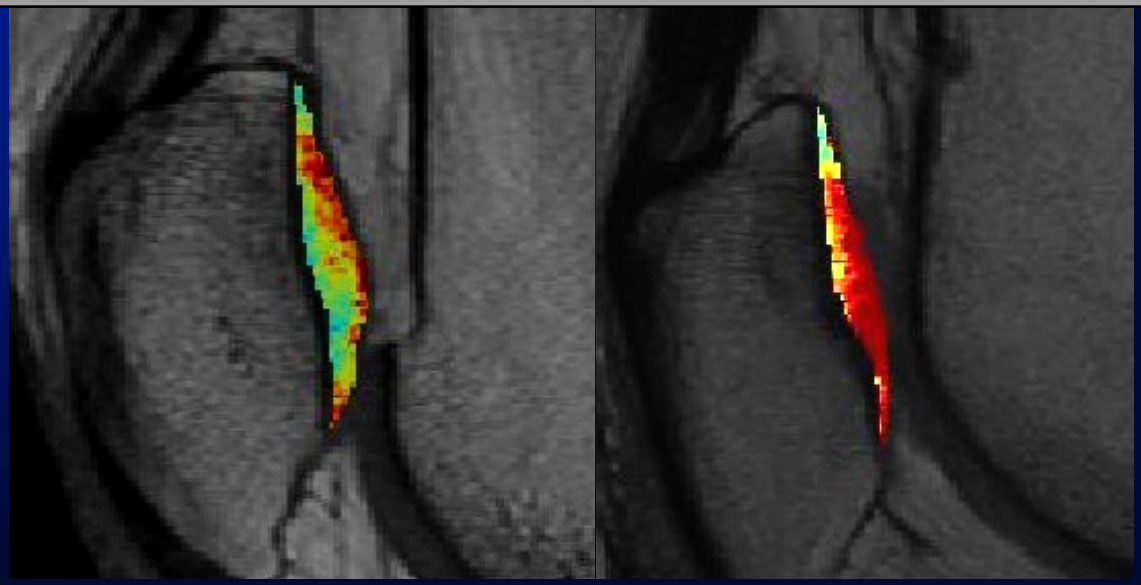
Current State of the Art in Compositional Imaging of Joint Tissues

Thomas M. Link, MD, PhD
Professor of Radiology

UCSF, San Francisco



Disclosures

No disclosures regarding presented lecture

Research funding from NIH

Compositional Imaging of Joint Tissues

- What is the rationale?
- What techniques are available?
- What tissues and what joints can we examine?
- What have clinical studies shown?
- What is required to apply it in clinical practice?

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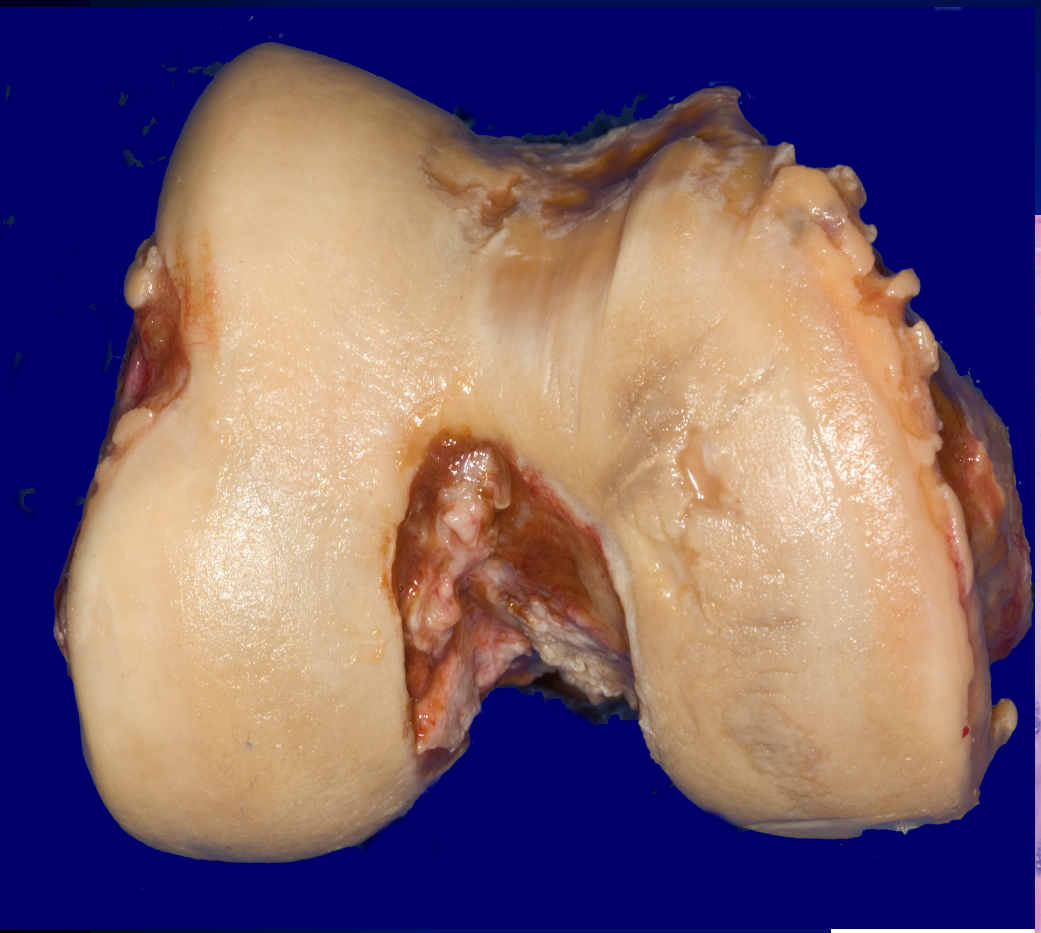
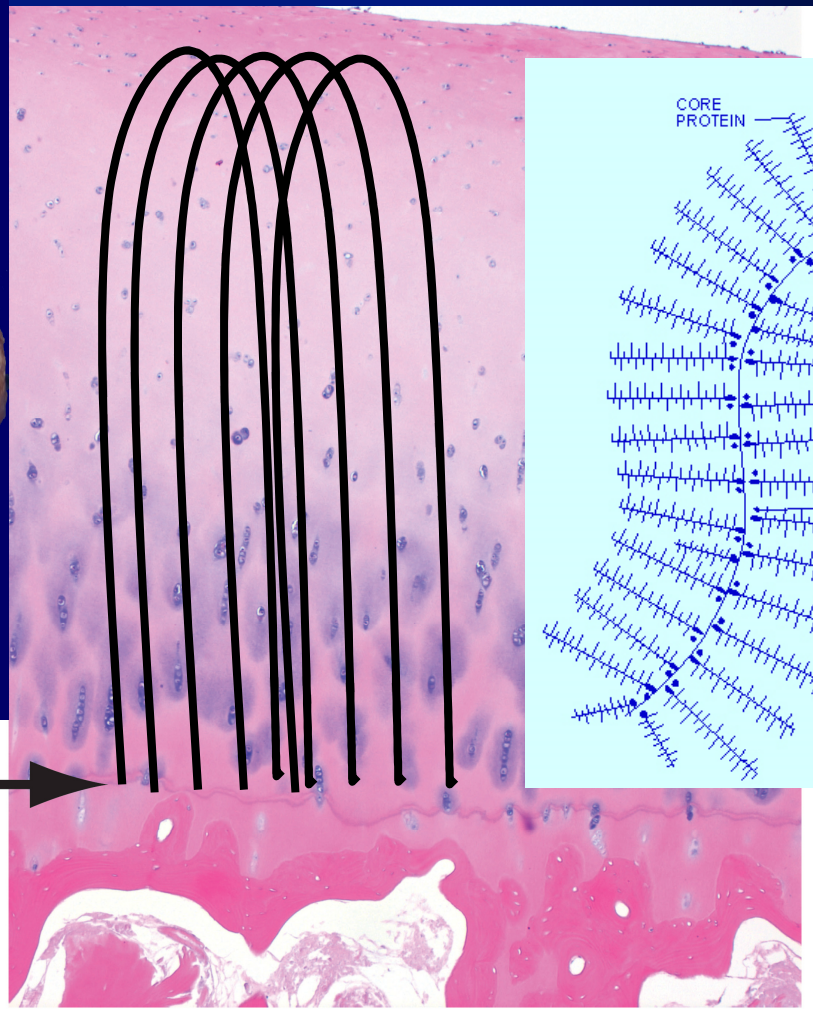
Analyzing the cartilage matrix



Glycosaminoglycans
Collagen



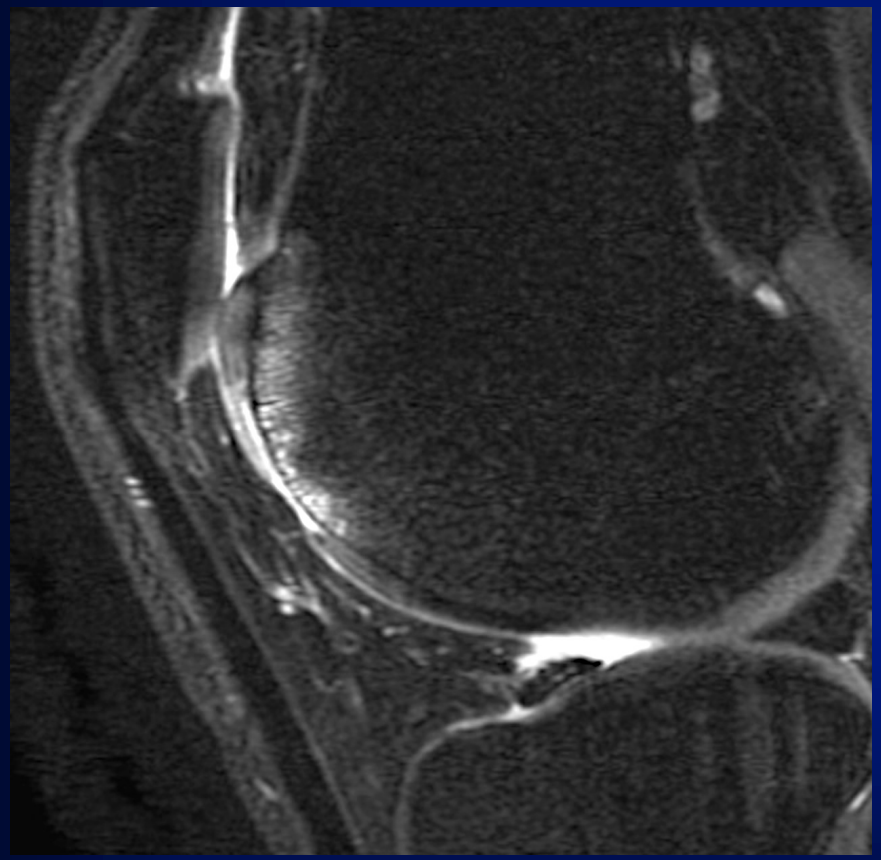
Link
Cartilage Imaging
Springer 2011

Compositional MRI

Rationale:

Morphological MRI shows irreversible changes

Morphology

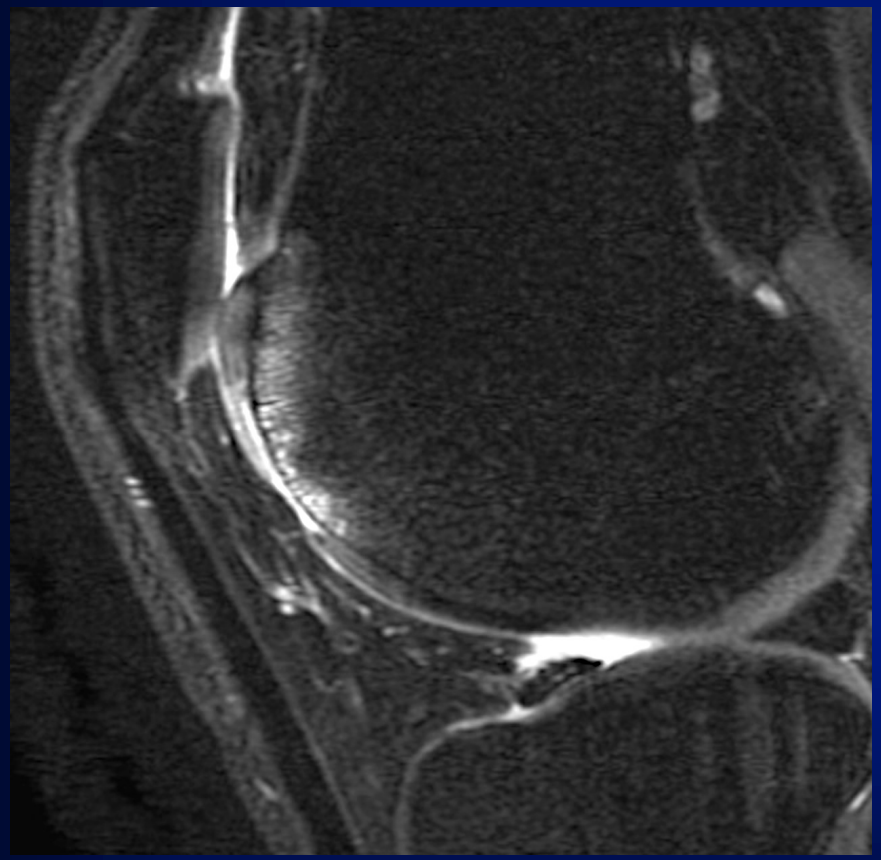


Compositional MRI

Early matrix abnormality before cartilage loss

May be reversible
Disease course may be modified

Morphology



Matrix composition

How exactly would it impact patient management?

