. Kollmorgen TA, Malek RS, Barrett DM. Laser prostatectomy: two and a half years' experience with aggressive multifocal therapy. *Urology* 1996;48(2):217-222.
17. Kuntzman RS, Malek RS, Barrett DM, Bostwick DG. Potassium-titanyl-phosphate laser vaporization of the prostate: a comparative functional and pathologic study in canines. *Urology* 1996;48(4):575-583.
18. Malek RS, Barrett DM, Kuntzman RS. High-power potassium-titanyl-phosphate (KTP/532) laser vaporization prostatectomy: 24 hours later. *Urology* 1998;51(2):254-256.
19. Kauffman EC, Kang HW, Choi BB. The effect of laser-fiber sweeping speed on the efficiency of photoselective vaporization of the prostate in an ex vivo bovine model. *J Endourol* 2009;23(9):1429-1435.
20. Osterberg EC, Kauffman EC, Kang HW, Koullick E, Choi BB. Optimal laser fiber rotational movement during photoselective vaporization of the prostate in a bovine ex-vivo animal model. *J Endourol* 2009;25(7):1209-1215.
21. Shim M, Kwon T, Kim SC, Ha SH, Ahn TY. Changes in serum prostate-specific antigen levels after potassium-titanyl-phosphate (KTP) laser vaporization of the prostate. *Korean J Urol* 2010;51(2):111-114.
22. Capitán C, Blázquez C, Martin MD, Hernández V, de la Peña E, Llorente C. GreenLight HPS 120-W laser vaporization versus transurethral resection of the prostate for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia: a randomized clinical trial with 2-year follow-up. *Eur Urol* 2011;60(4):734-739.
23. Gu X, Strom K, Spaliviero M, Wong C. Intermediate outcomes of GreenLight HPS laser photoselective vaporization prostatectomy for symptomatic benign prostatic hyperplasia. *J Endourol* 2011;25(6):1037-1041.
24. Spaliviero M, Strom KH, Gu X, Araki M, Culkin DJ, Wong C. Does Greenlight HPS laser photoselective vaporization prostatectomy affect sexual function? *J Endourol* 2010;24(12):2051-2057.
25. Spaliviero M, Araki M, Culkin DJ, Wong C. Incidence, management, and prevention of perioperative complications of GreenLight HPS laser photoselective vaporization prostatectomy: experience in the first 70 patients. *J Endourol* 2009;23(3):495-502.

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Open clinical uro-oncology trials in Canada

George Rodrigues, MD, Eric Winquist, MD
London Health Sciences Centre, London, Ontario, Canada

BLADDER CANCER

A PHASE II PROTOCOL FOR PATIENTS WITH STAGE T1 BLADDER CANCER TO EVALUATE SELECTIVE BLADDER PRESERVING TREATMENT BY RADIATION THERAPY CONCURRENT WITH CISPLATIN CHEMOTHERAPY FOLLOWING A THOROUGH TRANSURETHRAL SURGICAL RE-STAGING

Trial ID: RTOG 0926
Coordination: Radiation Therapy Oncology Group (RTOG)
Trial design: A randomized phase II study assessing a bladder preservation strategy for T1G2G3 bladder cancer.
Patient population: Operable patients with stage T1 disease (T1G2 or T1G3) for whom radical cystectomy is being considered as the next conventional step in therapy by standard urologic guidelines.
Sample size & primary endpoint: n = 37, rate of freedom from radical cystectomy at 3 years

PROSTATE ADENOCARCINOMA

LOCALIZED PROSTATE CANCER

Low Risk

A RANDOMIZED PHASE II TRIAL OF HYPOFRACTIONATED RADIOTHERAPY FOR FAVORABLE RISK PROSTATE CANCER

Trial ID: RTOG 0938
Coordination: Radiation Therapy Oncology Group (RTOG)
Trial design: A randomized phase II study assessing two hypo fractionated radiotherapy regimens in low risk prostate cancer.
Patient population: Histologically confirmed diagnosis of adenocarcinoma of the prostate within 180 days of randomization; Gleason scores 2-6; Clinical stage T1-2a; PSA < 10 ng/mL.
Sample size & primary endpoint: n = 174, EPIC Bowel score at 1 year after therapy

Intermediate Risk

A PHASE III PROSPECTIVE RANDOMIZED TRIAL OF DOSE-ESCALATED RADIOTHERAPY WITH OR WITHOUT SHORT TERM ANDROGEN DEPRIVATION THERAPY FOR PATIENTS WITH INTERMEDIATE RISK PROSTATE CANCER

Trial ID: RTOG 0815
Coordination: RTOG
Trial design: A randomized controlled trial to demonstrate an overall survival (OS) advantage for the addition of short term (6 months) ADT versus no additional ADT in the context of dose escalated RT for patients with intermediate risk prostate cancer.
Sample size & primary endpoint: n = 1520, overall survival

PROSTATE FRACTIONATED IRRADIATION TRIAL (PROFIT)

Coordination: Ontario Clinical Oncology Group (OCOG)

Trial design: A phase III study assessing the relative efficacy of dose-escalated radiation therapy (78 Gy in 39 fractions) versus a hypofractionated course of radiation (6000 Gy in 20 fractions).

Patient population: Intermediate-risk prostate cancer.

Sample size & primary endpoint: n = 1204, biochemical (PSA) failure

A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED PHASE III TRIAL TO EVALUATE THE EFFECTIVENESS OF A PHOSPHODIESTERASE 5 INHIBITOR, TADALAFIL, IN PREVENTION OF ERECTILE DYSFUNCTION IN PATIENTS TREATED WITH RADIOTHERAPY FOR PROSTATE CANCER

Trial ID: RTOG 0831

Coordination: RTOG

Trial design: A phase III placebo randomized trial to determine whether tadalafil maintains spontaneous (off-drug) erectile function, as measured by the International Index of Erectile Function (IIEF), as compared to placebo at weeks 28-30 after initiation of radiation therapy for prostate cancer.

Patient population: Men with clinical stage T1b-T2b adenocarcinoma of the prostate and no distant metastases (M0), and their spouses/partners.

Sample size & primary endpoint: n = 218, International Index of Erectile Function Questionnaire (IIEF)

High Risk

ANDROGEN DEPRIVATION THERAPY AND HIGH DOSE RADIOTHERAPY WITH OR WITHOUT WHOLE-PELVIC RADIOTHERAPY IN UNFAVORABLE INTERMEDIATE OR FAVORABLE HIGH RISK PROSTATE CANCER: A PHASE III RANDOMIZED TRIAL

Trial ID: RTOG 0924

Coordination: RTOG

Trial design: Demonstrate that prophylactic neoadjuvant androgen deprivation therapy (NADT) and whole-pelvic radiation therapy (WPRT) will result in improvement in overall survival (OS) in patients with "unfavorable" intermediate risk or "favorable" high risk prostate cancer compared to NADT and high dose prostate and seminal vesicle (SV) radiation therapy (P + SV RT) using intensity modulated radiotherapy (IMRT) or EBRT with a high dose rate (HDR) or a permanent prostate (radioactive seed) implant (PPI) boost in a phase III clinical trial.

Patient population: Patients who are most likely to benefit from androgen deprivation therapy and whole-pelvic radiotherapy, defined as: a) Having a significant risk of lymph node involvement (e.g. > 15%, based on the Roach formula) OR b) Being in one of the following risk groups: GS 7-10 + T1c-T2b (palpation) + PSA < 50 ng/mL (includes intermediate and high risk patients) GS 6 + T2c-T4 (palpation) or > 50% biopsies + PSA < 50 ng/mL GS 6 + T1c-T2b (palpation) + PSA > 20 ng/mL.

Sample size & primary endpoint: n = 2580 for a primary endpoint of overall survival

RANDOMIZED PHASE III STUDY OF NEO-ADJUVANT DOCETAXEL AND ANDROGEN DEPRIVATION PRIOR TO RADICAL PROSTATECTOMY VERSUS IMMEDIATE RADICAL PROSTATECTOMY IN PATIENTS WITH HIGH-RISK, CLINICALLY LOCALIZED PROSTATE CANCER

Trial ID: NCIC PRC3
Coordination: Intergroup (Cancer and Leukemia Group B)
Trial design: A phase III comparison of neoadjuvant chemohormonal therapy with goserelin or leuprolide for 18-24 weeks with docetaxel IV every 3 weeks for up to six courses followed by radical prostatectomy with staging pelvic lymphadenectomy versus radical prostatectomy with staging lymphadenectomy alone.
Patient population: High-risk prostate cancer.
Sample size & primary endpoint: n = 750, 3 year biochemical progression-free survival

POST-RADICAL PROSTATECTOMY

RADICALS: RADIOTHERAPY AND ANDROGEN DEPRIVATION IN COMBINATION AFTER LOCAL SURGERY

Trial ID: NCIC PR13
Coordination: Intergroup (MRC)
Trial design: Phase III clinical trial with randomizations both for radiotherapy timing, and for hormone treatment duration.
Patient population: Men who have undergone radical prostatectomy for prostatic adenocarcinoma within 3 months, post-operative serum PSA less than 0.4 ng/ml. Uncertainty in the opinion of the physician and patient regarding the need for immediate post-operative RT.
Sample size & primary endpoint: n = 5100, disease free survival

BIOCHEMICALLY RELAPSED PROSTATE CANCER

A MULTICENTER CLINICAL STUDY OF THE SONABLATE® 500 (SB-500) FOR THE TREATMENT OF LOCALLY RECURRENT PROSTATE CANCER WITH HIFU

Trial ID: FSI-003
Coordination: Focus Surgery Inc.
Trial design: Single arm phase II.
Patient population: Men with locally recurrent prostate cancer following external beam irradiation.
Sample size & primary endpoint: n = 202, absence of biochemical failure and negative prostate biopsy rate at 12 months

A PROSPECTIVE PHASE II TRIAL OF TRANSPERINEAL ULTRASOUND-GUIDED BRACHYTHERAPY FOR LOCALLY RECURRENT PROSTATE ADENOCARCINOMA FOLLOWING EXTERNAL BEAM RADIOTHERAPY

Trial ID: RTOG 0526
Coordination: RTOG
Trial design: Single arm phase II.
Patient population: Men with biopsy-documented local recurrence > 30 months after external beam radiotherapy.
Sample size & primary endpoint: n = 96, late treatment-related GI/GU adverse events of brachytherapy

A PHASE II TRIAL OF SHORT-TERM ANDROGEN DEPRIVATION WITH PELVIC LYMPH NODE OR PROSTATE BED ONLY RADIOTHERAPY (SPPORT) IN PROSTATE CANCER PATIENTS WITH A RISING PSA AFTER RADICAL PROSTATECTOMY

Trial ID: RTOG 0534
Coordination: RTOG
Trial design: Phase II comparing radiotherapy alone to radiotherapy with short-term androgen deprivation.
Patient population: Males who have undergone radical prostatectomy, followed by PSA rise to > 0.2 ng/ml.
Sample size & primary endpoint: n = 1764, 5-year freedom from progression

A STUDY OF ANDROGEN DEPRIVATION WITH LEUPROLIDE, +/- DOCETAXEL FOR CLINICALLY ASYMPTOMATIC PROSTATE CANCER SUBJECTS WITH A RISING PSA

Trial ID: XRP6976J/3503
Coordination: sanofi-aventis
Trial design: A phase III comparison of androgen deprivation with or without docetaxel in men with rising PSA followed by radical prostatectomy.
Patient population: No metastases and PSA doubling time ≤ 9 months
Sample size & primary endpoint: n = 412, progression-free survival

METASTATIC PROSTATE CANCER

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDY OF EARLY VERSUS STANDARD ZOLEDRONIC ACID TO PREVENT SKELETAL RELATED EVENTS IN MEN WITH PROSTATE CANCER METASTATIC TO BONE

Trial ID: NCIC PRC2
Coordination: Intergroup (Cancer and Leukemia Group B)
Trial design: A phase III study comparing treatment with zoledronic acid at the time of initiation of androgen deprivation therapy for metastatic prostate cancer to treatment at time of progression to hormone-refractory disease.
Patient population: Metastatic prostate cancer with at least one bone metastasis by radiographic imaging receiving androgen deprivation therapy.
Sample size & primary endpoint: n = 680, time to first skeletal related event

CASTRATE RESISTANT PROSTATE CANCER

A MULTINATIONAL PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EFFICACY AND SAFETY STUDY OF ORAL MDV3100 IN CHEMOTHERAPY-NAÏVE PATIENTS WITH PROGRESSIVE METASTATIC PROSTATE CANCER WHO HAVE FAILED ANDROGEN DEPRIVATION THERAPY

Trial ID: PREVAIL
Coordination: Medivation/ProTrials Research Inc.
Trial design: Randomized double-blind multicentre study comparing MDV3100 to placebo.
Patient population: Asymptomatic metastatic castration-resistant prostate cancer and no prior chemotherapy.
Sample size & primary endpoint: n=1680, progression-free and overall survival

A PHASE III, RANDOMIZED, DOUBLE-BLIND, MULTICENTER TRIAL COMPARING ORTERONEL PLUS PREDNISONE WITH PLACEBO PLUS PREDNISONE IN PATIENTS WITH CHEMOTHERAPY-NAIVE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Trial ID: NCT01193244
Coordination: Millennium Pharmaceuticals, Inc.
Trial design: Phase III.
Patient population: Asymptomatic metastatic castration-resistant prostate cancer and no prior chemotherapy.
Sample size & primary endpoint: n = 1454, radiographic progression-free survival and overall survival

A RANDOMIZED PHASE III STUDY COMPARING STANDARD FIRST-LINE DOCETAXEL/PREDNISONE TO DOCETAXEL/PREDNISONE IN COMBINATION WITH CUSTIRSEN (OGX-011) IN MEN WITH METASTATIC CASTRATE RESISTANT PROSTATE CANCER

Trial ID: SYNERGY
Coordination: Teva/Oncogenex
Trial design: Randomized multicentre study of the addition of custirsen to docetaxel chemotherapy.
Patient population: Metastatic castration-resistant prostate cancer planned for treatment with docetaxel.
Sample size & primary endpoint: n=800, overall survival

A RANDOMIZED, OPEN LABEL, MULTI-CENTER STUDY COMPARING CABAZITAXEL AT 25 MG/M2 AND AT 20 MG/M2 IN COMBINATION WITH PREDNISONE EVERY 3 WEEKS TO DOCETAXEL IN COMBINATION WITH PREDNISONE IN PATIENTS WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER NOT PRETREATED WITH CHEMOTHERAPY

Trial ID: NCT01308567
Coordination: sanofi aventis
Trial design: Phase III
Patient population: Metastatic castration resistant prostate cancer and not previously treated with chemotherapy.
Sample size & primary endpoint: n = 1170, overall survival

A PHASE II STUDY OF MAINTENANCE THERAPY WITH TEMSIROLIMUS IN ANDROGEN-INDEPENDENT PROSTATE CANCER AFTER FIRST LINE CHEMOTHERAPY WITH DOCETAXEL

Trial ID: OZM-018
Coordination: Sunnybrook Health Sciences Centre Odette Cancer Centre
Trial design: Single arm phase II.
Patient population: CRPC in remission after docetaxel.
Sample size & primary endpoint: n = 30, time to treatment failure

A MULTICENTRE, SINGLE-ARM, OPEN LABEL CLINICAL TRIAL INTENDED TO PROVIDE EARLY ACCESS TO CABAZITAXEL IN PATIENTS WITH METASTATIC HORMONE REFRACTORY PROSTATE CANCER PREVIOUSLY TREATED WITH A DOCETAXEL-CONTAINING REGIMEN AND TO DOCUMENT SAFETY OF CABAZITAXEL IN THESE PATIENTS

Trial ID: NCT01254279
Coordination: sanofi aventis
Trial design: Phase III.
Patient population: Metastatic hormone refractory prostate cancer previously treated with a docetaxel-containing regimen.
Sample size & primary endpoint: n = 808, overall survival

RANDOMIZED, OPEN LABEL MULTI-CENTER STUDY COMPARING CABAZITAXEL AT 20 MG/M2 AND AT 25 MG/M2 EVERY 3 WEEKS IN COMBINATION WITH PREDNISONE FOR THE TREATMENT OF METASTATIC CASTRATION RESISTANT PROSTATE CANCER PREVIOUSLY TREATED WITH A DOCETAXEL-CONTAINING REGIMEN

Trial ID: NCT01308580
Coordination: sanofi aventis
Trial design: Phase III.
Patient population: Metastatic castration resistant previously treated with a docetaxel-containing regimen.
Sample size & primary endpoint: n = 1200, overall survival

RENAL CELL CANCER

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE THERAPY FOR SUBJECTS WITH LOCALIZED OR LOCALLY ADVANCED RCC FOLLOWING NEPHRECTOMY III STUDY TO EVALUATE THE EFFICACY AND SAFETY OF PAZOPANIB AS ADJUVANT

Trial ID: PROTECT/VEG113387
Coordination: GlaxoSmithKline Inc.
Trial design: Double-blind placebo-controlled phase III.
Patient population: Resected predominantly clear cell renal cell cancer at higher risk of recurrence.
Sample size & primary endpoint: n = 1500, disease-free survival

A RANDOMIZED PHASE II STUDY OF AFINITOR (RAD001) VS SUTENT (SUNITINIB) IN PATIENTS WITH METASTATIC NON-CLEAR CELL RENAL CELL CARCINOMA

Trial ID: ASPEN/NCT01108445
Coordination: Duke University
Trial design: Double-blind placebo-controlled phase III.
Patient population: Measurable metastatic predominantly non-clear cell renal cell cancer.
Sample size & primary endpoint: n = 108, progression-free survival

A PHASE II STUDY OF RO4929097 IN PATIENTS WITH ADVANCED RENAL CELL CARCINOMA THAT HAS PROGRESSED AFTER VEGF/VEGFR DIRECTED THERAPY

Trial ID: PHL-077
Coordination: Princess Margaret Hospital Phase II Consortium
Trial design: Single arm 2-stage phase II.
Patient population: Metastatic predominantly clear cell renal cell carcinoma with measurable disease treated with at least one prior antiangiogenic therapy (+/- one mTOR inhibitor).
Sample size & primary endpoint: n = 39, objective response rate

A RANDOMIZED, BLINDED, PHASE 2 DOSE-RANGING STUDY OF BMS-936558 (MDX-1106) IN SUBJECTS WITH PROGRESSIVE ADVANCED/METASTATIC CLEAR-CELL RENAL CELL CARCINOMA WHO HAVE RECEIVED PRIOR ANTI-ANGIOGENIC THERAPY

Trial ID: NCT01354431
Coordination: Bristol-Myers Squibb
Trial design: Phase II.
Patient population: Patients with either progressive and/or advanced/metastatic Clear-Cell Renal Cell Carcinoma after prior antiangiogenic treatment.
Sample size & primary endpoint: n = 39, objective response rate

MESSAGE TO OUR READERS

Dear Colleagues,

The 2011 Joint Meeting of the New England and Mid-Atlantic Sections of the AUA will be a historic one for several reasons. First and foremost, it is the first time we have combined the collective talents of our two great sections into one tremendous educational program to serve all our members. In fact it is the first time ever that the Mid-Atlantic section has run a joint meeting with any other section. In addition, this meeting will debut the scientific program and abstracts in *The Canadian Journal of Urology (CJU)* electronic FlipBook Edition compatible with many hand held devices and platforms, including the iPad, to further enhance our participants learning experience. With internet access you can view the CJU FlipBook Edition at **www.canjurol.com/preview**. An alternative is to download the PDF of the October meeting issue which is available at **www.canjurol.com** "October 2011".

The meeting will also feature innovations such as electronic poster viewing via display kiosks with full poster download capabilities. With a record number of over 270 submissions for the meeting, the scientific programming across all areas of Urology promises to be very strong. In addition to AUA President Dr. Sushil Lacy, special guest faculty will include Dr. Mani Menon, Dr. Mark Moyad, Dr. David Bloom, and Dr. Paul Lange among others.

We all are looking forward to a great meeting at the Swan Hotel in Orlando and the opportunity for our section members to interact during the many educational and social venues of the program. The New England and Mid Atlantic leadership is proud to have partnered with *The Canadian Journal of Urology* to not only provide an enduring print version of the scientific program and abstracts that will be more widely distributed but also the electronic FlipBook Edition that will provide an alternative media for the program.

We all look forward to meeting you in Orlando.

Leonard G. Gomella, MD
Thomas Jefferson University
Philadelphia, PA
Editor-in-Chief, CJU

Timothy B. Hopkins, MD
UMass Memorial Medical Center
Worcester, MA
President, NE-AUA

Harry P. Koo, MD
VCU Medical Center
Richmond, VA
President, MA-AUA

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bioLITEC®
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for their support in publishing the following scientific program and abstracts from the New England & Mid-Atlantic sections of the AUA 2011 Joint Annual Meeting.

SCIENTIFIC PROGRAM

WEDNESDAY, NOVEMBER 2, 2011

2:00 pm – 8:00 pm **REGISTRATION**

THURSDAY, NOVEMBER 3, 2011

6:30 am – 6:00 pm **REGISTRATION**

7:30 am **CONTINENTAL BREAKFAST VISIT EXHIBITS**
Swan Ballroom V-X

7:30 am – 10:30 am **EXHIBITS OPEN**
Swan Ballroom V-X

8:00 am – 12:00 pm **HOSPITALITY SUITE**
Macaw & Terrace

8:00 am – 8:20 am
INTRODUCTION & WELCOME
Swan Ballroom I-IV

Timothy B. Hopkins, MD
President, New England Section of the AUA

Harry P. Koo, MD
President, Mid-Atlantic Section of the AUA

Sushil S. Lacy, MD
President, American Urological Association

8:20 am – 9:10 am
SCIENTIFIC SESSION I:
GENERAL UROLOGY/ BPH
Swan Ballroom I-IV
Moderators: Cameron R. Barnes, MD
Virginia Urology, Richmond, VA
Jeffrey A. Ranta, MD
Greenwich Urological Associates, Greenwich, CT

5 minute presentations, 2 minute discussions

8:20 am

1. **Trends in Surgical Management of Benign Prostatic Hyperplasia**
Nora Lee[1], Hui Xue[2], Lori B. Lerner[3]
[1]*Boston University Medical Center,Boston, MA;* [2]*Harvard University, Boston, MA;* [3]*Boston Veterans Affairs Hospital, Boston, MA*

8:27 am

2. **Prostate Atypia: Repeat Biopsy Results Within One Year of Diagnosis**
Cory D. Harris[1], Stuart Kesler[2], Joseph R. Wagner[3]
[1]*University of Connecticut, Farmington, CT;* [2]*Harford Hospital, Hartford, CT;* [3]*Hartford Hospital, Hartford, CT*

8:34 am

3. **Single Dose Intramuscular Ceftriaxone an Effective Alternative to Accepted Transrectal Prostate Biopsy Prophalaxsis**
Ravi Kacker[1], Spender Platt[2], Micheal Kearney[2]
[1]*Brigham and Women's Hospital, Boston, MA;* [2]*Beth Israel Deaconess Medical Center, Boston, MA*

8:41 am

4. **A Prospective Single-Center 3 Year Study of the Efficacy and Safety of the GreenLight Laser HPS in Men with Clinical BPH**
Gregg Eure
Eastern Virginia Medical School, Virginia Beach, VA

8:48 am

5. **Neurophysiologic Intraoperative Monitoring of Somatosensory Evoked Potentials to Detect Neurologic Injuries Due to Patient Positioning**
Marc D. Manganiello, Jay Shils, Carl Borromeo, Jill C. Buckley
Lahey Clinic, Burlington, MA

8:55 am

6. **A Contemporary Study of Renal Cysts in Representative US Population**
Steve Dong, Neesha Patel, Chandan Kundavaram, Deborah Glassman, Demetrius Bagley
Thomas Jefferson University, Philadelphia, PA

9:02 am

7. **Exploring the Volume-Outcomes Relationship for Adrenal Surgery**
Jay Simhan[1], Marc C. Smaldone[1], Daniel Canter[1], Fang Zhu[1], Russell Starkey[1], Karyn B. Stitzenberg[2], Robert G. Uzzo[1], Alexander Kutikov[1]
[1]*Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, PA;* [2]*University of North Carolina Hospitals, Chapel Hill, NC*

9:10 am – 9:30 am
HEALTH POLICY UPDATE
Swan Ballroom I-IV
Mark T. Edney, MD
Peninsula Urology Associates, Salibury, MD

Arthur E. Tarantino, MD
Connecticut Surgical Group, Hartford, CT

9:30 am – 10:00 am **COFFEE BREAK**
VISIT EXHIBITS
Swan Ballroom V-X

10:00 am – 10:50 am
WYLAND F. LEADBETTER MEMORIAL LECTURE
Swan Ballroom I-IV
Robotic Urologic Surgery at 10 Years: Quo Vadis?
Mani Menon, MD
Henry Ford Hospital, Detroit, MI

10:50 am – 12:15 pm
SCIENTIFIC SESSION II: URO-ONCOLOGY I
Swan Ballroom I-IV
Moderators: Alexander Kutikov, MD
Fox Chase Cancer Center, Philadelphia, PA
Joseph R. Wagner, MD
Connecticut Surgical Group, Hartford, CT

10:50 am – 10:55 am
HIGHLIGHTS FROM WASHINGTON D.C. – PROSTATE CANCER
Joseph F. Renzulli, MD
The Miriam Hospital, Providence, RI

10:55 am – 12:00 pm
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

10:55 am

8. **Primary Spermatic Cord Tumors: Disease Characteristics, Prognostic Factors and Treatment Outcomes**
Dayron Rodríguez[1], Aria F. Olumi[2]
[1]*Harvard Medical School and Harvard School of Public Health, Boston, MA;* [2]*Department of Urology, Massachusetts General Hospital, Boston, MA*

11:02 am

9. **Men with Hereditary Prostate Cancer Have Improved Outcomes after Radical Prostatectomy in the PSA Era**
John B. Eifler, Jr., Misop Han, Sally Isaacs, Elizabeth Humphreys, William Isaacs, Patrick C. Walsh
Brady Urological Institute, Baltimore, MD

11:09 am

10. **Interventions for Urinary Morbidity Long Term after Prostate Cancer Treatment**
Peter Chang[1], Meredith M. Regan[2], John T. Wei[3], Larry A. Hembroff[4], Chris S. Saigal[5], Jeff M. Michalski[6], Eric A. Klein[7], David P. Wood, Jr.[3], Martin G. Sanda[8],
The PROST-QA Study Group[8]
[1]*Beth Israel Deaconess Medical Center/Brigham and Women's Hospital, Boston, MA;* [2]*Dana Farber Cancer Institute, Boston, MA;* [3]*University of Michigan School of Medicine, Ann Arbor, MI;* [4]*Institute for Public Policy and Social Research, Michigan State University, East Lansing, MI;* [5]*UCLA Center for Health Sciences, Los Angeles, CA;* [6]*Washington University School of Medicine, St. Louis, MO;* [7]*Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH;* [8]*Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA*

11:16 am

11. **Denosumab Treatment for Prolonging Bone Metastasis-Free Survival in Men with Castrate-Resistant Prostate Cancer**
Paul Sieber[1], Matthew Smith[2], Fred Saad[3], Robert Coleman[4], Neal Shore[5], Karim Fizazi[6], Bertrand Tombal[7], Kurt Miller[8], Lawrence Karsh[9], Ronaldo Damiao[10], Teuvo Tammela[11], Blair Egerdie[12], Hendrik Van Poppel[13], Joseph Chin[14], Juan Morote[15], Tomasz Borkowski[16], Zhishen Ye[17], Amy Kupic[17], Roger Dansey[17], Carsten Goessl[17]
[1]*Urological Associates of Lancaster, Lancaster, PA, USA;* [2]*Massachusetts General Hospital Cancer Center, Boston, MA, USA;* [3]*University of Montreal Hospital Center, CRCHUM, Montreal, Quebec, Canada;* [4]*Weston Park Hospital, Sheffield, UK;* [5]*Carolina Urological Research Center, Myrtle Beach, SC, USA;* [6]*Institut Gustave Roussy, University of Paris Sud, Villejuif, France;* [7]*Université Catholique de Louvain Cliniques Universitaires Saint Luc, Bruxelles, Belgium;* [8]*Charité Berlin, Berlin, Germany;* [9]*The Urology Center of Colorado, Denver, CO, USA;* [10]*Hospital Universitario Pedro Ernesto, Rio de Janeiro, Brazil;* [11]*Tampere University Hospital, Tampere, Finland;* [12]*Urology Associates Urologic Medical Research, Kitchener, ON, Canada;* [13]*Universitair Ziekenhuis Gasthuisberg Leuven, Belgium;* [14]*London Health Sciences Centre, London, Canada;* [15]*Hospital Vall d'Hebron Barcelona, Spain;* [16]*Medical University of Warsaw, Szpital Dzieciatka Jezus, Warsaw, Poland;* [17]*Amgen Inc., Thousand Oaks, CA, USA*

11:23 am

12. Radical Perineal Prostatectomy: A Viable Minimally Invasive Option for Treatment of Localized Prostate Cancer

Thomas K. Huisman, Robert M. Chiaramonte, Burkhardt H. Zorn
Southern Maryland Hospital Center, Clinton, MD

11:30 am

13. Comparison of Positive Surgical Margin Rates in High Risk Prostate Cancer

Niall J. Harty[1], Spencer Kozinn[1], Jessica DeLong[1], David Canes[1], Andrea Sorcini[1], Jason Gee[1], Mark Silverman[1], Robin Ruthazer[2], John Libertino[1], Ali Moinzadeh[1]
[1]*Lahey Clinic, Burlington, MA;* [2]*Tufts Medical Center, Boston, MA*

11:37 am

14. Predictors of Positive Surgical Margins after Radical Prostatectomy: Analysis of a Contemporary Single Institution Series

Francisco Gelpi, Leonard G. Gomella, Costas Lallas, Peter McCue, Chandan Kundavaram, Xiaolong Liu, Edouard J. Trabulsi
Thomas Jefferson University Hospital, Philadelphia, PA

11:43 am

15. Prospective Study of Testosterone Suppression and Recovery after 6 Months of Androgen Deprivation Therapy and Radiation for Clinically Localized Prostate Cancer

Adam R. Metwalli[1], Aref N. Dajani[2], Robert Brookland[1], Heather Thomas[3], Ronald F. Tutrone[1]
[1]*Chesapeake Urology Associates, Baltimore, MD;* [2]*Independent Statistical Consultant, Greenbelt, MD;* [3]*Chesapeake Urology Research Associates, Baltimore, MD*

11:50 am

16. Too Few or Too Many Prostate Biopsies? Results from an Academic Center

Benjamin J. King, Brian H. Irwin, Thomas D. Trainer, Mark K. Plante, Samuel J. Trotter, Scott D. Perrapato
University of Vermont College of Medicine, Burlington, VT

12:00 pm – 12:15 pm
POINT/COUNTERPOINT
Adjuvant vs. Salvage Radiation Therapy following Radial Prostatectomy

Adjuvant Radiation Therapy
Misop Han, MD
John's Hopkins Hospital, Baltimore, MD

Salvage Radiation Therapy
Jim C. Hu, MD
Brigham and Women's Hospital, Boston, MA

10:50 am – 12:15 pm
CONCURRENT POSTER SESSION I: BASIC SCIENCE
Mockingbird
Moderators: Georgi Guruli, MD
Virginia Commonwealth University Medical School, Richmond, VA
John A. Taylor, III, MD
University of Connecticut Health Center, Farmington, CT

10:50 am – 11:05 am **POSTER VIEWING TIME**

11:05 am – 12:00 pm
POSTER PRESENTATIONS
Posters listed with times will be giving a two minute oral presentation followed by a one minute discussion

11:05 am

P1. Sphingosine Kinase-2 Deficient Mice Exhibit Diminished Renal Inflammation/Renal Fibrosis in Response to Unilateral Ureteral Obstruction

Shobha Thangada[1], Timothy Hla[2], **Fernando Ferrer**[1]
[1]*Connecticut Children's Medical Center/University of Connecticut Health Center, Hartford/Farmington, CT;* [2]*Weill Cornell Medical College Center for Vascular Biology, New York, NY*

11:08 am

P2. Regulation of Kinetochore Protein Expression by COX-2 Signaling in Prostate Cancer Cells

Jared Bieniek, Chandra Childress, Wannian Yang
Geisinger Medical Center, Danville, PA

11:11 am

P3. Comparison of Intraprostatic Ethanol Diffusion Using a Microporous Hollow Fiber Catheter vs. Standard Needle

Benjamin J. King[1], Mark K. Plante[1], Masatoshi Kida[1], Travis K. Man-Gow[1], Rick Odland[2], **Peter Zvara**[1]
[1]*University of Vermont, Burlington, VT;* [2]*Twin Star Medical, Minneapolis, MN*

11:14 am

P4. Inhibition of Inflammatory and Apoptotic Mediators Improves the Bladder Dysfunction that is Associated with Type 2 Diabetes

Zongwei Wang[1], Zhiyong Cheng[2], Vivian Cristofaro[3], Jijun Li[1], Xingyuan Xiao[1], Rongbin Ge[1], Pablo Gomez[4], Edward Gong[4], Klemen Strle[1], **Aria F. Olumi**[1]
[1]*Massachusetts General Hospital, Boston, MA;* [2]*Howard Hughes Medical Institute, Children's Hospital Boston, Boston, MA;* [3]*VA Boston Healthcare System, Boston, MA;* [4]*Children's Hospital Boston, Boston, MA*

11:17 am

P5. A Non-invasive Mirna Based Assay to Detect Bladder Cancer in Cell-free Urine

Jessica DeLong, Spencer Kozinn, Niall Harty, Kelly Summerhayes, Ian Summerhayes, Antonia Holway, Kimberly Rieger-Christ

The Lahey Clinic, Burlington, MA

11:20 am

P6. The In Vitro Anti-tumor Activity of Docetaxel in Combination with Inositol Hexaphosphate (IP-6) in Castrate-Resistant PC3 and DU-145 Prostate Cancer Cell Lines

Adam Luchey, Can Talug, Dale Riggs, Barbara Jackson, Dana Point, Stanley Zaslau, Stanley Kandzari

West Virginia University, Morgantown, WV

11:23 am

P7. Impact of Endothelin Axis Modification in Cancer Immunotherapy and Transplantation in Murine Model

Jeffrey P. Wolters, P. Joseph Yannie, Ekaterine Goliadze, Maryellen Dolat, Georgi Guruli

Virginia Commonwealth University, Richmond, VA

11:26 am

P8. Molecular Profiling of Erlotinib Resistance in an In-Vitro Bladder Cancer Model

William C. Faust, Marc Manganiello, Justin Zbrzezny, Christina Deliyiannis, Jason Gee, John Libertino, Antonia Holway, Kimberly R. Christ

Lahey Clinic, Cambridge, MA

11:29 am

P9. A New Method for Objective Analysis of Detrusor Rhythm during the Filling Phase

Ashley B. King[1], Adam Klausner[1], Samuel Robinson[1], David Rapp[2], Vikram Sabarwal[1], John Speich[1], Harry Koo[1], Paul Ratz[1]

[1]*Virginia Commonwealth University, Richmond, VA;* [2]*Virginia Urology Center for Incontinence and Pelvic Floor Reconstruction, Richmond, VA*

11:32 am

P10. Improved Detection of Prostate Cancer by the Combined Application of ERG and AMACR Immunohistochemical Stainings in Prostate Biopsy Specimens

George Leighton Lee

CPDR/WRAMC/USUHS, Rockville, MD

11:35 am

P11. Gene Expression Signature of High BMI Prostate Cancer Patients Identifies the Statin Target Gene SCD1

Patrick Parker

CPDR/WRAMC/USUHS, Rockville, MD

11:38 am

P12. NS11021, a BK Channel Opener, Effects Significant Changes on Mouse Urinary Bladder Function during Urodynamics

Hagop Sarkissian, Tom Heppner, Peter Zvara, Mark Plante, Mark Nelson

University of Vermont, Burlington, VT

11:41 am

P13. The Relation between Leptin and Prostate Cancer Cell Line LnCaP

Mohamad W. Salkini, Dake Ruggs, Barbara Jacksom

West Virginia University, Morgantown, WV

11:44 am

P14. The Effects of Social and Environmental Stimuli in a New Murine Model for Interstitial Cystitis/ Painful Bladder Syndrome

Adam Luchey, Dale Riggs, Barbara Jackson, Can Talug, Stanley Kandzari, James Coad, Yara Daous, Dana Point, Morris Jessop, Stanley Zaslau

West Virginia University, Morgantown, WV

11:47 am

P15. F-box Protein 10, an NF-KB-dependent Anti-apoptotic Protein, Regulates TRAIL-induced Apoptosis through Modulating c-Fos/c-FLIP

Rongbin Ge[1], Zongwei Wang[1], Qing Zeng[2], Xiaoyin Xu[2], **Aria Olumi[1]**

[1]*Mass General Hospital, Boston, MA;* [2]*Brigham and Women's Hospital, Boston, MA*

11:50 am

P16. Multi-Institutional Evaluation of a MicroRNA Expression Profile Defining the Invasive Bladder Tumor Phenotype

Marc D. Manganiello[1], William C. Faust[1], Justin M. Zbrzezny[1], Christina Deliyiannis[1], Michelle Waknitz[2], Wei Huang[2], Jason R. Gee[1], John A. Libertino[1], Antonia H. Holway[1], Kimberly R. Christ[1]

[1]*Lahey Clinic, Burlington, MA;* [2]*University of Wisconsin, Madison, WI*

11:53 am

P17. Sphingosine-1- Phosphate 2 Receptor Induces Ccl2 Expression in Neuroblastoma/A Targeted Inhibition Strategy

Mei-Hong Li[1], Timothy Hla[1], **Fernando Ferrer[1]**

[1]*Connecticut Children's Medical Center/University of Connecticut Health Center, Hartford/Farmington, CT;* [2]*Weill Cornell Medical College/Center for Vascular Biology, New York, NY*

11:56 am

P18. Clinicopathological Correlation of Gli1 Expression in a Population Based Cohort of Patients with Newly Diagnosed Bladder Cancer

Einar F. Sverrisson[1], Michael Scott Zens[2], Alan Schned[1], John D. Seigne[1], Margaret R. Karagas[2]
[1]*Dartmouth Hitchcock Medical Center, Lebanon, NH;* [2]*Dartmouth Medical School, Hanover, NH*

11:59 am

P19. Increased Alpha 1a and 1b Expression in the Castrated Rat Prostate

Allen D. Seftel[1], Michael DiSanto[1], Xinhua Zhang[1], Rani Sellers
[1]*Cooper University Hospital, Camden, NJ;* [2]*Albert Einstein College of Medicine, Bronx, NY*

12:02 am

P20. Up-regulation of Transforming Growth Factor-β and the Counter-regulatory Effects of Hepatocyte Growth Factor in Fetal Sheep Bladder Outlet Obstruction

Nora G. Lee[1], Hao Fan[2], Craig A. Peters[3]
[1]*Boston University Medical Center, Boston, MA;* [2]*University of Virginia, Charlottesville, VA;* [3]*Children's National Medical Center, Washington, DC*

12:15 pm – 1:45 pm
CONCURRENT LUNCH SYMPOSIUM
Swan Ballroom I-IV
Advanced Prostate Cancer Disease Awareness: Novel Mechanisms of Androgen Regulation and Modulation in Disease Progression
Supported by Janssen Biotech, Inc.

12:15 pm – 1:45 pm
CONCURRENT LUNCH SYMPOSIUM
Pelican
Individualized Approach: the Clinical Value of Toviaz 4mg and 8mg
Supported by Pfizer

2:00 pm – 7:15 pm **EXHIBIT HALL OPEN**
Swan Ballroom V-X

1:45 pm – 2:50 pm
SCIENTIFIC SESSION III: FEMALE UROLOGY, NEUROUROLOGY AND VOIDING DYSFUNCTION
Swan Ballroom I-IV
Moderators: Paula B. Bellin, MD
Hahnemann Urology Associates, Worcester, MA
Leslie M. Rickey, MD
University of Maryland Medical Center, Baltimore, MD

1:45 pm – 1:50 pm
HIGHLIGHTS FROM WASHINGTON D.C. – FEMALE UROLOGY, NEUROUROLOGY AND VOIDING DYSFUNCTION
David E. Rapp, MD
Virginia Urology, Richmond, VA

1:50 pm – 2:35 pm
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

1:50 pm

17. Fluid Intake and Risk of Stress, Urgency, and Mixed Urinary Incontinence

Ying Jura[1], Mary Townsend[2], Gary Curhan[3], Neil Resnick[4], Francine Grodstein[3]
[1]*Massachusetts General Hospital, Boston, MA;* [2]*Harvard School of Public Health, Boston, MA;* [3]*Brigham and Women's Hospital, Boston, MA;* [4]*University of Pittsburg Medical Center, Pittsburg, PA*

1:57 pm

18. Long-Term Treatment Interval of Percutaneous Tibial Nerve Stimulation: 18 Month Study Results

Jeffrey A. Ranta[1], Ken Peters[2], Donna Carrico[2]
[1]*Greenwich Urological Assoc. P.C., Greenwich, CT;* [2]*William Beaumont Medical Center, El Paso, TX*

2:04 pm

19. Sexual Function Following TVTO Placement: Minimum 12 Month Follow Up

Ashley B. King[1], Jeffrey P. Wolters[1], Adam P. Klausner[1], David E. Rapp[2]
[1]*Virginia Commonwealth University, Richmond, VA;* [2]*Virginia Urology Center for Incontinence and Pelvic Floor Reconstruction, Richmond, VA*

2:11 pm

20. Ileal Loop Urinary Diversion for Non-Bladder Cancer Indications - Long-term Outcomes and Complications

Ellen Goldmark, Melissa Heuer, Toby C. Chai
University of Maryland, Baltimore, MD

2:18 pm

21. Short-term Outcomes of Robotic Assisted Sacrocolpopexy for Pelvic Organ Prolapse

Veronica Triaca, Heidi Hallonquist, Cathy Yi, Katherine Cail
Concord Hospital, Concord, NH

2:25 pm

22. **Is Complete Cure Necessary for Satisfaction in Patients Undergoing Concurrent Anti-incontinence and Prolapse Surgery?**
Jeffrey P. Wolters[1], Ashley B. King[1], Adam P. Klausner[1], David E Rapp[2]
[1]*Virginia Commonwealth University, Richmond, VA;* [2]*Virginia Urology Center for Incontinence and Pelvic Floor Reconstruction, Richmond, VA*

2:35pm – 2:50pm
POINT/COUNTERPOINT
Male Perineal Sling versus the Artificial Urinary Sphincter for a Man with Moderate Post-prostatectomy Incontinence

Male Perineal Sling
William I. Jaffe, MD
Pennsylvania Presbyterian Medical Center, Philadelphia, PA

Artificial Urinary Sphincter
Arthur P. Mourtzinos, MD
Tufts Medical School, Boston, MA

1:45 pm – 2:50 pm
CONCURRENT SCIENTIFIC SESSION I: STONES/ENDOUROLOGY
Pelican
Moderators: Alan D. Jenkins, MD
University of Virginia School of Medicine, Charlottesville, VA
Peter L. Steinberg, MD
Maine Medical Center, Portland, ME

1:45 pm – 1:50 pm
HIGHLIGHTS FROM WASHINGTON D.C. – STONES/ENDOUROLOGY
Brian H. Eisner, MD
Massachusetts General Hospital, Boston, MA

1:50 pm – 2:35 pm
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

1:50 pm

23. **Assessment of Radiation Exposure from Diagnostic Imaging in Patients Undergoing Ureteroscopy with Laser Lithotripsy for Upper Tract Stones**
Brooke A. Harnisch, Jessica E. Kreshover, Aylin Bilgutay, Richard K. Babayan, David S. Wang
Boston University and Boston Medical Center, Boston, MA

1:57 pm

24. **Ureteral vs Renal Laser Lithotripsy- Are They Really Equal?**
Levi A. Deters, Vernon M. Pais, Jr.
Dartmouth Hitchcock Medical Center, Lebanon, NH

2:04 pm

25. **Radiation Exposure during Extracorporeal Shockwave Lithotripsy**
Eugene Kramolowsky[1], Nada L. Wood[1], Susan Taylor[2], Ruth Butler[1], Matthew Bassignani[1], Dean Broga[3]
[1]*Virginia Urology, Richmond, VA;* [2]*Washington and Lee University, Lexington, VA;* [3]*Virginia Commonwealth University, Richmond, VA*

2:11 pm

26. **Relationship Between Protein Intake and Urine Composition in Patients with Nephrolithiasis**
Brian H. Eisner[1], Sonali Sheth[1], Stephen P. Dretler[1], Benjamin Herrick[2], Vernon M. Pais, Jr.[2]
[1]*Massachusetts General Hospital, Boston, MA;* [2]*Dartmouth Hitchcock Medical Center, Lebanon, NH*

2:18 pm

27. **Nationwide Trends in Imaging Utilization during the Emergency Department Evaluation of Flank Pain, 2000-2008**
Elias Hyams[1], Frederick Korley[2], Brian Matlaga[1]
[1]*Brady Urological Institute, Johns Hopkins School of Medicine, Baltimore, MD;* [2]*Department of Emergency Medicine, Johns Hopkins School of Medicine, Baltimore, MD*

2:25 pm

28. **Percutaneous Nephrolithotomy in Patients with Neurogenic Bladder Dysfunction**
Matthew Mason, Sevann Helo, Noah Schenkman
University of Virginia, Charlottesville, VA

2:35pm – 2:50pm
POINT/COUNTERPOINT
Imaging and Management of Nephrolithiasis in Pregnancy

Imaging: Low Dose CT
Management: Conservative with Chronic Stenting
Julio G. Davalos, MD
Chesapeake Urology Associates, Baltimore, MD

Imaging: Ultrasound
Management: Treatment with Ureteroscopy
Vernon M. Pais, Jr., MD
Dartmouth Hitchcock Medical Center, Lebanon, NH

2:50 pm – 3:20 pm **COFFEE BREAK**
VISIT EXHIBITS
Swan Ballroom V-X

3:20 pm – 4:00 pm
PANEL DISCUSSION:
Management of Complications of the Lower Urinary Tract
Swan Ballroom I-IV
Moderators: Jill C. Buckley, MD
Lahey Clinic, Burlington, MA
Kurt A. McCammon, MD
Eastern Virginia Medical School, Norfolk, VA
Panelists: William I. Jaffe, MD
Pennsylvania Presbyterian Medical Center, Philadelphia, PA
Leonard Zinman, MD
Lahey Clinic, Burlington, MA

3:20 pm – 4:00 pm
CONCURRENT POSTER SESSION II: ONCOLOGIC DISEASES
Mockingbird
Moderators: Aria F. Olumi, MD, FACS
Massachusetts General Hospital, Boston, MA
Edouard J. Trabulsi, MD
Jefferson Medical College, Philadelphia, PA

3:20 pm – 3:30 pm **POSTER VIEWING TIME**

3:30 pm – 4:00 pm
POSTER PRESENTATIONS
Posters listed with times will be giving a two minute oral presentation followed by a one minute discussion

3:30 pm – 3:33 pm

P21. Delayed Ureteral Complications following Complex Partial Nephrectomy
Jose Reyes, Daniel Canter, Jay Simhan, Marc Smaldone, Ervin Teper, Alexander Kutikov, David Y.T. Chen, Robert G. Uzzo
Fox Chase Cancer Center, Philadelphia, PA

