Diagnostic potential of simultaneous ^{18}F-FACBC PET/MRI in high risk prostate cancer patients

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Introduction: Existing imaging techniques have limitations in detection and staging of prostate cancer. Specifically, MRI has low accuracy in detecting lymph node metastasis (N-stage). The leucine amino acid analog 1-amino-3-fluorine 18-fluorocyclobutane-1-carboxylic acid (^{18}F-FACBC) has shown promising results in assessment of primary and metastatic prostate cancer [1, 2]. The purpose of the present study was to establish a protocol for a simultaneous ^{18}F-FACBC PET and multiparametric MR examination of the prostate and the pelvic lymph nodes for precise staging and grading of high risk prostate cancer patients. Further, the aim is to evaluate the diagnostic potential with histopathology as the gold standard.

Methods: High risk prostate cancer patients (Gleason score ≥8 and/or PSA>20 and/or ≥cT3 cancer) scheduled for prostatectomy with extended pelvic lymph node dissection were recruited for the study and underwent a fully integrated PET/MRI examination (3 T Biograph mMR, Siemens, Erlangen, Germany) prior to surgery. The PET/MRI protocol was tailored to provide MR images of diagnostic quality for clinical preoperative evaluation in addition to dynamic PET images of the prostate gland and pelvic lymph nodes. A schematic overview of the implemented PET/MRI protocol is shown in Figure 1. In the first bed position (BP1) the prostate is in isocenter and a localizer, T2 weighted images (T2WI) in three orthogonal planes and transversal diffusion weighted images (DWI) are acquired. The table is then moved to the second bed position (BP2) in which both the prostate and pelvic lymph nodes are covered by the PET field of view. Immediately after tracer injection, PET data are acquired in list mode for 25 minutes. Simultaneously, MR images for attenuation correction (AC), coronal T1 (T1WI) and DWI and T2 SPACE are acquired. Eventually the table is moved back to BP1 where PET data are acquired in list mode for 20 min with simultaneous acquisition of AC, spectroscopy (MRSI) and dynamic contrast enhanced MR images (DCE-MRI). Two radiologists evaluated the MR examination according to the PI-RADS criteria [3] while PET-data will be evaluated by a nuclear medicine physician. After surgery a pathologist examined HES stained slides of the prostate gland and resected lymph nodes and outlined cancer foci and described cancer stage (TNM) and grade (Gleason score).

Time	30 min	Tracer injection	25 min	20 min
Localization	BP1		BP2	BP1
PET			PET (listmode)	PET(listmode)
MRI	Localizer, T2WI, DWI		AC, T1WI, DWI, T2 space	AC, MRSI, DCE-MRI

Figure 1: Schematic overview of the PET/MRI protocol. BP1/2= first /second bed position

Results: Fifteen patients have so far been included in the study (median age 67.1, mean PSA 14.6, cTNM T2-T3b, Gleason score from diagnostic biopsies 3+4 to 4+5, mean injected activity 323 MBq). The first visual inspection of the datasets reveal that all patients had high, non-uniform uptake of ^{18}F-FACBC in the prostate gland mainly corresponding either to areas suspicious for cancer from the MR images (Figure 2) or to areas suspicious for BPH (Figure 3). Tracer uptake has also been observed in histopathologically verified lymph node metastasis (Figure 4).

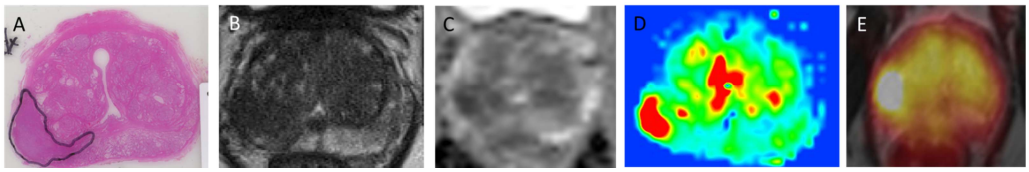

Figure 2: HES slide (A), T2W image (B), ADC map (C), K_{trans} map (D) and PET image overlaid T2W image (E) from 71 year old patient (PSA 10.7 ng/ml, cT2, GS 4+5) show good correspondence between histopathology, MR images and ^{18}F-FACBC uptake.

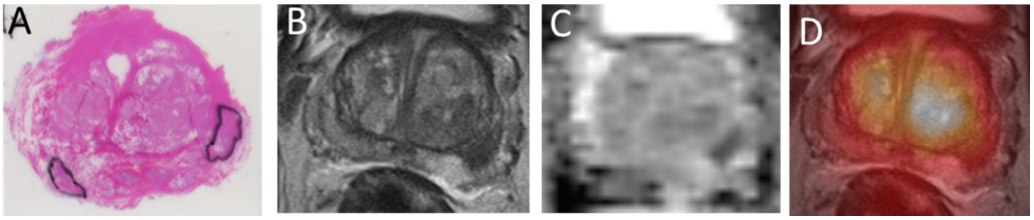

Figure 3: HES slide (A), T2W image (B), ADC map (C) and PET image overlaid T2W image (D) from 65 year old patient (PSA 9 ng/ml, cT3a, GS 3+5) show high uptake of ^{18}F-FACBC in area corresponding to central gland nodules.

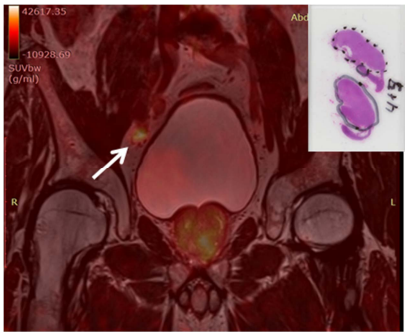

Figure 4: Coronal view of patient (66 years old, PSA 3.7 ng/ml, cT3b, GS 4+4) with lymph node metastasis verified by histopathology showing high uptake of ^{18}F-FACBC (white arrow). On histopathology long axis diameter was 15 mm and short axis diameter was 8 mm.

Discussion: High risk prostate cancer patients can have a full clinical PET/MRI examination in 75 minutes with the implemented protocol. Initial results indicate that there is good agreement between cancer suspect areas on PET and MR. There has however also been observed uptake in benign areas of the central gland. Further analysis including dynamic uptake curves is needed to evaluate whether tumor-uptake can be separated from non-malignant uptake. Uptake of ^{18}F-FACBC has been observed in lymph node metastasis and the study will be extended to include a total of 32 patients to further evaluate the diagnostic potential of ^{18}F-FACBC with particular emphasis on comparing the performance of multiparametric MRI and ^{18}F-FACBC PET in detection of regional lymph node metastasis.

References: 1: Schuster et al, J Nucl Med, 2007. 48(1): p. 56-63. **2:** Nanni et al, Clin Genitourin Cancer, 2014. 12(2): p. 106-10. **3**: Barentsz et al, Eur Radiol, 2012. 22(4): p. 746-57.