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Magnetic resonance imaging evaluation of weight-bearing subchondral trabecular bone in the knee

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Abstract

Objective—Changes in weight-bearing subchondral bone are central to osteoarthritis (OA) pathophysiology. Using MR, knee trabecular bone is typically assessed in the axial plane, however partial volume artifacts limit the utility of MR methods for femorotibial compartment subchondral bone analysis. Oblique-coronal acquisitions may enable direct visualization and quantification of the expected increases in femorotibial subchondral trabecular bone.

Methods—MR acquisition parameters were first optimized at 3 Tesla. Thereafter, five volunteers underwent axial and coronal exams of their right knee. Each image series was evaluated visually and quantitatively. An anatomically standardized region-of-interest was placed on both the medial and lateral tibial plateaus of all coronal slices containing subchondral bone. Mean and maximum marrow signal was measured, and “bone signal” was calculated.

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Results—The MR acquisition had spatial resolution $0.2 \times 0.2 \times 1.0$ mm and acquisition time 10.5 min. The two asymptomatic knees exhibited prominent horizontal trabeculae in the tibial subchondral bone, while the one confirmed OA knee had disorganized subchondral bone and absent horizontal trabeculae. The subchondral bone signal was 8–14% higher in both compartments of the OA knee than the asymptomatic knees.

Conclusion—The weight-bearing femorotibial subchondral trabecular bone can be directly visualized and changes quantified in the coronal-oblique plane. Qualitative and quantitative assessments can be performed using the resultant images and may provide a method to discriminate between the healthy and OA knees. These methods should enable a quantitative evaluation of the role of weight-bearing subchondral bone in the natural history of knee OA to be undertaken.

Keywords

Knee; MR; Subchondral bone; Osteoarthritis; Trabecular bone; Osteoporosis

Introduction

Changes in subchondral and adjacent trabecular bone are central to osteoarthritis (OA) pathophysiology. Although damage to articular cartilage can occur in people with early OA, evidence suggests that subchondral bone is also involved [1–11], motivating evaluation of bone changes in the OA population.

The structure and characteristics of the subchondral trabecular bone of the human OA knee have not been evaluated longitudinally in vivo using MR or any other 3D imaging technique. Human [12, 13] and equine [14] cadaveric MR and micro-CT studies indicate subchondral bone volume fraction increases with OA. Macroradiograph studies [15–18] indicate subchondral bone trabeculae increase in number and extent with OA, and, based on fractal analysis, possibly overlay regions of bone loss [15]. This finding is in agreement with radiographic findings of subchondral plate thickening and sclerosis [19, 20] in patients with established osteoarthritis. DXA [9, 21–26] data suggest subchondral bone density is increased in knees with radiographically demonstrated sclerosis. Bone scans [27, 28] of the hand and knee have demonstrated bony pathology prior to radiography, and potentially identify and differentiate progression to bone formation, remodeling, or OA. It would be helpful to use 3D imaging to characterize changes in the subchondral bone-articular cartilage functional unit in a longitudinal population-based study such as the Osteoarthritis Initiative (OAI).

MR is useful for longitudinal assessments because it is noninvasive and does not require contrast agents or utilize ionizing radiation. However, MR of in vivo trabecular architecture can require long acquisition times (19 min) [12, 29, 30]. Recently, shorter time acquisitions have been evaluated using higher signal-to-noise ratio (SNR) 3 Tesla (T) MR systems [31–37].

MR images of knee trabecular bone are traditionally acquired in the axial plane [29, 37–39]. In this orientation, however, the lowest image resolution (slice) is parallel to the articular surfaces of the femorotibial compartments and orthogonal to the long axis of the major trabeculae. While excellent for assessing the patellofemoral trabecular structure, the axial plane does not provide good visualization of the femorotibial subchondral bone because the slices containing the subchondral bone have partial volume averaging with the joint [40]. Coronal acquisitions directly visualize the femorotibial subchondral bone, and, thus, may be sensitive to the presence and progression of OA.