Life style changes:
physical activity
weight loss

Identify patients at risk who may benefit from early surgery (e.g. femoro-acetabular impingement)

Compositional Imaging of Joint Tissues

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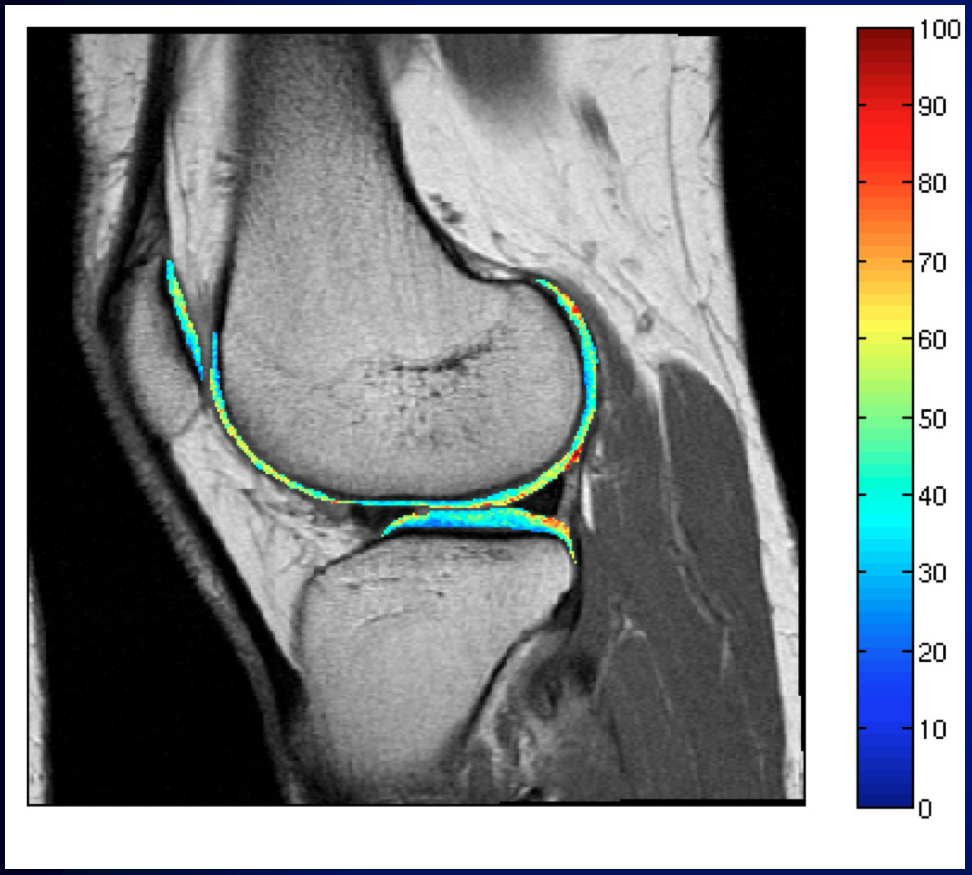
Advanced Quantitative MRI

Biochemical Analysis of Cartilage

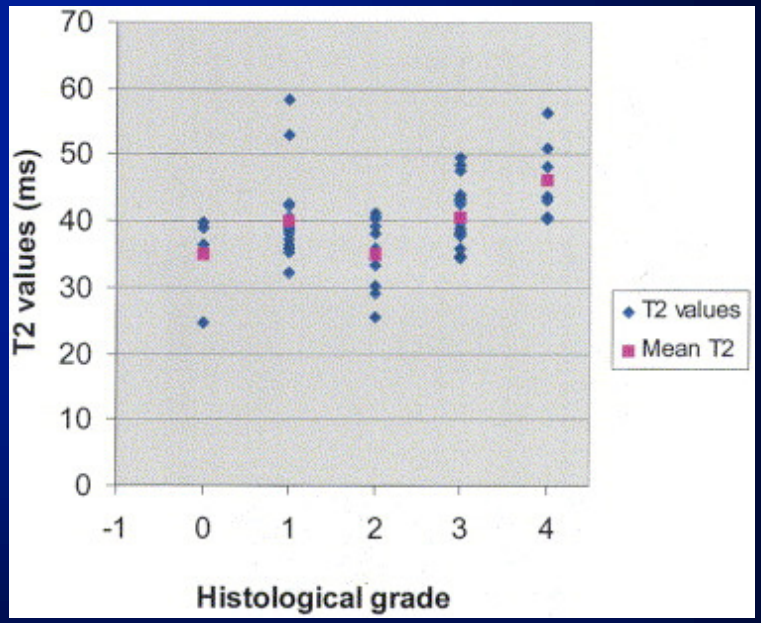
T2 Relaxation Time Measurement
T1rho
dGEMRIC
Sodium Imaging
gagCEST

Collagen, Water Content
Proteoglycan Content

T2 Relaxations Time Measurement

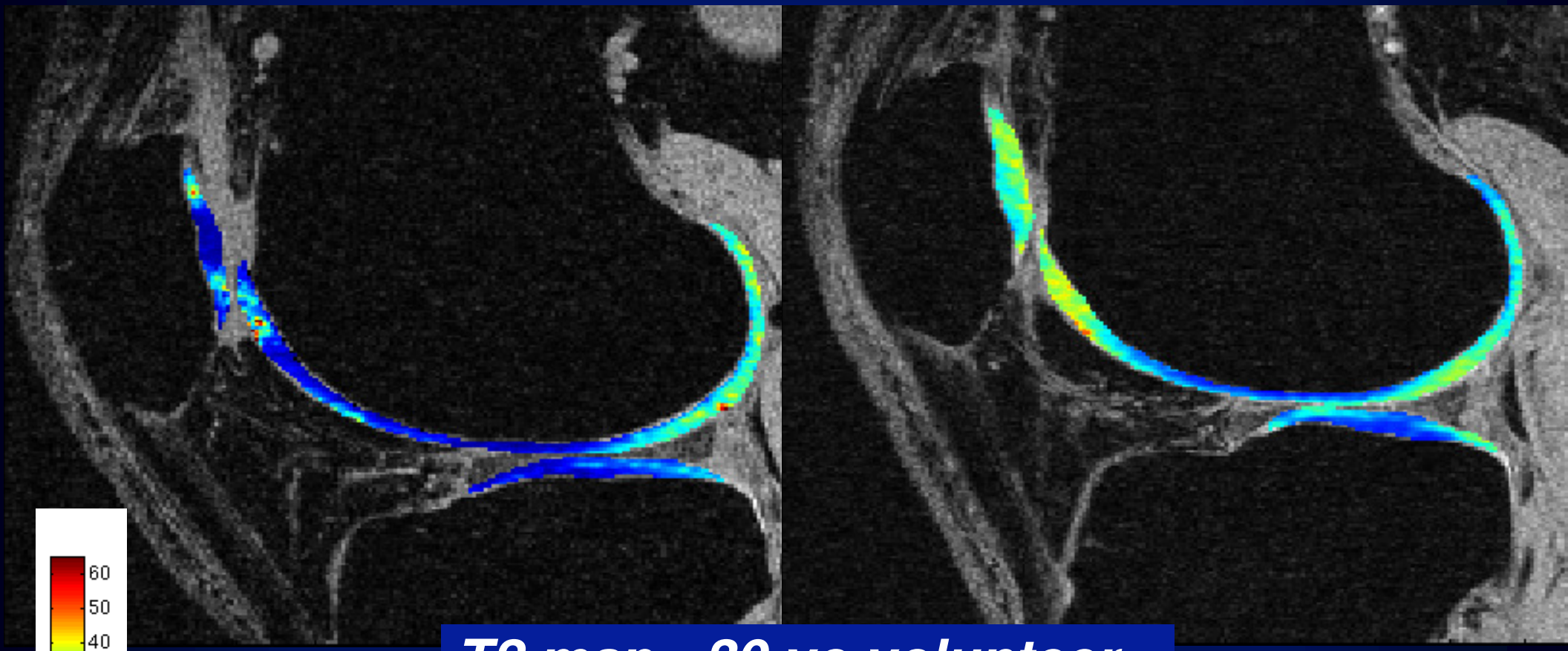


T2 quantifies water content and collagen integrity



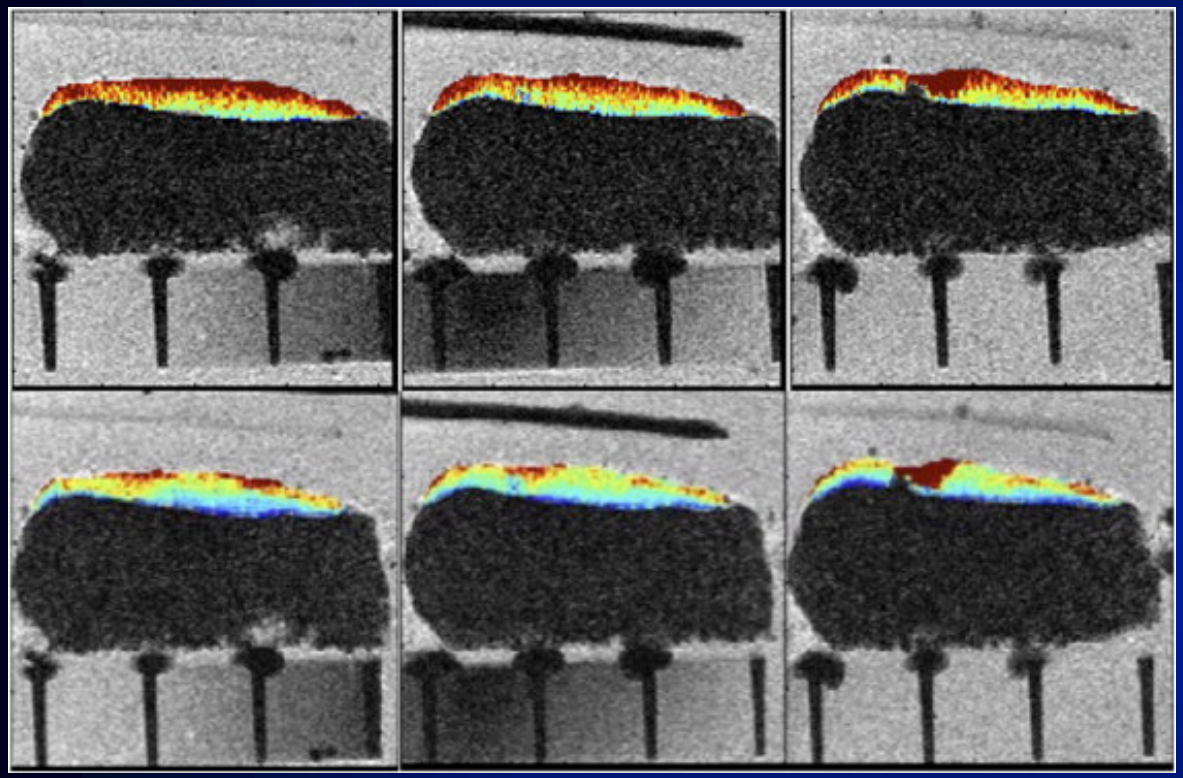
Dunn et al. Radiology 2004, 232:592-8
David-Vaudey E et al. Magn Reson Imaging. 2004 Jun;22(5):673-82.
Mosher TJ et al. Arthritis Rheum. 2004 Sep;50(9):2820-8

