Multimodality Multiparametric and Motion Musculoskeletal Imaging: Structure and Function

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DISCLOSURES

- Research Grants
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  - Globus Medical
  - Image Analysis Group
  - Pfizer

- MAB
  - Carestream
  - Image Analysis Group
  - GE

Call for Action to Invest in Musculoskeletal Health and Control the Burden of Musculoskeletal Conditions

Musculoskeletal disorders are the most common causes of severe long-term pain and physical disability, affecting hundreds of millions of people across the world.
Functional Imaging

- Medical imaging usually performed in static, non-loaded non-physiologic state
- Motion is an integral function of the MSK system
- Evaluating joint dysfunction could be enhanced by functional imaging
- Functional Imaging for MSK

Functional Imaging: Impetus

- Some disorders of muscles, tendons, nerves, and joints are better or only seen dynamically
  - during motion of the extremity
  - muscle contraction
  - Compression/provocative maneuvers
  - position change

Functional Imaging: Types

- Positional
- Loaded/weight bearing
- Dynamic-Kinematic
- Biochemical
Functional Imaging Intersections

- Positional
- Load/weight bearing
- Biochemical
- Dynamic, Kinematic

Wrist: DRUJ Instability

- Positional CT or MRI
  - Pronation, neutral, supination
  - Image bilateral wrists
OA patient with tendon rupture

Normal
supination

Normal
pronation

OA
supination

OA
pronation

ruptured tendon (Ext. dig. quinti prop.)

TFCC morphology:
Ulnar - radial deviated position

Ulnar-deviated position Radial-deviated position

Ulnar - neutral - radial deviated position

Ulnar-deviated position Neutral position Radial-deviated position
Fat suppressed MRI of Shoulder at 0.3T

Abduction, external rotation  Neutral

Courtesy of M Dohi, MD - JISS

Labrum Morphology:
position dependent shape

IR  ER

ABER Imaging Plane

ABduction External Rotation
Surface Coils
Coronal Localizer
ABER prescribed oblique along axis of humerus
Internal Impingement in ABER Position

courtesy of Col Timothy Sanders MD, WHMC
Normal configuration of hip with sufficient joint clearance allows unrestricted range of motion (top).

In pincer impingement, excessive acetabular overcoverage leads to early liner contact between femoral head-neck junction and acetabular rim, resulting in labrum degeneration and significant cartilage damage. Posterior portion of labrum is damaged (contrecoup) due to subtle subluxations (center).

In cam impingement, aspherical portion of femoral head-neck junction is jammed into acetabulum (bottom).
Figure: Sagittal intermediate-weighted dynamic MR images (3000/24) show a hip in extension (a) and flexion (b).
A 24-year-old man, competitive javelin thrower, who had a history of ulnar collateral ligament reconstruction 5 years earlier and recently felt a pop and recurrent pain while throwing...
Lumbar Spine Motion on Discography

- One possible cause of back pain in patients with intervertebral disk degeneration is decreased stability of the motion segment.
- Axial rotations between lumbar spinal vertebrae can be measured noninvasively with CT or MRI.
- Concordant pain at discography predicts increased axial rotation at a lumbar disc level.
- Rotation averaged 0.6° for the normal discs, 1.4° for discs with nonconcordant pain, and 1.8° for discs with concordant pain.

Functional Imaging

Loaded/weight bearing
EOS System

- Low dose biplane x-ray system utilizing two perpendicular x-ray beams with a novel detector
- Performed in an upright, weight-bearing position: assesses kyphoscoliosis
- Commonly used in pediatric scoliotic patients
- Improved visualization of thoracic spine

Intervertebral Disc: Anatomy

NUCLEUS: Soft hydrated
ANULUS: Concentric lamellae
- Angle alternates to form cross-woven reinforced structure
Define morphologic changes in the disk

Spine “Functional” Imaging: Positions

- Supine with axial loading (simulated weight bearing)
- Seated
- Upright

Made of hardened plastic, DynaWell™ L-Spine is free of any material that would disturb the magnetic field of the MRI scanner.

The key features are:
- Cushioned vest: with adjustable straps
- Stretch cords: on either side of vest
- Calibration instrument: at top of the foot plate
- Foot plate: at base of scanner
DynaWell: Literature

Physiologic Changes of Spinal Canal

Cross-sectional area of the spinal canal is smallest in extended position.

