Multimodality Multiparametric and Motion Musculoskeletal Imaging: Structure and Function

John A. Carrino, M.D., M. P. H.
Vice Chairman, Department of Radiology and Imaging
Hospital for Special Surgery
Professor of Radiology, Weill Cornell Medicine
New York, NY

AAPM 2018

HSS

DISCLOSURES

- Research Grants
  - GE (Institutional)
- Consultant
  - 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

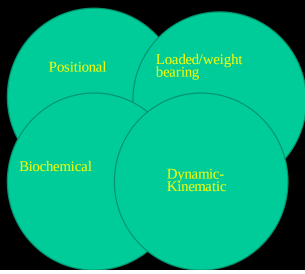
Functional Imaging: Impetus

- 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

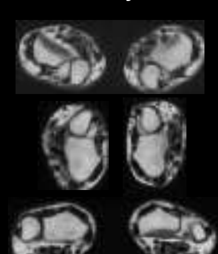
Functional Imaging Intersections



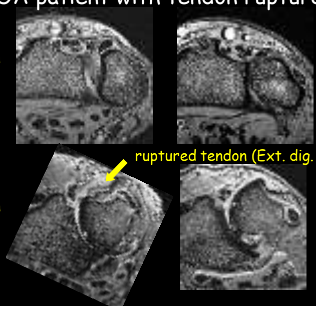
Functional Imaging

Wrist: DRUJ Instability

- Positional CT or MRI
  - Pronation, neutral, supination
  - Image bilateral wrists

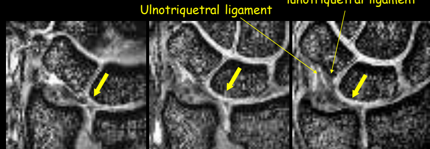


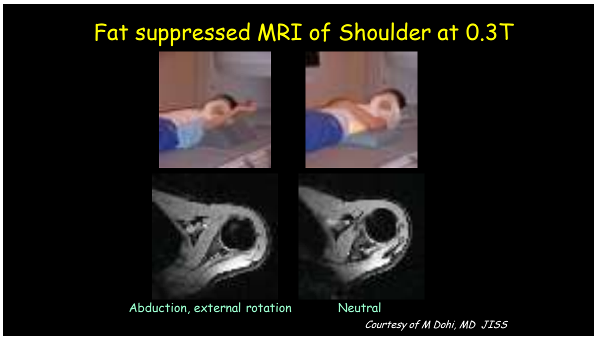
OA patient with tendon rupture

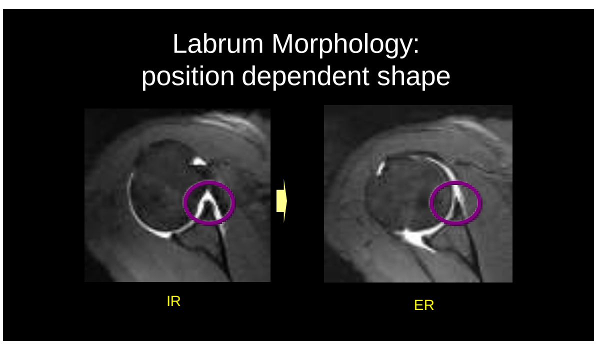


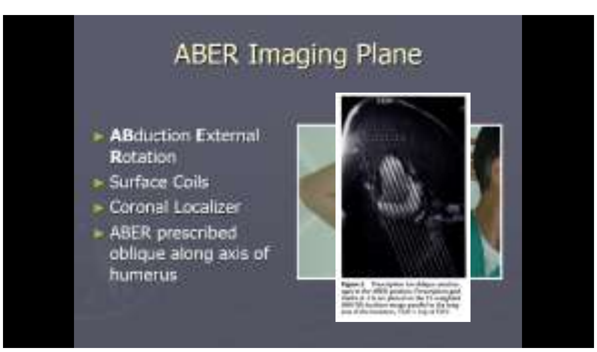
TFCC morphology: Ulnar – radial deviated position

Ulnar – neutral - radial deviated position




Fat suppressed MRI of Shoulder at 0.3T
Abduction, external rotation
Neutral
Courtesy of M Dohi, MD JISS

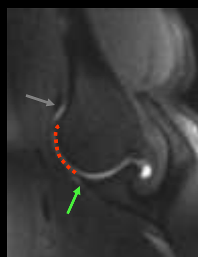

Labrum Morphology:
position dependent shape
IR
ER


ABER Imaging Plane
ABduction External Rotation
Surface Coils
Coronal Localizer
ABER prescribed oblique along axis of humerus

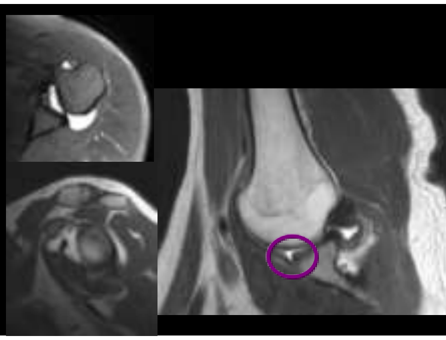
Inferior Glenohumeral Ligament

ABER
T1 fat sat

ANTERIOR



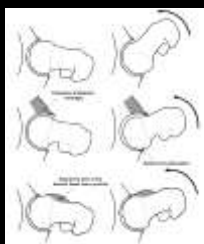
POSTERIOR



Internal Impingement in ABER Position

courtesy of Col Timothy Sanders MD, WHMC

FAI



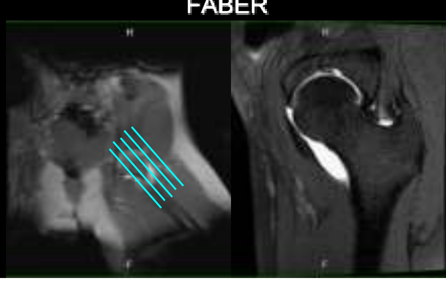
Normal configuration of hip with sufficient joint clearance allows unrestricted range of motion (top).

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

In cam impingement, aspherical portion of femoral head–neck junction is jammed into acetabulum (bottom).

