EDITORIAL

Letter regarding "^{18}F-Fluciclovine PET/CT performance in biochemical recurrence of prostate cancer: a systematic review"

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Rais-Bahrami and colleagues have provided an informative overview of the applications of ^{18}F-fluciclovine (FACBC, Axumin®, Blue Earth Diagnostics Ltd) positron emission tomography (PET) for detection and localization of disease in men with biochemically evidence of recurrent prostate cancer [1]. The authors found that the detection rate of metastatic lesions with ^{18}F-fluciclovine PET was overall correlative to prostate-specific antigen (PSA) levels, but that even at low PSA levels of <0.5 ng/mL, ^{18}F-fluciclovine was able to detect a majority of lesions. Additionally, Rais-Bahrami et al importantly found that ^{18}F-fluciclovine PET affected patient management and targeted ^{18}F-fluciclovine radiotherapy planning resulted in improved outcomes. It should be noted that, as with most PET radiopharmaceuticals, the literature regarding use of ^{18}F-fluciclovine in the setting of prostate cancer is limited by small sample sizes and a large heterogeneity of study design, limiting the ability to generalize the findings of specific studies to the disease spectrum as a whole. To this point, the authors of this review evaluated 315 articles, but limited inclusion for data analysis to prospective studies of ≥25 patients with biochemical recurrent prostate cancer. This effort to avoid variability from small sample design, resulted in a review of only 6 relevant articles and 3 conference presentations. Thus, while this review may avoid some bias, the resulting small sample size has remarkable heterogeneity and does not allow for an in-depth analysis of many of the more unanswered questions regarding the utility of ^{18}F-fluciclovine PET in the setting of prostate cancer. For example, within this small data set, there was inconsistent inclusion of: use of a reference standard, androgen deprivation therapy (ADT) status [2, 3], radical prostatectomy [4, 5], radiation therapy [2, 4], Gleason score, and initial nodal status [6, 7]. Additionally, there was heterogeneity in the actual imaging amongst the studies, with included studies starting PET scanning immediately after injection of ^{18}F-fluciclovine [7], 2 minutes [6] after, and with the reminder following the standard 3-5 minute delay post injection. All of these variables have been shown to affect diagnostic outcomes in the literature. Given their self-imposed constraints, the authors made an attempt to correct for the aforementioned variables. Ultimately, however, the disparate nature of each study leads to wildly variable conclusions, such as patient-level detection rates which varied from 26% [6] to 83% [5]. The overall value of ^{18}F-fluciclovine in the setting of biochemical recurrent prostate cancer is well established, but there are many unresolved questions regarding the diagnostic accuracy of ^{18}F-fluciclovine PET that a more targeted review and thoughtful approach to the literature inclusion may reveal. Some areas of uncertain utility for ^{18}F-fluciclovine include: PET-MRI in the setting of prostate-intact prostate cancer [8], ^{18}F-fluciclovine PET for osseous metastatic disease [9], and the continuing applicability of ^{18}F-fluciclovine in the United States with the recent FDA approval of ^{68}Ga PSMA-11 [10]. This last point is particularly pertinent given that the two studies that the review article included that compared ^{68}Ga PSMA-11 to ^{18}F-fluciclovine [6, 7] came to vastly different conclusions regarding the comparative accuracy of ^{18}F-fluciclovine PET. For ^{18}F-fluciclovine to maintain its role in the United States as the de facto molecular imaging agent for biochemical prostate cancer, more targeted analysis must be performed to assure the molecular imager and ordering physicians of its relevancy.

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