

When (How) MRI Became the Gold Standard

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Target audience: Radiologists and imaging scientists interested in assessing MRI of cartilage

Outcome/Objectives:

1. To become familiar with MRI pulse sequences that characterize cartilage morphology
2. To become familiar with quantitative techniques that illustrate cartilage biochemistry

Purpose:

The conventional standard for assessment of cartilage has been conventional radiographs, which do not directly depict cartilage but rather provide an indirect measure of cartilage loss. MRI pulse sequences have existed for two decades that accurately depict cartilage based on surgical standards but arthroscopy is a flawed standard for cartilage assessment. Histology via biopsy provides discrete and focal cartilage biochemistry assessment but arguably not the more important “macroscopic” picture of cartilage status, and further requires surgical violation of the cartilage structural integrity.

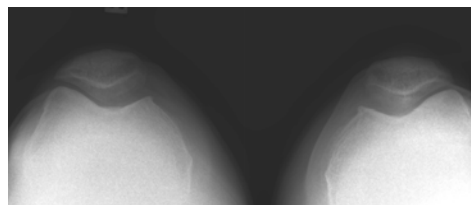
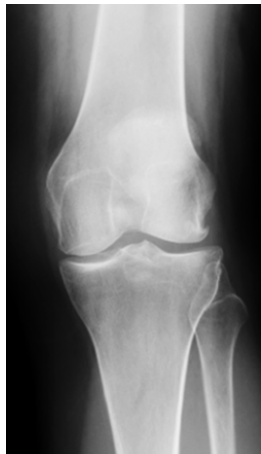
Methods and Results: Review of pertinent literature of MRI of cartilage

“Standard”

- something established by authority, custom, or general consent as a model or example
- authority as a rule for the measure of quantity, weight, extent, value or quality
- Traditional “standards” for cartilage assessment: histology, surgery, mechanical testing

Conventional Radiographs

- ◆ Imaging mainstay for assessment of joint space
 - conventional radiographs do not depict articular cartilage but provide an indirect measure of cartilage loss
 - Remain the FDA standard for osteoarthritis assessment!
 - Recommended views: Non-weight bearing radiographs underestimate degree of joint space narrowing
 - Femorotibial joint: AP standing and PA flexed
 - Semiflexed views (30 - 60) more closely approximate normal anatomic standing position than fully extended view
 - Mechanical axis: standing view hip to ankle; center of femoral head to center of ankle should fall just medial to center of knee joint

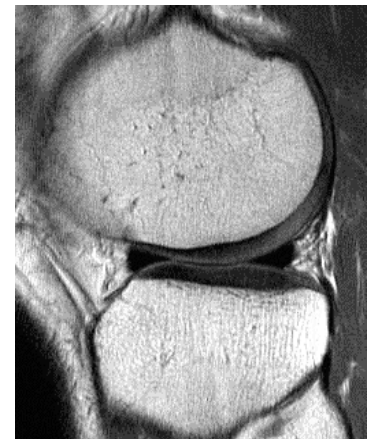


Diagnostic Arthroscopy: how reproducible is it?

- Marx et al: Multirater agreement of arthroscopic grading of knee articular cartilage (*AJSM* 2005)
 - 6 surgeons from 5 centers
 - combined partial thickness lesions : kappa range 0.34-0.87
 - Not combined: overall kappa 0.47
- “Blind” areas:
 - Knee: posterior surfaces (require nonroutine portals); posterolateral tibia (covered by meniscus)
 - Hip: medial and posteromedial
 - Wrist: DRUJ, midcarpal
 - Ankle: inferior gutters, hindfoot

