Characterization of Cartilage using Diffusion Imaging and Correlation with T1p/T2 relaxation times: A Longitudinal Evaluation in Knee Osteoarthritis

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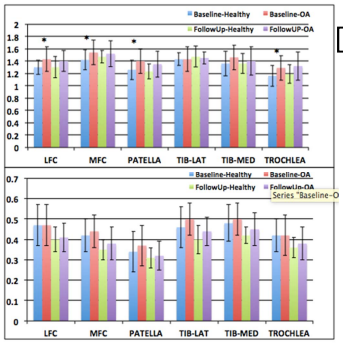
Purpose: Osteoarthritis (OA) is a common degenerative disorder occurring mainly due to aging and abnormal loading of the joint, resulting in a series of biochemical and morphological changes in the joint. Research has shown that subtle changes in tissue microstructure correlate with restricted diffusion of water, which manifest in signal changes on diffusion weighted (DWI) MR images[1,2]. In previous works, we demonstrated a novel diffusion sequence using a stimulated echo (STE) diffusion preparation with magnetization prepared angle modulated partitioned k-space (MAPSS) acquisition for knee cartilage imaging at 3T[3]. The goal of this work is to, a). to longitudinally evaluate the diffusion values at one year and b). analyze any correlation between 3 potential OA biomarkers: diffusion, T1ρ and T_2 in a bigger data set. MR T1p and T_2 quantification values are non-invasive biomarkers for cartilage degeneration since they associated with proteoglycan and collagen content respectively in the cartilage and increased T1ρ and T_2 is seen in OA[4].

Methods: Subject characteristics are shown in Figure 1(a). Subjects were a part of ongoing study in our institution and were scored according to both KL and WORMS[5,6] classification. The sequence parameters for the stimulated echo diffusion sequence were: image matrix:256x128, field of view:14cm, bandwidth:62.5kHz, slice thickness: 4mm, number of slices:22, number of directions: 6, δ:4.25ms, Tmix:150ms, b_0-value:0.86sec/mm^2, b-value:260.4sec/mm^2, maximum gradient amplitude:3.3x10^{-5} T/mm and scan time:7 minutes. To maintain stimulated echo behavior, the non-diffusion weighted image (b=0) has very small diffusion gradients (amplitude 0.25x10^{-5} T/mm). For calculating the Mean Diffusivity (MD) and Fractional Anisotropy (FA) values, the articular cartilage was divided into six compartments namely, lateral femoral condyle (LFC), medial femoral condyle (MFC), patella, trochlea, lateral tibia (LT) and medial tibia (MT) during semi-automatic segmentation done using in house software in Matlab[7]. A non-linear rigid registration of diffusion-weighted images was applied using Rview. The MD and FA values were calculated using a non-linear diffusion tensor-fitting algorithm in Matlab. The T1ρ and T_2 sequences had the following parameters: FOV=14cm, 256x128 matrix, slice thickness=3mm, number of slices:30 slices, TSL=[0,2,4,8,12,20,40,60ms], spin lock frequency=500Hz, TE=[0,3.4,6.8,10.3,20.5,34.2,47.8,61.5ms], TR/TE=5.2/2.9ms. The composite tip-down and tip-up RF pulses were used to compensate for B_0 and B_1 inhomogeneities and the 3T exam used 2x phase ARC acceleration. The segmentations from diffusion images were superimposed over the T1ρ and T_2 images and adjusted for using the same in house software. Independent two tail t-tests and chi-squared tests were performed to compare differences in subject age, gender and BMI. For longitudinal analysis one way ANOVA was performed. Lastly, the T1ρ and T_2 values were correlated with MD and FA values using Pearson's correlation for entire baseline cohort. The correlation was classified as low (<0.5), moderate (>0.5 but <0.7) and strong (>0.7).

Results and Discussion: The MD and FA values for both baseline and follow up cohorts are similar to previously reported values (Figure 1b)[8,9]. In the baseline cohort, the MD values of all knee compartments except the lateral and medial tibia region of OA (KL≥2) subjects were significantly higher ($p \leq 0.05$) from healthy subjects (KL0 and 1). The FA values were not significantly different between healthy controls and subjects with OA. MD values were higher in OA subjects compared to healthy subjects in all six compartments with the lateral tibia showing marginal increase. FA values did not lower with higher KL scores. In the follow up cohort similar trends were observed.

