time points and then dividing the point-by-point changes by the standard deviation of the paired-measurement noise. The standardized thickness points with z-values lower than 1.96 ($p < 0.05$) were marked and counted as points with significant cartilage loss. The proportion of marked points was reported as the percentage of significant cartilage loss at the femur cartilage and the tibia cartilage. Finally, all the 12-month and 24-month change maps were aggregated into a single standardized change map. The significant cartilage loss maps were aggregated into a single heat-map that showed the prevalence and localization of the significant changes in cartilage thickness. The difference between 24-month changes and 12-month changes were used to estimate the standardized response of the mean (SRM) of the methodology.

Results: One knee observation was dropped due to poor segmentation quality. As seen in Fig. 1, heat maps showed different patterns of loss among the no-denuded, the low-denuded and the high-denuded groups. The entire femur showed an average significant 12-month loss on 6.9% of its surface. The loss progressed towards an 8.9% loss with a SRM of 0.48 (0.31 to 0.65). The tibia progressed from a 7.0% loss to an 8.6% loss with a SRM of 0.25 (0.08 to 0.42). The knees with no-denuded areas showed cartilage loss at 5.4% of their femoral cartilage and progressed towards a 7.8% loss with a SRM of 0.73 (0.45 to 1.01) and 74.5% (60.1% to 85.2%) of the knees worsening the affected area. The tibia progressed from a 5.9% loss towards a 7.9% loss with a SRM of 0.39 (0.11 to 0.67). Subjects with small denuded areas showed a 12-month, 24-month loss of 7.1%, 8.6% respectively with a 0.36 SRM in the entire femur. Subjects with large denuded areas showed a 12-month, 24-month loss of 9.1%, 11.0% respectively with a 0.36 SRM.

Conclusion: The image analysis technology used in this study provided quantitative and statistical maps that showed the prevalence and location of changes in cartilage thickness. The spatial localization and the prevalence of those changes were different in the different OA groups studied in this work, indicating the degree of heterogeneity of the disease presentation and progression. Furthermore, the methodology showed that early stage OA (Bone free of denuded areas) is very dynamic with cartilage loss progressing at the annual rate of 2.2% ($0.45 < SRM < 1.01$). Future work will compare the rate and localization of the changes among the non-exposed OAI cohort, a symptomatic worsening OAI group, and an age matched symptom stable OAI group.

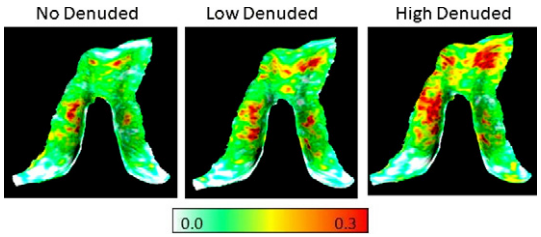

Fig. 1. Heat map of proportion of subjects that show significant changes in cartilage thickness in three different populations.

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PREDICTION OF THE ONSET OF KNEE PAIN BY QUANTITATIVE MRI: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: The purpose of this study was to evaluate the ability of structural changes in cartilage thickness to predict the future onset of knee pain as measured by the KOOS pain.

Methods: The symptomatic knee of 138 subjects at baseline, 12 month and 24 month DESS sagittal MRI knee images from OAI data progression cohort releases 0.C.2, 1.C.2 and 3.C.1 were segmented by a multi-atlas based segmentation algorithm. Images were evaluated for image quality and segmentation quality. All the local thicknesses measurements at the cartilage surface were projected back into the cartilage volume and mapped into to the digital atlas space. After that, cartilage voxles were compared voxel by voxel to the atlas' cartilage surface thicknesses creating atlas-referenced thickness maps. At baseline atlas-referenced maps of thickness values were statistically described by mean, variance and distribution percentiles. Furthermore, the 12 month data and the 24 month thickness maps were compared back to the baseline maps and the voxel-by-voxel longitudinal thickness change maps for every subject were computed. The change maps were described by mean change, variance of change and proportions of areas with significant changes. The quantification of curvature and thickness were done on the central regions of the knee, the entire femur and tibia cartilage. The KOOS scores were downloaded from the OAI site (http://www.oai.ucsf.edu) and used to associate the quantitative MRI measurements to changes in KOOS pain. Only subjects with an enrolment KOOS pain larger than 80 were considered for this analysis. Individual subject changes between the 36 month, 24 month and 12 month to the enrolment assessment of KOOS pain were compared to each subject qMRI baseline assessment and to each subject proportion of significant thickness changes observed between the baseline observations to the 12month. Furthermore, the area under the curve (AUC) of the ROC was computed for the test of predicting a positive change in pain. Finally a linear model with enrolment BMI was constructed to further study the association of the qMRI data to the change in knee pain. Significant associations were defined by beta coefficients different from zero.