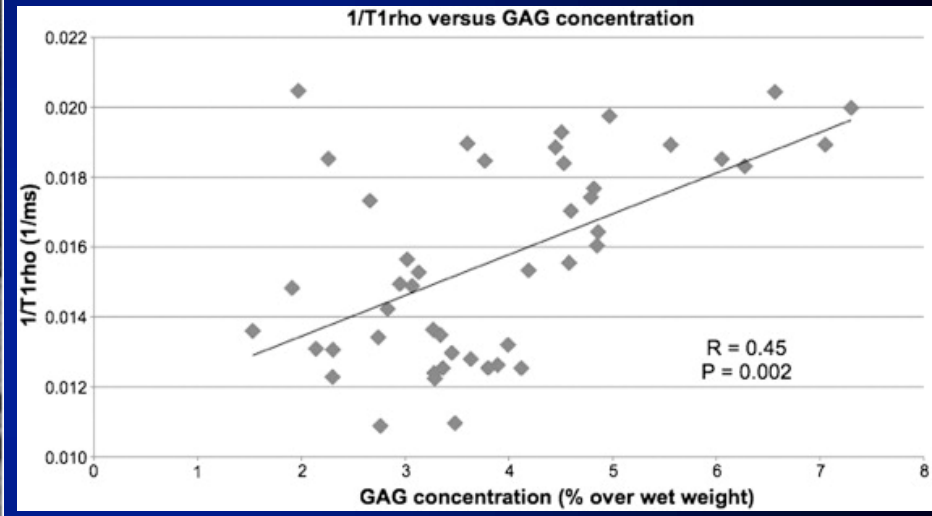
T2 mapping



T2 map - 30 yo volunteer
Before and after marathon

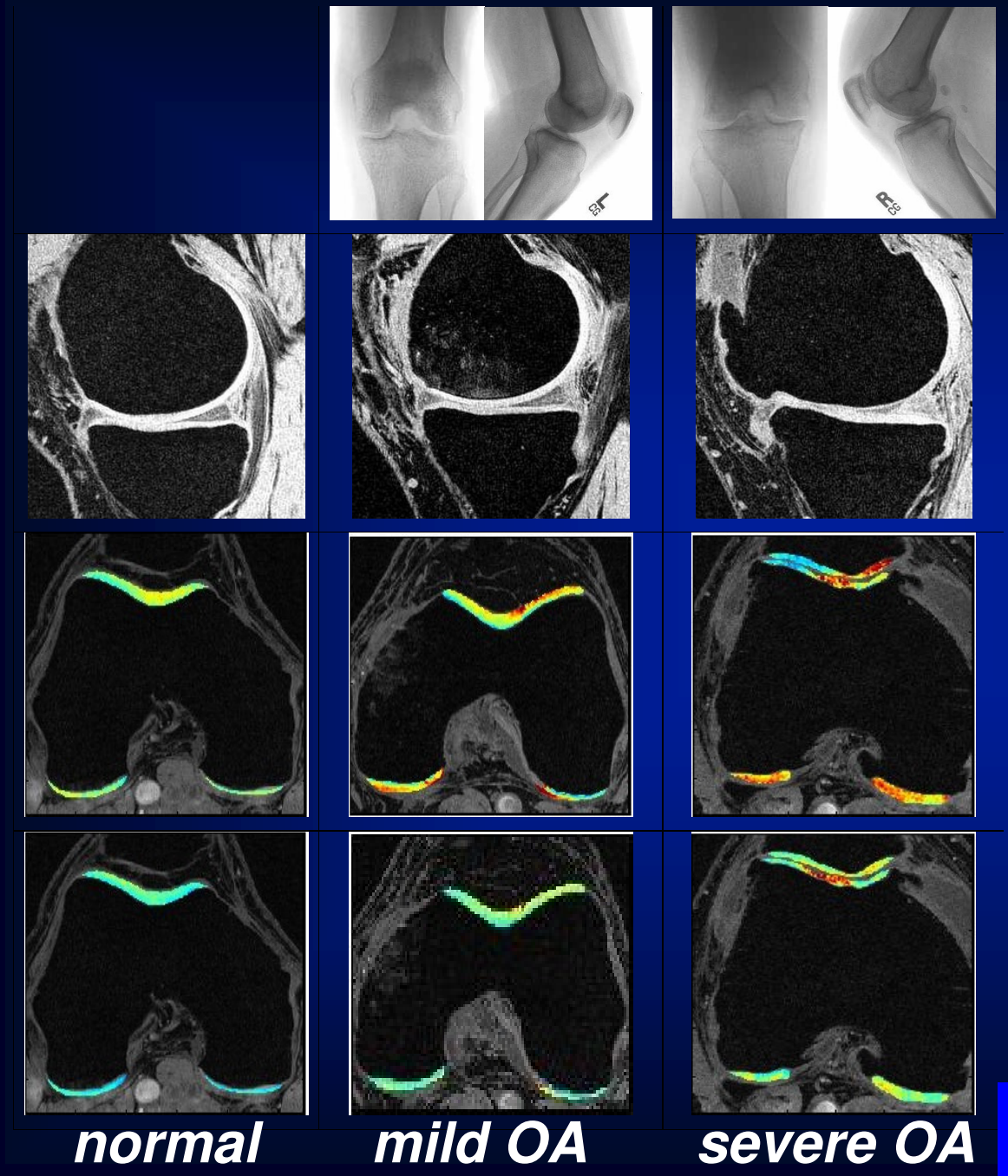
T1rho Measurement





T1rho quantifies macromolecules
In particular glycosaminoglycans

Regatte et al.; J Magn Reson Imaging 2006; 23:547-553
Li et al. MRM 2005; 54: 929-936, Li et al. Magn Reson Imaging. 2011 Apr;29(3):324-34

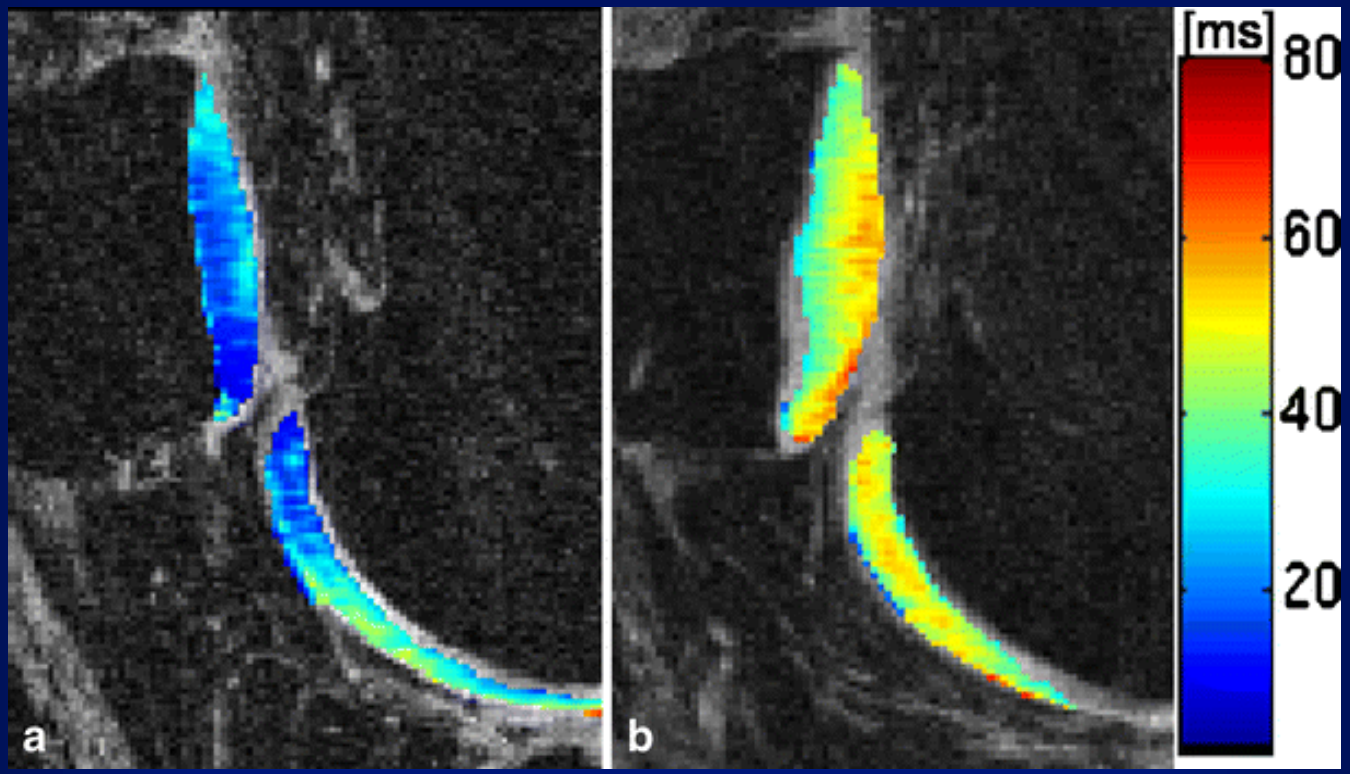


T1rho-relaxation time is higher in OA patients than in normals

and increases with degree of disease

Li, X et al, Osteoarthritis and Cartilage, 2007

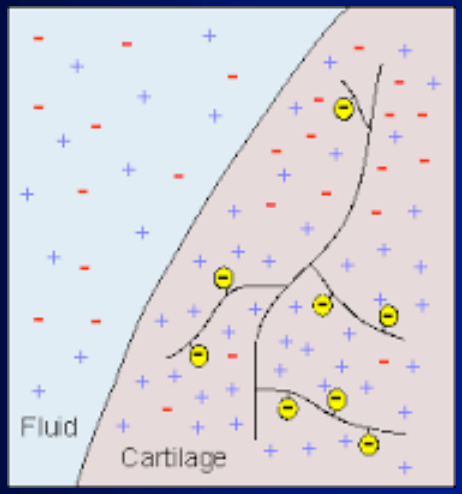
T1rho Measurement



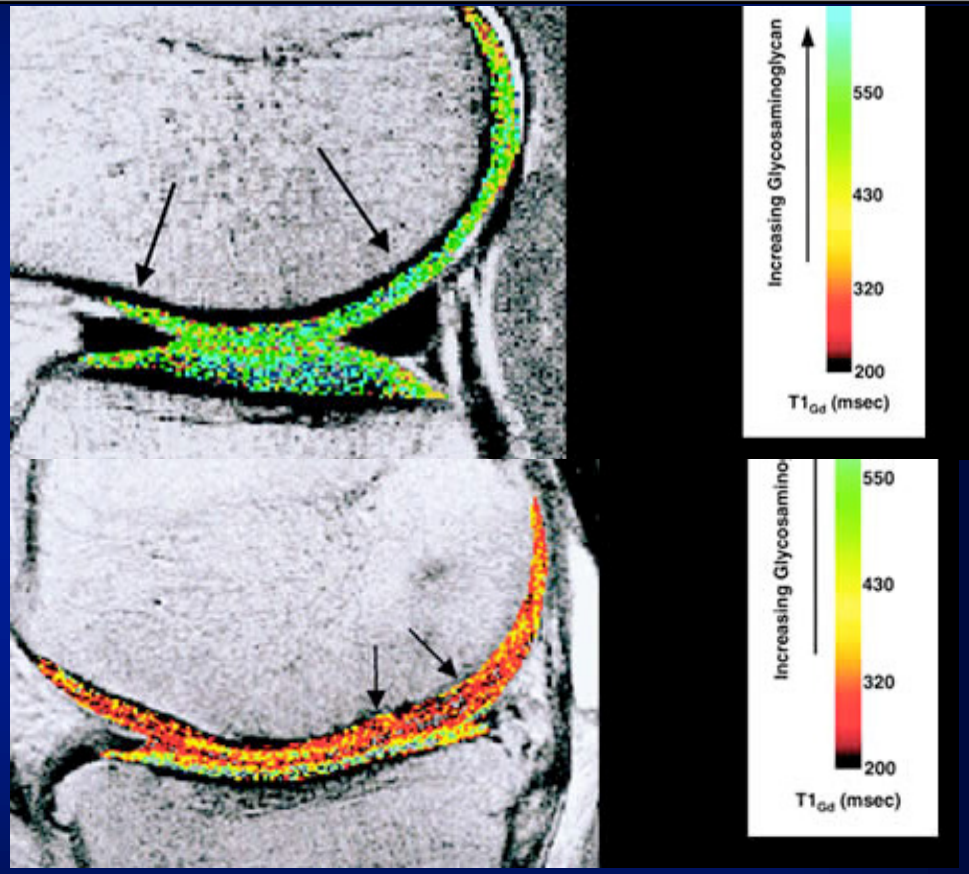
T1rho higher in patients with cartilage defects