P22. Comparing Post-operative Complication Rates Between Neoadjuvant Chemotherapy and Chemotherapy Naïve Patients who Undergo Cystectomy for Bladder Cancer
Jack W. Lambert, III, Stephen Riggs, Matthew Ingham, Bethany Barone
Eastern Virginia Medical School, Norfolk, VA

3:33 pm – 3:36 pm

P23. Durable Oncologic Outcomes after Radio frequent Ablation for T1 Renal Cell Carcinoma in Poor Surgical Candidates
Sarah P. Psutka, Francis J. McGovern, Peter Mueller, W. Scott McDougal, Debra Gervais, Adam S. Feldman
Massachusetts General Hospital, Boston, MA

P24. Comparing Outcomes in Elderly Patients after Laparoscopic Radical Nephrectomy, Open Partial Nephrectomy and Cryoablation for Renal Masses
Jack W. Lambert III, Stephen Riggs, Joshua Logan, Dave Staneck, Mary H. James, Bethany Barone
Eastern Virginia Medical School, Norfolk, VA

P25. Modifying Utilization of Urine Cytology Testing During Follow-up for Patients with Urothelial Carcinoma
Mohummad M. Siddiqui, Aria F. Olumi
Massachusetts General Hospital, Boston, MA

P26. Surgical Outcomes of Non-hilar Clamping Partial Nephrectomy; An Updated Twenty Year Experience
Justin M. Zbrzezny[1], William C. Faust[1], Marc D. Manganiello[1], Matthew F. Wszolek[1], Yoojin Lee[2], John A. Libertino[1]
[1]*Lahey Clinic Medical Center, Burlington, MA;* [2]*Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA*

P27. Pyeloperfusion as a Protective Mechanism for Radiofrequency Ablation of Renal Carcinoma Contiguous to the Ureter: Technique, Results and Complications
Jairam R. Eswara[1], Debra Gervais[1], Peter Mueller[1], Ron Arellano[1], Colin Cantwell[2], Raul Uppot[1], Francis McGovern[1]
[1]*Massachusetts General Hospital, Boston, MA;* [2]*St. Vincents, Dublin, Ireland*

P28. Masses Treated by Thermal Ablation are Low or Moderately Complex as Measured by the R.E.N.A.L-Nephrometry Scoring System
Jose Reyes, Daniel Canter, Jay Simhan, Marc Smaldone, Ervin Teper, Alexander Kutikov, Rosalia Viterbo, David Y.T. Chen, Richard E. Greenberg, Robert G. Uzzo
Fox Chase Cancer Center, Philadelphia, PA

P29. Renal Oncocytoma Diagnosed by Percutaneous Biopsy can be Safely Followed but Must Not Be Forgotten
Sameer M. Deshmukh, Brian F. Chapin, Brian H . Eisner, Jairam Eswara, Francis J. McGovern, W. Scott McDougal, Peter Mueller, Anthony Samir, Adam S. Feldman
Massachusetts General Hospital, Boston, MA

P30. R.E.N.A.L. Nephrometry Score is a Surrogate for Surgical Difficulty
Tom S. Floyd, Jr.[1], Jennifer Davila-Aponte[1], Kasey Morrison[1], Lorna Herbert[2], Noah Schenkman[1], Tracey L. Krupski[1]
[1]*University of Virginia, Charlottesville, VA;* [2]*UCLA, Los Angeles, CA*

P31. Role of Tumor Location and Provider Specialty in Selecting Patients for Percutaneous Versus Surgical Cryoablation of the Small Renal Mass
Christopher J. Long[1], Daniel J. Canter[2], Marc C. Smaldone[2], Ervin Teper[2], David Y.T. Chen[2], Richard Greenberg[2], Rosalia Viterbo[2], Robert G. Uzzo[2], Alexander Kutikov[2]
[1]*Temple University Hospital, Philadelphia, PA;* [2]*Fox Chase Cancer Center, Philadelphia, PA*

3:36 pm – 3:39 pm

P32. Short-term Complications after Cystectomy in Patients Treated with Neoadjuvant Chemotherapy is only Associated with Comorbidity
Sarah P. Psutka, Adam S. Feldman, Richard J. Lee, Aria F. Olumi
Massachusetts General Hospital,Boston, MA

3:39 pm – 3:42 pm

P33. Pathologic Upstaging Following Complete Transurethral Resection and Early Cystectomy for Clinical Stage T1 Bladder Cancer
Sheaumei Tsai, John A. Libertino, Andrea Sorcini, Karim J. Hamawy, Ali Moinzadeh, David Canes, Jason R. Gee
Lahey Clinic, Burlington, MA

3:42 pm – 3:45 pm

P34. Smoking Knowledge Assessment and Cessation Trends in Patients with Bladder Cancer Presenting to a Tertiary Referral Center
Mark S. Hockenberry[1], Thomas J. Guzzo[1], Phillip Mucksavage[2], Trinity J. Bivalacqua[3], Mark P. Schoenberg[3]
[1]*University of Pennsylvania School of Medicine, Philadelphia, PA;* [2]*University of California, Irvine, CA;* [3]*Johns Hopkins School of Medicine, Baltimore, MD*

P35. Perioperative Systemic Chemotherapy Confers a Cancer-Specific Survival Benefit in T3 Urothelial Carcinoma of the Renal Pelvis
Mohummad Minhaj Siddiqui, Richard J. Lee, Shulin Wu, Chin-Lee Wu, Adam S. Feldman
Massachusetts General Hospital, Boston, MA

P36. The Impact of Tumor Size on the Rate of Synchronous Metastasis and Survival in Renal Cell Carcinoma Patients - A Population Based Study
Johann P. Ingimarsson[1], Sverrir Hardarson[2], Vigdis Petursdottir[2], Eirikur Jonsson[2], Gudmundur V. Einarsson[2], Tomas Gudbjartsson[2]
[1]*Dartmouth-Hitchcock Medical Center, Lebanon, NH;* [2]*Landspitali University Hospital, Reykjavik, Iceland*

P37. Hand Assisted vs Robotic Assisted Laparoscopic Partial Nephrectomy; Comparison of Short-Term Outcomes
Sammy E. Elsamra, **Andrew Leone**, Michael Lasser, Simone Thavaseelan, George Haleblian, Gyan Pareek
Warren Alpert Medical School of Brown University, Providence, RI

P38. The Impact of the Learning Curve on Robot Assisted Pelvic Lymph Node Dissection during Radical Prostatectomy: An Update on the Brown University Experience
George A. Turini III, Simone Thavaseelan, Michael S. Lasser, Joseph F. Renzulli II, Gyan Pareek, George E. Haleblian
Brown University, Providence, RI

3:45 pm – 3:48 pm

P39. Radical Prostatectomy Outcomes in Men Aged 70 or Older with Low-Risk Prostate Cancer
Jeffrey K. Mullins, Misop Han, Alan W. Partin, Patrick C. Walsh, H. Ballentine Carter
Johns Hopkins Medical Institutions, Baltimore, MD

P40. Should Anterior Prostatic Fat During Radical Prostatectomy Undergo Pathological Examination?
Brooke A. Harnisch[1], Kevin Tomera[2], Ingolf A. Tuerk[2]
[1]*Boston University School of Medicine and Boston Medical Center, Boston, MA;* [2]*St. Elizabeth's Medical Center, Brighton, MA*

3:48 pm – 3:51 pm

P41. Directed Prostate Biopsies Utilizing Contrast-Enhanced Ultrasound with Flash Replenishment Imaging
Xiaolong S. Liu[1], Ethan J. Halpern[2], Flemming Forsberg[2], Leonard G. Gomella[1], Edouard J. Trabulsi[1]
[1]*Thomas Jefferson University, Department of Urology, Philadelphia, PA;* [2]*Thomas Jefferson University, Department of Radiology, Philadelphia, PA*

P42. Changes in Pre-operative and Pathologic Characteristics in Patients Undergoing Radical Prostatectomy by Era
John B. Eifler, Jr., Elizabeth B. Humphreys, Alan W. Partin, Misop Han
Brady Urological Institute, Baltimore, MD

3:51 pm – 3:54 pm
P43. Long-term Prognostic Significance of Close Prostatectomy Margins
Gregory J. Wirth, Jian Lu, Shulin Wu, Aria Olumi, Chin-Lee Wu
Massachusetts General Hospital, Boston, MA

3:54 pm – 3:57 pm
P44. Validation in CaPSURE of Predicted Sexual Outcome after Primary Prostate Cancer Treatment by PROSTQA
Mehrdad Alemozaffar[1], Meredith M. Regan[2], Natalia Sadetsky[3], Peter Carroll[3], Martin G. Sanda[1], Matt Cooperberg[3]
[1]*Beth Israel Deaconess Medical Center, Boston, MA;* [2]*Dana Farber Cancer Institute, Boston, MA;* [3]*University of California San Francisco, San Francisco, CA*

P45. Nationwide Comparison of Operative Outcomes for Robotic, Laparoscopic, and Open Radical Prostatectomy
Mehrdad Alemozaffar[1], Martin G. Sanda[1], Derek Yecies[2], Meir J. Stampfer[3], Stacey A. Kenfield[3]
[1]*Beth Israel Deaconess Medical Center, Boston, MA;* [2]*Boston University Medical School, Boston, MA;* [3]*Harvard School of Public Health, Boston, MA*

P46. Predictors of Positive Retroperitoneal Lymph Nodes in Patients with High Risk Testicular Cancer
Ravi Kacker, Stephen Williams, Graeme S. Steele, Jerome P. Richie
Brigham and Women's Hospital, Boston, MA

3:57 pm – 4:00 pm
P47. Determinants of the Adoption of Minimally Invasive Radical Prostatectomy in the United States
William D. Ulmer[1], Sandip Prasad[2], Xiangmei Gu[3], Stuart Lipsitz[4], Jim C. Hu[5]
[1]*Harvard Medical School, Boston, MA;* [2]*University of Chicago Medical Center, Chicago, IL;* [3]*The Center for Surgery and Public Health, Brigham and Women's Hospital, Boston, MA, Boston, MA;* [4]*The Center for Surgery and Public Health, Brigham and Women's Hospital, Boston, MA;* [5]*Division of Urologic Surgery, Brigham and Women's Hospital, Boston, MA*

4:00 pm – 4:45 pm
PAUL SCHELLHAMMER LECTURE ON UROLOGIC ONCOLOGY
Swan Ballroom I-IV
Some Possibly Heretical Observations about Local Control and New Therapies in Prostate Cancer
Paul H. Lange, MD
University of Washington School of Medicine, Seattle, WA

4:45 pm – 5:45 pm
PRODUCT SHOWCASE: PRESENTATIONS BY INDUSTRY EXPERTS/SCIENTISTS
Swan Ballroom I-IV

5:45 pm – 7:15 pm **WELCOME RECEPTION**
Swan Ballroom V-X

7:15 pm – 8:15 pm
YOUNG UROLOGISTS FORUM:
Jeopardy – New England vs. Mid-Atlantic Residents
Pelican
Moderators: Tracey L. Krupski, MD
University of Virginia, Charlottesville, VA
Joshua M. Stern, MD
Mystic Valley Urology Associates, Stoneham, MA
Section Resident Committee Representatives:
Tiffany M. Sotelo, MD
George Washington University, Washington, DC
John A. Taylor, III, MD
University of Connecticut Health Center, Farmington, CT

FRIDAY, NOVEMBER 4, 2011

6:30 am – 2:00 pm **REGISTRATION**

7:00 am – 8:00 am
CONCURRENT BREAKFAST SYMPOSIUM
Swan Ballroom I-IV
Identifying Bone Metastases and Preventing Skeletal-related Events in Prostate Cancer
Supported by Amgen

7:00 am – 8:00 am
CONCURRENT BREAKFAST SYMPOSIUM
Pelican
Testosterone Suppression: An Innovative Approach
Supported by Ferring

7:30 am – 8:00 am
CONTINENTAL BREAKFAST, VISIT EXHIBITS
Swan Ballroom V-X

7:30 am – 12:15 pm **EXHIBITS OPEN**
Swan Ballroom V-X

7:50 am – 8:00 am
SESSION HIGHLIGHTS FROM THURSDAY
Swan Ballroom I-IV

8:00 am – 12:00 pm **HOSPITALITY SUITE**
Macaw & Terrace

8:00 am – 9:20 am
SCIENTIFIC SESSION IV:
RESIDENT PRIZE ESSAY COMPETITION
Swan Ballroom I-IV
Moderators: Adam P. Klausner, MD
Virginia Commonwealth University Medical Center, Richmond, VA
Adam S. Feldman, MD
Massachusetts General Hospital, Boston, MA

7 minute presentations, 3 minute discussions

8:00 am

29. Complications of Pediatric Urologic Minimally Invasive Surgery
Shailen Sehgal[1], Matthew Christman[2], Pasquale Casale[2]
[1]*University of Pennsylvania, Philadelphia, PA;* [2]*Children's Hospital of Philadelphia, Philadelphia, PA*

8:10 am

30. Erythrocytosis and Testosterone Therapy: The Influence of Treatment Modality and Body Composition
Ravi Kacker[1], William Conners[2], Abraham Morgentaler[2]
[1]*Brigham and Women's Hospital, Boston, MA;* [2]*Men's Health Boston, Boston, MA*

8:20 am

31. Accelerated Gastrointestinal Recovery with Use of Alvimopan after Radical Cystectomy with Urinary Diversion
Anup A. Vora[1], Andrew Harbin[1], Robert Rayson[1], Keith Christiansen[1], Reza Ghasemian[2], Jonathan Hwang[1], Mohan Verghese[1]
[1]*Georgetown University, Washington, DC;* [2]*Washington Hospital Center, Washington, DC*

8:30 am

32. Complications of Salvage Cystectomy after Failed Bladder-Sparing Therapy for Muscle-Invasive Bladder Cancer
Jairam R. Eswara, Jason Efstathiou, Niall Heney, Jonathan Paly, Donald Kaufman, W. Scott McDougal, Francis McGovern, William Shipley
Massachusetts General Hospital, Boston, MA

8:40 am

33. Objective Measures of Renal Mass Anatomic Complexity Predict Rates of Major Complications Following Partial Nephrectomy
Jay Simhan, Marc C. Smaldone, Kevin J. Tsai, Daniel J. Canter, Tianyu Li, Alexander Kutikov, Rosalia Viterbo, David Y.T. Chen, Richard E. Greenberg, Robert G. Uzzo
Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, PA

8:50 am

34. Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP): Development and Validation of a Practical Health-Related Quality of Life Instrument for Use in the Routine Clinical Care of Prostate Cancer Patients
Peter Chang[1], Konrad M. Szymansk[2], Jonathan J. Chipman[3], Mark S. Litwin[4], Paul L. Nguyen[5], Robert Cook[6], Andrew A. Wagner[7], William C. DeWolf[7], John T. Wei[8], Martin G. Sanda[7]
[1]*Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Boston, MA;* [2]*McGill University Health Centre, Montreal, QC, Canada;* [3]*Dana-Farber Cancer Institute, Boston, MA;* [4]*David Geffen School of Medicine and School of Public Health, University of California-Los Angeles, Los Angeles, CA;* [5]*Brigham and Women's Hospital/Dana Farber Cancer Institute, Boston, MA;* [6]*Seven Hills Urology, Centra Health, Lynchburg, VA;* [7]*Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA;* [8]*University of Michigan School of Medicine, Ann Arbor, MI*

9:00 am

35. Ability of Ureteroscopic Biopsy to Accurately Grade and Stage Upper Tract Urothelial Carcinoma Lesions: Results from a Multi-institutional Cohort of Patients
Thomas Clements, Jamie Messer, Jay Raman
Milton S. Hershey Medical Center, Hershey, PA

9:10 am

36. Bilateral Same-Session Ureteroscopy: Safety and Efficacy
Jessica E. Kreshover[1], Jules Manger[2], Richard K. Babayan[1], David S. Wang[1]
[1]*Boston University Medical Center, Boston, MA;* [2]*University of Virginia Health System, Charlottesville, VA*

9:20 am – 10:10 am
SCIENTIFIC SESSION V: LAPAROSCOPY/ROBOTICS
Swan Ballroom I-IV
Moderators: Daniel Eun, MD
Pennsylvania Hospital, Philadelphia, PA
David S. Wang, MD
Boston Medical Center, Boston, MA

9:20am – 9:25am
HIGHLIGHTS FROM WASHINGTON D.C. – LAPAROSCOPY/ROBOTICS
Vernon Orton, III, MD
Virginia Commonwealth University Medical Center, Richmond, VA

9:25 am – 10:10 am
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

9:25 am
37. Should Robotic Assisted Radical Prostatectomy Be Extraperitoneal Like Open Surgery?
Kevin Tomera[1], Brooke A. Harnisch[2], Jaspreet Batra[1], Ingolf Tuerk[1]
[1]*St. Elizabeth's Medical Center, Brighton, MA;* [2]*Boston University and Boston Medical Center, Boston, MA*

9:32 am
38. Oncologic Outcome of Laparoscopic and Open Radical Prostatectomy
Gregory J. Wirth, Sarah P. Psutka, Shulin Wu, Chin-Lee Wu, Douglas M. Dahl
Massachusetts General Hospital, Boston, MA

9:39 am
39. Comparison of Extraperitoneal and Transperitoneal Pelvic Lymph Node Dissection During Minimally Invasive Radical Prostatectomy
Jeffrey K. Mullins, M. Eric Hyndman, Lynda Z. Mettee, Christian P. Pavlovich
Johns Hopkins Medical Institutions, Baltimore, MD

9:46 am
40. The Impact of Prostate Size, Median Lobe, and Prior Benign Prostatic Hyperplasia Intervention on Robotic-Assisted Radical Prostatectomy: Technique and Outcomes
Keith J. Kowalczyk, Andy C. Huang, Nathanael D. Hevelone, Stuart R. Lipsitz, Hua-yin Yu, Blakely A. Plaster, Channa A. Amarasekara, William D. UImer, Stephen B. Williams, Jim C. Hu
Brigham and Women's Hospital/Harvard Medical School, Boston, MA

9:53 am
41. Robotic Pyeloplasty in Adults over 50 Years-Old: Outcomes Compared to a Younger Cohort
F. Cameron Hill, **Jules P. Manger**, Noah S. Schenkman
University of Virginia, Charlottesville, VA

10:00 am
42. The Safety of Aspirin in the Perioperative Period in Urologic Robotic Surgery
Ankur Parikh, Yvette Henry, Peter Berger, Daniel Rukstalis
Geisinger Medical Center, Danville, PA

9:20 am – 10:10 am
CONCURRENT SCIENTIFIC SESSION II: IMPOTENCE/ PENO-SCROTAL SURGERY
Pelican
Moderators: Andrew Charles Kramer, MD
University of Maryland Medical Center, Baltimore, MD
Nelson Bennett, Jr., MD
Institute of Urology, Burlington, MA

5 minute presentations, 2 minute discussions

9:20 am
43. Microvascular Arterial Bypass Surgery: Prospective Outcomes Study Using Validated Instruments
Christopher E. Graziano, **Ricardo Munarriz**
Boston Medical Center, Boston, MA

9:27 am
44. 10-year Analysis of Adverse Event Reports to the Food and Drug Administration Related to the use of Phosphodiesterase Type-5 Inhibitors
Gregory Lowe, Raymond Costabile
University of Virginia, Charlottesville, VA

9:34 am
45. Outcomes of Surgical Management for Perineal Gangrene
Jairam R. Eswara, W. Scott McDougal
Massachusetts General Hospital, Boston, MA

9:41 am
46. VED Registry in Men Treated for Prostate Cancer: Initial Results of a Prospective, Multi-institutional Dataset
Edouard J. Trabulsi[1], John C. Rewcastle[2], Gerry Brock[3], Craig Donatucci[4], Run Wang[5], John Mulhall[6]
[1]*Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA;* [2]*University of Southern California, Los Angeles, CA;* [3]*University of Western Ontario, London, ON, Canada;* [4]*Duke University, Durham, NC;* [5]*University of Texas Medical School at Houston, Houston, TX;* [6]*Memorial Sloan-Kettering Cancer Center, New York, NY*

9:48 am

47. Urethral Reconstruction Outcomes Using Patient Reported Preoperative and Postoperative Questionnaires in Combination with Uroflometry
Jessica DeLong, Jill Buckley
The Lahey Clinic, Burlington, MA

9:55 am

48. Post-Operative Complications of the Exaggerated Lithotomy Position
Mary H. James, Paul D. McAdams, Britton E. Tisdale, Gerald H. Jordan, Kurt A. McCammon
Eastern Virginia Medical School, Norfolk, VA

10:00 am – 10:30 am **COFFEE BREAK**
VISIT EXHIBITS
Swan Ballroom V-X

10:30 am – 11:20 am
HUGH HAMPTON YOUNG LECTURE
Swan Ballroom I-IV
The First Successful Orchidopexy: When, Where and Why?
David A. Bloom, MD
University of Michigan, Ann Arbor, MI

11:20 am – 12:15 pm
SCIENTIFIC SESSION VI: SOCIOECONOMICS/PRACTICE MANAGEMENT
Swan Ballroom I-IV
Moderators: Stephen F. Schiff, MD
Urologic Surgeons of New England, Providence, RI
Tiffany M. Sotelo, MD
George Washington University, Washington, DC

5 minute presentations, 2 minute discussions

11:20 am

49. "Never Events" - The Incidence and Cost Implications of "Preventable" Complications in an Academic Urology Practice
Elias Hyams, Brian Matlaga
Brady Urological Institute, Johns Hopkins School of Medicine, Baltimore, MD

11:27 am

50. "Academic Ranking Score": A Reproducible Metric of Thought Leadership in Urology
Alexander Kutikov, Boris Rozenfeld, Jay Simhan, **Jose Reyes**, Brian L. Egleston, Mohit Sirohi, Raymond Hwang, Robert G. Uzzo
Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, PA

11:34 am

51. Influence of Surgeon and Hospital Volume on Radical Prostatectomy Costs
Stephen B. Williams, Channa A. Amarasekera, Xiangmei Gu, Stuart R. Lipsitz, Paul L. Nguyen, **Keith J. Kowalczyk**, Jim C. Hu
Brigham and Women's Hospital, Boston, MA

11:41 am

52. Cost-effectiveness of Percutaneous Renal Mass Biopsy to Guide the Management of Small Solid Renal Masses (≤4cm)
Steven L. Chang[1], Toni K. Choueiri[2], Michelle S. Hirsch[1], Stuart G. Silverman[1]
[1]*Brigham and Women's Hospital, Boston, MA;* [2]*Dana-Farber Cancer Institute, Boston, MA*

11:48 am

53. Impact of Poverty Level and Education on 24-hour Urine Composition in Patients with Nephrolithiasis
Brian H. Eisner[1], Sonali Sheth[1], Stephen P. Dretler[1], Benjamin Herrick[2], Vernon M. Pais, Jr.[3]
[1]*Massachusetts General Hospital, Boston, MA;* [2]*Dartmouth Hitchcock Medical Center, Lebanon, NH;* [3]*Dartmouth Hitchcock Medical Center, Lebanon, NJ*

11:55 am

54. Cost Comparison of Hand Assisted (HALPN) vs Robotic Assisted Laparoscopic Partial Nephrectomy (RALPN)
Sammy E. Elsamra, Andrew Leone, Michael Lasser, Simone Thavaseelan, George Haleblian, Gyan Pareek
Warren Alpert Medical School of Brown University, Providence, RI

12:02 pm

55. Measurement of Spatial Distribution in Prostate Biopsy
Misop Han, Chunwoo Kim, Doyoung Chang, Hyungju Kim, Doru Petrisor, Dan Stoianovici
Johns Hopkins Medical Institutions, Baltimore, MD

11:20 am – 12:15 pm
CONCURRENT POSTER SESSION III: NON-ONCOLOGIC DISEASES
Mockingbird
Moderators: Mark K. Plante, MD
Fletcher Allen Health Care, Burlington, VT
Christine L. Sears, MD
National Naval Medical Center, Bethesda, MD

11:20 am – 11:30 am **POSTER VIEWING TIME**

11:30 am – 12:15 pm
POSTER PRESENTATIONS
Posters listed with times will be giving a two minute oral presentation followed by a one minute discussion

11:30 am – 11:33 am

P48. Association of Bladder Sensation Measures and Bladder Diary in Patients with Urinary Incontinence
Ashley B. King[1], Jeffrey P. Wolters[1], Adam P. Klausner[1], David E. Rapp[2]
[1]*Virginia Commonwealth University, Richmond, VA;* [2]*Virginia Urology Center for Incontinence and Pelvic Floor Reconstruction, Richmond, VA*

P49. Bladder Compliance in Men with Lower Urinary Tract Symptoms
Kristina Wittig[1], Jerry Blaivas[2], Jeffrey Weiss[3], Georgia Panagopoulos;[4]
[1]*University of Connecticut Health Center, Farmington, CT;* [2]*Weill Cornell Medical Center, New York, NY;* [3]*SUNY Downstate, Brooklyn, NY;* [4]*Lenox Hill, New York, NY*

P50. Predictive Factors for Patient Satisfaction with Sacral Neuromodulation in Chronic Voiding Dysfunction
Michelle L. Ramirez, Michelle L. Persun, Phillip C. Ginsberg, Richard C. Harkaway
Albert Einstein Medical Center, Philadelphia, PA

11:33 am – 11:36 am

P51. The Association Between Psychological and Lower Urinary Tract Symptoms: A Population Based Study in Finland
Andrew Winer[1], Johnson Tsui[1], Fernando Cabrera[1], Jeffrey P. Weiss[1], Kari A. O. Tikkinen[2]
[1]*SUNY Downstate, New York, NY;* [2]*Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland*

P52. Recurrent Urinary Tract Infection in Intermittently Catheterized Spinal Cord Injury Patients
Leonard U. Edokpolo, Karen B. Stavris, Harris E. Foster, Jr.
Yale University School of Medicine, New Haven, CT

11:36 am – 11:39 am

P53. A Once-daily Titratable Gel Formulation for Transdermal Oxybutynin Delivery for OAB
David R. Staskin[1], Evan Goldfisher[2], Kaushik Dave[3]
T*ufts University School Of Medicine, Boston, MA;* [2]*Hudson Valley Urology, Poughkeepsie, NY;* [3]*Antares Pharma, Ewing, NJ*

11:39 am – 11:42 am

P54. Presentation and Management of Complications of Male Perineal Slings: Are Complications Under-reported?
Arthur Mourtzinos[1], William I. Jaffe[2]
[1]*Lahey Clinic Medical Center, Burlington, MA;* [2]*Pennsylvania Presbyterian Medical Center, Philadelphia, PA*

11:42 am – 11:45 am

P55. Effect of Percutaneous Tibial Nerve Stimulation on Fecal Incontinence: Results from a Double-Blind, Randomized, Sham-Controlled Trial for Over Active Bladder
Jeffrey A. Ranta[1], Ken Peters[2], Donna Carrico[2]
[1]*Greenwich Urological Assoc. P.C., Greenwich, CT;* [2]*William Beaumont Medical Center, El Paso, TX*

11:45 am – 11:48 am

P56. Differential Diagnosis of Overactive Bladder in Women
Brian K. Marks[1], Jerry G. Blaivas[2], **Fernando Cabrera**[1], Johnson F. Tsui[1], Jeffrey P. Weiss[1]
[1]*SUNY Downstate, Brooklyn, NY;* [2]*Urology, Weill Cornell Medical College, New York, New York, NY*

P57. Does Patient Obesity Impact the Effectiveness of Extracorporeal Shockwave Lithotripsy?
Eugene Kramolowsky[1], Nada L. Wood[1], Mark Monahan[1], Ruth Butler[1], Susan Taylor[2]
[1]*Virginia Urology, Richmond, VA;* [2]*Washington and Lee University, Lexington, VA*

11:48 am – 11:51 am

P58. Risk of Infection Stones in Patients with Non-Obstructing Renal Stones
Boris Gershman, Jairam R. Eswara, Dianne E. Sacco
Massachusetts General Hospital, Boston, MA

11:51 am – 11:54 am

P59. Contemporary 24-hour Urine Collection Analysis Reveals High Risk Stone Formers May Be at Increased Risk for Recurrence in Summer and Winter Months
Sammy E. Elsamra, Michael Lasser, Simone Thavaseelan, George Haleblian, Gyan Pareek
Warren Alpert Medical School of Brown University, Providence, RI

11:54 am – 11:57 am

P60. Submilisievert Computed Tomography for the Evaluation of Urolithiasis
Brian H. Eisner, Naveen Kulkarni, Daniella Pinho, Guarav Desai, Raul Uppot, Dushyant V. Sahani
Massachusetts General Hospital, Boston, MA

P61. The Impact of Body Mass Index Reduction on 24-Hour Urine Parameters
Michael M. Maddox, Simone Thavaseelan, Gyan Pareek, George Haleblian
Brown University, Providence, RI

11:57 am – 12:00 pm

P62. Management of Residual Fragments Following Percutaneous Nephrolithotomy: A Cost Analysis
Michelle J. Semins, **Elias Hyams**, Brian R. Matlaga
Johns Hopkins Hospital, Baltimore, MD

P63. Percutaneous Nephrolithotomy (PCNL) in the Septuagenarian, Octogenarian and Nonagenarian is Safe: Outcomes and Complications
Shubha De[1], Simone Thavaseelan[2], **Liza Aguiar[2]**, Gyan Pareek[2], George Haleblian[2]
[1]*Dalhousie University, Halifax, NS, Canada;* [2]*Brown University, Providence, RI*

12:00 am – 12:03 pm

P64. Baseline Body Mass Index (BMI) has no Effect upon Normalization of Testosterone Concentrations with Testosterone 2% Gel
Adrian Dobs[1], John McGettigan[2], Paul Norwood[3], Susan Potts[4], Errol Gould[4]
[1]*The John Hopkins University, Baltimore, MD;* [2]*Quality of Life Medical and Research Center, Tucson, AZ;* [3]*Valley Endocrine and Valley Research, Fresno, CA;* [4]*Endo Pharmaceuticals, Chadds Ford, PA*

P65. Penile Prosthesis Placement in Patients with Corporal Fibrosis Secondary to Infection, Peyronie's disease, or Priapism: Techniques, Outcomes, and Complications
Vikrant Uberoi, Ricardo Munarriz
Boston University, Boston, MA

12:03 pm – 12:06 pm

P66. Outcomes of KTPLAP and TURP in Patients with Impaired Detrusor Contractility
Daniel A. Thorner, **Fernando Cabrera**, Jerry G. Blaivas, Johnson Tsui, Dmitry Volkin, Jeffrey P. Weiss
SUNY Downstate, Brooklyn, NY

12:06 pm – 12:09 pm

P67. Nocturia Reduction after Cooled ThermoTherapy for Symptomatic Benign Prostatic Hyperplasia
Aaron F. Brafman[1], Stephen J. Eyre[2], Lori B. Lerner[3]
[1]*Boston University School of Medicine, Boston, MA;* [2]*Brigham, Boston, MA;* [3]*VA Boston Healthcare System, Boston, MA*

12:09 pm – 12:12 pm

P68. Efficacy and Safety Follow-Up Results 3 - 7 1/2 Years after Single Treatment with Transrectal NX-1207 in Multi-Center Prospective Blinded Randomized Controlled Studies of Men with Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia
Neal Shore[1], Sheldon Freedman[2], Barton Wachs[3], **Barrett Cowan[4]**
[1]*Carolina Urologic Research Center, Myrtle Beach, SC;* [2]*Sheldon Freedman, MD LTD, Las Vegas, NV;* [3]*Atlantic Urology Medical Group, Long Beach, CA;* [4]*Urology Associates, Englewood, CO*

P69. Rapid Ambulatory Pathway Laser Prostatectomy is Safe- Results within the Global Period
Cullen Jumper[1], Paul Snyder[2], **Ronald Yap[2]**
[1]*Dartmouth-Hitchcock Medical Center, Lebanon, NH;* [2]*Concord Hospital Center for Urologic Care, Concord, NH*

P70. Northern New England Renal Trauma: How it Differs from the Big City
Elizabeth B. Johnson, Levi A. Deters, Paul A. Merguerian
Dartmouth Hitchcock Medical Center, Lebanon, NH

P71. Prospective Robotically-Assisted Laparoscopic Pyeloplasty Analysis in Pediatrics
Kelly Chiles[1], Katherine W. Herbst[2], Christina Kim[2]
[1]*University of Connecticut, Farmington, CT;* [2]*Connecticut Children's Medical Center, Hartford, CT*

12:12 pm – 12:15 pm

P72. Effects of Spinal Cord Detethering on Children with Currarino Syndrome
Nora G. Lee, Joseph G. Borer, Carlos R. Estrada, Shahram Khoshbin, Stuart B. Bauer
Children's Hospital Boston, Boston, MA

12:15 pm – 1:45 pm
X-RAY AND PATHOLOGY COMPETITION
Swan Ballroom I-IV
Chairs: Robert A. Older, MD
University of Virginia, Charlottesville, VA
Robert H. Young, MD
Massachusetts General Hospital, Boston, MA

12:15 pm – 1:45 pm
AUA COURSE OF CHOICE: UPDATE ON AUA-CANCER RELATED GUIDELINES PREPARATION FOR CERTIFICATION
Pelican
Speakers: Sam Chang, MD
Vanderbilt University School of Medicine, Nashville, TN
Thomas J. Guzzo, MD
University of Pennsylvania, Philadelphia, PA
Dinesh Singh, MD
Yale University School of Medicine, New Haven, CT

1:45 pm **ADJOURN: FREE AFTERNOON**

1:00 pm – 5:00 pm **GOLF TOURNAMENT**
Celebration Golf Course

2:00 pm – 4:00 pm **TENNIS TOURNAMENT**
Tennis Courts

6:30 pm – 10:00 pm **AROUND THE WORLD DINNER**
Lake Terrace

SATURDAY, NOVEMBER 5, 2011

6:30 am – 12:00 pm **REGISTRATION**

7:00 am – 8:00 am
BREAKFAST SYMPOSIUM
Pelican Room
Current Treatment Options for Patients with BCG-Refractory CIS of the Urinary Bladder and Advanced Prostate Cancer
Supported by Endo Pharmaceuticals

7:30 am – 12:00 pm **EXHIBITS OPEN**
Swan Ballroom V-X

7:30 am – 8:00 am **CONTINENTAL BREAKFAST VISIT EXHIBITS**
Swan Ballroom V-X

8:00 am – 12:00 pm **HOSPITALITY SUITE**
Macaw & Terrace

8:00 am – 8:30 am **NEAUA BUSINESS MEETING**
Swan Ballroom I-IV

8:00 am – 8:30 am **MAAUA BUSINESS MEETING**
Pelican

8:30 am – 8:40 am **SESSION HIGHLIGHTS FROM FRIDAY**
Swan Ballroom I-IV

8:40 am – 9:45 am
SCIENTIFIC SESSION VII: URO-ONCOLOGY II (Renal & Urothelial Cancer)
Swan Ballroom I-IV
Moderators: Jay D. Raman, MD
Pennsylvania State/Hershey Medical Center, Hershey, PA
Andrew A. Wagner, MD
Beth Israel Deaconess Medical Center, Boston, MA

8:40am – 8:45am
HIGHLIGHTS FROM WASHINGTON D.C. – URO-ONCOLOGY II (Renal & Urothelial Cancer)
Steven L. Chang, MD, MS
Brigham and Women's Hospital, Boston, MA

8:45 am – 9:30 am
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

8:45 am
56. Cost Comparison of Open, Laparoscopic, and Robot-assisted Partial Nephrectomy
Mehrdad Alemozaffar[1], Steven L. Chang[2], Mayellen Sun[1], Ravi Kacker[1], Andrew A. Wagner[1]
[1]*Beth Israel Deaconess Medical Center, Boston, MA;* [2]*Brigham and Women's Hospital, Boston, MA*

8:52 am
57. Multi-Institutional Validation of the Predictive Value of Preoperative Hydronephrosis for Advanced Stage Upper-Tract Urothelial Carcinoma
Thomas Clements, Jamie Messer, Jay Raman
Milton S. Hershey Medical Center, Hershey, PA

8:59 am
58. Pathologic Down-staging with Gemcitabine and Cisplatin Neoadjuvant Chemotherapy for Muscle-Invasive Urothelial Carcinoma of the Bladder
Sarah P. Psutka, Aria F. Olumi, Adam S. Feldman, Philip Saylor, Donald Kaufman, Richard J. Lee
Massachusetts General Hospital, Boston, MA

9:06 am

59. Safety and Efficacy of Robot-Assisted Partial Nephrectomy: A Large Single Institution Experience

Kevin J. Tsai, Jay Simhan, Marc C. Smaldone, Alexander Kutikov, David Y.T. Chen, Robert G. Uzzo, Rosalia Viterbo
Fox Chase Cancer Center, Philadelphia, PA

9:13 am

60. Positive Surgical Margins after Partial Nephrectomy for pT1 Localized Renal Cell Carcinoma: Local Recurrence and RCC-Specific Survival

William C. Faust, Patrick A. Kenney, Eric Burks, Calvin Chen, Alireza Moinzadeh, John A. Libertino
Lahey Clinic, Cambridge, MA

9:20 am

61. Ureteral Stent Placement at the Time of Urinary Diversion Decreases Post-Operative Morbidity

Jeffrey K. Mullins[1], Thomas J. Guzzo[2], Mark W. Ball[1], Phillip M. Pierorazio[1], John B. Eifler[1], Thomas W. Jarrett[3], Mark P. Schoenberg[1], Trinity J. Bivalacqua[1]
[1]*Johns Hopkins Medical Institutions, Baltimore, MD;* [2]*University of Pennsylvania, Philadelphia, PA;* [3]*The George Washington University, Washington*

9:30am – 9:45am
POINT/COUNTERPOINT
The Role of Biopsy in Renal Masses

Biopsy
Peter A. Pinto, MD
National Cancer Institute, Washington, DC

Observation or Intervention
Douglas M. Dahl, MD
Massachusetts General Hospital, Boston, MA

8:40 am – 9:45 am
CONCURRENT SCIENTIFIC SESSION III: PEDIATRICS
Pelican
Moderators: Jonathan A. Roth, MD
Urology for Children, Voorhees, NJ
Adam Hittleman, MD
Yale University School of Medicine, New Haven, CT

8:40 am – 8:45 am
HIGHLIGHTS FROM WASHINGTON D.C. – PEDIATRICS
Bartley G. Cilento, Jr., MD, FACS
Children's Hospital, Boston, MA

8:45 am – 9:30 am
ABSTRACT PRESENTATIONS
5 minute presentations, 2 minute discussions

8:45 am

62. Fetal Closure of Myelomeningocele Does Not Improve Lower Urinary Tract Function

Vikrant Uberoi[1], Nora G. Lee[1], Pablo Gomez[2], Paul J. Kokorowski[2], Shahram Khoshbin[3], Stuart B. Bauer[2], Carlos R. Estrada[2]
[1]*Boston University, Boston, MA;* [2]*Children's Hospital Boston, Boston, MA;* [3]*Brigham and Women's Hospital, Boston, MA*

8:52 am

63. Incidence of Repeat Dextranomer/Hyaluronic Acid Copolymer Injection Among Pediatric Health Information System Hospitals

Katherine Herbst[1], John H. Makari[2], Christina Kim[2], Fernando Ferrer[2], Anthony Caldamone[3]
[1]*Connecticut Children's Medical Center, Hartford, CT;* [2]*Connecticut Children's Medical Center/University of Connecticut Health Center, Hartford/Farmington, CT;* [3]*Hasbro Children's Hospital/Brown University School of Medicine, Providence, RI*

8:59 am

64. Renal Trauma in Children: Mechanism of Injury and Outcomes at a Rural Northern New England Level I Trauma

Elizabeth B. Johnson, Levi A. Deters, Paul A. Merguerian
Dartmouth-Hitchcock Medical Center, Lebanon, NH

9:06 am

65. Comparing Minimally Invasive Surgery for Vesicoureteral Reflux: Dextranomer Hyaluronic Acid Injection Versus Robotically-assisted Laparoscopic Ureteral Reimplantation

Kelly Chiles[1], Katherine W. Herbst[2], John H. Makari[2], Fernando A. Ferrer[2], Christina Kim[2]
[1]*University of Connecticut, Farmington, CT;* [2]*Connecticut Children's Medical Center, Hartford, CT*

9:13 am

66. Repair of Complex Hypospadias Using Buccal Mucosa Grafts

Spencer I. Kozinn[1], Alan Retik[2], Richard Lee[2], Bartley Cilento[2], Stuart Bauer[2], Joseph Borer[2], Sohee Kim[2], David Diamond[2]

[1]Lahey Clinic, Burlington, MA; [2]Childrens Hospital Boston, Boston, MA

9:20 am

67. Evaluation of Urethral Stricture Disease in a Pediatric Population Using Sonographic Voiding Urethography

Luriel I. Smith-Harrison, Jessica Hammett, Sean Corbett, Laurence Watson

University of Virginia, Charlottesville, VA

9:30am – 9:45am

POINT/COUNTERPOINT

Laparoscopic Robotic Assisted vs. Open Infant Pyeloplasty

Laparoscopic Robotic Assisted Infant Pyeloplasty

Sarah M. Lambert, MD

The Children's Hospital of Philadelphia, Philadelphia, PA

Open Infant Pyeloplasty

Daniel B. Herz, MD

Dartmouth-Hitchcock Medical Center, Lebanon, NH

9:45 am – 10:15 am **COFFEE BREAK**
VISIT EXHIBITS
Swan Ballroom V-X

10:15 am – 11:00 am

NEAUA GUEST SPEAKER

Swan Ballroom I-IV

Fad Diets & Dietary Supplements: What Works and What is Worthless from A to Z?

Mark Moyad, MD

University of Michigan Medical Center, Ann Arbor, MI

11:00 am – 11:30 am

ETHICS PANEL DISCUSSION

Swan Ballroom I-IV

Moderators: David A. Diamond, MD
Children's Hospital, Boston, MA

Adam P. Klausner, MD
Virginia Commonwealth University Medical Center, Richmond, VA

Panel: David A. Diamond, MD
Children's Hospital, Boston, MA

Adam P. Klausner, MD
Virginia Commonwealth University Medical Center, Richmond, VA

Deborah J. Lightner, MD
Mayo Clinic, Rochester, MN

11:30 am – 12:00 pm

PRESIDENTIAL ADDRESS

Swan Ballroom I-IV

Timothy B. Hopkins, MD, NEAUA President
New England Section of the American Urological Association

Harry P. Koo, MD, MAAUA President
Mid-Atlantic Section of the American Urological Association

12:00 pm – 1:30 pm

LUNCH SYMPOSIUM

Swan Ballroom I-IV

Immunotherapy for the Treatment of Advanced Prostate Cancer

Supported by Dendreon

1:30 pm **ADJOURN**

3:00 pm – 5:00 pm **SECTION BEACH OLYMPICS**

6:30 pm – 7:30 pm **PRESIDENTS' RECEPTION**
Swan Ballroom V-X & Foyer

7:30 pm – 10:00 pm **PRESIDENTS' BANQUET**
Swan Ballroom V-X & Foyer

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1

Trends in Surgical Management of Benign Prostatic Hyperplasia

Nora Lee[1], Hui Xue[2], Lori B. Lerner[3]
[1]*Boston University Medical Center, Boston, MA;* [2]*Harvard University, Boston, MA;* [3]*Boston Veterans Affairs Hospital, Boston, MA*

Introduction: Surgical management of benign prostatic hyperplasia (BPH) has evolved, including techniques that can be used with the growing population of anticoagulated patients. We evaluated current trends in procedure utilization amongst American urologists.

Methods: A 90-item on-line survey was sent via email to: American Urological Association; Veterans Administration; Society for Government Service Urologists; Endourological Society. Data concerning utilization of 12 BPH surgical techniques were analyzed and compared to surgeons' demographics using categorical data analysis.

Results: 600 urologists replied; 570 currently perform BPH surgery. Table 1 shows procedure utilization. Urologists' age, year of residency completion, and region of country had no influence on technique utilization, except in Northeastern (less monopolar TURP, p=0.04) and New York Sections (less PVP, p=0.01). Academic versus private settings were no different other than RP and Button which occur more often in academics (RP 7% vs 2%, button TURP 28% vs 21%). High volume surgeons are more likely to perform monopolar and bipolar TURP, whereas low volume surgeons are more likely to perform PVP, HoLAP, and HoLEP.

Conclusions: Change in technology has altered urologists' surgical approach to BPH. OP and monopolar TURP are still the most utilized procedures, however, bipolar and laser therapies are becoming more common. Lower volume surgeons appear to perform more laser techniques. Academic programs did not influence preference in technique except with robotic surgery and Button.

TABLE 1.

Surgical technique	Percentage of respondents who utilize the procedure
Open prostatectomy	78%
Monopolar transurethral resection of prostate (TURP)	73%
Photoselective vaporization (PVP)	58%
TURis button TURP	24%
Bipolar TURP	20%
Holmium laser ablation of prostate (HoLAP)	18%
Holmium laser enucleation of prostate (HoLEP)	8%
Diode laser vaporization	8%
Thulium laser ablation of prostate	4%
Robotic simple prostatectomy	3%
Laparoscopic simple prostatectomy	1%
Thulium laser enucleation of prostate	0%

2

Prostate Atypia: Repeat Biopsy Results Within One Year of Diagnosis

Cory D. Harris[1], Stuart Kesler[2], Joseph R. Wagner[3]
[1]*University of Connecticut, Farmington, CT;* [2]*Harford Hospital, Hartford, CT;* [3]*Hartford Hospital, Hartford, CT*

Introduction: Atypical glands suspicious but not diagnostic for malignancy (atypia) is a descriptive term found in pathology reports of prostate needle biopsies. Prior reports suggest this finding carries a 40% risk of prostate cancer on subsequent biopsies. We investigated the incidence of atypia on biopsy specimens and pathologic findings on repeat biopsy.

Methods: We retrospectively reviewed our database of prostate needle biopsies performed from November 1987 to March 2011. 10,720 patients underwent 13,595 biopsies. 567 of the 10,720 patients (5.3%) had at least one biopsy with atypia; 623 of the 13,595 biopsies (4.6%) contained atypia. Patients undergoing a repeat prostate biopsy within one year of a diagnosis of atypia were identified. Patients with a prior history of prostate cancer were excluded.

Results: 284 patients met these inclusion criteria and underwent 305 sets of prostate biopsies within one year of a diagnosis of atypia. 103 patients (36%) were found to have prostate cancer. Rates of prostate cancer, atypia, high grade prostatic intraepithelial neoplasia, and benign histology are shown in Table 1. Pathologic results in 4 patients were unavailable.

Conclusions: Unlike high grade prostatic intraepithelial neoplasia, a significant number of men with atypia are found to have prostate cancer on repeat biopsy within one year. Immediate repeat biopsy should be recommended in this patient population.

TABLE 1.

Pathology Results on Repeat Biopsies for Atypia	
Total Number of Biopsies	305
Prostate cancer	103 (33.8%)
Atypia	56 (18.4%)
HPIN	18 (5.9%)
Benign	124 (40.7%)
Unknown	4 (1.3%)

3

Single Dose Intramuscular Ceftriaxone an Effective Alternative to Accepted Transrectal Prostate Biopsy Prophalaxsis

Ravi Kacker[1], Spender Platt[2], Micheal Kearney[2]
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[2]*Beth Israel Deaconess Medical Center, Boston, MA*

Introduction: Intramuscular Ceftriaxone 1gm given as a single dose immediately prior to transrectal prostate biopsy is an inexpensive, convenient, and effective form of prophylaxsis but currently is not included in the AUA Best Practice Statement and National Quality Forum (NQF) Consensus Standards. We report our experience using intramuscular Ceftriaxone in a multi-language, resident clinic where the rate of noncompliance with standard oral prophylaxsis has been historically high.

