Evaluation of bone quality in calcanei of young and postmenopausal women through ADC measurement

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Target audience: Translational researchers interested in noninvasive assessment of bone quality

Purpose: Even though bone mineral density (BMD) has been the accepted standard for osteoporosis diagnosis, BMD has a low predictive value on patients' risk for future fractures[1]. Thus, new approaches for examining patients at risk for developing osteoporosis would be desirable. Recently, a porous system model suitable for investigating the microstructural proprieties of cancellous bone, by using diffusion MRI techniques, was described and experimentally corroborated[2,3,4]. The model is based on the schematic representation for which water is more prevalent in the boundary zone while fat occupies primarily the central zone of each cancellous bone pore[1]. Therefore water component in bone marrow diffuses in the interstitial space between bone and fat and its diffusion process is affected by the strong internal magnetic field gradient (IMFG) located at the interface bone-water[1,4]. With the development of osteoporosis cancellous bone pores became more and more large and interconnected, increasing water apparent diffusion coefficient ADC. Aim of the present work is to test ADC measurement in calcaneus cancellous bone as new potential indicator to evaluate the bone quality. Toward this goal, ADC measurement and its reproducibility was performed together with diffusion signal behaviour study as a function of b value, and correlation between ADC, marrow fat content (Mfc), BMD and age.

Methods and Materials:

Subjects Fifty-eight calcanei in total were studied: nine from young healthy (mean age 33±10, age range 22-45 y), nine from postmenopausal healthy (mean age 64± 6, age range 53-70 y), twenty from osteopenic (mean age 63±8, age range 50-75 y), and twenty from osteoporotic (mean age 66±7, age range 52-74 y) women were investigated at 3.0T. Postmenopausal volunteers were classified as healthy osteopenic or osteoporotic subjects, according to their vertebral T-score values obtained by using QCT. This study was approved by the local Ethics Committee and written informed consent was obtained in all cases before study initiation.

Experiments: ADC in calcaneus was evaluated from DWI images acquired in a single sagittal section of the calcaneus using a 3T Allegra Siemens scanner. A spin-echo segmented echo-planar imaging (EPI) sequence (repetition time, TR=1500 ms, echo time, TE=96 ms; field of view, FOV=192x192 mm^2; matrix, 128x128; epi factor, 7; diffusion gradient along the anterior-posterior direction) was employed in a first phase by using five different b-values (b=0, 1000, 3000, 5000, 8000, 10000 s/mm^2). Then b=8000 s/mm^2 and TE=86 ms was selected to collect data from all subjects. A volume of interest (voxel size, 15x15x15 mm^3) in the central zone of the calcaneus was also selected for collecting ^{1}H spectra (TR/TE=5000/22 ms; number of signal-averages NS=32) using a single-voxel spectroscopy PRESS sequence.

Analysis: ADC values were obtained from DWI images, using the relation: $I_b=I_0 \cdot \exp(-b \cdot ADC) + c$, where I_0 and I_b are the mean signal intensities at b=0 s/mm^2 and b=8000 s/mm^2. All ^{1}H spectra were analyzed using the LC Model method. Mfc was calculated for all subjects according to the following equation: $Mfc = [I_{fat}/(I_{fat} + I_{wat})] \cdot 100$, where I_{wat} is the water peak area (at about 4.7 ppm) and I_{fat} is the sum of partially overlapping lipid peaks.

All measured variables in the calcaneus were compared between the three bone density groups and the young women group by a one-way analysis of variance (one-way ANOVA). Pearson correlation coefficients (r) were calculated to assess linear correlation between pairs of variables for all subjects and for all subjects belonging to each bone density group. A P value less than 0.05 was considered statistically significant.

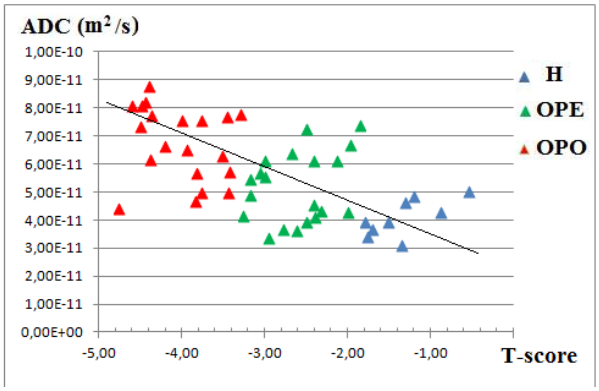

Fig. 1. ADC *vs* T-score measured in osteopenic (green triangle), osteoporotic (red triangle) women and in age matched healthy control (blue triangle).