Li et al. MRM 2005; 54: 929-936
Stahl et al. Eur Radiol. 2009 Jan;19(1):132-43

dGEMRIC
delayed Gd-DTPA enhanced MRI of cartilage

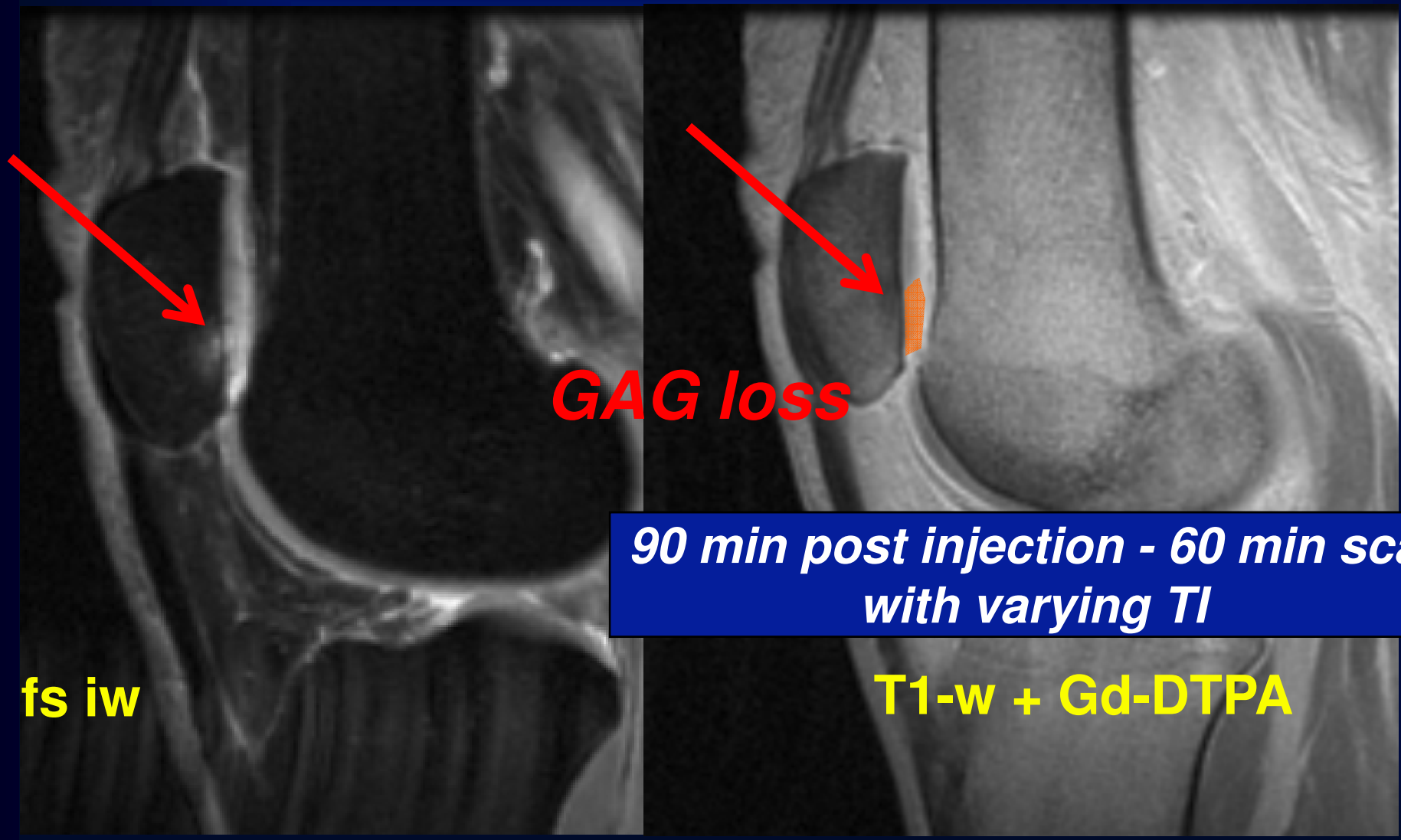


Gd Enhancement can be quantified and serves as surrogate marker for glycosaminoglycan (GAG) content
- the higher the enhancement the lower the GAG content



Burstein et al. Invest Radiol, 2003 35:634
Williams et al. Arthritis Rheum. 2005 Nov;52(11):3528-35.

dGEMRIC – requires exercise after Gd injection

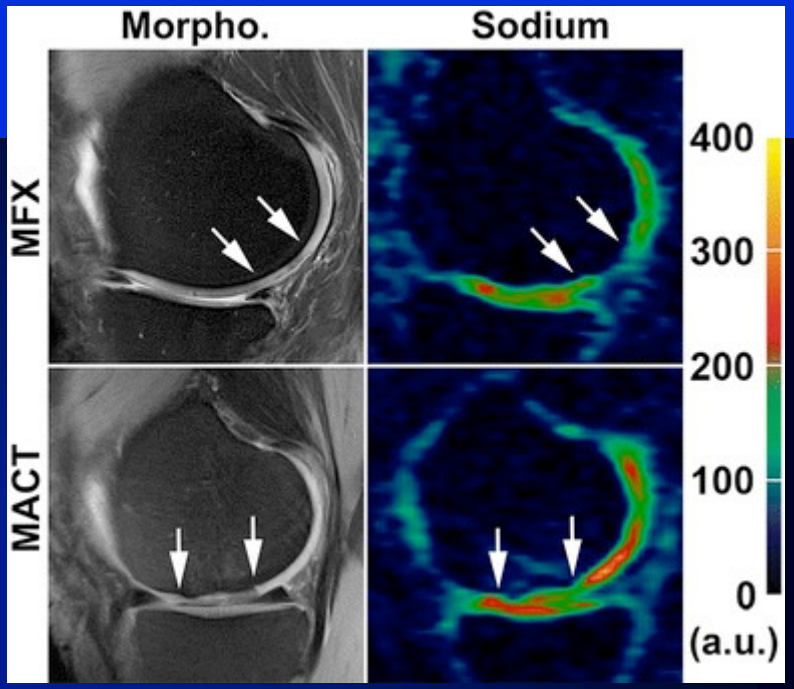


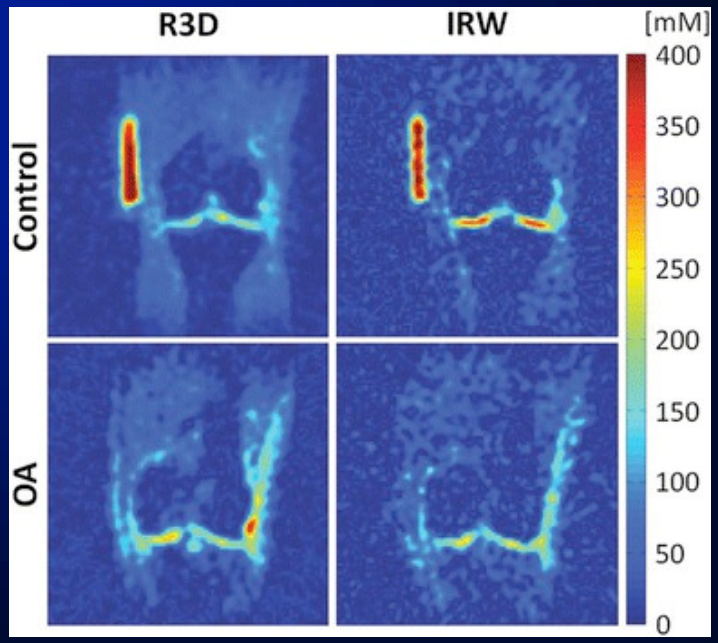
Sodium Imaging

Quantifies proteoglycan content

But requires multinuclear capabilities of the MR system, dedicated sodium coils, and high field strength (7T) to guarantee an adequate signal-to-noise ratio

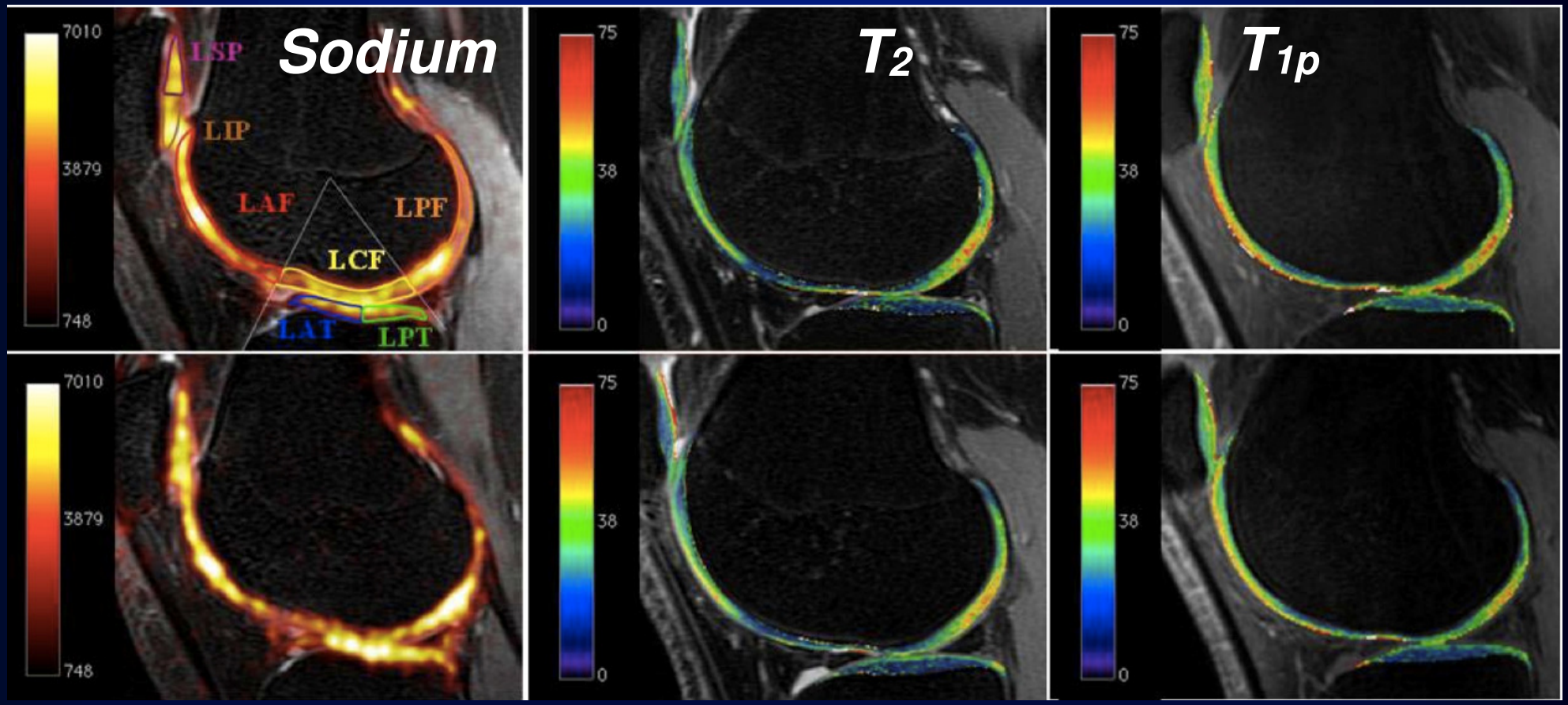
Limited spatial resolution





Sodium Imaging

Stanford Basketball Study

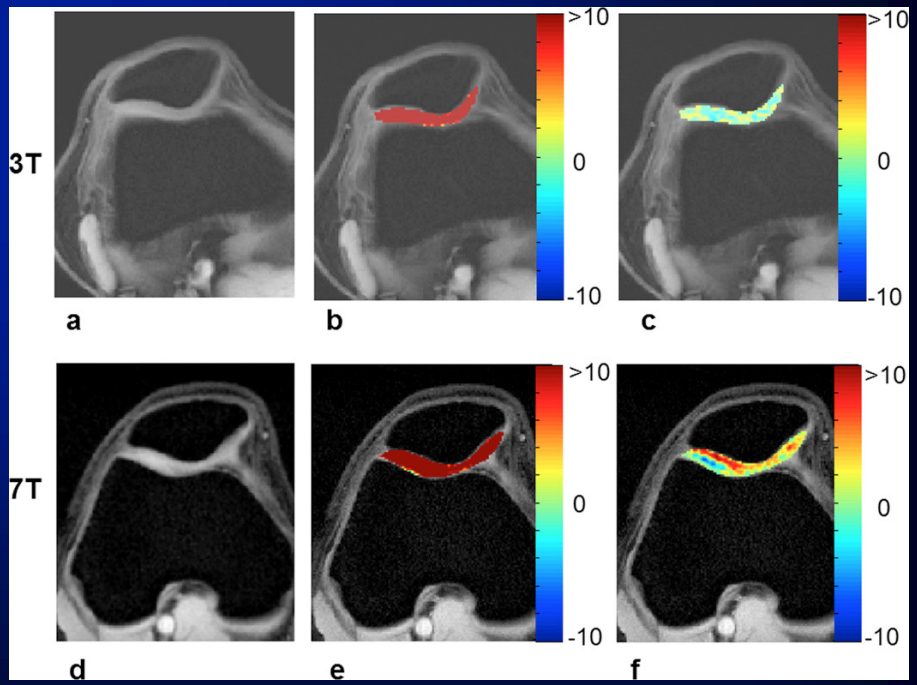


Courtesy Garry Gold - Vogelsong, et al, ISMRM 2011

GagCEST MRI

Chemical exchange saturation transfer (CEST) MR contrast enhancement technique
*Enables **indirect detection of molecules with exchangeable protons = GAG***