For the same cohorts, the cartilage MD and FA values based on WORMS (whole organ magnetic resonance imaging scoring) classification were also compared. In the baseline data set, increasing MD and decreasing FA values was observed for all knee compartment except for MFC MD and lateral tibia region for FA. Additionally, MFC FA value was significantly different between healthy and OA subjects. For the follow up cohort, MD values were higher in OA subjects compared to healthy controls except for medial tibia region with the patella and lateral tibia compartments approaching significance. FA values decreased in medial tibia region and were not significantly different in any of the six compartments. In diffusion weighted sequences motion induced phased errors and partial volume effect introduces undesirable effects that may have resulted in variation in the diffusion values. LFC, patella, trochlea, lateral and medial tibia show moderate positive correlation with MD values. Patella, MFC and trochlea FA T1ρ values show negative correlation with FA values. Medial tibia and patella MD values show positive correlation and LFC, patella FA T_2 values show correlation with diffusion values.



b

a

Subject Characteristic	Baseline (n=44)				Follow up (n=20)			
	Control (n=22)		OA (n=22)		Control (n=10)		OA (n=10)	
	Female	Male	Female	Male	Female	Male	Female	Male
Age (years)	53.8 (8.3)	55.1 (9.4)	60.2 (9.1)	55.7 (8.9)	50 (10.8)	52 (9.1)	60.6 (2.3)	53.2 (10.2
BMI (Kg/m^2)	24.5 (4.02)	25.3 (3.08)	24.7 (3.49)	26.8 (1.44)	24.2 (3.3)	23.1 (3.4)	28 (3.3)	25.9 (1.8)
Gender (F:M)	14:8	14:8	12:10	12:10	7:3	7:3	3:7	3:7

c

Knee Compartment	MD	p value	FA	p value
LFC	0.16	0.34	-0.3	0.05
MFC	0.1	0.5	-0.13	0.4
PATELLA	0.3	0.07	-0.4	0.01
TIBIA-LAT	0.14	0.38	-0.17	0.3
TIBIA-MED	0.42	0.007	-0.2	0.2
TROCHLEA	0.04	0.8	-0.24	0.13

d

Knee Compartment	MD	p value	FA	p value
LFC	0.24	0.16	-0.11	0.5
MFC	0.13	042	-0.2	0.2
PATELLA	0.24	0.13	-0.38	0.01
TIBIA-LAT	0.21	0.1	0.09	0.57
TIBIA-MED	0.5	0.001	-0.07	0.6
TROCHLEA	0.33	0.04	-0.43	0..006

Fig. 1(a). Table showing subject characteristics for data sets;(b) Bar graph showing mean diffusivity (MD, mm^2/sec) (top) and Fractional anisotropy (FA) (bottom) values of baseline and follow up cohort based on KL scores (denotes significance, error bar indicates std. deviation); (c) Table showing correlation between T_2 MD and FA values and values (along with p-values (d) T1p and diffusion MD and FA) for 44 baseline subjects.*

Conclusion: In our study, significant differences between healthy and OA subjects were seen in both the baseline and follow up diffusion values, suggesting the use of diffusion as tool for early diagnosis for OA at 3T. Diffusion, T1ρ and T_2 quantitative measurements have demonstrated potential to reflect biochemical composition of cartilage in early OA. To our knowledge this is the first study where the correlation between three potential biomarkers has been studied. These non-invasive OA biomarkers when used complementarily with standard morphological cartilage imaging may potentially increase a clinician's ability to detect subtle early cartilage matrix changes associated with early OA and help them design treatment strategies and follow up accordingly.

References: [1] Filidoro et al., MRM 2005; 53:993-998; [2] Raya et al.,Radiology 2012;262:550-559; [3] Guha et al; ISMRM 2013: 21,3543; [4] Li et al, Osteoarthritis and Cartilage 2007;15:789-797; [5] Kellgren et al.,Ann Rheum Dis 1957;16:494-501; [6]. Peterfy, C.G et al. Osteoarthritis and Cartilage 2004; 12:177-190; [7] Carbadillo-Gamio et al, Med Img Anal 2008; 12(2):120-135; [8] Bieri et al, MRM 2012; 67:691-700; [9] Starosweicki et al., MRM 2012; 67(4):1086-1096.