Topographic Modifications of T1-Gd in Early Osteoarthritic Tibial Cartilage by MRI at Microscopic Resolution

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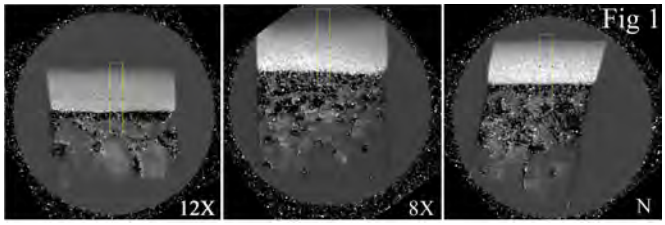
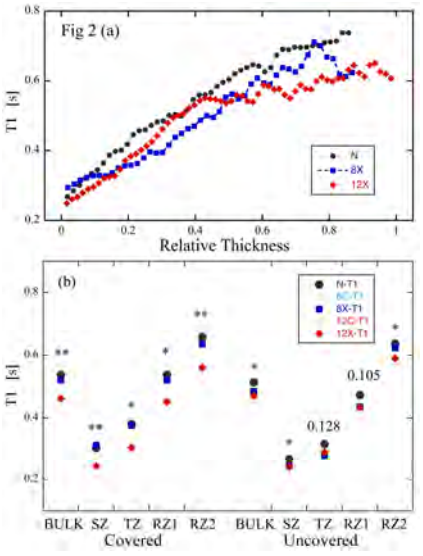
INTRODUCTION

Degeneration of cartilage is a hallmark of osteoarthritis (OA), which is one of the most common types of arthritis (1) and can be characterized by changes in molecular structure and composition across its unique sub-tissue zones. Early degenerative changes include depletion of proteoglycan (PG), alterations in PG-collagen interaction, and disruption of collagen structure. Early OA is localized and progresses slowly, which causes cartilage to have different pathological degradations at different time points and locations (2), contributing to the difficulty of establishing an accurate diagnostic standard. A sensitive technique for non-destructively detecting the structural, topographical, and functional changes in early OA would, therefore, be extremely valuable for monitoring of disease progression and for evaluating of the treatment efficacy. Since T1 relaxation times are correlated with the mechanical properties of cartilage (3), this study aimed to quantify the topographical and sub-tissue zonal changes of T1 in healthy and osteoarthritic tibial cartilage, using an experimental OA model on canine knee joints.



MATERIALS AND METHODS

Twelve skeletally mature dogs underwent anterior (cranial) cruciate ligament transection (ACLx) in one knee joint. Six animals were sacrificed 8 weeks post surgery and the other six dogs were sacrifices 12 weeks post surgery and they were handled according to the protocols approved by the Institutional Review Boards. The five rectangular blocks (3x2.5x4~5 mm) were harvested from the central load-bearing area of medial tibia from each knee. Each block was immersed in 1mM gadolinium (Gd-DTPA2-) contrast agent and stored at 4˚C until experiment. Quantitative μMRI T1 imaging experiments were performed on a Bruker AVANCE II 300 NMR spectrometer equipped with a 7-Tesla/89-mm vertical-bore superconducting magnet and micro-imaging accessory (Bruker instrument, Billerica, MA) and a custom-made 5-mm solenoid coil. Each cartilage specimen was placed in the magnet at the magic angle. The echo time (TE) was 7.2 ms and the repetition time (TR) was 0.5 s. The imaging slice thickness was 0.8 mm, which was transversely located in the middle of the 4~6 mm-long specimen. The 2D in-plane pixel size was 17.6μm. Healthy tissue data was from an on-going project using the tissue from the same source (4). One-way ANOVA with Bonferroni correction was used to test the differences in individual zones among the five groups of tissue (12-wks OA (12X), 8-wks OA (8X), 12-wks Contralateral (12C), 8-wks Contralateral (8C), and Normal (N)). Kruskal-Wallis Sum Test was performed to compare the meniscus-covered and the meniscus-uncovered areas in each 12X, 8X, 12C, 8C, and N and paired student t-test was performed between the contralateral and the OA in each OA stage of topographical group. A p-value of less than 0.05 represented statistical significance. (*, †: p<0.05; **, ††: p<0.01; ***, †††: p<0.001)



