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Water diffusion in cancellous bone

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ABSTRACT

In this paper, by means of in vivo experiments, a porous system model suitable for investigating the structural properties of cancellous bone by using diffusion MRI techniques is described and corroborated. Toward this goal a cancellous bone model is described on the basis of some recent evidence obtained in both calf bone samples and human vertebrae. Then, the calcaneus and the femoral neck of healthy, osteopenic and osteoporotic subjects were investigating, as classified by the bone mineral density (BMD) parameter, by measuring the apparent diffusion coefficient (ADC), together with the marrow fat content (Mfc) and assessing associations between bone mineral-density index T-score, Mfc and ADC. MR spectroscopy (1H-MRS) and diffusion weighted imaging (DWI) with *b*-value = 2500 s/mm^2 and *b*-value = 8000 s/mm^2 to investigate femoral neck and calcaneus, respectively, were obtained in each subject using a 3T MR scanner. One-way ANOVA and Pearson correlation analyses were applied.

ADC results as a function of Mfc and BMD obtained in calcaneus and femoral neck, seem to validate the cancellous bone model described in this paper. Although the MR results are still preliminary, and based on a small number (n = 60) of subjects, they suggest the ability of the ADC parameter to identify enhanced risk of osteoporosis. As a consequence, diffusion assessment in combination with 1H-MRS investigations obtained in large populations, might increase our pathophysiological understanding of osteoporosis and might also improve the diagnosis of osteoporosis.

1. Introduction

Cancellous bone tissue is a marvellous biological material. It is a complex porous composite of calcified tissue (the trabecular plates network) interdispersed with soft marrow. Cancellous bone is characterized by a broad range of pore sizes that are associated with different degrees of interconnection. The bone marrow in pores consists of different relative percentages of water and fat, depending on the particular skeletal site [1]. Moreover, water is more prevalent in the boundary zone while fat occupies primarily the central zone of each pore, as recently demonstrated [2]. Water in the boundary zones of pores is also due to the presence of the endosteum, a thin membrane of soft tissue comprised of a linear chain of cells that lines the medullary cavity [3].

Pore sizes in human cancellous bone are in the range 1μm–1 mm, where inter trabecular plates space ranges approximately from 100μm to 1–2 mm. On the other hand, the space between fat and bone in the boundary of each pore ranges from less than 1 to 10–20 μm [3].

The importance of studying the cancellous bone microstructure lies in the fact that the bone may fracture. The ability of bone to resist fracture depends on its porous microstructure, on the quality of the connectivity of the trabecular solid phase and on the quality of bone marrow [4]. Osteoporosis is the bone disorder where bone strength is reduced, resulting in increased risk of fracture. With the development of osteoporosis, pores of cancellous bone become more connected (i.e. trabecular network becomes more disconnected), and the mean size of pore diameter and the bone marrow fat content (Mfc), increases [5,6]. The clinical diagnosis of osteoporosis is currently performed on the basis of bone-mineral density (BMD) quantification [7]. However, the poor correlation between fracture prevalence and BMD [8,9] indicates a search for new methods to assess osteoporosis disease in bones.

An accurate investigation of cancellous bone tissue could potentially be found with diffusion-weighted imaging (DWI) [10] and diffusion tensor imaging (DTI) [11] magnetic resonance (MR) methods.

During the past few decades, DWI and DTI have become powerful MR methods to provide quantitative information on microstructural rearrangement and changes in both material [12,13] and human tissue investigations [14,15]. Specifically, diffusion imaging methods allow the measurement of water proton displacements at the cellular level by probing motion on the micrometer length scale which is orders of magnitude smaller than the macroscopic MR resolution (usually 1–3 mm in clinical scanners).

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Despite the great potential of diffusion methods, DWI of human bone tissues has not attracted much attention during the last years [16] due to two main problems: (1) technical issues mainly related to magnetic susceptibility variation and motion sensitivity [16]; (2) the lack of a valid cancellous bone model. Currently, thanks to the development of high performance magnetic field gradients and parallel imaging techniques, the main technical problems have been solved.

In this paper, by means of in vivo experiments, a porous system model is described and corroborated, suitable for investigating the structural properties of cancellous bone by using diffusion techniques. Towards this goal a cancellous bone model is described on the basis of some recent evidence obtained in both calf bone samples [2,17–18] and human vertebrae [19–22]. The underlying evidence exploited to develop the cancellous bone model are the following:

(1) water is more prevalent in the boundary zone while fat occupies primarily the central zone of each cancellous bone pore [2]; (2) bone marrow fat increases from axial skeleton (vertebral site) to peripheral skeletal sites. Mfc values extracted from the vertebrae, the femoral neck and the calcaneus of postmenopausal women was found to range from 50% to 70%, 60% to 88% and 78% to 98%, respectively [1,2,5,6,19,22,23]. Moreover, it has been recently underlined that osteoporotic decreases in the BMD correlate with increases in the bone-marrow fat in the lumbar vertebrae [19,20] and in the proximal femur [24].

The calcaneus and the femoral neck of healthy, osteopenic and osteoporotic subjects were investigated using a 3T MRI scanner as classified by the BMD parameter, by measuring the apparent diffusion coefficient (ADC), together with the Mfc and assessing associations between BMD, Mfc and ADC.