Tannast M et al. AJR 2007;188:1540-1552

FABER



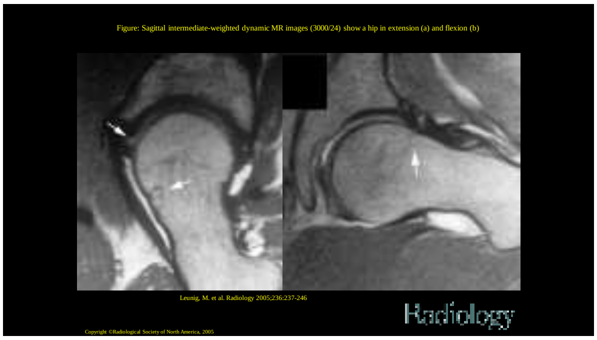
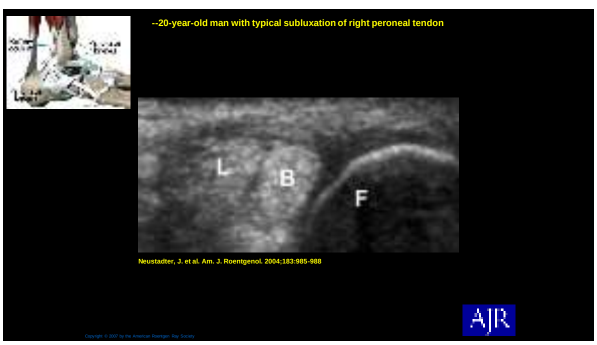
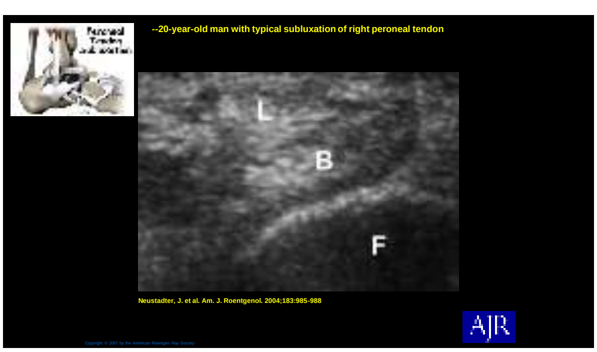


Figure: Sagittal intermediate-weighted dynamic MR images (3000/24) show a hip in extension (a) and flexion (b)
Leunig, M. et al. Radiology 2005;236:237-246
Radiology
Copyright ©Radiological Society of North America, 2005


--20-year-old man with typical subluxation of right peroneal tendon
L
B
F
Neustadter, J. et al. Am. J. Roentgenol. 2004;183:985-988
AJR

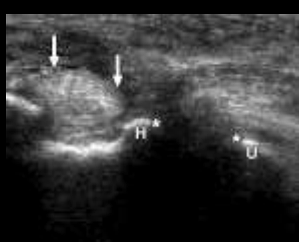

--20-year-old man with typical subluxation of right peroneal tendon
L
B
F
Neustadter, J. et al. Am. J. Roentgenol. 2004;183:985-988
AJR

--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

Nazarian, L. N. Am. J. Roentgenol. 2008;190:1621-1626

AJR

--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



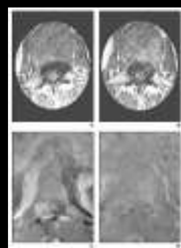
Nazarian, L. N. Am. J. Roentgenol. 2008;190:1621-1626

AJR

Donna G. Blankenbaker, Victor M. Haughton, Baxter P. Rogers, M. Elizabeth Meyerand, and Jason P. Fine. Axial Rotation of the Lumbar Spinal Motion Segments Correlated with Concordant Pain on Discography: A Preliminary Study. Am. J. Roentgenol., Mar 2006; 186: 795 - 799.

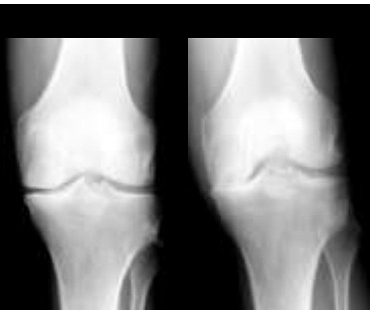
Lumbar Spine Motion on Discography

- 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

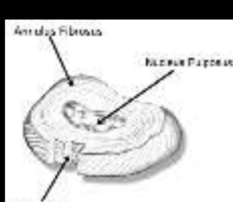
Loaded/weight bearing



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 re-inforced structure

Degenerative Disk Disease: Conventional Imaging Approach

Define morphologic changes in the disk

Spine "Functional" Imaging: Positions

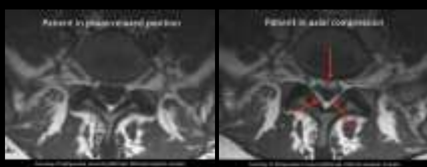
- **Supine with axial loading (simulated weight bearing)**
- **Seated**
- **Upright**