Articular cartilage

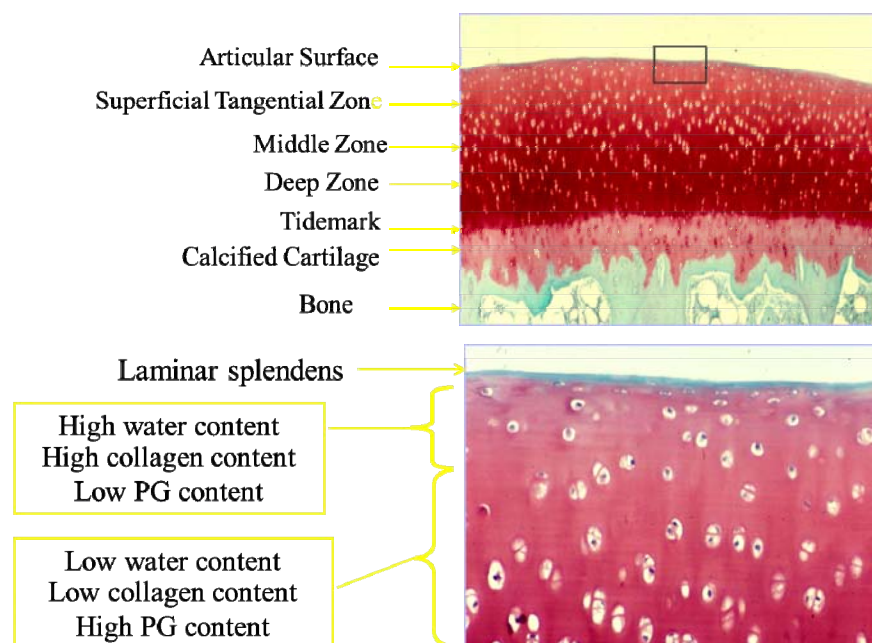
- ◆ Signal properties dependent on:
 - ◆ Cellular composition of collagen, proteoglycans and water
 - ◆ MR pulse sequence utilized
 - Moderate TE FSE more sensitive to partial thickness lesions (*JBJS* 1998; 80A(9):1276-1286)
 - Sensitivity 87%; specificity 94%; accuracy 92%
 - kappa = 0.93
 - Fat suppressed 3D GRE or 3D FSE with isotropic voxels more amenable to semiautomatic segmentation and volume quantification methods
- ◆ Orientation of collagen in different laminae of cartilage



Advantages of MR Imaging

- ◆ Direct multiplanar capabilities
- ◆ Superior soft tissue contrast
- ◆ More sensitive than radiographs in detecting focal chondral lesions and subchondral bony abnormalities prior to subchondral sclerosis
- ◆ Direct visualization of articular cartilage allows for accurate, reproducible measurement of cartilage thickness and assessment of morphologic change

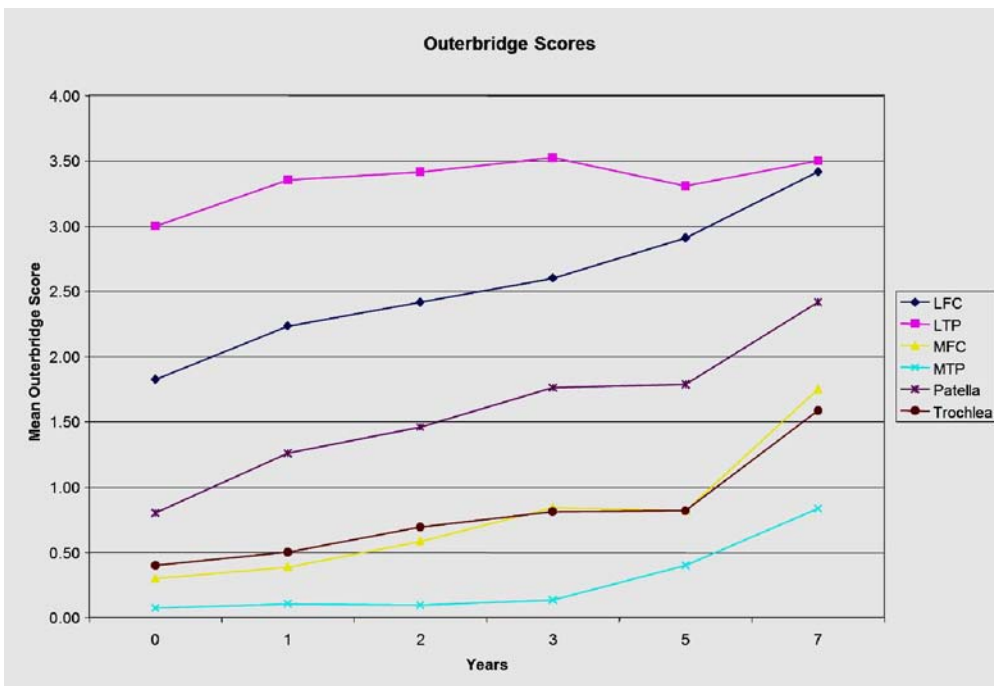
Cartilage is soft tissue: viscoelastic substance with strong imaging and biomechanical anisotropy that is a function of its extracellular matrix