Our objectives were to optimize the 3 T MR acquisition, qualitatively assess the ability of coronal and axial 3D images to visualize the weight-bearing subchondral femorotibial bone, and assess the utility of coronal 3D images for quantitative analysis.

Methods

This study was performed with the local Institutional Review Board approval in accordance with the Declaration of Helsinki.

The MR acquisition parameters of an axial 3D gradient-recalled echo (GRE or FISP) sequence were first optimized at 3 T (Trio, Siemens Medical Solutions, Erlangen, Germany) using a quadrature transmit/receive knee coil (USA Instruments, Aurora, OH). Historically, 1.5 T parameters [29, 38, 41–43] for trabecular bone used an axial 3D GRE acquisition with echo time (TE) 4.5 ms, repeat time (TR) 30 ms, flip angle 40°, and spatial resolution 0.195×0.195×1 mm. The TR we used was decreased to 20 ms to shorten the acquisition because of the expected increase in SNR at 3 T [35, 36]; all other variables were held constant. Thereafter, the epiphyseal marrow signal, SNR, and contrast-to-noise ratio (CNR) compared to muscle and subcutaneous fat were maximized by systematically varying the flip angle between 10° and 70°. Signal was measured in the mid-tibial plateau, medial subcutaneous fat, soleus muscle, and in a medial region outside the knee (noise). The bone marrow signal, SNR, and bone marrow-to-subcutaneous fat CNR as well as bone marrow-to-muscle CNR were plotted as a function of flip angle. This optimization was performed in two volunteers, one asymptomatic and one with clinical and radiographic diagnosis of knee OA.

The double coronal-oblique orientation was used, as previously described for weight-bearing femoral and tibial cartilage morphometry [44, 45]. This orientation positions the posterior edge of the medial and lateral femoral condyles in the same slice [44]. Thereafter, the head/foot orientation is aligned parallel to the femoral diaphysis [45]. This reproducible orientation has provided reliable assessment of femorotibial cartilage loss in OA by optimizing the measurement plane to be perpendicular to weight-bearing knee cartilage and subchondral bone [44, 46, 47].

The optimized acquisition parameters of the coronal-oblique 3 T MR acquisitions for visualization and quantitation of femorotibial subchondral trabecular bone were as follows: 1 mm slice thickness, in-plane spatial resolution 0.2×0.2 mm, 12 cm imaging field-of-view, 512×512 matrix (interpolated to 1024×1024), 72 slices, TE 4.92 ms (fat-water in-phase), TR 20 ms, flip angle 50°, readout bandwidth 180 Hz/pixel, phase encode right/left, and no partial Fourier reconstruction options. With these parameters, the chemical shift artifact of 2.4 pixels shifted superior, outside the femoral subchondral bone (Fig. 1). The double oblique-coronal acquisition required 10.5 min.

Five volunteers were recruited for the purpose of acquiring measurements from subjects with a spectrum of right knee pain severity and clinical disease. Volunteers were at least 40 years old and did not have inflammatory arthritis, arthroplasty, or any MR contraindications. Only one subject had prior radiographs. Both an axial and a coronal-oblique 3D GRE were acquired of the right knee for each participant and basic demographic information as well as the frequency and severity of knee symptoms were recorded.

The axial and coronal images were evaluated for qualitative differences between the tibial plateaus. A standardized region-of-interest (ROI) was manually placed on all coronal slices containing medial tibial subchondral bone (superficial levels 1 and 2 [10]), and the mean and maximum signal intensities were then measured (Analyze version 7.0, Mayo Clinic, Rochester, MN). The ROI dimensions were approximately 200×50 voxels with slight variation because the superior margin was drawn to conform to the shape of the cartilage-

bone interface, including the subchondral bone but excluding osteophytes and articular cartilage (Fig. 1). The tibial plateau was selected for manual measurement because its contour was flatter than the femoral condyle, optimizing the uniformity of the ROI size. In the future, use of an automated analysis method should allow measurement of both bones. “Bone signal” of the ROI, defined as $1 - (\text{mean signal}/\text{maximum signal})$, was used to estimate the percentage of bone within the ROI (akin to bone volume fraction, but without coil inhomogeneity correction [40]). Average bone signals for the central 20 slices (weight-bearing portion) of each femorotibial compartment were calculated for all subjects. Bone signal topographs of the medial and lateral tibial plateaus were created by plotting the bone signal for each coronal slice for each patient versus the slice location in each knee.

