Quantitative MRI biomarkers for Knee Pain and Other Symptoms

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Although much is known about the stuctural pathogenesis of Osteoarthritis, studies associating MRI-measurable structural changes to clinical outcomes of knee pain and other symptoms are nonexistent. The objectives of this work were to evaluate the association between MRI-derived quantitative structural measurements and KOOS-measured clinical symptoms of pain and dysfunction, and to evaluate the ability of the imaging measurements to predict changes in clinical outcomes.

Material and methods: An automated, atlas-based segmentation algorithm using an anatomical reference atlas was used to segment 3D DESS sagittal MRI images of the symptomatic knee of 133 subjects from the OAI Progression Cohort (0.C.2, 1.C.2, 3.C.1) at baseline, 12-month and 24-month visits. After segmentation, all local thickness measurements at the cartilage surface and local curvature measurements at the subchondral bone plate (SBP) for each of the time points were normalized spatially to the anatomical reference atlas. Measurements at each cartilage surface voxel were then compared voxel to the corresponding atlas' cartilage surface voxels, creating atlas-referenced maps of cartilage thicknesses and SBP curvature. Mean, variance and distribution percentiles were calculated for baseline atlas-referenced thickness and curvature maps. To evaluate the longitudinal changes in curvature and thickness, 12 and 24 month thickness and curvature maps were compared back to the baseline maps and the voxel-by-voxel longitudinal thicknesses and curvature change maps for every subject were computed. The mean change, variance of change and percentiles distribution of change were then calculated for the change maps. The cartilage of the central regions of the knee and that of the entire femur and tibia were quantified; but only changes in femoral cartilage were included for this analysis. KOOS scores, paired KL scores, and average joint space width for each subject (http://www.oai.ucsf.edu) were used to evaluate the association between MRI measurements and knee pain and other symptoms as measured by the KOOS tool. The MRI measurements of subjects with a KL score lower than 4 were contrasted to changes in KOOS pain and KOOS other symptoms using odds ratios to compare subjects with low MRI based measurements to subjects with high MRI measurements in a low, medium and high uniform stratification of the analyzed population.

Results and Conclusion: Seven subjects' image sets were eliminated resulting in 107 subjects' data. From these 107 subjects 36% subjects showed an increase in pain and 39% in symptoms over the two year observation. At baseline, an average cartilage thickness was associated to an increase in pain, while average curvature of the femoral SBC was associated to an increase in KOOS' other symptoms**.** The correlation analysis of KOOS pain and KOOS other symptoms to common OA variables at two years showed that change in pain was associated with changes in cartilage thickness while change in other symptoms was associated with changes in the average SBC curvature. Odds ratios of the low exposed (n=35) sub**j**ects to the high exposed subjects (n=35) showed statistically significant increase in knee pain or in other symptoms Table 1.

In this study, knee cartilage thickness and bone curvature modestly predicted changes in KOOS pain and KOOS other symptoms. Change in thickness was associated with an increased prevalence of pain and changes in curvature with an increased prevalence of other knee symptoms. The results of this study are promising evidence that MRI-derived structural biomarkers may have clinical utility, however additional work is needed to characterize such biomarkers across larger and more varied subject populations.

KOOS PAIN (n=70)			
Index	ODDS Ratio	95% CI	
5% Thickness Change Percentile	***2.83***	***1.27***	***6.33***
KL/BMI	***2.60***	***1.04***	***6.52***
Average Curvature Change	1.89	0.98	3.65
BMI	1.78	0.91	3.47
Average Curvature	1.67	0.84	3.29
Other Symptoms	1.00	0.52	1.91
Baseline PAIN	0.75	0.36	1.55
Average Thickness	0.67	0.31	1.43
Mean X-ray Joint Space Width	0.67	0.35	1.28
Min X-ray Joint Space Width	0.56	0.29	1.10

KOOS Other Symptoms (n=70)			
Index	ODDS Ratio	95% CI	
Average Curvature Change	***2.63***	***1.35***	***5.11***
BMI	***2.00***	***1.10***	***3.63***
KL/BMI	1.25	0.69	2.27
Baseline PAIN	1.17	0.63	2.15
5% Thickness Change Percentile	1.13	0.68	1.89
Average Curvature	0.93	0.51	1.68
Average Thickness	0.86	0.46	1.58
Min X-ray Joint Space Width	0.63	0.36	1.09
Mean X-ray Joint Space Width	0.61	0.34	1.10
Other Symptoms	0.53	0.27	1.02

Table 1. Odds ratios of the low exposed (n=35) subects to the high exposed subjects (n=35) in showing an increase in knee pain (left table) or an increase in other symptoms (right table). *Italic* numbers are statistically diferent from one ($p<0.05$)