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Potential diagnostic role of the MRI-derived internal magnetic field gradient in calcaneus cancellous bone for evaluating postmenopausal osteoporosis at 3 T

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ABSTRACT

Introduction: Bone mineral density (BMD) result has a low predictive value on patients' risk for future fractures. Thus, new approaches for examining patients at risk for developing osteoporosis would be desirable. Magnetic resonance (MR) investigations in cancellous bone have been shown to yield useful quantitative information on both trabecular-bone microstructure and bone marrow composition.
This work was undertaken to address the hypothesis that the effective internal magnetic field gradient (IMFG), a new MR parameter, discriminates between healthy, osteopenic and osteoporotic postmenopausal women, classified on the basis of bone mineral density (BMD) criteria. The work builds on preliminary results indicating that IMFG, measured in trabecular-bone pores and quantified by spin-echo decay and water diffusion MR near the bone–bone marrow interface depends on both the bone marrow water rate of diffusion and the magnetic susceptibility difference ($\Delta\chi$) between water and bone.
Materials and methods: MR relaxometry, MR spectroscopy and diffusion-weighted MR imaging of the heel was performed in fifty-five women (mean age, 62.9 ± 6.6 years) at 3 T. Moreover, in order to study the reproducibility of IMFG measurement, five young women (mean age 31.0 ± 3.2 years; age range, 28–36 years) were scanned and rescanned. The study protocol was approved by the local Ethics Committee. Quantitative Computer Tomography (QCT) of the L1–L3 vertebral segments was performed to classify the postmenopausal women into three groups according to QCT BMD: healthy (n = 8); osteopenic (n = 25); and osteoporotic (n = 22). In all subjects, BMD T-scores, marrow fat content (Mfc), T2*, apparent diffusion coefficient (ADC) and IMFG (estimated from the additional spin-echo decay due to diffusion of water in local magnetic field gradients), were assessed in the whole calcaneus as well as in three calcaneal subregions: subtalar, tuber calcaneus, and cavum calcaneus. Between-group comparisons to assess group differences and Pearson correlation analysis were performed. Short and long-term coefficients of variation (CV_S and CV_L, respectively) were evaluated in young subjects.
Results: Reproducibility of the IMFG measurement was satisfactory. No significant difference was found in the IMFG measurement performed in both calcaneus and subtalar calcaneal region between the two separate sessions comprised of five young women. Mfc did not significantly differ between groups. The IMFG in the subtalar region was significantly different between all three groups ($P < 0.01$), being greatest in healthy women, intermediate in those with osteopenia, and lowest in osteoporotic subjects. Conversely neither T2* nor ADC is able to discriminate healthy subjects from those with osteopenia and osteoporosis. Increased inter-trabecular space, as it typically occurs in patients with osteoporosis, modifies water diffusion, conferring higher ADC values, thereby lowering the IMFG.
Conclusion: The IMFG measured in the calcaneal subtalar region shows a high ability in identifying healthy subjects. The new quantitative MR method based on measurement of the IMFG may provide a new means for assessing patients with osteoporosis.

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Introduction

Osteoporosis is a systemic skeletal disease that predisposes bone to fracture. The condition is characterized by a decrease in bone density

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and strength, resulting in increased bone fragility. The clinical diagnosis of osteoporosis is currently performed on the basis of bone mineral density (BMD) [1]. However, the poor correlation between fracture prevalence and BMD [2,3] suggests that other factors may contribute to bone fragility, such as micro-architectural deterioration of bone tissue, increased bone porosity, and alteration of bone marrow quality [3–5].

Magnetic resonance (MR) techniques applied to cancellous bone allow investigation of both trabecular network and bone marrow. MR relaxometry has been shown to yield quantitative information on trabecular-bone density (mainly via T_2^* measurements) as well as on bone micro-architecture [3,6–8]. T_2^* probes the trabecular-bone microstructure by virtue of its sensitivity to magnetic susceptibility differences ($\Delta\chi$) between bone and marrow [6]. Therefore, an increase in inter-trabecular space, which typically occurs in osteoporosis, prolongs marrow T_2^* [3,6–8].

Further, proton MR spectroscopy of cancellous bone marrow provides information on bone marrow composition via analysis of marrow fat content (Mfc). At vertebral and femoral skeletal sites, Mfc has been reported to correlate negatively with BMD and positively with age [9–14]. Diffusion MR has also been used to investigate the lumbar vertebral bone although so far failed to show a clear relationship between apparent diffusion coefficient (ADC) and either subjects' age or BMD [15–18]. On the other hand, diffusion assessment in the femoral neck [19] and calcaneus [20] has recently suggested the great potential of diffusion tensor imaging (DTI) [19,21] and diffusion-weighted imaging (DWI) [20] techniques for the pathophysiological understanding of osteoporosis disease.

A new potential surrogate marker for osteoporosis, the internal magnetic field gradient (IMFG), has recently been proposed [22,23]. In cancellous bone, the susceptibility mismatch between the solid matrix and interstitial liquid marrow generates internal gradients at the interface between the bone and marrow [22–27].