Smallest foraminal dimensions in extended position.
Recumbent

Upright-Extension

Kinetic Central Spinal Canal Stenosis

J. Randy Jinkins, MD

CT Multi-Detector CT (MDCT)

MDCT:
Fan Beam (1-2 Detector Rows)
Multiple Reconstructive Techniques
Helical (Spiral) Acquisition
Mammography Imaging in OI

Cone-Beam CT (CBCT)

CBCT:
Cone Beam, Large Area Flat Detector
Single Rotation (without X-ray Divergence)
Mechanically Simple – Novel Platforms
New Applications: ENT/Dental, IGS

Multi-Detector CT (MDCT)

Intraoperative C-arm

Flat Panel Detector
Applications of Cone-Beam CT

- Flat-panel detector (FPD)
- Compact gantry
- Siting / standing examination
- Weight-bearing scans
- High isotropic spatial resolution
- Multi-mode Rad / Fluoro / CBCT
- Simplified logistics
- Modest imaging dose

* Zbijewski et al. Med Phys 2011
* Carrino et al. Radiology 2014
** Tuominen et al. AJR 2013
** Huang et al. Skeletal Radiol 2015

Extremity CBCT

- Carestream OnSight 3D
- CurveBeam pedCAT
- Planmed Verity

Applications of Weight-Bearing CBCT

Anatomical metrics in weight-bearing CBCT

- Tibial Tuberosity – Trochlear Grove Distance

CBCT vs. RA in weight-bearing

- Improved detection of arthritis and impingement
- Consistent with prior study

Challenges

- Establish clinical significance of CBCT metrics and weight-bearing
- No "gold standard" reference values – ongoing work.

1. Hirschmann Eur Radiol 2015 (Planmed Verity)
3. Hirschmann Eur Radiol 2014 (Planmed Verity)
4. Netto Foot Ankle Ortho 2016 (OnSight3D)
5. Lepojarvi Foot Ankle Internat 2016 (Planmed Verity)
7. Burssens Foot Ankle Surgery 2016 (pedCAT)
8. Lintz Foot Ankle Internat 2017 (pedCAT)
9. Collan Foot and Ankle Surgery 2013 (Planmed Verity)
10. Richter Journal Foot Ankle Surgery 2016 (pedCAT)
11. Richter Foot Ankle Surg. 2014 (pedCAT)
12. Ellis Foot Ankle Inter 2010 (Philips Eleva)
13. Barg Foot Ankle Internat 2017 (Review)
Joint Space Analysis in OA

**Joint Space Width (JSW)**
- Detection and staging of OA
- Currently measured with weight-bearing RAD
- More accurate positioning with CBCT
- Improved sensitivity
- High inter-reader agreement
- Weight-bearing (WB) vs. Non-weight bearing (NWB)
  - Significant difference in JSW for OA
  - No significant difference in JSW for non-OA

**Additional metrics accessible to CBCT**
- Meniscal extrusion (ME)
  - Weight bearing aids detection of ME
  - ME changes between WB and non-WB in OA patients
- Osteophytes and cysts in OA
  - Higher sensitivity and specificity in CBCT than RAD

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**Dynamic Kinematic Imaging**

- **Dynamic**
  - "real-time"
- **Kinematic**
  - "joint in motion"
Dynamic Kinematic Ultrasound

Advances in sonographic technology, including higher resolution probes, power Doppler sonography, extended field-of-view imaging, and compound imaging, have contributed to expand its clinical applications.


Dynamic Joints

- Move
- Move
- Move
- Move

Continuous Movement
Dose = 0.5mSv

Continuous Exposure
Dose = 1mSv
• KINEMATIC MRI OF THE PFJ

POSITIONING DEVICE

Knee GRE
TR/TE/FA=38/17/40, Slice Thickness 2mm

Courtesy of M Dohi, MD JISS
3T Open-Bore MRI

- Improved off iso-center imaging (TrueForm™ design)
- Large patients
  - Athletes
  - Bariatric
- More positioning options (decubitis)
- Mild claustrophobia
- Functional Joint Imaging
- High Field Strength 3T

Johns Hopkins Bayview Med CTR
Siemens Verio
Courtesy of Mark Bohlman, MD

Functional Imaging

T2 TSE, 43 sec acquisition, 6 partitions, 5mm SL, 256 matrix, 26 cm FOV

70 cm open bore broadens clinical possibilities: Kinematic Imaging

T2 TSE, 38 sec acquisition, 6 partitions, 5mm SL, 256 matrix, 32 cm FOV

High Field Strength 3T open bore innovation.
Unique Applications

1. Volume Scan
   • ONE Rotation
   • ONE Heart Beat

2. Dynamic Volume Scan
   • ONE Examination
   • New Diagnostic Tool
Dynamic Volume CT

- 16 cm coverage per rotation
- 320 X 0.5mm detector elements
- 350 msec rotation time
- 650 lb patient couch

The subject's knees are positioned within the CT gantry (Viewed from the other side of gantry). The subject's knees are secured with a strap to prevent translation during flexion and extension of the knee. The CT gantry is tilted away from the subject in order to maximize knee motion.

