Association of MR Relaxation Times and Functional Behavior of Osteoarthritic Cartilage using Loaded Knee MRI

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INTRODUCTION: Magnetic resonance imaging (MRI) can be used as a tool for studying biomechanics and biochemical composition of the cartilage, in-vivo in human subjects, i.e. cartilage-on-cartilage contact [1], deformation of cartilage [3], proteoglycans (PG) and collagen content [4], which are known to be altered due to cartilage degeneration in early stages of osteoarthritis. Changes in the biochemical properties of cartilage likely affect the mechanical behavior of cartilage. Though the relationship between mechanical properties and composition of the cartilage has been studied in specimens and cadavers, in in-vivo human studies have been limited to T_2 relaxation times.[5] No studies have reported in-vivo tibiofemoral joint contact mechanics in human subjects with osteoarthritis (OA) under static joint loading using high-field MRI. The objective of this study is to investigate the changes in cartilage-on-cartilage contact patterns and deformation of tibio-femoral cartilage under physiological loading in subjects with and without OA. Additionally, we will compare the biomechanical behavior of cartilage with biochemical changes associated with OA.

METHODS: Thirty female subjects (10 controls and 20 OA patients) participated in the study (age: >40 years and BMI: 20-35 kg/m^2). The study was approved by the CHR of our institution and written consent was obtained from all subjects. MR imaging was performed using a 3T scanner (General Electric, WI), an 8-channel phased array TR knee coil, and an in-house built loading apparatus mounted on the scanner table (Fig.1.a). Two sets of MR images of one knee (controls: dominant knee; patients: knee with severe OA) were acquired. Subjects were positioned supine on top of the loading apparatus, in 20° of knee flexion and 10° of foot external rotation (placed on a footplate and supported in place). The first set of images were acquired with no load applied, and the next set was acquired while applying a load of 50% of the subject's weight at the bottom of subjects' foot by a footplate through a pulley system, intended to simulate static standing conditions. The imaging protocol included four sequences: coronal 3D water excitation spoiled gradient-echo (SPGR) images, coronal fat-saturated T_2-weighted FSE images, multi-slice coronal $T_{1\rho}$-weighted images based on SPGR acquisition, and multi-slice T_2-weighted images covered the same region as the $T_{1\rho}$ sequence, all using previously published pulse sequence parameters. The subjects were categorized based on the individual WORMS scoring of medial and lateral compartments (*medial*: absence of lesions (WORMS 0 or the Normal group) =16 subjects, and focal cartilage lesions (WORMS >0 or the OA group) =12 subjects; *lateral*: Normal=21 subjects, and OA group=7 subjects). Cartilage of the femoro-tibial joint (medial and lateral compartments) as well as contact regions were segmented on SPGR images using a semi-automated spline-based software program and superimposed over reconstructed $T_{1\rho}$ and T_2 maps to compute $T_{1\rho}$ and T_2 relaxation times. Contact area was computed by triangulation (Fig.1.b). Data were pooled and stratified into two equal groups (Low and High) at the median value of $T_{1\rho}$ and T_2 relaxation times. The change in contact area and cartilage deformation was measured within these groups. Paired student's t-test (α=0.05) was used to analyze the effect of loading on contact area and deformation.

RESULTS: Cartilage-on-cartilage contact area in the medial compartment was significantly larger than in the lateral compartment in both normal and OA subjects under loading condition (P<0.01). The average $T_{1\rho}$ and T_2 relaxation times, change in contact area, and change in cartilage thickness of subjects with OA were higher when compared to normal subjects (Table 1). The pooled data show that the relative change of cartilage thickness in the medial compartment was significantly higher than in the lateral compartment (-5.26 ± 9.9% vs. -1.9 ± 9.2%, P=0.042). The differences (between normal and OA groups) in contact area, $T_{1\rho}$ and T_2 were larger in the lateral compartment when compared to the medial compartment (42.02 mm^2, 108.78% vs. 21.82 mm^2, 24.46% for contact area), (6.73 ms, 16.69% vs. 2.43 ms, 5.56% for $T_{1\rho}$) and (4.22 ms, 13.89% vs. 2.4 ms, 7.86% for T_2). When data were further stratified based on compartments (medial and lateral) with each $T_{1\rho}$ group (Low-$T_{1\rho}$ and High-$T_{1\rho}$), the same trend was observed in the change in contact area (Fig.1.c), but not in cartilage deformation (Fig.1.d).

