Imaging of Joint Osteoarthritis

- Radiographs provide information largely about standing alignment
- Standardized, reproducible MR sequences should be utilized
- Objective evaluation of cartilage following repair
- Quantitative MR evaluation:
  - Should ideally assess both PG and collagen
  - Whereas PG depletion generally precedes collagen disruption, most argue that the collagen network is the most “important” matrix component

Cartilage Structure

- Deep radial zone (40-60%): collagen oriented perpendicular to subchondral zone—strong angular dependence: vertical striations evident and short T2 values
- Transitional zone (20-30%): more random collagen orientation—less angular dependence and longer T2s
- Superficial zone (<10%): parallel to surface (beyond resolution of clinical MRI)

Imaging of Cartilage Structure

- Free water (accounts for bulk of MRI signal)
- Bound to PG by electrostatic charge (assess fixed charge density)
  - Sodium MRI
  - Gd-DTPA-2 techniques (dGEMRIC)
    - Correlated to static (compressive) mechanical properties at 9.4T*
  - T1 rho imaging
- Associated with collagen fibrils Quantitative T2 mapping:
  - Assess alterations in collagen orientation
  - Correlated to dynamic mechanical properties at 1.5T and 9.4T*
- Diffusion tensor weighted imaging

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

* 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; Osteoarth Cartilage 2009 (Epub)
Whole-Organ MRI (WORMS) Score  
*Osteoarthritis & Cart* 2004; 12: 177-90

- Cartilage signal and morphology
- Marrow edema pattern
- Subarticular cysts
- Subarticular bone attrition (subchondral flattening)
- Osteophytes
- ACL/PCL (torn, intact)
- MCL/LCL (torn, intact)
- Menisci (0-4; include postop changes)
- Synovitis (0-3 based on % involvement of maximum potential distention; no distinction made between effusion and synovitis)

0-7: none, equivocal, small, small to moderate, moderate, mod-large, large, very large

**T2 mapping at HSS: Issues of PSD**

- Conventional Spin Echo (SE) (multiple acquisitions) vs. *Conventional* multi-slice, multi-echo (MSME) sequence
- Similar range of TEs
- *Stimulated echo* component due to imperfect slice-selective refocusing pulses
- *Magnetization transfer contrast* (MTC) between slices
- Substantial *inaccuracy in T2 calculation* for articular cartilage

**T2 mapping at 1.5T: Issues of PSD**

- Modified multi-slice, multi-echo (MSME) sequence
- ↓↓ ↓↓ Slice-selective refocusing pulse gradient amplitude reduced (relative to excitation pulse)
  - ↓↓ Stimulated echo contribution
- ↑↑ ↑↑ Cross talk
  - Requires interleaved slice acquisition (forced 2 acquisition)
- Assumes a monoexponential decay
- T2 calculated by natural logarithm of mean signal of the ROI and performing a weighted least squares fit

Maier et al; *J MRI* 2003; 17(3):358-364

**Quantitative MR in hip disease**

- Kim et al studied pts with DDH and found the dGEMRIC index was sensitive to OA changes as well as symptoms (WOMAC) (*JBJS* 2003; 85A:1987-1992)
- F/U study of pts with DDH treated with osteotomy showed that pts. who clinically failed osteotomy had more OA on radiographs and lower dGEMRIC indices, but dGEMRIC index was more predictive of failure (*Cunningham et al; JBJS 2006; 88A:1540-1548*)
- Nishii et al studied pts with DDH with mild or no OA and nl controls with T2 mapping at 3T; prolongation of T2 was noted in the majority of the early OA pts (*Osteoarthritis and Cart 2008; 16:227-233*)

**Articular Cartilage Injury following Acute ACL Tear**

- Spindler et al (*AJSM 1993; 21:551-557*) evaluated 54 pts with ACL tear and ACLR
  - 46% (25/54) had articular lesion at arthroscopy (LFC>LTP>MFC>MTP)
- Johnson et al (*AJSM 1998; 26:409-414*) evaluated 10 pts with acute ACL tear underwent biopsy of LFC during ACLR
  - Chondrocyte degeneration, loss of PG, osteocyte necrosis and empty lacunae degeneration
- Tiderius et al (*Arthritis and Rheumatism 2005; 52:120-127*) evaluated cartilage glycosaminoglycan loss in the acute ACL injury with delayed post-gadolinium MRI
  - 15 out of 24 patients (63%) had loss of GAG in both medial and lateral femorotibial surfaces
  - Suggests generalized alteration in matrix within the knee cartilage following ACL injury