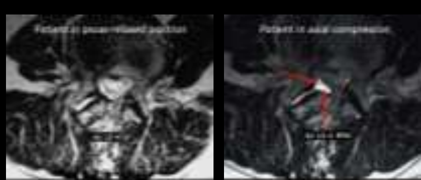
DynaWell

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

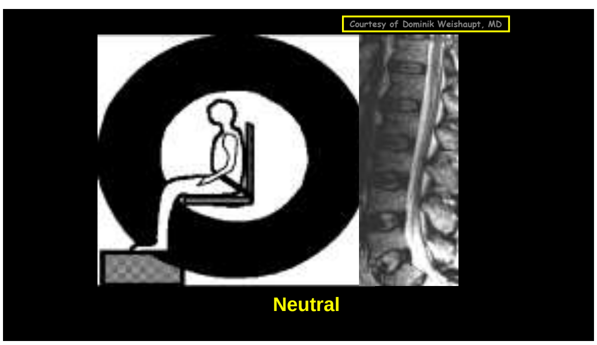


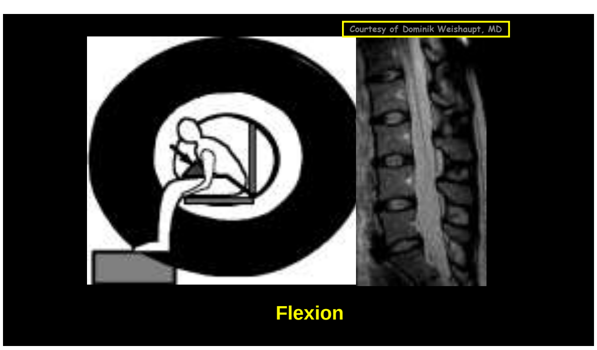


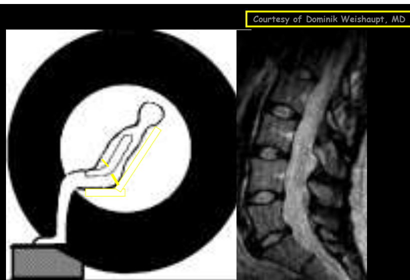
DynaWell: Literature

- Danielson B, Willén J: Axially loaded Magnetic Resonance Imaging of the lumbar spine in asymptomatic individuals. *Spine 2001; 26: 2601-06.*
- Kimura S, Steinbach G, Watenpaugh D, Hargens A: Lumbar spine disc height and curvature responses to an axial load generated by a compression device compatible with magnetic resonance imaging. *Spine 2001; 26: 2596-2600.*
- Willén J, Danielson BI: The diagnostic effect from axial loading of the lumbar spine during Computed Tomography and Magnetic Resonance Imaging in patients with degenerative disorders. S*pine 2001; 26: 2607-14.*
- Danielson BI, Willén J, Gaulitz A, Niklason T, Hansson TH: Axial loading of the spine during CT and MR in patients with suspected lumbar spinal stenosis. *Acta Radiologica 1998; 39: 604-611.*
- Tallroth K: Plain CT of the degenerative lumbar spine. *European Journal of Radiology 1998; 27: 206-213.*
- Willén J, Danielson BI, Gaulitz A, Niklason T, Schönström N, Hansson TH: Dynamic effects on the lumbar spinal canal. Axially loaded CT - Myelography and MRI inpatients with sciatica and/or neurogenic claudication. *Spine 1997; 22 (24): 2968-2976.*


Seated/
Standing MRI
FONAR
http://www.fonar.com/


Courtesy of Dominik Weishaupt, MD
Neutral

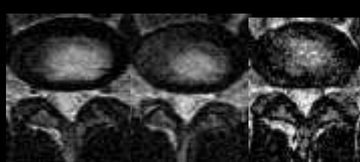

Courtesy of Dominik Weishaupt, MD
Flexion



Extension

Physiologic Changes of Spinal Canal

Schmid MR et al AJR 1999;172:1095



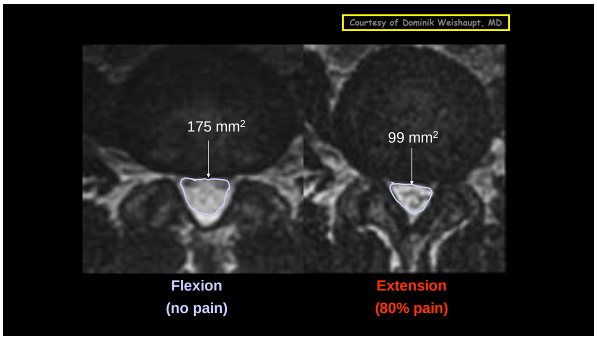
Neutral Flexion Extension

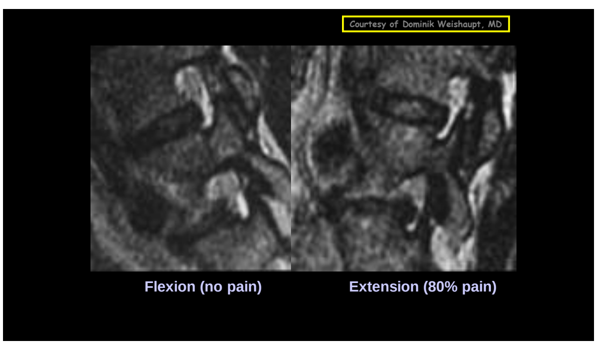
Cross-sectional area of the spinal canal is smallest in extended position

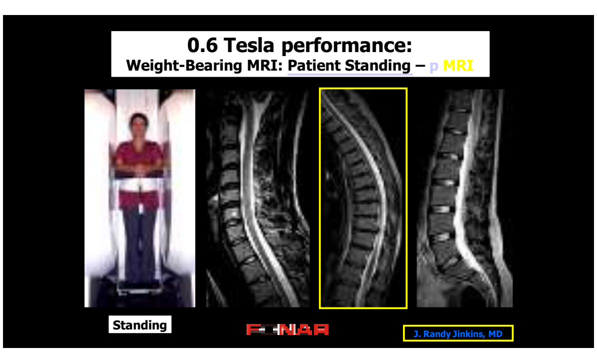
Neuroforamina in different Body - Positions

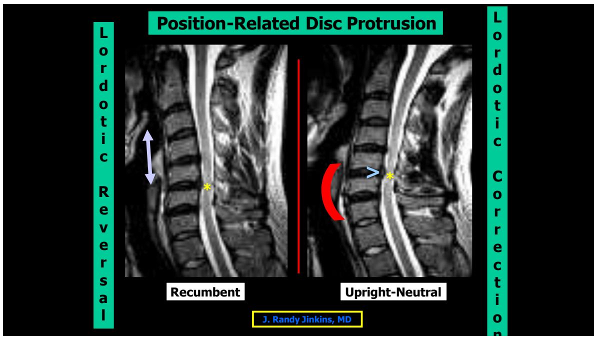
Neutral Flexion Extension

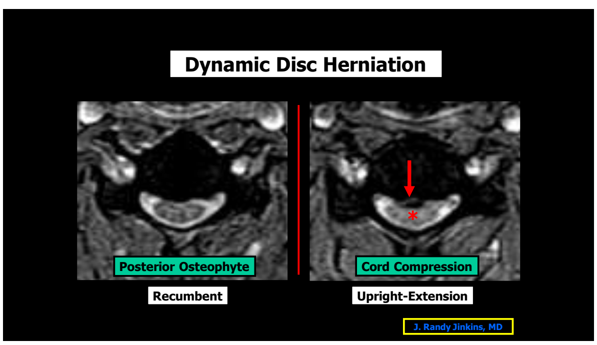
Smallest foraminal dimensions in extended position

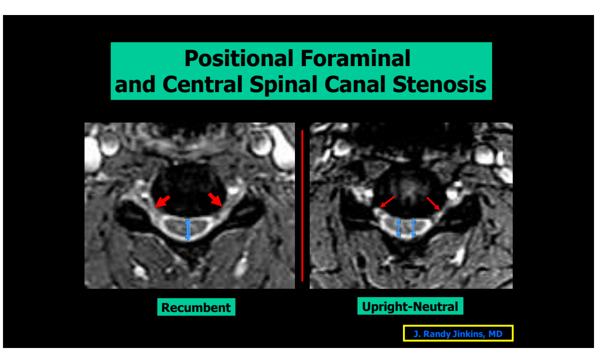

Courtesy of Dominik Weishaupt, MD
175 mm²
99 mm²
Flexion
(no pain)
Extension
(80% pain)