Materials & Methods: Retrospective chart review identified 234 men who underwent prostate biopsy between September 2009 and December 2010. 73 of these men received intramuscular Ceftriaxone prior to biopsy in resident clinic, whereas in private clinics at the same center 104 men received prophylaxsis with oral Bactrim plus Ciprofloxacin and 57 men received oral Ciprofloxacin alone. All patients were either seen in follow-up or called one week after biopsy. Infectious and non-infectious complications were determined from the chart.

Results: Of patients who received prophylaxis with oral Ciprofloxacin plus Bactrim and Ciprofloxacin alone, 2 (1.9%) and 1 (1.8%) respectively developed a postoperative febrile infection requiring hospital admission and treatment with intravenous antibiotics. No patients receiving intramuscular Ceftriaxone prophylaxis required admission for any postoperative complication. 1 patient who received Ceftriaxone and 1 patient who received Ciprofloxacin plus Bactrim were treated as outpatients with oral antibiotics for a nonfebrile urinary tract infection.

Conclusions: Bacterial resistance and the potential for noncompliance with patient-controlled prophylaxsis may lead to serious infectious complications after prostate biopsy. Intramuscular ceftriaxone offers a provider-controlled alternative equally effective as standard methods of surgical prophylaxsis.

4

A Prospective Single-Center 3 Year Study of the Efficacy and Safety of the GreenLight Laser HPS in Men with Clinical BPH

Gregg Eure
Eastern Virginia Medical School, Virginia Beach, VA

Introduction: To demonstrate safety and efficacy of treatment with the 532 nm KTP (120 watt) laser for patients with male lower urinary tract symptoms (LUTS) and clinical benign prostatic hyperplasia (BPH) in a prospective single surgeon study under a unified protocol.

Materials & Methods: A prospective, single-arm study with a single surgeon conducted in the US. Thirty-five consecutive patients were enrolled and 33 underwent treatment with the KTP 532 nm laser. The study included subjects aged ≥ 45 years who were indicated for surgical intervention for obstructive BPH. Subjects are followed at 3 months, 6 months, 1 year, and annually through 5 years. Mean age was 65.6±7.7 years.

Results: All actively participating subjects have completed at least 2 years of follow-up. Length of stay was 3.9±4.4 hrs, length of catheterization 21.7±3.2 hrs, procedure time was 55.9±23.4 min, and total energy used 189±84.8 kJ. The table shows baseline and follow-up data with mean±SD.

	Baseline	3 mo	6 mo	12 mo	24 mo
IPSS	23.8±4.7	7.8±4.5	5.0±3.2	6.1±4.6	6.6±4.5
QoL	4.4±1.2	1.3±1.3	1.0±1.1	0.9±1.0	1.3±1.0
Qmax (ml/s)	12.4±4.9	21.9±8.9	21.0±8.6	19.9±9.2	18.0±9.0
PVR (ml)	109.8±81.3	60.6±51.3	69.0±52.7	62.7±36.6	64.7±38.7
TRUS (cc)	67.2±31.5		34.7±22.8		
PSA	2.5±1.6		2.2±2.2	2.7±2.2	3.3±2.7

Adverse events were all mild including urgency, dysuria, retrograde ejaculation and hematuria with the exception of 1 bladder neck contracture.

Conclusions: In this single-center prospective single arm study, the 532 nm KTP laser provided 17.2 point (72.3%) improvement in IPSS at 24 mo, with a commensurate QoL improvement, reduction in PVR and improvement in Qmax, while inducing a volume decrease of 48.4%. Observed AEs were as expected for surgical ablation of prostate tissue.

5

Neurophysiologic Intraoperative Monitoring of Somatosensory Evoked Potentials to Detect Neurologic Injuries Due to Patient Positioning

Marc D. Manganiello, Jay Shils, Carl Borromeo, Jill C. Buckley
Lahey Clinic, Burlington, MA

Introduction: To determine if intraoperative somatosensory evoked potential (SSEP) monitoring could detect and prevent peripheral positioning related neuropathies in high risk urologic patients.

Materials & Methods: 64 patients underwent urethral reconstruction and intraoperative neuromonitoring by a single surgeon from March 2009 through August 2010. Electrodes were placed at the wrist to stimulate peripheral nerves. The SSEPs were recorded at the brachial plexus, cervical spine, and cortex. The functional integrity of the pathway was monitored using the characteristic SSEP waveform parameters (amplitude and latency) from the various recording sites. When significant waveform changes occurred, the patient was re-positioned. Patients were assessed postoperatively for neurologic deficits.

Results: 9 of the 64 patients experienced significant intra-operative SSEP changes. 8 of these SSEP reductions were detected within ten minutes of the beginning of the case and returned to baseline with repositioning of the affected extremity. In these 9 patients, there were no postoperative events. 2 of the 64 patients awoke with neurologic symptoms that were not detected intraoperatively. One experienced transient bilateral forearm numbness and hand extensor weakness. The second patient experienced right upper extremity sensory and motor weakness requiring extensive neurologic assessment and prolonged physical therapy with 95% resolution of symptoms at 3 months.

Conclusions: SSEP is a useful monitoring tool to detect common position related neuropathies. SSEP monitoring may help avoid positioning related neuropathies in high risk patients. Detection of potential peripheral nerve damage largely occurred within the first ten minutes after positioning with resolution after re-positioning and no post-operative events.

6

A Contemporary Study of Renal Cysts in a Representative US Population

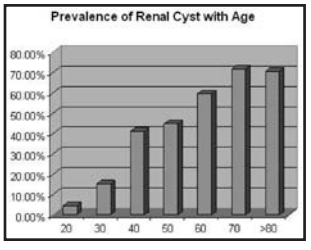
Steve Dong, Neesha Patel, Chandan Kundavaram, Deborah Glassman, Demetrius Bagley
Thomas Jefferson University, Philadelphia, PA

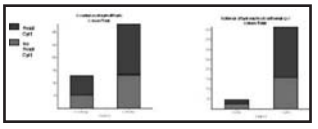
Introduction: With the rise of imaging studies, incidental findings of renal cysts are frequent. Primary care physicians refer patients to urologists to question their prevalence and significance. Contemporary data is sparse when attempting to answer this common question.

Methods: We evaluated 466 patients who underwent renal imaging. The presence of renal cysts in each patient was correlated to their demographics and associated urologic findings. Films of studies that did not mention the presence of cysts were reviewed.

Results: The incidence of renal cysts increased with age (Graph 1). They more often occurred unilaterally (62.3%versus 37.4%). There is no correlation with nephrolithiasis, however cysts are negatively correlated with hydronephrosis (Graph 2). In addition, they were more commonly seen in Caucasians than in African or Asian-Americans (59.1% vs. 38.7 and 38.1%, respectively). Reviewing the films revealed 32/212(17%) of reports without mention of cyst, in fact had cysts. Furthermore, 3/4 reports of "complex" cysts or "septations" on cysts were described without Bosniak classification.

Conclusions: Renal cysts prevalence increases with age and is inversely associated to hydronephrosis. Radiologists often omit notations of renal cysts because they are considered benign, thus leading to underreporting. Bosniak classification is infrequently used, but could help define the clinical significant cysts.





7

Exploring the Volume-Outcomes Relationship for Adrenal Surgery

Jay Simhan[1], Marc C. Smaldone[1], Daniel Canter[1], Fang Zhu[1], Russell Starkey[1], Karyn B. Stitzenberg[2], Robert G. Uzzo[1], Alexander Kutikov[1]
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Introduction: Although centralization of surgical procedures to high volume centers has been described previously, patterns of care for adrenal surgery are unknown. We investigated trends in regionalization of care for patients undergoing adrenalectomy using hospital discharge data from 3 Northeastern states.

Materials & Methods: Using 1996-2009 hospital discharge data from NY, NJ and PA, all patients >=18 years undergoing adrenalectomy were identified. Hospital volume status was assigned by quintiles based on number of procedures performed on a per-hospital basis in 1996 and divided as very low volume hospital (VLVH), low (LVH), moderate (MVH), high (HVH) and very high (VHVH). Outcome variables were examined by volume status over time using logistic regression models.

Results: From 1996 to 2009, 8,338 patients underwent adrenalectomy with a shift towards regionalization to VHVHs (17 to 42%, p<0.001). For each successive year, odds of having surgery performed at a VHVH increased by 9% (OR 1.09 [CI 1.08-1.10]). There were significant differences in patient age, race, geographic location, and payer group (p<0.0001) comparing VLVHs to VHVHs. Patients at VHVHs were less likely to be >=55 years (OR 0.76 [CI 0.72-0.80]), insured through Medicaid (OR 0.59 [CI 0.40-0.85]), or be uninsured (OR 0.30 [CI 0.21-0.43]). Controlling for year treated, patients were less likely to die in the hospital if treated at a VHVH (OR 0.38 [CI 0.19-0.75]).

Conclusions: These data demonstrates centralization of adrenalectomy to VHVHs since 1996 with improved clinical outcomes. Inequities in access to care to higher volume centers appear to exist and require further investigation.

8

Primary Spermatic Cord Tumors: Disease Characteristics, Prognostic Factors and Treatment Outcomes

Dayron Rodríguez[1], Aria F. Olumi[2]
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[2]*Department of Urology, Massachusetts General Hospital, Boston, MA*

Introduction: Experience with management of spermatic cord tumors (SCT) is uncommon. Therefore, in order to better elucidate the disease characteristics of SCT we utilized a large population-based cancer registry to characterize the demographic, pathological, treatment characteristics and outcomes.

Materials & Methods: The Surveillance, Epidemiology, and End Results (SEER) database (1973-2007) was queried.

Results: 362 patients were identified with SCT. The annual incidence of SCT was 0.5 cases per 1,000,000, and did not change over time. The most common histologic types were liposarcoma (46%), leiomyosarcoma (20%), histiocytoma (13%), and rhabdomyosarcoma (9%). The median age for diagnosis of rhabdomyosarcomas was (26.3yrs), while for other SCT was (64.7yrs) (p< 0.001), suggesting a different biologic behavior in rhabdomyosarcomas than other SCT's. On multivariate analysis, a worst outcome was associated with an undifferentiated tumor grade, distant stage, positive lymph nodes, and leiomyosarcoma or histiocytoma cell histology. Radiotherapy improved survival in patients with lymph node metastasis (median 81.5 months vs. 120.4, p-value = 0.043), but not in patients without metastasis. Lymphadenectomy made no difference in survival in patients with or without lymph node involvement.

Conclusions: This series represents the largest cohort of SCT studied to date. While liposarcoma is the most common, leiomyosarcoma and histiocytoma histologic subtypes are the most aggressive. Radiotherapy improves survival in patients with lymph node metastasis; however, lymphadenectomy does not significantly affect survival.

9

Men with Hereditary Prostate Cancer Have Improved Outcomes after Radical Prostatectomy in the PSA Era

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Brady Urological Institute, Baltimore, MD

Introduction: The impact of PSA testing on stage and oncologic outcome in men with hereditary prostate cancer (HPC) remains unknown.

Materials & Methods: A pre-PSA era cohort of 690 men who underwent radical prostatectomy (RP) by a single surgeon between 1982 and 1989 was compared to a PSA era cohort of 4046 men who underwent RP between 1993 and 2007 and had detailed family history available. Men with sporadic prostate cancer (SPC) were compared to patients with a family history consistent with HPC, defined as a family with 3 generations affected, 3 first-degree relatives affected or 2 relatives affected before age 55.

Results: In the pre-PSA era cohort, no statistically significant difference was found in pathologic stage, biochemical recurrence free survival (BRFS), or disease-specific survival (DSS) between patients with HPC and those with SPC (Table 1). In the PSA era cohort, men with HPC presented at a younger age than men with SPC ($p<0.0001$), had lower mean PSA ($p=0.0016$), were more likely to have organ-confined disease ($p=0.001$) and less likely to have a pathologic Gleason score greater or equal to 7 ($p=0.001$). Men with HPC had higher 10-year BRFS than men with SPC ($p=0.0034$) and a trend towards higher DSS ($p=0.06$).

Conclusions: Men undergoing RP who meet the criteria for HPC in the PSA era have less advanced disease and are less likely to recur.

Table 1

	Pre PSA Era			PSA Era		
Variables	Sporadic	HPC	HPC vs Sporadic	Sporadic	HPC	HPC vs Sporadic
N	511 (74.1%)	35 (5.0%)		2634 (65.1%)	336 (8.3%)	
Mean age	59.5	57.3	**p = 0.025**	58.4	56.1	**p < 0.0001**
Mean PSA	8.1 (SD 11.9)	9.6 (SD 9.8)	p = 0.28	6.5 (SD 8.6)	5.6 (SD 3.9)	**p = 0.0016**
Median PSA	4.6	7.5		5.4	4.7	
RP GI 7 (%)	40.3	40	p = 0.97	43.3	33.7	**p = 0.001**
Palpable Disease (%)	82.8	88.6	p = 0.37	27.3	23.1	p=0.103
OC (%)	37.7	31.4	p = 0.45	68.8	77.8	**p = 0.001**
Pos SM (%)	26.1	31.4	p = 0.5	13	11.3	p=0.39
SVI (%)	13.4	17.1	p = 0.53	4.7	3.9	p = 0.5
LN (%)	9.4	5.7	p = 0.46	1.9	0.6	p = 0.08
5-yr BCFS	76	74		82	89	
10-yr BCFS	67	74	p = 0.78	73	79	**p = 0.0034**
5-yr DSS	99	94		99	100	
10 -yr DSS	95	88		96	100	p = 0.06
20-yr DSS	84	85	p = 0.96			

10

Interventions for Urinary Morbidity Long Term after Prostate Cancer Treatment

Peter Chang[1], Meredith M. Regan[2], John T. Wei[3], Larry A. Hembroff[4], Chris S. Saigal[5], Jeff M. Michalski[6], Eric A. Klein[7], David P. Wood, Jr.[3], Martin G. Sanda[8], The PROST-QA Study Group[8]
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Introduction: Urinary medication usage and/or procedural interventions to manage post-treatment urinary morbidity - concrete and clinically relevant endpoints - have not been previously compared after primary PCa treatment.

Materials & Methods: A multicenter prospective cohort of 1,201 PCa patients who underwent radical prostatectomy (RP, 603), external radiotherapy (XRT, 298) or brachytherapy (BT, 302) from 2003 to 2006 had quality-of-life data collected from pre- to 2 years post-treatment. Treatment group differences in urinary medication usage, procedural interventions, and EPIC-26 overall urinary bother were analyzed using longitudinal logistic regression.

Results: The number of XRT patients using urinary medications pre-treatment (n=53; 22%) remained unchanged post-treatment (n=56; 26%). BT patients required more urinary medications from pre- (n=50; 19%) to post-treatment (n=109; 46%; $p < 0.0001$). Conversely, RP patients used significantly fewer urinary medications from pre- (n=76; 14%) to post-treatment (n=32; 6%; $p < 0.0001$). Urinary medication usage at 2 years was lower after RP and XRT than after BT ($p < 0.001$), whereas procedural interventions were similar after XRT, RP, and BT, respectively (5%, 7%, and 10%; $p = 0.20$). The number of patients experiencing moderate to severe overall urinary bother from pre- to post-treatment was unchanged in XRT (24 to 23), increased in BT (20 to 37), and decreased in RP (58 to 38).

Conclusions: Long-term medical intervention for urinary problems was more common after radiotherapy, especially brachytherapy, than after prostatectomy, suggesting that the previously underappreciated burden of obstructive urinary problems after radiation is paramount to the accepted burden of incontinence after prostatectomy.

11

Denosumab Treatment for Prolonging Bone Metastasis-Free Survival in Men with Castrate-Resistant Prostate Cancer

Paul Sieber[1], Matthew Smith[2], Fred Saad[3], Robert Coleman[4], Neal Shore[5], Karim Fizazi[6], Bertrand Tombal[7], Kurt Miller[8], Lawrence Karsh[9], Ronaldo Damiao[10], Teuvo Tammela[11], Blair Egerdie[12], Hendrik Van Poppel[13], Joseph Chin[14], Juan Morote[15], Tomasz Borkowski[16], Zhishen Ye[17], Amy Kupic[17], Roger Dansey[17], Carsten Goessl[17]
[1]*Urological Associates of Lancaster, Lancaster, PA, USA;* [2]*Massachusetts General Hospital Cancer Center, Boston, MA, USA;* [3]*University of Montreal Hospital Center, CRCHUM, Montreal, Quebec, Canada;* [4]*Weston Park Hospital, Sheffield, UK;* [5]*Carolina Urological Research Center, Myrtle Beach, SC, USA;* [6]*Institut Gustave Roussy, University of Paris Sud, Villejuif, France;* [7]*Université Catholique de Louvain Cliniques Universitaires Saint Luc, Bruxelles, Belgium;* [8]*Charité Berlin, Berlin, Germany;* [9]*The Urology Center of Colorado, Denver, CO, USA;* [10]*Hospital Universitario Pedro Ernesto, Rio de Janeiro, Brazil;* [11]*Tampere University Hospital, Tampere, Finland;* [12]*Urology Associates Urologic Medical Research, Kitchener, ON, Canada;* [13]*Universitair Ziekenhuis Gasthuisberg Leuven, Belgium;* [14]*London Health Sciences Centre, London, Canada;* [15]*Hospital Vall d'Hebron Barcelona, Spain;* [16]*Medical University of Warsaw, Szpital Dzieciatka Jezus, Warsaw, Poland;* [17]*Amgen Inc., Thousand Oaks, CA, USA*

Introduction: Men with castrate-resistant prostate cancer (CRPC) are at increased risk for developing bone metastasis, which can result in pain and bone-related complications called skeletal-related events. This study assessed the ability of denosumab to prolong bone metastasis-free survival in men with CRPC at increased risk of developing bone metastasis.

Methods: Adult men with non-metastatic CRPC at high risk for developing bone metastasis (PSA value ≥8.0 ng/mL and/or PSA doubling time ≤10.0 months) and total serum testosterone of <50 ng/dL were randomized 1:1 in a blinded manner to receive subcutaneous injections of denosumab 120 mg or placebo monthly. Calcium and vitamin D supplements were advised. The primary endpoint of bone metastasis-free survival was determined by time to first bone metastasis or death from any cause. This trial was event driven. The first patient enrolled in February 2006.

Results: A total of 1432 subjects enrolled. Denosumab significantly improved bone metastasis-free survival compared with placebo (hazard ratio [HR] 0.85; 95% CI: 0.73, 0.98; P=0.03; median increase of 4.2 months), and significantly improved time to first occurrence of bone metastasis. Overall survival was similar between treatment groups. Overall rates of adverse events (AEs) and serious AEs were similar between groups, with the exception of ONJ and hypocalcemia.

Conclusions: In patients with CRPC, denosumab significantly prolonged bone metastasis-free survival by delaying time to bone metastasis.

12

Radical Perineal Prostatectomy: A Viable Minimally Invasive Option for Treatment of Localized Prostate Cancer

Thomas K. Huisman, Robert M. Chiaramonte, Burkhardt H. Zorn
Southern Maryland Hospital Center, Clinton, MD

Introduction: Although a proven technique for over 100 years, Radical Perineal Prostatectomy (RPP) has recently fallen out of favor as a surgical procedure of choice for treatment of localized prostate cancer. We report our experience with RPP and compare our results with contemporary data for other surgical treatments.

Materials & Methods: A retrospective review of 300 consecutive RPP patients in a single institution was performed. Patient demographics, hospital stay, perioperative and postoperative morbidity, postoperative complications and biochemical disease-free survival were reviewed.

Results: Demographics: Average patient age was 61.5 years (range 36-76). Mean pre-op Gleason sum was 6(4-8). Average PSA was 6.5 (1.4-23.7). Average OR time was 100 minutes. Average EBL was 354 cc. Only 4/300 patients needed transfusion (1.3%) Average hospital stay was 1.3 days, but for the last 250 cases all patients have been discharged on POD 1. Average length of catheterization 7 days. Overall continence 91.4% (dry- no pads) and 5% minimal (1 ppd). 64% of bilateral nerve sparing patients have spontaneous erectile function.

Conclusions: RPP is a well-tolerated and effective treatment for clinically localized prostate cancer. It is associated with less morbidity, shorter hospital stays and quicker recovery times than traditional retropubic prostatectomy. It compares favorably to robotic prostatectomy and may represent a cost-effective alternative, especially in specific patient populations, including morbidly obese patients, patients with renal transplant or history of extensive prior abdominal surgeries. These findings are increasingly relevant as the rising cost of health care delivery continues to come under intense scrutiny.

13

Comparison of Positive Surgical Margin Rates in High Risk Prostate Cancer

Niall J. Harty[1], Spencer Kozinn[1], Jessica DeLong[1], David Canes[1], Andrea Sorcini[1], Jason Gee[1], Mark Silverman[1], Robin Ruthazer[2], John Libertino[1], Ali Moinzadeh[1]
[1]*Lahey Clinic, Burlington, MA;* [2]*Tufts Medical Center, Boston, MA*

Introduction: High risk prostate cancer (HRCaP) represents a complex disease entity. We compared positive surgical margin (PSM) rates for patients with HRCaP who underwent open radical retropubic (RRP), robotic (RALP), and laparoscopic (LAP) prostatectomy.

Materials & Methods: We performed a review of prostate cancer patients at our institution that underwent RRP, RALP, or LAP between January 2000 and March 2010. Patients were considered to have HRCaP if they had biopsy or final pathologic Gleason score ≥ 8, PSA ≥ 20, or pathologic stage of T3a or higher. PSM was defined by the presence of tumor at the inked surface of the specimen. Patients who received neoadjuvant hormonal therapy and those who underwent a perineal prostatectomy were excluded.

Results: We identified 513 patients with HRCaP. Sixty-eight patients were excluded. Of the 445 patients, surgical technique was RRP (n=153), RALP (n=152), and LAP (n=140). No age difference was noted between the three groups. Overall PSM was 52.9% for RRP, 50% for RALP, and 41.4% for LAP. The PSM rate did not differ between the three groups nor when comparing RRP to RALP and LAP combined. There was no statistical difference between the three groups in terms of the number of patients with a pathologic stage of T3 or higher. A higher preoperative PSA value was associated with a positive margin (p=0.04).

Conclusions: In patients with HRCaP, the PSM rate does not differ based on the surgical approach. Patients with a higher preoperative PSA value were more likely to have a PSM.

14

Predictors of Positive Surgical Margins after Radical Prostatectomy: Analysis of a Contemporary Single Institution Series

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Introduction: Positive surgical margins (PSM) after radical prostatectomy (RP) are an important adverse pathologic feature associated with increased risk of disease recurrence. A contemporary single-institution series of RP was examined in order to analyze multiple factors and their relationship with PSM.

Methods: A retrospective review of 1,300 patients in an institutional IRB-approved RP database was performed. Factors assessed included: age, obesity, pre-operative PSA, surgeon, EBL, surgical approach, post-operative stage, post-operative Gleason score, extracapsular extension (ECE), seminal vesical involvement (SVI), perineural invasion (PNI), and prostate weight. Prostate specimens underwent whole mount step sectioned pathologic analysis and confirmatory second level review at a multidisciplinary genitourinary pathology conference. Multivariate logistic regression analysis was performed.

Results: Recognized factors associated with higher PSM included: surgical Gleason score (p=0.002), pathologic stage (pT3/4 vs. pT2) (OR=6.23 p=<0.001), SVI (OR=4.99, p=<0.001), PNI (OR= 4.65, p=<0.001), preoperative PSA (OR=1.11, p= <0.0001), and obesity (OR=1.06, p=0.0002). Younger patient age (OR= 0.98, p< 0.05) and larger prostate weight (OR= 0.98, p=<0.001) were associated with a lower chance of PSM. No statistical difference was appreciated regardless of surgical approach (open, laparoscopic, robotic-assisted, or conversion), surgeon, EBL, or ECE.

Conclusions: PSM after RP are associated with multiple demographic, operative, and pathologic factors. In this series, it was also observed that younger patients and larger prostates had lower PSM. Furthermore, obesity was associated with higher rates of PSM: the cause and implication of this association are unclear, but are consistent with the finding that obesity is related to worse prostate cancer outcomes.

15

Prospective Study of Testosterone Suppression and Recovery after 6 months of Androgen Deprivation Therapy and Radiation for Clinically Localized Prostate Cancer

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Introduction: Testosterone suppression and recovery is not uniform among men who have received LHRH Agonist therapy for the treatment of prostate cancer. We prospectively measured testosterone levels before, during, and for 12 months after cessation of LHRH therapy in men undergoing radiation for clinically localized prostate cancer.

Materials & Methods: From 2001 to 2003, 29 patients with T1c-T3 prostate cancer undergoing definitive radiation combined with 6 months of Eligard 22.5 mg were enrolled in a 12 month open label study of Testosterone suppression and recovery. Patients were followed at Months 1, 3, 7, 9 and 12 with serum Testosterone and PSA.

Results: Median time to Castrate testosterone as defined by Testosterone less than 20ng/dL was 3 months with a mean of 2.68 months and 25 of 29 achieved at least one value at that level. Only 13 (44.8%) patients had sustained suppression of testosterone less than 20ng/dL for the entire 6 month intended duration of therapy. Only 9 of the 29 subjects had returned to within 90% of their baseline testosterone level by 12 months. Median time to recovery of 90% of baseline testosterone was 15 months with a mean of 13.8 months.

Conclusions: Testosterone suppression with standard LHRH agonist therapy may require as long as 3 months to achieve testosterone levels equivalent to surgical castration. Less than half have sustained suppression of testosterone for the full duration of therapy. ADT also results in prolonged testosterone suppression that may persist more than a year after therapy has been discontinued.

16

Too Few or Too Many Prostate Biopsies? Results from an Academic Center

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Introduction: Given the variability in indications for and cancer detection rates from trans-rectal ultrasound (TRUS)-guided biopsy, we evaluated the prostate cancer (PCa) detection rate in males undergoing 12-core needle biopsies at a single academic center. We then identified the proportion of men with PCa who met the criteria for active surveillance (AS).

Materials & Methods: A retrospective analysis of 603 consecutive patients undergoing TRUS-guided biopsies after meeting standard-of-care criteria including at least one of the following: abnormal digital rectal exam, PSA>4ng/mL, PSA velocity >0.7ng/mL and/or positive family history in 1st degree relative were identified within an IRB-approved pathologic database. Klotz and Nam criteria (PSA≤10ng/ml, clinical stage T1-T2a, Gleason score ≤6, <3 cores involved, <50% of a single core involved) were used as determinants for AS candidacy. AS candidacy and PCa detection rates were calculated.

Results: Two-hundred eighty-five of the 603 (47.3%) prostate biopsies resulted in a diagnosis of PCa with 75 (26.3%) of those patients meeting Klotz and Nam criteria for AS. The remaining 73.7% of PCa diagnoses were classified as intermediate/high-risk cases.

Conclusions: The cancer detection rate at our center of 47.3% is well-above the rate reported in the PLCO screening trial of 36.8% as well as the rates seen in other large-scale PCa screening trials. Given the fact that favorable-risk PCa nationally represents ~50-60% of new diagnoses, further research should be done to clarify strict biopsy indications in order to help eliminate the variability in PCa detection rates between centers. With appropriate biopsy indications, we may see increased detection of intermediate/high-risk PCa as seen in this study.

P1

Sphingosine Kinase-2 Deficient Mice Exhibit Diminished Renal Inflammation/ Renal Fibrosis in Response to Unilateral Ureteral Obstruction

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Introduction: The objective of this study is to investigate the role of sphingosine kinase-2 in modulating renal injury induced by unilateral ureteral obstruction (UUO). Congenital Urinary tract obstruction is an important cause of renal injury and failure in children. While many aspects of the obstructive injury cascade are understood, this has not translated into therapeutic benefit. Sphingosine Kinase-2 (Sphk-2) is a metabolizing enzyme responsible for production of the bioactive lipid Sphingosine-1 Phosphate (S1P), which plays a major role in regulating the immune system, tissue injury and re-generation. Because of this, multiple Sphk inhibitors are under development and in the future Sphk inhibitors may see broad clinical use.

Materials & Methods: Genetically engineered Sphk-2 deficient and wild type mice were used in UUO model experiments. Contralateral kidneys served as control. Evaluation time points were 1,5 and 10 days. The renal pathology was examined by light microscopy. Expression levels of alpha-smooth muscle actin, TGF-b and Collagen type 1 were analyzed by RTPCR, immuno-histochemistry and western blotting.

Results: Wild type and Spkh-2 knock out mice showed significant differences. Mice expressing sphingosine kinase-2 showed extensive renal damage characterized by thickened cortical lesions, interstitial fibroblastic proliferation, focal interstitial hemorrhage, necrosis in lining of tubular epithelium and atrophic tubules. Sphk-2 knock out mice did not demonstrate this pattern of injury. Alpha smooth muscle actin and TGF-b expression levels were elevated in wild type obstructed kidneys when compared to knock out mice.

Conclusions: Our initial studies show that Sphk-2 -S1P pathway is implicated in the pathogenesis of obstructive renal injury.

P2

Regulation of Kinetochore Protein Expression by COX-2 Signaling in Prostate Cancer Cells

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Introduction: Kinetochores anchor microtubules to chromosomes during mitosis and without proper attachment, cell division is arrested at the mitotic checkpoint. *In vitro* prostate cancer cell viability assays have revealed a cell growth arrest phenomenon following treatment with cyclooxygenase-2 (COX-2) inhibitors. We hypothesized that treatment of prostate cancer cells with COX-2 inhibitors will arrest cell growth at mitosis through regulation of kinetochore proteins.

Materials & Methods: LNCaP and PC3 prostate cancer cells were cultured and treated with a COX-2 inhibitor, celecoxib, a highly-selective COX-2 inhibitor, CAY10404, and a celecoxib analogue without COX-2 inhibition, OSU03012. Cells were lysed at 48 hours and probed for kineotchore proteins: CENP-A, PlK1, and ZWINT. Immunofluorescence (IF) was performed using antibodies to CENP-B, DNA, and tubulin in treated and untreated cells. Additional cells were treated with COX-2 inhibitors and kinase inhibitors to investigate the mechanism of action.

Results: Inhibition of COX-2 by celecoxib and CAY10404 induced a dramatic down-regulation of the kinetochore proteins in LNCaP cells. OSU03012 had no effect. IF staining showed that treatment with COX-2 inhibitors diminished kinetochore structure and blocked mitosis in LNCaP cells. Mixed results from co-treatment with COX-2 inhibitors and MAP kinase inhibitors suggest a complex mechanism involving MAP kinase pathways.

Conclusions: COX-2 inhibition of prostate cancer cells down-regulates kinetochore protein levels leading to mitotic arrest. These results correlate with recent epidemiologic studies showing a reduced incidence of prostate cancer among men taking COX-2 inhibitors. Further studies are needed to determine the chemopreventative and chemotherapeutic potential of celecoxib in human prostate cancer.

P3

Comparison of Intraprostatic Ethanol Diffusion Using a Microporous Hollow Fiber Catheter versus Standard Needle

Benjamin J. King[1], Mark K. Plante[1], Masatoshi Kida[1], Travis K. Man-Gow[1], Rick Odland[2], **Peter Zvara[1]**
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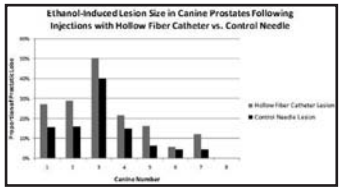
Introduction: Transurethral intraprostatic ethanol chemoablation of the prostate has demonstrated promising preliminary clinical results for treatment of BPH with some variability in clinical outcomes. This is likely due to injectable backflow along the needle tract with uneven prostatic distribution. The objective of this study was to compare tissue diffusion of an intraprostatic injection using a new microporous hollow fiber catheter (MiHFC) to that of a standard needle.

Materials & Methods: The prostates of eight mongrel dogs (weighing 70 - 88 lbs) were exposed and a single injection of 99% ethanol was delivered into each lobe using the MiHFC and a standard needle. The prostates were harvested and fixed en block in 10% formalin. The lesions were traced on scanned hematoxylin & eosin histology sections. Three dimensional reconstructions were performed using 2.5 mm step-sections. The volume of each ethanol-induced prostatic lesion was calculated using stereology.

Results: Ethanol-induced tissue changes were seen bilaterally in seven of eight prostates injected. One prostate was harvested without injection, acting as a negative control. Statistical analysis of data compiled from all treated prostates showed significantly larger histological changes ($p \leq 0.01$) on the side injected by the MiHFC (Figure).

Conclusions: The use of a MiHFC consistently resulted in larger ethanol-induced tissue lesions. The advantage shown with the MiHFC indicates its potential for developing into a new method to treat prostate disease.



P4

Inhibition of Inflammatory and Apoptotic Mediators Improves the Bladder Dysfunction that is Associated with Type 2 Diabetes

Zongwei Wang[1], Zhiyong Cheng[2], Vivian Cristofaro[3], Jijun Li[1], Xingyuan Xiao[1], Rongbin Ge[1], Pablo Gomez[4], Edward Gong[4], Klemen Strle[1], **Aria F. Olumi[1]**
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Introduction: To evaluate the molecular pathways associated with bladder dysfunction in type 2 diabetes (T2D), we used a genetic mouse model with hepatocyte-specific double knockout of Insulin Receptor Substrates 1 & 2 (DKO) that develops T2D.

Materials & Methods: Bladders from different age DKO/floxed control mice were harvested and functional alterations were evaluated by muscle strip experiment ex vivo and cystometric experiment in vivo. Affymetrix mouse gene chip was employed to evaluate the expression of 45,000 genes in bladder. Cytokines in serum were determined using the Multiplex kit. Cultured Bladder Smooth Muscle Cell (BSMC) contraction in vitro was assayed by collagen gel retraction. The presence of macrophages, extent of apoptosis and expression of specific proteins were assessed with IHC and Western blot respectively.

Results: Young DKO mice exhibited hyperactive bladders (higher amplitudes of tension and frequency of contraction), while older mice demonstrated hypoactivity. Over 20 inflammatory genes were upregulated in the bladder of diabetic mice, most of which belonged to the TNF superfamily. Metabolic (ATPase, Rho GTPase, Rho kinase) and apoptotic-related (Caspase-3) genes were also upregulated. TNF-alpha was significantly upregulated in serum, and it stimulated the contraction of BSMC in culture. Systemic treatment with neutralizing TNFR1 in DKO mice corrected the diabetic cystopathy without affecting serum glucose.

Conclusions: The bladder of T2D mice transition from a hyperactive to a hypoactive state. Inflammatory/apoptotic mediators are upregulated in diabetic bladder dysfunction, and targeted systemic inhibition of TNFR improves bladder function without alteration of serum glucose.

Concurrent Poster Session I: Basic Science
10:50 am-12:15 pm

P5

A Non-invasive Mirna Based Assay to Detect Bladder Cancer in Cell-free Urine
Jessica DeLong, Spencer Kozinn, Niall Harty, Kelly Summerhayes, Ian Summerhayes, Antonia Holway, Kimberly Rieger-Christ
The Lahey Clinic, Burlington, MA

Introduction: MicroRNAs (miRs) are small, non-coding segments of regulatory RNA that are powerful biomarkers of disease severity and prognosis. Previous work from this group indicated the potential for identification of miRNAs that play a role in urothelial carcinoma of the bladder (UCB). In this study we isolated RNA from cell-free urine to identify a miRNA profile that could be used as a non-invasive diagnostic assay to detect the presence of UCB and provide a discriminatory signature for different stages of progression.

Materials & Methods: Total RNA was isolated from cell-free urine of patients with UCB and controls. Samples were grouped according to grade and stage. MiRNAs were profiled by qRT-PCR array on pooled samples within each group. Validation of miRNAs was performed on individual samples using qRT-PCR.

Results: 236 miRNAs were detected in at least one pooled sample; the number of miRNAs detected correlated with disease progression. The control group and the >=T2 group expressed 8 and 228 miRNAs, respectively. Of miRNAs present in both cancer and non-cancer groups, 13 had significantly higher levels in the cancer group. Statistical analysis adjusted for multiple comparisons demonstrated differences between groups based on miRNA expression levels including a panel of miRNAs that discriminated between cancer and cancer-free patients with high sensitivity and specificity.

Conclusions: We demonstrated successful isolation of miRNAs from cell-free urine. Utilizing this non-invasive assay, we identified miRNAs capable of discriminating between cancer-free patients and patients with UCB, providing evidence that miRNA profiling holds promise for the development of valuable clinical tools.

P6

The In Vitro Anti-tumor Activity of Docetaxel in Combination with Inositol Hexaphosphate (IP-6) in Castrate-Resistant PC3 and DU-145 Prostate Cancer Cell Lines
Adam Luchey, Can Talug, Dale Riggs, Barbara Jackson, Dana Point, Stanley Zaslau, Stanley Kandzari
West Virginia University, Morgantown, WV

Introduction: Inositol Hexaphosphate (IP-6) regulates the cell cycle, apoptosis, and cellular proliferation in prostate cancer lines *in vitro*. We hypothesized that when combined with Docetaxel (DOC), IP-6 results in an additive reduction in cellular proliferation in castrate-resistant prostate cancer cell lines (CPCL), PC3 and DU-145, thereby increasing effectiveness and minimizing toxicity of DOC.

Materials & Methods: PC3 and DU-145 CPCL were cultured using standard techniques and incubated with IP-6 (0.25 and 0.5mM/well) and/or DOC (2.5 and 5nM/well). Cell viability was measured by MTT at 24, 48 and 72 hours thereafter. Statistical analysis was performed by ANOVA, with individual comparisons made by the Tukey test.

Results: Significant reductions ($P<0.001$) in cellular growth were noted in both cell lines and at all time frames with the combination of DOC and IP-6 compared to control. At 24 hours with DU-145, there was significance in kill rate with the combination of DOC 5nM/IP-6 0.5mM versus each agent alone ($P<0.001$), but not with PC3. At 48 and 72 hours with PC3, but not DU-145, the combinations of DOC 2.5nM/IP-6 0.25mM produced significantly higher kill rates than DOC 5mM ($P<0.001$).

Conclusions: When combined, DOC and IP-6 exhibited an additive reduction in cellular proliferation in both CPCL. IP-6, when combined with DOC 2.5nM, achieved a significant reduction in cellular proliferation equal to that observed with DOC 5.0nM. These results indicate that a lower dose of DOC with IP-6 could potentially lead to a more effective and less toxic treatment for castrate-resistant prostate cancer and warrants further investigation.

P7

Impact of Endothelin Axis Modification in Cancer Immunotherapy and Transplantation in Murine Model
Jeffrey P. Wolters, P. Joseph Yannie, Ekaterine Goliadze, Maryellen Dolat, Georgi Guruli
Virginia Commonwealth University, Richmond, VA

Introduction: The aim of this study was to determine if modification of the endothelin axis would alter the growth of murine prostate cancer as well as murine skin graft survivability.

Materials & Methods: One group of mice were injected with RM1 (prostate cancer) cells subcutaneously. Modified dendritic cells (DC) were injected into the contralateral flank. We used TNFa, BQ788 (ET_B receptor antagonist) and RM1 cell lysates for DC modification. In transplant experiments, Balb/C mice received an allographic skin transplant from C57B/6 mice and were treated either with BQ123(ET_A receptor antagonist) or water. Grafts were considered dead when complete separation was noted.

Results: In the prostate cancer experiment the mice were treated with DC alone (1), DC+TNFa(2), DC+RM1 lysate (3), DC+TNF+ BQ788 (4), and TNFa+BQ788+RM1 lysate (5). By day 28, mean tumor size reached 1824.08±229.86 mm^3 in the Group 1, 1845.42±302.34 mm^3 in the Group 2, 1502.67±367.13 mm^3 in the Group 3, 1400.16±188.88 mm^3 in Group 4, and 922.58±90.86 mm^3 in Group 5. Difference in tumor sizes between Groups 1 and 5 was statistically significant ($P=0.002$). In the transplant experiment graft survival was 11.0±0.7 days in control group and 15.8±1.1 days in the group treated with BQ123 ($P<0.001$).

Conclusions: We have shown for the first time that modification of the endothelin axis on dendritic cells might alter immune response and prolong graft survival. Further, ET_B receptor blockade seems to stimulate proinflammatory immune response, a feature that may be useful in the treatment of malignant tumors.

P8

Molecular Profiling of Erlotinib Resistance in an In-Vitro Bladder Cancer Model
William C. Faust, Marc Manganiello, Justin Zbrzezny, Christina Deliyiannis, Jason Gee, John Libertino, Antonia Holway, Kimberly R. Christ
Lahey Clinic, Cambridge, MA

Introduction: We previously reported differential sensitivity of 17 urothelial carcinoma of the bladder (UCB) cell lines to the EGFR inhibitor erlotinib where lines displaying EMT characteristics showed greater resistance. In this study we evaluated the correlation between microRNA (miRNA) expression levels and erlotinib resistance in an*in-vitro* model of UCB.

Methods: Erlotinib sensitivity was determined by clonogenic assay in 46 UCB cell lines randomly divided into training and test sets. MiRNA expression levels were determined by microarray analysis and confirmed by qRT-PCR. Multilogistic regression analysis and the Random-Forest Algorithm were used to identify microRNAs predictive of sensitivity.

Results: In the training group, 62 miRNAs were significantly different between the 16 sensitive and 14 resistant cell lines. In the resistant group, 38 miRNAs were up-regulated and 24 miRNAs were down-regulated. A predictive model using two miRNAs, resulted in the misclassification of 1 resistant and 2 sensitive lines. Sensitivity and specificity was 93% and 87.5%, respectively, for the detection of resistance while the area under the receiver operator characteristic curve was 0.9554. In the test set of cell lines, the classifier had a PPV of 50% and a NPV of 100%.

Conclusions: MiRNAs are a powerful new tool in the molecular diagnosis and treatment of UCB. We have found a group of previously uncharacterized miRNAs that accurately predicts the response of UCB cell lines to erlotinib treatment. Next steps involve bringing this molecular information to the clinic, and using molecular profiles to guide chemotherapeutic treatment decisions in patients with UCB.

P9

A New Method for Objective Analysis of Detrusor Rhythm during the Filling Phase
Ashley B. King[1], Adam Klausner[1], Samuel Robinson[1], David Rapp[2], Vikram Sabarwal[1], John Speich[1], Harry Koo[1], Paul Ratz[1]
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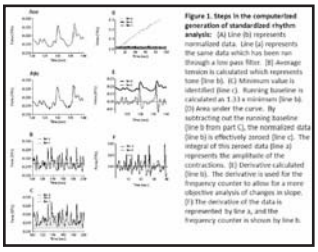
Introduction: A standardized model for quantitative analysis of detrusor rhythmic contraction currently does not exist. The goal of this study was to develop a computer program for analyzing detrusor rhythm.

Materials & Methods: Seventeen detrusor strips from 12 rats of 3 different strains (Wistar, WKY, and SHR) were used to analyze rhythm. At optimal length, prostaglandin-E2 (PGE2) was added in half-log increments from 1.0x10-9M to 1.0x10-6M. Then maximum and minimum force values were obtained using KCl and Ca2+-free solution containing EGTA, respectively. A computer program was developed using DASYLab 10.0 to analyze the effects of PGE2 on frequency (contractions/5min), amplitude (5min area under the curve), and tone (5min average) in a step-wise fashion shown in Figure 1. The computer generated frequency count was compared to human assessment.

Results: PGE2 induced a concentration-dependent increase in frequency, amplitude, and tone. These effects were documented in a reproducible, consistent way using the computer program, and the frequency count was significantly different from human assessment.

Conclusions: A computer program for rhythm analysis was developed and tested using detrusor strips of rats from different genders and strains. The program analyzed detrusor rhythm in terms of frequency, amplitude, and contractile tone in an objective and reproducible manner. Further testing may allow this program to compare the effects of different agents on rhythmic activity during the filling phase.



P10

Improved Detection of Prostate Cancer by the Combined Application of ERG and AMACR Immunohistochemical Stainings in Prostate Biopsy Specimens
George Leighton Lee
CPDR/WRAMC/USUHS, Rockville, MD

Introduction: Biochemical markers, such as AMACR and p63 have improved diagnostic precision of prostate cancer. Recently, recurrent *TMPRSS2-ERG* genomic fusion has been demonstrated in half of prostate cancers. We have developed a monoclonal anti-ERG antibody that demonstrated 99.9% specificity in detecting the protein product of recurrent *ERG* fusions. Previously we have shown that when *AMACR* and *ERG* mRNA expression were examined together, 96.4% of cases were positive for at least one of the two markers. We reasoned that by combining ERG with AMACR immunohistochemical staining, diagnostic sensitivity and specificity can be improved in prostate biopsy specimens.

Materials & Methods: In a retrospective set of 88 patients undergoing prostate biopsies, prostate cancer was identified in 44 patients. Ten of these patients subsequently underwent radical prostatectomy. We evaluated 385 slides from the 88 biopsy sets by IHC with 350 stained for ERG only and 35 stained for both ERG and AMACR.

Results: AMACR was detected in 28 of 31 (90.3%) and ERG in 37 of 70 (52.8%) of tumor positive biopsies evaluated. Of the three biopsies with benign tissue only, one had AMACR positive glands. However, in six other biopsies, both neoplastic and benign glands were positive for AMACR. ERG positivity in benign glands was detected in only 1/280 (0.4%) of biopsies (specificity >99%). Of the three slides with AMACR negative tumors, two were positive for ERG.

Conclusions: Our findings highlight that detection of ERG oncoprotein when combined with AMACR has potential to improve diagnostic sensitivity and specificity in prostate biopsy specimens.

P11

Gene Expression Signature of High BMI Prostate Cancer Patients Identifies the Statin Target Gene SCD1
Patrick Parker
CPDR/WRAMC/USUHS, Rockville, MD

Introduction: Obesity is one of the largest medical challenges in the USA. Recent studies highlighted the association of obesity with prostate cancer aggressiveness. However, obesity-associated gene expression alterations need to be better understood. The objective of this study was to evaluate elevated BMI-associated prostate cancer gene expression signatures.

Materials & Methods: Prostate cancer cells and matching non-adjacent normal epithelial cells were selected by laser capture microdissection from frozen radical prostatectomy specimens of patients with normal- and high BMI. Gene expression analyses were performed by using HG-U133A Affymetrix microarrays. Tumor-over-normal gene expression ratios were calculated and data were further analyzed by applying a three-fold cutoff. To pinpoint central regulatory nodes of gene expression alterations knowledge-based pathway analysis, gene ontology and comparative meta-analysis of obesity related independent datasets were performed.

Results: Bioinformatic analyses revealed associations of high BMI with cholesterol and lipid metabolism associated genes within fatty acid synthesis and oxidation-reduction pathways. The identified high BMI-associated genes were tightly connected to genes involved in lipid metabolism, cholesterol homeostasis, and tumorigenesis. The analysis highlighted the association of stearoyl-CoA desaturase (*SCD1*) with elevated BMI.

Conclusions: Our study revealed that *SCD1*, a known target of atorvastatin, may play a mechanistic role in the recently noted beneficial effects of statin treatment in reducing biochemical recurrence of prostate cancer.