Imaging of Cartilage Structure

- Water proton pools:
 - Free water (accounts for bulk of MRI signal)
 - Bound to PG by electrostatic charge (assess fixed charge density)
 - Sodium MRI
 - GAG CEST
 - Gd-DTPA² techniques (dGEMRIC)
 - T1 rho imaging
 - Associated with collagen fibrils Quantitative T2 mapping:
 - Assess alterations in collagen orientation
 - Diffusion tensor weighted imaging

Cartilage injury following acute, isolated ACL tear: Immediate and longitudinal effect with clinical/MRI follow up. *Am J Sports Med* 2012; 40:276-285



Outerbridge Scores over Time N=42 knees (40 patients; mean age 37 years)

Isolated ACL tear as a traumatic model of OA adjusting for age, sex and type of surgery:

- 100% of isolated ACL tears sustain chondral damage at the time of pivot shift
 - ◆ Spindler et al (*AJSM* 1993; 21:551-557) evaluated 54 pts with ACL tear at ACLR: 46% had articular lesion at arthroscopy
- Risk of cartilage loss doubled from baseline to year one for LFC, LTP and MFC (tripled for patella)
- By year 7-11, risk for LFC was 50 times baseline (30x for patella, 19x for MFC)
- Progressive prolongation of T2 compared to year 1 for LFC and patella
- Nonsurgical vs. ACLR group (adjusted for age, sex and time): Higher risk of cartilage loss over MTP for nonsurgical group (P=0.003) with higher odds ratio effect (5.9; 95% CI)
- Each increase in MFC OB score resulted in 13 pt decrease in IKDC (p=0.0002)

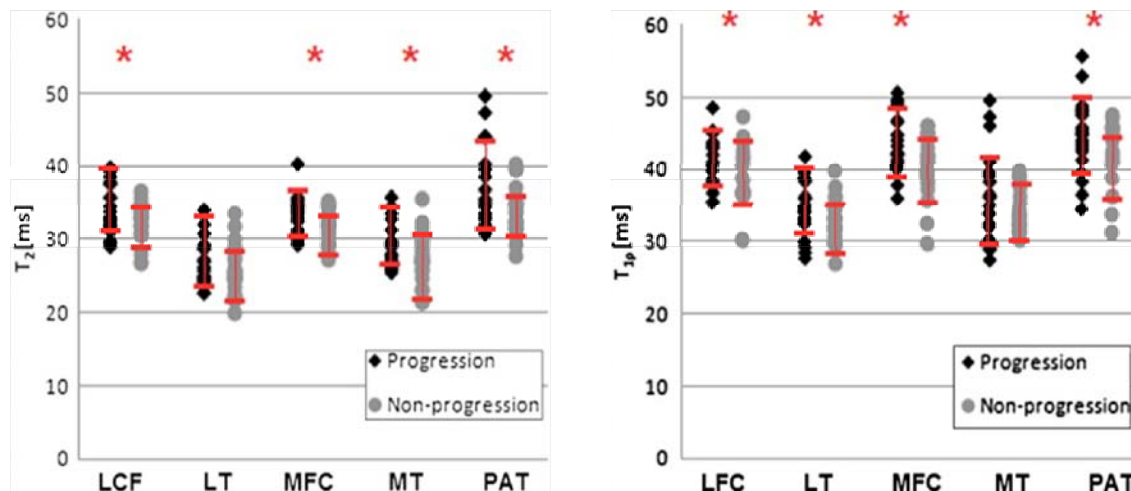
- Each level increase in MTP resulted in 2.4 point decrease in ARS ($p=0.0015$)