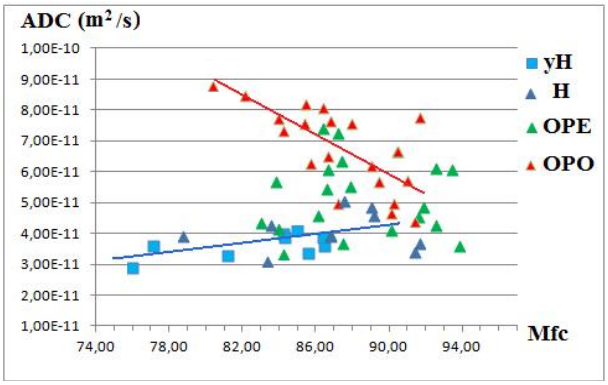

Fig. 2. ADC *vs* Mfc measured in young healthy (light blue square) and healthy (blue triangle), osteopenic (green triangle), osteoporotic (red triangle) postmenopausal women.

Results and discussion: All ADC values of cancellous bone water show a lower ADC value due to the presence of IMFG, as confirmed by simulations. Their short time and long time reproducibility is acceptable. Young healthy women are characterized by the lowest ADC values =[3.6±0.4]*10^{-11}m^2/s and the lowest standard deviation. ADC values were significantly lower in healthy (ADC=[4.1±0.7]*10^{-11}m^2/s) than in osteopenic (ADC=[5.2±1.3]*10^{-11}m^2/s) and osteoporotic (ADC=[6.7±1.3]*10^{-11}m^2/s) subjects. Moreover ADC values significantly discriminate between osteopenic and osteoporotic women. The highest ADC values in osteoporotic group may be a consequence of pore enlargement and increase in interconnections between adjacent pores in the trabecular bone network due to formation of perforations of trabecular plates. A significant linear correlation was found between ADC and T-score values (**Fig. 1**) and no-correlation was found between ADC and age in postmenopausal subjects. On the other hand, a significant correlation (r=0.53) was found between ADC and age when all healthy subjects (young and postmenopausal women) are considered. Although Mfc values didn't discriminate between different bone density groups (according to previous results)[3,5], results displayed in **Fig. 2** show a dependence of ADC values on Mfc in osteoporotic and healthy group. In healthy subjects, the positive linear correlation may indicate both trabecular-bone network and metabolic changes due to normal aging. Please note that for highest Mfc, ADC values of all healthy, osteopenic and osteoporotic women move to a common value. This result is in agreement with the cancellous bone model previously described[2,3] and suggests that postmenopausal women characterized by a low fat content can be better classified as healthy, osteopenic and osteoporotic subjects on the basis of ADC results in calcaneus. Because the yellow bone marrow increases with aging, graph in **Fig. 2** suggests that, ADC investigations could be also useful in pediatric investigations of pathologies involving changes in trabecular-bone density.

Conclusion: In the present study, we have quantified the compartment-specific water ADC changes in calcaneal bone of healthy subjects characterized by a large age range (22-69 y) and of osteopenic and osteoporotic patients at 3.0T employing DWI and MRS techniques. ADC data from human calcanei shows the ability of diffusion measurement to obtain complementary information, compared to those provided by BMD for investigating cancellous bone quality.

References: [1]Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet 2002;359:1929-1936. [2] De Santis S, Rebuzzi M, Di Pietro G, Fasano F, Maraviglia B, Capuani S. In vitro and in vivo MR evaluation of internal gradient to assess trabecular bone density. Phys Med Biol 2010;55:5767. [3]Capuani S. Diffusion in cancellous bone. Micropor Mesopor Mater 2013;178:34. [4]Manenti G, Capuani S, Fanucci E, et al. Diffusion tensor imaging and magnetic resonance spectroscopy assessment of cancellous bone quality in femoral neck of healthy, osteopenic and osteoporotic subjects at 3T: Preliminary experience 2013;55:7. [5]Rebuzzi M, Vinicola V, Taggi F, Sabatini U, Wehrli FW, Capuani S. Potential diagnostic role of the MRI-derived internal magnetic field gradient in calcaneus cancellous bone for evaluating postmenopausal osteoporosis at 3T. Bone 2013;57:155. [6]Wehrli FW, Hilaire L, Fernández-Seara M, Gomberg BR, Song HK, Zemel B, Loh L, Snyder PJ. Quantitative magnetic resonance imaging in the calcaneus and femur of women with varying degrees of osteopenia and vertebral deformity status. J Bone Min Res 2002;17:2265-2273.