P12

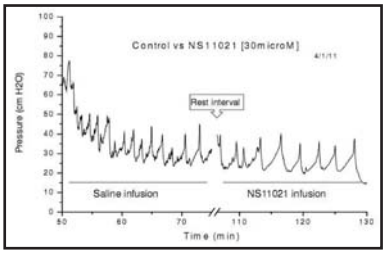
NS11021, a BK Channel Opener, Effects Significant Changes on Mouse Urinary Bladder Function During Urodynamics
Hagop Sarkissian, Tom Heppner, Peter Zvara, Mark Plante, Mark Nelson
University of Vermont, Burlington, VT

Introduction: Large conductance Ca^{2+} activated potassium (BK) channels are ubiquitous throughout excitable and non-excitable tissues. BK knockout mice exhibit urinary frequency and urinary leakage. Their bladders show increased intravesicular pressures, increased excitability and spontaneous contractions. Therefore, the current project sought to investigate a novel BK channel opener, NS11021, and examine its effect on bladder function in partially obstructed (pBOO), overactive and normal controls.

Materials & Methods: Bladder domes of pBOO and normal, C57BL/6 mice, were implanted with polyethylene tubing. Subsequently, conscious, continuous cystometrography was performed. CMG had three separate phases: control/saline infusion (0.75mL/hr), an established rest period, then, continuous intravesicular infusion phase of 30microM of NS11021 solution.

Results: In mice with pBOO or with overactivity on CMG (n=5), NS11021 infusion improved CMG parameters significantly. Quantitatively, a 43% increase in threshold pressure ($p<0.001$), an 82% increase in intermicturition interval ($p<0.001$), a 32% decrease in filling pressure ($p<0.001$) and a 9% decrease in peak pressure. In normal mice, i.e. those without overactivity, NS11021 had no effect.

Conclusions: In mice with pBOO and overactivity, intravesicle infusion of NS11021, seemed to effect significant functional changes in bladder characteristics on CMG, including marked decreases of phasic, non-voiding contractions. These results may have translational implications in the future for the treatment of bladder overactivity in certain patient populations.



P13

The Relation between Leptin and Prostate Cancer Cell Line LnCaP

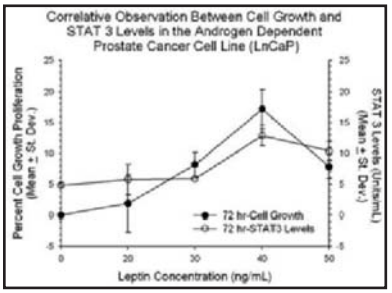
Mohamad W. Salkini, Dake Ruggs, Barbara Jacksom
West Virginia University, Morgantown, WV

Introduction: Leptin, the adipocyte-derived hormone is associated with an increased risk of multiple cancers including prostate cancer. We hypothesized that leptin would change hormone dependent prostate cancer cells to hormone independent cells. Signal transducer and activator of transcription 3 (STAT3) plays a key role in many cellular processes such as cell growth and apoptosis. Increased expression of STAT 3 in LnCaP prostate cancer cells precedes the transition into castrate resistance status.

Materials & Methods: The androgen dependent human prostate cancer cell line, LnCaP, was exposed to Leptin at different concentrating (0, 20, 30, 40 and 50 ng/mL). Cell viability and STAT3 protein were assayed using MTT and ELISA respectively after 72 hours of exposure to leptin. All data is reported as means ± standard deviation.

Results: A gradual increase in LnCaP cellular proliferation was observed and reached statistical significance at concentrations of 30 (8.2% ± 2.0), 40 (17.2% ± 3.2) and 50 ng/ml (7.8% ± 2.0) of Leptin (P<0.001). STAT3 levels increased steadily along with the proliferation and reached statistical significance at 40 ng/ml concentration of Leptin (12.9 ± 1.7 units/ml, P<0.05). The described changes peaked at concentration 40ng/ml of leptin.

Conclusions: Increased Leptin levels induced significant *in vitro* cellular proliferation and increase STAT-3 levels of hormone dependent prostate cancer cells. These findings demonstrate some of the effects of obesity on prostate cancer.



P14

The Effects of Social and Environmental Stimuli in a New Murine Model for Interstitial Cystitis/Painful Bladder Syndrome

Adam Luchey, Dale Riggs, Barbara Jackson, Can Talug, Stanley Kandzari, James Coad, Yara Daous, Dana Point, Morris Jessop, Stanley Zaslau
West Virginia University, Morgantown, WV

Introduction: The treatment and etiology of Interstitial Cystitis (IC) is still unclear. The objective was to develop a murine model to evaluate the bladder response to environmental stressors, which have been shown to exacerbate IC symptoms.

Materials & Methods: Forty-one BalB/c (6-7 weeks old) were randomized into the Control Group (CG, n=20) and the Chronic Stress Group (CS, n=21) and allowed to acclimatize for two weeks. CS underwent unpredictable, random, chronic stressors daily: succession of light/dark cycles every 15-30 minutes, changes to bedding (removal, being replaced with water, cage tilt), and social stress (cage rotation). After 10 weeks the mice were sacrificed. The bladders were formalin-fixed and paraffin-embedded, then evaluated with light microscopy using H&E, giemsa and PAS to determine weight, mast cells and urothelial thickness. Statistical significance was determined using the non-parametric Mann-Whitney method.

Results: The bladder weight of CG was 39.4±7.41mg compared to CS of 50.08±11.06mg (p<0.001).

		Mean ± Std Dev	Median	Min	Max
Urothelial Mast Cells	Control (n=20)	2.57 ± 1.28	2.40	1.00	5.00
(per 200x field; p=0.048)	Stressed (n=21)	1.83 ± 1.03	1.40	0.50	4.30
Detrusor Mast Cells	Control (n=20)	1.02 ± 0.67	0.90	0.00	2.63
(per 200x field; p=0.928)	Stressed (n=21)	1.04 ± 0.74	0.80	0.10	2.90
Urothelial Thickness µm	Control (n=20)	6.2 ± 0.3	6.2	5.7	6.5
(p<0.0001)	Stressed (n=21)	5.6 ± 0.3	5.7	5.3	10.0

Conclusions: This study demonstrates a murine model exposed to noxious environmental stimuli to produce the clinical features of IC. This can be used to study the pathogenesis and treatment of the human condition. We hypothesize that stressors may exacerbate IC by thinning the urothelium to the peripheral nerve fibers rather than increasing mast cells. Additional directions include response to reversal of stressors, medications including intravesical agents, and the study of neurogenic and biochemical pathways.

P15

F-box Protein 10, an NF-kB-dependent Anti-apoptotic Protein, Regulates TRAIL-induced Apoptosis through Modulating c-Fos/c-FLIP

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Introduction: Tumor necrosis factor-related apoptosis–inducing-ligand (TRAIL) holds great promise as an anti–cancer-agent, but some tumors develop resistance to TRAIL. Previously, we have shown that the AP–1 family member, c–Fos, is an important modulator of apoptosis. Although FBXL10 has been implicated to regulate an AP–1 family protein, c–Jun, its role in mediating apoptotic pathways has not been previously investigated. Here, we report that FBXL10 is a novel NF–kB-dependent anti–apoptotic-molecule and regulates TRAIL-induced-apoptosis through modulating c-Fos/c-FLIP.

Methods: RT–PCR, Western blot and immunofluorescence assays were applied to evaluate protein expression. RNAi, ChIP, EMSA, hydrodynamic–based-transfection were performed to analyze the interaction among FBXL10/c–Fos/NF–kB. Prostate xenografts were carried out for in–vivo analyses.

Results: FBXL10 was suppressed and c–Fos was upregulated in TRAIL-sensitive cancers after treatment with TRAIL. However, in TRAIL-resistant cancers, FBXL10 and c–Fos were not affected. Silencing of FBXL10 sensitized resistant cells to TRAIL. Conversely, over–expression of FBXL10 repressed TRAIL–induced apoptosis. To behave as an anti–apoptotic molecule, we found that FBXL10 directly binds and represses c–Fos promoter. In addition, FBXL10 regulates c–FLIP, another anti–apoptotic molecule, by a c–Fos dependent pathway. We also found that expression of FBXL10 is NF–kB–dependent, and TRAIL down–regulate FBXL10 via inhibiting NF–kB signaling. Using ChIP and EMSA assays, we found that NF–kB–p65 directly binds the FBXL10 promoter, and promotes expression of FBXL10.

Conclusions: Differentiating molecular mechanisms between TRAIL-sensitive and TRAIL-resistant cancer cells will improve the efficacy of apoptotic therapies. In this study, we demonstrate that FBXL10 plays an anti–apoptotic role and indicates a novel NF–kB/FBXL10/c–Fos/c–FLIP signaling pathway in TRAIL–mediated apoptosis.

P16

Multi-Institutional Evaluation of a MicroRNA Expression Profile Defining the Invasive Bladder Tumor Phenotype

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Introduction: MicroRNAs (miRNAs) are small, non-coding segments of regulatory RNA that have emerged as powerful biomarkers of disease severity and prognosis. We previously reported a miRNA profile (miR-200c, miR-141, and miR-30b) capable of differentiating invasive from noninvasive urothelial carcinoma of the bladder (UCB) with a sensitivity of 100% and a specificity of 96%. The goal of this project is to validate this profile with an expanded sample pool that includes tissues from an independent institution.

Materials & Methods: MiRNA expression levels in tumor tissue and cell lines were quantified by qRT-PCR. Fifty UCB cell lines and 157 UCB tumors (76 noninvasive and 81 invasive) were evaluated. Downstream targets were assessed via Western blot analysis.

Results: On multi-institutional analysis, the original miRNA panel remained capable of distinguishing between invasive and non-invasive UCB, however, the sensitivity and specificity were both reduced to 82%. To address this we identified additional miRNAs that were correlated with invasive potential in a screen of 50 cell lines. When evaluated in tumor samples from both institutions, several of these additional miRNAs were significantly different between invasive and non-invasive tumors.

Conclusions: Multi-institutional analysis of our panel of miRNAs capable of defining the invasive bladder tumor phenotype was confirmed albeit with a slightly reduced sensitivity and specificity. Expansion of miRNA analysis in UCB cell lines resulted in the identification of additional miRNAs with differentiating potential, several of which were found to significantly discriminate invasive from non-invasive tumors. Improvements in specificity and sensitivity with these additional miRNAs will be evaluated.

P17

Sphingosine-1-Phosphate2ReceptorInducesCcl2ExpressioninNeuroblastoma/a Targeted Inhibition Strategy

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Introduction: Neuroblastoma (NB) is the most common extracranial solid tumor of childhood. The bioactive lipid sphingosine-1-phosphate (S1P) and its five specific receptors ($S1P_{1-5}$) and known to impact tumor growth and progression. Preliminary data derived from human angiogenesis array showed that S1P induced the secretion of angiogenesis-related proteins VEGF and monocyte chemoattractant protein 1(MCP-1; CCL2), an important inflammatory chemokine in NB. Recently, we have shown that S1P/$S1P_2$ signaling mediates VEGF expression and thus promotes NB growth. In the present study, we investigated the mechanism of S1P-induced CCL2 expression in NB.

Materials & Methods: Quantitative real-time PCR detected mRNA levels of S1PRs and CCL2 in NB SK-N-AS cells and tissues. CCL2 ELISA detected CCL2 protein secretion in SK-N-AS cells. Gain and loss of functions studies were performed using S1PR antagonists, adenoviral transduction and siRNA. NB murine xenograft models were used to test the efficacy of a selective $S1P_2R$ inhibitor *in-vivo*.

Results: $S1PR_{1-3}$ and CCL2 mRNA were abundantly expressed in NB tissues. In NB SK-N-AS cells S1P induced CCL2 mRNA expression and protein secretion in time- and concentration-dependent manners. Antagonism of $S1P_2$ by specific $S1P_2$ antagonist JTE-013 blocked S1P-induced CCL2 mRNA expression and protein secretion. Overexpression of $S1P_2$ by adenoviral transduction into SK-N-AS cells increased CCL2 secretion while knockdown of $S1P_2$ by $S1P_2$ siRNA transfection decreased CCL2 secretion. The $S1P_2R$ inhibitor JTE-013 suppressed tumor growth in NB xenograft models.

Conclusions: Taken together, our data demonstrate that S1P induced CCL2 expression in NB cells via $S1P_2$ and maybe a potential therapeutic target.

P18

Clinicopathological Correlation of Gli1 Expression in a Population Based Cohort of Patients with Newly Diagnosed Bladder Cancer

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Introduction: Gli transcription factors are the primary effectors of the Hedgehog signaling pathway which has been linked to several different human tumors including cancers of the skin, brain, colon, prostate, blood and pancreas. We assessed the clinicopathological correlation of Gli1 expression in bladder cancer.

Materials & Methods: Bladder cancer cases were identified from the New Hampshire State Department of Health and Human Services Cancer Registry as histologically confirmed primary bladder cancer diagnosed between January 1st 2002 and July 31st 2004. Immunohistochemistry was performed to detect Gli1 and TP53. We computed Odds ratios and their 95% CI for Gli1 positivity for pathology stage using T code from TNM, invasiveness and grade using both WHO 1973 and WHO ISUP criteria.

Results: A total of 194 men and 67 women were included in the study. No difference were noted in sex, age, smoking status or high risk occupation when stained for Gli1. There was a statistical difference in Gli1 staining when comparing Ta and T1 tumors (OR 0.38, CI 0.21-0.93) and when comparing lower grade tumors (grade 1-2) and high grade tumors (grade 3) (OR 0.44, CI 0.21-0.93). Invasive transitional cell carcinoma was less likely to stain for Gli1 than noninvasive tumors but on multivariate analysis the difference was not statistically significant (OR 0.61, CI 0.29-1.27).

Conclusions: Gli1 may have a role in transitional cell cancer differentiation. Our data provides additional information on the role of effectors of Hedgehog signaling in the molecular pathogenesis of bladder cancer.

P19

Increased Alpha 1a and 1b Expression in the Castrated Rat Prostate

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Introduction and Objectives: Male aging is accompanied by hypogonadism and worsening LUTS/BPH. The hypogondal state should lead to diminution in LUTS/ BPH symptoms. To understand these paradoxical clinical effects, we used a castrate rat model examining contractility and mRNA expression of eNOS, nNOS, PDE5, TGFβ1, ROKα, ROKβ, alpha 1a, alpha 1b, alpha 1d, total myosin, non-muscle myosin and the smooth muscle specific transcriptional factor myocardin.

Methods: Male adult Sprague-Dawley rats (275 to 330 g) were divided into sham, surgical castration, surgical castration with testosterone proprionate (T) supplementation. Organ bath contractility studies, competitive and Real-Time RT-PCR, and histological examination were performed.

Results: The castrate model was validated histologically. The prostate and seminal vesicles atrophied. T supplementation reinstated weight. Total myosin immunostaining was essentially unchanged, though the glandular cells changed morphologically. Castration significantly decreased KCl and phenylephrine (PE)-induced prostate strip contraction in a dose-dependent manner. Alpha receptor subtypes 1a and 1b significantly increased by 2-fold. nNOS decreased 5-fold while eNOS increased 2-fold. ROKβ decreased 2-fold while ROKα showed no change. PDE5 was reduced 3.3-fold. TGFβ1 increased 4-fold. Competitive RT-PCR of the control prostate displayed around 50% SMA and 50% SMB, 85% SM1 and 15% SM2, 70%LC17a and 30%LC17b myosin isoforms. After castration, SMB, SM1 and LC17b increased by 20%, 15% and 5%, respectively. Total myosin, non-muscle myosin and myocardin significantly decreased 2-fold, 5-fold and 3-fold, respectively.

Conclusions: Castration increases prostate alpha 1a and 1b mRNA expression, possibly accounting for LUTS symptoms seen in the aging male faced with hypogonadism.

P20

Up-regulation of Transforming Growth Factor-β and the Counter-regulatory Effects of Hepatocyte Growth Factor in Fetal Sheep Bladder Outlet Obstruction

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Introduction: Obstructive nephropathy is a major cause of renal insufficiency in children. Transforming growth factor-β1 (TGF-β1) plays a central role in the pathogenesis of obstructive renal injury. Hepatocyte growth factor (HGF) has been found to reduce fibrosis and tissue injury, but its relationship to TGF-β1 is less defined. We hypothesize that renal TGF-β will be increased in a fetal sheep model of bladder outlet obstruction (BOO) with a coordinate and compensatory increase in HGF.

Materials & Methods: Six fetal sheep underwent partial BOO at 95 days gestation via a metal urethral ring and urachal ligation. These and four age-matched controls were sacrificed at 135 days gestation (term). Kidneys were retrieved, drained, and weighed. Formalin-fixed mid-sagittal kidney sections were obtained. Immunohistochemical localization of TGF-β1, TGF-β receptor type2 (TGF-βR2), and HGF was performed and quantified morphometrically.

Results: Obstructed kidneys showed significantly greater TGF-β1 and TGF-βR2 staining compared to controls (p=0.048 and p=0.026 respectively). TGF-β1 was largely localized to tubules and moderately to the interstitium, whereas TGF-βR2 staining was heavily localized to tubules. HGF staining in obstructed kidneys was significantly greater than in controls (p=0.017), and localized to tubules and less so to the interstitium.

Conclusions: TGF-β1 and TGF-βR2 are up-regulated in sheep subjected to BOO with predominantly tubular presence. HGF is coordinately up-regulated and co-localized, likely as a compensatory mechanism to counteract effects of TGF-β1. HGF appears to be an important co-factor in the pathophysiology of congenital obstructive nephropathy and may be useful diagnostically and therapeutically in preventing/attenuating renal injury.

17

Fluid Intake and Risk of Stress, Urgency, and Mixed Urinary Incontinence

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Introduction: Many women with urinary incontinence restrict their fluid intake in an effort to manage their urinary symptoms. Additionally, women without incontinence might limit their fluid intake hoping to prevent incontinence despite the lack of evidence. Because low fluid intake is associated with increased risks of several chronic diseases, more studies are needed. We prospectively investigated the relation between total fluid intake and incident urinary incontinence in the Nurses' Health Study cohorts.

Materials & Methods: We measured daily fluid intake using food frequency questionnaires among 65,167 women, aged 37-79 years, without incontinence at baseline (2000-2001). Women reported incontinence incidence on questionnaires during 4 years of follow-up. Multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards models.

Results: We found no association between total fluid intake and risk of incident incontinence (multivariable-adjusted HR 1.04, 95% CI 0.98-1.10 comparing top to bottom quintile of fluid intake). In analyses of incontinence type, total fluid intake was not associated with risks of incident stress, urgency, or mixed incontinence (HR 0.91, 95% CI 0.77 - 1.06 for stress; HR 1.13, 95% CI 0.88 - 1.44 for urge; and HR 1.12, 95% CI 0.89 - 1.42 for mixed incontinence comparing top to bottom quintile of fluid intake). We also found no associations between specific beverages (e.g. juice, soda, alcohol etc.) and incontinence risk.

Conclusions: No significant risk of incident urinary incontinence was found with higher fluid intake in women. Women should not restrict their fluid intake to prevent incontinence development.

18

Long-Term Treatment Interval of Percutaneous Tibial Nerve Stimulation: 18 Month Study Results

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Introduction: The Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) Study evaluates long term therapy effectiveness of percutaneous tibial nerve stimulation (PTNS) for OAB. The objective of this review is to evaluate the treatment interval frequency through 18 months of sustained therapy.

Methods: Following treatment success after 12 weekly PTNS treatments, subjects were on a set tapering protocol of PTNS for 3 months and then received ongoing therapy on a Personal Treatment Plan as determined by the investigator and subject to maintain sustained improvement in the subject's OAB symptoms. Questionnaires were completed every 3 months and voiding diaries were completed every 6 months.

Results: Of the PTNS subjects eligible to continue into the STEP Study, 52/60 (87%) were enrolled. The mean treatments/month by follow-up intervals were: 1.9 (3-6 months), 1.3 (6-9 months), 1.2 (9-12 months), 1.2 (12-15 months) and 1.1 (15-18 months). Median treatments/month were: 1.8 (3-6 months), and 1.1 (6-9, 9-12, 12-15, 15-18 months). All OAB-q domains and voiding diary parameters at 6, 12, and 18 months were significant for improvement compared to baseline for frequency, incontinence episodes, nighttime voids and moderate to severe urgency episodes ($p<0.001$).

Conclusions: Sustained significant efficacy of PTNS was demonstrated over 18 months with a mean and median of 1.1 treatments/month following initial success after twelve 30-minute weekly treatments.

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Sexual Function Following TVTO Placement: Minimum 12 Month Follow Up

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Introduction: The effect of anti-incontinence surgery on sexual function is not clear based on the current literature. The study aim was to examine the impact of TVTO on sexual function and vaginal symptoms.

Methods: This study is a retrospective review of thirty-three undergoing TVTO with a minimum of 12 month follow-up. Outcomes were assessed using validated questionnaires, with focus on the International Consultation on Incontinence Questionnaire-Vaginal Symptoms (ICIQ-VS). The ICIQ-VS is a validated measure assessing impact of vaginal symptoms and associated sexual matters on quality of life and treatment outcome. Incontinence impact questionnaire (IIQ-7) was used a secondary measure of quality of life. Quality of life scores were also compared to patient perceived level of improvement.

Results: Mean age was 61.8 years old (±13.6) with average parity of 2.1 children (±1.2). Improvements in ICIQ vaginal symptom (6.7 to 3.8, $p<0.01$), sexual function (4.1 to 2.7, $p=0.13$), and quality of life scores (3.2 to 1.6, $p<0.01$) were seen in comparison of baseline and 12-month questionnaire evaluations. VS QOL scores demonstrate score improvement, stability, and deterioration in 14, 14, and 5 patients, respectively. Pearson's correlation of QOL outcomes and patient perceived level of improvement demonstrated weak correlations (VS-QOL versus improvement ($r=-0.37$), IIQ versus improvement ($r=0.36$), $p<0.05$, both comparisons).

Conclusions: Anti-incontinence surgery is associated with improvements in validated measures of sexual function and vaginal symptoms. The vast majority of patients reported symptom stability or improvement in these endpoints. Vaginal symptom QOL outcomes and patient perceived improvement were weakly correlated.

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Ileal Loop Urinary Diversion for Non-Bladder Cancer Indications - Long-term Outcomes and Complications

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Introduction: We evaluated complications and patient satisfaction following supravesical urinary diversion for non-bladder cancer indications.

Materials & Methods: This IRB approved retrospective study was performed in 26 females and 10 males who underwent ileal loop diversion for non-bladder cancer indications by a single surgeon between 1999 to 2010. Charts were reviewed and patients were contacted to assess outcomes, complications and satisfaction following surgery.

Results: Of the 36 patients, indications for urinary diversion were: neurogenic bladder (18), radiation cystitis (11), prostatic brachytherapy complications (3), refractory incontinence (3) and recurrent urinary tract infection (1). All patients were left with their native bladders. Complications occurred in 18 patients (50%) including: UTI (25%), ureteral stenosis (19%), stomal hernia (14%), pyocystis (8%), bowel leak, (6%), and nephrolithiasis (6%). Fourteen patients were deceased at time of our review (mean 27 months after surgery). Nineteen of the surviving 22 patients (86%) were interviewed. Their mean age was 62 years and mean time from surgery was 39 months. Patients had a mean overall satisfaction score of 8.63 ± 1.83 on a scale from 0-10 (10 = most satisfied). When asked if they would repeat the surgery 14 (74%) said yes, 2 (11%) said no, and 3 (16%) said they were unsure.

Conclusions: In selected patients, ileal loop diversion can be used to manage recalcitrant lower urinary tract complications. Despite a relatively high complication rate, long-term patient satisfaction remains high. The bladder may be left in place given the low pyocystis rate.

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Short-term Outcomes of Robotic Assisted Sacrocolpopexy for Pelvic Organ Prolapse

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Introduction and Objectives: We present short term surgical and quality of life outcomes in a cohort of patients that underwent robotic assisted sacrocolpopexy (RASCP) for symptomatic pelvic organ prolapse.

Methods: A prospective analysis was performed to evaluate perioperative and quality of life outcomes following RASCP for the treatment of symptomatic POP. All patients underwent multi-disciplinary evaluation including examination with a urologist and gynecologist. Prolapse was graded by the Baden-Walker staging. Candidates underwent RASCP with/without supracervical hysterectomy and urethral sling. Patients were followed postoperatively with physical examination and questionnaires (PFDI, ISS, AUASS, AUAQOL). Data was available at 3, 6 and 12 months following surgery.

Results: From 4/2010 to 4/2011, 58 patients with POP underwent RASCP. All patients underwent concomitant mid-urethral sling, (8 miniarc, 50 PVS), 30 patients underwent concomitant robotic assisted supracervical hysterectomy. Mean patient age was 59.9 years (range 45 - 80). Mean EBL was 50cc. Mean operative time was 156 minutes. Mean operative prolapse stage was 3.2 on Baden-Walker staging (0-4). Mean length of stay was 48hrs. There were no conversions. There was one bowel injury. Mean follow up was 6 months. One patient demonstrated apical recurrence at 6 months postop. Patients demonstrated statistically significant QOL improvement following surgery based on mean scores PFDI (3.6 vs 1.9, $p<0.05$), ISS (2.2 vs 0.8, $p<0.05$) and AUASS (3.75 vs 1.5, $p<0.05$) and AUAQOL (4.3 vs 1.2 $p<0.05$).

Conclusions: RASCP is a safe and highly efficacious treatment option for women with symptomatic POP. Patients reported an improvement in their QOL.

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Is Complete Cure Necessary for Satisfaction in Patients Undergoing Concurrent Anti-incontinence and Prolapse Surgery?

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Introduction: Simultaneous repair of SUI and prolapse has become increasingly common. In these cases, determinants of patient satisfaction are further complicated given the fact that complete surgical success may be achieved in one component but not the other. The study focus was to determine if patients report satisfaction if success is only achieved with respect to a single outcome when concurrent surgeries are performed.

Materials & Methods: We performed a retrospective review of post-operative results on 92 consecutive women undergoing variety of AI procedures and/or prolapse repair. Multiple validated outcome measures were used to evaluate success following AI surgery (ICIQ-FLUTS, SUI item, pad use, subjective SUI cure) and prolapse (ICIQ-VS, POPQ stage). Multiple statistical analyses (Pearson's correlation, Mann-Whitney, and Fischer's exact) were performed to assess for association between outcome measures and patient satisfaction.

Results: Eighty women (87%) reported satisfaction following surgery with mean follow-up of 12 months. Cure of both prolapse (POPQ stage <2) and SUI (subjective cure) was associated with satisfaction ($p<0.05$). Satisfaction rates among these dual cure patients were comparable to satisfaction rates in women who had cure of only one entity (prolapse OR incontinence). ICIQ-VS improvement correlated with overall post-op satisfaction ($p<0.05$) while the other examined measures did not demonstrate statistically significant correlation with post-op satisfaction.

Conclusions: Not surprisingly, cure of both incontinence and prolapse in the setting of a concominant procedure was associated with statistically significant satisfaction. Interestingly, these satisfaction rates do not differ greatly from those in patient's who reported cure of only one problem.

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Assessment of Radiation Exposure from Diagnostic Imaging in Patients Undergoing Ureteroscopy with Laser Lithotripsy for Upper Tract Stones

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Introduction: Patients with urolithiasis who undergo ureteroscopy (URS) are commonly diagnosed with CT, X-ray, and renal ultrasound. There has been recent concern that these patients are at increased risk for radiation exposure above the annual limit of 50 millisieverts (mSv) due to diagnostic imaging, especially with CT scan. Therefore, we evaluated the number of imaging studies and the amount of radiation exposure to patients undergoing URS for upper tract stones.

Methods: An IRB approved retrospective study was conducted on patients who underwent URS between 2003-2007. Total number of imaging studies was analyzed over 1-14 months. Time period of data collection was determined from the initial diagnosis of the stone until 6 weeks following completion of URS. Radiation dose was calculated using effective radiation dose standards.

Results: 286 patients were identified. Mean size of stone was 8.71 +/- 4.2 mm. The most common stone location was renal (43%). Patients underwent an average of 1.6 CT scans (range 0 to 6) over an average of 5 months. 124 patients (43%) received $\geq$ 50mSv which is equivalent to a $\geq$ 2 CT scans. Smaller stone size and stone location increased the probability of receiving $\geq$ 2 CT scans in one year ($p=0.02$). Patient age, stent placement, and/or post surgical complications were not significant.

Conclusions: 43% received $\geq$ 50mSv of radiation over one year. Smaller size and mid/distal location of the stone significantly increased the risk of receiving a higher number of imaging studies emphasizing the increased radiation risk to patients with urolithiasis.

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Ureteral vs Renal Laser Lithotripsy- Are They Really Equal?

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Objective: The role of ureteroscopic laser lithotripsy (ULL) is well established for the management of ureteral stones and is increasingly accepted for renal stones. However, stone location is not currently differentiated by procedural name or billing code. We hypothesized that these cases are not equivalent in terms of the surgeon's work as measured by the operating time, and we assessed if significant variations exist within the umbrella of CPT 52353: "ureteroscopic lithotripsy".

Methods: We retrospectively reviewed records of all patients undergoing unilateral ULL under the care of one fellowship trained endourologist between 2008 and 2010. Patients who underwent simultaneous additional endoscopic procedures, including bilateral ureteroscopy, were excluded. Demographics, operative time, stone size and location, and presence of previously placed stent were assessed and compared. Cohorts were designated according to stone location -- ureteral or renal.

Result: Of the total 213 ULL cases reviewed, 115 were ureteral stones and 98 renal stones. Renal stones had a significantly increased mean operative time of 112 minutes versus 70 minutes for ureteral stones ($p<0.001$). Renal stone size was significantly larger (11.3mm vs 7.7mm, $p<0.001$), and these cases had a higher preoperative stent rate (55% vs 37%, $p=0.0128$).

Conclusion: Despite bundling within a single CPT code, ureteroscopic management of renal stones and ureteral stones were markedly different, with a significant increase in operative time for renal stones. Renal stone size was significantly larger, as can be expected. In the same manner as resection of bladder tumors and lithotripsy of bladder stones, CPT differentiation should be considered.

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Radiation Exposure during Extracorporeal Shockwave Lithotripsy
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Introduction: Efforts should be made to minimize patient radiation exposure during extracorporeal shockwave lithotripsy (SWL).

Materials & Methods: Fluoroscopy time (FT) and radiation effective dose (Deff) were determined for 422 consecutive SWL. Standard imaging protocol was applied and adjusted based on clinical situation. Fluoroscopic imaging was done prior to; at 1,000 and 2,000 shocks; and at completion. Patient Deff was calculated using Monte Carlo simulation rendered by PCXMC software.

Results: 422 ESL (259 males; 163 females [79 of child bearing age]) were analyzed. Mean FT was 95.4 seconds (range 21-600); average Deff per patient was 0.847 mSv (range 0.116- 5.878). Digital exposures were not routinely done. FT based on stone size (<25mm2 = 94.1sec; 25-75 mm2 = 95.7 sec; >75 mm2 = 95.9 sec) was not significant. Estimated average Deff for patients was 0.784 mSv (<25mm2); 0.863 mSv (25-75 mm2); and 0.882 mSv (>75 mm2), respectively. No significant difference was noted regarding stone location [(ureteral 0.940 mSv); (renal 0.770 mSv)]. FT for females under age 49 was 94.2 +/-5.9 sec and mean Deff was 0.785 mSv (range 0.165-4.325). Deviation from the imaging protocol occurred in 36 ESL treatments (8.5%) with mean FT of 258.3 +/- 16.0 sec (range 185-600) and mean Deff of 2.336 mSv.

Conclusions: Radiation exposure during SWL is comparable to that of a conventional radiograph of the abdomen (KUB) at 0.7 mSv. Implementation of a standard imaging protocol during SWL results in a reliable means to minimize radiation exposure to the patient.

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Relationship Between Protein Intake and Urine Composition in Patients With Nephrolithiasis
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Introduction: Epidemiologic studies have demonstrated that high dietary protein intake may increase risk of nephrolithiasis. The current study examines the relationship between dietary protein intake and 24-hour urine composition in patients with nephrolithiasis.

Materials & Methods: A retrospective review was performed. Multivariate linear regression examined the relationship between protein intake and 24-hour urine composition. Regression models adjusted for known risk factors for stone disease. Urine urea nitrogen was used as a surrogate for dietary protein intake.

Results: 460 patients were included in the study. Female:male ratio was 184:276 (i.e. 40% female), mean age was 52.4 years (SD 14.3), mean BMI was 28.7 (SD 6.3). Mean 24-hour urine urea nitrogen was 12.1 g/day (SD 4.5). On multivariate linear regression, increasing dietary protein intake was significantly associated with increasing urine calcium (β = 4.53, 95% CI 0.51 to 8.54), uric acid (β = 0.012, 95% CI 0.007 to 0.018), sodium (β = 1.45, 95% CI 0.85 to 1.96), and volume (β =0.073, 95% CI 0.04 to 0.10). Increasing dietary protein was also significantly associated with decreasing urine citrate (β =-23.3, 95% CI -34.8 to -11.8) and pH (β =-0.05, 95% CI -0.07 to -0.04). There was no association between protein intake and urine oxalate.

Conclusions: Among known risk factors for nephrolithiasis, increasing dietary protein intake appears to increase urine calcium and uric acid, while decreasing urine citrate and pH. Restriction of protein intake, therefore, should reduce patient risk for both calcium oxalate and uric acid nephrolithiasis.

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Nationwide Trends in Imaging Utilization during the Emergency Department Evaluation of Flank Pain, 2000-2008
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Introduction: Patients with acute flank pain are most commonly evaluated in the emergency department (ED) with computed tomography (CT). At present, however, our understanding of radiographic practice patterns in the emergency evaluation of flank pain is limited. Therefore, we performed a study to characterize the utilization of conventional radiography (CR), ultrasound (US), and CT in the ED evaluation of patients with acute flank pain.

Materials & Methods: A retrospective cross-sectional analysis of ED visits using data from the National Hospital Ambulatory Medical Care Survey (2000-2008) was performed. Specific visits for a complaint of either flank pain or kidney pain were further analyzed.

Results: Over the time period studied, there was a significant increase in the utilization of CT ($p<0.0001$), a significant decline in the use of CR ($p=0.0156$), and the utilization of US remained stable ($p=0.3012$). Over that same time period, the proportion of patients with flank pain who were diagnosed with a kidney stone remained stable, at approximately 20% ($p=0.4441$).

Conclusions: Between 2000 and 2008, there was a significant increase in the utilization of CT in the emergency evaluation of CT utilization, but the proportion of patients with flank pain who were diagnosed with a kidney stone remained stable.

28

Percutaneous Nephrolithotomy in Patients with Neurogenic Bladder Dysfunction
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Introduction: Patients with neurogenic bladder (NGB) dysfunction are at increased risk of urolithiasis, and frequently develop large renal stones requiring percutaneous nephrolithotomy (PNL). Patients with myelomeningocele (MMC) have NGB but typically have abnormal body habitus, making percutaneous access and surgical positioning more difficult. Recent literature suggests that the many patients with NGB possess metabolic rather than infectious stones.

Materials & Methods: We reviewed the medical records of all patients who underwent PNL at our institution from 2001 to 2010. Patients with NGB were selected for this study. Comparison was made between patients with MMC versus other forms of neurologic disease.

Results: A total of 26 patients with NGB underwent 39 PNL procedures between 2001 and 2010. The majority of patients had infectious stones. Major complications were sepsis or bleeding requiring transfusion. There was no significant difference in stone size, peri-operative complications, stone composition, stone-free rate, or radiation exposure between patients with or without MMC.

Results:

	MMC	Non-MMC	All NGB patients	p-value
Patients (#)	11	15	26	
Stone procedure episodes (#)	18	21	39	
Avg peri-op decrease in Hct (%)	5.3	4.1	4.6	0.53
Avg peri-op change in GFR (mL/min)	-6	-15	-11	0.17
Major peri-op complications	11%	5%	8%	0.46
Avg initial stone area (mm2)	423	580	513	0.31
Patients with infectious stones	80%	88%	84%	0.57
Stone free at 3 months	64%	56%	59%	0.62
Avg fluoro dose (mGy)	1031	901	959	0.71

Conclusions: Our experience failed to confirm recent reports suggesting a high number of metabolic stones, and supports previous findings that this population has a high percentage of infection stones. Despite the abnormal body habitus of most patients with myelomeningocele, PNL remains equally effective and safe when compared to other patients with NGB and normal body habitus.

P21

Delayed Ureteral Complications Following Complex Partial Nephrectomy
Jose Reyes, Daniel Canter, Jay Simhan, Marc Smaldone, Ervin Teper, Alexander Kutikov, David Y.T. Chen, Robert G. Uzzo
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Introduction: The recent AUA guidelines for management of the clinical T1 renal mass highlight the role of nephron sparing surgery (NSS). As detailed in the recent guidelines, nephron preservation is associated with a higher risk of major urologic complications. Ureteral complications including delayed ureteral stricture (DUS) formation after NSS is an uncommonly reported event. Here we report the incidence of DUS after complex NSS in order to identify the potential risk factors.

Materials & Methods: Using our institutional kidney cancer database, we identified 720 patients who underwent NSS from January 1, 2000 through December 31, 2010 and identified eleven (1.5%) patients with a DUS. Patient and tumor characteristics were reviewed.

Results: Median tumor size and R.E.N.A.L. Nephrometry score was 4.1 (2-7.2) cm and 10p (4p-11p), respectively. Eighty percent of tumors were located in the mid or lower pole of the kidney. Eight (72.7%) patients with DUS experienced a postoperative urinary leak. Two (18.2%) patients experienced a postoperative retroperitoneal hemorrhage with one of these patients requiring selective embolization. All ureteral strictures were in the upper third of the ureter and were diagnosed at a minimum of 10 weeks postoperatively (median 154 days, range 70-400).

Conclusions: Ureteral stricture formation is an uncommon and under reported event following complex NSS. Risk factors include tumor complexity, imperative indications, mid or lower pole location, postoperative urinary leak and hemorrhage. Although uncommon, postoperative DUS can occur after NSS for complex renal masses, necessitating patient counseling and diligent postoperative surveillance.

P22

Comparing Post-operative Complication rates between Neoadjuvant Chemotherapy and Chemotherapy Naïve Patients who undergo Cystectomy for Bladder Cancer
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Introduction: Although it may appear implicit that patients who receive neoadjuvant chemotherapy (NC) for bladder cancer would have higher complication rates post-operatively, there has been sparse literature published on this subject. Our single institution study compares complication rates between NC and chemotherapy (CT) naïve patients who underwent radical cystectomy (RC).

Methods: We performed a retrospective review from our bladder cancer database of 208 patients and we included any patient from 2004-2011 who underwent cystectomy for bladder cancer. 13 patients were excluded from analysis because they died prior to cystectomy. Immediate post-operative and 90 day complications were recorded for all patients.

Results: Interestingly, 60.5% of patients in the NC group and 71.3% in chemotherapy naïve group had at least one complication. The Clavien-Dindo classification scores were 2.39 and 2.55 for the NC and CT naïve groups, respectively. There was a total of 347 post-operative and 90 day complications in 208 patients, or 1.73 complications per patient.

	Neoadjuvant	CT naive
Number of patients	50	158
Age (years)	65.7	68.1
Gender	41M/9F	131M/27F
EBL (mL)	1214	898
Length of stay (days)	10	11.7
Follow up (months)	20.8	27.5
OR time (minutes)	422	402
ASA score	2.78	2.77
Preoperative albumin	3.87	4.01

Conclusions: Patients who underwent NC had a 10.8% lower post-operative complication rate than CT naïve patients. Therefore, in our single institution study NC does not confer an increased complication risk and the potential risk for complications should not deter urologists from the pursuing this option for patients.

P23

Durable Oncologic Outcomes after Radiofrequent Ablation for T1 Renal Cell Carcinoma in Poor Surgical Candidates
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Introduction: Long-term oncologic outcomes for radiofrequency ablation (RFA) of renal cell carcinoma (RCC) are limited.

Methods: Between 1998 and 2008, 311 biopsy-proven RCC were treated with RFA in 274 patients. Exclusion criteria included history of prior RCC or known metastatic RCC at time of RFA (n=92). 26 were lost to follow-up prior to their 6-month imaging study. We retrospectively reviewed the long-term oncologic outcomes for 193 patients. Mean follow-up was 4.6 yrs (range 1-12, SD 2.3).

Results: Mean age was 71 years. Mean Charlson Score was 5.46. Tumor size averaged 3.1cm (SD 1.3cm) and 64 (33%) were endophytic. Tumor breakdown by stage was T1a: n=153 (79%), T1b: n=37 (19%), and T2: n=3 (2%). Initial treatment success rate was 89%. There were 6 local recurrences (3%) in 4 patients with T1b disease and 2 patients with T2 disease with an average time-to-recurrence of 2.9 years (SD 0.7). 95% of patients with T1a RCC were disease free at last follow-up, in comparison to 81% of those with T1b and 33% of those with T2 disease (p=0.008). At last follow-up 178 (92%) patients were disease-free. 16 (8.2%) developed metastatic disease and 4 patients (2%) died of RCC. Mean disease-free survival was 4.3 years (SD 2.4).

Conclusions: In patients who are poor surgical candidates, RFA results in durable local control and a low risk of disease recurrence in T1 RCC. Higher stage, however, correlates with a lower disease free survival and should be considered when evaluating treatment options.

P24

Comparing Outcomes in Elderly Patients after Laparoscopic Radical Nephrectomy, Open Partial Nephrectomy and Cryoablation for Renal Masses
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Introduction and Objectives: There is minimal research comparing morbidity and mortality in elderly patients undergoing various types of treatment for renal cell carcinoma (RCC). This study compares open partial nephrectomy (OPN), laparoscopic radical nephrectomy (LN) and cryoablation (CA) in patients 70 years or older and evaluates outcomes between these cohorts.

Methods: We performed a retrospective review using our RCC database of 500 patients from 2001-2009. Inclusion criteria were any patient older than 70 years of age who underwent OPN, LN, or CA. 101 patients were identified of which 28, 38 and 35 had OPN, LN, or CA, respectively.

Results: Recurrence free survival (RFS) for the entire cohort was 98.0%, overall survival (OS) was 88.1%, and cancer specific survival (CSS) was 98.0%. The average follow up was 25.3 months. Only one patient (in the LN cohort) required hemodialysis (HD). The mean percentage decrease from pre to post-operative glomerular filtration rate (GFR) for OPN, LN and CA were 7%, 33%, and 10.7% respectively. The complication rates were 78.6%, 36.7%, and 31.4% in the OPN, LN, and CA cohorts, respectively.

Conclusions: Our data suggests that patients 70 years or older who undergo partial nephrectomy experienced increased morbidity given their higher complication rate. Only one patient in the LN cohort went on to require HD, questioning the ultimate benefit of nephron sparing surgery in this age group.

Concurrent Poster Session II: Oncologic Diseases
3:20 pm-4:00 pm

P25

Modifying Utilization of Urine Cytology Testing During Follow-up for Patients with Urothelial Carcinoma
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Introduction: Urine cytology is routinely used at initial diagnosis and during follow-up of patients with urothelial carcinoma (UC). We hypothesized that urine cytology results at time of initial diagnosis in UC is representative of the urine cytology when patients recur.

Materials & Methods: A retrospective review of patients newly diagnosed with stage Ta or T1 bladder UC in 2004-2005 was performed. Data were collected from January 2004 to March 2011 regarding demographics, urine cytology, pathology, bladder UC recurrence, and follow-up. 161 patients were evaluated of whom 43 were excluded due to loss to follow-up (17) or unavailable initial cytology in the medical record (26).

Results: 118 patients were evaluated with a mean follow-up of 61.8 months. Positive urine cytology was seen in 46/118 (39%) of patients at initial diagnosis. A total of 76/118 (64%) had recurrent bladder UC with a mean recurrence time of 16 months. In patients with recurrent disease, cytology evaluation had a sensitivity of 76% for detection of recurrence amongst patients who had a history of positive cytology with their initial tumor. However, amongst patients with a history of negative cytology with their initial tumor, cytology only had a sensitivity of 17% during recurrence. Cytology result remained a significant predictor of positive cytology results with tumor recurrence in multivariate analysis when controlling for grade, tumor size, and multifocality ($p<0.0001$).

Conclusions: Urine cytology is a useful diagnostic test for follow-up of patients with UC only in those who have a positive result during the first diagnosis of UC.

P26

Surgical Outcomes of Non-hilar Clamping Partial Nephrectomy; An Updated Twenty Year Experience
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Introduction: Non-clamping partial nephrectomy has superior renal outcomes and equivalent oncologic outcomes compared to hilar clamping partial nephrectomy in initial investigations. Potential hindrances to widespread acceptance include concerns over technical difficulty and the associated learning curve. Our purpose is to demonstrate durable renal, perioperative and oncologic outcomes from a multi-surgeon, single institution experience over the past twenty years.

Methods: 695 non-clamping partial nephrectomies were performed at our institution between 1990 and 2010. 469 patients with inadequate follow up, familial renal cancer syndrome, solitary kidney, or benign pathology were excluded. Patient demographics, operative data, complications, oncological outcomes, and percent change of early and late glomerular filtration rate (GFR) of the remaining 226 patients were analyzed. Patients were placed into 3 chronological groups (1st third, 2nd third, 3rd third) based on date of surgery, and the above parameters were compared using Student's T-test to investigate changes over time.

Results: Patient demographics, operative outcomes, complications, surgical margins, local recurrence, overall and disease specific survival, and percent change in eGFR were statistically similar among the three groups. Loss of renal function among the early and late time points was not observed. Over time more partial nephrectomies were performed for bilateral tumors ($p=0.05$), less were performed for advanced disease ($p=0.05$), and length of hospital stay decreased ($p=0.05$).

Conclusions: Over 20 years experience, non-clamping partial nephrectomy has durable and consistent outcomes in regards to postoperative renal function, peri-operative complications and disease specific survival. This supports an acceptable learning curve and potential widespread application of this technique.

P27

Pyeloperfusion as a Protective Mechanism for Radiofrequency Ablation of Renal Carcinoma Contiguous to the Ureter: Technique, Results and Complications
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Introduction: Radiofrequency-ablation (RFA) is an effective means of renal tumor ablation. Ablation of masses adjacent to the ureter risks ureteral injury/stricture. Placement of a ureteral catheter and pyeloperfusion with dextrose 5% in water (D5W) has been used as a method of reducing the risk of ureteral injury/stricture.

Materials & Methods: Between November 2005 and July 2010, 46 patients (52 ablations) required pyeloperfusion to protect the ureter. Patients were selected for retrograde-pyeloperfusion during RFA if the tumor was located within 1.5cm of the ureter. Pyeloperfusion was performed via a 5 Fr ureteral catheter and retrograde instillation of D5W. Tumors were classified as central, exophytic, or mixed according to the Gervais classification system. All procedures were performed under CT-guidance.

Results: 52 RFAs with pyeloperfusion were performed with an 87% success rate. Median tumor diameter was 3.3 cm. 14/45 (31%) patients had major complications according to the Society of Interventional Radiology classification, but 2 patients (4%) developed a ureteral stricture managed with stenting. 5 patients (10%) had significant hematuria, 2 (4%) had urinomas requiring IR-drainage, and 1 had pseudoaneurysm requiring angioembolization. 2 patients (4%) had delayed abscesses: 1 patient underwent IR-drainage of the abscess, 1 underwent nephrectomy for possible recurrent tumor, but was found to be an abscess with no evidence of malignancy.

