

Assessment of bone marrow adipose tissue and glucose metabolism in a whole body MR/PET system: distribution patterns and correlation with anthropometric data

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Purpose: Human bone marrow consisting of red (hematopoietic) marrow and marrow adipose tissue (MAT) is a complex and dynamic organ which is involved in a large number of physiological processes. The distribution, composition and metabolic activity of bone marrow is mutable and can be influenced by various conditions such as age, body weight, endocrinologic and hematologic factors, drugs etc.. Bone marrow may also be changed in oncological, degenerative and inflammatory diseases[1]. Lately, it was also reported that MAT resembles both, white and brown adipose tissue [2]. Therefore, the metabolic activity of MAT could differ from subcutaneous white fat.

Cross-sectional imaging techniques such as CT and MRI can provide whole-body assessment of bone marrow distribution and - to a variable extent - also provide information about the composition of bone marrow within the skeleton. Metabolic activity of the bone marrow can be visualized using ¹⁸F-FDG-PET as this tracer physiologically accumulates in bone marrow [3]. Sambuceti et al. have recently given a first estimation of distribution and metabolism of bone marrow throughout the skeleton using ¹⁸F-FDG-PET/CT[1].

In MRI studies, accurate differentiation of fat and water can be performed using proton chemical shift imaging [4, 5]. In this technique, the different resonant frequencies of precessing fat and water protons are made use of to obtain quantitative information about water and fat content of the studied tissues [6]. Thus, objective quantification of the regional fat content of the bone marrow can be performed throughout the skeleton.

In the last years, the two modalities PET and MRI have been combined in clinical MR/PET scanners. They offer the possibility to assess structural and functional characteristics of bone marrow by analyzing the spatial distribution and fat fraction of bone marrow in correlation with its metabolic activity.

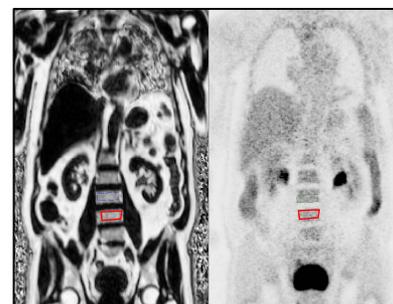
The aim of the study was twofold: first, to comprehensively assess composition and metabolic activity of bone marrow throughout the human skeleton in vivo with respect to the fat content using a simultaneous MR/PET scanner; second, to analyze the influence of anthropometric and endocrinologic factors on bone marrow composition and metabolic activity such as age, body mass index and blood glucose level.

Methods: Retrospective analysis of 10 patients who underwent whole-body MR/PET after a clinically indicated PET/CT with ¹⁸F-FDG (mean age 47 ± 19 years; range: 23 – 73 years; 9 male, 1 female) was performed. Inclusion criteria were: interval between imaging and last treatment > 6 months; MRI scan covering neck to upper thigh; age > 18 years, no osseous metastases. Clinical indication for PET/CT was: melanoma (n=4), lymphoma (n=1), CUP (n=1), breast cancer (n=1), lung cancer (n=1), colon cancer (n=1), Caroli syndrome with recurrent cholangitis (n=1).

All included patients fasted overnight. Before tracer injection (mean dose ¹⁸F-FDG 353±22MBq; range: 317-386MBq), blood glucose levels were measured (mean: 118±18mg/dl, range: 97-159mg/dl). During the uptake phase, patients were instructed to rest. MR/PET was performed on average 120 ± 7 min after radiotracer injection in a clinical whole-body 3T MR/PET (Biograph mMR, Siemens Healthcare). A 3D T1-weighted spoiled gradient-echo sequence with Dixon-based fat-water separation used for the generation of segmentation-based PET attenuation correction maps was used for fat fraction quantification: repetition time (TR) 3.6 ms, echo time (TE) TE₁ 1.23 ms, TE₂ 2.46 ms; excitation angle 10°; bandwidth 965 Hz/pixel; matrix size 79x192; pixel size 4.1x2.6x2.6 mm³; 128 slices per slab; parallel imaging acceleration factor 2; time of acquisition(TA) 19s. PET acquisition lasted 6 minutes per bed. PET data were reconstructed using an iterative three-dimensional (3D) ordered-subset expectation maximization (OSEM) algorithm with three iterations, 21 subsets and Gaussian filter of 3 mm.