Results

Parameter optimization

For both volunteers, a flip angle greater than 45° resulted in no additional increase in absolute bone marrow signal (Fig. 2), and a flip angle greater than 50° resulted in no additional increase in SNR (Fig. 3). The CNR between bone and muscle did not vary substantively as a function of the flip angle (Fig. 4) whereas the CNR between bone and subcutaneous fat was minimized at a flip angle of 35° . Thus the optimal 3 T flip angle was 50° with a TR of 20 ms for epiphyseal bone marrow. This finding was independently confirmed on the same volunteers at a later date and the optimized flip angle was identical.

Bone measurements

The five subjects in the measurement group (age 48.6 ± 2.3 years; Table 1) included two without any knee pain or other clinical OA symptoms; one with rare, mild knee pain; one with constant, severe medial knee pain; and one with radiographic medial knee OA (Kellgren Lawrence grade 3 [19]).

Qualitative image review focused on easily visualized differences in the subchondral and trabecular bone of the tibial plateau (Fig. 5a, b). As expected from clinical MR imaging, the axial images provided limited insight to the femorotibial subchondral bone compared to the coronal-oblique images. The subjective findings include (1) organized horizontal trabeculae in asymptomatic knees, which were absent in the OA knee; (2) smooth contour of the tibial subchondral bone in the asymptomatic knees, which was irregular in the OA knee; (3) flattened tibial plateau in the OA knees, which was not seen in the asymptomatic knees; and (4) apparently thickened subchondral bone on the medial tibial plateau and the medial femoral condyle of the OA knee. On the OA knee (Fig. 5b), the thickened subchondral bone on the medial femoral condyle was substantially greater than the chemical shift artifact found on the lateral femoral condyle.

Bone signal is reported as the mean and maximum of the 20 central slices of bone (Table 1) and as bone signal topographs of the medial and lateral tibia (Figs. 6 and 7). In all cases, the medial tibial bone signal was greater than the lateral tibial bone signal. The OA knee with definite medial disease had 14% higher mean bone signal in the central region of the medial tibia (slices 10–30) as compared to asymptomatic knees (Table 1). However, in the relatively unloaded lateral tibia, the OA knee had only 8% higher bone signal than the asymptomatic knees (Table 1). In the lateral compartment, the bone signal of the painful knees was between the asymptomatic and OA values. In the medial compartment, the asymptomatic knees showed lower bone signal than the knee with definitive medial OA but were within measurement error of the knee with constant severe pain. As expected, the bone signal topographs demonstrated greater bone signal from the slices corresponding to the

central weight-bearing portions of the knee than the anterior and posterior margins of the knee for all tibias (Fig. 6).

Discussion

In this exploratory study, coronal-oblique images with $0.2 \times 0.2 \times 1.0$ mm spatial resolution directly visualized the femorotibial subchondral trabecular bone and enabled both qualitative assessment and quantitative measurements. Knee trabecular bone has been evaluated in OA by other authors using MR [12, 29, 37–39]. Axial images provide good assessments of the patellofemoral joint but only limited information of the weight-bearing femoral condyles and tibial plateau. Much of the pathology of OA occurs in the subchondral bone immediately beneath the articular surfaces of the tibial plateau. Therefore, it is important to optimize analysis of these regions. When analyzing axial acquisitions, slices that cover the immediate subchondral bone are typically discarded because of partial volume averaging of the subchondral bone with the joint space. As expected, the oblique-coronal acquisition directly visualized the subchondral trabecular bone in the weight-bearing femorotibial joint as the images were directly orthogonal to the central weight-bearing tibial plateau and overcame the limitations of the axial acquisitions [44, 45].