Conclusions: RFA for renal masses is well-tolerated. Pyeloperfusion for ablations adjacent to the ureter led to only 2 ureteral strictures but also 2 delayed abscesses. Our rate of complications is slightly higher than that of other contemporary RFA series.

P28

Masses Treated by Thermal Ablation are Low or Moderately Complex as Measured by the R.E.N.A.L-Nephrometry Scoring System
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Introduction: Despite the AUA Guidelines listing thermal ablation (TA) as a treatment option for the clinical T1 renal mass, treatment decision-making for renal lesions remains subjective. The R.E.N.A.L.-Nephrometry scoring system (NS) was introduced to objectify salient renal mass anatomy and standardize academic reporting. Preliminary reports have evaluated its utility in terms of surgical decision-making and predicting post-operative complications. In this study, we characterize our experience with renal lesions undergoing TA using NS.

Materials & Methods: We queried our prospectively maintained kidney cancer database of 2,312 patients and identified 39 patients who underwent TA with available Nephrometry scores. Patient clinical, tumor, peri-operative, and oncologic characteristics were reviewed.

Results: Median patient age, serum creatinine, estimated glomerular filtration rate, and Charlson Comorbidity Index were 71 (range=57-86) years, 1.39 (range=0.7-3.5) mg/dl, 57.5 (range=23.3-93.8) ml/min, and 2 (range=0-5), respectively. Chronic kidney disease stage III or higher was present in 56% of patients. Median NS was 6 (4-10). Low (NS=4-6), moderate (NS=7-9), and high (NS=10-12) complexity tumors were observed in 20 (51%), 17 (44%), and 2 (5%) patients. Minor (Clavien I-II) and major (Clavien III-IV) complications occurred in 4 (10%) and 1 (3%) patients, all of whom had moderate complexity tumors. Five (13%) patients had a recurrence, 4 of whom had moderate complexity tumors.

Conclusions: In our institutional experience, 95% of lesions undergoing TA are low or moderate complexity as measured by the R.E.N.A.L-Nephrometry scoring system. There appears to be a direct relationship between increasing tumor complexity and the incidence of peri-procedural complications and disease recurrence.

P29

Renal Oncocytoma Diagnosed by Percutaneous Biopsy Can Be Safely Followed but Must Not Be Forgotten

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Introduction: Percutaneous needle biopsy is emerging as an option for identifying benign renal neoplasms. The natural history of *in situ* renal oncocytoma has not been well characterized. We present radiographic and clinical outcomes of patients diagnosed with oncocytoma by a percutaneous needle biopsy.

Materials & Methods: We performed a retrospective review of 899 patients who underwent percutaneous core biopsy of a renal mass at our institution from 1997-2010. We excluded patients with ≤ 12 months follow-up, leaving 40 patients who were diagnosed with oncocytoma by dedicated genitourinary pathologists. Follow-up and treatment outcomes were assessed.

Results: 38/40 patients underwent active surveillance with serial cross-sectional imaging. Median follow-up time was 26.0 months. Median tumor size was 2.5 cm. Median growth rate was 0.1 cm/year. 1 patient underwent delayed intervention (radical nephrectomy) due to an increase in lesion size from 6.6 cm to 7.1 cm over a 9 month period. Surgical pathology confirmed oncocytoma. 2/40 patients received immediate treatment via radical nephrectomy (1) or RFA (1). Tumor sizes were 4.3 cm and 2.6 cm, respectively. Indications for treatment were baseline size and imaging characteristics (1) or patient preference (1). In 1 patient (4.3 cm tumor) who underwent immediate surgery, surgical pathology revealed papillary RCC, Fuhrman Grade 2.

Conclusions: Renal oncocytoma is a slow growing lesion which, in our series, had a median growth rate of 0.1 cm/year. The biopsy diagnosis of oncocytoma may allow patients to avoid the need for intervention; however, our data highlight the need for close follow-up with serial imaging.

P30

R.E.N.A.L. Nephrometry Score is a Surrogate for Surgical Difficulty

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Introduction: As health care costs increase, so does the demand for comparative efficacy studies. Surgical efficacy studies are problematic as technical complexity is difficult to quantitate. The RENAL nephrometry score (NS) is a standardized system for describing kidney tumors attempting to quantify surgical complexity. Aside from one observational report, these methods have not been externally evaluated. We tested the hypothesis that higher NS correlates with surgical difficulty during partial nephrectomy (PN).

Materials & Methods: Using a retrospective database of laparoscopic or open PN performed from 2005-2010 containing patient demographic data, operating details and post-operative glomerular filtration rate (eGFR). CT or MRI scans were used to generate RENAL NS. Surgical difficulty was defined by blood loss, operating room time, ischemia time (IT) and length of stay, while eGFR was considered indicative of post-operative renal function. Univariate and multivariate analyses identified associations among the measured characteristics. All statistical analysis used SAS 9.2.

Results: In 139 patients, higher NS correlated with IT in both univariate (p=0.0002) and multivariate analysis (p=0.0010) when controlling for potential confounders. NS also correlated significantly with post-operative eGFR in univariate analysis (p = 0.0302) and displayed a trend in multivariate analysis (p=0.0824). NS was not correlated with other surrogates for surgical complexity.

Conclusions: Surgical clamp time is a logical surrogate for technical difficulty. Higher RENAL NS strongly predicted surgical clamp time during PN suggesting it serves as substitute for clinical judgment. NS may also reflect long term outcome of PN, as reflected by its correlation with post-operative GFR.

P31

Role of Tumor Location and Provider Specialty in Selecting Patients for Percutaneous Versus Surgical Cryoablation of the Small Renal Mass

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Introduction: To determine how tumor location and provider specialty effect selection of tumors for surgical (SCA) and percutaneous (PCA) cryoablation of small renal masses (SRMs).

Materials & Methods: MEDLINE search was performed of the published literature in which cryoablation was used as therapy for localized renal masses. Tumor location was recorded amongst three categories: (1) anterior, posterior, and lateral; (2) upper, mid, and lower pole; and (3) endo-, meso-, and exophytic. Reports were stratified by medical specialty, defined as Urology, Radiology, or both.

Results: 46 studies, encompassing 1,955 lesions treated by surgical (n=29) or percutaneous (n=17) cryoablation were analyzed. Reporting rates for SCA versus PCA are 35% (10/29) vs. 47% (7/17) for anterior/posterior lesions. SCA was performed in 40% of reported anterior lesions, compared to PCA in 75% of posterior lesions. Reporting rates for Urologists were 31% for SCA and 60% for PCA. Radiologists reported location in 20% of their reports. The combined approach report rates were SCA 67% and PCA 50%.

Conclusions: While efficacy does not differ between SCA and PCA, health care cost and patient morbidity significantly favors PCA. Tumor location is classically the primary determinant in selection of SCA vs. PCA, yet data regarding tumor location is vastly under reported in the literature. Moreover, over 30% of lesions treated with surgical cryoablation appear to be posterior lesions. These findings raise significant quality of care issues, since some of the most co-morbid urologic patients appear to be exposed to unnecessary risks with SCA.

P32

Short-term Complications after Cystectomy in Patients Treated with Neoadjuvant Chemotherapy is Only Associated With Comorbidity

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Introduction: We wished to evaluate the complication rates after cystectomy in patients who received neoadjuvant chemotherapy for treatment of muscle-invasive urothelial carcinoma (MI-UC).

Methods: We evaluated patients with MI-UC who received neoadjuvant chemotherapy cisplatin and gemcitabine between January 2003 and February 2011 (n=32). Patients were excluded if they also received neoadjuvant radiation therapy (n= 15). Any complication within 90 days of surgery was graded using the Clavien-Dindo system.

Results: Median patient age was 70 years with a median American Society of Anesthesiologists (ASA) score of 3. Patients received a median of 3 cycles of chemotherapy a median of 119 days prior to RC. Ileal conduits were performed in all except for 3 cases, in which orthotopic neobladders were performed. Pelvic lymphadenectomy was aborted in 2 cases due to extensive fibrosis. Median operative time was 9.5 hours with median EBL of 900cc. 25 complications were identified in 10 patients (59%). Complications were classified as grade 1 in 6% (1), grade 2 in 41% (7), grade 3 in 12% (2) and grade 4 in 6% (1). Increased risk of complication was associated with ASA Score ≥ 3 (p=0.03), whereas number of cycles of neoadjuvant GC, duration between CG and RC, type of urinary diversion, BMI, or preoperative hydronephrosis did not (P>0.05).

Conclusions: The early complication rates in patients treated with neoadjuvant CG before cystectomy is associated with ASA score, while the number of cycles of chemotherapy, type of urinary diversion or interval between chemotherapy and RC do not affect morbidity.

P33

Pathologic Upstaging Following Complete Transurethral Resection and Early Cystectomy for Clinical Stage T1 Bladder Cancer

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Introduction: Early cystectomy is advocated for clinical stage T1 (cT1) bladder cancer with frequent pathologic upstaging in recent multicenter studies. However, details such as timing, tumor size and completeness of resection prior to cystectomy may be difficult to obtain and were noted as potential confounding variables. Herein we evaluate these factors in a contemporary single institution analysis of cT1 bladder cancer patients undergoing radical cystectomy.

Materials & Methods: From 2000-2011, 120 patients underwent early cystectomy for cT1 disease. Inclusion criteria consisted of documented evidence of visibly complete TURBT and uninvolved muscularis propria in the TUR specimen. Estimated tumor size at TUR and time interval from initial T1 diagnosis to cystectomy were correlated with final pathologic stage.

Results: Of 120 cT1 patients undergoing early radical cystectomy, 51 (42%) satisfied the inclusion criteria. Sixteen (31%) of 51 were upstaged to pT2 (n=6), pT3 (n=7) or pT4 (n=3) disease. Occult nodal metastases were identified in 4 (8%) patients. The mean interval from initial T1 diagnosis to cystectomy was 10.3 months in the non-upstaged group, versus 6.8 months in the upstaged group (p=0.15, t-test). No significant difference in upstaging was observed on the basis of tumor size (p=0.69, Fisher's).

Conclusions: In our series, pathologic upstaging of cT1 bladder cancer occurred in 31% of patients despite visibly complete TURBT. Neither the interval from diagnosis to radical cystectomy nor tumor size at TUR correlated significantly with pathologic stage. Better preoperative staging modalities are needed in assigning cT1 patients to radical cystectomy versus other treatment.

P34

Smoking Knowledge Assessment and Cessation Trends in Patients with Bladder Cancer Presenting to a Tertiary Referral Center

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Introduction: Smoking is the leading risk factor for bladder cancer (BC) in industrialized nations. Little information is available regarding BC patients' knowledge of smoking's risks and the role of their urologists in initiating smoking cessation at the time of diagnosis.

Materials & Methods: A smoking knowledge and cessation questionnaire was administered to 71 patients referred to a tertiary referral center for BC from April 2008 to June 2009. The questionnaire captures data on demographics, BC history, smoking status and history, risk factor knowledge, and cessation patterns.

Results: The mean age of the cohort was 65.1 (range: 42-86) years and 72% were male. At the time of referral, 71 (100%) patients knew smoking was a risk factor for lung cancer compared to 61 (86%) for that of BC. Only 36 (51%) patients knew smoking was the leading risk factor for BC. Of the 17 (24%) patients smoking at the time of their BC diagnosis, 12 (71%) were counseled by their referring urologist to quit smoking, however the significant majority (76%) were not offered any specific intervention.

Conclusions: The association between smoking and BC was not as well known as that of lung cancer in our cohort of patients. Most current smokers were advised to stop smoking by their primary urologist; however few were offered any intervention to aid cessation. Urologists should assume a more active role both in educating patients regarding smoking's link to BC and in initiating smoking cessation.

P35

Perioperative Systemic Chemotherapy Confers a Cancer-Specific Survival Benefit in T3 Urothelial Carcinoma of the Renal Pelvis

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Introduction: Limited and conflicting data are available regarding adjuvant and neoadjuvant chemotherapy in patients with locally advanced upper tract urothelial carcinoma (UTUC) of the renal pelvis. Here we present our experience with treatment of patients with T3 UC of the renal pelvis.

Methods: Patients diagnosed with UTUC at the Massachusetts General Hospital between January 1993 and March 2011 were reviewed. Forty-one patients with T3 disease of the renal pelvis on pathology were included. Ten patients received neoadjuvant (3) or adjuvant (7) chemotherapy. The mean follow-up was 41 months.

Results: The mean age 69 years old and 56% of the patients were female. There was no significant difference between the chemotherapy and control groups in age (66.2 vs 69.7 years, p=0.3), gender (60% vs 55% Female, p=0.8), high grade (84% vs 80%, p=0.8), lymphovascular invasion (50% vs 69%, p=0.4), N+ status (33% vs 32%, p=0.9), and positive margins (10% vs 9.7%, p=0.9). No significant difference in survival was seen amongst patients with parenchymal versus peri-hilar fat invasion (p=0.3). A significant difference in five-year disease-specific survival was seen between the group who received perioperative chemotherapy (5-yr survival 70%) and the group who did not receive any chemotherapy (5-yr survival 36.5%). When adjusted for age in a multivariate analysis, the use of perioperative chemotherapy significantly improved survival (HR 3.9).

Conclusions: Adjuvant or neoadjuvant chemotherapy confers a survival benefit in patients with T3 UTUC of the renal pelvis. Further prospective studies are warranted to validate these results.

P36

The Impact of Tumor Size on the Rate of Synchronous Metastasis and Survival in Renal Cell Carcinoma Patients. A Population Based Study

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Introduction: Complete or partial nephrectomy has been the predominant treatment for small incidentally diagnosed renal cell cancers (RCC). Some authors have suggested active surveillance as a treatment option, especially among patients with higher peri-operative risks, arguing that patients with small tumors have lower metastatic rates and better survival. The aim of the study is to test that argument for in a nationwide population registry.

Materials & Methods: 791 histopathologically confirmed RCCs with known tumor size were diagnosed in Iceland between 1971 and 2005. Histological material and TNM staging were centrally reviewed. Synchronous metastases (SM) were recorded. Cancer-specific survival was calculated. Cubic-spline analysis compared size and metastatic rate. Multivariate analysis was applied to compare size to other known prognostic factors. Median follow-up was 6.7 years.

Results: With increased tumor size, synchronous metastasis (SM) rate increases in a non-linear fashion (10.6, 25.3, 35.2 and 49.6%) and five year survival decreases (86.1, 71.8, 53.0 and 32%) for tumors ≤ 4, 4.1-7.0, 7.1-10.0 and >10 cm, respectively. In multivariate analysis, size was a significant independent prognostic factor for synchronous metastasis (OR=1.08, p=0.01) and cancer specific survival (OR=1.09, p<0.01), while TNM stage was the strongest predictor of cancer specific survival (OR=2.58, p<0.01).

Conclusions: Size dose affect rates of SM and cancer related mortality. Size may aid in prognostication, but the TNM stage proves a superior marker. The relatively high (10.6%) propensity of tumors ≤ 4cm to metastasize should be kept in mind when advising active surveillance.

P37

Hand Assisted versus Robotic Assisted Laparoscopic Partial Nephrectomy; Comparison of Short-Term Outcomes

Sammy E. Elsamra, **Andrew Leone**, Michael Lasser, Simone Thavaseelan, George Haleblian, Gyan Pareek
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Introduction: Robotic assisted laparoscopic partial nephrectomy (RALPN) may offer superior outcomes compared with laparoscopic partial nephrectomy (LPN). However, no previous analysis compared RALPN to hand assisted laparoscopic partial nephrectomy (HALPN). Herein, we compared our experience with RALPN and HALPN.

Materials & Methods: The records of LPN from 2006 to 2010 were reviewed. Patient age, tumor pathology, grade, stage, size of tumor, estimated blood loss (EBL), hospital length of stay (LOS), and change in creatinine were noted. Comparison was performed by Student's t-test.

Results: Of 69 patients, 47 underwent HALPN (2006-2010) and 21 underwent RALPN (2008-2010). Exclusion criteria included concurrent laparoscopic cholecystectomy (n = 4 HALPN) and conversion to open (n = 2 RALPN). Table 1 shows number of cases, mean age, tumor size, operative time, room time, EBL, LOS, change in Cr, proportion clamped, and complications for each group.

Conclusions: Our data reveals that while LOS is significantly shorter for RALPN, operative and room times were significantly shorter for HALPN. There was a non-statistically significant decreased complication rate associated with HALPN, with no conversions to open procedure in the HALPN cohort. Hilar vessel clamping was utilized in the minority of HALPN versus the majority of RALPN. One may consider HALPN for its benefit of decreased technical difficulty, tactile feedback, shorter operative and room times, decreased need for hilar clamping and similar complication rate.

TABLE 1. Comparison between HALPN and RALPN

	HALPN	RALPN	p-value
Number of Cases	42		19
Tumor Size	2.5 cm (1.4)	2.5 cm (1.2)	0.94
Estimated Blood Loss	136 ml (151)	178 ml (249)	0.54
Surgery Time	149 min (39)	212 min (53)	<0.001
Room Time	203 min (42)	275 min (47)	< 0.001
Length of Stay	4.2 days (1.4)	3.5 days (0.6)	0.44
Proportion with Hilar Vessel Clamping	1 of 42 (2.38%)	17 of 19 (89.47%)	z=6.6**significant**
Change in Cr (last Cr obtained in hospital minus pre-op Cr)	0.004	-0.025	0.44
Complication Rate	5 of 42 (11.9%)	4 of 19 (21%)	z=0.54**not significant**

P38

The Impact of the Learning Curve on Robot Assisted Pelvic Lymph Node Dissection during Radical Prostatectomy: An Update on the Brown University Experience

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Introduction: Pelvic lymph node dissection (PLND) provides important staging and prognostic information. In 2009, our institution reported on the yield of Robot-Assisted Laparoscopic PLND (RALPLND) in comparison to an age-matched cohort undergoing open PLND. Herein, we assess our continued experience with RALPLND to determine if LN yield has improved as our robotica program has matured.

Materials & Methods: 178 patients underwent radical prostatectomy with PLND between 2006 and 2010. Open PLND was performed in 78 and RALPLND in 100. Data was collected through an IRB approved blinded prospective database by an independent third party committee. Final pathology reports were retrospectively reviewed. Standard template dissection was carried out in both cohorts.

Results: Both cohorts had similar age and Gleason grade ($p>0.05$). Mean yield for open and RAL PLND were 6.9 and 4.1, respectively ($p<0.001$). Within the RAL cohort, 3.2 nodes were collected on average in the first 50 cases, compared to 5.5 in the most recent 50 ($p<0.001$). While there was a significant difference between LN yield of our open cohort and that of the first 50 robotic cases, there was no significant difference when compared to our most recent 50 cases ($p=0.114$).

Conclusions: We previously published data documenting lower LN yield during RALPLND compared to open PLND. Our current study demonstrates a statistically significant improvement in LN yield as robotic experience is gained. While patients with high-risk disease may benefit from open PLND during a program's early robotic experience, with time, RALPLND can provide LN yields similar to open dissection.

P39

Radical Prostatectomy Outcomes in Men Aged 70 or Older with Low-Risk Prostate Cancer

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Introduction: A recent study of SEER data considered men aged $\geq$ 70 years with moderately differentiated prostate cancer (PCa) as having lower-risk disease (Miller et al, JNCI 2006). This study also concluded that a significant portion of these men were overtreated with radical prostatectomy (RP) or radiation therapy. We examined the proportion and outcomes of men aged $\geq$ 70 years who underwent RP with low-risk disease at our institution over the past three decades.

Materials & Methods: Our institutional RP database with more than 19,000 men was queried for elderly men aged ≥70 years with low risk PCa (PSA≤10 ng/ml, biopsy Gleason $\leq$ 6, and clinical stage T1c/T2a). Pathologic and survival outcomes were assessed.

Results: Between 1983 and 2010, 169 elderly men with low risk PCa (0.88%) underwent RP. Gleason score at RP was $\geq$ 7 in 55 (32.5%). Pathologic stage was pT2 in 119 (70.4%), pT3a in 43 (25.4%), pT3b in 6 (3.6%), and N1 in 1 (0.6%). Actuarial 5- /10-yr biochemical recurrence-free survival, PCa-specific survival, and overall survival probability following RP were 88%/ 77%, 98% /87%, and 87%/63%, respectively.

Conclusions: Less than 1% of men undergoing RP at our institution were elderly men with low risk PCa. However, many of these men were found to have higher risk disease after RP. These cancers may be life-threatening in men with few comorbidities. Treatment recommendation in elderly men with low risk PCa should made after careful consideration of life expectancy based on comorbidities and potential adverse outcomes from the treatment.

P40

hould Anterior Prostatic Fat during Radical Prostatectomy Undergo Pathological Examination?

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Introduction: Dissection of the anterior fat overlying the prostate allows for visualization during robotic prostatectomy. However, this fat is usually not sent for pathologic analysis. One study has demonstrated that anterior prostatic fat (APF) can harbor lymph nodes involved with prostate cancer. Therefore, the purpose of this study was to evaluate APF and the incidence for positive nodes.

Methods: An IRB approved retrospective study was conducted on patients who underwent robotic prostatectomy and had APF sent for pathologic analysis. Clinical and pathological data was analyzed.

Results: 101 patients were identified. Mean age was 57 +/- 8.3 years. 9/101 patients (8.9%) had APF lymph nodes. A total of ten lymph nodes were found (range 1-2). Overall, 2/101 patients (2%) had positive APF nodes despite negative lateral nodes. The pre-operative biopsy Gleason score and prostate specific antigen was 4+3 and 5.5 ng/ml for patient 1 and 4+3 and 2.6 ng/ml for patient 2. BMI didn't differ among patients with and without APF nodes 27.8 ± 2.4 vs. 27.9 ± 3.6 (kg/m^2 ± SD). Final pathological data is summarized in Table 1.

Conclusions: APF lymph nodes were positive for metastatic prostate cancer in 2% of patients despite having negative lateral pelvic lymph nodes. Ultimately, this finding lead to pathological upstaging stressing the importance of examining this specimen.

TABLE 1. Final pathological data for patients with positive APF nodes

	Seminal vesicle invasion	Extraprostatic extension	Perineural invasion	Lymphovascular invasion	Positive lateral pelvic lymph nodes	Pathological staging
Patient one	(-)	(-)	(+)	(-)	No	pT3a N1Mx
Patient two	(-)	(-)	(+)	(+)	No	pT2c N1Mx

Concurrent Poster Session II: Oncologic Diseases
3:20 pm-4:00 pm

P41

Directed Prostate Biopsies Utilizing Contrast-Enhanced Ultrasound with Flash Replenishment Imaging

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Introduction: To evaluate the detection of prostate cancer from directed prostate biopsies with contrast-enhanced ultrasound using flash replenishment with maximum intensity projection (MIP) MicroFlow Imaging (MFI) compared to systematic biopsy.

Materials & Methods: 259 patients underwent pre and post-contrast enhanced transrectal ultrasound (TRUS) evaluation of the prostate using MFI (Toshiba America Medical Systems, Tustin, CA). Contrast enhanced images were obtained while infusing Definity®, an encapsulated liposomal suspension of perfluoropropane microbubbles. MFI is an imaging technique that utilizes high power flash pulses to destroy contrast microbubbles followed by lower power pulses to show contrast replenishment. Up to 6 MFI guided prostate biopsies were taken per patient followed by a standard systematic 12 core biopsy protocol.

Results: Prostate cancer was found in 110/259 (42%) patients. 249/3108 (8%) of the systematic cores compared to 187/1175 (15.9%) of the directed cores were positive for cancer. In 12 patients prostate cancer was detected only in targeted biopsy. Among patients with a positive biopsy, the odds ratio for a positive core with targeted biopsy versus systematic biopsy was 3.1 (95% CI: 2.4-4.0, p<0.001). Mean percentage of biopsy core involvement was 32% among patients with a positive targeted core, compared with 15% among patients who were not detected by targeted biopsy (p<0.001). Higher grade cancer (Gleason score > 6) was more common among patients with a positive targeted biopsy (53% versus 18%, p<0.001).

Conclusions: Targeted biopsy of the prostate using contrast-enhanced TRUS MFI may selectively detect higher grade cancers as compared with systematic 12 core biopsy.

P42

Changes in Pre-operative and Pathologic Characteristics in Patients Undergoing Radical Prostatectomy by Era

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Introduction: In 2005, the International Society of Urological Pathology (ISUP) modified the Gleason scoring system to reduce interobserver variability. We sought to evaluate the recent trends in stage and grade for patients presenting for radical prostatectomy at a single high-volume center.

Materials & Methods: A total of 18,743 men underwent radical prostatectomy from 1982-2010. We compared the distribution of pathologic stage and grade at presentation according to 5 different eras of prostate cancer management.

Results: A higher proportion of men undergoing RP presented with PSA 0-4 since 2005 than from 1999-2005 (p<0.001). Since 2005, more patients underwent radical prostatectomy for biopsy Gleason 7-10 prostate cancer (23.6% from 1999-2005 vs 36.0% after 2005, p <0.001), in patients being upgraded from Gleason 6 to Gleason 7 at RP (20.3% from 1999-2005 vs 26.7% after 2005, p<0.001). However, patients with pathological Gleason 7-10 disease were more likely to have PSA between 0 and 4 ng/ml (20% vs 14%, p <0.001) and organ-confined disease (54% vs 50%, p = 0.005) in the era after 2005 than from 1999-2005.

Conclusions: Since 2005, patients are more likely to present with intermediate to high grade disease. However, these patients are more likely to have a low PSA and organ-confined disease than in previous eras.

	Era					
	1982-1988	1989-1991	1992-1998	1999-2005	2006-2010	Total
Clinical Stage						
T1a/b	115 (14)	63 (9)	46 (<1)	25 (<1)	12 (<1)	261 (1.4)
T1c	19 (2)	94 (13)	2459 (55)	5639 (75)	3890 (75)	12101 (64)
T2a	348 (42)	243 (33)	1095 (24)	1371 (18)	812 (16)	3869 (21)
T2b	245 (30)	206 (28)	637 (14)	401 (5)	270 (5)	1759 (9)
T2c	68 (8)	75 (10)	177 (4)	56 (<1)	40 (<1)	416 (2)
T3	16 (2)	40 (5)	51 (1)	20 (<1)	17 (<1)	144 (<1)
Serum PSA						
0-4	194 (42)	206 (29)	803 (18)	1839 (24)	1511 (29)	4553 (25)
4-10	148 (32)	275 (39)	2531 (57)	4789 (64)	3183 (61)	10926 (60)
10-20	76 (17)	155 (22)	886 (20)	749 (10)	353 (7)	2217 (12)
> 20	37 (8)	71 (10)	226 (5)	134 (2)	78 (2)	546 (3)
Bx Gleason score						
2-5	268 (34)	200 (28)	356 (8)	37 (<1)	2 (<1)	863 (5)
6	374 (47)	320 (44)	3164 (70)	5731 (76)	3321 (63)	12910 (69)
7	115 (14)	154 (21)	803 (18)	1544 (20)	1548 (30)	4164 (22)
8-10	37 (5)	44 (6)	164 (4)	235 (3)	320 (6)	800 (4)
Pathological stage						
OC	305 (37)	224 (31)	2514 (56)	5550 (74)	3729 (72)	12322 (66)
EPE, GI < 7	200 (24)	198 (27)	691 (15)	653 (9)	304 (6)	2046 (11)
EPE, GI ≥ 7	166 (20)	201 (27)	911 (20)	986 (13)	899 (17)	3163 (17)
SVI, LN-	79 (10)	44 (6)	213 (5)	243 (3)	181 (3)	760 (4)
LN+	69 (8)	67 (9)	152 (3)	93 (1)	71 (1)	452 (2)
	819	734	4481	7525	5184	18743

P43

Long-term Prognostic Significance of Close Prostatectomy Margins

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Introduction: Current guidelines state that close prostatectomy margins (<0.1 mm from the inked margin) should be reported as negative on pathology reports. However, this recommendation remains controversial and relies on little evidence. The aim of this study is to evaluate the impact of close margin status on the long-term risk of biochemical recurrence following radical prostatectomy.

Materials & Methods: Eight-hundred ninety-four consecutive patients who underwent radical prostatectomy for localized prostate cancer at Massachusetts General Hospital between 1993 and 1999 were identified. Associations between margin status, Gleason score, pathological stage, pre-operative PSA, prostate weight, age with the risk of biochemical recurrence were examined.

Results: Negative prostatectomy margins occurred in 644 of 894 cases (72%). Of these patients, 100 (15.5%) had close margins. Overall, median time to recurrence was 3.5 years, median follow-up of patients in remission 9.9 years. Cumulative recurrence-free survival differed significantly among the three types of margins (p<0.001). On multivariate analysis, close margin status constituted a significant independent predictor of recurrence (HR 2.23, 95%CI 1.08 - 4.99). Subgroup analysis showed the same impact on prognosis in low-risk tumors. Gleason score and positive margins were the strongest predictors of recurrence.

Conclusions: In this study, margin closeness constituted an independent prognostic factor. However, it was clearly subordinated to Gleason grade and frank positive margins. Our findings reaffirm the need of regular, long-term postoperative follow-up, in particular of patients otherwise considered to be at low-risk.

P44

Validation in CaPSURE of Predicted Sexual Outcome after Primary Prostate Cancer Treatment by PROSTQA

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Introduction: Patients with localized prostate cancer undergoing radical prostatectomy (RP), external radiation therapy (XRT), or brachytherapy (BT) are often concerned about erectile function (EF) following treatment. We developed models for individualized sexual outcome expectations following prostate cancer treatment at academic centers and sought to validate them in a community-based cohort.

Methods: The PROSTQA cohort was utilized to create models predicting the likelihood of EF at 2 years following therapy for localized prostate cancer with RP, XRT, or BT (N=1027), based on pre-treatment patient, disease, treatment and HRQOL characteristics. CaPSURE participants (N=1931), were used for validation by AUC from fitting univariable logistic regression of reported 2-year EF on model-predicted probability, and calibration by examining model-predicted probability vs. observed EF at 2 years.

Results: The PROSTQA models performed well in predicting EF at 2-years following treatment with AUC's of 0.76, 0.81, and 0.89 for men undergoing RP, XRT, and BT, respectively. Calibration showed that predicted rates of EF based on the PROSTQA-derived models corresponded to the observed outcome in the CaPSURE cohort across a broad range of predicted probabilities. Table 1

Conclusion: Validation in a community-based cohort of predictive models for recovery of EF following treatment of localized prostate cancer with RP, XRT, and BT at academic centers based on pretreatment EF and various patient and treatment characteristics suggest that these models are generalizable.

Table 1. PROSTQA Outcomes and Observed CaPSURE Erectile Function recovery at 2 years

Treatment type	N	Mean PROSTQA-estimated 2 yr erectile recovery	Observed proportion 2 yr erectile recovery in CaPSURE
Prostatectomy	1058	0.22	0.23
External Radiotherapy	240	0.13	0.15
Brachytherapy	350	0.22	0.27

P45

Nationwide Comparison of Operative Outcomes for Robotic, Laparoscopic, and Open Radical Prostatectomy

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Introduction: Multi-center, community-based evaluations of robot-assisted laparosopic prostatectomy (RALP) and radical retropubic prostatectomy (RRP) are lacking. We sought to evaluate perioperative and oncologic outcomes of RALP and RRP for prostate cancer in a nationwide cohort.

Methods: The Health Professionals Follow-up Study (HPFS) cohort of 51,529 men was interrogated to evaluate outcomes of men who underwent RALP (N=172) and RRP (N=573) from 2000 to 2009.

Results: Tumor severity was slightly greater among RRP than RALP patients (Table 1). RRP patients were more likely than RALP to undergo lymphadenectomy (85.4% vs. 46.5%, respectively, p<0.0001), experienced greater mean estimated blood loss (858.9 vs. 206.0 ml, respectively, p<0.0001), were more likely to receive blood transfusions (26.3% vs. 4.7%, respectively, p<0.0001), and had longer mean hospital stays (2.9 vs. 1.9 days, p=0.0001) (Table 2). Oncologic outcomes between RRP and RALP revealed no difference in pathologic stage, gleason score, positive surgical margins, or psa-specific survival (Table 3).

Conclusions: In this nationwide, community-based cohort RALP was associated with shorter hospital stay and less blood loss than RRP, while yielding similar oncologic outcomes.

Table 1. Preoperative Tumor Characteristics

	Total (N = 745)	RALP (N = 172)	RRP (N = 573)	p value
Clinical T-Stage				
T1	68.9	77.3	66.5	0.01 (T1 vs T2+)
T2	31.0	22.7	33.3	
T3	0.1	0	0.2	
T4	0	0	0	
PSA				
Median (ng/dl)	5.5	5.2	5.7	0.04
Biopsy Gleason Score				
<6	3.5	1.2	4.2	0.04
6	59.1	55.9	60.1	
7	29.9	37.1	27.8	
8+	7.4	5.9	7.9	

Table 2. Perioperative Outcomes

	Total (N = 745)	RALP (N = 172)	RRP (N = 573)	p value
Nerve-Sparing				
Bilateral	69.4	71.6	68.8	0.82
Unilateral	14.7	14.2	14.8	
None	15.9	14.2	16.4	
Seminal Vesicle Removal				
% Patients	97.1	97.6	97.0	
Lymph Node Dissection				
% Patients	77.0	47.0	85.6	<0.0001
Hospital Stay				
Mean (days)	2.7	1.9	2.9	0.0001
EBL				
Mean (cc)	712.8	206.0	858.9	<0.0001
Transfusions				
% Patients	26.3	4.7	30.4	<0.0001
Mean Units	2.0	2.8	2.0	0.54

Table 3. Oncologic Outcomes

	Total (N = 745)	RALP (N = 172)	RRP (N = 573)	p value
Pathologic T-Stage				
T2	79.3	79.3	79.3	1.0
T3	20.6	20.7	20.6	
T4	0.14	0	0.2	
Gleason Score				
< or =6	45.2	37.1	47.6	0.07
7	46.5	55.7	43.9	
8	3.9	3.6	4.0	
9+	4.3	3.6	4.6	
Positive Margins				
% Patients	23.1	26.1	23.1	0.47
Extracapsular Extension				
% Patients	23.1	19.8	24.1	0.29

P46

Predictors of Positive Retroperitoneal Lymph Nodes in Patients with High Risk Testicular Cancer

Ravi Kacker, Stephen Williams, Graeme S. Steele, Jerome P. Richie
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Introduction: Percent of embryonal carcinoma and lymphovascular invasion (LVI) in the primary tumor are risk factors for occult retroperitoneal metastatic disease. High risk patients with clinical stage I and IIA non-seminomatous germ cell tumor who underwent primary retroperitoneal lymph node dissection (P-RPLND) were identified to discern any other risk factors for metastatic disease.

Materials & Methods: Patients who had undergone RPLND at our institution from 1993 to 2009 were identified and clinical charts reviewed. Ninety patients with orchiectomy specimens containing greater than 30% embryonal carcinoma who underwent P-RPLND were identified and peri-operative data was obtained.

Results: 90/353 (25%) patients had greater than 30% embryonal carcinoma and underwent P-RPLND. Of these, 45 (50%) had combined LVI. Median follow-up time was 1.1 years. Positive lymph nodes identified at RPLND were noted in 30 (46%) and 15 (60%) of patients with CSI vs. CSII disease. On multivariate analysis, embryonal carcinoma (OR 1.02, 95%CI 1.00-1.04) and LVI (OR 3.52, 95%CI 1.43-8.67) were associated with positive lymph nodes at RPLND. The positive predictive value for 100% embryonal carinoma was 65.5% although the negative predictive value for 30% embryonal carinoma was 85.7%.

Conclusions: Embryonal carcinoma and LVI were significantly and independently associated with risk for occult retroperitoneal metastatic disease. These results should be taken into consideration when counseling patients about appropriate treatment options.

P47

Determinants of the Adoption of Minimally Invasive Radical Prostatectomy in the United States

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Introduction: Minimally invasive radical prostatectomy (MIRP) with and without robotic-assistance has been rapidly adopted. However the relative influence of tumor, patient, surgeon, and hospital characteristics driving its use over conventional open radical prostatectomy (ORP) remains poorly characterized.

Materials & Methods: Using Surveillance, Epidemiology and End Results-Medicare linked data, we identified 1,428 MIRP and 5,452 RRP during 2003-2005. We assessed the relative contribution of pathologic, demographic, surgeon and practice characteristics on utilization of MIRP vs. RRP.

Results: In multilevel models for men undergoing prostatectomy, surgeon factors accounted for 87.9% of variance in the receipt of MIRP versus RRP. Hospital factors accounted for 77.9% of the variance. In partitioned multilevel models, unmeasured surgeon (78%) and patient (79.3%) factors explained largest amount of variance in the use of MIRP that was attributable to each. Surgeon age explained 15.4% of variance. Surgeons less than 40 vs. over 60 years of age were more likely to use MIRP (OR, 25.9; 95% CI, 3.2-209.8, p=0.002). Surgeon volume comprised only 0.07% of surgeon variance. Hospital bed size accounted for 10.9%. Demographics were the largest patient contributors to variance in MIRP use (6.1%) while tumor characteristics contributed very little.

Conclusions: While increased utilization of MIRP is primarily driven by surgeon and hospital factors rather than patient demographic or tumor characteristics, young surgeon age was a major contributor while surgeon volume contributed very little to use of MIRP, which is worrisome given that higher surgeon volume and experience are associated with better radical prostatectomy outcomes and lower costs.

29

Complications of Pediatric Urologic Minimally Invasive Surgery

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Introduction: The incidence of any complication development with adult laparoscopic surgery is reported to be between 3.5 and 9.3%. To our knowledge, there are no large-scale, prospective published reports concerning the incidence of complications with Pediatric Urologic Minimally Invasive Surgery (PUMIS). We present our experience with complications in PUMIS.

Materials & Methods: We prospectively followed 600 minimally invasive cases performed at our institution. We described complications as any deviation from normal postoperative course, and categorized our complications according to the Clavien system.

Results: Median age was 3.2 yr. (0.4 - 18.8). Median follow-up was 29 months (12-83.4). There were 1895 port sites analyzed in the 600 cases. The 600 cases comprised of 116 testicular; 267 renal/ureteral; 209 bladder; 6 retroperitoneal lymph node dissections; and 2 pelvic cases for removal of Mullerian remnants. There were 7 port site complications (3 umbilical hernias and 4 lateral site superficial infections). Four children had intra-abdominal urinary leakage (1 nephroureterectomy; 1 pyeloplasty with stent migration; 1 nephrectomy; 1 ureteral reimplant). One ureteral reimplantation had a blood loss of 150 cc while the remaining cases were negligible for blood loss. There were 7 Clavien I and 5 Clavien IIIb complications in the 600 cases.

Conclusions: Incidence of complications with PUMIS was 2.0% overall which is slightly lower than the published incidence in adults undergoing minimally invasive surgery. Although it appears safe to perform PUMIS, we must continue to carefully monitor our outcomes in this evolving sub-specialty.

Scientific Session IV: Resident Prize Essay Competition

8:00 am-9:20 am

30

Erythrocytosis and Testosterone Therapy: The Influence of Treatment Modality and Body Composition

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Introduction: Erythrocytosis may be the most common complication of testosterone therapy (TTh) and guidelines recommend intervention for HCT over 54. Few clinical studies have examined the risk of erythrocytosis during TTh and the influence of treatment modality and body composition is not known.

Materials & Methods: Retrospective chart review identified 171 men who underwent TTh with topical gel, injections, or pellets and 146 men maintained a single treatment modality. Linear regression modeling was used to determine factors that correlate with changes in HCT for 76 men with adequate lab and body composition data.

Results: During the first year of therapy, 2 (7.4%) and 0 of 27 patients on topical therapy developed HCT > 50 and 54 respectively compared to 21 (29.2%) and 3 (4.2%) of 72 on injections (p=0.03; 0.56) and 13 (27.7%) and 2 (4.3%) of 47 on pellets (p=0.0411;0.53). For those without erythrocytosis during the first year, 4 (3.8%) patients subsequently developed HCT over 54. Increased age (p=0.0238), low baseline HCT (p=0.0034), and elevated T during therapy (p=0.5463) correlate with greater increases in HCT. Increased baseline fat percentage is associated with maximum HCT during therapy (p=0.048) but a response in terms of body composition is not related to a response in HCT.

Conclusions: Topical therapies have a lower risk of erythrocytosis compared to other modalities. Older and obese patients may be a greater risk for erythrocytosis. Until the clinical implications of erythrocytosis are better understood, HCT should be monitored during the duration of testosterone therapy.

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Accelerated Gastrointestinal Recovery with Use of Alvimopan after Radical Cystectomy with Urinary Diversion

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Introduction: Radical cystectomy, while being the gold standard treatment for muscle-invasive cancer, is associated with significant morbidity, with rates of gastrointestinal complications being reported as high as 20%. Alvimopan is a peripherally-acting, mu-opioid receptor antagonist that has been shown in randomized-control trials to accelerate gastrointestinal recovery in patients undergoing bowel resection with primary anastamosis. We report our experience with gastrointestinal recovery for patients undergoing cystectomy with urinary diversion treated with alvimopan.

Materials & Methods: From 1/2008 to 3/2011, 41 consecutive patients underwent radical cystectomy with urinary diversion performed by a single surgeon. The first 25 patients in our study did not receive alvimopan and were kept with nasogastric-decompression until return of flatus. The latter 16 patients received perioperative alvimopan and were without postoperative nasogastric-decompression.

Results: Time to first flatus (3.2 vs 5.6 days, p=<0.01) and bowel movement (3.7 vs 6.0 days, p=<0.01) were significantly shorter in those patients who received alvimopan. Additionally, initiation of clear liquid (4.2 vs 6.3 days) and regular diet (5.9 vs 7.3 days p=<0.01) were accelerated in the alvimopan cohort. There were no incidences of prolonged ileus in those patients who received perioperative alvimopan (0% vs 24%, p=0.03).

Conclusions: Urinary diversion status post radical cystectomy is associated with significant gastrointestinal morbidity. In our experience, the use of alvimopan perioperatively significantly accelerates the rate of GI recovery and reduces the incidence of post-operative ileus.

Pre- & Postoperative Comparison Between Patients With & Without Alvimopan

	Without Alvimopam	With Alvimopam	p-value
Age	70.1	69.7	0.90
BMI	29.7	28.0	0.64
Length of Hospital Stay (days)	9.6	8.7	0.55
Length of Nasogastric Decompression (days)	5.5	0	<0.01
Time to First Flatus (days)	5.6	3.16	<0.01
Time to First Bowel Movement (days)	6.0	3.6	<0.01
Time to Initiation of Clear Liquid Diet (days)	6.3	4.2	<0.01
Time to Initiation of Regular Diet (days)	7.4	5.9	0.09
Incidence of Prolonged Postoperative Ileus	24%	0%	0.03

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Complications of Salvage Cystectomy after Failed Bladder-Sparing Therapy for Muscle-Invasive Bladder Cancer

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Introduction: Radical cystectomy has been the gold standard for muscle-invasive bladder cancer. Combined-modality-therapy (CMT) involving transurethral resection of bladder tumor (TURBT), external-beam radiation, and chemotherapy is an effective alternative to cystectomy in selected patients. Salvage cystectomy is reserved for those failing CMT. We characterized complications associated with salvage cystectomy.

Materials & Methods: From 1986-2007 of 285 patients undergoing undergoing bladder-sparing therapy, 91 patients (32%) underwent salvage cystectomy at our institution following CMT for T2-T4aNxM0 bladder cancer. Patients underwent TURBT followed by chemoradiation (40Gy). Early assessment was performed by cystoscopy/rebiopsy. Patients with complete response continued with consolidation chemoradiation (total dose 64Gy). Immediate salvage cystectomy (50/91) was performed for persistent disease, while delayed salvage cystectomy (41/91) was performed for an invasive recurrence. Medical records were reviewed classifying complications using the Clavien system.

Results: Median age was 69.4yrs (27.5-88.9), median follow-up was 20mos (0-252). 99% (90/91) underwent ileal diversion. 69% (63/91) had complications of any grade within 90 days. 16% (15/91) experienced major complications <90 days. 21% (19/91) required readmission <90 days. 90-day mortality was 2.2% (2/91). Significant cardiovascular/hematologic complications [PE, MI, DVT, transfusion] <90 days were more common in the immediate cystectomy group (37% vs. 15%, p=0.02). Tissue-healing complications [fascial dehiscence, wound infection, ureteral stricture, anastamotic stricture, stoma/loop revisions] were more common in the delayed group (35% vs. 12%, p=0.05).

Conclusions: Salvage cystectomy is associated with acceptable morbidity, though complication rates are slightly higher than for other cystectomy series. Immediate cystectomies have more CV/hematologic complications, while delayed cystectomies have more tissue-healing complications.

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Objective Measures of Renal Mass Anatomic Complexity Predict Rates of Major Complications Following Partial Nephrectomy

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Introduction: We evaluated whether increasing tumor complexity, quantitated by Nephrometry score (NS), is associated with increased complication rates following PN using the Clavien-Dindo classification system (CCS).

Methods: We queried our prospectively maintained kidney cancer database for patients undergoing PN for whom NS was available from 2007 to 2010. Tumors were categorized into low (NS 4-6), moderate (NS 7-9), and high (NS 10-12) complexity lesions. Complication rates within 30 days were graded (CCS I-V), stratified as minor (CCS I-II) or major (CCS III-V), and compared between groups.

Results: 390 patients (mean age 58.0±11.9yrs, 66.9% male) undergoing PN (44.6% open, 55.4% robotic) for low (28%), moderate (55.6%) and high (16.4%) complexity tumors (mean tumor size 3.74±2.4cm) from 2007-2010 were identified. Tumor size, EBL, and ischemia time all significantly differed (p<0.0001) between groups, while patient age, BMI, and operative time were comparable. Stratified by CCS, minor and major complication rates for all patients were 26.7% and 11.5%. Minor complication rates were comparable (26.6 vs. 24.9 vs. 32.8%, p=0.45), while major complication rates differed (6.4 vs. 11.1 vs. 21.9%; p=0.009) amongst tumor complexity groups. Controlling for age, gender, BMI, tumor size, operative time, and tumor complexity, prolonged operative time (OR 3.4, CI [1.6-7.1]) and high NS (OR 3.9, CI [1.4-10.9]) were associated with the postoperative development of a major complication.

Conclusions: Increasing tumor complexity is associated with the development of major complications after PN. This association should be validated externally and integrated into the decision-making process when counseling patients with complex renal tumors.

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Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP): Development and Validation of a Practical Health-Related Quality of Life Instrument for Use in the Routine Clinical Care of Prostate Cancer Patients

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Introduction: Measuring prostate cancer patient HRQOL in routine clinical practice is hindered by lack of instruments enabling efficient real-time, point-of-care scoring of multiple HRQOL domains. We sought to develop an instrument for this purpose.

Materials & Methods: The EPIC for Clinical Practice (EPIC-CP) is a one-page, 16-item questionnaire to measure urinary incontinence, urinary irritation, bowel, sexual, and hormonal HRQOL domains that we constructed by eliminating conceptually overlapping items from the 3 page EPIC-26, and revising the questionnaire format to mirror the AUA Symptom Index, thereby enabling practitioners to calculate HRQOL scores at point of care. We administered EPIC-CP to a new cohort of PCa patients in community-based and academic oncology, radiation, and urology practices to evaluate the instrument's validity and ease of use for clinical practice.

