Quantitative MRI (qMRI) Features Predict Symptomatic Knee Pain During the Next Year: Data from the OAI

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INTRODUCTION: Predicting those who will develop near-term chronic knee pain may accelerate the development of effective OA therapies

OBJECTIVE:. The purpose of this work was: 1) To describe the qMRI differences between subjects with and without symptomatic knee pain; 2) To develop a 12-month predictive index of symptomatic knee pain based on qMRI analysis

METHODS: Subjects from the Osteoarthritis Initiative (OAI) with increasing untreated right knee pain were selected for this study. Those whose right knee symptomatic pain scores (RKSX) were 2, indicating "Pain most days of a month in past 12m" and whose corresponding RKSX scores for the prior year were lower were included. Age, BMI and gender matched subjects without right knee pain were selected as a control cohort. 3D DESS WE MRI images were analyzed using software (Qmetrics Technologies, Rochester, NY) that automatically segmented articular cartilage into whole femur, tibia and patella, and sub-regional central medial femur, central lateral femur, medial tibia, lateral tibia, medial trochlea, lateral trochlea, medial patella, and lateral patella. A human observer verified the success of the segmentations. Segmentations that failed to accurately delineate cartilage tissue were removed from the analysis. Cartilage volume, area, thickness, curvature and DESS signal contrast properties were computed for each region. Descriptive statistics were generated for thickness, curvature and signal contrast measurements. All measurements were adjusted for BMI, age and gender differences. Next, the measurements were z-transformed using the rank inverse normal transform. Finally, individual measurements were classified as low-control-quartile ($p<0.25$), mid-control-range ($0.25<p<0.75$) and top-control-quartile ($p>0.75$). At each class the z-score was maintained. The qMRI analyses at the time of recording the RKSX=2 observation (T-0) and year prior (T-1) were selected. Matching T-0 visit was determined for the control group, based on the T-0 visit of the age-gender-BMI matched case subject. Multivariate logistic models were used to build a Knee-pain predictor. The model selection was found using a bootstrapped-step-wise feature selection algorithm based on the Integrated Discrimination Improvement (IDI). Knee-pain-models were developed for the T-1 and T-0 time points, and both models were internally validated using a tenfold cross-validation. The odds ratio (OR) for each model feature was evaluated. Finally, we determine the practicality of the index to select patients that will develop pain in the next by determining of the number of subjects that could be correctly predicted with a 5% false positive rate

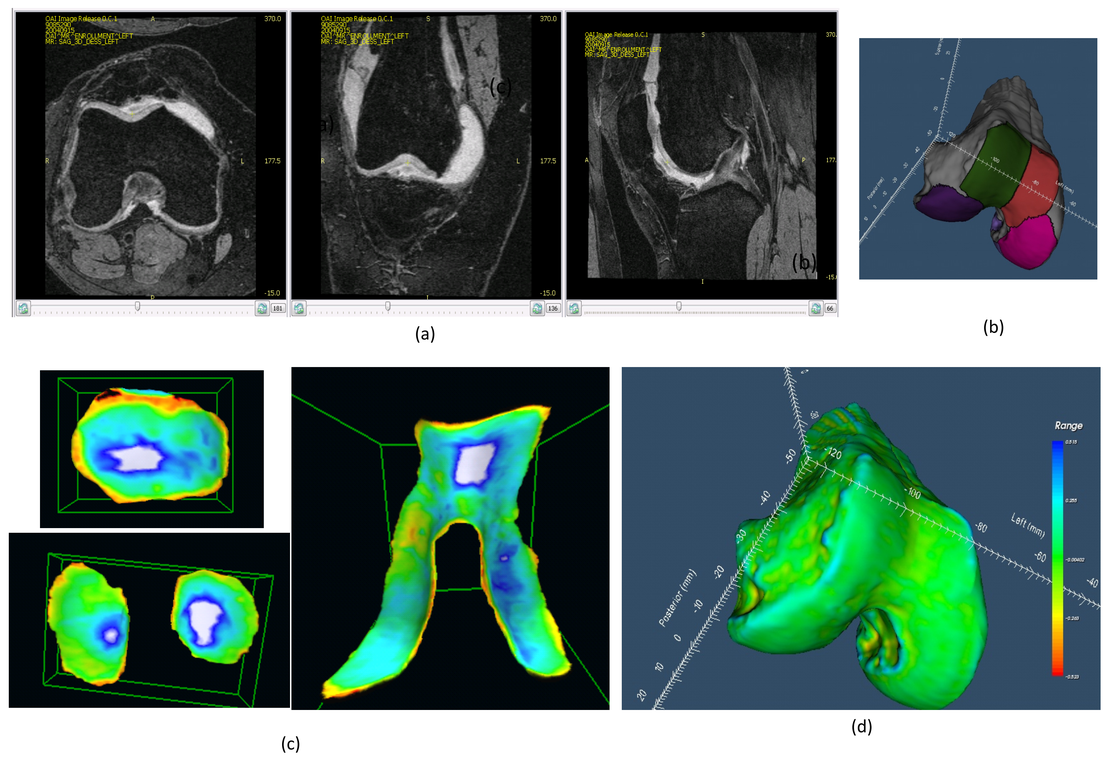

Figure 1: (a) DESS images used to predict future pain. (b) The segmented images were divided into several anatomical ROIs. (c) Cartilage Thickness maps of patella, tibia and femoral cartilage. (d) Curvature map of the femur.

