Osteoarthritis and Cartilage (2008) **16,** 1150–1159
Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.
doi:10.1016/j.joca.2008.02.018

Osteoarthritis and Cartilage

International Cartilage Repair Society

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Relationship between trabecular bone structure and articular cartilage morphology and relaxation times in early OA of the knee joint using parallel MRI at 3 T

R. I. Bolbos Ph.D., Doctor†*, Jin Zuo Ph.D., Doctor†, Suchandrima Banerjee B.E.†‡, Thomas M. Link M.D., Professor†, C. Benjamin Ma M.D., Assistant Professor§, Xiaojuan Li Ph.D., Assistant Professor† and Sharmila Majumdar Ph.D., Professor†‡

† *Musculoskeletal Quantitative Imaging Research, Department of Radiology, University of California San Francisco, San Francisco, CA, USA*

‡ *Joint Graduate Group in Bioengineering, University of California Berkeley, Berkeley, CA, USA*

§ *Department of Orthopaedic Surgery, University of California San Francisco, San Francisco, CA, USA*

Summary

Objective: To evaluate trabecular bone structure in relationship with cartilage parameters in distal femur and proximal tibia of the human knee at 3 Tesla (3 T) using high-resolution magnetic resonance imaging (MRI) with parallel imaging.

Method: Sixteen healthy controls and 16 patients with mild osteoarthritis (OA) were studied using a 3 T magnetic resonance (MR) scanner and an eight-channel phased-array knee coil. Axial 3D GeneRalized Autocalibrating Partially Parallel Acquisition (GRAPPA)-based phase cycled Fast Imaging Employing Steady State Acquisition (FIESTA-c) images were acquired in order to quantify the trabecular bone structure. For assessing cartilage morphology (thickness, volume), sagittal high-resolution 3D spoiled gradient echo (SPGR) images were acquired. In a subset of the subjects, sagittal images were acquired for measuring T1ρ and T2 relaxation times, using 3D T1ρ and T2 mapping techniques.

Results: Good measurement reproducibility was observed for bone parameters, the coefficients of variations (CVs) ranging from 1.8% for trabecular number (app. Tb.N) to 5.5% for trabecular separation (app. Tb.Sp). Significant differences between control and OA groups were found for bone volume fraction bone volume over total volume (app. BV/TV) and app. Tb.Sp in all compartments. Significantly increased values in T1ρ and T2 were demonstrated in OA patients compared with controls at the femur, but not at the tibia. T1ρ was negatively correlated with app. BV/TV, app. Tb.N and app. Tb.Sp both at the medial femoral condyle (MFC) and lateral tibia (LT), while T2 was only correlated at the LT. Also, medial tibia (MT) T1ρ was negatively correlated with app. BV/TV ($R^2 = -0.49$, $P < 0.05$) and app. Tb.N ($R^2 = -0.42$, $P < 0.05$) from the opposite side of lateral femoral condyle (LFC). Significant correlations were found between trabecular bone parameters and cartilage thickness and normalized volume, mainly at LT, tibia (T) and femur (F).

Conclusion: At this early stage of OA, an overall decrease in bone structure parameters and an increase in cartilage parameters (T1ρ, T2) were noticed in patients. Trabecular bone structure correlated with articular cartilage parameters suggesting that loss of mineralized bone is associated with cartilage degeneration.
Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.

Key words: Osteoarthritis, Trabecular bone, Cartilage, Magnetic resonance imaging, T1ρ, T2.

Introduction

Osteoarthritis (OA) is a degenerative joint disease which typically affects the weight-bearing knee joints. It was suggested that pathological alterations at early stage of OA primarily affect the articular cartilage and the underlying bone[1–3]. The articular cartilage's early changes consist in increase in water content, loss of proteoglycans (PGs) and disruption of collagen fibers[4], while for trabecular bone, the volumetric mineral density decreases due to incomplete mineralization of trabecular structure[5]. As the early OA stages are practically asymptomatic, the need of an early detection method is necessary.