Results: 175 treated and 132 untreated PCa subjects completed EPIC-CP (N = 307). EPIC-CP domain scores correlated highly with respective domain scores from longer versions of EPIC ($r > 0.92$ for all domains). EPIC-CP showed high internal consistency (Cronbach's alpha = 0.64-0.84) and sensitivity to PCa treatment-related effects ($p < 0.05$ in each of 5 HRQOL domains). Patients completed EPIC-CP efficiently (96% in <10 minutes, and 11% missing items). It was deemed 'very convenient' by clinicians in 87% of routine clinical encounters, and clinicians accurately scored completed questionnaires 94% of the time.

Conclusions: EPIC-CP is a valid instrument that enables patient-reported HRQOL to be measured efficiently and accurately at the point of care, and can thereby facilitate improved emphasis and management of patient-reported outcomes.

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Ability of Ureteroscopic Biopsy to Accurately Grade and Stage Upper Tract Urothelial Carcinoma Lesions: Results from a Multi-institutional Cohort of Patients

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Introduction: We present a multi-institutional cohort of patients with UTUC who underwent surgical resection to characterize the association of ureteroscopic biopsy and final pathology.

Materials & Methods: Preoperative URS biopsy data was available in 238 patients at 5 academic medical centers. URS biopsies were performed using either a brush biopsy kit or a mechanical biopsy device. The association between URS biopsy and final pathologic data was determined.

Results: 154 men and 84 women, with a median age of 70 years were included. On URS biopsy, 88 (37%) patients had a positive brush, 140 (59%) were staged as non-MI, and 10 (4%) had MI disease. In addition, 140 (59%) biopsies were low grade while 98 (41%) were high grade. RNU pathology, demonstrated non-MI tumors in 140 (59%) patients, MI UTUC in 98 (41%), and high-grade disease in 150 (63%), positive LN in 18(8%). On univariate analysis, high URS biopsy grade was associated with high RNU grade ($p<0.001$), MI UTUC ($p<0.001$), and LN positive UTUC ($p=0.02$) on RNU pathology. Conversely, URS biopsy stage was only associated with final UTUC disease grade ($p=0.005$), but not stage ($p=0.16$) or LN positivity ($p=0.24$). In a multivariate model that controlled for gender, age, and tumor location, URS grade (but not stage) was associated with high RNU grade ($p<0.0001$) and MI UTUC ($p<0.0001$).

Conclusions: Results from a contemporary large multi-institutional cohort of patients further supports that URS biopsy grade, but not stage, is associated with final pathology. Such information may play a valuable role for risk stratification regarding ablative versus extirpative therapies for UTUC.

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Bilateral Same-Session Ureteroscopy: Safety and Efficacy

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Introduction: Bilateral same-session ureteroscopy (URS) was initially avoided due to fear of increased morbidity particularly bilateral ureteral injury. However, improvements in endourologic technology and surgeon experience have minimized complications. We sought to evaluate the safety and efficacy of bilateral same-session ureteroscopy at our institution.

Materials & Methods: Retrospective chart review was conducted on all URS cases for renal and ureteral stones performed by a single surgeon from August 2003 through November 2008. Bilateral same-session cases were then isolated. Quantitative and qualitative analysis was performed.

Results: A total of 459 operative cases were identified. Of this, 86 (20%, 172 renal units) were performed as bilateral same-session ureteroscopies. There were no intraoperative complications described in any of the bilateral procedures--no ureteral perforation, episodes of lost access, or aborted cases. Seventy-eight patients (90.7%) had adequate stone clearance after one procedure and 8 (9.3%) required an additional procedure within 1 year. There were two major complications (2.3%) both being post-operative urosepsis. There were 13 (15.1%) minor complications. These included ER visits for post-operative pain and urinary tract infection without fever.

Conclusions: To date, this is the largest series to demonstrate that bilateral ureteroscopy can be successfully performed on patients with renal and/or ureteral stones in the same session. With appropriate patient selection, bilateral same-session ureteroscopy performed by the experienced surgeon is a safe and efficacious treatment for bilateral nephrolithiasis.

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Should Robotic Assisted Radical Prostatectomy Be Extraperitoneal Like Open Surgery?

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Introduction: The standard approach for open radical prostatectomy is extraperitoneal but most robotic surgeons have limited themselves to the transperitoneal approach. We compare our surgical and oncological results for extraperitoneal (EP-RARP) to transperitoneal (TP-RARP) robotic assisted radical prostatectomy.

Methods: We examined our departmental, IRB approved, retrospective database of RARP. Between October 2008 to March 2011, 611 patients underwent RARP of which 382 had EP-RARP.

Results: EP-RARP was comparable to TP-RARP with mean operative times (126 vs. 124 minutes), estimated blood loss was identical at 150mls, similar nodal yield (8.3 vs. 8.5), low positive surgical margin rate (9.8 vs. 9.6%) despite 26% of patients having pT3 disease. Hospital stays were overnight (1.01 vs. 1.04 days) . The importance of lymphadenectomy is confirmed by our 9.6% yield. Major complications were only 0.6% with a small bowel obstruction and renal failure in the transperitoneal group (table attached).

Conclusions: The advantage of extraperitoneal approach for open surgery is avoiding bowel complications. An experienced robotic surgeon can perform extraperitoneal radical prostatectomy retaining this advantage without oncological or surgical compromise.

Table 1: EP-RARP vs. TP-RARP data

	Total	Extraperitoneal	Transperitoneal
Number	611	382	239
Age(mean± s.d.)	59.84±7.18	59.49±7.09	60.71±7.38
BMI kg/m^2	28.3 ±4.26	27.2 ±3.31	31.0 ±5.14
Number of pts with BMI> 30kg/m^2	157	89	68
PSA(ng/dl)	5.9 ±5.0	5.9 ±5.1	6.0 ±4.6
Prostate size	49 ±19	49 ±17	50 ±23
OR time (minutes)	125 ±21	126 ±20	124 ±24
EBL(ml) median	150 ±154	150 ±166	150 ±100
Pathologic stage pT3a,pT3b	26%	25.6%	30%
PSM- prostate surgical margins	9.7%	9.8%	9.6%
Lymphadenectomy	188pts	144pts	44pts
Nodal Yield	8.4 ±4.2	8.3 ±3.8	8.5 ±5.3
Node positive	9.6%	6.4%	13.6%
Post operative Complications (Clavien grade 4 number or greater)	0.6% (4pts)	STEMI x2	Small bowel obstruction and renal failure; anastomotic disruption and renal failure
Length of stay	1.03	1.01	1.04

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Oncologic Outcome of Laparoscopic and Open Radical Prostatectomy
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UNABLE TO BE PUBLISHED

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Comparison of Extraperitoneal and Transperitoneal Pelvic Lymph Node Dissection during Minimally Invasive Radical Prostatectomy
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Introduction: Pelvic lymph node dissection (PLND) during radical prostatectomy (RP) has prognostic and possible therapeutic benefits. We assessed whether an extraperitoneal minimally-invasive RP (MiRP) allows for standard-template PLND comparable to transperitoneal MiRP+PLND.

Methods: A retrospective clinicopathologic study of 914 consecutive patients who underwent MiRP (laparoscopic or Da Vinci™ robot-assisted laparoscopic) with bilateral PLND by one surgeon (CPP) from 2001- 2010 was performed. Low-risk patients generally received a limited dissection (external iliac nodes) when PLND was performed. Those with intermediate and high-risk disease generally received a standard PLND (external iliac and obturator nodes). Patients were stratified into groups based on operative approach (extraperitoneal vs. transperitoneal) for most analyses.

Results: Overall, 192 patients had transperitoneal MiRP+PLND, and 377 had extraperitoneal MiRP+PLND. The extraperitoneal group had higher BMI (p=0.03), a higher percentage of low-risk (p=0.003) and a lower percentage of intermediate-risk disease (p=0.006). Lymph node yield (LNY) was higher with extraperitoneal PLND overall (6.5 vs. 5.3, p=0.003). When stratified by risk category, LNY was greater in the extraperitoneal group for patients with low-risk disease only (6.6 vs. 4.9, p=0.008). There was no difference in nodal yield in intermediate/high-risk patients receiving standard PLND by either transperitoneal or extraperitoneal approach (6.0 vs. 5.5, p=0.36 and 8.0 vs. 5.8, p=0.14, respectively). Lymph node involvement was rare overall. Estimated blood loss and complication rates were comparable between operative approaches.

Conclusions: The extraperitoneal MiRP approach does not compromise the oncologic efficacy or safety of routine PLND.

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The Impact of Prostate Size, Median Lobe, and Prior Benign Prostatic Hyperplasia Intervention on Robotic-Assisted Radical Prostatectomy: Technique and Outcomes
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Introduction: Large prostate size, median lobes, and prior benign prostatic hyperplasia (BPH) surgery pose technical challenges during robotic-assisted radical prostatectomy (RARP). We describe technical modifications to overcome BPH sequelae and associated outcomes.

Materials & Methods: Retrospective study of prospective data on 951 RARP performed from September 2005 to November 2010. Outcomes were analyzed by prostate weight, prior BPH surgery (n=59), and median lobes >1cm (n=42). Estimated blood loss (EBL), blood transfusions, operative time, positive surgical margins (PSM), and urinary and sexual function were compared.

Results: In unadjusted analysis, men with larger prostates and median lobes experienced higher EBL (213.5 vs. 176.5 mL, p<0.001 and 236.4 vs. 193.3 mL, p=0.002), and larger prostates were associated with more transfusions (4 vs. 1, p=0.037). Operative times were longer for men with larger prostates (164.2 vs. 149.1 minutes, p=0.002), median lobes (185.8 vs. 155.0 minutes, p=0.004) and prior BPH surgical interventions (170.2 vs. 155.4 minutes, p=0.004). Men with prior BPH interventions experienced more prostate base PSM (5.1% vs. 1.2%, p=0.018), but similar overall PSM. In adjusted analyses, median lobes increased both EBL (p=0.006) and operative times (p<0.001) while prior BPH interventions also prolonged operative times. However, prostate size did not affect EBL, PSM or recovery of urinary or sexual function.

Conclusions: Large prostate size and BPH characteristics pose challenges that increase operative times and EBL during RARP, but do not affect recovery of urinary or sexual function. Technical modifications to overcome median lobes and prior BPH surgeries improve both perioperative and long term outcomes.

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Robotic Pyeloplasty in Adults over 50 years-old: Outcomes Compared to a Younger Cohort
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Introduction: Ureteropelvic junction (UPJ) obstruction frequently presents in the pediatric population. With improved life expectancy and increased use of imaging, more patients are presenting with UPJ obstruction after age fifty. We hypothesized that objective measures of surgical outcomes of pyeloplasty would be equivalent in our adult populations older than and younger than 50 years-old.

Methods: An IRB-approved retrospective database of surgical management of UPJ obstruction by a single surgeon between November 2006 and October 2010 was created. Of 69 patients, 22 patients (32%) were older than 50 years of age. Diuretic renography and creatinine were obtained pre- and post-operatively and patients were followed for two years postoperatively. Univariate analysis was performed with standard statistics.

Results: The two groups were equivalent with regards to age, gender, laterality, and etiology. Postoperatively, patients greater than 50 years-old were found to have a greater increase in ipsilateral differential function on renography than the younger cohort (6.28% vs. 1.05%, p=0.04). There was no difference between the two groups with regards to other postoperative outcomes.

TABLE 1. Outcomes pyeloplasty in adults over 50 years old and those younger than 50 years old

Outcome	< 50	> 50	p value
LOS (days)	1.95	2.00	0.88
Change in eGFR (mL/min)	4.95	1.41	0.25
Change in differential function (%)	1.05	6.28	0.04*
Change in t ½ (minutes)	-5.85	-21.55	0.17
Symptomatic relief (%)	87	100	0.31

Conclusions: This is, to our knowledge, the first study to address the surgically relevant outcomes of robotic pyeloplasty in an older cohort. We demonstrated that in those greater than 50 years old, there is a greater improvement in differential function on renography and equivalence of other outcomes, compared to a younger cohort.

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The Safety of Aspirin in the Perioperative Period in Urologic Robotic Surgery
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Introduction: Robotic surgery is increasingly performed for radical prostatectomy and nephrectomy. Many patients have significant cardiac histories requiring aspirin and have significant thromboembolic risk when it is held. Our objective is to provide the first evaluation of the safety of aspirin in the perioperative period for robotic prostatectomy and nephrectomy.

Materials & Methods: A retrospective study of a pre-existing prospectively collected quality improvement database was performed. All patients who underwent robotic radical prostatectomy or robotic nephrectomy by a single surgeon between August 2008 and August 2010 were identified. We compared patients operated after November 2009 in whom aspirin had been administered the day of surgery with those who underwent surgery before November 2009 in whom aspirin had been held. Kruskall-Wallis tests or 2-sample T-tests were used to compare continuous variables.

Results: We identified 44 patients who underwent prostatectomy without recent aspirin and 51 who received preoperative aspirin. There were no significant differences between the 2 groups in baseline characteristics. Operative time (182 vs 174 min, p=0.19), median blood loss (175 vs 100 mL, p=0.12), and length of hospital stay (1 vs 1 day, p=0.08) were similar between the 2 groups. In the nephrectomy cohort, 12 patients had not received aspirin and 14 had. Again, there were no differences in median blood loss (65 vs 50 mL, p=0.96), median operative time (176 vs 140 min, p=0.14), or median hospital stay (2 vs 2 days, p=0.74).

Conclusions: Continuing aspirin in patients undergoing robotic radical prostatectomy and radical nephrectomy appears to be safe.

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Microvascular Arterial Bypass Surgery: Prospective Outcomes Study Using Validated Instruments
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Introduction: Penile microarterial bypass surgery may be the only treatment capable of restoring normal erectile function without the necessity of chronic use of vasoactive medications or placement of a prosthesis. Lack of standardization in patient selection, hemodynamic evaluation, surgical technique and limited long-term outcome data using validated instruments have resulted in this surgery being considered experimental. In this study we report long-term outcome data using validated questionnaires in young men (younger than 55) free of vascular risk factors who underwent microvascular arterial bypass surgery.

Materials & Methods: This is a single institution prospective institutional review board approved study of 38 men (mean age 28.2 ± 8.7 years) who underwent microvascular arterial bypass surgery between 2000 and 2010.

Results: Mean preoperative and postoperative penile rigidity measures without and with phosphodiesterase type 5 inhibitors were 43%, 75% and 77%, 94%. Mean total International Index of Erectile Function score, Erectile Function domain, and question 3 and 4 scores preoperatively and postoperatively were 41.5 ± 17.0, 16.4 ± 8.2, 2.9 ± 1.9 and 2.5 ± 1.8, and 53.5 ±13.3, 23.7 ± 5.8, 4.2 ± 1.5 and 3.7 ± 1.5. Preoperative and postoperative Center for Epidemiologic Studies Depression Scale scores were 18.4 ± 15.1 and 14.2 ± 13.1. Short-term complications included emesis and dysuria. Long-term complications were loss of penile length and decreased penile sensation.

Conclusions: In patients with no vascular risk factors and pure cavernous arterial insufficiency, microvascular arterial bypass surgery provides long-term improvements in erectile function, depression and overall satisfaction.

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10-year Analysis of Adverse Event Reports to the Food and Drug Administration Related to the use of Phosphodiesterase Type-5 Inhibitors
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Introduction: To ensure public safety all Food and Drug Administration (FDA) approved medications undergo post-approval safety analysis. Phosphodiesterase type-5 inhibitors (PDE5-i) are generally regarded as safe and effective.

Methods: We performed a non-industry sponsored analysis of the reports for sildenafil, tadalafil, and vardenafil to evaluate the overall cardiovascular and mortality events in the past 10 years. Summarized reports of adverse events for each PDE5-i were requested from the Center for Drug Evaluation and Research within the FDA. These data are available under the Freedom of Information Act and document the reports of adverse events entered into the computerized system maintained by the Office of Surveillance and Epidemiology. The data was analyzed for overall number of adverse events (AEs), number of objective cardiovascular events, and reported deaths.

Results: Overall 14818 AEs were reported for sildenafil. Events associated with death numbered 1824 (12.3%) and those associated with cardiovascular adverse events numbered 2406 (16.2%). Tadalafil was associated with 5548 AEs and those associated with cardiovascular adverse events and deaths were 7.8% and 4.3% of these reports respectively. Vardenafil was associated with 6085 events, with cardiovascular adverse events and deaths at 5.3% and 2% respectively. Only 10% of adverse events were reported by the manufacturers.

Conclusions: Adverse events associated with death are concerning and remain above 5% of total reported events. Limitations of this data set exist but it is important that these reports be reviewed outside of the pharmaceutical industry in order to provide due diligence and transparency.

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Outcomes of Surgical Management for Perineal Gangrene
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Introduction: Perineal gangrene is a potentially lethal disease whose cure depends on rapid diagnosis and surgical intervention.

Materials & Methods: We identified 36 patients at our institution from 7/95-11/10 diagnosed with Fourniers/perineal gangrene. Fourniers Gangrene Severity Index (FGSI) was used to stratify illness severity. Wound closure was performed by split-thickness skin-graft (STSG), primary-closure, or healing by secondary-intention.

Results: Median age of patients in this series was 54 years (33-91). Median length of stay was 19 days (6-92) and number of surgical procedures was 4 (1-10). 4 patients (11%) were bacteremic at presentation. Median WBC was 18.2 th/mm3 (8.9-37.0), and creatinine was 1.3 mg/dl (0.7-7.4). Median FGSI was 5 (0-16), and follow-up was 19 months (0-99). The most common comorbidities were hypertension (58%), type-2 diabetes (47%), alcoholism (14%), end-stage renal failure (14%), and coronary artery disease (14%). The most common etiologies were GU trauma (25%), perirectal abscess (17%), and GU instrumentation (11%). The most common wound culture pathogens were coagulase-negative Staphylococcus (33%) and beta-hemolytic Streptococcus (28%). Mortality <7 days was 6% (2 pts), <30 days was 9% (3 pts), and <1 year was 9%. 12 patients (33%) underwent STSG, 10 (28%) were closed primarily, and 14 (39%) healed by secondary-intention.

Conclusions: There is a spectrum of severity in patients with perineal gangrene with the most severe form classically referred to as Fourniers. This accounts for the variable mortality reported for this disease. Irrespective of initial presentation the cosmetic and functional results of wound closure were excellent for all those who survived.

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VED Registry in Men Treated for Prostate Cancer: Initial Results of a Prospective, Multi-institutional Dataset

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Introduction: The VED Registry is an IRB approved prospective multicenter database for men prescribed a Vacuum Erection Device (VED). We report initial data collected from men who have undergone prostate cancer (PCa) treatment.

Materials & Methods: Patients were sent questionnaires to be completed and returned at the time of receipt of the VED and at 3, 6 and 12 months. Baseline questionnaires consisted of a brief history including information on (PCa) diagnosis and treatment (Tx), the IIEF and an ED treatment inventory. Follow-up questionnaires included the full IIEF, ED treatment inventory and a VED questionnaire. Only PCa patients are included in this analysis.

Results: In 12 months 395 questionnaires were returned 210 from PCa patients. Baseline SHIM scores are summarized in the table; note that some men were unsure of their treatment details. Similar dissatisfactions (scale: 1-5) were observed for post prostatectomy rehabilitation with Viagra (1.0±0.9), Levitra (2.0±1.0) and Cialis (1.7±0.0). The 3-month dataset is small and analysis is premature. However it was noted that VED satisfaction score was 2.0±1.4 and 45.0% of 22 patients reported an increase in the length of their erect penis at 3-months.

Conclusions: The data is embryonic but the ability to collect large amounts of patient data has been demonstrated and it is anticipated the VED Registry will contribute significantly to post prostatectomy ED knowledge. Supported by Firma Medical Co.

Baseline SHIM Scores

	All (n)	Full Gland (n)	Unilateral NS (n)	Bilateral NS (n)	Focal (n)
Prostatectomy (all)	8.9±9.6 (131)	11.6±10.4 (32)	11.6±9.0 (7)	9.4±10.3 (50)	-
Robotic/Lap	8.8±9.4 (107)	11.7±10.6 (21)	9.3±7.4 (6)	8.9±10.3 (45)	-
Open	9.5±10.4 (24)	11.4±10.5 (11)	25±N/A (1)	14.0±10.8 (5)	-
Radiation (all)	13.4±8.3 (23)	-	-	-	-
Cryoablation	3.1±6.7 (28)	3.2±6.9 (14)	(0)	(0)	2.5±6.1 (6)

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Urethral Reconstruction Outcomes Using Patient Reported Preoperative and Postoperative Questionnaires in Combination With Uroflometry

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Introduction: There is a paucity of data regarding self-reported outcomes following urethral reconstruction. We compared preoperative and postoperative AUA symptom score (AUASS), quality of life (QOL), erectile function, flow rate (FR), and post-void residual (PVR) in patients undergoing urethral reconstruction for complex stricture disease.

Materials & Methods: Under an IRB-approved chart review, 86 patients were identified with complete pre and postoperative data, and an additional 20 patients with only postoperative data. All cases were performed at our institution over a 2.5-year period. Patient demographics, type of surgery, AUASS, QOL score, IEFF, FR and PVR were collected for all patients. Patients were followed at 3 and 6 months postoperatively, then yearly with questionnaires, FR and PVR. Flexible cystoscopy (17fr) was performed at 6 months. Statistical analysis was performed using the Wilcoxon signed rank test.

Results: Average patient age was 46.8 (range 17-81) years. Twenty-two anastomotic, 73 onlay and 11 fasciocutaneous flap urethroplasties were performed. The median individual change when comparing pre and postoperative data in our cohort was an improvement of 12 for AUASS, 4 for QOL, and no change in IIEF (table 1).

Conclusions: Patients undergoing urethral reconstruction for complex stricture disease experienced a significant improvement in self-reported outcomes that correlated with functional uroflow studies. Patients can expect to maintain their erectile function. This data may be helpful when counseling patients prior to surgical intervention.

TABLE 1. Median preoperative and postoperative patient reported and diagnostic data

	Preoperative	Postoperative	Median Change	p-value
AUA symptom score	16	2	-12	<0.0001
QOL	5	1	-4	<0.0001
IIEF	23	24	1	0.2155
FR	9	23	12	<0.0001
PVR	66	24	-32	<0.0001

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Post-Operative Complications of the Exaggerated Lithotomy Position

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Introduction: The exaggerated lithotomy position provides excellent exposure to the perineum during urethral surgery. Recent studies have reported a high complication rate for this position suggesting that its use should be limited. We present our experience with the exaggerated lithotomy position.

Methods: Data was retrospectively reviewed on 105 patients who underwent surgery in the exaggerated lithotomy position at a single institution. Positioning related complications and time in exaggerated lithotomy position were collected.

Results: All patients except one underwent urethral reconstruction. Average time in the exaggerated lithotomy position was 172 minutes (105-230 minutes). Twenty three patients (21.9%) had complications felt to be positioning related, the majority of which resolved without additional treatment or sequelae. The most common findings were paresthesias of the lower extremity seen in 20 patients (19.0%) and musculoskeletal back pain in 4 patients (3.8%). All but 3 of these patients (87%) had spontaneous resolution of these symptoms prior to discharge. Average time to resolution was 2.3 days. The symptoms in the remaining 3 patients continued to improve at time of discharge and did not warrant further intervention. A single patient (0.9%) had a pulmonary embolus. Medical work-up revealed the presence of lupus anticoagulants, an additional risk factor for thrombosis. No patients had neurapraxia, rhabdomyolysis or compartment syndrome.

Conclusions: The exaggerated lithotomy position provides unequaled access to the perineum for urethral reconstruction. With appropriate equipment and attention to proper positioning, there is a relatively low risk of even minor, self-limited complications and is therefore our position of choice.

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"Never Events" - The Incidence and Cost Implications of "Preventable" Complications in an Academic Urology Practice

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Introduction: In 2008, the Center for Medicare Services enumerated a list of "preventable" adverse events and began restricting payments for associated costs. These included certain unambiguous preventable errors like wrong site surgery, but also certain medical/surgical complications that might result from non-modifiable risk factors. In this study, we investigated the incidence of current or proposed "never events" during a one year period in a tertiary level academic urology practice. Also we sought to quantify inpatient costs directly attributable to these events.

Methods: We reviewed a prospectively maintained database of patient morbidity and mortality in our urology department from July 2009-June 2010. Incidence of current and proposed "never events" were collated. Inpatient billing records for infection-related events were specifically reviewed.

Results: Table 1 demonstrates the incidence of various current and proposed "never events." Infection-related events generated hospital costs of $168,428.28 (mean $7655.83/patient; range $1.26-70,151.94).

Conclusions: While "never events" are relatively rare in an academic urology practice, they can generate substantial cost burden if reimbursement is strictly limited. For high risk patients, it may be impossible to determine whether specific events are preventable even when best practices are followed. Furthermore, determining which costs are directly attributable to an event during a complex hospital course may not be routinely feasible. Health care policy that seeks to incentivize quality care needs to recognize these methodological issues.

Table 1.

Event	Overall Incidence (5305 cases)	Adult Incidence (4032)	Pediatric Incidence (1273)
C. difficile infection (6)	0.11% (6)	0.12% (5)	0.08% (1)
Surgical site infection (12)	0.23% (12)	0.17% (7)	0.39% (5)
Catheter-associated UTI (8)	0.15% (8)	0.17% (7)	0.08% (1)
Infected device (1)	0.02% (1)	0.03% (1)	0% (0)
Hospital acquired pneumonia (4)	0.08% (4)	0.10% (4)	0% (0)
Deep venous thrombosis/ pulmonary embolism (17)	0.32% (17)	0.42% (17)	0% (0)
Hip fracture (1)	0.02% (1)	0.03% (1)	0% (0)
Anesthesia-related (3)	0.06% (3)	0.05% (2)	0.08% (1)
Positioning-related (5)	0.09% (5)	0.12% (5)	0% (0)
Narcotic overdose (2)	0.04% (2)	0% (0)	0.16% (2)

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"Academic Ranking Score": A Reproducible Metric of Thought Leadership in Urology
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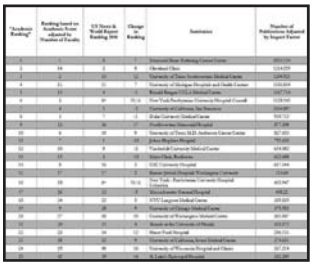
Introduction: U.S. News & World Report (USNWR) rankings of hospitals are an integral marketing strategy for healthcare systems. Nevertheless, the methodology utilized appears flawed due to the disproportionate reliance on "reputation", as determined by querying approximately 125 urologists. In an effort to develop an improved measure of a urology department's contribution, we have developed the "Academic Ranking Score" (ARS).

Methods: All publications as first or last author from 2005-2010 were identified using an active faculty list for each urology department. The ARS was derived by normalizing the tabulated publications by the Impact Factor of the journal of publication. The 2010 USNWR Top-50 urology hospitals were then re-ranked based on ARS (Table 1).

Results: 6,437 urological publications were indexed to calculate ARS. Two of the top 3 programs in the USNWR rankings dropped out of the top 10. Meanwhile, the top 10 academically ranked programs moved an average of >5 positions (range 0-17). No correlation was seen between programs ranked in the top 10 by USNWR and our ARS method (Spearman's rho -0.1, p=0.75). When adjusting ARS on a per-FTE basis to eliminate bias of size, the disparity in rank lists persisted (Spearman's rho -0.33, p=0.23).

Conclusions: ARS departmental rankings determined through quantification of recent academic contribution differs substantially from the USNWR. Our integration of objective measures into an overall ranking system replaces subjective opinions with up-to-date, merit-based assessments.



51

Influence of Surgeon and Hospital Volume on Radical Prostatectomy Costs
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Introduction: While higher radical prostatectomy (RP) hospital and surgeon volume is associated with better outcomes, the effect of provider volume on healthcare costs remains unclear.

Materials & Methods: We used SEER-Medicare data to identify 5,964 men who underwent RP from 2003-2005. We categorized hospital and surgeon RP volume during the study period into quartiles (low, intermediate, high, very high). Costs from inpatient, outpatient, and physician services were assessed from RP until 90 days postoperatively.

Results: Higher surgeon volume was associated with lower RP costs (low $11,925; intermediate $11,680; high $11,649; very high $10,384, p<0.001) while higher hospital volume was associated with greater costs (low $10,910; intermediate $11,006; high $11,696; very high $12,132, p<0.001). In adjusted analyses, the cost savings of an additional RP by surgeon volume was $10.6 (95% CI: 4.4-16.8, p<0.001) while the marginal cost for an additional RP by hospital volume was $6.8 (95% CI: 4.1-9.6, p<0.001). Moreover, RP costs were higher for single vs. married men ($383.9, 95% CI: 138.4-629.4, p=0.002) and Black ($599.0, 95% CI: 296.7-901.3, p<0.001) and Hispanic ($500.9; 95% CI: 65.8-936.1, p = 0.024) vs. white men. Finally, there was significant geographic variation, and the RP cost differential between the most and least costly SEER regions was $3988.4 (95% CI: 3361.6-4615.2, p<0.001).

Conclusions: Higher RP surgeon volume leads to significant savings; however, higher RP hospital volume increased costs. These findings should be considered when balancing health care reform initiatives to improve quality while reducing health care expenditures.

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Cost-effectiveness of Percutaneous Renal Mass Biopsy to Guide the Management of Small Solid Renal Masses (≤4cm)
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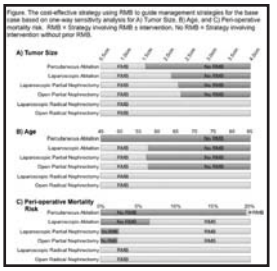
Introduction: We assessed the cost-effectiveness of percutaneous renal mass biopsy (RMB) to guide management decisions for small solid enhancing renal masses (SRM, ≤4cm).

Materials & Methods: We developed a decision-analytic model estimating the costs and benefits of RMB prior to competing treatments: percutaneous/laparoscopic ablation, laparoscopic/open partial nephrectomy, laparoscopic/open radical nephrectomy. For RMB, we modeled a 10% non-diagnostic rate, 97.5% sensitivity, 91.2% specificity and 0.01% complication rate. Positive or non-diagnostic RMB led to treatment; negative RMB led to active surveillance. Our base case was a healthy 65-year old patient with an asymptomatic unilateral 3cm SRM. Model inputs were estimated from the literature. Outcomes were measured in quality-adjusted life-years (QALY) and 2008 US$, respectively. We used a societal perspective, lifetime horizon, 3% discount rate, 3-month cycle length, and a $50,000/QALY willingness-to-pay threshold. The model results and alternative clinical scenarios were tested with sensitivity analysis.

Results: In the base case, RMB was cost-effective prior to radical nephrectomy options for all scenarios. Conversely, for partial nephrectomy or ablation options, management without prior RMB was cost-effective; however, RMB was cost-effective with smaller tumors, younger and less healthy patients (Figure).

Conclusions: For healthy 65-year old patients, RMB is cost-effective to guide management of any SRM prior to radical nephrectomy. It is also recommended for patients with smaller SRM, younger age, and worse health prior to partial nephrectomy or ablative therapies.



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Impact of Poverty Level and Education on 24-hour Urine Composition in Patients with Nephrolithiasis
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Introduction: Socioeconomic status and education level have been shown to affect health outcomes. We examined the relationship between poverty level, education level, and 24-hour urine composition in patients with nephrolithiasis.

Materials & Methods: A retrospective review was performed. Poverty level and education level for each zip code were determined from US Census Bureau Data. Multivariate linear regression examined the relationship between poverty level, education level, and 24-hour urine composition. Regression models adjusted for known risk factors for stone disease.

Results: 435 patients were included in the study. Female:male ratio was 173:262 (i.e. 40% female), mean age was 52.5 years (SD 14.4), mean BMI was 28.6 (SD 6.5). On multivariate linear regression, increasing poverty was associated with significant increases in urine calcium (B = 1.51, 95% CI 0.16 to 2.86). There were no other associations between poverty level and any urine constituents or supersaturations. Increasing level of education was associated with significant decreases in urine calcium (B = -1.26, 95% CI -2.42 to - 0.10), supersaturation of calcium oxalate (B = -0.04, 95% CI -0.09 to -0.006), and supersaturation of calcium phosphate (B = -0.013, 95% CI -0.03 tp -0.0002). There were no other associations between education level and any urine constituents or supersaturations.

Conclusions: In this study of stone formers, increasing poverty and lower education level were both associated with increased urine calcium. Further studies are important to elucidate the mechanisms underlying these findings.

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Cost Comparison of Hand Assisted (HALPN) vs Robotic Assisted Laparoscopic Partial Nephrectomy (RALPN)

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Introduction: While many studies tout the benefits of RALPN, none have evaluated the financial cost of this approach. Herein, we evaluate the financial cost of RALPN as compared to HALPN at our institution.

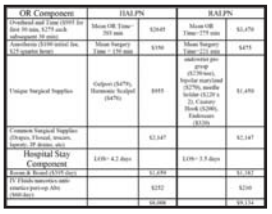
Materials & Methods: The records of all HALPN and RALPN between 2006 and 2010 were reviewed. Total cost of each procedure was based on operative room cost (time cost of room, anesthesia time cost, and supply) and hospital stay cost. These costs were applied to the mean HALPN and RALPN patient (Table 1).

Results: 47 patients underwent HALPN and 21 patients underwent RALPN. Room time and operative time were significantly shorter for the HALPN cohort whereas LOS was significantly shorter in the RALPN cohort. The decreased LOS led to a cost savings of $319 for the RALPN cohort. The increased time in the OR led to an increased cost of $950 (OR time fee and anesthesia fee). Further, the cost of surgical supplies was $495 greater for the RALPN. There is an overall savings of $1128 if HALPN is selected (Figure 1).

Conclusions: HALPN is significantly less expensive than RALPN and should be considered for its financial value.

TABLE 1. Comparison of OR Times and LOS for HALPN vs RALPN

	HALPN	RALPN	p value
Number of Cases	43	19	
Surgery Time (min)	150	221	<0.01
Room Time (min)	203	275	<0.01
Length of Stay (days)	4.2	3.5	<0.02



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Association of Bladder Sensation Measures and Bladder Diary in Patients with Urinary Incontinence

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Introduction: Investigation suggests the involvement of afferent actions in the pathophysiology of urinary incontinence. Current diagnostic modalities do not allow for the accurate identification of sensory dysfunction. We previously reported urodynamic derivatives that may be useful in assessing bladder sensation. This study further investigated these derivates by assessing for a relationship with 3-day bladder diary.

Methods: We performed a retrospective review of 120 women evaluated for urinary incontinence. Statistical analysis assessed for a relationship between bladder diary parameters and two previously reported urodynamic derivatives (First Sensation Ratio (FSR)(FS/Capacity), Bladder Urgency Velocity (BUV)(Capacity-FS)). Subset analysis was performed in patients without stress urinary incontinence (SUI) to isolate patients with urgency symptoms. Analysis was also performed to identify a possible relationship between these derivatives and the presence/absence of detrusor overactivity (DO).

Results: No association was demonstrated between bladder diary parameters and FSR/BUV. However, subset analysis demonstrated an association between DO and BUV, with a lower BUV identified in patients without DO ($p<0.05$). Subset analysis of patients without SUI demonstrated a weak association between voiding frequency and FSR ($r=-0.39$) and between daily incontinence episodes and BUV ($r=-0.35$). However, these failed to demonstrate statistical significance.

Conclusions: No association between bladder diary and FSR/BUV was seen. This is not unexpected since bladder diary may reflect numerous pathologies including not only sensory dysfunction but also SUI and DO. However, weak associations identified in patients without SUI suggest that further investigation is needed to assess the utility of FSR/BUV in characterizing sensory dysfunction in patients with urge-predominant symptoms

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Measurement of Spatial Distribution in Prostate Biopsy

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Introduction: Prostate biopsy is typically performed freehand with transrectal ultrasound (TRUS) guidance. However, it is difficult to determine the accuracy of the spatial distribution of TRUS-guided biopsy.

Materials & Methods: A simulation model was built to accurately measure *in-vitro* biopsy locations. This model consists of (1) a gelatin-based pelvic mockup with precisely defined geometry of a prostate and rectal cavity, (2) an optical tracking system (Polaris®, NDI, Ontario, Canada) to measure the relative locations, (3) TRUS probe, and (4) biopsy needle (Figure 1). Overall, this system measures the precise locations where biopsy cores are sampled. The measurement errors of the instrument are within 1 mm. After defining the gold standard using a 12-core sextant biopsy plan, we determined how closely an experienced urologist can perform a biopsy compared to the gold standard.

Results: Results from a simulated biopsy are shown in Figure 2. The simulated biopsy cores were often clustered and a large portion of the prostate gland was undersampled. The average error distance was 8.86 mm.

Conclusions: TRUS-guided prostate biopsies may not closely follow sextant biopsy distribution. An alternate targeting method may be needed for uniform sampling during TRUS-guided prostate biopsy.

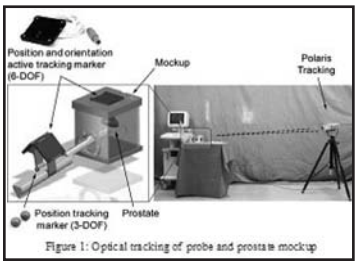

Figure 1: Optical tracking of probe and prostate mockup

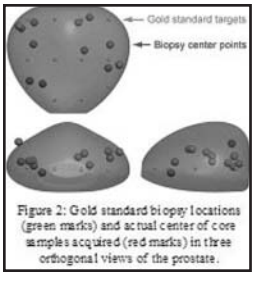

Figure 2: Gold standard biopsy locations (green marks) and actual center of core samples acquired (red marks) in three orthogonal views of the prostate.

P49

Bladder Compliance in Men with Lower Urinary Tract Symptoms

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Introduction: To determine whether there is a relationship between bladder compliance in men with lower urinary tract symptoms (LUTS) and the degree of urethral obstruction, prostate size, detrusor overactivity, and age.

Materials & Methods: Retrospective observational study of consecutive men 18 years of age or older, identified from our database, who underwent evaluation for persistent LUTS. All patients underwent history & physical examination, voiding diary, urinalysis & urine culture, cystoscopy & videourodynamics. Exclusion criteria: urethral stricture, prostate cancer, prostate surgery, active bladder cancer, neurogenic bladder. Urethral obstruction was defined by the Schafer bladder outlet obstruction nomogram (grades obstruction 0-6). Prostate size was defined as 0-4+ (0 = smaller than normal, 1+ = normal, 2 - 4+ = increasing prostatic size).

Results: Of 314 patients screened, 229 were excluded because of one or more exclusion criteria. The 85 remaining patients ranged in age from 31-89 yrs (mean = 63, SD = 13). An inverse correlation was found between bladder compliance & Schafer obstruction grade (Spearman's rho= -.276, p=.011). No correlation was noted between bladder compliance and prostate size (Spearman's rho=.076, p=. 50), detrusor overactivity (Spearman's rho= -.17, p=.33) or age (Spearman's rho=.01, p=.93).

Conclusions: Since low bladder compliance is an important risk factor for the development of upper urinary tract disease, proactive treatment and careful monitoring of patients with high degrees of urethral obstruction should be considered.

P50

Predictive Factors for Patient Satisfaction with Sacral Neuromodulation in Chronic Voiding Dysfunction

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Introduction: Sacral neuromodulation is an FDA-approved treatment for a variety of voiding dysfunctions that are refractory to conservative treatment. Studies have shown success rates of up to 80%; however, more than 20% of patients who undergo a successful test stimulation period, defined by at least 50% improvement in symptoms, fail to respond. We sought to identify other predictive factors for successful treatment of lower urinary tract symptoms with InterStim® neuromodulation.

Materials & Methods: We retrospectively analyzed 51 patients with chronic, nonobstructive frequency and urgency refractory to medical therapy who were treated with staged placement of the InterStim® device. Two cohorts were identified: those who were satisfied with treatment and those who were not according to a subjective grading scale. Variables were analyzed using paired t-tests.

Results: Of the 51 patients evaluated, 3 patients were excluded secondary to infection. Of the 48 remaining patients, 77% were female. Thirty-nine patients (81%) were satisfied with their improvement in symptoms, while 9 patients (19%) were dissatisfied. Age, sex, weight, the number of anticholinergic medications previously used, and the number of prior urologists sought in treatment were comparable between the two groups ($p>0.05$). Approximately 18% of patients in satisfied group were using chronic narcotic medication for pelvic pain control compared to 67% in the dissatisfied group ($p=0.002$).

Conclusions: Sacral neuromodulation is a successful means of treatment for refractory chronic voiding dysfunction. Regardless of undergoing staged placement after a successful stimulation trial, those who use chronic narcotics are less likely to be satisfied with Interstim® therapy.

P51

The Association Between Psychological and Lower Urinary Tract Symptoms: A Population Based Study in Finland

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Introduction: Our aim in this population based study is to determine if lower urinary tract symptoms (LUTS) are more prevalent in patients with anxiety and/or mood disorders.

Methods: In 2003-2004, questionnaires were mailed to 6,000 randomly selected Finnish people aged 18-79 years. LUTS information was collected by questionnaire using the validated Danish Prostatic Symptom Index with an additional question from the American Urological Association Symptom Index. The questionnaire included items related to mood and anxiety disorder. Patients were grouped into two categories, those with and those without a mood/anxiety disorder. Prevalence and odds ratios of LUTS were calculated for both groups.

Results: Of 6,000 subjects, 3,597(60%) responded, of whom 1,709(48%) were men and 1888(52%) were women. 300(5%) reported having a mood disorder/anxiety, of whom 116(39%) were males and 184(61%) were females. Prevalence of LUTS between those with and without mood disorder/anxiety is depicted in Table 1.

Conclusions: Among individuals with self-reported anxiety/mood disorders, there is increased prevalence of LUTS. The increased odds ratio for LUTS in these patients suggests a link between mental health and reported LUTS.

Table 1: Prevalence of LUTS in Patients With and Without Mood Disorder or Anxiety

LUTS Symptom	Patients Without Mood Disorder or Anxiety (95% CI)	Patients With Mood Disorder or Anxiety (95% CI)	Odds Ratio (95% CI)
Frequency	5.2% (4.4-5.9%) (n=166)	12.8% (9.0-16.6%) (n=38)	2.7 (1.9-3.5)
Urgency	7.3% (6.4-8.2%) (n=238)	16.6% (12.4-20.9%) (n=49)	2.5 (1.8-3.5)
Dysuria	0.4% (0.2-0.7%) (n=14)	1.3% (0.1-2.7%) (n=4)	3.1 (1.0-9.6)
Nocturia	2.5% (2.0-3.0%) (n=333)	3.4% (1.3-5.4%) (n=54)	1.9 (1.4-2.7)
Weak Stream	0.4% (0.2-0.6%) (n=12)	1.3% (0.1-2.7%) (n=4)	3.7 (1.2-11.5)
Hesitancy	3.6% (3.9-5.3%) (n=102)	10.5% (7.0-14.0%) (n=23)	2.6 (1.6-3.7)
Terminal Dribbling	6.6% (5.7-7.4%) (n=212)	14.3% (10.3-18.3%) (n=42)	2.4 (1.7-3.4)
Incomplete Voiding	3.2% (2.6-3.8%) (n=148)	7.9% (4.8-10.9%) (n=31)	2.4 (1.6-4.1)

*All odds ratios were significant with p-value<0.05 with the exception of Dysuria, which had a p-value of 0.058

P52

Recurrent Urinary Tract Infection in Intermittently Catheterized Spinal Cord Injury Patients

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Introduction: Clean intermittent catheterization (CIC) is widely accepted for neurogenic bladder management in spinal cord injury (SCI). We studied our population of SCI patients for the association of recurrent urinary tract infections (UTI) with the long-term use of CIC for neurogenic bladder management.

Materials & Methods: Retrospective study of 61 SCI subjects. Subjects were selected from patients followed by one physician at our institution between 2000 and 2010. 930 records were generated with diagnosis codes for "neurogenic bladder" and "spinal cord injury." Initial review of these records identified 210 SCI patients. 51 males and 10 females followed for at least one year were included. Patients with urinary diversion or those not using CIC were excluded. Subjects experiencing recurrent symptomatic UTI's were identified by their use of medical UTI prophylaxis (PRx) with either oral antibiotics or methenamine/vitamin C.

Results: 41 (67%) subjects required medical PRx for recurrent symptomatic UTI's (8 (80%) females and 33 (65%) males). There was no statistically significant difference between percentage of males and females requiring PRx. Date of initial PRx use was noted in 39 of 41 subjects and the results demonstrate 28 (72%) required PRx within 2 years after initiation of CIC.

Conclusions: Although CIC is believed to have the fewest complications compared with other methods, most SCI patients managed with long-term CIC will require medical PRx for prevention of symptomatic UTI within 2 years after its initiation. This highlights the continued need for advances in bladder management to improve quality of life in SCI patients.

P53

A Once-daily Titratable Gel Formulation for Transdermal Oxybutynin Delivery for OAB

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Introduction: A prospective randomized double-blind placebo-controlled trial of a once-daily titrable dose transdermal oxybutynin gel (TTOG) formulation. To date there are no titrable transdermal agents for OAB.

Materials & Methods: 12 week study ages 19-89 years with symptoms of urgency (UUI) and/or mixed UI for >3 months. Inclusion: >1-2 urge episodes and >8 voids/day. Three treatment arms: 84mg and 56mg TTOG and placebo. Primary: change from baseline in (UI) using a 3-day diary. Secondary: change from baseline in urinary frequency and volume voided. Primary analysis: modified intent to treat. Diaries: baseline, and weeks 1,2,4,8, and 12. Statistics: transformation for group comparison (predefined). IRB approved. Gel formulation supplied (Anturol) and study funding by Antares Pharma, Inc., Ewing, NJ.

Results: 626 patients (87% female) were included: TTOG 84mg (N=214), 56mg (N=210), and placebo (N= 202). Both doses of TTOG were statistically superior to placebo for UUI reduction and volume voided; 84mg dose for urinary frequency (Table 1). AEs:mild to moderate / non-prompted rates of dry mouth n= 26 (12.1%)/84mg and n= 23 (11.0%)/56mg TTOG and n=10 (5.0%)/placebo. CNS AEs were similar between both active arms and placebo group.

Conclusions: This is the first report of a TTOG. Significant improvement noted for OAB symptoms at both doses. Side effects were mild to moderate with low levels of skin reactivity. TTOG provides an additional alternative for managing OAB symptoms.

TABLE I	Treatment Group		
Endpoints	TT-Oxy gel 84mg/day (n=195)	TT-Oxy gel 56mg/day (n=171)	Placebo gel (n=166)
UUI/week, mean			
Baseline	43.6	50.1	45.8
Median Change	−18.7[x]	−21.0[xx]	−16.3
Micturitions/24 h			
Baseline , mean	11.4	11.7	10.5
Change, mean	−2.9[y]	−2.2[ns]	−1.9
Mean Voided Volume, ml			
Baseline	196.9	196.2	182.0
Change	29.0[z]	21.1[zz]	10.4

x ~ p =0.033 xx ~ p =0.028 y ~ p =0.0005 z ~ p =0.0499 zz ~ p =0.0017

P54

Presentation and Management of Complications of Male Perineal Slings: Are Complications Under-reported?