Controversy:
*"… not expected to be clinically useful at 3T, but **holds promise at 7T** and may be a viable clinical technique …"*



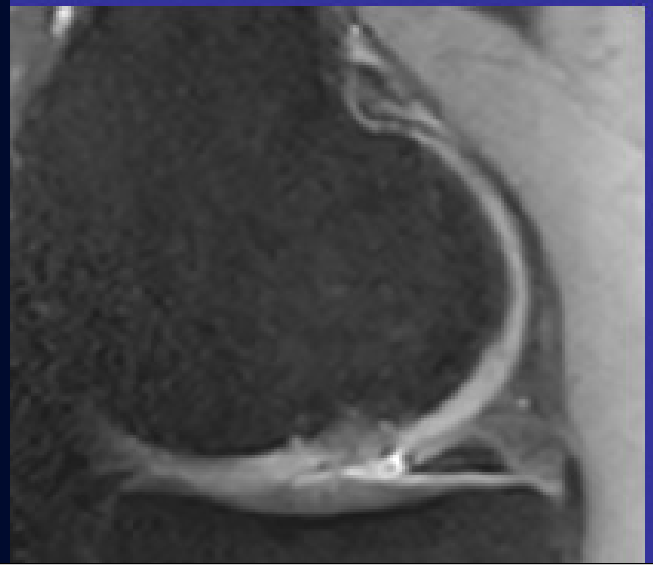
Ling et al. Proc Natl Acad Sci U S A. 2008 Feb 19;105(7):2266-70
Singh et al. Magn Reson Med. 2012 Aug;68(2):588-94

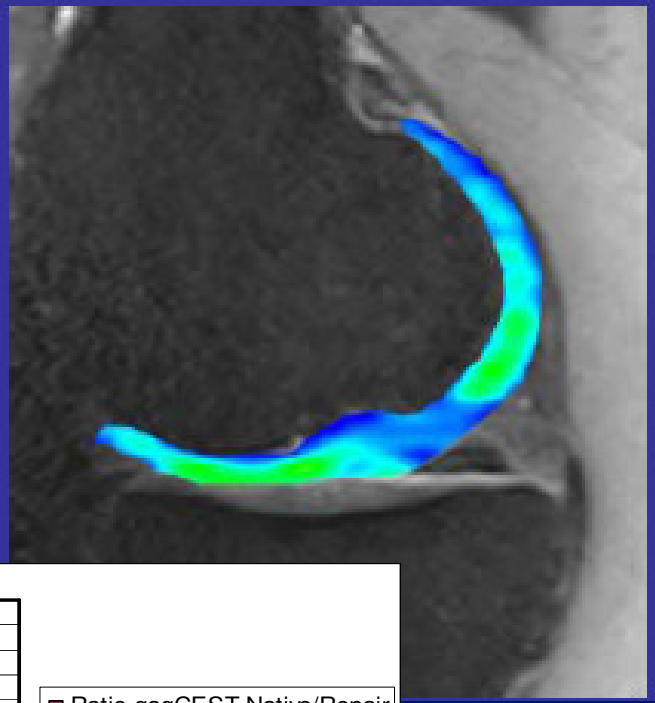
GagCEST MRI

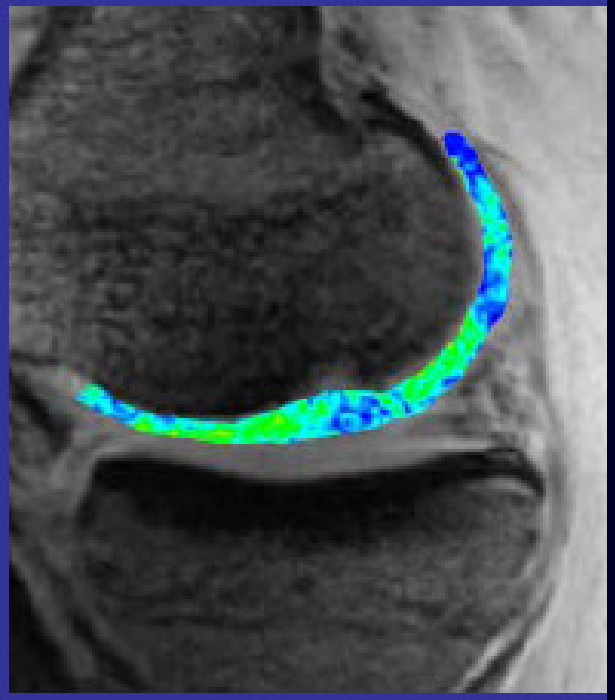
PD fs

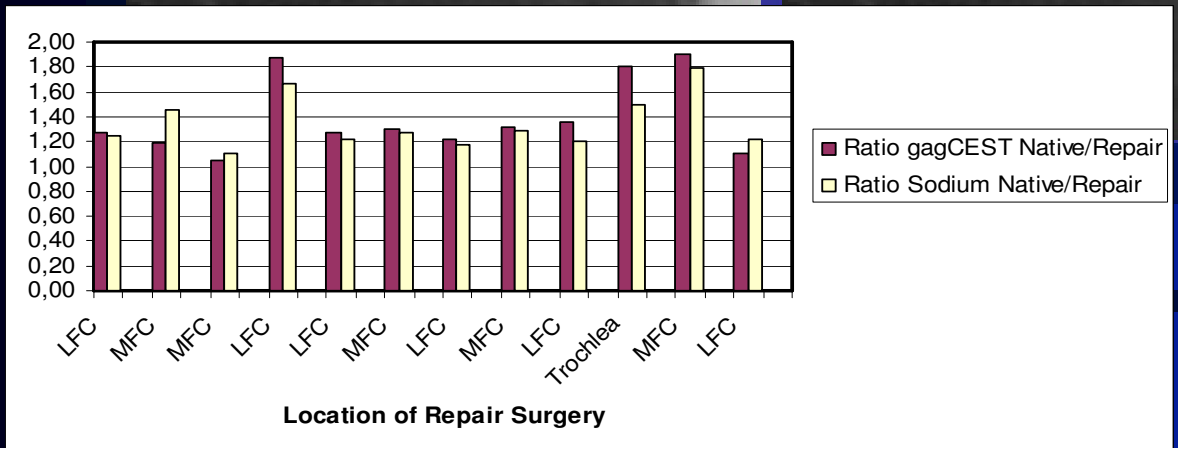
^{23}Na

CEST









Courtesy Prof. Siegfried Trattnig

Schmitt et al RADIOLOGY 2011 Jul;260(1):257-64

Compositional Imaging of Joint Tissues

- What is the rationale?
- What techniques are available?
- What tissues and what joints can we examine?
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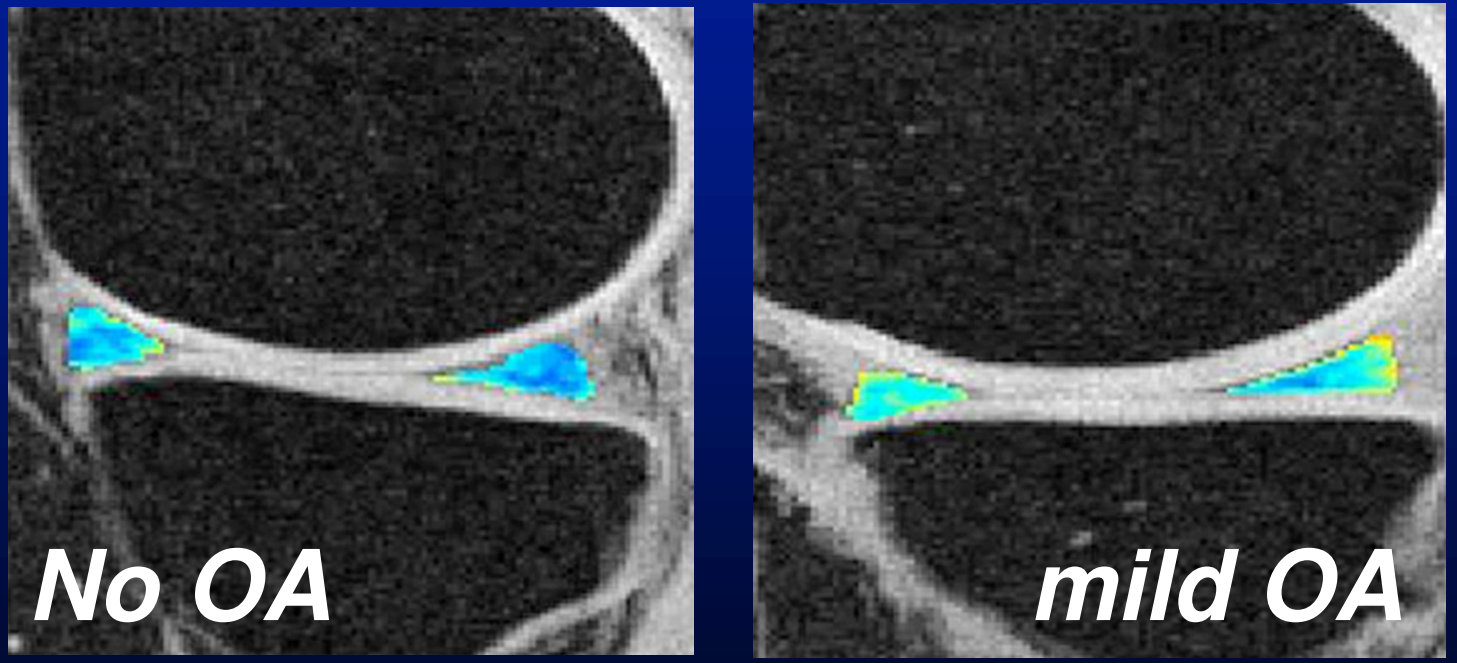
UCSF MQIR

Tissues and Joints

- Most studies focus on hyaline cartilage
- Increasingly also on menisci

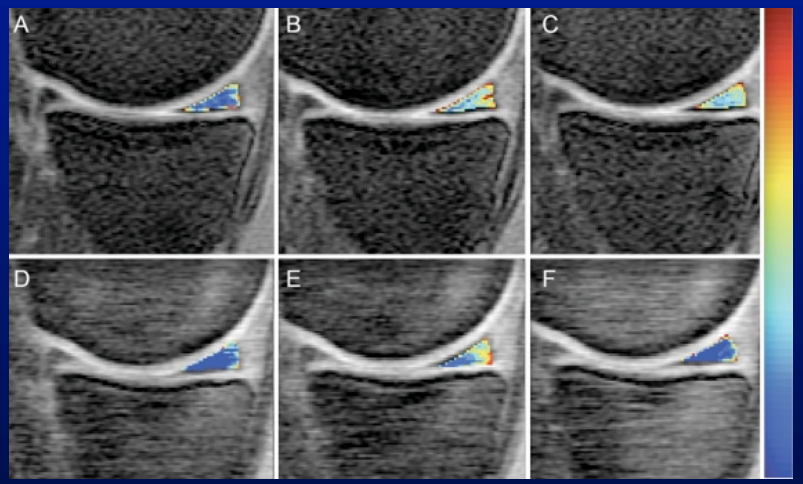


Rauscher et al. Radiology. 2008 Nov;249(2):591-600

Tissues and Joints

Menisci

- Significant differences in T1rho and T2 between normal controls, mild and severe OA subjects
- Changes in T2 and T1rho after running a marathon
- Increase in lateral meniscal T1rho after ACL tears



