Comparison of Dynamic PET Imaging with $^{18}$F-FCH and $^{18}$F-DCFPyL for Prostate Cancer: Why do they behave differently?

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**Purpose.** Positron emission tomography (PET) imaging with $^{18}$F-fluorocholine (FCH) was widely used for imaging prostate cancer (PCa); however, many studies showed that choline uptake is not always higher in tumour regions. However, the prostate-specific membrane antigen (PSMA) ligand, $^{18}$F-DCFPyL, is able to localize and detect PCa nodules with high contrast to background normal prostatic tissue. Therefore, here we investigated whether the difference between the two tracers can be explained by their kinetic behaviour in PCa.

**Methods.** Patients aged 18 years or older with pathologically confirmed PCa underwent dynamic PET imaging. Seven patients with histologically confirmed PCa (mean prostate-specific antigen (PSA), 10.7 ± 7.9 ng/mL; Gleason score 3+4, proportion of prostate involved with tumour 20%) were evaluated with dynamic $^{18}$F-DCFPyL PET, and another seven patients with similar characteristics (mean PSA, 7.9 ± 3.8 ng/mL, Gleason score 3+4, tumour involvement 20%) underwent dynamic $^{18}$F-FCH PET. The dynamic PET imaging protocol consisted of 10 images at 10 s each, 5 at 20 s, 4 at 40 s, 4 at 60 s and 4 at 180 s (total acquisition time of 22 min). Based on prostate sextant biopsy and a standardized uptake value (SUV) map constructed from the sum of the last 4 dynamic frames (12-22 min post injection), tumour and normal tissue regions of interest (ROI) were segmented. The ROI were evaluated semi-quantitatively using the SUV map and quantitatively using Johnson-Wilson-Lee model modified open 3-compartment model kinetic parameters: F (Blood flow), $K_1$ (Influx rate constant), $k_2$ (Efflux rate constant), $k_3$ (Binding rate constant), $k_4$ (Dissociation rate constant) and $K_i$ (Normalized net uptake rate) which describes the blood flow delivery to tissue and subsequent binding to target and were estimated from the time-activity curves.

**Results.** Amongst SUV and the kinetic parameters for $^{18}$F-DCFPyL, $k_4$ and $K_i$ were the best combination of parameters to discriminate tumour from normal tissue using logistic regression with backward elimination while SUV and $K_i$ were the best combination for $^{18}$F-FCH. The normalized washout from the bound pool, as estimated by the inverse of binding potential ($k_3/k_4$), of $^{18}$F-DCFPyL from normal tissue was greater than tumour while for $^{18}$F-FCH both normal tissue and tumour had similar normalized washout. The binding rate constant ($k_3$) of $^{18}$F-FCH was higher than $^{18}$F-DCFPyL for both normal tissue and tumour.

**Discussion.** Kinetic analysis of $^{18}$F-DCFPyL is more sensitive than the semi-quantitative SUV for detecting and differentiating tumour from normal prostatic tissue. The $^{18}$F-DCFPyL contrast between tumour and normal tissue is due to the differential normalized washout. In contrast, the lack of $^{18}$F-FCH contrast between tumour and normal tissue is due to similar normalized washout. The large binding rate constant of $^{18}$F-FCH vs $^{18}$F-DCFPyL suggested that the former has a faster uptake rate and at time interval when binding dominates, SUV could be used to differentiate sensitively tumour from normal tissue.