The present work builds on recent work showing that in cancellous bone the water component in the bone marrow is prevalent in the boundary zones of the pores, while fat occupies the central inter-trabecular space [23]. Water in the boundary zones of pores is located in the endosteum, a thin membrane of soft tissue that lines the medullary cavity. Moreover, due to a biological division of the bone marrow compartment, granulocytes and other non-fat entities accumulate at the boundary of the marrow space adjacent to the endosteum [28].

An estimate of the IMFG can be obtained from the spin-echo (SE) signal by quantifying the additional decay of the echo amplitude due to diffusion of water in local magnetic field gradients [23], analogous to an approach practiced to investigate porous media [29,30]. The local IMFG, obtained using the aforementioned method, is a temporally averaged quantity since the water molecules sense a multitude of local gradients as they diffuse near the interface between the fatty marrow and bone.

In micro-imaging experiments previously performed in cancellous bone samples water IMFG was found to be proportional to the trabecular-bone density [23]. Furthermore, preliminary data obtained in vivo from the human calcaneus at 3 T [23] indicate a progressive reduction of the IMFG with age, suggesting IMFG to parallel the physiological reduction of trabecular-bone density.

The aim of the present work was to assess the potential of IMFG to detect trabecular-bone status in postmenopausal women. Toward this goal we examined the heel of healthy, osteopenic and osteoporotic subjects at 3 T, as classified by quantitative computed tomography (QCT) BMD, by measuring the IMFG at various calcaneal sites and assessing its associations with T-scores, Mfc, T_2^* and age.

Materials and methods

IMFG and T_2^*

In the trabecular bone, the susceptibility mismatch between the solid matrix and interstitial bone marrow generates internal gradients of magnitude depending on the geometry and orientation of the trabeculae with respect to the static magnetic field direction scaling with magnetic field strength. The interface separating two materials of different magnetic susceptibility gives rise to an induced local magnetic field B_{ind}, which produces heterogeneities in the static magnetic field B_0 generating the so-called internal gradient g_i. For surfaces with complex geometries the calculation of B_{ind} is difficult but the following relation is well known [31]:

$$B_{ind} \propto \Delta\chi B_0 A \cos(\alpha) \tag{1}$$

where $\Delta\chi$ is the susceptibility difference between the two materials, A is the surface separating the materials and α the angle between the static field and the surface normal.

The gradient-echo (GE) signal is given as:

$$S(\mathrm{TE}) = S(0)\exp\left(\frac{-\mathrm{TE}}{T_2^*}\right) \tag{2}$$

with $S(\mathrm{TE})$ being the signal intensity at time TE, $S(0)$ the signal intensity at time $\mathrm{TE} = 0$ and T_2^* depending on the local magnetic field heterogeneities ΔB (due to the static and transient magnetic field) and on T_2 spin–spin relaxation time (linked to the intrinsic coherence loss of the spin system):

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma\Delta B \tag{3}$$

Dephasing of the transverse magnetization due to susceptibility differences produces T_2^* shortening. Thus, the resulting loss in coherence becomes greater as the fraction of the solid network in the surrounding homogeneous liquid spin system increases. Conversely, the increase in trabecular spacing reduces the spatial field inhomogeneity, thereby prolonging T_2^*.

The decay of the GE amplitude is the result of coherence loss in the static dephasing regime phase [32,33]. In this regime, MR signal decay resulting from the local differences in the nuclear frequencies occurs faster than the diffusion phenomena. As a consequence diffusion effects are negligible in the GE signal decay [32,33]. In contrast, a spin-echo (SE) type sequence (such as the MCSE sequence used in this work) is less sensitive to induced magnetic field inhomogeneities. This is because the 180° RF pulse refocuses dephasing from static magnetic field inhomogeneity. However, in the trabecular bone, diffusion of water in the local magnetic field gradients becomes important; molecules interchange their positions resulting in a small phase difference between their nuclear magnetic moments and this action generates an irreversible signal loss [34], thereby acting as a mechanism for irreversible (i.e. T_2) signal loss. In this case the signal decay, as a function of TE, is given by [34–36]:

$$\begin{aligned} S(\mathrm{TE}) &= S(0)\exp\left(-\frac{\mathrm{TE}}{T_2^{\mathrm{APP}}}\right) \\ &= S(0)\exp\left[-\left(\frac{\mathrm{TE}}{T_2}\right) - \frac{1}{12}(\gamma\cdot\mathrm{IMFG}\cdot\mathrm{TE})^2\cdot\mathrm{ADC}\cdot\mathrm{TE}\right] \end{aligned} \tag{4}$$

where ADC is the apparent diffusion coefficient, IMFG is the effective internal magnetic field gradient and:

$$\frac{1}{T_2^{\mathrm{APP}}} = \frac{1}{T_2} + \frac{1}{12}(\gamma\cdot\mathrm{IMFG}\cdot\mathrm{TE})^2\cdot\mathrm{ADC} \tag{5}$$

is the apparent transverse relaxation rate.

Thus, in SE-type measurements of porous systems, the additional decay of the echo amplitude is due to diffusion of mobile molecules in the effective local magnetic field gradient, IMFG. As a consequence, in porous systems such as in the trabecular bone, IMFG can be quantified

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