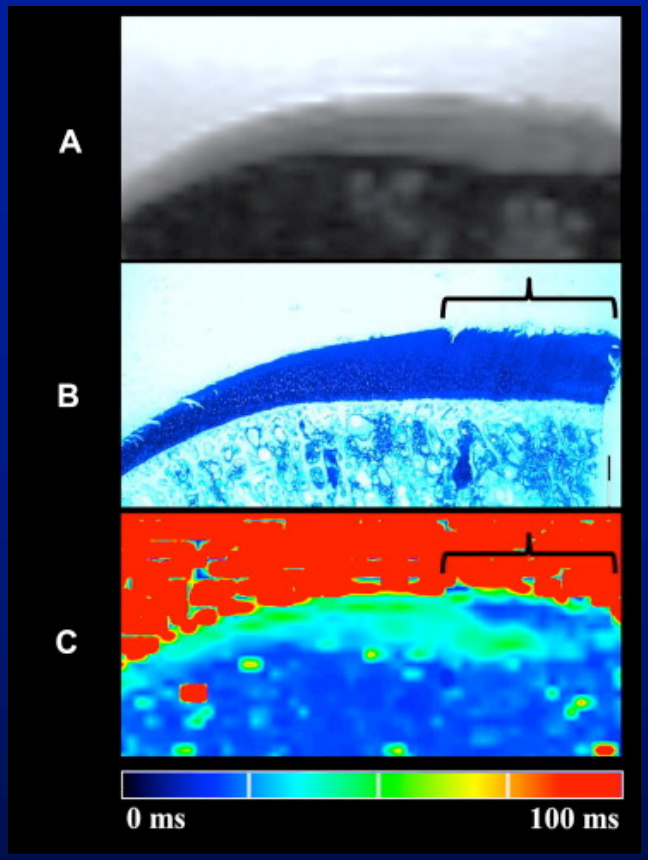
Rauscher et al. Radiology. 2008 Nov;249(2):591-600
Wang et al. Eur J Radiol. 2012 Sep;81(9):2329-36
Stehling et al. Skeletal Radiol. 2011 Jun;40(6):725-35
Wang et al. J Magn Reson Imaging. 2015 Feb;41(2):544-9

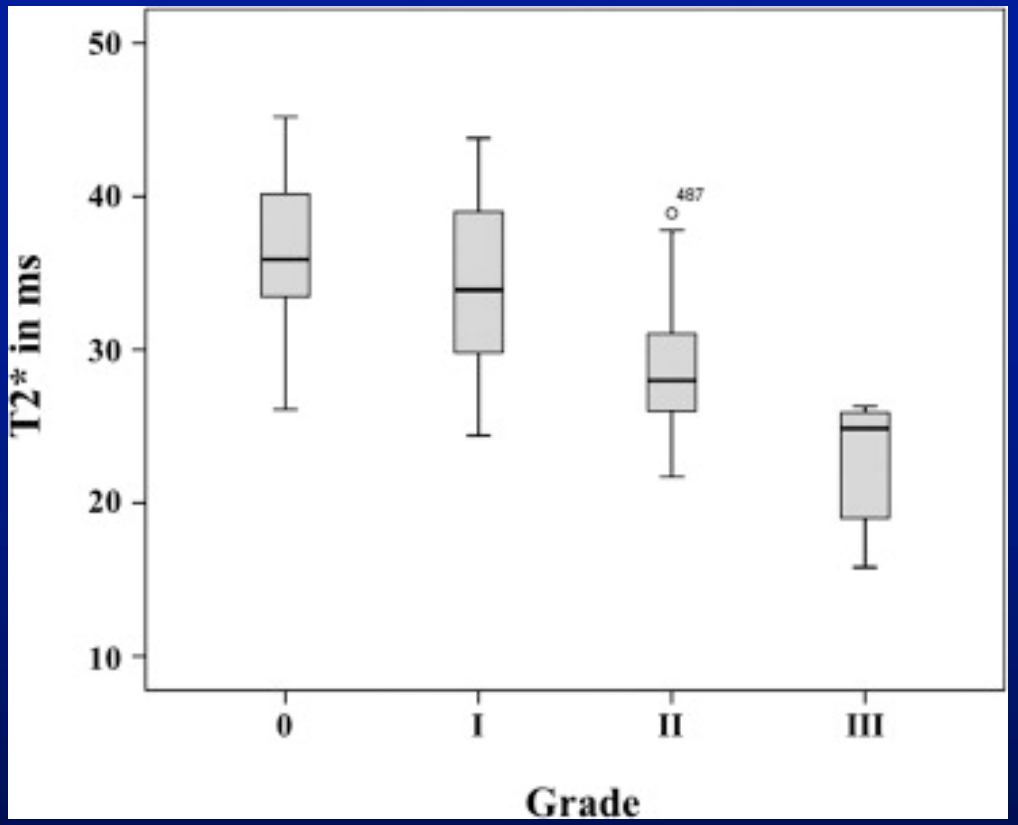
Tissues and Joints

- Most studies focus on knee joint
- Increasingly also on hip

Morgan et al. Orthop Traumatol Surg Res. 2014 Dec;100(8):971-3
Subburaj et al. Magn Reson Imaging. 2013 Sep;31(7):1129-36

Tissues and Joints

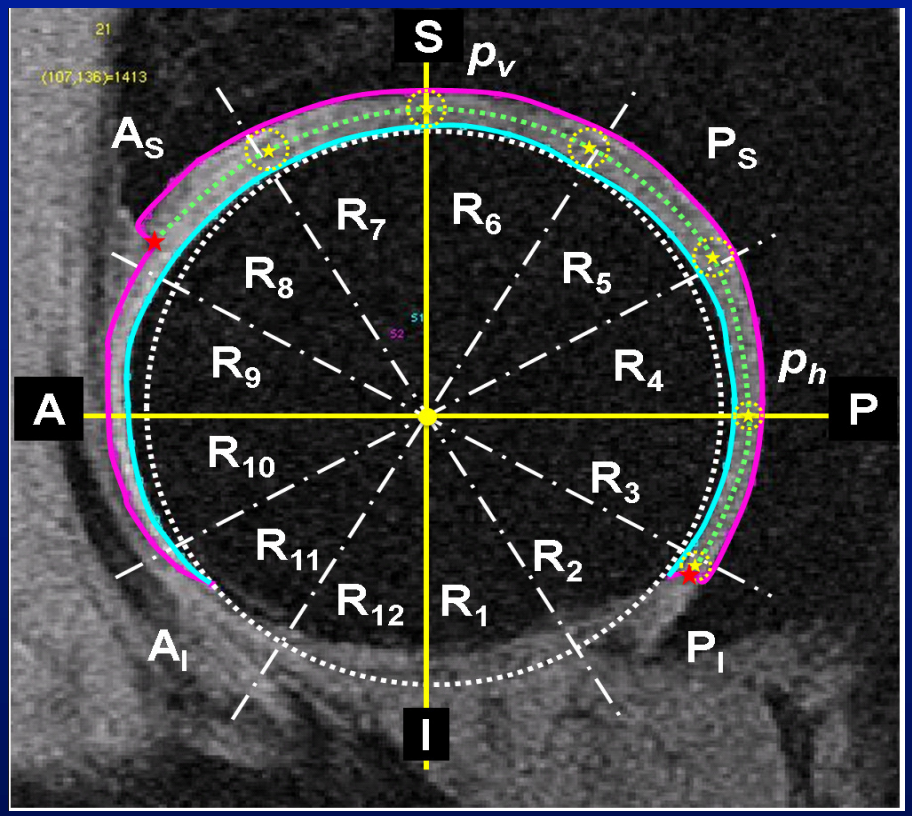


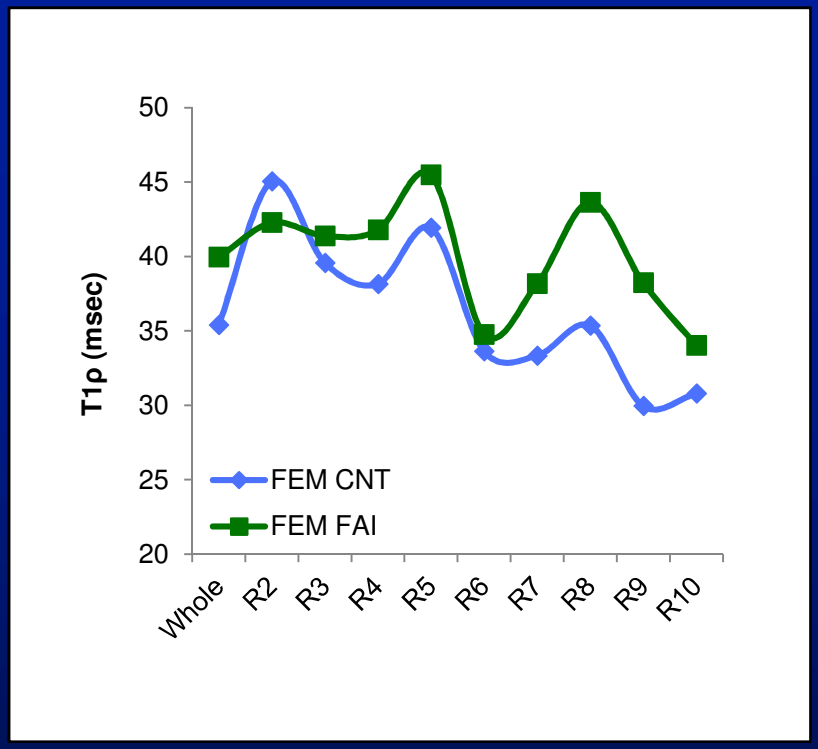


*Ex vivo validation in femoral head specimens**
T2 values decreased with increasing Mankin cartilage scores*

*Bittersohl et al. Osteoarthritis Cartilage. 2012 Jul;20(7):653-60**
Nishii et al. Radiology. 2010 Sep;256(3):955-65

Tissues and Joints





Increase in T1rho at the anterior-superior region of the femoral head/acetabulum in patients with FAI*

Morgan et al. Orthop Traumatol Surg Res. 2014 Dec;100(8):971-3
*Subburaj et al. Magn Reson Imaging. 2013 Sep;31(7):1129-36**

