Internal gradient evaluation in spongy bone as a potential NMR parameter to detect osteoporosis disease

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Introduction

Osteoporosis is a bone disease associated with an increased risk of bone fracture. The main features of osteoporosis are a low bone mass and a decrease in the architectural competence. Currently, the diagnosis of osteoporosis is based on bone mineral density (BMD) measurements. However, the poor correlation between fracture prevalence and BMD assessments suggests that other factors contribute in determining bone fragility. Indeed, the trabecular micro architecture of spongy bones affected by osteoporosis is characterized by structural rearrangements and/or disruption, and the quality of the bone marrow is altered. So far, T_2* is the most used MR parameter to evaluate spongy bone status [1]. T_2* probes the micro-structure of the trabecular bone, due to its sensitivity to the microscopic field in-homogeneities which are caused by differences in magnetic susceptibility between the solid bone structure and the liquid bone marrow. Several studies confirmed that an increase of the inter-trabecular space, which occurs in patients with osteoporosis, prolonges T_2* value. In this study we propose an alternative way of evaluating the influence of the susceptibility differences in spongy bone which are linked to trabecular bone density and structural rearrangements. It is based on the evaluation of the internal gradient G_i extracted from the Spin-Echo (SE) decay, which is usually used for the investigation of porous systems [2,3]. When considering the spongy bone, G_i values are not only affected by differences of magnetic susceptibility, but also by fat and water diffusion of the trabecular bone marrow. Aims of this work were: 1) to evaluate the G_i of the spongy bone in vitro, in order to relate this quantity with bone properties; 2) To assess, in vivo, the potential ability of G_i to describe the spongy bone status when applied to human calcanei.

Methods and Materials: In porous systems as the spongy bone, which are characterized by strong internal gradients G_i is no longer possible to describe the SE signal decay as: $S(TE)=M_0\exp(-TE/T_2)$ because the influence of G_i must be considered. As a consequence, the SE decay is more properly described by: $S(TE)=M_0\exp(-TE/T_2^{true}-(\gamma G_i)^2 x D x TE^3/12)$, which takes also into account the spin diffusion D between the two pulses in regions of different magnetic field [2,3,4]. Considering this contribution, it is possible to quantify the G_i with a simple fitting procedure. In this study, Gi was obtained along x direction, perpendicular to the static magnetic field from the Levengerg-Marquardt (L-M) fit using measured D (in the same direction x) and T_2^{true} parameters. Spongy bone samples were excised from calf distal femur and analyzed using a 9.4 T Bruker Avance NMR system with a micro-imaging probe. Spectroscopic CPMG sequence (TE=100μs, TR=1s) was applied to measure T_2^{true}, and PGSTE sequence (TE/TR=18/6000ms, Δ=400ms, b values from 200 to 60000s/mm^2) was performed to measure D for both fat and water components in bone marrow. A MSME sequence at various TEs (6,8,10,14,18,20,24,30,40,60,80ms), TR=1000ms, FOV=6mm, matrix 256x256, slice thickness 0.5mm, pixel dimension 23x23μm^2 was applied to obtain SE images in three regions with different trabecular density, as reported in Fig. a) and b). The trabecular bone density across the sample in fig. b) varied continuously from the lower zone, where the inter-trabecular space were larger (fig. a.3), to the upper zone where they were closely spaced and smaller (fig. a.1). In-vivo study were performed on human calcanei of three subjects (two women, one 24 and one 40 years old, and one 33 years old man). We hypothesized that, between the two women, there was a different spongy bone quality, due to their different age. Moreover, more packed trabeculae are expected to characterize the spongy bone in men compared to women. Sagittal view SE images (Fig. d)) were acquired at 3T using SEMC sequence at various TEs (20, 30, 40, 50, 80, 100 ms), TR=1500ms, FOV=192mm, matrix 256x256, slice thickness 5mm, while the diffusion coefficient D was evaluated as ADC from sagittal diffusion weighted images using a SE segmented-EPI sequence at two different b-values (0 and 8000 s/mm^2) with diffusion gradient along phase direction, TE/TR=109/2500ms. The G_i was obtained by a fitting procedure selecting all the calcaneus area (Fig. d) and e)).