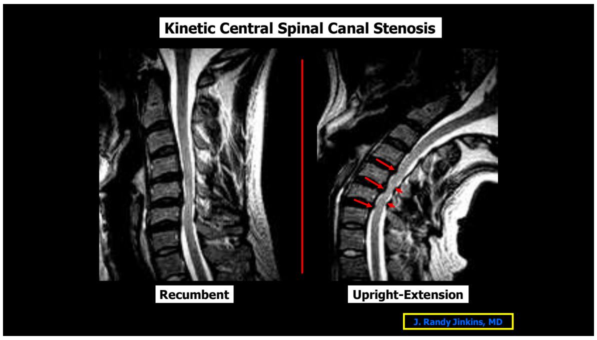

Courtesy of Dominik Weishaupt, MD
Flexion (no pain)
Extension (80% pain)

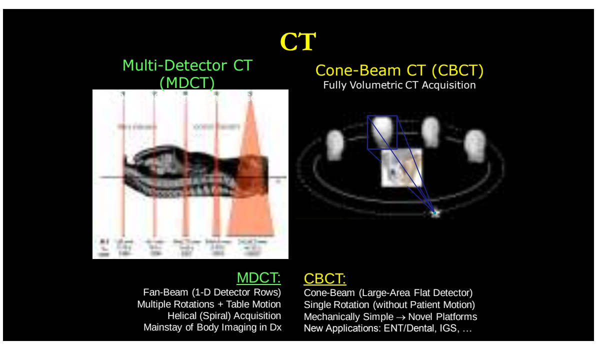

0.6 Tesla performance:
Weight-Bearing MRI: Patient Standing – p MRI
Standing
J. Randy Jinkins, MD

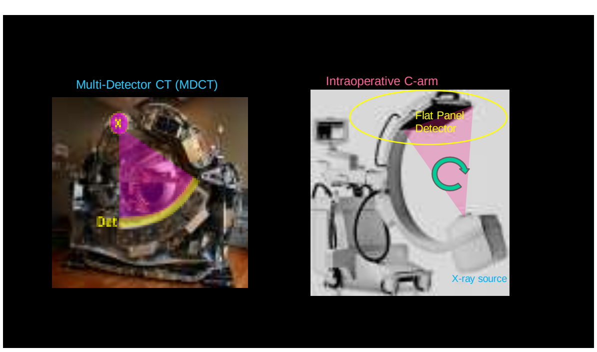

Position-Related Disc Protrusion
Lordotic Reversal
Lordotic Correction
Recumbent
Upright-Neutral
J. Randy Jinkins, MD

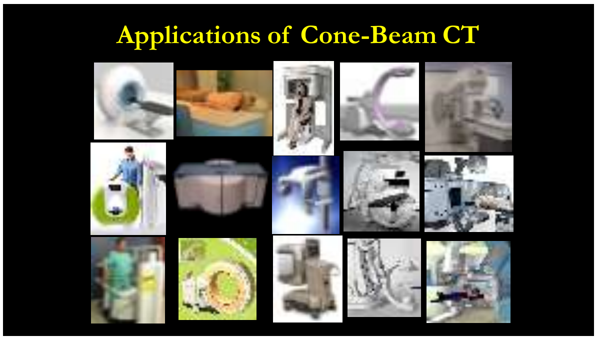

Dynamic Disc Herniation
Posterior Osteophyte
Cord Compression
Recumbent
Upright-Extension
J. Randy Jinkins, MD


Positional Foraminal and Central Spinal Canal Stenosis
Recumbent
Upright-Neutral
J. Randy Jinkins, MD

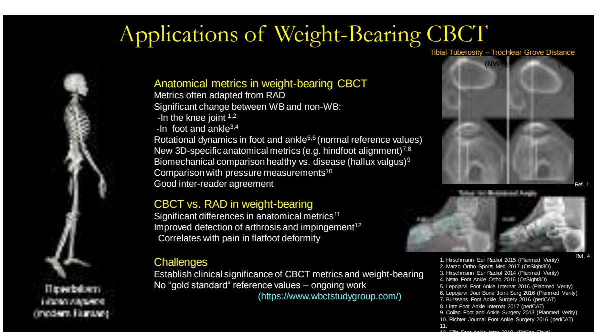

Kinetic Central Spinal Canal Stenosis
Recumbent
Upright-Extension
J. Randy Jinkins, MD


CT
Multi-Detector CT (MDCT)
Cone-Beam CT (CBCT)
Fully Volumetric CT Acquisition
MDCT:
Fan-Beam (1-D Detector Rows)
Multiple Rotations + Table Motion
Helical (Spiral) Acquisition
Mainstay of Body Imaging in Dx
CBCT:
Cone-Beam (Large-Area Flat Detector)
Single Rotation (without Patient Motion)
Mechanically Simple → Novel Platforms
New Applications: ENT/Dental, IGS, …


Multi-Detector CT (MDCT)
X
Det
Intraoperative C-arm
Flat Panel Detector
X-ray source


Applications of Cone-Beam CT

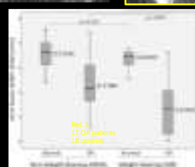

Extremity CBCT
Carestream OnSight 3D*
carestream.com
Planmed Verity**
planmed.com
CurveBeam pedCAT
curvebeam.com
System Configuration
Flat-panel detector (FPD)
Compact gantry
Sitting / standing examination
Capabilities
Weight-bearing scans
High isotropic spatial resolution
Multi-mode Rad / Fluoro / CBCT
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


