INTRODUCTION
There is large interest in using quantitative magnetic resonance imaging (qMRI) to identify degenerative changes of osteoarthritis (OA) in cartilage. The objective of this study was to use qMRI to identify a series of image metrics on knee MRI that can be used to identify early detection and progression of OA in asymptomatic individuals. In normal cartilage, there is a spatial distribution of cartilage MRI T2 values that is strongly influenced by the highly anisotropic organization of the collagen matrix and regional variation in cartilage water content. Differences on T2 mapped sequences between normal and damaged cartilage can sometimes be observed on a clinical basis (Fig. 1). We hypothesize that loss of the normal spatial distribution of cartilage MRI T2 values, as quantified by texture features, will identify distinctive signatures of OA prior to symptomatic or radiographic evidence of OA. This change in T2 signal heterogeneity could be used to predict symptomatic disease progression.

METHODS
Cohorts: The Osteoarthritis Initiative (OAI) was used to select control and rapid OA progression populations of knee cartilage T2 maps. The control population from the OAI was used for collecting asymptomatic, healthy individuals (n=89). The incidence cohort was used to identify a rapid progression population of OA defined as patients that were asymptomatic with no radiographic signs of OA at the initial time point (WOMAC<3; KL-2) that had a large increase in WOMAC score (greater than 10) at the three year time point (n=120).

Segmentation and Registration: DESS sequences were used for semi-automated segmentation. The approximate anatomic center of the femoral condyle is user defined, and a radial search is completed identifying bone-cartilage and cartilage-soft tissue edge points. These edges can be redefined by the user. A path framework is used to connect these points. Image analysis and visualization software design was completed using the Insight Toolkit and the Visualization Toolkit, respectively. DESS and T2 sequences were registered using a Matus mutal information metric.

Feature Extraction and Classification: Approximately 800 image features and texture measures were extracted from each image to develop a texture based metric. A linear discriminant score, the support vector machine (SVM) method, was used to design a classification model to discriminate image features associated with the control and rapid OA progression populations based only on the baseline MRI. Repeated random 50-50 splits of the cohorts were used to divide the overall populations into independent training and test data sets. Margin based feature elimination (MFE) was used to eliminate redundant and uninformative features.

RESULTS
Image features were extracted from the two cohorts described above and a linear discriminant score, SVM, was used to quantify signal heterogeneity by assembling a texture metric composed of key texture image features to predict rapid OA progression given an independent series of cases. Using the entire image feature set, the average accuracy of our texture metric at predicting rapid progression of OA was measured at 79±4% with a sensitivity of 82±6% and a specificity of 76±7%.

Only a small subset of these image features is essential for accurate prediction of OA progression. Using MFE to eliminate redundant and uninformative features, only 20 of the initial approximately 800 features are essential. When this small subpopulation of features was used, our model had a similar accuracy of 75±6% with a sensitivity of 79±7% and a specificity of 69±7% (Fig 2A). Accordingly, these essential features can be considered "image biomarkers". These features included grey level run length, grey level co-occurrence matrix, entropy, and local energy measures. A large majority of the errors in classification occurred with texture metric values in close proximity to the decision boundary.

DISCUSSION:
Structural changes in knee cartilage can be measured by quantifying signal heterogeneity in T2 maps, and can predict rapid OA progression in asymptomatic individuals. Texture image features were extracted from two groups, healthy controls and asymptomatic individuals without radiographic signs of OA that were known to have a large change in their WOMAC score at a future time point in three years. Features from these two groups were compared using SVM scores to identify a small subset of features that could build a texture metric to quantify signal heterogeneity. This method had an overall accuracy of 76% in predicting rapid OA progression in asymptomatic individuals.

For most individuals, this change in signal heterogeneity primarily occurs in only one of the three main knee compartments suggesting that on an individual basis one of the compartments plays a dominant role in predicting OA progression.

SIGNIFICANCE
A series of image metrics on MRI T2 maps of knee articular cartilage predicts rapid symptomatic progression of OA in asymptomatic subjects prior to symptomatic or radiographic evidence of OA. This defines a series of biomarkers that can predict rapid OA progression.

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