Additionally, by using a higher magnetic field strength of 3 T, a shorter image acquisition time was achieved with identical spatial resolution and higher SNR as at 1.5 T. This is not the first application of trabecular bone MR imaging at 3 T [35–37]. One group evaluated 3 T MR results compared to those at 1.5 T for the wrist [35] and a second group for the calcaneus [36]. Both groups used a 3D GRE acquisition, the sequence with the widest clinical research applicability [30], without optimizing the 3 T acquisition. A third group [37] used a fast steady-state acquisition sequence at 3 T with parallel imaging in the axial plane to quantify the trabecular bone of the knee. All groups found 3 T MR to provide an equivalent or better measure of the trabecular bone structure than 1.5 T.

Several approaches were used to take advantage of the improved SNR of the 3 T systems. Group one [35] acquired two different spatial resolution acquisitions at each field strength with nearly identical acquisition parameters (25° flip angle, 7.5 ms TE, and 15 ms TR for 1.5 T; 25° flip angle, 8.4 ms TE, and 17 ms TR for 3 T). The SNR at 3 T was found to be 16 times higher than at 1.5 T (approximately four times is expected) and likely indicates lower noise detection chain electronics were used at 3 T. The 3 T SNR advantage was used to obtain higher spatial resolution images ($0.2 \times 0.2 \times 0.2$ mm) and enabled greater contrast to be obtained for the spongy bone in the wrist between normal and markedly osteoporotic subjects. Group two [36] held the flip angle and resolution constant, but allowed small differences in TE and TR to be used at the two field strengths (5.1 and 20.0 ms for 1.5 T; 4.3 and 18.5 ms for 3 T). Significantly higher correlations were found between the structural parameters measured using 3 T MR and those from micro-CT measurements. Trabecular dimension was thought to be accentuated at 3 T due to increased magnetic susceptibility at the higher field strength. Group three [37] used a fast steady-state sequence (60° flip angle, 4.2 ms TE, and 11 ms TR) with parallel imaging to achieve a 10 min scan time and $0.2 \times 0.26 \times 1$ mm resolution axial acquisition in the knee. Sixteen patients with early knee OA (Kellgren-Lawrence grade [19] 1 or 2) and 16 asymptomatic volunteers were evaluated. The early OA patients had an overall decrease in trabecular bone structure parameters in both the distal femur and proximal tibia compared to the normal controls, indicating loss of mineralized bone.

In this exploratory study, we first evaluated the relationship between the flip angle and bone marrow CNR and SNR to optimize the 3 T parameters. We then used the parameters for the qualitative and quantitative analyses for remainder of the study.

In asymptomatic knees the subchondral tibial bone appeared organized, and the contour of the tibial plateau was smooth and concave. In comparison, the OA knee had disorganized trabeculae and an irregular and flattened tibial plateau contour. Near the articular surface, the subchondral bone in the OA knee had a thickened, irregular contour, as well as the trabecular orientation changes findings that have been described on radiographic assessments [10, 15–20] and bone morphogenesis identified by histopathology [11].

The coronal-oblique images enabled quantification of “bone signal,” akin to “bone volume fraction” [40] (but without coil inhomogeneity correction), in the subchondral trabecular bone of the medial and lateral tibial plateaus. As expected, these values were higher than trabecular apparent bone volume fraction as they were measured at the superficial levels 1 and 2 [10] of tibial subchondral bone. Both medial and lateral bone signal were higher (14 and 8% respectively) in the knee with established medial knee OA, likely indicating a higher fraction of trabecular bone. The asymptomatic knees had lower values and the painful knees without a clinical diagnosis of knee OA had intermediate values. This result might be expected because of the visibly disorganized bone in the OA knee.

