LETTER TO THE EDITOR

Overcoming challenges associated with 18F-DCFPyL PET imaging in prostate cancer

Arosh S. Perera Molligoda Arachchige, MD[1,2]

[1]Department of Radiology, Istituto Clinico Humanitas, Milan, Italy

[2]Department of Biomedical Sciences, Humanitas University, Milan, Italy

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Editor:

We read with great interest the article by Dr. Rowe et al who provide a brief introduction on 18F-DCFPyL PET scans for practices and academic groups that are adopting it for use in their patients with prostate cancer.[1] Indeed, prostate-specific membrane antigen (PSMA) PET is becoming a standard method of evaluating patients with newly diagnosed high-risk and biochemically recurrent prostate cancer. The first of these PSMA PET radiopharmaceuticals to receive U.S. Food and Drug Administration approval for prostate cancer evaluation was Gallium-68-labelled prostate-specific membrane antigen (^{68}Ga–PSMA-11) followed by 18F-DCFPyL, a second-generation low molecular weight radiofluorinated PSMA-targeted positron emission tomography (PET) radiotracer, approved in 2021 to help identify suspected metastasis or recurrence in patients with prostate cancer.[2]

Address correspondence to Dr. Arosh S. Perera Molligoda Arachchige, Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini, Pieve Emanuele, Milan 20090, Italy

18F-DCFPyL PET/CT is one of the most versatile PET agents for metastatic prostate cancer with high sensitivity as described by the authors. However, it must be noted that a commonly encountered limitation is the identification of several false-positive findings and tumor mimics since it can be uptaken by both benign and malignant lesions. Interestingly, previous studies have shown that binding of 18F-DCFPyL at prostate cancer cells increases over time. Thus, the dual-phase protocol which employs both early and delayed scans may be helpful in separating benign lesions from malignant ones associated with prostate cancer. In a study by Tian et al which was designed to retrospectively analyze the incremental diagnostic value of 18F-DCFPyL dual-phase imaging (1 and 2h) in patients with prostate cancer, compared with benign tissues, the uptake of 18F-DCFPyL in prostate-related malignant lesions increased over time and may be helpful for more precise evaluation of benign and prostate-related malignant lesions since SUVmax metrics and SUV ratio of early and delayed imaging of prostate cancer-related malignant lesions being significantly higher compared with those of benign lesions ($p < 0.05$) were good indicators for differential diagnosis.[3]

Moreover, understanding the cause of uptake by benign lesions may help us implement strategies to distinguish them. For example, a common cause

of bone uptake is healing old fractures.[4] Several studies have described increased 68Ga-PSMA-11 and 18F-DCFPyL uptake in healing fractures at multiple sites, such as vertebrae, sacrum, ribs, and distal radius.[4] Furthermore, as suggested by Schmuck et al using 68Ga-PSMA I&T, an early dynamic followed by a static delayed image acquisition also leads to an improved tumor-to-nontumor ratio, in particular in the prostate gland and this may be relevant for 18F-labeled PSMA PET agents as well.[5] It is worth investigating whether this is applicable to 18F-DCFPyL.

Lastly, since the urinary excretion of 18F-DCFPyL is high, the modification of current imaging protocols to reduce the overall effective dose as well as the absorbed doses to the testes and urinary bladder may help increase the overall detection rate. These strategies include intravenous application of furosemide, oral hydration, or voiding prior to imaging.[2] All 18F-labeled agents have shown better target-to-background ratios in delayed scans and thus, future protocols should not start imaging acquisition prior to 90 min after radiotracer administration.[2] We believe that each of the aforementioned aspects could be taken into consideration when designing future studies in order to overcome the current challenges faced in 18F-DCFPyL prostate cancer imaging. □

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