Applications of Weight-Bearing CBCT
Tibial Tuberosity – Trochlear Grove Distance
(NWB)
Anatomical metrics in weight-bearing CBCT
Metrics often adapted from RAD
Significant change between WB and non-WB:
-In the knee joint [1,2]
-In foot and ankle[3,4]
Rotational dynamics in foot and ankle[5,6] (normal reference values)
New 3D-specific anatomical metrics (e.g. hindfoot alignment)[7,8]
Biomechanical comparison healthy vs. disease (hallux valgus)[9]
Comparison with pressure measurements[10]
Good inter-reader agreement
Ref. 1
CBCT vs. RAD in weight-bearing
Significant differences in anatomical metrics[11]
Improved detection of arthrosis and impingement[12]
Correlates with pain in flatfoot deformity
Ref. 4
Challenges
Establish clinical significance of CBCT metrics and weight-bearing
No "gold standard" reference values – ongoing work
(https://www.wbctstudygroup.com/)
1. Hirschmann Eur Radiol 2015 (Planmed Verity)
2. Marzo Ortho Sports Med 2017 (OnSight3D)
3. Hirschmann Eur Radiol 2014 (Planmed Verity)
4. Netto Foot Ankle Ortho 2016 (OnSight3D)
5. Lepojarvi Foot Ankle Internat 2016 (Planmed Verity)
6. Lepojarvi Jour Bone Joint Surg 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.
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[1]
  - Improved sensitivity
  - High inter-reader agreement
- Weight-bearing (WB) vs. Non-weight bearing (NWB)[1]
  - Significant difference in JSW for OA
  - No significant difference in JSW for non-OA

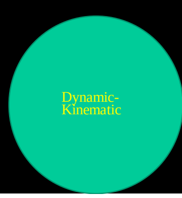


Additional metrics accessible to CBCT

- Meniscal extrusion (ME)
  - Weight bearing aids detection of ME[2]
  - ME changes between WB and non-WB in OA patients[1]
  - Higher sensitivity and specificity in CBCT than RAD[2]

1. Thawait Eur Radiol 2015 (OnSight3D)
2. Segal Phys Sportsmed 2015 (pedCAT modified for knees)

Functional Imaging



Dynamic Kinematic Imaging

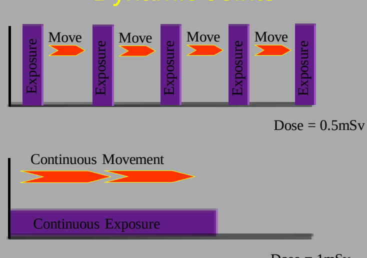
- Dynamic
  - "real-time"
- Kinematic
  - "joint in motion"

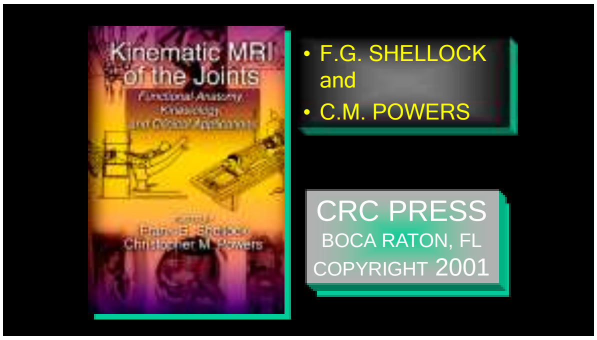
Dynamic Kinematic Ultrasound

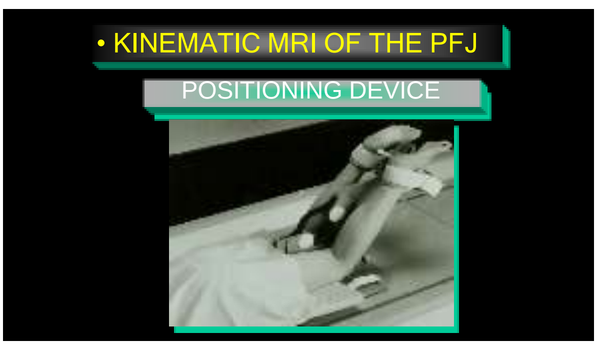
Advances in sonographic technology, including higher resolution probes, power Doppler sonography, extended field-of-view imaging, and compound imaging, have contributed to expand its clinical applications

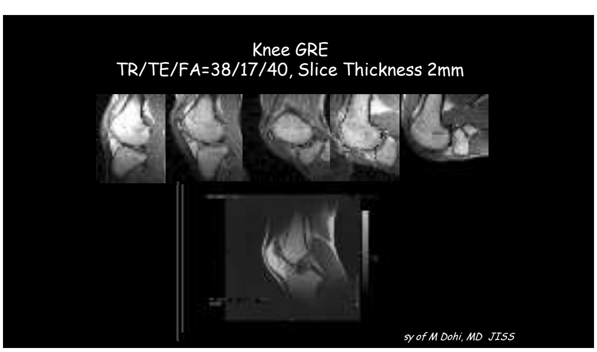
V. Khoury, E. Cardinal, and N. J. Bureau. Musculoskeletal Sonography: A Dynamic Tool for Usual and Unusual Disorders Am. J. Roentgenol., January 1, 2007; 188(1): W63 - W73.

Dynamic Joints




Kinematic MRI of the Joints
• F.G. SHELLOCK and
• C.M. POWERS
CRC PRESS
BOCA RATON, FL
COPYRIGHT 2001


• KINEMATIC MRI OF THE PFJ
POSITIONING DEVICE


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

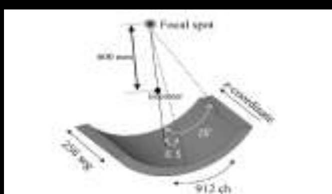
T2 TSE, 43 sec acquisition, 6 partitions, 5mm SL, 256 matrix, 26 cm FOV

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

70 cm open bore broadens clinical possibilities: Kinematic Imaging

Courtesy of Singapore General Hospital, Singapore

256-detector row CT

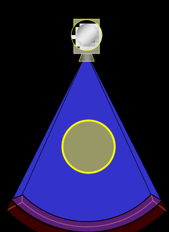


Mori et al.: Physical performance evaluation of a 256-slice CT-scanner

Med. Phys. 31 (6) June 2004

Unique Applications

1. Volume Scan
   - ONE Rotation
   - ONE Heart Beat
2. Dynamic Volume Scan
   - ONE Examination
   - New Diagnostic Tool



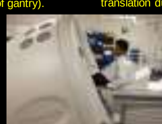
Dynamic Volume CT

Aquilion ONE

– 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.