The subject is a 38-year-old man with healthy knee.
Characterization of changes in PF loading with dynamic 3D CT

- Primary objectives: to show the efficacy of using dynamic 3D CT imaging technology paired with computational modeling and analysis, in its application to furthering our understanding of kinematics and biomechanics of the knee with respect to patellofemoral instability. In particular, we hope to show how realignment procedures will centralize the patella and reduce patellar subluxation and instability as well as reduce the pressure applied to lateral cartilage, thereby improving function and slowing cartilage degeneration.

- Secondary objectives: to examine the efficacy of realignment surgeries (including tibial tubercle transfers and MPFL reconstructions) in the way they 1) unload the lateral patellofemoral cartilage and 2) correlate with changes in the patient's pain and functional status.

Computational and experimental pressure patterns superimposed over the image of the patella for one knee at 60° of flexion. Pressure changes related to VMO weakness are shown for intact cartilage and cartilage with a lateral lesion.

Functional Imaging Intersections
Disc Structure

- Avascular
- Low oxygen tension
- Acid pH
- Extracellular matrix
- Cell density <0.5%

Courtesy of Lee Riley

Intervertebral Disc: Three Major Constituents

1. WATER
2. COLLAGEN
3. AGGREGAN
   - Proteoglycan core
   - GAG chains

Intervertebral Disc: Function

Compression → Water Movement
Mechanical loading of the intervertebral disc will result in a complex set of physical changes that may be transduced as mechanical stimuli to the cells.


Intervertebral Disc Degeneration

With Degeneration

• Loss of proteoglycan and water
• Fibrocartilage formation and disorganization of the anular architecture


MRI Cartilage Biomarkers
- Collagen
  - Diffusion
  - T2 maps
- GAG
  - dGEMRIC
  - Sodium Imaging* - T1rho*

*most benefit from higher field

Early Detection of Disc Degeneration
T1, Na, T2, dGEMRIC
DIFFUSION (DTI)
T2 Mapping

- Loss of proteoglycans → loss of the fixed negative charge density → can be mapped negatively
- T2 variations could be related to:
  - Known distribution of water content
  - Distribution of proteoglycan content with cartilage depth
  - Collagen network organization in different zones of cartilage
- T2 relaxation times of the IVD correlate strongly with water content and weakly with PG content


T2 mapping

Single-echo imaging of the disc sample, features enhance sensitivity to the proton motion with conventional T2-weighted imaging.

Na MRI

- [Na] measured from sodium MRI correlates to [PG] measurement in discs (bovine samples)
- High field MRI 3T with special coil to detect sodium

**T1 ρ:**
Spin-lock MRI technique

Generates a new type of contrast, with images that reflect low frequency interactions (chemical exchange rate between macromolecules and free water).

**EARLY DETECTION:**
T1 ρ

Representative T1-weighted images and quantitative T1 maps for 2 lumbar spine sections.

T1 ρ values were higher in the younger, non-degenerate disks.

Average T1ρ in nucleus had a strong linear correlation with GAG content.

Johannessen et al. Spine 2006; 31:1253-1257

**Diffusion**

- Diffusion imaging is a method for measuring the displacement distribution of water molecules *in vivo.*

Brownian Motion: 3D Random motion
**Diffusion terms**

- **Isotropic**: Diffusion occurs along all directions, (with no preferred direction for diffusion), as in free water.
- **Anisotropic**: Diffusion is restricted and has directional dependence, as when it comes into contact with cell membranes and other large structures.

**Diffusion Imaging: Technique**

Refocusing Gradient:

- Some protons will have moved during the time interval between pulses (Diffusion)
- Measured signal is reduced by amount of diffusion

**Diffusion Techniques**

- The diffusion of water occurs unequally in different directions
- **Diffusion Weighted Imaging (DWI)** measures the relative amount of water diffusion occurring in a voxel
- **Diffusion Tensor Imaging (DTI)** measures the direction and magnitude of water diffusion in 3 dimensions in a voxel
Intervertebral disc specimens (L1 to L5). Regions of interest of MR scans that were performed are visible as white squares on the anterior annulus fibrosus, nucleus pulposus, and posterior annulus fibrosus.