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Goals of OA Biomarkers

1. *Predict disease*
2. *Show efficacy of intervention and therapy*

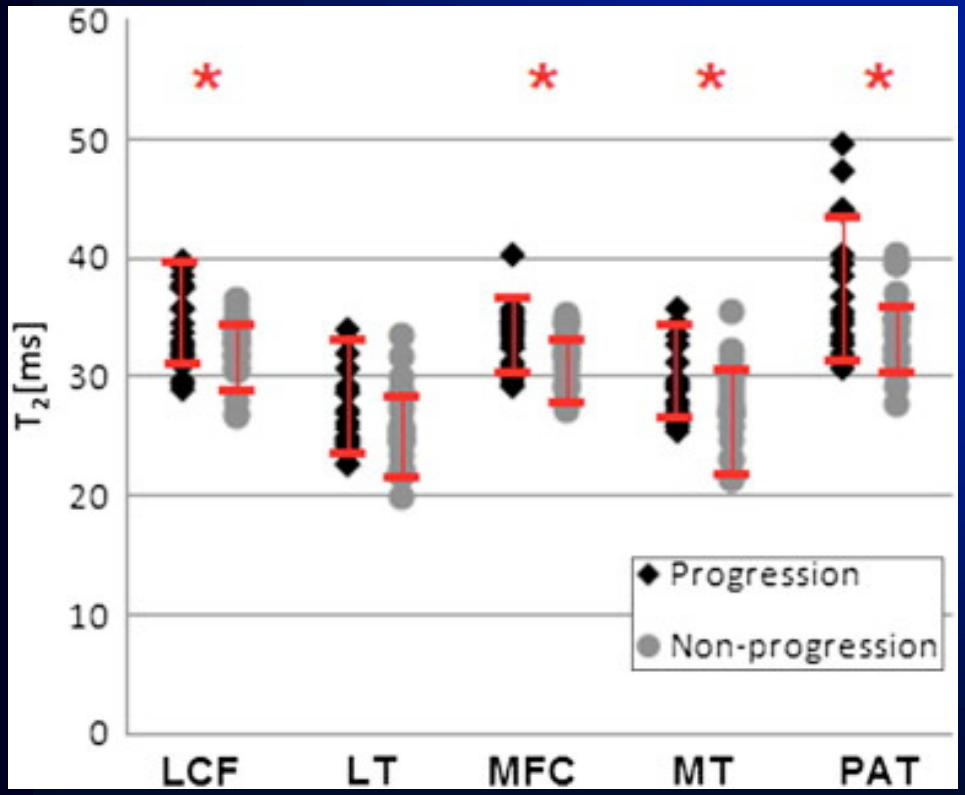
Clinical Significance

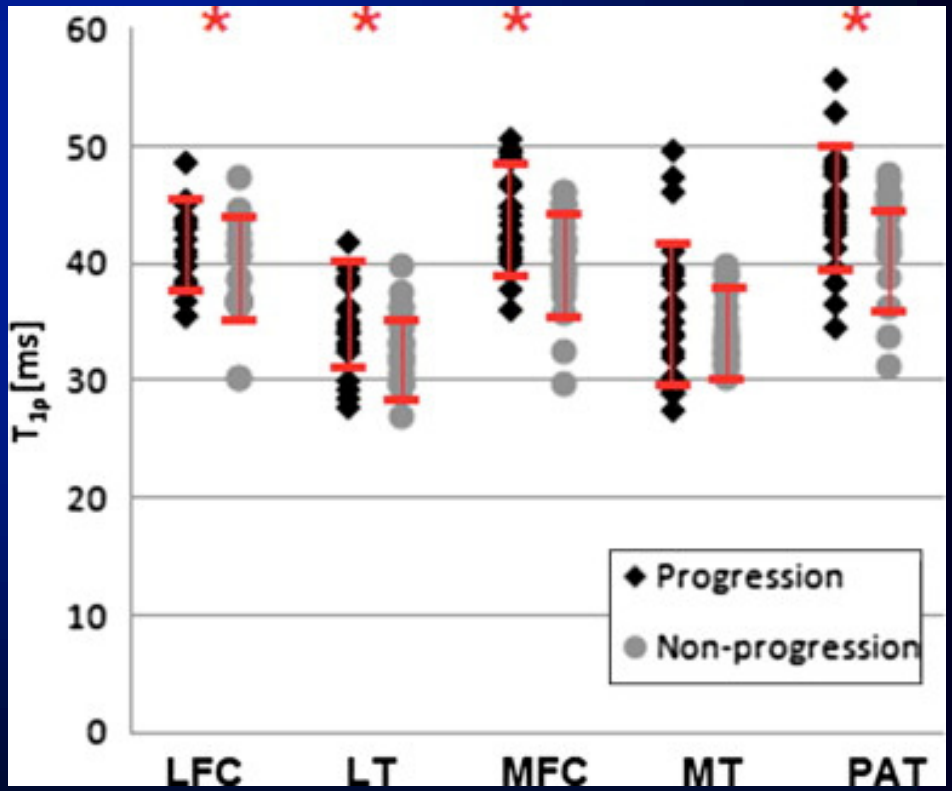
1. T1 rho and T2 predict cartilage loss and radiographic OA

Prasad et al. Osteoarthritis Cartilage. 2013 Jan;21(1):69-76.
Liebl et al. Ann Rheum Dis. 2014 Mar 10. [Epub ahead of print]

T1 rho and T2 predict cartilage loss

55 subjects with normal knees or mild OA
examined over 2 years with 3T MRI
2 groups with and without progression





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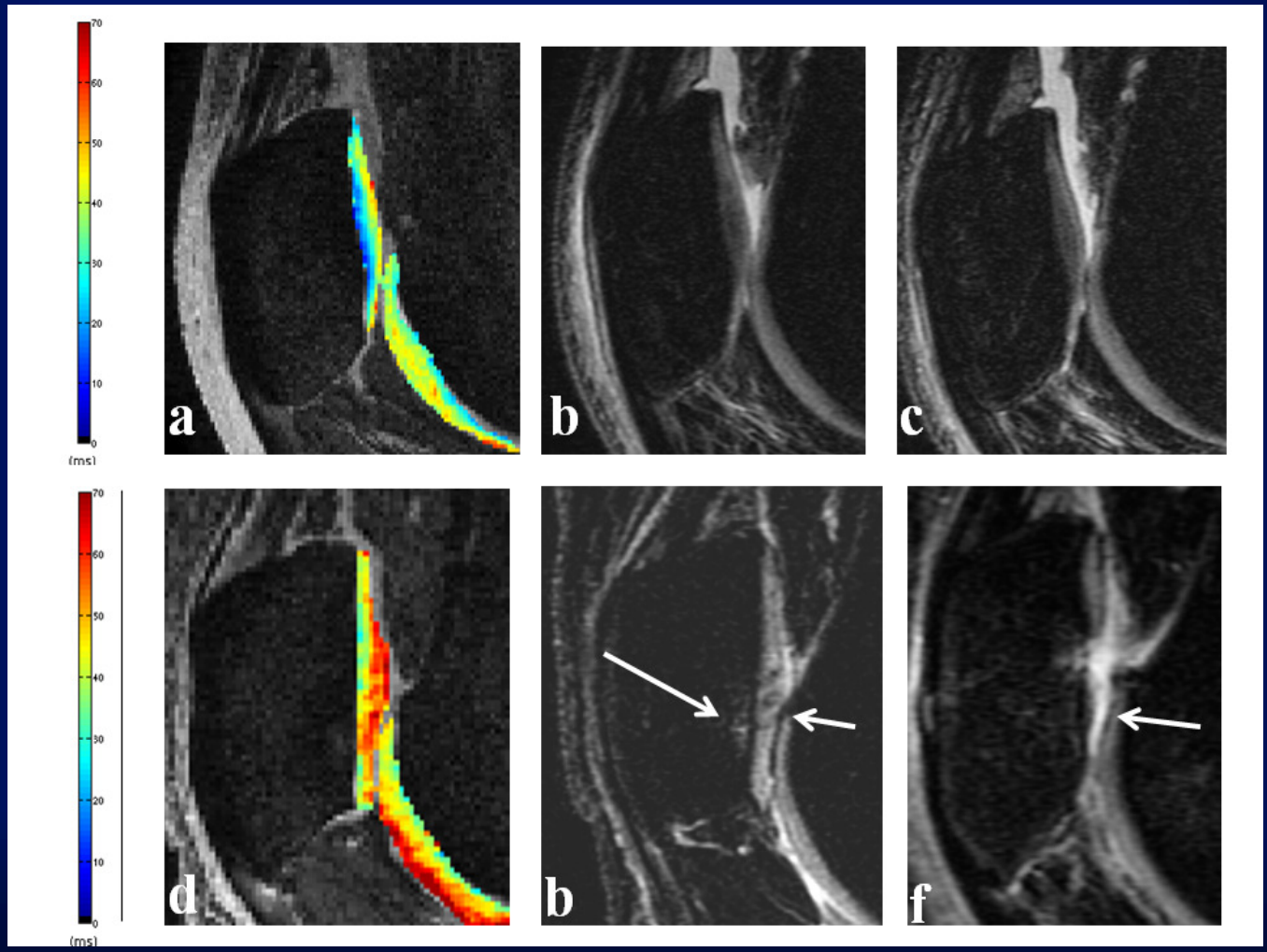


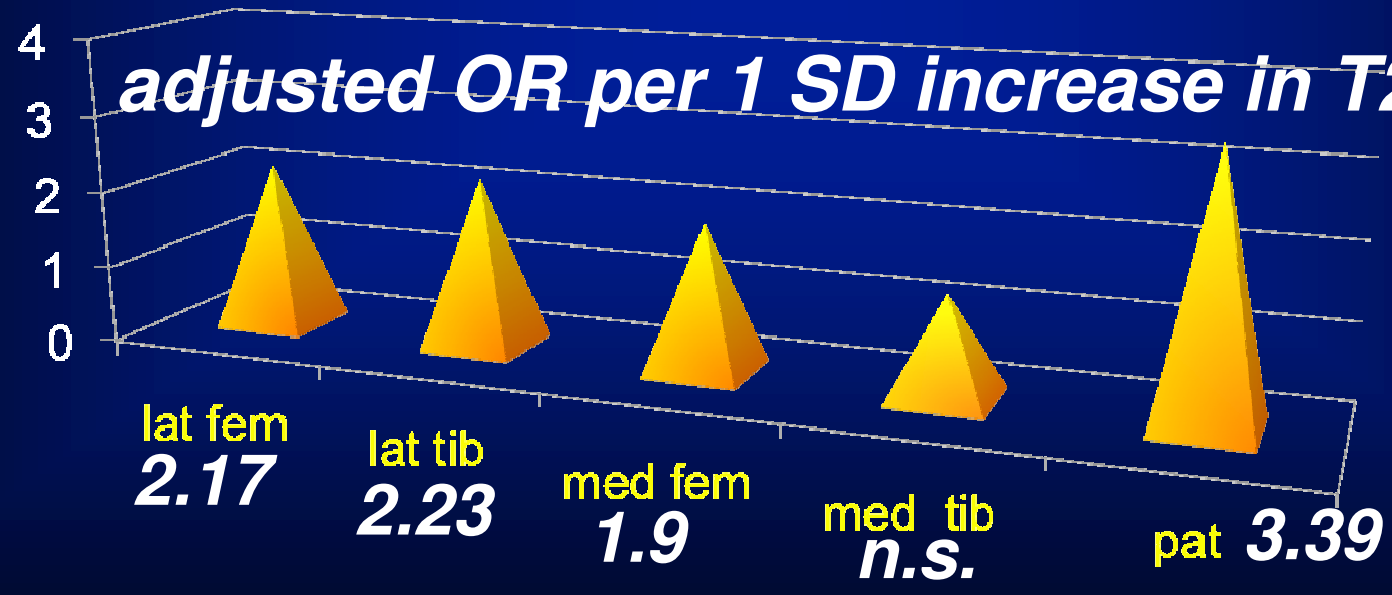
T1rho

Prasad et al. Osteoarthritis Cartilage. 2013 Jan;21(1):69-76.

T2 predicts radiographic OA

Osteoarthritis Initiative

50 knees with baseline KL grade of 0 developed KL 2 or more over a 4-year period
80 controls with no change in KL grade
baseline T2 values in all compartments except medial tibia were significantly higher



Liebl et al. Ann Rheum Dis. 2014 Mar 10. [Epub ahead of print]

Clinical Significance

2. T2 and T1rho show effect of intervention

- reversible cartilage changes after running -

Luke et al. Am J Sports Med. 2010 Nov;38(11):2273-80
Stehling et al., Skeletal Radiol. 2011 Jun;40(6):725-35

Marathon runners

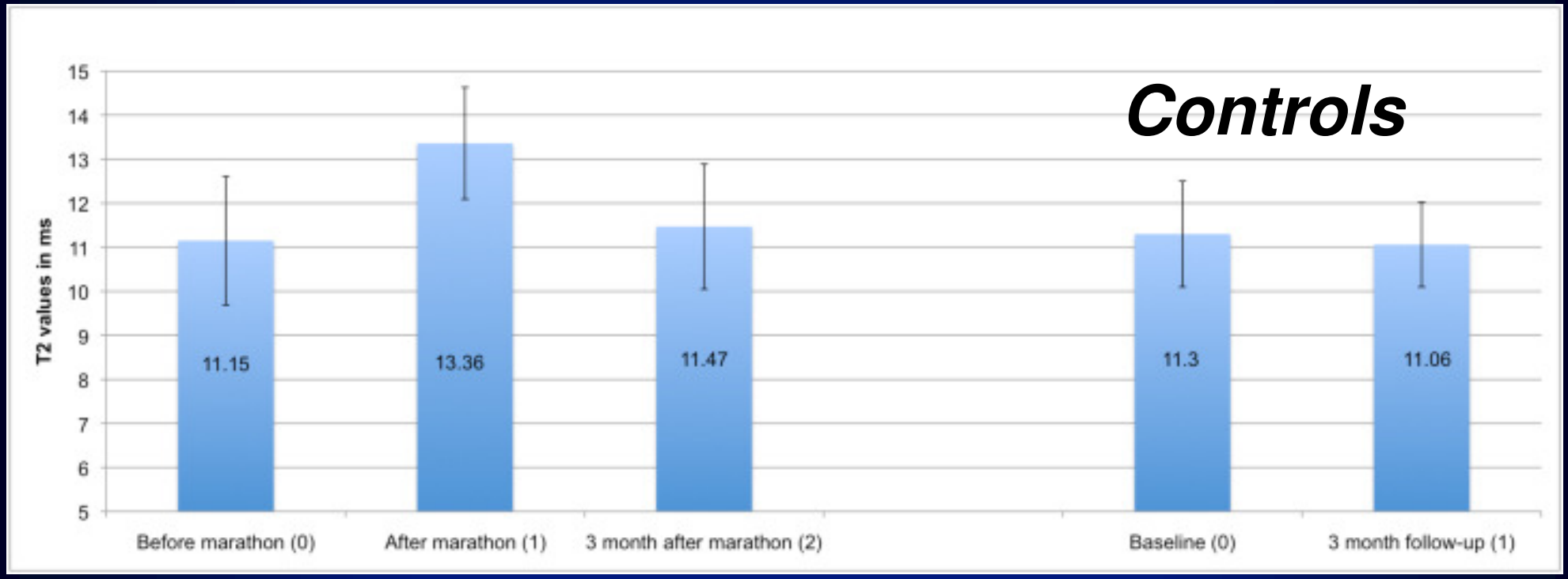
marathoners (n=10) and
controls (n=10)
without clinical symptoms
age: 18-40 years

