INTRODUCTION
Detection of subsurface alterations to the cartilage extra-cellular matrix, prior to the breakdown of the articular surface, is a primary goal of diagnostic imaging of patients with traumatic joint injury and of the physicians who treat them. Ultrashort T2-Enhanced T2* (UTE-T2*) mapping has the potential to non-invasively assess cartilage molecular integrity in vivo. In vitro, UTE-T2* has been shown to reflect the cartilage collagen matrix integrity as determined by polarized light microscopy, and to be sensitive to signal from deep layers of calcified and uncalcified cartilage with T2* values as short as 1.3 ms. The purpose of this study is to examine the diagnostic potential of clinical UTE-T2* mapping to detect early degenerative changes in articular cartilage following traumatic joint injury.

METHODS
Fifty-two human subjects underwent examination of their knee articular cartilage on a Siemens 3T clinical MRI scanner (MAGNETOM Trio TIM 3T, Siemens Medical Solutions, Erlangen, Germany) using an 8-channel knee coil (In vivo Inc., Gainesville, Florida, USA). All subjects provided informed consent to IRB-approved protocols. Thirty-five subjects undergoing arthroscopy to treat acute anterior cruciate ligament or meniscus injury (mean age = 35.0 yrs; mean BMI = 28.3; 19 female and 17 asymptomatic volunteers (mean age = 27.6 yrs; mean BMI = 24.6; 9 female), with no known or suspected knee injury or disease, were included. UTE-T2* and standard T2 images were acquired on all surgical subjects and 3 asymptomatics. The remaining 14 asymptomatics underwent either UTE-T2* imaging (n=7) or standard T2 imaging (n=7) only.

UTE-T2* maps in the sagittal plane centered on the femoral tubial joint were acquired with an AWOS sequence (acquisition-weighted stack of spirals) as previously described. Standard T2 maps were acquired using the NIH-sponsored Osteoarthritis Initiative (OAI) sequence UTE-T2*, and standard T2 maps were generated with a mono-exponential fitting routine using MRIMapper software (C Beth Israel Deaconess and MIT 2006). Regions of interest (ROIs) were manually segmented from a single section from each subject to separately evaluate the superficial and deep halves of the cartilage thickness in the central femoral condyle. During surgery, targeted arthroscopic exams were conducted on the area of the central weight-bearing zone of the medial femoral condyle.

RESULTS
UTE-T2* values from the superficial layer of articular cartilage to the central femoral condyle vary significantly with disease status. MRI UTE-T2* differences in deep articular cartilage between patient and asymptomatic subjects with cartilage deemed arthroscopically ‘firm’ (Scope 0), or softened while retaining an intact articular surface (Scope 1) are significantly elevated compared to asymptomatic subjects, P=0.014 P=0.003, respectively. Error bars are ± SEM.

DISCUSSION
MRI UTE-T2* differences in deep articular cartilage between patient subjects with cartilage morphology ‘normal’ tissue compared to asymptomatic controls suggests that UTE-T2* mapping is sensitive to sub-clinical, subsurface matrix changes. This human clinical study shows quantitative and noninvasive MRI evidence for subsurface cartilage changes following joint injury that was not detectable by the gold-standard arthroscopic palpation. Continued longitudinal study is needed to determine whether elevated cartilage UTE-T2* values are potential markers of subsurface injury that lead to OA.

SIGNIFICANCE
The ability to diagnose, stage and quantify cartilage injury prior to articular surface breakdown is important for identifying early disease states that may be amenable to molecular, biological, and mechanical interventions to delay the onset of OA.

REFERENCES

ACKNOWLEDGEMENTS
Funding support provided by the NIH (ROI AR052784 (Chu)).