Features associated with more rapid progression of OA

- More advanced radiographic disease at the time of initial evaluation
- High baseline BMI
- Baseline meniscal tear, extrusion
- Progressive BME lesion
- * Maximum BML assoc. with WB pain
- Eckstein et al; Arthritis Rheum 2009; 61:1218-1225
- Roemer et al; Radiology 2009; 252:772-780
- Biswal et al; Arthritis Rheum 2002;46:2884-92
- Roemer et al; Radiology 2009
- Hunter et al; Arthritis Rheum 2006; 54:1529-35
- Roemer et al; Ann Rheum Dis 2009; 68:1461-65
- *Lo et al; Osteoarthritis Cartilage 2009 (Epub)

T1 rho and T2 predict cartilage loss

55 subject with no or mild OA
Follow-up over 2 years
2 groups with and without progression



Prasad et al. Osteoarthritis Cartilage. 2012 Oct 8 epub

Assessment of cartilage matrix depletion by QMRI as predicted by subchondral bone impaction on 3D CT in FAI patients

- T2 and T1rho values in and outside of the zone of collision (identified on CT) were compared
- T2 Mapping Results (n=30 hips)
 - Superficial In vs. Superficial Out- difference in means: 8.93 ms, ($p<0.001$)
 - Deep In vs. Deep Out – difference in means: 12.59 ms ($p<0.001$)
 - Superficial In vs. Deep In- difference in means: .43 ms, ($p=.657$) → indicating loss of stratification in the zone of collision
 - Superficial Out vs. Deep Out - difference in means: 3.22 ms ($p<0.001$)
- T1rho (n=22 hips)
 - In vs. Out – difference in means: 9.10 ms, ($p<0.001$)

MRI as Primary Outcome Measure: Cartilage Repair

- ◆ Signal intensity of tissue (ROI)
- ◆ Integrity/hypertrophy of periosteal flap
- ◆ Morphology; presence/absence of displacement (ACI/ OCA)
- ◆ Interface with native cartilage
- ◆ Volume of repair “fill”
- ◆ Appearance/morphology of subchondral bone
- ◆ Assess adj./opp. articular cartilage
- ◆ Presence/absence of inflammatory synovitis
- ◆ MR observation of cartilage repair tissue (MOCART)

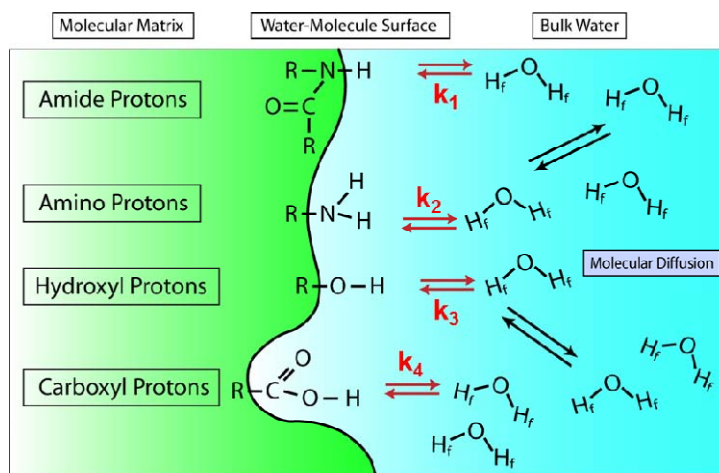
Marlovits et al; Eur J Radiol 2006; 57:16-23

- Correlated to KOOS and VAS; significant correlation for fill, structure, subchondral bone, SI
- ICC (3 readers); κ range: 0.765-1.00