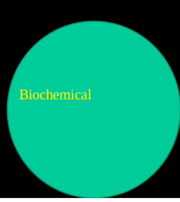
AJR

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 patients' 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



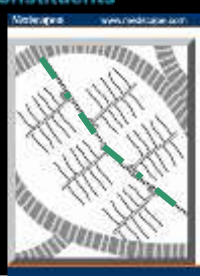
Disc Structure

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

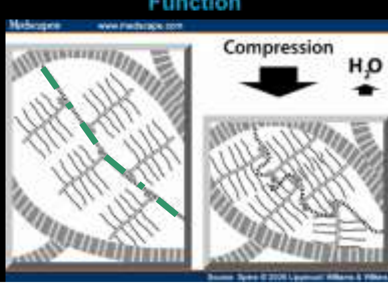
Courtesy of Lee Riley

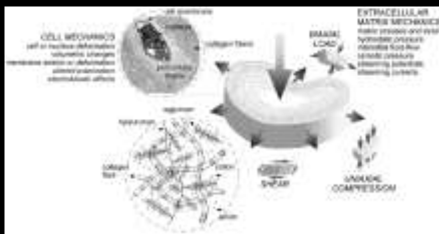
Intervertebral Disc: Three Major Constituents

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



Intervertebral Disc: Function





Setton L. A., Chen J. J Bone Joint Surg 2006:88:52-57

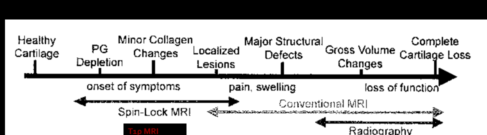
TBTS

Intervertebral Disc Degeneration

With Degeneration

- *Loss of proteoglycan and water
- *Fibrocartilage formation and disorganization of the anular architecture

Musculoskeletal Imaging Spectrum: OA



1. Lawrence RC, et al. Arthritis Rheum 41:778-779, 1998.
2. Gunzberg R, et al. Degenerative Disc Disease. Lippincott: 2004.
3. Regatte, RR. Academic Radiology, 2004 11(7): 741-749.
4. Johannessen, et al. Spine. 31(11): 1253-1257.

I. Structure: Homogeneous, bright white.
Distinction of Nucleus and Anulus. Clear
Signal Intensity: Hyperintense
Height of Intervertebral Disc: Normal

II. Structure: Inhomogeneous with or without horizontal bands
Distinction of Nucleus and Anulus. Clear
Signal Intensity: Hyperintense
Height of Intervertebral Disc: Normal

III. Structure: Inhomogeneous, gray
Distinction of Nucleus and Anulus. Clear
Signal Intensity: Intermediate
Height of Intervertebral Disc: Normal to slightly decreased

IV. Structure: Inhomogeneous, gray to black
Distinction of Nucleus and Anulus. Lost
Signal Intensity: Intermediate to hypointense
Height of Intervertebral Disc: Normal to moderately decreased

V. Structure: Inhomogeneous, black
Distinction of Nucleus and Anulus. Lost
Signal Intensity: Hypointense
Height of Intervertebral Disc: Collapsed disc space

[1] Classification and images reprinted from Pfirrmann CWA *et al.* *SPINE* 26(17): 1874-1875, 2001.

MRI Cartilage Biomarkers

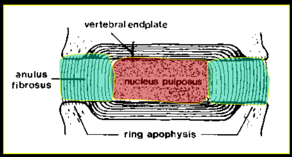
- Collagen
  - Diffusion
  - T2 maps
- GAG
  - DGEMRIC
  - Sodium Imaging*
  - T1rho*

*most benefit from higher field

Early Detection of Disc Degeneration

T1 ρ
Na
T2
dGEMRIC

DIFFUSION
(DTI)

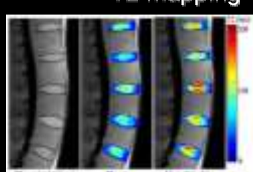


T2 Mapping

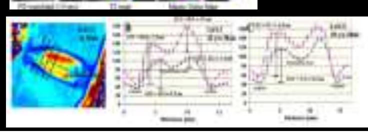
- loss of proteoglycans ➔ loss of the fixed negative charge density ➔can be mapped negatively
- T2 variations could be related to
  - known distribution of water content
  - the distribution of proteoglycans content with cartilage depth
  - collagen network organization in different zones of cartilage
- T2 relaxation times of the IVD correlate strongly with water content and weakly with PG content

Marinelli NL, Haughton VM, Muñoz A, Anderson PA. T2 relaxation times of intervertebral disc tissue correlated with water content and proteoglycan content. Spine (Phila Pa 1976). 2009 Mar 1;34(5):520-524.

T2 mapping

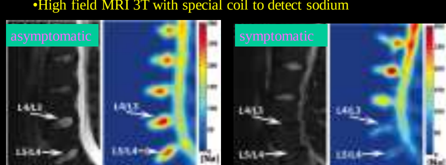


Magic echo imaging of the disc reveals features enhances sensitivity to the nucleus pulposus over conventional T2-weighted imaging.



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



Wang C, McArdle E, Fenty M, Witschey W, Elliott M, Sochor M, Reddy R, Borthakur A. Validation of sodium magnetic resonance imaging of intervertebral disc. Spine (Phila Pa 1976). 2010 Mar 1;35(5):505-10.

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

Average T1rho in nucleus had a strong linear correlation with GAG content

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

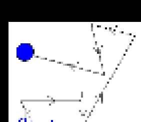
T1 rho values were higher in the younger, non-degenerate disks.

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



www.gcsescience.com/e14-smoke-particles.htm

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)

↓

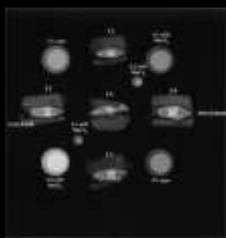
Measured signal is reduced by amount of diffusion

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

MRI - “Quality of IVD Diffusion”



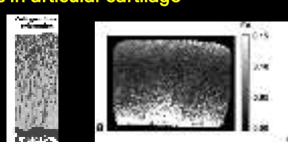
Intervertebral disc specimens (L1 to L5). Regions of interest of MR scans that were performed are visible as white squares on the anterior anulus fibrosus, nucleus pulposus, and posterior anulus fibrosus.

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

Antoniou et al. MRI 2004; 22: 963-972.