Quantitative magnetic resonance imaging (qMRI) could serve as an early marker of changes in the mechanical properties of cartilage and underlying bone. qMRI provides a way to directly assess the integrity (thickness and volume) and composition (T1ρ, T2) of the articular cartilage *in vivo* in OA. Eckstein *et al.*[6] evaluated the precision of qMRI when performed on 1.5 T and 3 T magnets, reporting errors from 1% to 4% for cartilage thickness and volume measurements. In the last years, significant interest focused on imaging cartilage biochemical composition. In particular, T1ρ and T2 relaxation time mapping techniques have been proposed to quantitatively examine the early stages of cartilage degeneration. T2 mapping represents a significant marker of cartilage degeneration by its sensitivity to tissue hydration and biochemical composition related to the integrity of collagen in the cartilage extracellular matrix[7–9]. Quantitative T1ρ mapping based on

*Author correspondence and reprint requests to: Dr Radu I. Bolbos, Ph.D., Department of Radiology, University of California San Francisco, 185 Berry Street, Suite 350, San Francisco, CA 94107, USA. Tel: 1-415-353-4928; Fax: 1-415-353-3438; E-mail: radu.bolbos@radiology.ucsf.edu

Received 29 October 2007; revision accepted 22 February 2008.

spin-locking technique represents a potential of MRI to reflect changes in biochemical composition of cartilage with early OA, such as PG loss[10–13]. These studies demonstrated that the higher the values of these relaxation parameters, the more significant changes take place within the cartilage organization (collagen fibers) and composition (PG). Li *et al.*[14] quantified the cartilage volume and thickness as well as T1ρ and T2 values at 3 T and compared these parameters between normal and OA patients. They found that the average T1ρ and T2 values were significantly increased in OA patients compared with controls, whereas no significant difference was found in terms of cartilage volume and thickness. They suggested that, based on these significantly higher values of the T1ρ and T2 relaxation times obtained in patients, early degeneration could take place within the cartilage composition before the morphological changes occur.

Remarkable progress in high-resolution MRI (HR-MRI) over the last 15 years offers now a new promising noninvasive tool for depicting trabecular microstructure *in vivo*[15,16]. Trabecular bone consists of a network of oriented elements or trabeculae (~80–100 μm) that are usually spaced ~200 μm apart. Given the size of the trabeculae, spatial resolution is perhaps the single most critical parameter since this is required to be in the order of the trabeculae structural dimension for an accurate representation of topology, scale and orientation of trabecular bone networks. Since spatial resolution and signal-to-noise ratio (SNR) are inversely related, imaging at even higher spatial resolutions would entail a very long acquisition time to maintain a reasonable SNR. The currently achievable spatial resolution for *in vivo* trabecular bone imaging is ~130–190 μm in plane and ~500 μm through plane with an acquisition time of 15–20 min[17,18].

Several qMRI techniques have recently been introduced for the noninvasive assessment of structure and composition of trabecular bone and articular cartilage. An *ex vivo* study investigated human cadaver patellae employing qMRI and several reference methods, demonstrating the relationship between structural and mechanical properties of articular cartilage and trabecular bone with different stages of degeneration[19]. Beuf *et al.*[1] performed an *in vivo* MRI study and demonstrate significant variations in trabecular bone structure within the knee joint in patients with OA. Other previous studies using the same *in vivo* MRI technique[2,3] demonstrated that cartilage degeneration in the knee joint is associated with changes in trabecular bone structure, and that cartilage loss on one side of the knee joint is related to loss of mineralized trabecular bone on the opposite side of the knee joint.

Over the last few years, parallel MRI acquisition strategies have been proposed and have seen increased acceptance in the MRI community. In parallel MRI, spatial information contained in the component coils of an array is used to partially replace spatial encoding normally performed by gradients, thereby reducing imaging time[20–22]. One of them, GeneRalized Autocalibrating Partially Parallel Acquisition (GRAPPA) technique is particularly suitable for small field-of-view imaging[22]. Structural depiction of trabecular bone has been seen to be preserved in images in GRAPPA based parallel MRI. In this work, we apply GRAPPA based parallel MRI method to shorten the acquisition time involved in high-resolution MRI of trabecular bone, thereby reducing patient motion induced artifacts. The time saved can also allow more flexibility in the protocol design.