The information obtained by the ADCs, particularly of the nucleus pulposus, can potentially be used in combination with quantitative T1, T2, and MT parameters to noninvasively obtain a quantitative assessment of the disc matrix composition and structural integrity.

**DTI values reflect the orientation of collagen fibers in articular cartilage**


**Orientations of anisotropy exhibit a layered morphology that agree with light micrographs of the disc**

*Hsu et al MRM 1999; 41:992-999
**Basis for Ultrashort TE Sequence**

**Transverse Magnetization Decay**

- Total magnetization
  - Long T2 component
  - Short T2 Component

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**Symphysis Intervertebral Disc**

- Firmest attachment of disc to vertebral body is at outer bony ring
- Lamellar bands of disc penetrate the ring as Sharpey’s fibers

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**Normal UTE Appearance CEP**

- well-defined linear signal intensity found, at least partially, near all cartilaginous endplate (CEP)
Degeneration CEP with UTE MRI

- focal loss or irregularity

Note: what is DCE-MRI

Why is inflammatory perfusion important?

Conclusion: 107 patients

Subclinical joint inflammation in 20% detected by imaging techniques explains the structural deterioration in RA patients in clinical remission who are receiving conventional therapy with:

- 12 times higher odds of deterioration in joint with increased PD signal (odds ratio 12.21, P < 0.001)
- 4.5 times higher odds using MRI synovitis and osteitis

Mikael Boesen, MD, Phd
Dynamic Curves

Enhancing tissues (active synovitis) vs Non-enhancing (bone, muscle, healthy tissue)

Validation: DCE-MRI

DCE-MRI is an imaging technique based on sequential acquisition of rapid MRI sequences before and during the infusion of a contrast agent. DCE-MRI can discriminate patients with active disease from patients with remission regardless of MRI scanner strength.

Techniques for quantification of DCE-MRI:
- Region of Interest (ROI) Subtraction
  - Visual
  - Time consuming, difficult to reproduce, not sensitive
- RAMRIS
  - First attempt to standardise
- Computer-aided analysis of DCE-MRI with integrated patient motion correction

Impact of motion correction on the quality of MRI data:

DCE-MRI correlates well with synovial activity and inflammation.
Quantitative DCE-MRI is a stable, reproducible, and robust technique.

Arthritis and Rheum 1994
Arthritis and Rheum 2003
European J. of Radiology 2007

- DCE-MRI vs Histology, 2013
- DCE-MRI vs US Doppler, 2007
- DCE-MRI vs artefactual motion artifacts
- DCE-MRI vs dual source CT, 2011
- DCE-MRI in healthy controls, 2013
- Dynamic range: 2013
- Relative and inter observer variability for quantitative DCE-MRI: 2012
IVD: Endplate Perfusion

- Clinical studies using serial CE-MRI show a correlation between diffusion and morphologic DDD with endplate status being the most important factor influencing disc diffusion

- Characteristics of normal, aging and degenerative discs and the effect of pharmacologic modulation of enhancement with nimodipine have been described

dGEMRIC: Technique

- PG/GAG depletion causes areas of negative charge
- Need to use positively charged contrast material
- Delayed acquisition time

References:

Metabolite assessment by proton MR spectroscopy

- Location and amplitude of resonances yield information about which metabolites are present and in what concentration.

- Relies on the same physical principles as MRI.

- Biochemical (rather than anatomical) information about tissue content.

Functional Imaging Intersections

- Positional
- Loaded-weight bearing
- Biochemical
- Dynamic, Kinematic
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<td>Multidetector CT</td>
<td>High spatial resolution</td>
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**TABLE:** Comparison of imaging modalities’ characteristics for functional joint imaging

The biomarker development process

![Diagram](image)

**The Research Framework**

| TABLE 1: The Tiers Model of Diagnostic Efficacy |
|-----------------------------------------------|-----|
| Stage of Efficacy | Evaluation |
| Technical capacity | Validation, reproducibility |
| Diagnostic accuracy | Validation, specificity, precision values, RCC curves |
| Therapeutic impact | Validation, ability of diagnostic test to affect the diagnostic impact |
| Therapeutic outcomes | Ability of diagnostic test to influence therapeutic choice |
| Efficacy outcomes | Ability of diagnostic test to increase the length of survival |

**Fundamentals of Clinical Research for Radiologists**

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