Diffusion Tensor Imaging: Collagen Fiber Orientation

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



*Filidoro et al Magn Reson Med 2005; 53:993-998

Diffusion Tensor Imaging: Collagen Fiber Orientation

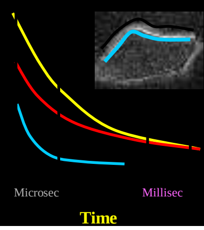
Orientations of anisotropy exhibit a layered morphology that agree with light micrographs of the disc

*Hsu et al MRM 1999; 41:992-999

Courtesy of Christine Chung and Won Bae, UCSD

Basis for Ultrashort TE Sequence

Transverse Magnetization Decay



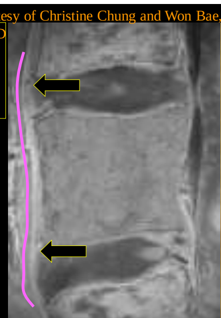
- Total magnetization
  - Long T2 component
  - Short T2 Component

Robson, et al., J Comput Assist Tomogr 2003; 27(6): 825-846

Courtesy of Christine Chung and Won Bae, UCSD

Symphysis – Intervertebral Disc

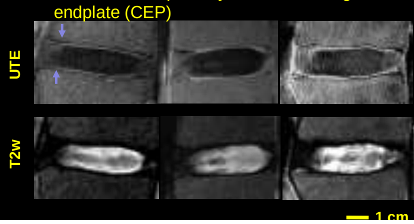
- Firmest attachment of disc to vertebral body is at outer bony ring
- Lamellar bands of disc penetrate the ring as Sharpey's fibers



Normal UTE Appearance CEP

Courtesy of Christine Chung and Won Bae, UCSD

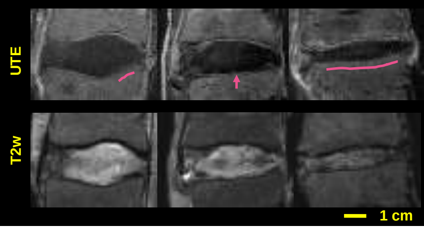
- well-defined linear signal intensity
  - –found, at least partially, near all cartilaginous endplate (CEP)

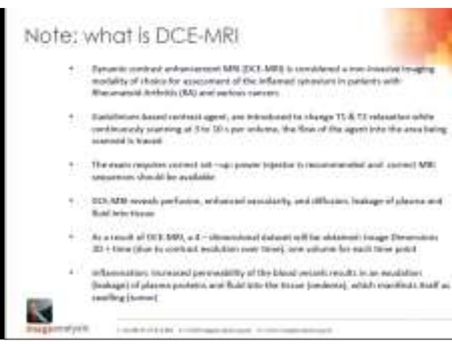


Degeneration CEP with UTE MRI

Courtesy of Christine Chung and Won Bae, UCSD

- focal loss or irregularity





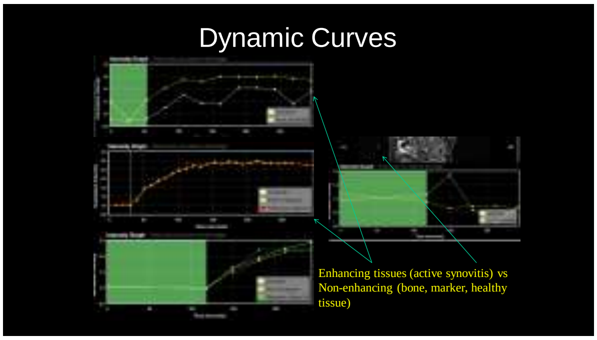
Why is inflammatory perfusion important?

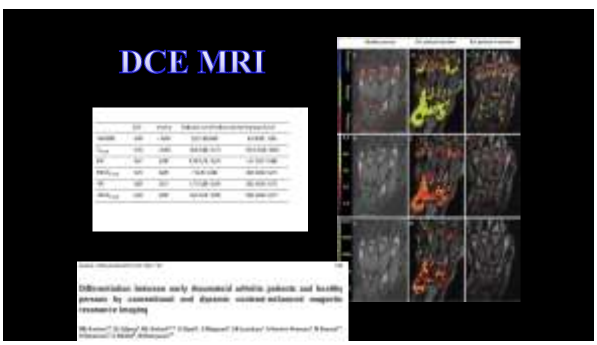
<u>**Conclusion: 107 patients**</u>

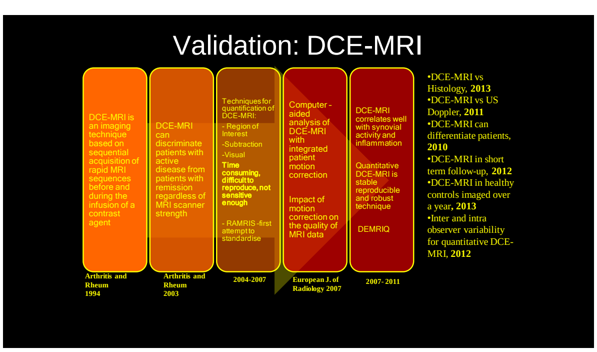
Subclinical joint inflammation in 20% detected by imaging techniques explains the structural deterioration in RA patients in clinical remission who are receiving conventional therapy with:

12 times higher odds of deterioration in joints with **increased PD signal** (odds ratio 12.21, $P < 0.001$). **4-5 timer higher odds** using **MRI synovitis** and **osteitis**

Mikael Boesen, MD, PhD


Dynamic Curves
Enhancing tissues (active synovitis) vs Non-enhancing (bone, marker, healthy tissue)


DCE MRI


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
Arthritis and Rheum 1994
DCE-MRI can discriminate patients with active disease from patients with remission regardless of MRI scanner strength
Arthritis and Rheum 2003
Techniques for quantification of DCE-MRI:
- Region of Interest
-Subtraction
-Visual
Time consuming, difficult to reproduce, not sensitive enough
- RAMRIS -first attempt to standardise
2004-2007
Computer - aided analysis of DCE-MRI with integrated patient motion correction
Impact of motion correction on the quality of MRI data
European J. of Radiology 2007
DCE-MRI correlates well with synovial activity and inflammation
Quantitative DCE-MRI is stable reproducible and robust technique
DEMRIQ
2007- 2011
•DCE-MRI vs Histology, 2013
•DCE-MRI vs US Doppler, 2011
•DCE-MRI can differentiate patients, 2010
•DCE-MRI in short term follow-up, 2012
•DCE-MRI in healthy controls imaged over a year, 2013
•Inter and intra 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

  Nguyen-mihn C, Haughton VM, Papke RA, An H, Censky SC. Measuring diffusion of solutes into intervertebral discs with MR imaging and paramagnetic contrast medium. AJNR 19:1781-1784, 1998.

  Rajasekaran S, Naresh Babu J, Arun R et al. A study of diffusion in human lumbar discs: A serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. Spine 29: 2654-2667, 2004.