CORR 2004;422: 214-223

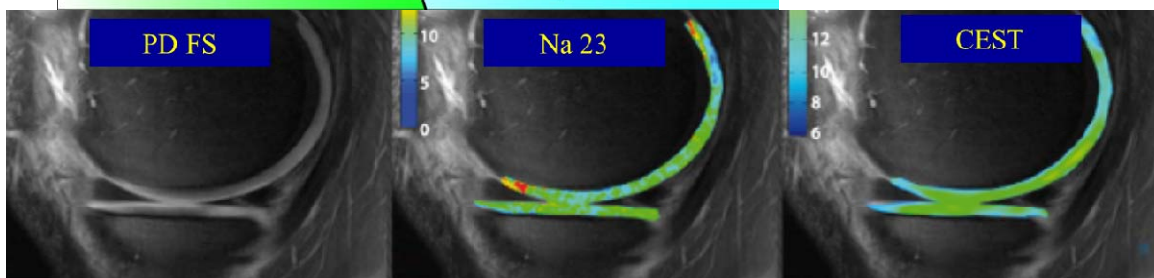
Chemical Exchange Saturation Transfer (CEST)



$$k_{ex} = 22.17 \cdot 10^{(pH-7)} \text{ Hz} \cdot f$$

$$f = \frac{[\text{labile protons}]}{[\text{water protons}]}$$

Siegfried Trattnig MD



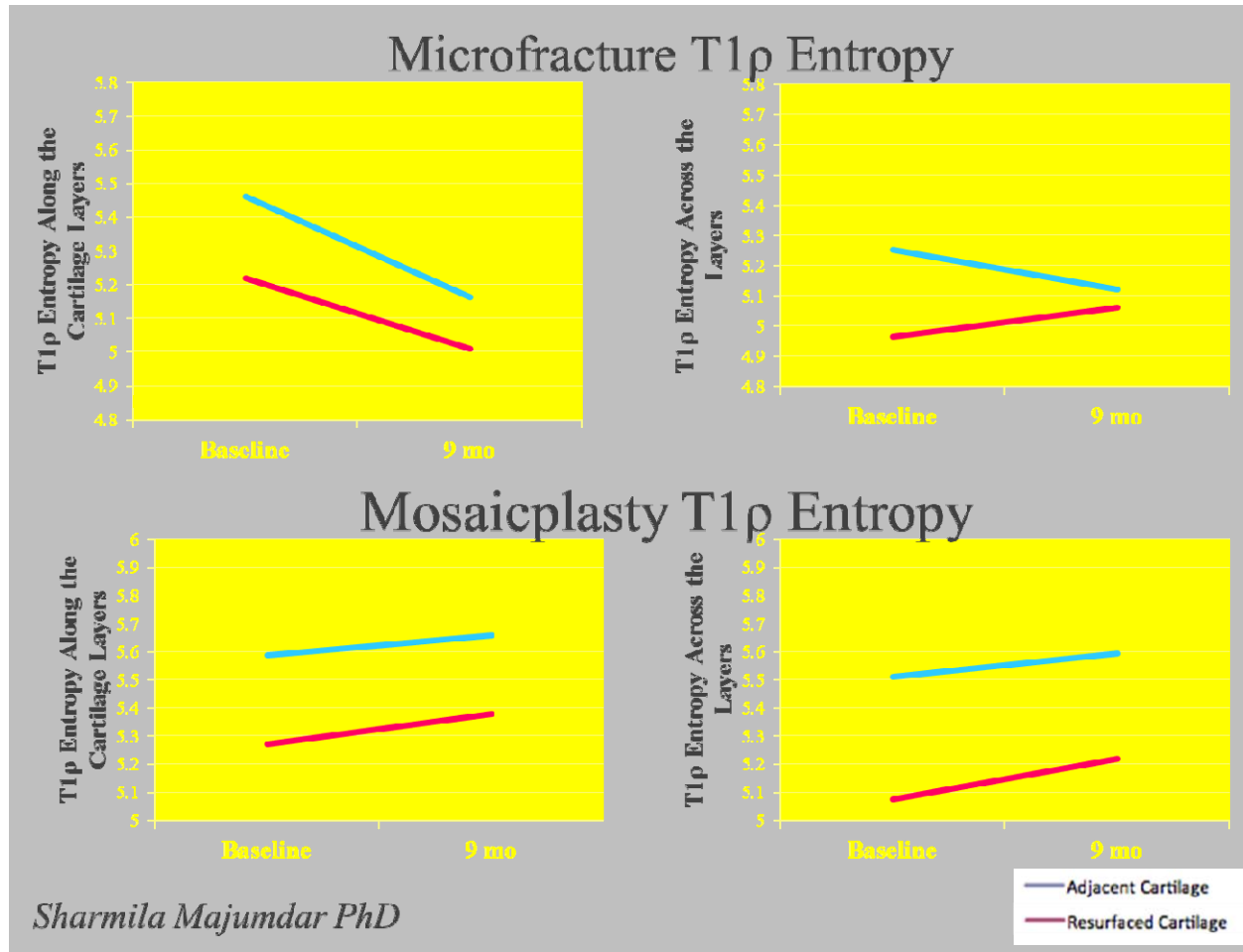
Schmitt et al RADIOLOGY (2011)