Therefore, the aim of this study is to use high-resolution magnetic resonance imaging (MRI) to evaluate the trabecular bone structure in the distal femur and the proximal tibia and to establish its relationship with articular cartilage of the human knee at 3T strength field using a parallel imaging protocol.

Material and methods

SUBJECTS

The study was performed in accordance with the rules and regulations the Committee for Human Research at our institution. Informed consent was obtained from all of the subjects after the nature of the examinations had been fully explained. An orthopedic surgeon recruited all subjects based on clinical investigation and diagnosis from antero-posterior weight-bearing radiographs. The severity of each subject's OA was evaluated based using the X-ray based Kellgren–Lawrence scale[23].

Sixteen normal control subjects who did not show any clinical symptoms of OA (seven female, nine male, age range 27–56 years; average = 36.3 years) were recruited and classified as control group. Sixteen patients (seven female, nine male, age range 29–72 years; average = 47.2 years) which exhibited mild radiographic signs of OA (K–L grades of 1 or 2) were classified as mild OA Group. A standardized questionnaire (Western Ontario and McMaster Universities Pain, Stiffness, and Physical Function scales, WOMAC)[24] for measuring the degree of pain, functional impairment and stiffness in all subjects through a five-point scale (none, slight, moderate, severe and extreme) was used. The subject characteristics are presented in Table I. Reproducibility of the trabecular bone structure measurements was assessed in four healthy controls (four male, age = 31–39 years) with repositioning between two measurements.

MRI PROTOCOL

MRI of the study knee of each subject was acquired at a 3 T GE Excite Signa MR scanner (General Electric, Milwaukee, WI) using an eight-channel phased-array knee coil (General Electric Medical Systems, WI).

Morphologic imaging

In order to quantify the trabecular bone structure, images were acquired with axial fully refocused steady state free-precession (SSFP) 3D phase cycled Fast Imaging Employing Steady State Acquisition (3D FIESTA-c) sequence. The sequence parameters were repetition time (TR)/echo time (TE) = 11/4.2 ms, acquisition matrix = 512 × 384, flip angle = 60°, field-of-view (FOV) = 10 cm, 90 slices, slice thickness = 1 mm, scanning time approximately 10 min. A modified sampling scheme allowed the sequence to be employed with autocalibration and twofold undersampling ($R = 2$), thus reducing the imaging time to nearly half of that in the conventional method[22].

A 3D spoiled gradient echo (SPGR) sequence was used for cartilage morphological measurements (thickness and volume) with the following parameters: TR/TE = 20/6.3, matrix size 512 × 512, FOV = 16 cm, locations per slab (LPS) = 100, slice thickness = 1 mm, flip angle = 18°.

T1ρ and T2 relaxation time mapping

Sagittal 3D T1ρ-weighted images were acquired based on spin-lock techniques and 3D SPGR acquisition. Basically, the sagittal 3D T1ρ-weighted

Table I
Summary of subject characteristics: age, weight and BMI values as well as WOMAC OA parameters are reported as mean ± SD. Kellgren–Lawrence grades are also shown. P *values indicate the significance level of differences between patients and controls*

	Patients	Controls	*P*-values
Study population [*n*]	16	16	
Age [years]	47.19 ± 11.54	36.25 ± 10.54	0.009
Weight [kg]	80.08 ± 17.70	70.44 ± 11.84	0.080
BMI	26.78 ± 4.83	22.64 ± 3.03	0.007
Kellgren–Lawrence grade [*n*]			
Grade 0	0	16	
Grade 1	7	0	
Grade 2	9	0	
WOMAC OA index			
Pain	5.31 ± 2.63	1.94 ± 2.95	0.002
Stiffness	3.25 ± 1.24	0.63 ± 0.93	<0.0001
Function	15.06 ± 7.60	2.81 ± 6.57	<0.0001