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Introduction: The AdVance and Virtue male slings are treatment options for post-prostatectomy incontinence (PPI), with the goal of reducing urinary incontinence without affecting voiding parameters. A concern of any procedure in treating men with PPI is the presence of significant complications. The purpose of this study was to report the presentation and treatment of complications from this minimally invasive treatment to a tertiary referral practice and to highlight complications reported in the food and drug administration (FDA) device failure database.

Materials & Methods: From January 2008 through March 2011, we reviewed all cases of AdVance and Virtue sling complications that presented to our institutions. The FDA manufacturer and user facility device experience (MAUDE) database was queried for self-reported complications.

Results: A total of 5 patients were referred to the Lahey Clinic and Penn Presbyterian Medical Center with complications following a male perineal sling. Treatments required a combination of surgical exploration, drainage and irrigation with antibiotics, mesh excision, and further surgery to treat the incontinence. The MAUDE database contained 11 major complications out of a total of 61 complications that were reported for the AdVance and Virtue male slings. There were significantly more major complications reported in MAUDE than in published literature.

Conclusions: Although rare, major complications of the male perineal slings are more common than they appear in the literature. Many of these cases may require additional reconstructive surgery and subsequent procedures for treatment of underlying incontinence.

P55

Effect of Percutaneous Tibial Nerve Stimulation on Fecal Incontinence: Results from a Double-Blind, Randomized, Sham-Controlled Trial for Over Active Bladder

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Introduction: The Objective of this study was to compare efficacy of percutaneous tibial nerve stimulation (PTNS) to validated-sham treatment in the subset of overactive bladder (OAB) subjects diagnosed with FI using a seven-level Global Response Assessment (GRA) questionnaire defining responders as those reporting FI symptoms a "moderately" or "markedly" improved.

Materials & Methods: The study was a multi-center trial with 220 OAB subjects of which 28 subjects (13%) experienced FI. Of these subjects, 15 were randomized to PTNS and 13 randomized to a validated sham intervention. Both groups received twelve weekly 30-minute intervention in which the PTNS group received stimulations delivered through a 34-guage needle electrode inserted near the posterior tibial nerve, and the sham therapy used a placebo needle and a TENS device using sensory and auditory methods to mimic the PTNS treatment without active treatment. Voiding diaries and validated questionnaires were completed at baseline, and after 6 and 12 treatments.

Results: Baseline characteristics were similar across both groups. The GRA for FI symptoms found 30.8% were responders in the PTNS group compared to 18.2% in the sham group aqfter 6 interventions and 45.5% and 18.2 after 12 treatments.

Conclusions: Although PTNS is not FDA cleared for use with those affected by FI in the United States, it suggests this treatment is not due to a placebo effect, is safe and effective, and has great potential for patients with FI

P56

Differential Diagnosis of Overactive Bladder in Women

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Introduction: The aim of this study is to evaluate the differential diagnosis in women with symptoms of overactive bladder (OAB).

Methods: This is a retrospective study demonstrating the differential diagnosis of women with symptoms of OAB using a previously validated OAB symptom questionnaire (OABSS). All patients underwent history and physical, OABSS questionnaire, 24-hour voiding diary, urinalysis, uroflow and post-void residual. Cystoscopy and urodynamics were completed when required for diagnosis. Selection criteria were developed to assign patients to the various diagnostic categories.

Results: 125 women (mean age 67) met inclusion criteria for OAB. Cystoscopy and urodynamics were completed in 106 (85%) women and detrusor overactivity was demonstrable in 54 (43.2%). The differential diagnosis for all patients and patients with OABSS≥9 is listed in Table 1. 103 (82.4%) patients had an OABSS≥9 with a mean OABSS of 15.4 (range 5-27, SD 5.5). The differential diagnosis of this subset of patients is listed in table along with mean OABSS for each category.

Conclusion: Women who present with OAB symptoms exhibit a differential diagnosis of concomitant urologic pathologies, we believe that OAB should be considered a symptom complex, not a syndrome. This series confirms that up to 79% of women with OAB symptoms have other diagnosable conditions, many of which may be remediable to treatment.

Table 1. Differential Diagnosis	**All Patients (N=125)**			**OABSS 9 (N=103)**		
Category	Number (%)	Mean OABSS	# DO	Number (%)	Mean OABSS	# DO
UTI	16 (13)	13.3	10	15 (15)	13.8	9
Sphincteric incontinence	46 (37)	14.7	25	42 (41)	15.4	23
POP	29 (23)	14.6	18	29 (28)	14.6	18
Neurogenic bladder	15 (12)	15.3	13	14 (14)	16.0	12
Bladder outlet obstruction	6 (5)	15.7	6	6 (6)	15.7	6
Miscellaneous	22 (18)	13.0	14	19 (18)	13.9	13
Idiopathic	26 (21)	13.5	13	21 (20)	15.0	11

***Each subject could be represented in more than one diagnostic category.**

P57

Does Patient Obesity Impact the Effectiveness of Extracorporeal Shockwave Lithotripsy?

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Introduction: The incidence of upper tract urinary stones is higher in obese patients with body mass index (BMI) ≥ 30. Does obesity impact stone free rate of SWL? We compared normal and overweight (BMI <30) patients with obese (BMI≥30) patients to determine stone free rate.

Materials & Methods: 1975 consecutive SWL procedures done on a Lithotron lithotriptor by 20 urologists using a consistent protocol for>95% of patients were reviewed. KV and number of shocks delivered were consistent in groups. Age and sex distribution was comparable. To evaluate outcomes, the group was divided into 1095 SWL patients with BMI of <30 (normal and overweight) and 880 patients with BMI ≥30 (obese). Size and location of the stones were compared as was stone free status on plain film of the abdomen and pelvis at 4-6 weeks (94% of patients). Statistical differences between groups were determined by Students-t or Chi-square analysis.

Results: Overall stone-free rate for patients with BMI <30 was 66.7% and 57.2% for BMI≥30 ($p<0.005$). Stone-free rate evaluated by stone location was 62.5% for renal; 72.1% for ureteral in non-obese and 53.1% for renal; 63.7% for ureteral in obese patients ($p<0.005$ renal; $p<0.010$ ureteral). Stone size analysis showed higher stone free rate in the non-obese patient, particularly for larger stones greater than 75 mm^2 (52.8% and 39.2%)($p<0.005$); <25 mm^2 (83.5% and 77.3%)($p<0.010$); 25-75 mm^2 (65.6% and 63.2%) (n.s); for BMI <30 and BMI ≥30 respectively.

Conclusions: SWL remains the mainstay of treatments but appears to be less effective in obese patients (BMI≥30).

P58

Risk of Infection Stones in Patients with Non-Obstructing Renal Stones
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Introduction: Non-obstructing renal stones are a potential cause of recurrent urinary tract infections. However, there is little clinical data to distinguish infected from uninfected renal stones.

Materials & Methods: We performed a retrospective review of patients who underwent unilateral ureteroscopy for non-obstructing renal stones from 9/2008 - 6/2010. Stone culture was routinely sent if a stone was retrieved. Patients were excluded if they had hydronephrosis, ureteral stones, indwelling stent, bilateral procedures, or ipsilateral percutaneous nephrolithotomy or shock-wave lithotripsy in the preceding 12 months. Stone dimensions were independently measured from CT images.

Results: Ureteroscopy was performed in 43 renal units in 41 patients with a mean of 2.3 stones per renal unit. Four (9.3%) renal units had a stone culture with at least one bacteria while 39 (90.7%) had no growth. Stone microbiology included alpha-hemolytic Streptococcus (1 stone), Enterococcus (2 stones), and coagulase-negative Staphylococcus (1 stone). Eight (18.6%) patients had a diagnosis of recurrent UTIs, but only 1 (2.3%) had a stone culture that correlated with at least one prior urine culture. Mean stone size was 7.14 ± 3.16 mm x 5.44 ± 2.24 mm in the axial plane. There was no statistically significant difference in stone length, width, height, axial ellipsoid area, or ellipsoid volume between patients with and without positive stone cultures.

Conclusions: Non-obstructing renal stones have a low but non-negligible incidence of infection in this patient population. Larger studies are needed to identify predictive variables for stone infection to guide patient selection for surgical intervention.

P59

Contemporary 24-hour Urine Collection Analysis Reveals High Risk Stone Formers May Be at Increased Risk for Recurrence in Summer and Winter Months
Sammy E. Elsamra, Michael Lasser, Simone Thavaseelan, George Haleblian, Gyan Pareek
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Introduction: Climate and geography have been shown to play a role in stone risk, with populations in warmer climates exhibiting a greater prevalence of nephrolithiasis. None of these studies are from the northeast and many reveal no decrease in urinary volume in the summer. We evaluated high-risk stone formers in our region to determine if a seasonal variation in urine volume exists.

Materials & Methods: 963 24-hour urine specimens from high risk stone formers (2005-2010) were stratified by season (Winter-Dec, Jan, Feb; Spring-Mar, Apr, May; Summer-Jun, Jul, Aug; Fall-Sep, Oct, Nov) and seasonal mean 24-hour urine volume was compared via Student T test.

Results: Of 963 urine studies, 472 (49%) were male and 482 (51%) female. Mean (± standard deviation) 24-hour urine volumes (liters) for spring, summer, fall, and winter were 1.9 ± 0.97, 1.79 ± 0.9, 2.02 ± 0.87, and 1.84 ± 0.76, respectively. Student's T-test was used to compare each season in a round-robin fashion. Significant differences were noted between summer and fall as well as winter and fall with both summer and winter associated with significantly lower volumes than fall (p=.007 and p=0.014, respectively).

Conclusions: High-risk stone formers in the northeast produce lower urine volumes in the summer *and* winter. Frigid winters may increase exposure to arid indoor heating with similar effects on hydration. Urologists treating high-risk stone formers, in the northeast, should be aware of *both* of these two seasonal variations to facilitate proper hydration counseling to high-risk stone formers.

P60

Submilisievert Computed Tomography for the Evaluation of Urolithiasis
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Introduction: We evaluated feasibility of submillisievert computed tomography (CT) examinations reconstructed with iterative reconstruction (IR) techniques in patients with urolithiasis.

Materials & Methods: 26 patients (mean age-38 yrs) with diagnosed urolithiasis, treated and on follow up underwent submillisievert dose unenhanced scan on 64 MDCT (Discovery CT750 HDCT, GE Healthcare) and 128 MDCT (Somatom Definition Flash, Siemens Health care). The scan protocol included 80 kV, auto mA 75-150 or Ref mA - 80, slice thickness 5mm for < 200 lbs and 100 kV, auto mA 75-150 or Ref mA - 80, slice thickness 5mm for > 200 lbs. Images were reconstructed using filtered back projection (FBP) and IR [ASIR(GE) 60% & 80% and IRIS (Siemens)]. All images were reviewed for image quality (scale 1-5), noise (scale 1-3), number and size of calculi and reader confidence on PACS work station. Comparison was made with the prior low dose FBP baseline CT scan.

Results: All 34 stones mean size (6.4mm, range 4-15 mm) was confidently diagnosed by two readers, yielding 100% sensitivity and accuracy. In 8 patients, stones had passed/resolved after treatment. In giving a differential diagnosis IR images were rated better than FBP (2.8 vs 1.7). The mean CTDI, DLP and mSv for submillisievert protocol was 1.2, 65.3 and 0.86 in comparison to 10.6, 363.4, and 5.4 for our baseline low dose exam with 82-88% dose reduction (p-0.0013).

Conclusions: Submillisievert unenhanced CT is a clinically feasible for diagnosis of urolithiasis with 82-88% dose reduction compared with standard non-contrast CT.

P61

The Impact of Body Mass Index Reduction on 24-Hour Urine Parameters
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Introduction: Studies have shown an association between obesity and lithogenic metabolic parameters in stone-forming patients. However, the relationship between obesity and nephrolithiasis is incompletely understood. We assessed the effect of change in body mass index (BMI) on changes in 24-hour urine profiles.

Materials & Methods: 505 consecutive stone-formers completed comprehensive metabolic evaluations between 2006 and 2010. BMI (kg/m^2) was measured at successive office visits, and 181 patients completed 24-hour urine collections separated by at least 3 months available for retrospective review. Delta-BMI was compared against 24-hour urine parameters and the correlation coefficients (R^2) were calculated.

Results: 140 of the 181 patients (77%) were obese (BMI≥25). The mean delta BMI in our population was +0.09kg/cm^2 (range -5.62 to +4.56) with a mean time between 24-hour urine collections of 8.9 months. Using a linear regression model, no significant correlation was found between delta-BMI and 24-hour urine parameters. In the subset of patients with a positive delta-BMI, there was a trend towards a decrease in urinary pH (R^2=0.08, fig 1).

Conclusions: Few studies have investigated the effect of weight loss on metabolic profiles. Our data did not suggest a clear correlation of change in BMI with change in 24-hour urine chemistries. Although weight loss may play a role in the management of stone-forming patients, the approach to stone prevention remains multi-faceted.

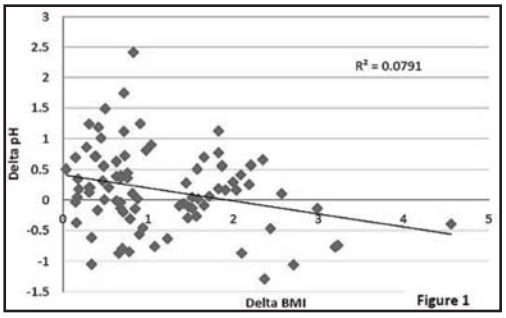

Figure 1

Concurrent Poster Session III: Non-Oncologic Diseases
11:20 am-12:15 pm

P62

Management of Residual Fragments Following Percutaneous Nephrolithotomy: A Cost Analysis
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Introduction: Residual fragments after percutaneous nephrolithotomy (PNL) have historically been managed with second-look flexible nephroscopy. As the utilization of tubeless PNL becomes more widespread, there has been an increased interest in second-look ureteroscopy for patients with residual stone fragments. We performed a cost analysis of immediate second-look flexible nephroscopy and second-look ureteroscopy for patients with residual stones following PNL.

Methods: We reviewed the records of patients who underwent PNL and then required a secondary procedure for the management of residual fragments following the initial PNL procedure. Cost data were obtained from administrative billing records. We defined total costs as operating room and post-anesthesia care unit expenses, as well as laboratory and professional (surgical and anesthesia) fees.

Results: The mean costs for second-look percutaneous nephroscopy were almost twice as high as the mean costs for second-look flexible ureteroscopy: $7609.72 versus $3752.93, p<0.05. We did not include in the analysis the costs of the initial PNL procedure for either group.

Conclusions: Our findings suggest that the costs of second-look PNL are significantly greater than the costs of second-look ureteroscopy for patients with a residual stone burden following PNL. It is important to note that costs are only one metric that are used to evaluate surgical efficacy for stone-removal procedures. However, an emerging surgical paradigm for patients with large or complex stone burdens may be a tubeless PNL procedure followed by flexible ureteroscopy for the management of a residual stone burden.

P63

Percutaneous Nephrolithotomy (PCNL) in the Septuagenarian, Octogenarian and Nonagenarian is Safe: Outcomes and Complications
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Introduction: PCNL is the standard of care for large volume upper tract stone disease. Patients presenting in their seventh to ninth decade of life are often considered to be at increased risk of peri-operative complications and poorer outcomes. We aim to compare outcomes of PCNL in septuagenarian, octogenarian and nonagenarians, compared to a younger population matched for stone burden.

Materials & Methods: Records of 231 PCNLs performed from 2006 to 2010 were reviewed. Demographics, age, ASA score, and length of stay (LOS) were assessed. Stone size, clearance, and complications were investigated. Patients over the age of 70y were compared to a stone size matched, age adjusted control group of 20 patients 30-60 years of age. Descriptive statistics and student's T-tests were used.

Results: A total of 32 PCNLs in 28 patients over 70y (n=15 aged 71-79, 9 aged 80-89, 4 aged 90-94) were performed. This cohort's mean age was 77y, ASA of 2.63, and had 2.86 comorbidities each. The control group had a mean age of 47y, significantly lower ASA scores of 1.78, and 1.10 comorbidities (p=0.001 and p=0.0001 respectively). Stone free rate was 63.3% in those >70y and 74% in the control group, without differences in surgical time or LOS. There was no statistically significant difference in frequency of complications and mean Clavien class between the two groups.

Conclusions: PCNL is safe and effective in patients over 70. Age, alone, should not be an excluding criterion. Concerns regarding anesthesia risk, prone positioning, bleeding and hospitalization should be considered individually.

P64

Baseline Body Mass Index (BMI) has no Effect upon Normalization of Testosterone Concentrations with Testosterone 2% Gel
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Introduction: This *post hoc* analysis examined the effect of body mass index (BMI) on testosterone (T) replacement therapy (TRT) in hypogonadal males (HM).

Materials & Methods: In a non-comparative trial, 129 HM with serum total T (STT) <250ng/dL or 2 consecutive STT concentrations <300ng/dL received once-daily T2% gel (Fortesta™, a new formulation applied to the front and inner thigh) for 90d. Starting dose was 40mg/day, adjusted on days 14, 35 and 60 if necessary according to predefined criteria in 10mg increments. BMI measurements were collected at baseline. Endpoints were average STT concentration over 24h (C_{avg} 0-24h) and maximum STT concentration (C_{max}) at 90d. Study objective was to raise STT C_{avg} 0-24h to a normal range of ≥300 and ≤1140ng/dL in ≥75% patients.

Results: At baseline, 8 patients (6%) had normal weight (BMI ≥18.5-≤24.9kg/m^2); 43 patients (33%) were overweight (BMI ≥25-≤29.9kg/m^2); and 78 patients (61%) were obese (BMI ≥30kg/m^2). Mean STT levels at baseline were 199.8 92.1ng/dL, 190.3 69.4ng/dL and 198.5 63.1ng/dL, respectively. STT concentrations at 35d and 90d were comparable across treatment groups (Table). T2% gel was generally well tolerated and most common adverse incidents were application-site reactions (16%) considered mild (19/24; 79%) to moderate (5/24; 21%).

Conclusions: Regardless of baseline BMI, patients responded similarly to T2% gel to maintain STT levels.

Table: Results at 35d and 90d

	Normal (n=8)	Overweight (n=43)	Obese (n=78)
STT C avg 0-24h, ng/dL (mean±SD)			
35d	409.1±152.7	414.9±133.3	404.6±166.4
90d	457.8±154.0	433.4±171.5	439.5±160.2
STT Cmax, ng/dL (mean±SD)			
35d	839.1±351.8	897.5±438.3	781.6±367.9
90d	947.4±269.6	821.8±341.1	818.6±373.6
STT normal range (≥300-≤1140ng/dL) (% patients)			
35d	75.0%	87.8%	70.1%
90d	75.0%	76.7%	78.2%
Average daily T2% gel dose, mg (mean±SD)	45.4±5.4	42.7±7.3	46.3±7.4

P65

Penile Prosthesis Placement in Patients with Corporal Fibrosis Secondary to Infection, Peyronie's Disease, or Priapism: Techniques, Outcomes, and Complications
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Introduction: Corporal fibrosis can make the insertion of a penile prosthesis very challenging. Various methods have been described regarding dilation of the fibrotic corpora. We describe our experience using cavernotomes, sharp corporal excision, or both techniques in conjunction. Our study investigates outcomes and complications of penile prosthesis placement in patients with corporal fibrosis.

Materials & Methods: This is a retrospective study of 20 patients with erectile dysfunction significant corporal fibrosis. Over an 8-year period, these patients underwent insertion of penile prosthesis. Most patients required use of cavernotomes and/or sharp corporal excision for corporal dilation. Charts were reviewed for cause of fibrosis, use of advanced measures of dilation, and outcomes after surgery.

Results: Corporal fibrosis was due to previously infected prosthesis in 8 patients, priapism in 9 patients, extrusion of prior prosthesis in 2 patients, and Peyronie's disease in one patient. During placement of penile prosthesis, cavernotomes were used in 8 patients, sharp corporal excision in 3 patients, and combination of sharp corporal excision and cavernotomes in 2 patients. Penile prosthesis was successfully placed in all 20 patients. Overall, 16 patients (80%) have had no complications to date. Complications included infection in 2 patients, urethral erosion in one patient, and malpositioned prosthesis in another patient. Interestingly, there were no complications in patients who had fibrosis secondary to priapism.

Conclusions: Penile prostheses can safely be placed in patients with significant corporal fibrosis, especially in patients with history of priapism. If dilation is challenging, cavernotomes and sharp corporal excision can be used safely.

P66

Outcomes of KTPLAP and TURP in Patients with Impaired Detrusor Contractility

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Introduction: We report outcomes in men with impaired detrusor contractility (IDC) treated with KTP laser ablation (KTPLAP) or transurethral resection of the prostate (TURP).

Materials & Methods: This was a retrospective study of consecutive patients with IDC who underwent KTPLAP or TURP. IDC was defined as bladder contractility index <100 or detrusor contraction of insufficient duration to empty bladder. Pre-operative uroflow(Qmax), post-void residual volume(PVR), videourodynamics, and cystoscopy were obtained. Post-operative Qmax, PVR, clean intermittent catheterization (CIC) need, and Patient Global Impression of Improvement(PGII) score were obtained.

Results: 56 men aged 29-91 years (mean=67) were included. Mean preop BCI, BOOI, and PVR for entire cohort was 51 (SD=30), 31 (SD=30), and 670 (SD=559) respectively. Mean preop IPSS and bladder capacity for the entire cohort was 14 (SD=8) and 904mL (SD=605mL) respectively. 5 (96%) subjects were available at 1 year follow-up and 53/56(95%) subjects completed PGII. 41 (73%) had successful outcomes (PGII score=1 in 20, 2 in 21). 6(11%) had little to no improvement (PGII score=3 in 2, 4 in 4), 6(11%) were worse (PGII score=5 in 1, 6 in 3, 7 in 2) and 11 still required CIC. Pre- and postop data is shown below.

Conclusions: 80% of patients with IDC who underwent KTPLAP/TURP had excellent outcomes based upon PGII and objective improvement in PVR, Qmax, and need for CIC. TURP/KTPLAP is viable for properly selected patients with IDC.

Table 1: Pre and Post-op Data

	Mean Qmax, mL/sec (SD)	Median Qmax, mL/sec (range)	Mean PVR mL (SD)	Median PVR mL (range)	# on CIC
Preop (n=56)	5 (5)	4 (0-23)	670 (559)	547 (0-2500)	27
Preop (n=56)	17 (10)	15 (0-44)	144 (249)	51 (0-1200)	11

P67

Nocturia Reduction after Cooled ThermoTherapy for Symptomatic Benign Prostatic Hyperplasia

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Introduction: Nocturia is a common complaint in benign prostatic hyperplasia (BPH) patients suggesting clinically significant disease. Cooled ThermoTherapy™ (CTT) is a minimally invasive BPH treatment. We explored how much nocturia improved after CTT and whether or not more than BPH could be contributing.

Methods: Using Urologix maintained data of 796 men from numerous multi-center studies we examined nocturia via American Urological Association Symptom Scores (AUASS), BPH Impact Index (BII), quality of life (QOL), and peak flow (Qmax) at baseline, 6 months, 1, 2, and 4 years post-CTT. Patients were divided into 3 groups by baseline nocturia score: 1) 0-1; 2) 2; 3) >2. One-way analysis of variance, Tukey's multiple comparison test, chi square, Pearson's correlation, and repeated measures regression analyses were performed.

Results: Groups 1 (N=119), 2 (N=228) and 3 (N=449) were similar in baseline prostate volume, body mass index, prostate specific antigen level, and diabetes and cardiac disease prevalence. Group 3 was older than the other groups and saw the greatest nocturia improvement post-CTT. BII, AUASS, QOL, Qmax and nocturia improvement was seen across groups post-CTT and sustained through 4 years. Nocturia improvement positively correlated to QOL, BII and AUASS across groups. Each point reduction in nocturia improved QOL by 0.5 and BII by 1.0. However, other unidentified factors also affected nocturia.

Conclusions: CTT leads to sustained improvements in nocturia, BII, AUASS, QOL and Qmax. QOL, BII and AUASS positively and predictably correlate with nocturia. No co-morbid predictors which correlate with the degree or lack of improvement were identified.

P68

Efficacy and Safety Follow-Up Results 3 - 7 1/2 Years after Single Treatment with Transrectal NX-1207 in Multi-Center Prospective Blinded Randomized Controlled Studies of Men with Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia

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Introduction: NX-1207 is an investigational prostate selective therapeutic protein drug for BPH which causes controlled atrophy of prostate tissue. NX-1207 2.5 mg is injected transrectally bilaterally into the transition zone. In 4 U.S. Phase 1-2 and Phase 2 studies NX-1207 efficacy measures reached statistical significance at 90 days. Subjects from these studies were assessed in blinded follow-up studies to determine long-term efficacy.

Methods: All available unselected subjects and controls were included. AUASI scores were measured at intervals of 7 years (Phase 1-2) and 3-5 years (Phase 2).

Results Obtained: Overall in separate follow up studies at 3 to 7 ½ years after a single dosage of NX-1207, 37 to 58% of subjects required no surgical treatments or medication for their BPH. After 7 ½ years, 58% of available Phase 1-2 subjects had no drug or surgical treatment for their BPH and had a mean improvement of 11.7 points in their AUASI scores. All Phase 2 follow-up study efficacy results reached statistical significance. There were no sexual side effects or significant adverse safety events attributable to study drug.

Conclusions: NX-1207 treatment offers an office based transrectal ultrasound guided injection procedure for the treatment of LUTS due to BPH. Follow-up results after a single treatment indicate significant symptomatic improvement with an acceptable safety profile. This research was supported by Nymox Corp.

P69

Rapid Ambulatory Pathway Laser Prostatectomy is Safe- Results within the Global Period

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Introduction: Though laser prostatectomy is becoming more commonplace, many patients are admitted postoperatively. We investigated the feasibility and safety of a rapid ambulatory discharge pathway following holmium laser ablation of the prostate (HoLAP) for the treatment of benign prostatic hyperplasia (BPH).

Materials & Methods: Between January 2007 and December 2009, 65 patients underwent HoLAP scheduled as a day surgical case by one surgeon. Patients were discharged from day surgery with a straight drainage catheter in place. Voiding trial occurred on postoperative day 3. Preoperative, intraoperative, and postoperative parameters within the 90 day global period were reviewed. Statistical analysis employed the Student's t-test with a two-tailed significance level of 0.05.

Results: The mean patient age was 64. Average ASA score was 2.2. Mean operative time was 44 minutes. Mean postoperative time until discharge was 2 hours 29 minutes. There were no readmissions after discharge. Within the 90-day global period, 13 patients described LUTS, 5 patients had post-operative urinary retention, and one patient had a UTI. Average AUA Symptom Score decreased from 21.3 to 7.6 postoperatively ($p<0.0001$). Average quality of life score decreased from 4.04 to 1.38 ($p<0.0001$) postoperatively. Average post-void residual decreased from 190.2 to 46.4 ml postoperatively ($p<0.0005$).

Conclusions: In appropriately selected patients, a rapid ambulatory pathway HoLAP can be safely performed with minimal mobidity in the global period.

P70

Northern New England Renal Trauma: How it Differs from the Big City

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Introduction: Renal injury occurs in up to 10% of blunt force injuries. Rural populations have a higher rate of trauma and are 50% more likely to suffer a trauma related death than their urban counterparts. We reviewed the mechanism of injury, management and outcomes of patient admitted with renal injury at a single rural level 1 trauma center. We hypothesize that the mechanisms of injury and the outcomes are different than in published urban data.

Materials & Methods: After institutional review board approval we retrospectively reviewed the charts of all adult patients (>19 years of age) admitted from 2006-2010 with renal trauma. Variables evaluated included age, gender, intoxication status, grade, mechanism of injury, and associated abdominal injuries. Management and outcomes were analyzed.

Results: Of the 104 patients admitted 80 (77%) were male and 24 (23%) female. Mean age was 44 years. Blunt force trauma accounted for the majority of injuries (98%). The most common mechanism of injury was motor vehicle collision (MVC) 36/104(35%), followed by recreation related activities 35/104 (34%), falls (16%), and motor cycle crash 17/104(16%). Winter related activities accounted for 19/24 (79%) of recreational injuries. Five patients (6%) required embolization and one required emergent nephrectomy. Mortality was 8/104(8%). MVC resulted in significantly more multiple intra-abdominal injuries (64% vs 29%, p=0.0173).

Conclusions: Unlike urban setting, our data from a rural center shows that recreational renal injuries were as common as MVCs. MVCs were found to result in significantly more multi organ injuries. Management of renal trauma remains mostly nonoperative.

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Prospective Robotically-Assisted Laparoscopic Pyeloplasty Analysis in Pediatrics

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Introduction: Dismembered pyeloplasty was historically done with an open incision, but less invasive techniques have taken a more prominent role. Many studies review outcomes in a retrospective fashion. We performed a prospective analysis of pediatric robotically-assisted laparoscopic pyeloplasties (RALP) to further establish the safety and effectiveness of this minimally invasive surgery.

Materials & Methods: After obtaining IRB approval, all patients scheduled for RALP after March 2009 were offered enrollment in our database.

Results: Twenty four of the twenty six enrolled patients have undergone surgery. Mean age is 5.4 years; mean weight is 27.3 kg. Two patients were redo repairs. Mean anesthesia time was 296 minutes, and mean surgical time from first incision to final suture was 188 minutes. Mean hospital stay was 1.4 days. Mean follow up was 8.5 months. Mean narcotic use per patient was 0.4 mg/kg of morphine intravenous equivalent. There were four postoperative complications (16%): two major and two minor. One patient had omental herniation during drain removal, one returned to the emergency room for bladder spasms, and two had repeat surgeries. Postoperative imaging revealed worsened hydronephrosis in two patients (8%). One patient underwent a re-do RALP and the other underwent endoscopic incision of scar tissue.

Conclusions: On this prospective review, we found RALP continues to be a safe and comparable alternative to open UPJ obstruction repair. We will continue with long-term follow up and active recruitment of patients. We hope this helps solidify benchmarks for robotic surgical results in pediatric UPJ obstructions.

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Effects of Spinal Cord Detethering on Children with Currarino Syndrome

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Background: Currarino Syndrome (CS) is an inherited disorder involving a triad: anorectal anomalies, sacro-coccygeal defect and presacral mass. Only a few case reports and series discussing this rare condition exist; none report its effects on the genitourinary tract. We present the urologic issues in CS patients and determine how spinal cord untethering affects urinary tract function.

Methods: We retrospectively reviewed 13 patients diagnosed with CS. We evaluated patients' urinary signs/symptoms and urodynamic (UDS) findings before and after cord untethering.

Results: All 13 with CS having a sacral defect and presacral mass were diagnosed between birth and 6 years (Table1). 92% had a tethered spinal cord that was surgically detethered between 8 months to 6 years (average 3 years). Four had recurrent urinary tract infections, 2 of whom had bilateral vesicoureteral reflux and both resolved spontaneously. Two had mild unilateral hydronephrosis without reflux. Three others with radiologic imaging were normal. Eleven underwent comprehensive UDS. Three of four with pre- and post-surgery UDS showed improvement (Table1). Six had only post-surgery UDS; 5 being abnormal with small capacity, poor compliance, detrusor overactivity (DO), sphincter dyssynergy or high voiding pressures. One infant had no spinal surgery and normal UDS.

Conclusions: CS is a rare disorder with few published reports regarding long-term implications. Although UDS parameters improved after surgery, all toilet-trained patients continued to have ongoing voiding issues.

Table 1.

Characteristics	N=13	Frequency	3
Female to male ratio	9:4	Urgency	5
Familial to sporadic ratio	8:5	Urinary incontinence	5
Presacral mass	13	Noctural bedwetting	3
Myelomeningocele	5	Recurrent urinary tract infection	4
Teratoma	5	Non-toilet trained patients	3
Lipoma	3	UDS evaluation	11
Full triad (including anorectal abnormalities)	7	Pre- > post-surgery UDS	4
		*Normal > normal	-
Anal stenosis	4	*Dyssynergy > synergy more than dyssynergy	-
Imperforate anus	2		
Anal duplication	1	*Small capacity, DO, dyssynergy	-
Tethered spinal cord	12	> Small capacity, multiple DO with dyssynergy; later normal capacity, no DO with synergy	
Surgical history			
Presacral mass resection	12		
Cord detethering	12	*DO > no DO	-
Voiding complaints in toilet trained patients	10	Post-surgery UDS	6
		No surgery UDS	1

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Cost Comparison of Open, Laparoscopic, and Robot-assisted Partial Nephrectomy

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Introduction and Objectives: Laparoscopic and robotic partial nephrectomy (LPN and RPN) are increasingly common minimally invasive alternatives to open partial nephrectomy (OPN) in the management of renal tumors. We compared the costs associated with each procedure.

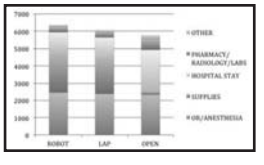
Methods: Hospital variable costs including operating room (OR) time, supplies, anesthesia, inpatient care, radiology, pharmacy, and laboratory charges were captured for the last 25 patients who underwent OPN, LPN, and RPN at our institution prior to September 2010.

Results: Our results are listed in Table 1. We found similar overall costs for OPN, LPN, and RPN ($5,774 vs. $6,074 vs. $6,374, p=0.1166) (Figure 1). OR supplies contributed a greater cost for LPN and RPN than OPN ($2,179 vs. $1,987 vs. $181, p<0.001), while the inpatient stay cost was disproportionately higher for OPN compared to LPN and RPN ($2,418 vs. $1,305 vs. $1,274, p<0.001). Sensitivity analysis demonstrated that RPN and LPN represent less costly alternatives to OPN (if OPN parameters are kept the same) if the average hospital stay for RPN and LPN is <2 days or OR time less than 204 and 196 minutes, respectively.

Conclusions: There were no statistically significant differences among variable costs associated with OPN, LPN, and RPN.

Table 1. Perioperative Outcomes and Costs

	Robot	Laparoscopic	Open	P-value RPN vs. LPN	P-value RPN vs. OPN	P-value LPN vs. OPN	Kruskal- Wallis analysis
Age (mean years)	55.9 ± 11.7	53.3 ± 13.7	61.9 ± 10.1	0.477	0.0554	0.0142	0.0432
Tumor Size (cm)	2.5 ± 1.0	3.3 ± 1.3	3.3 ± 1.4	0.0279	0.0298	0.900	0.0661
RENAL Score	6.08 ± 1.68	7.04 ± 1.70	7.00 ± 1.56	0.05	0.0532	0.932	0.0659
OR Time (min)	231.8 ± 44.2	223.8 ± 43.2	238.3 ± 119.5	0.536	0.804	0.572	0.732
EBL	178 ± 205.7	154 ± 114.5	275.4 ± 170.0	0.613	0.0742	0.0047	0.0079
Length of Hospital Stay (days)	2.48 ± 0.68	2.72 ± 0.67	4.6 ± 1.68	0.353	0.0001	0.0001	0.0001
Overall Cost	6374 ± 1318	6074 ± 758	5774 ± 2420	0.329	0.281	0.557	0.1166
Supply Costs	2178 ± 225	629 ± 125	180 ± 118	0.0001	0.0001	0.0001	0.0001
Hospital Costs	1304 ± 891	3260 ± 469	2418 ± 1501	0.0001	0.0025	0.0101	0.0001



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Multi-Institutional Validation of the Predictive Value of Preoperative Hydronephrosis for Advanced Stage Upper-Tract Urothelial Carcinoma

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Introduction: The presence of hydronephrosis (HN) has been implicated as a predictor of poor outcomes for patients diagnosed with bladder cancer. Smaller reports suggest a similar negative relationship exists for upper-tract urothelial carcinoma (UTUC).

Materials & Methods: 469 pts with localized UTUC from 6 tertiary referral centers who underwent a radical nephroureterectomy (91%) or segmental ureterectomy (9%) without neoadjuvant chemotherapy were integrated into a database. Preoperative HN data variables were available in 408 pts.

Results: 192 pts (47%) had ≥ pT2 disease, 145 (36%) had non-organ confined disease and 298 (73%) had high grade disease on final pathology. Forty-six percent of pts had tumors in the renal pelvis, 27% in the ureter, and 27% in both. Preoperatively, 223 pts (55%) had HN (39% low grade and 61% high grade). HN was associated with ≥ pT2 stage ($p<0.001$) and non-organ confined disease ($p<0.001$). On preoperative multivariate analysis that adjusted for the effects of gender, age, and tumor location, HN was an independent predictor of muscle invasive disease (HR 7.4, $p<0.001$), non-organ confined disease (HR 5.5, $p<0.001$), and high pathologic grade (HR 1.6, $p=0.03$). Even after controlling for ureteroscopic biopsy grade and urinary cytology (n=172), HN remained an independent predictor of muscle invasive stage (HR 12.0, $p<0.001$) and non-organ confined disease (HR 5.1, $p<0.001$).

Conclusions: The presence of preoperative HN is a significant predictor for advanced stage UTUC. This imaging modality may improve preoperative risk stratification to guide use of endoscopic versus extirpative surgery and/or the need for neoadjuvant chemotherapy regimens.

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Pathologic Down-staging with Gemcitabine and Cisplatin Neoadjuvant Chemotherapy for Muscle-Invasive Urothelial Carcinoma of the Bladder

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Introduction: Neoadjuvant chemotherapy (NC) with MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin) improves survival in muscle invasive urothelial cancer (MI-UC) with patients who achieve pathologic complete response (PCR) following radical cystectomy (RC). Gemcitabine/Cisplatin (GC) NC is increasingly employed due to lower toxicity, however, its effectiveness as neoadjuvant therapy is controversial. We describe pathologic and clinical outcomes following NC and RC.

Methods: We retrospectively evaluated patients with MI-UC who received NC between 2003 and 2011 (n=37). Those who were treated with neoadjuvant radiation therapy (n= 15) were excluded. We compared initial clinical stage at surgery to final pathological stage and assessed overall-median progression free-survival.

Results: Twenty-two patients who received NC were included. Seventeen patients (77.3%) were treated with GC, 3 (13.6%) with MVAC, and 2 (9.1%) with other regimens. The mean time from start of NC to RC was 108 days (SD 94). 10 (59%) patients treated with GC achieved PCR (pT0) from clinical stage T2 (n=5), cT3 (n=2) and cT4 (n=3), and 3 (18%) were downstaged to pTIS from cT2. Two patients treated with MVAC were downstaged to pT1. Mean metastasis-free survival was 14 months (SD 0.8). At a mean post-operative follow-up of 24 months (range 2-71, SD 22), 15 (68%) of patients were disease free. 14 of these patients had received GC.

Conclusions: Neoadjuvant GC for MI-UC was associated with a 59% PCR rate at RC and was well tolerated. These data compare favorably with published data on GC and MVAC as NC, and warrant further study.

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Safety and Efficacy of Robot-Assisted Partial Nephrectomy: A Large Single Institution Experience

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Introduction: Although it is an acceptable treatment option for small renal masses, the role of robot-assisted partial nephrectomy (RPN) in complex tumors is not well understood.

Materials & Methods: We provide a large institutional study of demographics, tumor anatomic complexity, perioperative outcomes, pathology, complications, and follow-up data for RPN cases from 2007-2010.

Results: 174 patients (mean age 56.7±12.7yrs, 63.7% male, mean tumor size 2.95±1.63cm) with mean follow-up 17.5±9.8mos underwent RPN during the study period. Lesion complexity stratified by Nephrometry score was low, moderate, and high in 83 (47.7%), 81 (46.6%), and 10 (5.7%) patients. 95 (54.6%) patients had predominantly endophytic or entirely intraparenchymal tumors while 100 (57.5%) had tumors <7mm of the renal sinus or collecting system. Mean warm ischemia time was 27.8±11.5min, and 12.0% (n=21 pts) were performed without hilar clamping. Mean operative time was 203.2±69.0min, and mean EBL was 118.6±129.6mL. Transfusions were required in 9 (5.2%) patients. Final pathology was pT1a (85.3%), pT1b (9.6%), pT2 (0.6%), pT3 (4.5%). Histology was malignant in 78.7% of tumors: 68.6% clear cell, 24.8% papillary, 5.9% chromophobe, and 0.7% were undefined. There were 4 (2.3%) positive margins on final pathology. Major (Clavien III-IV) and minor (Clavien I-II) complication rates were 6.8% and 22.7%. Mean change in postoperative GFR was 4.21 mL/min /1.73m2. Local recurrence was noted in 2 patients (1.1%) and progression in 1 patient (0.6%).

Conclusions: Our RPN experience demonstrates minimal morbidity and acceptable oncologic results with excellent functional preservation in intermediate and high complexity renal tumors.

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Positive Surgical Margins after Partial Nephrectomy for pT1 Localized Renal Cell Carcinoma: Local Recurrence and RCC-Specific Survival

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Introduction: In patients undergoing partial nephrectomy for localized Renal Cell Carcinoma (RCC), positive surgical margin (PSM) is thought to increase risk for local recurrence. Our objective is to describe the natural history of PSM following partial nephrectomy for RCC.

Methods: We identified 1044 patients who underwent partial nephrectomy at a single institution from 1988 to 2010. 45 patients had PSM (4.3%) confirmed by single pathologist review. Patients with familial kidney cancer, benign pathology, ≥pT2 disease, or follow up less than 6 months were excluded (n = 22). Clinical, pathological, and follow up data were analyzed for the remaining cohort (n = 23). RCC-specific survival and local recurrence were calculated.

Results: Mean age at diagnosis was 63 ± 11 years. 82% of cases (19/23) were open while 4 were laparoscopic. 6 patients (26%) had a solitary kidney. 52% (12/23) of patients had vascular clamping. Mean tumor size was 3.2 ± 1.3 cm, and 17/23 (74%) were pT1a. Surveillance imaging was performed every 6 months for two years, and yearly thereafter. Median follow up was 28 months. No patient had elective invasive management of their PSM. Only 1/23 (4.3%) patient developed local recurrence 1.8 years after surgery. This was treated with systemic therapy as the patient had synchronous distant metastases. Among all patients with PSM, 3-year RCC-specific survival was 90%.

Discussion: Local recurrence was rare among patients with PSM after partial nephrectomy for pT1 RCC at 28 months follow up. Post-operative surveillance is reasonable in patients with PSM after partial nephrectomy.

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Ureteral Stent Placement at the Time of Urinary Diversion Decreases Post-Operative Morbidity

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Introduction: The objective of this study is to determine the impact of stenting the ureteroenteric anastomosis on post-operative stricture rate and gastrointestinal recovery in continent and non-continent urinary diversion after radical cystectomy.

Materials & Methods: We retrospectively reviewed the clinical and pathologic data on 192 consecutive patients who underwent a radical cystectomy and bilateral pelvic lymphadenctomy from 2003-2007. Patients received either continent (orthotopic ileal neobladder, catheterizable reservoir) or non-continent (ileal conduit) urinary diversion with or without stent placement through the ureteroenteric anastomosis. Stricture rate, gastrointestinal recovery (ileus), length of hospital stay, and stricture were analyzed. Study end points were compared between four groups - stented and non-stented continent and stented and non-stented non-continent diversion.

Results: Overall, 36% patients were stented and 64% were non-stented at time of urinary diversion. Mean follow up was 25 months. The total ureteral stricture rate was 9.9%. There was no statistically significant difference in stricture rate (p=0.11) or length of hospital stay (p=0.081) in stented patients compared to non-stented patients. There was a significantly (p =0.014) greater ileus rate in patients who were not stented in both continent and non-continent urinary diversion. Endoscopic management of strictures was attempted in 42.1% of cases and was successful in 12.5% of cases.

Conclusions: Stenting of the ureteroenteric anastomosis in both continent and non-continent urinary diversion has no effect on post-operative stricture rate but is associated with lower rates of post-operative ileus.

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Fetal Closure of Myelomeningocele Does Not Improve Lower Urinary Tract Function

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Introduction: Recent data comparing prenatal to postnatal closure of myelomeningocele showed decreased need for ventriculoperitoneal shunting (VPS) and improved motor outcomes in patients closed prenatally. Ten patients closed in-utero are followed in our Spina Bifida program. We hypothesized that fetal repair of myelomeningocele would improve lower urinary tract (LUT) function.

Methods: Ten prenatally closed patients were matched (age, gender and spinal defect level) with 10 patients closed postnatally. Urologic outcomes were retrospectively reviewed including urodynamic (UDS) data, need for intermittent catheterization, and use of anti-cholinergics and prophylactic antibiotics.

Results: Mean patient ages at UDS for the prenatally versus postnatally closed groups were 6.3 years (range 7 months-12 years) and 6.6 years (range 5 months-13 years) respectively (p=0.87) with mean follow-up being 7.9 years (range 9 days-12 years) and 7.8 years (range 3 months-11 years) respectively. Each group had 5 lumbar and 5 sacral level defects. Urodynamic findings including bladder capacity, detrusor overactivity, detrusor pressure at capacity, and presence of sphincter dyssynergia were not significantly different between the groups. 7 patients in the prenatal group require intermittent catheterization compared with 9 patients in the postnatal group (p=0.58). There was no difference in rates of anti-cholinergic or antibiotic use between the two groups. Interestingly, there was no difference of VPS between the groups in our study.

Conclusions: While fetal closure of myelomeningocele has been shown to decrease rates of VPS and improve motor function, it is not associated with any significant improvement in LUT function when compared to matched patients closed postnatally.

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Incidence of Repeat Dextranomer/Hyaluronic Acid Copolymer Injection among Pediatric Health Information System Hospitals

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Introduction: Success rates after single dextranomer/hyaluronic acid (DxHA) injection for vesicoureteral reflux (VUR) are variable. Those failing initial injection are candidates for a 2nd injection. The purpose of this study is to analyze trends in the utilization of repeat DxHA injection among patients treated at hospitals participating in the Pediatric Health Information System Database (PHIS).

Materials & Methods: Billing records for patients who underwent DxHA injection for primary VUR between 1/1/2007 and 9/30/2009 were extracted from the PHIS database. Patient history was reviewed and patients with previous DxHA or ureteral reimplantation were excluded. Patient records with 1 to 3 years follow-up were analyzed to identify additional DxHA injection or reimplantation procedures.

Results: 24/43 hospitals submitted CPT Code level data during the study period. 2,817 patients who received initial injection were identified. 85% of patients were female. Median age at first injection was 5 years (+/- 3.7 yrs). 89% of patients received unilateral injection, 11% bilateral injection. 9% (254) had an additional procedure (9% of unilateral patients, 11% of bilateral patients). 190 (7%) of unilateral patients received a 2nd injection, 9 (0.4%) received a 3rd. Among bilateral patients, 8% received a 2nd unilateral injection, 1% received 2nd bilateral injections. 22 (0.8%) patients had subsequent reimplantation (20 unilateral, 2 bilateral).

Conclusions: Within the limits of the database, these results suggest that, in patients who have undergone DxHA injection, the rate of repeat DxHA injection is low and open reimplantation is much lower, indicating a trend for continued endoscopic management in this population with VUR.

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Renal Trauma in Children: Mechanism of Injury and Outcomes at a Rural Northern New England Level I Trauma

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Objective: Blunt abdominal trauma results in renal injury in 10% of pediatric cases. The published mechanism of injury is motor vehicle accidents(MVA) while recreational injuries are less common. No data is currently available on the mechanism of injury in a rural level I pediatric trauma center. We hypothesize that it is different.

Methods: After approval from the institutional review board, we retrospectively reviewed the medical records of 40 consecutive children with renal trauma between 2006 and 2010. Patients were stratified into two groups (under and over 16 years of age). Parameters reviewed included mechanism of injury, severity of injury, associated injuries, management and clinical outcomes.