Table 1: Top, subject characteristics at the time of pain incidence. Bottom, subject characteristics one year before pain

P0		n	BMI	Age
Cohort	Males	122	27.83 (3.66)	66.81 (9.57)
	Females	120	25.97 (5.27)	65.59 (9.40)
Case	Males	38(%49)	28.74 (4.12)	65.71 (8.90)
	Females	39(%51)	27.14 (5.70)	66.41 (9.13)
Control	Males	84(%51)	27.42 (3.38)	67.31 (9.87)
	Females	81(%49)	25.41 (4.99)	65.20 (9.55)

P1		n	BMI	Age
Cohort	Males	103	27.08 (3.12)	65.75 (9.49)
	Females	95	26.78 (4.97)	64.00 (9.73)
Case	Males	29(%48)	27.72 (3.77)	63.72 (8.93)
	Females	31(%52)	28.43 (4.97)	65.81 (9.44)
Control	Males	74(%54)	26.83 (2.82)	66.54 (9.64)
	Females	64(%46)	25.98 (4.81)	63.13 (9.82)

RESULTS: At pain incidence (RKSX=2), 77 cases with reliable qMRI analyses were included (38:39 Males:Females). 165 controls were matched at the incident point (84:81 Males:Females). The entire cohort had an average age of 66.21±9.5 years with a BMI of 26.9±4.6. Subjects with available prior year qMRI analyses included 60 cases and 138 controls. Table 2 shows the qMRI parameters that were able to separate cases from controls at the time of pain incidence and one year prior. The model at pain incidence indicated that superficial femur signal contrast, the curvature of the tibia, and patella were different between cases and controls with odds ratios of 3.38, 4.5 and 4.15 respectively. One year prior to the incidence of pain, the thickness of patella cartilage, the cartilage signal contrast of the medial patella and that of the femur were discriminant between subjects that progressed to pain and subjects that did not. The odds were 11.0, 3.0 and 1.8 respectively. The model at one year prior to pain onset was able to accurately predict 28% of the subjects that progress to pain with only 5% false positives.

CONCLUSIONS: The quantitative features of 3D WE DESS images are different between subjects with pain and those that will not develop symptomatic pain. Furthermore, the lack of signal contrast between cartilage and surrounding tissue as well as the presence of abnormal cartilage thickness in the patella and abnormal bone shape (curvature) are strong predictors the imminent onset of frequent knee pain. Based on these results it is possible to use qMRI to select patients that will develop chronic pain in the next year.

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Table 2: Top, MRI Features that are concordant with pain. Bottom, qMRI features that predict pain.

Model	Description	Cases	Control	Odds Ratio
T-0 AUC 0.80 (0.73-0.87), Sen 36% at 95% Specificity	Femur Contrast (Mean)	2.131 (0.608)	2.485 (0.562)	3.38(2.20-5.18) (-)
	Medial Patella Area	418.5 (63.7)	434.8 (85.7)	6.21(1.62-23.77)
	Tibia Curvature (Trimmed)	-0.012 (0.006)	-0.009 (0.006)	4.54(1.28-16.14)
	Tibia Area	1855.1 (247.1)	1930.5 (310.2)	7.20(1.86-27.83)
	Patella Curvature (Mean)	0.009 (0.008)	0.011 (0.006)	4.15(1.23-14.02)
	Lateral Trochlea Contrast (5%)	-2.453 (1.551)	-2.702 (1.612)	1.94(1.16-3.23) (+)
	Lateral Tibia Contrast (95%)	3.663 (0.877)	3.991 (0.852)	3.75(1.07-13.15)
T-1 AUC 0.82 (0.75-0.88) Sensitivity 0.28 at 0.95 Sensitivity)	Patella Thickness (5%)	0.708 (0.037)	0.714 (0.037)	11.01(2.38-50.93)
	Medial Patella Contrast (Std)	1.376 (0.294)	1.301 (0.222)	3.02(1.73-5.29) (+)
	Femur Contrast (Mean)	2.131 (0.608)	2.485 (0.562)	1.80(1.06-3.06) (-)
	Patella Contrast (Std)	1.777 (0.478)	2.000 (0.439)	2.15(1.24-3.70) (-)
	Lateral Patella Curvature (Std)	0.059 (0.005)	0.060 (0.007)	2.65(1.37-5.14) (-)
	Lateral Trochlea Thickness (Std)	0.678 (0.131)	0.668 (0.138)	0.11(0.03-0.52)

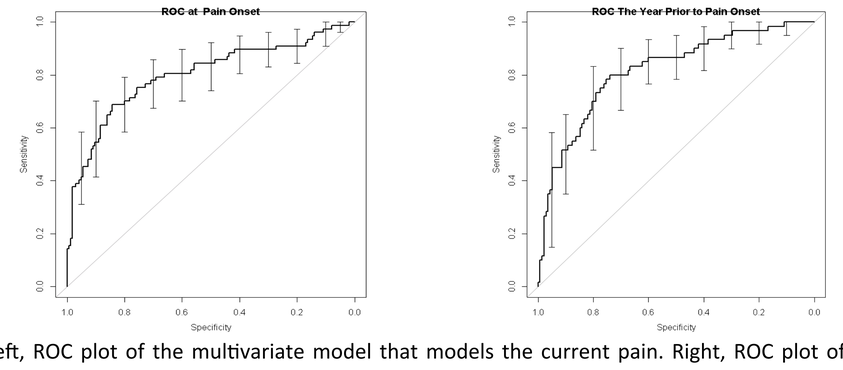

Figure 2: Left, ROC plot of the multivariate model that models the current pain. Right, ROC plot of the model that predicts future pain.