Texture analysis

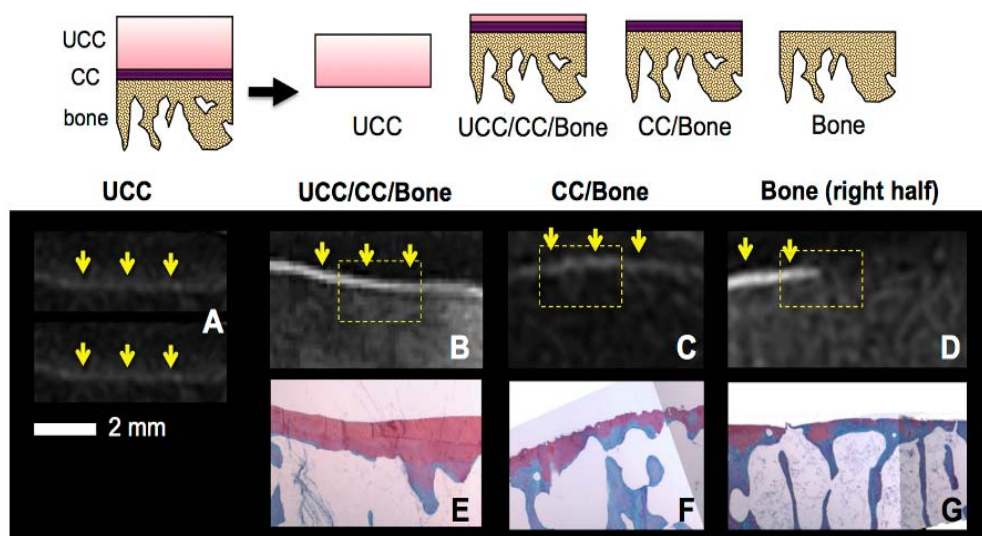
- Represents the classical definition of texture (smooth, rough, etc) with pixel intensities
- Grey Level Co-occurrence Matrix (GLCM) is a tabulation of how often different combinations of pixel intensities co-occur
 - Contrast group (dissimilarity, homogeneity); Orderliness (angular second moment, entropy); GLCM mean (variance, correlation: not simple pixel value but frequency of occurrence in combination with certain neighboring pixels, based on GLCM)

- Haralick *et al* (IEEE 1977) developed a 12 metrics (into contrast, orderliness, and statistical groups) of texture analysis based on the grey-level co-occurrence matrix (GLCM)
- Measures spatial distribution of pixel intensities in an image