Dixon images and PET data were co-registered and depicted in three planes for the evaluation using an institutional Matlab program (IMAGINE). Volumetric analysis of defined regions (humerus, thoracic spine, lumbar spine, sacrum, femur) was performed in a 3D analysis by manually outlining the different volumes of interest (VOI) on subsequent slices. Care was taken not to include cortical bone. Fat fraction (in %) and glucose uptake (SUVmean) of each VOI were recorded (Fig. 1). Spearman correlation coefficient was calculated.

Results: Fat fraction was highest in the extremities as assessed in humerus and femur and lowest in the thoracic vertebrae. SUVmean was negatively correlated with fat fraction (r=0.80, p<0.0001, Fig. 2). Significant correlations were found between fat content of the lumbar spine and age (r=0.77, p=0.009) as well as between BMI and sacral fat content (r=0.73, p=0.017). No significant correlation was found between blood glucose and fat fraction or SUVmean in any region.



Coronal fat-fraction image (left) and FDG-PET of the same patient (right). Exemplarily, one manually drawn contour (red) of the lumbar spine is shown. Contours were drawn on subsequent slices and composed for regional VOI analysis of BM.

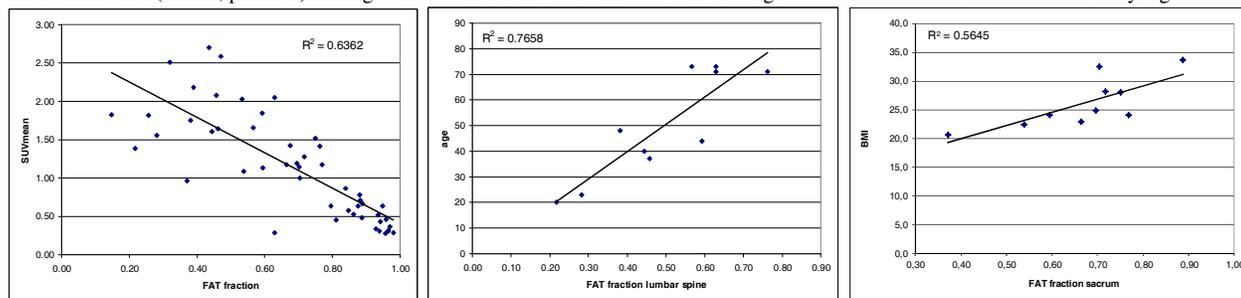


Fig. 2: Analysis of MAT and anthropometric data.

Significant correlation of bone marrow FAT fractions and SUVmean (left) age (middle) and BMI (right) were found.

Discussion: A significant negative correlation was found between presence of MAT (as represented by the fat fraction) and ¹⁸F-FDG-uptake (as represented by SUV) in bone marrow. This might indicate that MAT does not exhibit a comparably high metabolic activity as does BAT.

A significant correlation was found between age and MAT in the spine but not with MAT in the long bones which might indicate different physiologic patterns of MAT distribution with age. As MAT is also a fat depot, one might expect a correlation between BMI and MAT. However, a significant correlation was only found for the sacral fat fraction and BMI. This has to be elaborated further since all other MAT regions showed no dependency.

Our preliminary study has several limitations: first, patient number is rather small and does not allow for a representative gender-specific analysis. Second, all patients suffered from diseases possibly influencing bone marrow characteristics. However, we tried to reduce treatment related influences by excluding patients with therapy in the last 6 months before imaging. Third, the MR-based attenuation correction causes an underestimation of PET (ca. 8%) within bone. As this underestimation is present in all datasets, correlation analysis results should not be biased.

The present study indicates that the assessment of composition and metabolic activity of bone marrow by MR/PET has the potential to provide new insights in bone marrow physiology and might contribute to a deeper understanding of the physiology of MAT.

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