Multiparametric hybrid 18FDG-PET/MRI in patients with Multiple Myeloma: initial experience

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Objective:

Bone involvement is a prominent feature in multiple myeloma (MM) [1]. MRI for evaluating symptomatic bone sites is discussed as a possible gold standard for imaging of the axial skeleton [2]. ^{18}F-FDG PET can assist in evaluating treatment response, but the routine use in this disease is still controversial [3, 4]. PET/MRI hybrid scanner therefore can provide both metabolic and anatomic information through improved soft tissue contrast of MRI combined with PET-information and render a potentially new diagnostic approach [5]. Because of high cellularity, bone marrow infiltration by MM shows enhanced signal intensity on DWI (diffusion-weighted imaging) and recent publications indicate promising results regarding diagnosis and follow-up in myeloma patients [6]. This prospective multimodality single institution study intended to evaluate the benefit of PET/MRI-imaging in combination and comparison to DWI for characterizing myeloma-lesions.

Methods:

The study was conducted in accordance to the declaration of Helsinki with institutional approval by the local ethics committee. Fifteen patients newly diagnosed with Multiple Myeloma, according to the International Myeloma Working Group criteria (2003), were referred for whole-body PET/MRI including DWI. DWI conspicuities were matched to respective PET and static MRI findings through lesion-by lesion based analysis (Fig.1A and B). For imaging a hybrid PET/MRI 3.0 T scanner (Siemens mMR Biograph, Erlangen, Germany) was used, including T1w, T2wSTIR and axial triggered 2D echoplanar diffusion sequences, with the following parameters: TR/TE 2600/65 ms, matrix 128 × 128, FOV 380 × 380, resolution 3.7 × 3.02 × 5.0 mm³, 2 b-values (0, 800 s/mm^2). The PET detector contained eight rings of 56 detector blocks (64 lutetium oxyorthosilicate crystals each, 4x4x20mm). PET data were reconstructed with an iterative 3-D OSEM algorithm (two iterations, 21 subsets; image matrix 172 pixels). Feasibility of PET/MRI was verified by comparison to ^{18}F-FDG PET/CT. Data were assessed based on qualitative and semi-quantitative evaluation (standard uptake value- SUV; OSIRIX). Apparent diffusion coefficient (ADC)-values were calculated for the whole tumor volume using the open-source software "Medical Imaging and Interaction Toolkit-Diffusion" (MITK-DI; Fig.1C) [7] and compared to SUV-values. For measurement and calculations lesions had to be displayed on at least three slices in DWI with a volume of >0.5 cm³. Statistical analysis was performed with the SSPS 15.0 software including correlation analysis of ADC_{mean} and $SUV_{average}$ with the Pearson Correlation Coefficient. Results were considered significant for $p<0.05$.

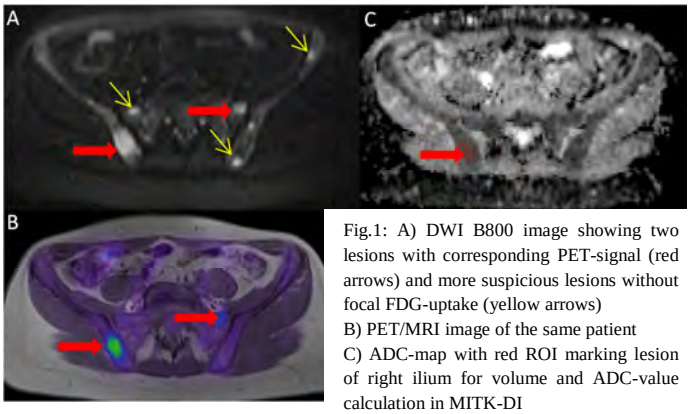
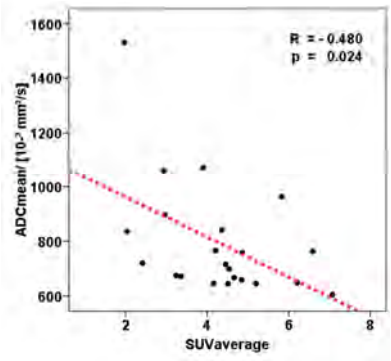


Fig.1: A) DWI B800 image showing two lesions with corresponding PET-signal (red arrows) and more suspicious lesions without focal FDG-uptake (yellow arrows)
B) PET/MRI image of the same patient
C) ADC-map with red ROI marking lesion of right ilium for volume and ADC-value calculation in MITK-DI

Results: DWI demonstrated a total of 62 focal MM lesions, of which 60 were confirmed in static MR images (2 ribs not suspicious in T1w or T2w-STIR). 47 of these 62 lesions correlated anatomically with the lesions that were also visible in PET, while 15 where DWI-positive and PET-negative (see Fig.1 A and B), all proving corresponding lesions in T2w-STIR. Three of these lesions exhibited diffuse PET-signal, the majority (11) were located in vertebrae or pelvis, all of those bones showed diffuse myeloma infiltration pattern in MRI. Seven PET positive lesions showed no DWI-correlate (4 ribs, 2 diffuse infiltration pattern, 1 outside FOV) and 6 neither correlate in static MRI (4 ribs, 2 due to diffuse infiltration in MRI). DWI failed to depict one lesion detected by static MRI-sequences due to location outside field of view. Correlation analysis of 22 lesions for $SUV_{average}$ and ADC_{mean} showed a significant negative correlation (Fig.2; R=-0.480, p=0.024).

Fig.2: Pearson correlation coefficient showing significant negative correlation (n = 22; R = -0.480; p = 0.024) of ADC_{mean} und $SUV_{average}$ values of myeloma lesions >0.5cm³



Discussion and Conclusion: Our study shows that for the detection of focal bone marrow infiltrates, PET and DWI can be complementary with PET displaying more lesions located in ribs, whereas DWI seems to have advantages discovering lesions in bones which are already diffusely infiltrated by myeloma cells and in which therefore "hot" foci are masked by the surrounding myeloma infiltrate. One lesion was missed in DWI compared to T1w/T2 STIR because it was out of the field of view. Therefore whole-body diffusion would render similar results to static MRI, which if applied to clinical examinations, could shorten MRI protocol and result in an acceptable exam time for patients with pain. Correlation of SUV and ADC is significant but weak. Although this result is theory-conform, expecting densely packed cells leading to lower ADC-values should result in higher FDG-uptake, it needs to be considered that tumor lesions can be very heterogeneous. Further studies with a bigger sample size investigating also patients after therapy would be of great interest in this context.

References: [1] International Myeloma Working Group, *Br J Haematol*., 2003. [2] Caers et al., *Haematologica*, 2014. [3] Zamagni et al., *Br J Haematol*., 2012. [4] Dimopoulos et al., *Blood*, 2011.[5] Buchbender et al., *J Nucl Med*., 2012. [6] Horger et al., *AJR Am J Roentgenol*., 2011. [7] Fritzsche et al., *Methods Inf Med*.2012.