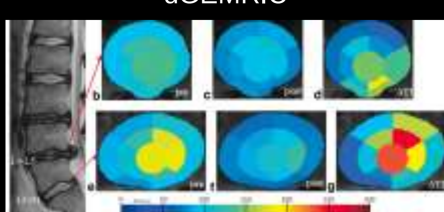
- Characteristics of normal, aging and degenerative discs and the effect of pharmacologic modulation of enhancement with nimodipine have been described

  Rajasekaran S, Venkatadass K, Naresh Babu J, Ganesh K, Shetty AP. Pharmacologic enhancement of disc diffusion and differentiation of healthy, ageing and degenerated discs. Eur Spine J. 17: 626-643, 2008.

dGEMRIC: Technique

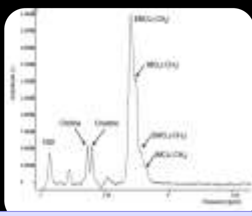
- PG/GAG depletion causes areas of negative charge
- Need to use positively charged contrast material
- Delayed acquisition time

dGEMRIC



Vaga S, Raimondi MT, Caiani EG, Costa F, Giordano C, Perona F, Zerbi A, Fornari M. Quantitative assessment of intervertebral disc glycosaminoglycan distribution by gadolinium-enhanced MRI in orthopedic patients. Magn Reson Med. 2008 Jan;59(1):85-95.

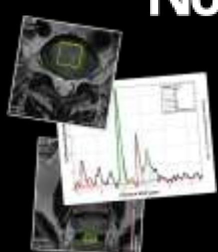
Metabolite Assessment by Proton MR Spectroscopy



Location and amplitude of resonances yields information about which metabolites are present and in what concentration

- Relies on same physical principles as MRI
- Biochemical (rather than anatomical) information about tissue content

Nocimed



Functional Imaging Intersections

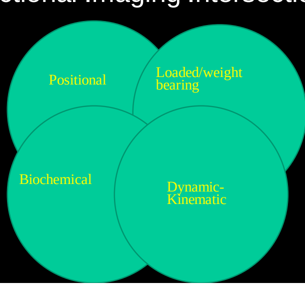


TABLE : Comparison of imaging modalities' characteristics for functional joint imaging

Modality	Advantages	Limitations
Fluoroscopy	• Dynamic image acquisition (sufficient temporal resolution) • Volumetric imaging • High spatial resolution	• Projectional technique with overlapping structures obscuring relationships of interest
Ultrasound	• Dynamic image acquisition (sufficient temporal resolution) • Imaging during activity • High spatial resolution • Non-ionizing radiation	• Limited contrast resolution with respect to osseous structures • Limited field of view with respect to entire joint imaging
MRI	• Very good contrast resolution for soft tissue structures • Non-ionizing radiation	• Insufficient temporal resolution to capture joint motion during single acquisition • Lesser spatial resolution • Bore size prohibiting physiologic motion
Multidetector CT	• High spatial resolution • Suitable contrast resolution between bone, ligament, tendon and muscle • Volumetric imaging • Dynamic image acquisition (sufficient temporal resolution)	• Limited field of view with respect to entire joint imaging (64-slice MDCT does not allow for greater than 32 mm coverage in the z direction during single acquisition)

The biomarker development process

Gray M. L. J Bone Joint Surg 2009;91:44-49

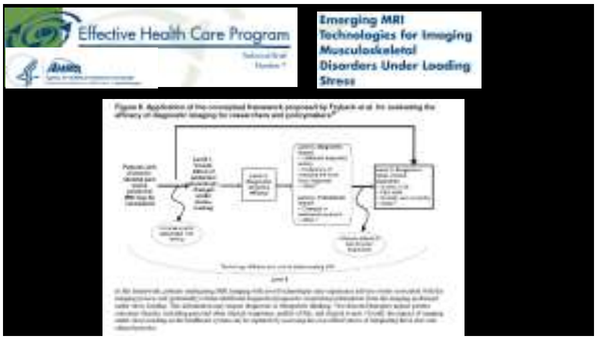
Fundamentals of Clinical Research for Radiologists

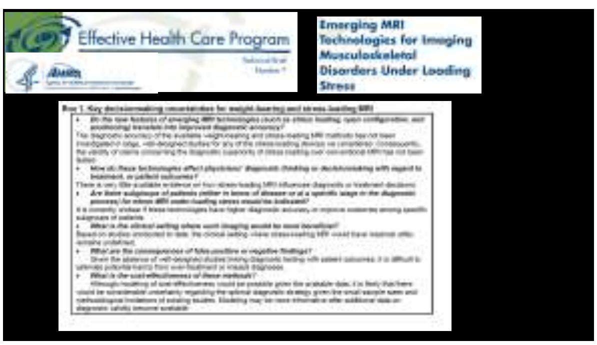
Jeffrey G. Jarvik[1]

The Research Framework

TABLE 1 Six-Tiered Model of Diagnostic Efficacy

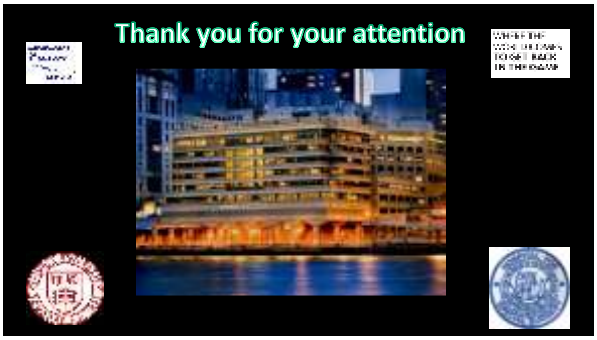
Stage of Efficacy	Definition
Technical capacity	Resolution, sharpness, reliability
Diagnostic accuracy	Sensitivity, specificity, predictive values, ROC curves
Diagnostic impact	Ability of a diagnostic test to affect the diagnostic workup
Therapeutic impact	Ability of a diagnostic test to affect therapeutic choices
Patient outcomes	Ability of a diagnostic test to increase the length or quality of life
Societal outcomes	Cost-effectiveness and cost utility





Acknowledgements: Functional Joint Imaging

- Frank Shellock
- Hiroshi Yoshioka
- Randy Jinkins
- Domick Weishaupt
- Shadpour Demehri
- William Morrison
- Garry Gold
- Chris Beaulieu
- Chloe Stevenson
- Rick Moore
- Ferenc Jolesz
- Carl Winalski
- Amir Zamani
- Viviane Khoury
- Jeff Siewerdsen
- Web Stayman
- Wojtek Zbijewski


Thank you for your attention