2. Materials and method

Thirty postmenopausal women (mean age, 64.5 ± 5.8 years, GROUP I), were recruited to investigate the calcaneus and thirty postmenopausal women (mean age, 71.5 ± 4.2 years, GROUP II), were recruited to investigate the femoral neck. The study was approved by the local Ethics Committee, and written informed consent was obtained from all subjects before entering the study. All subjects of GROUP I underwent quantitative computer tomography (QCT) to assess trabecular BMD of lumbar vertebrae L1–L3. T-scores were calculated for each woman, and subjects were grouped into three categories according to the following diagnostic classification criteria based on QCT BMD [25]: healthy, T-score $\geqslant -1.8$ (10 subjects), osteopenic, $-3.3 <$ T-score < -1.8 (10 subjects), osteoporotic, T-score $\leqslant -3.3$ (10 subjects). All subjects of GROUP II underwent femoral densitometry (DXA). DXA BMDs were measured in femoral neck and T-scores were calculated for each subject. The study population was divided into three groups [7]: healthy, T-score $\geqslant -1.0$ (10 subjects), osteopenic, $-2.5 <$ T-score < -1.0 (10 subjects), osteoporotic, T-score $\leqslant -2.5$ (10 subjects).

ADC was evaluated in GROUP I from DWI images acquired in a single sagittal section of the calcaneus using a 3T Allegra Siemens scanner. A diffusion weighted segmented echo-planar imaging (EPI) sequence (repetition time, TR = 1500 ms, echo time, TE = 86 ms; field of view, FOV = 192 $\times$ 192 mm^2; matrix, 128 $\times$ 128; epi factor, 7; diffusion gradient along the anterior-posterior direction) at two different b-values (b = 0 and 8000 s/mm^2) was run[2].

ADC was evaluated in GROUP II from DWI images acquired in coronal section of the femoral neck using a 3T Achieva, Philips scanner. A diffusion weighted segmented EPI sequence (TR/TE = 2500/104 ms; FOV = 160 $\times$ 142 mm^2; matrix, 72 $\times$ 49; epi factor, 7; diffusion gradient along left–right direction) at two different b-values (b = 0 and 2500 s/mm^2) was run [26]. The MRI imaging time for any patient was approximately equal to 5 min.

ADC values of bone-marrow water were obtained from DWI images, using the relation:

$$I_b = I_0 \cdot \exp(-b \cdot \mathrm{ADC}) \quad (1)$$

where I_b and I_0 are the mean signal intensities in the femoral neck region at b = 2500 s/mm^2 (for femur) or b = 8000 s/mm^2 (for calcaneus) and 0 s/mm^2, respectively. Values of b were selected as 2500 s/mm^2 (to investigate femoral neck which is characterized by a mean ADC of bone-marrow water equal to 3×10^{-10} m^2/s) and b = 8000 s/mm^2 (to investigate calcaneus which is characterized by a mean ADC of bone-marrow water equal to 5×10^{-11} m^2/s) to obtain the best compromise between a sufficient signal to noise ratio (SNR) of DWI and ADC maps (Fig. 1) and a sufficient diffusion weighted to detect slow diffusion regime of bone marrow water restricted between fat and bone [2]. In both cases the attenuation factor was approximately around 70–80% [26]. Moreover, a Gaussian diffusion approximation regime was assumed [27], as suggested by the experimental mono-exponential decay of the diffusion-sensitised EPI signal as a function of b values, recently shown in femoral neck [26].

A volume of interest (voxel size, 15 $\times$ 15 $\times$ 15 mm^3) in the central zone of the calcaneus (GROUP I) and in the femoral neck (GROUP II) 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.

All spectra were analyzed using the LC Model method [28]. Mfc was calculated for all subjects according to the following equation: $\mathrm{MFC} = [I_{\mathrm{fat}} + I_{\mathrm{wat}})] \cdot 100$, where I_{wat} is the water peak area (at about

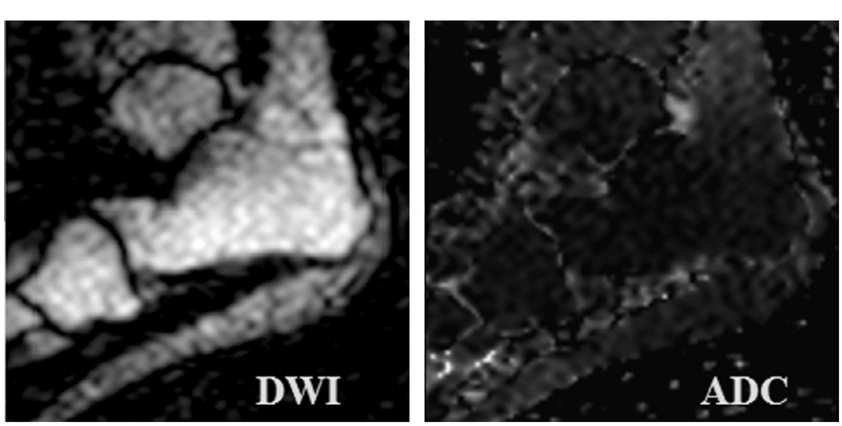

Fig. 1. An example of DWI (left) and ADC (right) sagittal view maps of a portion of foot examined in a 62-year-old woman. See the text for further details.