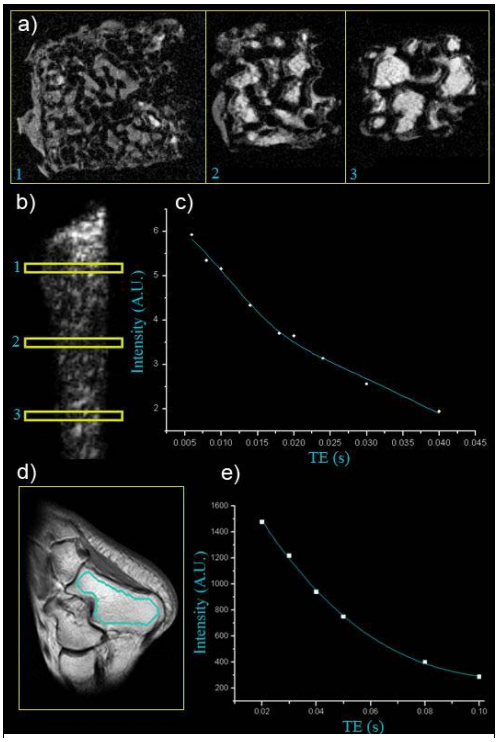

Fig. 1: a) SE images (TE=4,3ms) of a calf sample in three slices at different trabecular bone density. b) Slices positioning across the sample c) L-M fit of the SE signal from one slice d) SE images (TE=10ms) of a calcaneus spongy bone and the considered region to evaluate G_i e) L-M fit of the SE signal from the selected calcaneal zone

Results: The mean G_i value of water bone marrow decreased according to the water peak area. Moreover a decreasing G_i value was also evident when moving from zones adjacent to the trabecula (G_i=454mT/m in zone large 1 pixel close to trabecula) to zones located in the centre of the inter-trabecular space (G_i=288mT/m in zone large 5 pixel from trabecula). Conversely, the mean G_i value of fat bone marrow increased according to the fat peak area, and, again, when moving from zones adjacent to the trabecula (G_i=353mT/m in zone large 1 pixel close to trabecula) to zones located in the centre of the inter-trabecular space (G_i=491mT/m in zone large 5 pixel from trabecula). Moreover, by considering all areas from the selected slices (Fig. a)), the mean G_i was higher in the slice characterized by an higher trabecular bone density (G_i=6258±812mT/m) (a.1), it assumed an intermediate value in the slice characterized by an intermediate trabecular bone density (G_i=4398±665mT/m) (a.2), and it was lower in the slice characterized by a lower trabecular bone density (G_i=3712±451mT/m) (a.3). G_i was higher in the male subject (G_i=894±113mT/m), who showed a fat fraction in bone marrow equal to 93% and an ADC=(4.5±0.9)*10^{11}m^2/s. Both female subjects showed a fat fraction in bone marrow equal to 87%, with no age related differences. Conversely, the G_i values were remarkably different with a lower value (256±55mT/m) in the 40 years old and a higher value (G_i=477±40mT/m) in the 24 years old subject.

Discussion and Conclusion: As expected, we found that G_i magnitude in calf spongy bone samples increases according to the increase of trabecular density. Moreover, by evaluating G_i, ADC, T2 and the relative quantity of both water and fat bone marrow components in a single pixel, we may conclude that the G_i strongly depends on trabecular bone density and on the water to lipid fraction in bone marrow. Consistently the water to lipid fraction in bone marrow correlates with the ADC. These findings are relevant in suggesting the potential role of G_i as a reliable marker of the spongy bone status. Moreover, they clarify the properties underlying the peculiar contrast which is observed in DWI and DTI maps of the spongy bone. It has been recently indicated that BMD and architectural rearrangements of the trabecular bone are not the only factors which contribute to determine the bone resistance to fracture, but other components, such as the bone marrow and several proteins are involved as well. In this scenario, our results obtained in vivo indicate G_i as a potential diagnostic marker of osteoporosis. In fact the in vitro and in vivo results reported here, demonstrate that G_i values depend on both solid trabecular bone characteristics and liquid interstitial bone marrow quality.

References [1]Wehrli FW et al. Radiology 1991;179:615-621. [2]Jara H. et al., JMRI 1994;4:787-797; [3] Callaghan P.T, "Principles of Nuclear Magnetic Resonance Microscopy" Oxford University Press, Oxford (1991); [4] Sealand J, et al. Phys.Rev. E 2004;70:051305.