**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
- 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
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)

Cartilage Repair: Methods of Repair

- Articular cartilage has little to no capacity to undergo spontaneous repair
  - avascular; unable to regenerate across a physical gap
- Debridement
- Marrow stimulation (microfracture)
- Osteochondral transfer
  - autologous (mosaicplasty; OATS)
  - allograft (fresh cadaveric tissue)
- Tissue Engineered Cartilage (three requirements)
  - matrix scaffold
    - carbohydrate based polymers (polylactic acid)
    - protein based polymers (collagen, fibrin)
  - cells
    - chondrocytes
    - chondroprogenitor cell pools (cambial layer of periosteum and perichondrium)
    - mesenchymal stem cells from the bone marrow or synovial membrane
  - signaling molecules (growth factors or genes)
- Synthetic acellular techniques (scaffold)
  - polylactide-co-glycolide copolymer and calcium sulfate (porous)

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 adjacent/opposite 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

Imaging of Microfracture

- Prospective study of 48 patients treated with microfracture evaluated by validated clinical outcome instruments and cartilage sensitive MRI
  - bony overgrowth was noted in 25% of patients, but did not have a negative effect on clinical outcome scores
  - adverse functional scores after 24 months did correlate with poor percentage fill
  

24 year-old professional football player with unstable lesion MFC

- Welsch et al (Radiology 2008; 247:154-161) studied 20 pts following MFX or MACT with mean F/U 28.6 vs 27.4 mo
- MFX tissue showed reduced mean T2 whereas MACT showed mean T2 similar to control tissue (56.4msec); MFX showed no stratification while MACT did from deep to superficial areas

Imaging of Osteochondral Allografts

- Prospective, longitudinal study of cartilage defects treated with hypothermically stored fresh osteochondral allografts

Allografts remain intact without displacement
- fissures noted at the graft/host interspace in 78%
- poor incorporation was noted in 22% grafts: persistent bone marrow edema pattern and/or subchondral marrow fibrosis
- collapse of the subchondral bone in the graft was correlated to lack of bony integration based on signal characteristics
  • Sirlin et al. correlated MRI of shell osteochondral allografts to the results of antihuman leukocyte antigen antibody screening (Radiology 2001;219:35-43)
  - Pts. who expressed positive humoral immune responses were associated with decreased incorporation, greater marrow edema pattern and a higher proportion of surface collapse of their graft

T2* of meniscal repair
- Morphologic grading correlated well to T2*; however, T2* was more predictive of healing based on histology as standard
- T2* values are predictive of meniscal healing and show potential as a biomarker for meniscal integrity
- Regional differences indicating collagen disruption are detectable

Imaging & Cartilage OA/Repair Trials: cartilage morphology
- Preclinical outcome measures should parallel Phase I and Phase II clinical measures for repaired tissue
- Clinical trial challenges: morphology
  - Sufficient spatial resolution to detect partial thickness lesion, abnormal synovium, subchondral sclerosis
  - Standardize protocol, field strength, coils
  - Used cartilage sequence previously validated for accuracy and reproducibility for cartilage morphology
  - Issues of availability of QMRI sequences and standardization of postprocessing

Quantitative MRI in OA assessment: Issues of Data Acquisition
- Ideally assess both PG and collagen
- 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

Quantitative MRI in OA assessment: Issues of Data Interpretation
- Issues of sampling:
  - Thin cartilage: hip, ankle, wrist, shoulder
  - Avoid sampling the tidemark and the synovial fluid
  - Standardize # pixels for sampling and site of sampling
  - Need laminar data with deep and superficial sampling
  - For OA, may do 1-2 slices per compartment
  - For cartilage repair, sample within repair, native hyaline cartilage and at interface with host tissue

Clinical applications of QMRI of cartilage
- Provides objective assessment of matrix alteration in cartilage that often precedes morphologic alterations
- QMRI is best applied in conjunction with standardized, reproducible MR sequences and standardized OA scoring systems
- Objective evaluation of cartilage following repair that may obviate the need for surgical biopsy of repair tissue
Quantitative MR evaluation:

- should ideally assess both PG and collagen
- Registration methodology helpful for longitudinal analysis
- Need more longitudinal REGISTRY data performed on populations at increased risk for OA to provide information suitable for powering pharmaceutical intervention
- DDH, FAI, PF dysmorphism, ACL tears

References