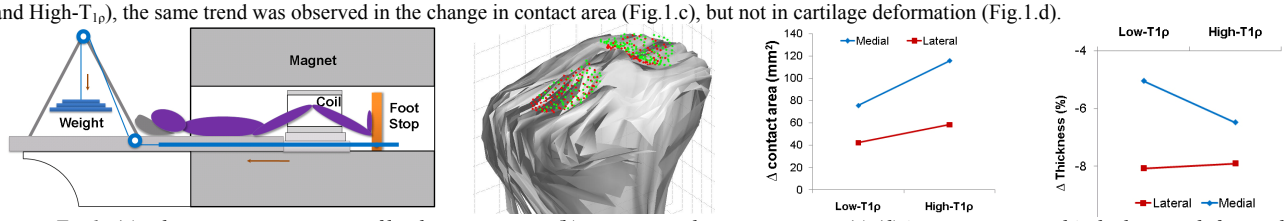

Fig.1: (a) schematic representation of loading apparatus, (b)superimposed contact regions, (c) (d) Δ contact area and Δ thickness in bifurcated data ($T_{1\rho}$)

Table 1: Change in cartilage-to-cartilage contact area, cartilage thickness, and MR relaxation times

Group	Δ Contact Area (mm^2)		Δ Cartilage thickness (%)		$T_{1\rho}$ (ms)		T_2 (ms)	
	Medial	Lateral †	Medial	Lateral	Medial	Lateral †	Medial †	Lateral †
Normal	78.95 (62.36)*	35.25 (33.2)**	-5.09 (11.12)	-2.69 (10.01)	43.66 (6.27)	40.35 (6.23)	30.61 (3.99)	30.38 (4.91)
OA	123.37 (63.55)*	88.87 (34.71)**	-7.02 (10.54)	-1.51(8.85)	46.09 (5.54)	47.08 (5.76)	33.01 (5.22)	34.60 (4.98)

*,** significant difference in unloaded and loaded conditions (* p<0.05; ** p < 0.01) † significant difference between normal and OA (p<0.05)

DISCUSSION: Higher contact area, contact deformation, $T_{1\rho}$, and T_2 values in subjects with OA are likely related to the reduced compressive stiffness of the cartilage due to the damaged collagen network[6]. Higher ratio of contact area and MR relaxation times (between OA and Normal group) of the lateral compartment suggests possible change in load sharing pattern due to OA. Support for this finding of altered loading mechanics in subjects with OA comes from Astephen et al [7] who reported that knee moment and angle data during self-selected gait were significantly different between healthy and OA subjects. We propose that damage to the collagen fiber network and decreases in PG content may reduce the compressive stiffness of the cartilage tissue, which is reflected in larger deformation and larger contact areas in subjects with OA. Consistent with our observations of contact area, cartilage deformation in OA patients was higher than in normal subjects. These results suggest that the structural degradation affects the load bearing capacity of cartilage. In conclusion, this study provides support for a strong relationship of the mechanical response of cartilage to physiological loading (cartilage-on-cartilage contact area and cartilage deformation) with MR relaxation ($T_{1\rho}$ and T_2) in both OA patients and normal subjects.

[1]. Li et al., *Am J Sports Med* 2005, 33, 102-7. [2]. Yao et al. *J Orthop Res* 2008, 26, 673-84. [3]. Eckstein et al., *Ann Rheum Dis* 2005, 64, 291-5. [4]. Zarins et al., *Osteoarthritis Cartilage*, 2010. [5]. Nishii et al., *JMRI,* 2008, 28, 175-80. [6]. Wong et al., *Bone* 2003, 33, 1-13. [7]. Astephen et al., *J Orthop Res* 2008, 26, 332-41.