DTI and MRS assessment of cancellous bone quality in femoral neck of healthy, osteopenic and osteoporotic subjects at 3T

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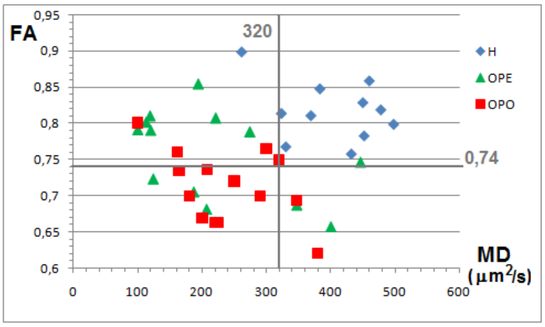
Introduction: Nowadays, the clinical diagnosis of osteoporosis is based on the quantification of bone mineral density (BMD) of those skeletal sites with high trabecular content, such as spine and proximal femur. Dual-energy X-ray absorptiometry (DXA) is the diagnostic tool currently recommended in clinical routine for BMD assessment (1). However, BMD quantification is characterized by a low predictive value on patients' risk of reporting bone fractures (2). This lack of sensitivity is likely to be due to the partial information that BMD provides on cancellous bone (CB) characteristics, assessing exclusively its mineral component (2,3). Other factors, such as topological rearrangement of trabecular bone (TB) microstructure, or composition of bone marrow (BM) may contribute in determining bone strength and its resistance to fractures. Indeed, CB is a porous system characterized by a solid TB network immersed in BM and characterized by different relative percentage of water and fats. Magnetic resonance (MR) techniques applied to CB allow investigation of both trabecular network and BM. An accurate investigation of CB architecture could potentially be obtained using diffusion tensor imaging (DTI) methods (4). DTI has been extensively used to study the structure of ordered biological tissue such as brain, myocardium, intervertebral disc and cartilage. Recently, some authors (5) demonstrated in vitro, that DTI is a promising method to investigate microstructural features of CB, through the study of the diffusive behavior of BM water in CB. Indeed, DTI method suggests that MD may be sensitive to the mean pore sizes increase in CB and that FA may be sensitive to the loss of anisotropy of the trabecolar bone network which occur with the onset of the osteoporotic disease. Other authors demonstrated in bovine bone samples, that water in CB is more prevalent in the boundary zone, while fats are rearranged primarily in the central zone of each pore (6). As a consequence water diffusion plays an important role for the characterization of microstructural features of CB, such as the anisotropy of the TB network. Moreover, the aforementioned observations suggest to detect just the water to perform DTI experiments in CB, and suggest that the water diffusion regime is influenced by fat quantity in BM. In summary, MD and FA values in CB depend on both the TB rearrangement and the marrow fat-water ratio content (FF) amount. Aim of this study was to assess the potential of DTI in combination with ^{1}H-MRS, to evaluate CB quality in the femoral neck of postmenopausal women.

Materials and Methods: 37 postmenopausal women in total (mean age, 69 years; range 52-81 years), underwent a DXA examination in femoral neck, to be classified as healthy subjects (H, n=11), osteopenic (OPE, n=13) and osteoporotic (OPO, n=13) patients on the base of their resulting T-scores (1). MR investigations were performed using a 3.0 T MR imaging system (Achieva, software release 2.5, Philips Healthcare, Best, The Netherlands) with a maximum gradient strength of 80 mT/m and a maximal slew rate 400 mT/m/ms. A 6-channel SENSE torso phased-array coil was used. MRS and coronal diffusion-weighted MR imaging of femoral neck were obtained in each subject using a spin-echo segmented echo-planar imaging (EPI) sequence (b-values 0 and 2500 mm^2/s, TE/TR=104/2500ms, EPI factor=7, number of slices 3, STH=5mm, acquisition matrix = 72x49, rectangular FOV 160x142 mm, NSA=4, along 6 non collinear direction). Single-voxel PRESS-sequence (TE/TR=30/4000ms, voxel:1.5x1.5x1.5cm^3, NSA=32 for selective water and fat resonances quantification was performed. Mean Diffusivity (MD) and Fractional Anisotropy (FA) were obtained from DTI acquisitions using Philips Diffusion Registration tool (version 4.0). To measure MD and FA in the femoral neck zone, a rectangular ROI (1,2x1,5 cm) was placed in the femoral neck location in b=0 image. This ROI was then automatically transposed onto MD and FA maps. FF = $[I_{fat}/(I_{fat} + I_{wat})]$, where I_{wat} is the water peak area (at about 4.65 ppm) and I_{fat} is the sum of three partially overlapping lipid peaks area (at about 0.9, 1.3 and 2.0 ppm) was evaluated from proton spectra. Mean $\pm$ SD values were calculated for each variable. Differences between groups were assessed with ANOVA and multiple comparisons were made with the Bonferroni test. P values <0.05 were considered statistically significant. Receiver Operating Characteristic (ROC) curve analysis was performed to test the sensitivity/specificity of FF and DTI parameters in discriminating between the three bone density groups. All statistical analyses were carried out with SPSS software, version 15.0 (SPSS Inc., Chicago, IL).