There is no report to date in the literature on the femorotibial subchondral bone in OA subjects in vivo. However, our findings are consistent with post-mortem studies of proximal tibiae in patients with mild OA and without OA [13], and in equine third metacarpal condyles [14], where the bone volume fraction and amount of sclerosis was found to be higher in knees with OA as compared to those without. A cadaveric study [12] of the proximal tibial plateaus from osteoarthritic patients found statistically significant correlation between apparent bone volume fraction determined using coronal 3 T MR and micro-CT bone with measured mechanical properties.

This work represents the first step in longitudinal assessment of the weight-bearing femorotibial compartment of the knee in OA patients and in subjects with risk factors for developing OA. Longitudinal studies are challenging due to the additional requirement of reproducibly identifying the same region of interest. The relatively flat surfaces of the central portion of the femorotibial joint in the coronal-oblique plane should improve the ability to reduce measurement variability over time. Image fusion techniques should also be more easily applied to these regions. A limitation is the relatively thick slice (1 mm) compared to the trabecular spacing, which results in partial volume averaging of the trabeculae, subchondral bone, and adjacent pathophysiology [48]. This reflects the compromise between SNR and acquisition time. Thicker slices may decrease sensitivity to change, decrease measurement reproducibility, and/or confound results. Validation of longitudinal sensitivity to change in quantitative trabecular measures [40], such as trabecular number and spacing, in addition to the bone signal reported here, is also needed.

In conclusion, we demonstrated that high quality MR images that directly visualize the subchondral trabecular bone of the femorotibial joint can be obtained in a clinically relevant 10.5 min acquisition time using widely available coronal-oblique 3D GRE techniques at 3 T. The coronal-oblique images were amenable to both qualitative and quantitative analysis. While these results are preliminary and in need of confirmation, the findings are compatible with visibly disrupted trabecular bone architecture and increased volume of subchondral bone occurring in OA, and are in agreement with human [12, 49] and equine [14] cadaveric studies. The methods presented here lay the ground work for longitudinal quantitative investigation into the role and pathophysiology of subchondral trabecular bone in knee OA based on large natural history studies, such as the Osteoarthritis Initiative [45, 49].

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Fig. 1.
The region-of-interest (ROI) conforms to the cartilage-bone interface on the medial tibial plateau. *Arrow* identifies chemical shift artifact on femoral condyle that does not interfere with subchondral bone analysis

Fig. 2.

Bone marrow signal versus flip angle. A flip angle of 45° to 50° maximizes bone marrow signal using a 3D GRE acquisition with a TR of 20 ms at 3 T

Fig. 3.
SNR versus flip angle. A flip angle of approximately 50° maximizes bone marrow SNR with a 3D GRE acquisition with a TR of 20 ms at 3 T

Fig. 4. CNR versus flip angle. CNR between bone marrow and muscle did not vary substantially as a function of flip angle (*green squares*). CNR between bone marrow and subcutaneous fat was minimized at a flip angle of 35° (*red triangles*)

Fig. 5.

a. Sample image from an asymptomatic volunteer (medial side is on right). In these knees, the subchondral bone appeared organized and the contour of the tibial plateau was smooth and concave. **b.** Sample image from a volunteer with known radiographic knee OA (KL 3 [19]) with medial joint space narrowing. This knee demonstrates disorganized trabeculae and an irregular and flattened tibial plateau contour with thickened subchondral bone

Fig. 6.
Medial tibia bone signal topographs

Fig. 7.
Lateral tibia bone signal topographs

Subject demographics and right medial knee pain characteristics. Bone signal versus knee OA. The mean and maximum bone signals were computed from the central tibial region (slices 10–30)

Table 1

Group	Gender	Age (years)	Pain/OA	MT mean bone signal	MT max bone signal	LT mean bone signal	LT max bone signal
1	M	47	No pain	0.65	0.72	0.60	0.67
1	F	48	No pain	0.65	0.72	0.61	0.66
2	F	51	Rare, mild knee pain	0.69	0.75	0.63	0.67
3	F	51	Severe constant pain	0.68	0.74	0.65	0.71
3	F	46	Definite medial OA	0.74	0.79	0.65	0.71