RESULTS

In all OA joints, the medial meniscus was partly torn or showed partial thickness erosions and osteophytes around the joint periphery; the medial tibia and femoral condyle had minor surface fibrillation and slightly yellowish color. In all contralateral knees, the meniscus was intact and the surface of tibial articular cartilage showed no visual evidence of disease. Quantitative T1 images (Fig 1), profiles (Fig 2a) and zonal averages (Fig 2b) of cartilage when soaked in gadolinium showed an increasing trend from the surface to deep cartilage in all 12X, 12C, 8X, 8C, and N. Fig 3 compares the averaged T1-bulk among the tissue groups. The mean T1-Gd values from the meniscus-covered area were significantly higher than those from the uncovered area for most sub-tissue zones (*) except most RZ2 and bulk. Between X and C, C had higher T1-Gd values than X at most zones and bulk for both covered (†) and uncovered areas (except uncovered area of 12X). Table 1 summarizes the mean T1-Gd and standard deviation at each sub-tissue zone as well as the bulk, with statistical determinations.

DISCUSSION: This study characterized experimental canine OA knee cartilage with the T1-Gd in OA cartilage at different stages, which were sensitive to early degradation. We measured mean T1-Gd not only bulk but also in each sub-tissue zone. With the number of sample at nineteen (six-12wks, six-8wks, and seven-normal), we observed significant changes in most of sub-tissue zones as well as bulk for both meniscus covered and uncovered area among the OA stages. We found topographical variations of T1-Gd between the meniscus-covered and uncovered area at each OA time-point at most sub-tissue zones except RZ2, while the difference is not significant at bulk and 12X. We also confirmed that the average T1-Gd decreased with OA advance and the thickness of OA cartilage increased at early stage of OA (2), which was expected because the increased water content at the early stage of OA. The detailed knowledge of the strain-modified T1-Gd profile in cartilage from μMRI would be useful in characterizing the event in mechanically induced joint diseases and injuries.

SIGNIFICANCES: This study presented the statistical comparisons of T1-Gd topography of articular cartilage in all sub-tissue zones during the development of OA. The results suggest that the progression of early OA in medial tibia cartilage varies topographically. We showed that the modifications to T1-Gd at different sub-tissue zones and bulk with OA could be detected by μMRI. This observation could help to design more effective protocols to detect the early stages of OA in the clinics. (The authors thank NIH for the R01 grants.)

REFERENCES: (1) Murphy et al., Arth. Rheuma. 59:1207, 2008; (2) McDevitt et al., J Bone Joint Surg Br. 58:94,1976; (3) Xia et al., Magn Reson Med. 65:1733, 2011; (4) Lee et al., Connect Tissue Res. 55:205, 2014.

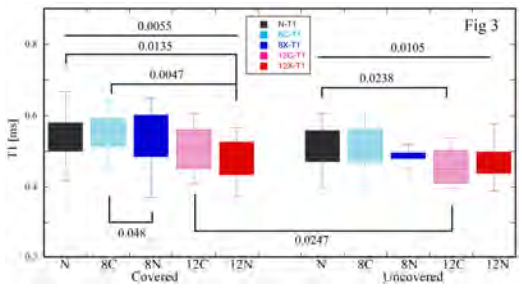


Table 1. The mean T1 values with standard deviation at each sub-tissue zone and bulk with statistical results

Zone	12wks-ACLx (12X)		12wks-Contralateral (12C)		8wks-ACLx (8X)		8wks-Contralateral (8C)		Normal (N)	
	Meniscus-covered	Meniscus-uncovered	Meniscus-covered	Meniscus-uncovered	Meniscus-covered	Meniscus-uncovered	Meniscus-covered	Meniscus-uncovered	Meniscus-covered	Meniscus-uncovered
Bulk	462±84	471±53	509±67*	456±49	521±101†	485±31	560±56	515±66	538±74	514±58
SZ	243±35††	240±32	278±45*	243±19	313±81**	245±25	314±43**	255±31	305±59**	268±30
TZ	306±63††	290±54	387±65**	295±45	377±98**	280±38	391±67**	308±46	380±76***	317±46
RZ1	452±105	436±75	518±83**	418±61	521±104*	436±43	560±70**	472±78	538±78**	473±72
RZ2	561±87	590±53†	634±59*	581±49	635±104†	624±38	682±55	648±83	658±77	636±59

(*: p<0.05, **: p<0.01, ***: p<0.001 Kruskal-Wallis Sum Test result between meniscus covered and uncovered areas at each sub-tissue zone of each OA stage; †: p<0.05, ††: p<0.01, Paired student t-test between Contralateral (C) and OA (X) on each topographical area of 12 wks and 8wks)