

MR Multi-parametric approach to evaluate osteoporosis at 3T: T2, T2*, ADC, Gi and 1H-MRS measurements in healthy, osteopenic and osteoporotic subjects.

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Introduction: One of the major limitations in the determination of the bone fracture risk is the inadequate evaluation of bone status, which is currently based on Bone Mineral Density (BMD). However, BMD provides exclusively a quantification of the bone mineral component. Other components, such as bone marrow (which is constituted by different quantities of lipids and water), are also present in spongy bone tissue, and may contribute in determining its resistance to fracture. So far, several MR-based methods have been developed for non-invasive assessment of osteoporosis in spongy bone [1,2]. Among these, MR-interferometry [1,2], which is based on T_2^* measurements, is currently considered the best candidate for the assessment of osteoporosis. However, due to their characteristics, there are other MR parameters, such as the Apparent Diffusion Coefficient (ADC) and the internal gradient G_i which might represent new potential indicators to evaluate bone quality. Recent studies suggest that ^1H -MRS provides quantitative information on the lipid and water content in spongy bone marrow which may be relevant for the diagnosis of osteoporosis at the earliest stages [3]. Aims of this study were: 1) to correlate T2, T2*, ADC and G_i of the spongy bone measured in the calcanei of healthy, osteopenic and osteoporotic women with their correspondent bone marrow fat content, assessed by ^1H -MRS and their T-score 2) to assess the ability of each MR parameter to predict the osteopenic and/or osteoporotic status of the spongy bone; 3) to identify the MR parameter which better predicts the risk of bone fracture.

Methods: Seventy postmenopausal women were recruited for this study. They first underwent a QTC examination to establish their bone status on the basis of BMD measurements, and divided in three subgroups: 1) healthy subjects (H) (N=10); 2), osteopenic subjects (OPE) (N=30), and osteoporotic patients with (OPO) (N=30). All subjects underwent an MR investigation of the calcaneus at 3.0T, including the following acquisitions: 1) FLASH sequence (TE_s/TR :5,7,10,20/1500ms, NS=1, square FOV=192mm, Matrix 128X128), 2) SEMC sequence (TE_s/TR :20,30,40,50,80,100, /1500ms NS=1, square FOV=192mm, Matrix 256X256); 3) SE-segmented-EPI diffusion-weighted sequence (TE/TR =109/2500ms, NS=4), using phase-diffusion gradient and b values (0-8000 s/mm²); 4) Single-Voxel Spectroscopy (TE/TR =22/5000ms, NS=32 and voxel size of 15x15x15 mm positioned in the centre of the calcaneus). ^1H -spectra were used to assess lipid and water content from the calcaneal bone marrow. In all acquisitions, no chemical presaturation pulses were used for either fat and water protons. T2 and T2* were evaluated assuming a mono-exponential decay behaviour, ADCs were evaluated from signal ratio using $b=8000$ and $b=0$, and G_i values were extracted using the following spin-echo relaxation time decay curve: $S(TE)=M_0\exp(-TE/T_2-ADCx(\gamma G)^2xTE^3/12)$. Finally, individual percentages of bone marrow fat content (Mfc%) were calculated from ^1H -spectra by assessing the Methylene-Methyl to water peaks area ratios. All the extracted measures were examined by Pearson's correlation coefficient p .