Sharmila Majumdar PhD



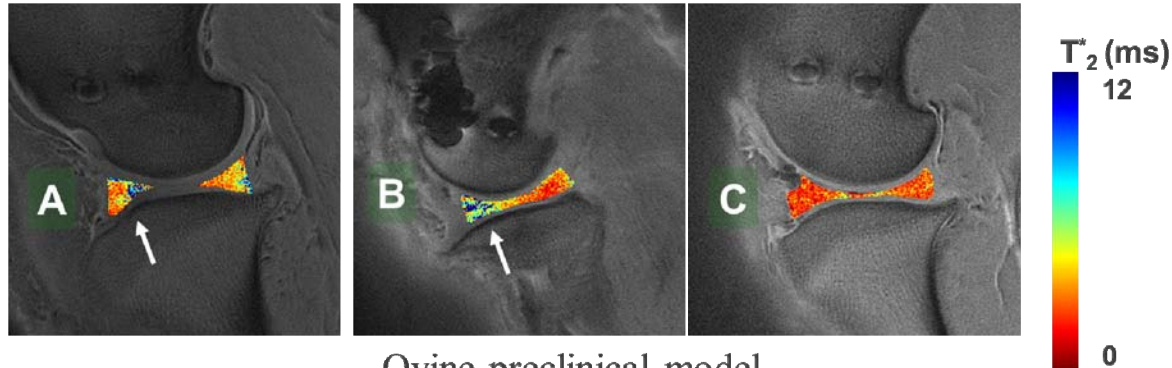
UTE MR Patterns of Calcified Layer Appearance at 3T



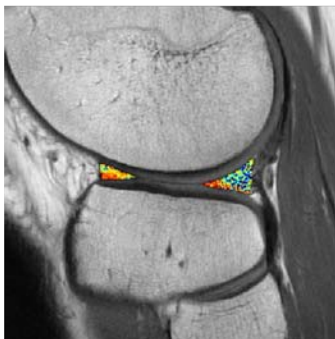
- (A-D) UTE MRI and (E-F) histology of prepared cartilage/bone samples: (A) UCC-only; (B) UC/CC/bone; (C) CC/bone; (D) bone-only. UCC=uncalcified cartilage, CC=calcified cartilage. (Arrows) high intensity linear signals.
Bae, et al., Radiology. 2010; 254(3): 837-845
Courtesy Christine Chung MD

T2* as a biomarker of the repaired meniscus

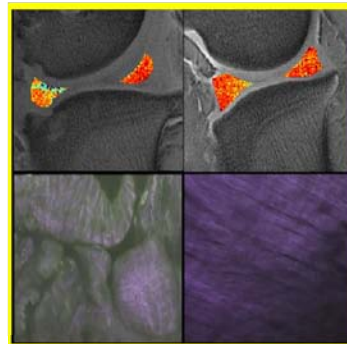
Koff et al Osteoarthritis & Cartilage 2013, 21:1083-91



Ovine preclinical model



T2* map of clinical lateral meniscal repair



Quantitative MRI in Cartilage Assessment

- Ideally assess both PG and collagen
- Provide objective, quantitative data
- Clinical trial challenges for reproducibility: QMRI
 - Add to scan time!!
 - Software availability
 - Magnetic field strength (Na^{23} , T1rho)
 - Contrast agents (dGEMRIC)
 - Magic angle prolongation (T2, T1rho)
 - Coil choice (Na^{23})
 - Parameters of acquisition (SNR, resolution, # echoes)
 - Post-processing algorithm (2 vs. 3 parameter fit)
 - Registration software
- Need dissemination of protocols and MR vendor engagement!!

Imaging of Joint Cartilage in 2014

- ◆ MRI is the standard by which we can assess cartilage morphology
- ◆ Standardized, reproducible MR sequences should be utilized

- ◆ Objective evaluation of cartilage following repair and provides macroscopic assessment of integration
- ◆ Quantitative MR evaluation:
 - ◆ should ideally assess both PG and collagen
 - ◆ Need more longitudinal REGISTRY data performed on populations at increased risk for OA to provide information suitable for powering pharmaceutical intervention to prevent OA progression
 - ◆ DDH, FAI, ACL tears
- ◆ New applications for QMRI: meniscus, ligament, tendon
- ◆ Need to strengthen links to cartilage mechanical properties

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