Results: One subject was removed due to poor segmentation quality. 43 subjects had a KOOS pain score greater than 80. Table 1 shows the association statistics. The atlas referenced standard deviation of cartilage thickness was a good predictor of an increase of pain at 12 month, 24 month and 36 month (Spearman $r = 0.4$, 0.42 and 0.31 respectively). Baseline to 12 month significant changes in tibia cartilage thickness were also associated to an increase in pain at 12, 24 and 36 month (Spearman $r = 0.42$, 0.34 and 0.34 respectively). The significant AUC were also found for the prediction of a 24 month increase of pain (AUC = 0.81) by the thickness referenced standard deviation. The linear model observed positive association of the atlas referenced standard deviation to the 24 month pain, and of the significant changes in tibia to the increase in 12 month pain. Figure 1 shows the ROC of the prediction of a 24 month vs. Baseline increase in pain. ROC curves indicate that an 80% prediction of pain onset can be achieved with less than 30% of false positives.

Association to Changes in KOOS Pain (n=43)

		Baseline Measurements			Proportion of Significant Thickness Changes (V1-V0)		linear Model
		BMI	Femur				
			Curvature	Thickness Std	Femur	Tibia	
Spearman (r)	12 Month vs. BL	0.08(0.624)	0.19(0.223)	**-0.40(0.008)***	-0.25(0.106)	**-0.42(0.005)****	0.54(0.000)
	24 Month vs. BL	0.06(0.719)	0.24(0.123)	**-0.42(0.005)****	-0.23(0.146)	**-0.34(0.024)**	0.43(0.004)
	36 Month vs. BL	0.17(0.271).	0.30(0.053)	**-0.31(0.045)**	*-0.27(0.078)*	**-0.34(0.024)***	0.52(0.000)
ROC AUC	12 Month vs. BL	0.510	0.622	0.676	0.620	0.753	0.758
	24 Month vs. BL	0.546	0.663	0.819	0.751	0.756	0.826
	36 Month vs. BL	0.504	0.737	0.689	0.612	0.692	0.748

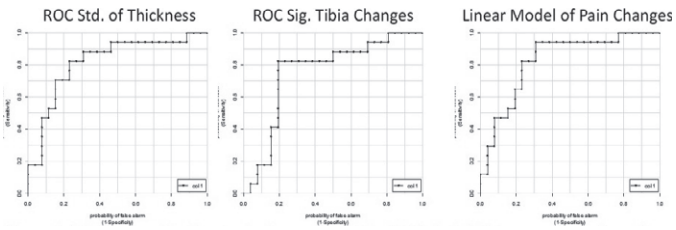

Fig. 1. Month vs Enrolment pain increase prediction ROC. Left: ROC curve of the atlas reference thickness. Middle: ROC curve of the significant changes in tibia thickness. Right: ROC of the linear model that includes BMI, curvature, standard deviation and significant changes.

Conclusion: The changes in cartilage morphology are good predictors of pain onset. ROC and correlation analysis indicate that structural changes in cartilage morphology can be used to predict the 2 year onset of knee pain with a true positive rate of 80% and 30% of false positives. These findings in combination with other risk factors can help in the design of prospective clinical trials requiring a good proportion of subjects showing significant progression in their pain symptoms.

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OSTEOPHYTES AND JOINT SPACE NARROWING ARE INDEPENDENTLY ASSOCIATED WITH PAIN IN FINGER JOINTS IN HAND OSTEOARTHRITIS

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Purpose: Hand osteoarthritis (HOA) can cause considerable pain, and one could assume that structural abnormalities play a role in the aetiology of this clinical feature. However, in earlier studies only limited associations