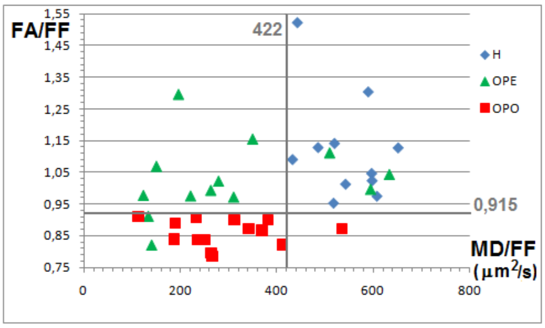


Fig.1 Scatter plots show FA values as a function of MD values (top graph) and FA/FF values as a function of MD/FF values (bottom graph) for each bone density group (normal: blue diamond, H; osteopenia: green triangle, OPE; osteoporosis: red square, OPO). In both plots cut-off values obtained from ROC curve analysis are reported in gray. Please note that, all data of H subjects displayed in FA/FF vs MD/FF graph, are located in a well defined region, for which MD/FF is equal or higher than 422 μm^2/s and FA/FF is equal or higher than 0.915.

Results and discussion: Higher FF was found in OPO patients as compared to H and OPE subjects. Higher MD and FA values were found in H subjects as compared to OPE and OPO patients. FF is able to just discriminate H subjects from OPO ones. Conversely MD and FA are able to discriminate H from OPE, and H from OPO subjects, but these MR parameters are not able to discriminate between OPE and OPO patients. Because both MD and FA are affected by the FF as well as the BMD, MD/FF and FA/FF parameters were considered to improve the diagnostic potential of DTI protocol to discriminate among subjects characterized by different BMD. Cut off values between the three bone density groups were determined using both the couple of parameters: MD, FA, and MD/FF, FA/FF (Fig. 1). Values of MD/FF and FA/FF are characterized by a higher sensitivity and specificity compared to MD and FA values in the discrimination between H, OPE and OPO subjects. By considering MD/FF and FA/FF variables, the sensitivity and the specificity for the detection of H subjects were 100% and 91.3% using MD/FF alone, with a cut-off value of 422 μm^2/s, while they were 92.3% and 85.7% using FA/FF alone, with a cut-off value of 0.915 for selecting OPO patients (see Fig. 1). The concordance between DTI-MRS and DXA method is equal to 81.1%.

Conclusion: We reported, for the first time, MD and FA results obtained from femoral neck of subjects characterized by different BMD, using a DTI-MRS protocol. Although our results are still preliminary, they show that MD/FF and FA/FF parameters, extracted from femoral neck, differentiate among H, OPE and OPO individuals classified according to DXA criteria. In particular, the DTI-MRS method seems to be highly sensitive and specific in identifying H subjects. As a consequence DTI assessment in femoral neck region of the skeleton, in combination with MRS might represent a potential MR procedure to improve the diagnostic confidence of osteoporosis on a single subject basis.

References: 1.WHO Scientific Group. World Health Organ Tech Rep Ser. 2000;921. 2. Kanis JA, *Lancet.* 2002;359:1929-1936. 3. Wehrli FW, et al. *J. Bone Min Res.* 2002;17:2265-2273. 4. Basser PJ, Pierpaoli C. *J Magn Reson B*. 1996;111:209-219. 5. S. Capuani et al. *Solid State NMR*. 2005;28:266-272; 6. S. De Santis et al. *Phys Med Biol.* 2010;55:5767-5785.