Results: Of the 40 patients, 26/40(65%) had recreational related injury. Snow sports was the most prevalent (14/26, 53.8%). MVAs accounted for 11/40 (27.5%) of injuries. Two injuries presented with co-existing urinary tract anomalies. Of the 18 children under 16 years of age the mechanism of injury was recreational in 14/18 (77.8%). Of these, 6 (42.9%) were related to winter sports. Only 2/18(11.1%) were related to MVA. Majority of injuries were grade III, two had vascular injuries with poor or no perfusion into the kidney. All patients were managed conservatively with two patients requiring embolization for bleeding.

Conclusions: Recreational sport injuries are the major cause of blunt renal trauma at our rural Level I pediatric trauma center. Most of these injuries were managed conservatively. Due to delay in transfer to our trauma center grade V trauma with renal devascularization resulted in loss of renal function.

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Comparing Minimally Invasive Surgery for Vesicoureteral Reflux: Dextranomer Hyaluronic Acid Injection versus Robotically-assisted Laparoscopic Ureteral Reimplantation

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Introduction: Two minimally invasive surgical (MIS) options for treatment of vesicoureteral reflux (VUR) are endoscopic Dextranomer Hyaluronic Acid injection (DI) and robotically-assisted laparoscopic ureteral reimplantation (RALUR). We compared outcomes of these MIS operations at our institution.

Materials & Methods: We performed a retrospective case review of our first 17 extravesical RALUR patients and 17 age matched patients who underwent DI. Voiding cystourethrogram was performed on all patients except one RALUR lost to follow up.

Results: Median age was 6 years (RALUR) and 5 years 11 months (DI). A total of 50 ureters were treated. Mean follow-up was twelve and ten months in the RALUR and DI group, respectively. Preoperatively, there was Grade I-II in 30% of RALUR and 41% of DI groups, Grade III in 57% of RALUR and 59% of DI groups, and Grade IV in 13% of RALUR and none of DI groups. RALUR had a significantly better outcome than DI (p=0.008). RALUR had complete resolution of VUR in 20 ureters (91%) and downgrading in 2 (9%). DI had complete resolution in 16 ureters (59%), downgrading in 3 (11%), and 8 (30%) had no improvement or worsening of VUR. Mean hospital stay for the RALUR group was 1.26 days; all DI patients were discharged the same day. One RALUR and three DI patients developed contralateral VUR.

Conclusions: Although small in volume and retrospective, this series revealed better results with RALUR compared to DI. We are currently enrolling patients prospectively to compare outcomes of DI, RALUR, and open reimplantation.

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Repair of Complex Hypospadias Using Buccal Mucosa Grafts

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Introduction: We aim to describe indications and outcomes for repair of complex hypospadias and chordee in the pediatric population using buccal mucosa grafts.

Methods: We retrospectively identified consecutive patients undergoing complex hypospadias repair using buccal mucosa grafts between 1995 and 2010. Demographic and surgical outcomes data was collected on all patients.

Results: SEE TABLE 1
A total of 21 patients underwent hypospadias repair with buccal graft. Approximately two thirds had penoscrotal/perineal disease, with the remainder mid-shaft or distal. All patients underwent initial repair in early childhood, and 71% were revised, just over half multiple times, prior to undergoing salvage repair using buccal grafts. In 16 patients, a staged approach was utilized with a mean interval of 10.8 months between surgeries, while 5 were completed in a single operation. All but one of the single stage patients required an additional major urethroplasty. Only 4 of the staged cohort necessitated major revision, one of the first stage and 3 of the second. The most common complication was recurrent stricture (8 patients), followed by urethrocutaneous fistula (3 patients), and diverticulum (one patient).

Conclusions: Hypospadias repair with buccal graft in a staged fashion is a good option for the most complex cases. Many of these patients will require revision, however, to achieve ultimate success. Attempts at single stage tubularized grafts had poor results in this small series.

Table 1.
Patient Characteristics

	n=21
Mean Age, yrs (range)	8.9 (1.33-17)
Indication for Surgery	
Repair Breakdown	8 (38%)
Fistula	4 (19%)
Diverticulum	4 (19%)
Stricture/Meatal Stenosis	13 (62%)
Chordee	4 (19%)
Multiple	10 (48%)
Mean Graft Length, cm	4.3 cm (1.5-11cm)
Mean Follow-up, mos	19

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Evaluation of Urethral Stricture Disease in a Pediatric Population Using Sonographic Voiding Urethography

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Introduction: Retrograde urethrography (RUG) is the gold standard for the diagnosis of male urethral stricture disease. This method requires instrumentation of the urethra, radiation exposure and in the pediatric population, general anesthesia. Current ultrasound techniques are able to mimic RUG with a faster and risk-free approach.

Materials & Methods: Prior to voiding, a conventional 7.5 MHz transducer is placed at the perineum. The transducer is aligned along the line of the proximal corpus spongiosum. While angled at the prostate, the patient is instructed to void. The now opened lumen, can be followed distally by adjustments in the angle of the probe. This method allows visualization of a significant length of the urethra, though very distal strictures require an experienced hand.

Results: Our initial series involves four boys with suspected urethral stricture. Chief complaints at presentation included hematuria, dysuria, splayed stream, and retention. All underwent sonographic urethrography (SUG), three underwent RUG, all had direct visualization internal urethrotomy, and two had dilation. Two boys required eventual urethroplasty. Sonographic urethrography was able to characterize strictures in three of the four boys. The ultrasound technique elicited no reports of discomfort.

Conclusions: When presented with a pediatric patient with the suspicion of stricture, sonographic ultrasonography provides a quick and risk-free technique for diagnosis. This technique is able to characterize the presence and extent of urethral stricture.

ELIGARD®
leuprolide acetate
Working with you for your patients

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Luteinizing Hormone-Releasing Hormone Analog

INDICATIONS AND CLINICAL USE

ELIGARD® (leuprolide acetate) is indicated for the palliative treatment of advanced prostate cancer (stage D2).
ELIGARD® should be administered by a health care professional.

Special Populations

Geriatrics (>70 years of age)

The majority (>70%) of the patients studied in the clinical trials for ELIGARD® were 70 years and older (see the CLINICAL TRIALS section of the Product Monograph).

Pediatrics (<12 years of age)

ELIGARD® is not indicated for use in children as safety and effectiveness have not been established in this group of patients.

Pregnant Women

ELIGARD® is contraindicated in women who are, or may become, pregnant while receiving the drug and in women who are nursing, as safety and effectiveness have not been established in this group of patients.

Nursing Women

ELIGARD® is not indicated for use in nursing women as safety and effectiveness have not been established in this group of patients.

Race

In clinical pharmacokinetic studies, mean serum leuprolide concentration profiles were similar among subjects after administration of ELIGARD® 7.5 mg (26 white, 2 black), ELIGARD® 22.5 mg (19 white, 4 black, 2 Hispanic), ELIGARD® 30 mg (18 white, 4 black, 2 Hispanic) and ELIGARD® 45 mg (17 white, 7 black, 3 Hispanic).

CONTRAINDICATIONS

ELIGARD® is contraindicated in patients with hypersensitivity to luteinizing hormone-releasing hormone (LH-RH), LH-RH analogs or any of the components of ELIGARD®. Anaphylactic reactions to synthetic LH-RH or LH-RH analogs have been reported in literature. For a complete listing, see the Dosage Forms, Composition and Packaging section of the Product Monograph.

ELIGARD® is contraindicated in women who are, or may become, pregnant while receiving the drug. There are possibilities that fetal harm and spontaneous abortions may occur. The use of ELIGARD® in nursing mothers is not recommended.

Safety Information

WARNINGS AND PRECAUTIONS

General

ELIGARD®, like other LH-RH analogs, causes a transient increase in serum concentration of testosterone during the first week of treatment. Patients may experience worsening of symptoms or onset of new symptoms, including bone pain, neuropathy, hematuria or ureteral or bladder outlet obstruction. Cases of spinal cord compression, which may contribute to paralysis with or without fatal complications, have been reported with LH-RH analogs. If spinal cord compression or renal impairment due to ureteral obstruction develops, standard treatment of these complications should be instituted.

Patients with metastatic vertebral lesions and/or with urinary tract obstruction should begin leuprolide therapy under close supervision.

Dependence/Tolerance

No drug dependence has been reported with the use of leuprolide.

Endocrine and Metabolism

Changes in bone density: Bone loss can be expected as part of natural aging and can also be anticipated during the hypoandrogenic state caused by long-term use of leuprolide acetate. In patients with significant risk factors for decreased bone mineral content and/or bone mass such as family history of osteoporosis, chronic use of corticosteroids or anticonvulsants or chronic abuse of alcohol or tobacco, leuprolide acetate may pose additional risk. In these patients, risk versus benefit must be weighed carefully before initiation of leuprolide acetate therapy.

Long-term administration of leuprolide will cause suppression of pituitary gonadotropins and gonadal hormone production with clinical symptoms of hypogonadism. These changes have been observed to reverse on discontinuation of therapy. However, whether the clinical symptoms of induced hypogonadism will reverse in all patients has not yet been established.

Renal and Hepatic

All clinical studies and kinetic evaluations have been conducted in patients with adequate hepatic and renal function.

Monitoring and Laboratory Tests

Renal function tests, blood urea nitrogen (BUN) and creatinine may rarely be elevated during the first few days of therapy in prostate cancer patients before returning to normal. In clinical trials with ELIGARD® however, no significant difference was observed from baseline to 7 days following injection in terms of the number of patients who demonstrated an elevation from normal to above normal levels of creatinine and BUN.

Response to ELIGARD® may be monitored by periodically measuring serum concentrations of testosterone and prostate specific antigen. Results of testosterone determinations are dependent on assay methodology. It is advisable to be aware of the type and precision of the assay methodology to make appropriate clinical and therapeutic decisions.

The effects of leuprolide on bone lesions may be monitored by bone scans, while its effects on prostatic lesions may be monitored by ultrasonography, and/or CT scan in addition to digital rectal examination. Intravenous pyelogram, ultrasonography, or CT scan may also be utilized to diagnose or assess the status of obstructive uropathy.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

ELIGARD®, like other LH-RH analogs, caused a transient increase in serum testosterone concentrations during the first 2 weeks of treatment (first week of treatment for 4-month and 6-month treatments). Therefore, potential exacerbations of signs and symptoms of the disease during the first few weeks of treatment are of concern in patients with vertebral metastases and/or urinary obstruction or hematuria. If these conditions are aggravated, it may lead to neurological problems such as weakness and/or paresthesia of the lower limbs or worsening of urinary symptoms (see WARNINGS AND PRECAUTIONS).

In clinical trials of non-orchiectomized prostate cancer patients treated with ELIGARD® 7.5 mg, 22.5 mg, 30 mg and 45 mg, none of the 1,338 injections and subsequent transient increases in testosterone were associated with an exacerbation of disease symptoms. Some adverse effects reported with ELIGARD® are due primarily to its pharmacological action of sex hormone suppression. The safety of ELIGARD® 7.5 mg (1-month) and ELIGARD® 22.5 mg (3-month) was evaluated in orchiectomized and non-orchiectomized patients with advanced prostate cancer in three clinical trials. The safety of ELIGARD® 30 mg (4-month) and ELIGARD® 45 mg (6-month) was evaluated in 50 and 63 patients with advanced prostate cancer, respectively. Local adverse events reported after injection of ELIGARD® 7.5 mg (1-month), ELIGARD® 22.5 mg (3-month), ELIGARD® 30 mg (4-month) and ELIGARD® 45 mg (6-month) were typical of those frequently associated with similar subcutaneously injected products and included transient burning and stinging (27.5% of injections) and pain at the site of injection (3.9% of injections), which were typically mild in intensity, brief in duration (one minute or less) and non-recurrent over time.

The majority of study injections were not associated with reports of injection site adverse events.

Other local adverse events that were rarely reported (<2.6%) following the administration of ELIGARD® 7.5 mg, 22.5 mg, 30 mg and 45 mg included erythema (1.7%), bruising (2.0%), pruritus (0.8%), induration and ulceration (0.3%). These events were mostly reported as mild and generally resolved within a few days post-injection.

Abnormal Hematologic and Clinical Chemistry Findings

Abnormalities of certain parameters were observed, but are difficult to assess in this population. For both ELIGARD® 7.5 mg and ELIGARD® 22.5 mg abnormal values were observed in ≥5% of the study population for the following analyses at any time during the study: increased eosinophils, neutrophils, BUN, total cholesterol, triglycerides, alanine aminotransferase (ALT), alkaline phosphatase (ALP) and creatine kinase (CK). Decreased red blood cell count, hematocrit and hemoglobin were observed.

In addition, for ELIGARD® 7.5 mg, decreased white blood cells, as well as increased sodium, lactate dehydrogenase (LDH) and international normalized ratio (INR) were observed for ≥5% of the study population. For ELIGARD® 22.5 mg, increased creatinine and aspartate aminotransferase (AST) were observed in ≥5% of the study population.

DRUG INTERACTIONS

Overview

No formal drug interaction studies have been conducted with ELIGARD®. No data is available on the interaction with alcohol.

Drug-Drug Interactions

Interactions with drugs have not been established.

Drug-Food Interactions
Interactions with food have not been established.

Drug-Herb Interactions
Interactions with herbal products have not been established.

Drug-Laboratory Interactions
Therapy with leuprolide results in suppression of the pituitary-gonadal system. Results of diagnostic tests of pituitary gonadotropic and gonadal functions conducted during and after leuprolide therapy may be affected.

To report an adverse event, contact the Canada Vigilance Program by toll-free telephone at 1-866-234-2345; by toll-free fax at 1-866-678-6789; online at www.healthcanada.gc.ca/medeffect; by e-mail at CanadaVigilance@hc-sc.gc.ca; or by regular mail at the Canada Vigilance National Office, Marketed Health Products Safety and Effectiveness Information Bureau, Marketed Health Products Directorate, Health Products and Food Branch, Health Canada, Tunney's Pasture, AL 0701C, Ottawa, ON K1A 0K9.

Administration

DOSAGE AND ADMINISTRATION

Dosing Considerations
ELIGARD® may be administered by a health care professional under the supervision of a physician. ELIGARD® 7.5, 22.5, 30 and 45 mg administered subcutaneously is designed to provide continuous sustained release of leuprolide for 1, 3, 4 and 6 months, respectively.

Recommended Dose and Dosage Adjustment
ELIGARD® 7.5 mg (1-month)

The recommended dose of ELIGARD® (1-month) is 7.5 mg administered monthly as a single subcutaneous injection after mixing with a special polymer formulation (see ADMINISTRATION). The total deliverable injection weight per dose is 250 mg including 7.5 mg leuprolide acetate. The total volume administered per dose is approximately 0.25 mL.

ELIGARD® 22.5 mg (3-month)

The recommended dose of ELIGARD® (3-month) is 22.5 mg administered every three months as a single subcutaneous injection after mixing with a special polymer formulation (see ADMINISTRATION). The total deliverable injection weight per dose is 375 mg including 22.5 mg of leuprolide acetate. The total volume administered per dose is approximately 0.37 mL.

ELIGARD® 30 mg (4-month)

The recommended dose of ELIGARD® (4-month) is 30 mg administered every four months as a single subcutaneous injection after mixing with a special polymer formulation (see ADMINISTRATION). The total deliverable injection weight per dose is 500 mg including 30 mg of leuprolide acetate. The total volume administered per dose is approximately 0.50 mL.

ELIGARD® 45 mg (6-month)

The recommended dose of ELIGARD® (6-month) is 45 mg administered every six months as a single subcutaneous injection after mixing with a special polymer formulation (see ADMINISTRATION). The total deliverable injection weight per dose is 375 mg including 45 mg of leuprolide acetate. The total volume administered per dose is approximately 0.375 mL.

Missed Dose
Maintaining testosterone suppression is important in treating the symptoms of hormone-dependent prostate cancer. Missing an appointment by a few days should not disrupt the benefits of treatment, but keeping a consistent schedule of ELIGARD® injections is an important part of treatment.

Administration
As with other drugs administered by subcutaneous injection, the injection site should be varied periodically. The specific injection location chosen should be an area with sufficient soft or loose subcutaneous tissue. In clinical trials, the injection was administered in the upper- or mid-abdominal area. Avoid areas with brawny or fibrous subcutaneous tissue or locations that could be rubbed or compressed (i.e., with a belt or clothing waistband).

As with all parenteral drug products, syringes, as well as reconstituted drug solutions, should be inspected visually for particulate matter, precipitate, discoloration and leakage prior to administration. Solutions showing particulate matter, precipitate, discoloration or leakage should not be used.

Prior to administration, the syringes are removed from the pouches or trays, the syringe tip caps are removed and the syringes are coupled. The product is prepared by passing the formulation from syringe to syringe until a homogenous solution (homogenous suspension for ELIGARD® 45 mg product) is achieved. The syringes are decoupled and the sterile needle is affixed to the male syringe. The Domrex™ Needle Guard[1] device must be affixed on the syringe prior to the injection to help prevent accidental needle stick injuries following the injection. The health care professional should carefully read the leaflet provided with the device before use.

Mixing and Administration Procedure
See the Product Monograph for instructions.

Supplemental Product Information

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

ELIGARD® 7.5 mg (1-month), 22.5 mg (3-month), 30 mg (4-month) and 45 mg (6-month)

The following possibly or probably related systemic adverse events were reported by ≥2% of the patients using ELIGARD® 7.5 mg, 22.5 mg, 30 mg and 45 mg in clinical studies:

Table 1. Incidence (%) of possibly or probably related systemic adverse events reported by ≥2% of patients treated with **ELIGARD® 7.5 mg** [1 injection every month for up to 6 months], **ELIGARD® 22.5 mg** [1 injection every 3 months for up to 6 months], **ELIGARD® 30 mg** [1 injection every 4 months for up to 8 months] and **ELIGARD® 45 mg** [1 injection every 6 months for up to 12 months]

		7.5 mg (*n*=128)	22.5 mg (*n*=117)	30 mg (*n*=90)	45 mg (*n*=111)
Body system	**Adverse event**	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**
Body as a whole	Malaise & Fatigue	21 (16.4)	—	—	—
	Dizziness	4 (3.1)	—	4 (4.4)	—
Cardiovascular	Vasodilation/Hot Flashes/Flushing*	70 (54.7)	66 (56.4)	66 (73.3)	64 (57.7)
General disorders	Fatigue	See Body as a whole	7 (6.0)	12 (13.3)	13 (11.7)
	Weakness	—	—	—	4 (3.6)
Genitourinary	Atrophy of the Testes*	6 (4.7)	—	4 (4.4)	8 (7.2)
	Testicular pain	—	—	2 (2.2)	—
	Gynecomastia*	—	—	2 (2.2)	4 (3.6)
Digestive	Gastroenteritis/Colitis	3 (2.3)	—	—	—
Gastrointestinal	Nausea	—	4 (3.4)	2 (2.2)	—
Musculoskeletal	Arthralgia	—	4 (3.4)	—	—
	Myalgia	—	—	2 (2.2)	5 (4.5)
	Pain in Limb	—	—	—	3 (2.7)
Renal and Urinary	Urinary frequency	—	3 (2.6)	2 (2.2)	—
	Nocturia	—	—	2 (2.2)	—
Skin	Pruritus (not otherwise specified)	—	3 (2.6)	—	—
	Alopecia	—	—	2 (2.2)	—
	Clamminess*	—	—	4 (4.4)	—
	Night sweats*	—	—	3 (3.3)	3 (2.7)
Psychiatric	Decreased libido*	—	—	3 (3.3)	—

* Expected pharmacological consequences of testosterone suppression.

In the ELIGARD® 7.5 mg clinical trial, hot flashes were reported as mild in 80% of patients, moderate in 18.6% of patients and severe in 1.4% of patients. A total of 84 hot flashes/flushing events were reported in the ELIGARD® 22.5 mg clinical trial; of these, 73 of 84 (87%) were described as mild and 11 of 84 (11%) as moderate. No severe events were reported in the ELIGARD® 22.5 mg study. In the patient population studied for ELIGARD® 30 mg, a total of 75 hot flashes were reported in 66 patients. Of these, 57 events (76%) were described as mild; 16 (21%) as moderate; 2 (3%) as severe. A total of 89 hot flash events were reported in the ELIGARD® 45 mg study. Of these, 62 events (70%) were described as mild and 27 events (30%) as moderate.

Less Common Clinical Trial Adverse Drug Reactions (<2%)

The following possibly or probably related systemic adverse events were reported by <2% of the patients using ELIGARD® 7.5 mg (1-month), 22.5 mg (3-month), 30 mg (4-month) and 45 mg (6-month) in clinical studies.

ELIGARD® 7.5 mg (1-month)
General: Sweating, insomnia, syncope
Gastrointestinal: Flatulence, constipation
Hematologic: Decreased red blood cell count, hematocrit and hemoglobin (anemia)
Metabolic: Weight gain
Musculoskeletal: Tremor, backache, joint pain
Nervous: Disturbance of smell and taste, depression, vertigo
Skin: Alopecia
Urogenital: Testicular soreness, impotence, decreased libido, gynecomastia, breast soreness

ELIGARD® 22.5 mg (3-month)
Cardiovascular: Hypertension, hypotension
General: Rigors, weakness, lethargy, pain (not otherwise specified), fever
Urinary: Difficulties with urination, pain on urination, scanty urination, bladder spasm, blood in urine and urinary retention
Reproductive and breast: Breast tenderness, testicular atrophy and pain, enlarged breasts, impotence
Gastrointestinal: Stomach upset, constipation, dry mouth

ELIGARD® 30 mg (4-month)
General: Lethargy
Reproductive: Breast enlargement*, erectile dysfunction*, reduced penis size*
Renal/Urinary: Urinary urgency, incontinence
Musculoskeletal: Muscle atrophy, limb pain
Psychiatric: Insomnia, depression, loss of libido*
* Expected pharmacological consequence of testosterone suppression.

ELIGARD® 45 mg (6-month)
In addition, the following possibly or probably related systemic adverse events were reported by 1% of the patients (2/111) using ELIGARD® 45 mg in the clinical study:
General: Lethargy
Reproductive: Penile disorder*
Renal/Urinary: Nocturia, aggravated nocturia
Psychiatric: Loss of libido*
* Expected pharmacological consequence of testosterone suppression.

Post-Market Adverse Drug Reactions

Post-market studies have not been conducted with ELIGARD®.

The full Product Monograph can be obtained at www.sanofi-aventis.ca or by contacting sanofi-aventis Canada Inc., 2150 St-Elzear Blvd West, Laval, Quebec H7L 4A8, at 1-800-265-7927.

OVERDOSAGE

There is no clinical experience with the effects of an acute overdose. Because the acute animal toxicity of the drug is low, adverse effects are not expected. No difference in adverse reactions was observed in patients who subcutaneously received either 1 or 10 mg/day leuprolide for up to three years or 20 mg/day for up to two years.

For management of suspected drug overdose, contact your regional Poison Control Centre.

STORAGE AND STABILITY

ELIGARD® should be kept refrigerated between 2-8°C (36-46°F).

ELIGARD® can be stored at room temperature (15-30°C) in original packaging for a period of 8 weeks prior to administration.

Once mixed, ELIGARD® should be discarded if not used within 30 minutes.

SPECIAL HANDLING INSTRUCTIONS

Allow the product to reach room temperature before using.

DOSAGE FORMS, COMPOSITION AND PACKAGING

ELIGARD® 7.5 mg (1-month)

(10.2 mg leuprolide acetate per syringe)

ELIGARD® 7.5 mg (1-month) is supplied in two separate, prefilled, sterile syringes whose contents are mixed immediately prior to administration. The two syringes are joined and the single dose product is mixed until it is homogenous. One syringe contains the ATRIGEL® Delivery System[2], and the other contains leuprolide acetate. The ATRIGEL® Delivery System is a polymeric (non–gelatin-containing) delivery system consisting of a biodegradable, 34% poly (DL-lactide-co-glycolide) (PLGH) polymer formulation dissolved in a biocompatible solvent, 66% N-methyl-2-pyrrolidone (NMP). PLGH is a co-polymer with a 50:50 molar ratio of DL-lactide to glycolide containing carboxyl end groups. The second syringe contains 10.2 mg lyophilized leuprolide acetate and is designed to deliver 7.5 mg of leuprolide acetate at the time of subcutaneous injection.

ELIGARD® 7.5 mg (1-month) is available in single use tray packaging. The tray packaging contains the two-syringe mixing systems, a 20-gauge half-inch needle, and two silicone desiccant pouches to control moisture uptake. A needle safety device, the Domrex™ Needle Guard (manufactured by Domrex Pharma Inc.), is also included to help prevent accidental needle stick injuries. An instructions leaflet is provided with the device.

ELIGARD® 22.5 mg (3-month)

(28.2 mg leuprolide acetate per syringe)

ELIGARD® 22.5 mg (3-month) is supplied in two separate, prefilled, sterile syringes whose contents are mixed immediately prior to administration. The two syringes are joined and the single dose product is mixed until it is homogenous. One syringe contains the ATRIGEL® Delivery System, and the other contains leuprolide acetate. The ATRIGEL® Delivery System is a polymeric (non–gelatin-containing) delivery system consisting of a biodegradable, 45% poly (DL-lactide-co-glycolide) (PLG) polymer formulation dissolved in a biocompatible solvent, 55% N-methyl-2-pyrrolidone (NMP). PLG is a co-polymer with a 75:25 molar ratio of DL-lactide to glycolide with hexanediol. The second syringe contains 28.2 mg lyophilized leuprolide acetate and is designed to deliver 22.5 mg of leuprolide acetate at the time of SC injection.

ELIGARD® 22.5 mg (3-month) is available in a single use pouch or tray packaging. The pouch and the tray packaging contain the two-syringe mixing system, a 20-gauge half-inch needle, and a silicone desiccant pouch (two for the tray packaging) to control moisture uptake. A needle safety device, the Domrex™ Needle Guard (manufactured by Domrex Pharma Inc.), is also included to help prevent accidental needle stick injuries. An instructions leaflet is provided with the device.

ELIGARD® 30 mg (4-month)

(35.8 mg leuprolide acetate per syringe)

ELIGARD® 30 mg (4-month) is supplied in two separate, prefilled, sterile syringes whose contents are mixed immediately prior to administration. The two syringes are joined and the single dose product is mixed until it is homogenous. One syringe contains the ATRIGEL® Delivery System, and the other contains leuprolide acetate. The ATRIGEL® Delivery System is a polymeric (non–gelatin-containing) delivery system consisting of a biodegradable, 45% poly (DL-lactide-co-glycolide) (PLG) polymer formulation dissolved in a biocompatible solvent, 55% N-methyl-2-pyrrolidone (NMP). PLG is a co-polymer with a 75:25 molar ratio of DL-lactide to glycolide with hexanediol. The second syringe contains 35.8 mg lyophilized leuprolide acetate and is designed to deliver 30 mg of leuprolide acetate at the time of subcutaneous injection.

ELIGARD® 30 mg (4-month) is available in a single use pouch or tray packaging. The pouch and the tray packaging contain the two-syringe mixing system, a 20-gauge $^5/_8$-inch needle, and a silicone desiccant pouch (two for the tray packaging) to control moisture uptake. A needle safety device, the Domrex™ Needle Guard (manufactured by Domrex Pharma Inc.), is also included to help prevent accidental needle stick injuries. An instructions leaflet is provided with the device.

ELIGARD® 45 mg (6-month)

(58.2 mg leuprolide acetate per syringe)

ELIGARD® 45 mg (6-month) is supplied in two separate, prefilled, sterile syringes whose contents are mixed immediately prior to administration. The two syringes are joined and the single dose product is mixed until it is homogenous. One syringe contains the ATRIGEL® Delivery System, and the other contains leuprolide acetate. The ATRIGEL® Delivery System is a polymeric (non–gelatin-containing) delivery system consisting of a biodegradable, 50% poly (DL-lactide-co-glycolide) (PLG) polymer formulation dissolved in a biocompatible solvent, 50% N-methyl-2-pyrrolidone (NMP). PLG is a co-polymer with an 85:15 molar ratio of DL-lactide to glycolide with hexanediol. The second syringe contains 58.2 mg lyophilized leuprolide acetate and is designed to deliver 45 mg of leuprolide acetate at the time of subcutaneous injection.

ELIGARD® 45 mg (6-month) is available in a single use tray packaging. The tray packaging contains the two-syringe mixing systems, a 18-gauge $^5/_8$-inch needle, and two silicone desiccant pouches to control moisture uptake. A needle safety device, the Domrex™ Needle Guard (manufactured by Domrex Pharma Inc.), is also included to help prevent accidental needle stick injuries. An instructions leaflet is provided with the device.

[1] Domrex™ Needle Guard is a trademark of Domrex Pharma Inc.

[2] ATRIGEL® is a registered trademark of QLT USA, Inc.

sanofi-aventis Canada Inc., Laval, Quebec H7L 4A8

ELIGARD®
leuprolide acetate
Working with you for your patients

CDN.LEU.10.05.02E

Vesicare®
solifenacin succinate

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Urinary Antispasmodic

INDICATIONS AND CLINICAL USE: VESICARE (solifenacin succinate) is indicated for the treatment of overactive bladder in adults with symptoms of urge urinary incontinence, urinary urgency and urinary frequency.

Geriatrics: In placebo controlled clinical studies, similar safety and effectiveness were observed between older (623 patients ≥ 65 years and 189 patients ≥ 75 years) and younger patients (1188 patients <65 years) treated with VESICARE.

Pediatrics: Safety and effectiveness in children have not yet been established.

CONTRAINDICATIONS

VESICARE should not be administered to patients with urinary retention, dependent on dialysis, gastroparesis or narrow angle glaucoma, or patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container.

Special Populations

For use in special populations, see WARNINGS AND PRECAUTIONS, Special Populations.

Safety Information

WARNINGS AND PRECAUTIONS

General: VESICARE, like other anticholinergic drugs, should be administered with caution in patients with impaired ability to sweat, to reduce the risk of heat prostration, and in patients with clinically significant bladder outflow obstruction because of the risk of urinary retention. VESICARE may cause blurred vision. Patients should be advised to exercise caution in driving or operating machinery until the drug's effect on vision has been determined.

Monitoring and Laboratory Tests: Monitoring of the QT/QTc interval and/or serum electrolyte levels may be appropriate in high risk patients who are being treated with VESICARE, such as: Patients with known congenital or acquired QT/QTc interval prolongation or electrolyte disturbances; Patients who are taking drugs that have been associated with QT/QTc interval prolongation and/or torsade de pointes such as Class IA (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) antiarrhythmic medications or those taking potent CYP3A4 inhibitors.

Cardiovascular: A study of the effect of solifenacin on the QT interval was conducted in 76 healthy women. The QTc interval prolongation effect appeared greater for the 30 mg compared to the 10 mg dose of solifenacin. Although the effect of the highest solifenacin dose (three times the maximum therapeutic dose) studied did not appear as large as that of the positive control moxifloxacin at its therapeutic dose, the confidence interval overlapped. This study was not designed to draw direct statistical comparison between the drugs or the dose levels. This observation should be considered in clinical decisions to prescribe VESICARE for patients with a known history of QT prolongation or patients who are taking medications known to prolong the QT interval. The effect of solifenacin on QTc interval change in males has not been investigated, and caution should be taken in extrapolating the findings of this study to male subjects. The effect of solifenacin on QTc interval change in elderly subjects with occult renal insufficiency, (in whom plasma concentration of solifenacin might be higher than those observed in younger subjects), has not been investigated.

Gastrointestinal: VESICARE, like other anticholinergics, should be used with caution in patients with decreased gastrointestinal motility.

Hepatic: VESICARE should be used with caution in patients with reduced hepatic function. Doses of VESICARE greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B). VESICARE is not recommended for patients with severe hepatic impairment (Child-Pugh C). (See DOSAGE AND ADMINISTRATION and ADVERSE REACTIONS).

Renal: Use with caution in patients with reduced renal function. Doses of VESICARE greater than 5 mg are not recommended in patients with severe renal impairment (CL_{cr} < 30 mL/min). (See DOSAGE AND ADMINISTRATION). VESICARE is contraindicated in dialysis dependent patients (see CONTRAINDICATIONS).

Sexual Function/Reproduction: No clinical data are available from reproductively competent women who have received long-term treatment with VESICARE. The potential risk to such women is presently unknown. Therefore, VESICARE should be used during pregnancy only if the potential benefit for the mother justifies the potential risk for the fetus. Women of childbearing potential should be considered for treatment only if using adequate contraception.

Special Populations

Pregnant Women: There are no adequate and well-controlled studies investigating the effects of solifenacin succinate in pregnant women. Therefore, VESICARE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women of childbearing potential should be considered for treatment only if using adequate contraception. The effect of VESICARE on labor and delivery in humans has not been studied.

Nursing Women: It is not known whether solifenacin is excreted in human milk. Because many drugs are excreted in human milk, VESICARE should not be administered during nursing. A decision should be made whether to discontinue nursing or to discontinue VESICARE in nursing mothers.

ADVERSE REACTIONS

Adverse Drug Reaction Overview: Expected side effects of antimuscarinic agents are dry mouth, constipation, blurred vision (accommodation abnormalities), urinary retention, and dry eyes. The most common adverse events reported in patients treated with VESICARE were dry mouth and constipation and the incidence of these side effects was higher in the 10 mg compared to the 5 mg dose group. Compared to twelve weeks of treatment with VESICARE, the incidence and severity of adverse events were similar in patients who remained on drug for up to 12 months. The most frequent reason for discontinuation due to an adverse event was dry mouth, 1.5%.

To report a serious or unexpected reaction to this drug, you may notify Health Canada at 1-866-234-2345 or Astellas Pharma Canada, Inc., at 1-888-338-1824.

DRUG INTERACTIONS

Overview: Concomitant medication with other medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. An interval of approximately 1 week should be allowed after stopping treatment with VESICARE, before commencing other anticholinergic therapy. The therapeutic effect of solifenacin may be reduced by concomitant administration of cholinergic receptor agonists. Solifenacin may reduce the effect of medicinal products that stimulate the motility of the gastrointestinal tract, such as metoclopramide.

Drugs Metabolized by Cytochrome P450: At therapeutic concentrations, solifenacin does not inhibit CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 derived from human liver microsomes.

CYP3A4 Inhibitors: In vitro drug metabolism studies have shown that solifenacin is a substrate of CYP3A4. Inducers or inhibitors of CYP3A4 may alter solifenacin pharmacokinetics. Therefore, the dose of solifenacin should be maintained at, or dropped to, 5 mg daily while patients are taking a potent CYP3A4 inhibitor such as ketoconazole, clarithromycin, erythromycin, diclofenac, nefazodone, verapamil and others.

Administration

DOSAGE AND ADMINISTRATION

Dosing Considerations :

Dose Adjustment in Renal Impairment: For patients with severe renal impairment (CL_{cr} < 30 mL/min), a daily dose of VESICARE greater than 5 mg is not recommended. VESICARE is contraindicated in dialysis dependent patients (see CONTRAINDICATIONS).

Dose Adjustment in Hepatic Impairment: For patients with moderate hepatic impairment (Child-Pugh B), a daily dose of VESICARE greater than 5 mg is not recommended. Use of VESICARE in patients with severe hepatic impairment (Child-Pugh C) is not recommended.

Dose Adjustment with CYP3A4 Inhibitors: When administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors, a daily dose of VESICARE should be maintained at, or dropped to, 5 mg daily.

Recommended Dose and Dosage Adjustment: The recommended dose of VESICARE is 5 mg once daily. If the 5 mg dose is well tolerated, the dose may be increased to 10 mg once daily. VESICARE should be taken with liquids and swallowed whole. VESICARE can be administered with or without food, without regard to meals. The maximum effect can be determined after 4 weeks at the earliest.

Missed dose: If a dose is missed, the next tablet should be taken as planned. Doses should not be doubled to make up for a missed dose.

Study References

1. Chapple CR, et al. *Eur Urol* 2005; 45: 464-470.
2. Chapple CR, et al. *Eur Urol* 2006; 49: 157-190.

SUPPLEMENTAL PRODUCT INFORMATION

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

VESICARE has been evaluated for safety in 1811 patients in randomized, placebo-controlled trials. In the four 12-week double-blind clinical trials, there were three intestinal serious adverse events in patients, all treated with VESICARE 10 mg (one fecal impaction, one

colonic obstruction, and one intestinal obstruction). The overall rate of serious adverse events in the double-blind trials was 2%. Table 1 lists adverse events, regardless of causality, that were reported in randomized, placebo-controlled trials at an incidence greater than placebo and in 1% or more of patients treated with VESICARE 5 or 10 mg once daily for up to 12 weeks.

Table 1. Percentages of Patients with Treatment-Emergent Adverse Events Exceeding Placebo Rate and Reported by 1% or More Patients for Combined Pivotal Studies

SYSTEM ORGAN CLASS MedDRA Preferred Term	Placebo (%)	VESICARE 5 mg (%)	VESICARE 10 mg (%)
Number of Patients	1216	578	1233
Number of Patients with Treatment-Emergent AE	634	265	773
Eye Disorders			
Vision Blurred	1.8	3.8	4.8
Dry Eyes NOS	0.6	0.3	1.6
Gastrointestinal Disorders			
Dry Mouth	4.2	10.9	27.6
Constipation	2.9	5.4	13.4
Nausea	2.0	1.7	3.3
Dyspepsia	1.0	1.4	3.9
Abdominal Pain Upper	1.0	1.9	1.2
Vomiting NOS	0.9	0.2	1.1
General Disorders and Administration Site Conditions			
Fatigue	1.1	1.0	2.1
Edema Lower Limb	0.7	0.3	1.1
Infections and Infestations			
Urinary Tract Infection NOS	2.8	2.8	4.8
Influenza	1.3	2.2	0.9
Pharyngitis NOS	1.0	0.3	1.1
Nervous System Disorders			
Dizziness	1.8	1.9	1.8
Psychiatric Disorders			
Depression NOS	0.8	1.2	0.8
Renal and Urinary Disorders			
Urinary Retention	0.6	0	1.4
Respiratory, Thoracic and Mediastinal Disorders			
Cough	0.2	0.2	1.1
Vascular Disorders			
Hypertension NOS	0.6	1.4	0.5

One young male subject developed a reversible increase in hepatic enzymes following a single dose of solifenacin during a Phase I study. Although causality has not been established, special attention should be paid to subjects who develop abnormal liver function tests after starting solifenacin and consideration given to discontinuing treatment.

Post-Market Adverse Drug Reactions: In addition to the adverse events observed in clinical trials, the following events have been reported in association with VESICARE use in worldwide postmarketing experience, although the frequency of events or a causal relationship with VESICARE could not always be confirmed: urinary retention; vomiting; peripheral edema; hypersensitivity reactions including rash, pruritus, and urticaria; dizziness; headache; and hallucination.

DRUG INTERACTIONS

Drug-Drug Interactions: Solifenacin is metabolised by CYP3A4. Simultaneous administration of ketoconazole (200 mg/day), a potent CYP3A4 inhibitor, resulted in a two-fold increase of the AUC of solifenacin, while ketoconazole at a dose of 400 mg/day resulted in a three-fold increase of the AUC of solifenacin. Therefore, the maximum dose of VESICARE should be restricted to 5 mg, when used simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors.

Table 2. Investigated Potential Drug-Drug Interactions

Drug name	Ref	Effect	Clinical Comment
Digoxin	CT	No significant effect on pharmacokinetics of digoxin in healthy subjects.	
Ketoconazole	CT	↑ solifenacin The mean C_{max} and AUC of solifenacin increased by 1.5 and 2.7-fold, respectively.	It is recommended not to exceed 5 mg daily dose of VESICARE when administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors.
Oral contraceptives (ocp)	CT	No significant effect on plasma concentration of combined OCPs (ethinyl estradiol/levonorgestrel).	
Warfarin	CT	No significant effect on pharmacokinetics of *R*-warfarin or *S*-warfarin.	

CT = Clinical Trial

Drug-Food Interactions: Co-ingestion of grapefruit juice with VESICARE may increase the serum level of solifenacin.

Drug-Herb Interactions: Interactions with herbal products have not been established and caution should be taken if such agents are used by patients.

Drug-Laboratory Test Interactions: Interactions with laboratory tests have not been investigated.

OVERDOSAGE

Acute: Overdosage with VESICARE can potentially result in severe anticholinergic effects and should be treated accordingly. The highest dose of solifenacin succinate accidentally given to a single patient was 280 mg in a 5-hour period, resulting in mental status changes. The patient was given charcoal treatment and recovered without sequelae.

Chronic: Intolerable anticholinergic side effects (fixed and dilated pupils, blurred vision, failure of heel-to-toe exam, tremors and dry skin) occurred on day 3 in normal volunteers taking 50 mg daily (5 times the maximum recommended therapeutic dose) and resolved within 7 days following discontinuation of drug.

Treatment of Overdosage: In the event of overdose with VESICARE treat with gastric lavage and appropriate supportive measures. ECG monitoring is also recommended.

Complete Product Monograph available upon request.

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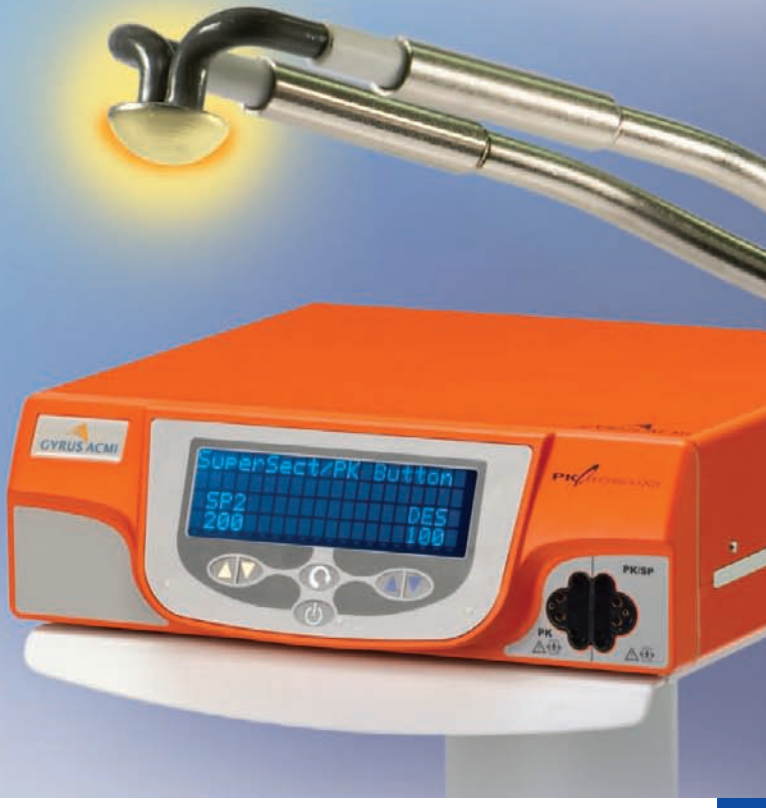

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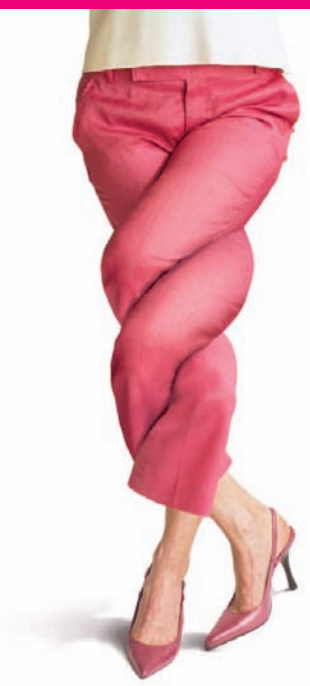
Vesicare

Help your Overactive Bladder patients with the discomfort of urgency.



Vesicare 5 mg/10 mg treatment resulted in a similar reduction of micturitions per 24 hours compared to tolterodine ER 4 mg[1]

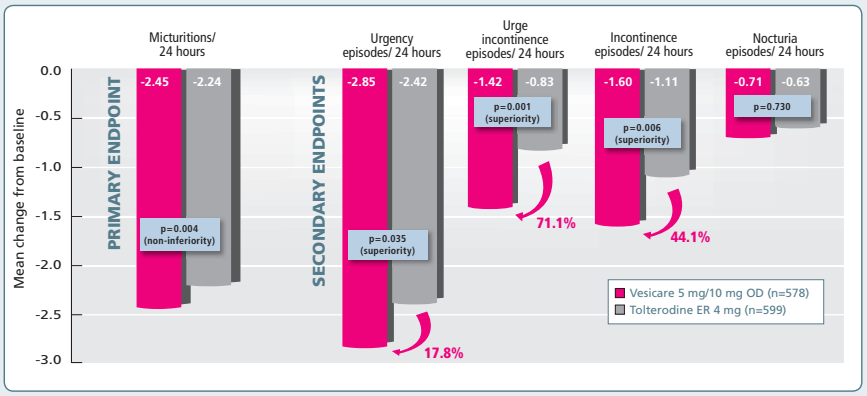
Vesicare 5 mg/10 mg demonstrated a greater reduction in urgency and urge incontinence episodes from baseline than tolterodine ER 4 mg[1]

- Urgency: -47%(-2.85) vs. -41%(-2.42), respectively
- Urge incontinence: -61%(-1.42) vs. -39%(-0.83), respectively

Discontinuation rates due to adverse events were 3.5% and 3.0%, respectively for Vesicare 5 mg/10 mg and tolterodine ER 4 mg[1,2]

- The most commonly reported adverse events were:
  Dry mouth: 30% vs. 24%, respectively; $p<0.05$[2]
  Constipation: 6.4% vs. 2.5% respectively; $p<0.05$[2]

IMPROVEMENT IN OAB SYMPTOMS AFTER 12 WEEKS[1]



Adapted from Chapple et al., 2005. Prospective, double-blind, double-dummy, two-arm, parallel-group, 12 week trial in OAB patients. After a 2 week, single–blind, placebo run-in, patients were randomized to receive either Vesicare 5 mg OD or tolterodine ER 4 mg OD. After 4 weeks of treatment, patients had the option of either continuing with their original dose or requesting a dose increase. However regardless of dose decision (dummied throughout), only Vesicare treated patients were given an increase from 5 mg to 10 mg OD based on product labeling (dose increase was not approved for tolterodine ER).

INDICATIONS: Vesicare (solifenacin succinate) is indicated for the treatment of overactive bladder in adults with symptoms of urge urinary incontinence, urinary urgency and urinary frequency. Safety and effectiveness in children have not yet been established.

CONTRAINDICATIONS: Patients with urinary retention, dependent on dialysis, gastroparesis or narrow angle glaucoma. Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container.

WARNINGS: Women of childbearing potential should be considered for treatment only if using adequate contraception.

ADVERSE EVENTS: Expected side effects of antimuscarinic agents are dry mouth, constipation, blurred vision (accommodation abnormalities), urinary retention, and dry eyes. The most common adverse events reported in patients treated with Vesicare were dry mouth and constipation and the incidence of these side effects was higher in the 10 mg (27.6% and 13.4%, respectively) compared to the 5 mg (10.9% and 5.4%, respectively) dose group (4.2% and 2.9% for placebo, respectively).

Vesicare: Demonstrated Efficacy vs. Tolterodine ER.

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Helps Control Urgency

See prescribing summary on page A16