Results: No significant age difference was present among groups. T_2^* -values were significantly higher in OPO compared to H subjects (T_2^* -values: [13.8±2.8]ms and [10.1±1.9]ms respectively; $p=0.0005$) and significantly higher in OPE (T_2^* -value: [12.8±2.8]ms) compared to H women ($p=0.005$), while no significant difference was found between OPE and OPO subjects. T_2 -values were able to discriminate H from OPO subjects ($p=0.01$) and OPE from OPO ($p=0.05$) but not H from OPE. G_i -values were significantly different ($p=0.01$) between OPO and OPE and between OPO and H, but not between OPE and H subjects. Conversely ADC-values were significantly higher in OPO compared to OPE subjects (ADC-values: $[6.5\pm1.6]\cdot10^{-11}\text{m}^2/\text{s}$ and $[5.4\pm1.2]\cdot10^{-11}\text{m}^2/\text{s}$ respectively; $p=0.025$), in OPE compared to H women (ADC-value: $[3.9\pm1.0]\cdot10^{-11}\text{m}^2/\text{s}$; $p=0.005$), and in OPO compared to H subjects ($p=0.0005$). Any significant difference was found among Mfc% values of the three groups. A linear correlation (LC) was also found between ADC and Mfc% values in H subjects, while a feeble LC and no LC were found in OPO and OPE women respectively (Fig.1.A). Moreover, a feeble trend towards LC was found between T_2^* and Mfc% values in H subjects, while no LC was found in OPE and OPO groups (Fig. 1.B). Conversely, an high LC was found between G_i and Mfc% values in H subjects, and a feeble LC was found in the other two groups.

Discussion and Conclusion: Our results, obtained in women calcanei spongy bone at 3T, indicate the ability of ADC to discriminate among H, OPE and OPO groups better than all the others considered MR parameters. Specifically, ADC like T_2^* identifies OPE subjects at risk of developing osteoporosis. ADC discriminates also between OPE and OPO, while T_2^* does not. These observation about ADC measured in calcanei, together with the Mfc% values results (which were about equal in the three groups), bring forward some different conclusions with respect to relevant evidence previously obtained from vertebral spongy-bone [4]. Indeed some authors have demonstrated that in vertebral spongy bone Mfc% values and total lipids content are significantly higher in OPO as compared to H subjects. Moreover ADC of vertebral bone marrow does not change as a function of bone density. These different conclusions may be due to the skeletal-site dependence of Mfc%, which is higher in calcaneus (from about 80% to 90%) than in vertebral (from about 50% to 70%) spongy bone. As a consequence the ADC values and the ADC behaviour are different in vertebral and calcaneal spongy bone.

Our results show the great potentiality of ADC measurements in the diagnosis of osteoporosis when calcaneus spongy bone is investigated. Moreover the combination of ADC (and/or T_2^*) and ^1H -spectroscopy assessment might contribute in a better prediction of bone fracture risk. Finally, this study highlights that the best parameter to assess the bone status is skeletal-site dependent, and changes according to the examined part.

References: [1] Wehrli FW et al. Radiology 1991;179:615-621. [2] Link TM, et al. Radiology 1998;209:531-536. [3] Yeung DKW, JMIRI 2005;22:279-285. [4] Griffith JF et al. Radiology 2006;241:831-838.

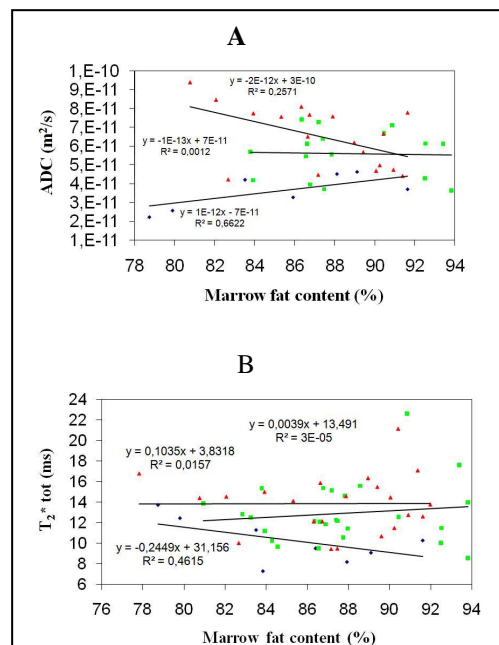


Fig.1 The peculiar behaviour of ADC and T_2^* measured values in the calcaneus spongy bone as function of Marrow fat content percentage (Mfc%). Their linear correlations (R^2 coefficient), and their functional linear dependency $y(x)$ are also showed. Blue diamonds indicate Healthy subjects, green squares indicate Osteopenic subjects and red triangles indicate Osteoporotic ones.