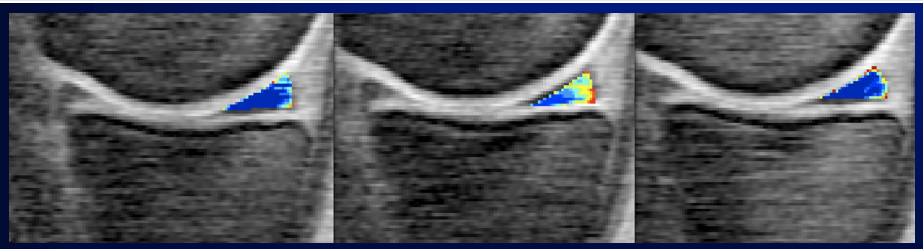
3T MRI T2 and T1rho
of knee cartilage and menisci

Before marathon, directly after
marathon and after 3 months

Luke et al. Am J Sports Med. 2010 Nov;38(11):2273-80
Stehling et al., Skeletal Radiol. 2011 Jun;40(6):725-35

Marathon runners

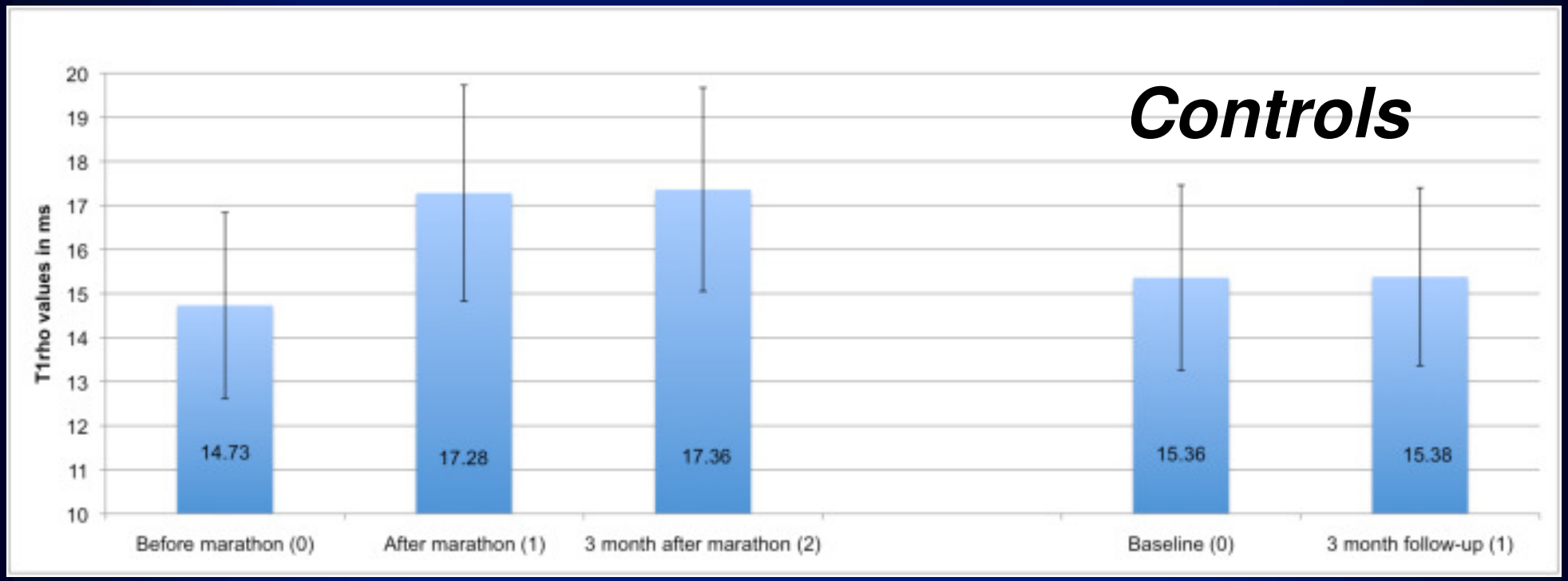


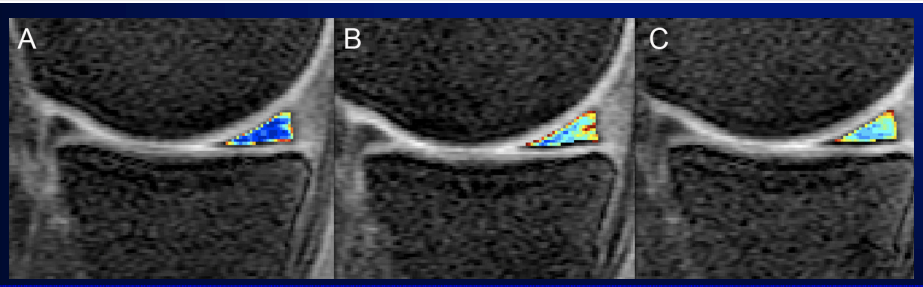


T2-Measurements

Luke et al. Am J Sports Med. 2010 Nov;38(11):2273-80
Stehling et al., Skeletal Radiol. 2011 Jun;40(6):725-35

Marathon runners





T1rho-Measurements

Luke et al. Am J Sports Med. 2010 Nov;38(11):2273-80
Stehling et al., Skeletal Radiol. 2011 Jun;40(6):725-35

Clinical Significance

2. T2 shows effect of intervention

- Physical activity -

Hovis et al. Arthritis Rheum. 2011 Aug;63(8):2248-56
Lin et al. Osteoarthritis Cartilage. 2013 Oct;21(10):1558-66

Osteoarthritis Initiative

128 individuals (71 f, 57 m)

age: 45-55 years

asymptomatic (WOMAC, Pain =0)

but risk factors for OA

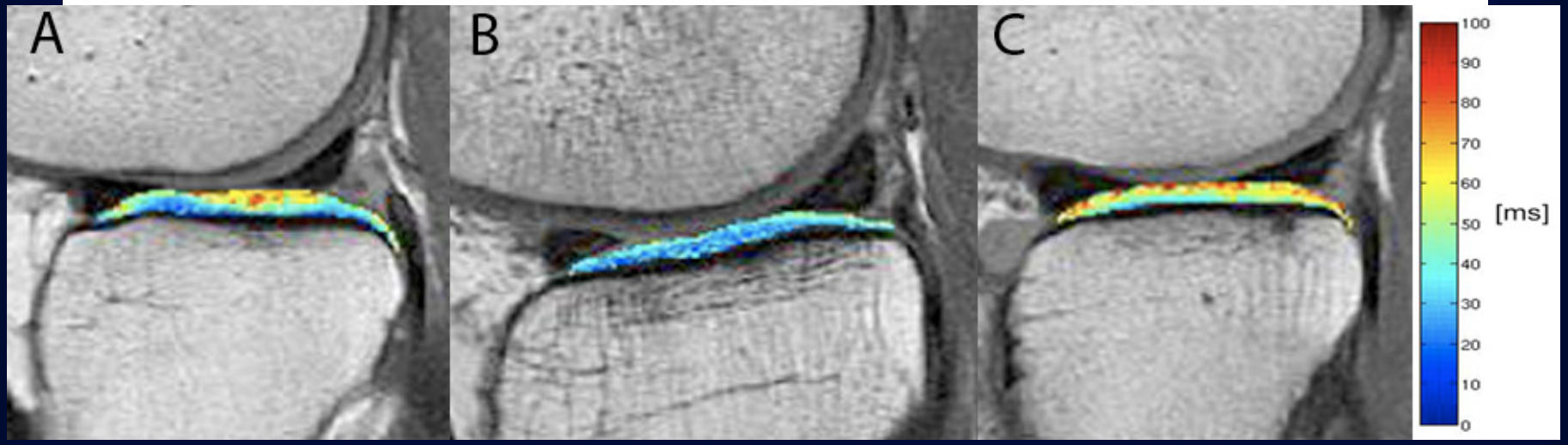
MRI

- Cartilage defects (WORMS)
- T2 relaxation time measurements

PASE (physical activity score for the elderly)

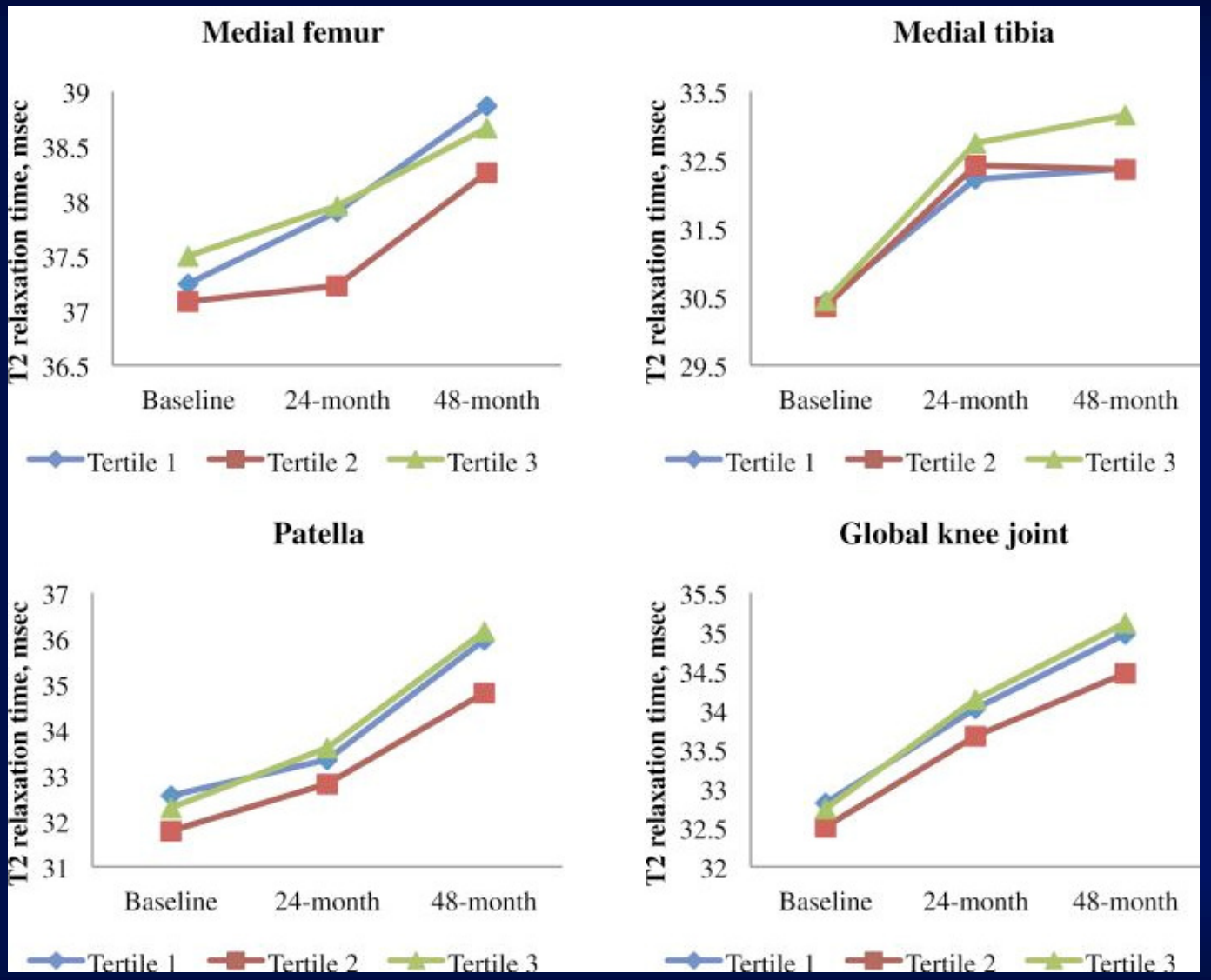
T2 cross-sectional – 3 exercise levels

	All Subjects			
	Exercise Level §			
T2 Values	**E_1 (n=26)**	**E_2 (n=50)**	**E_3 (n=56)**	**p value†**
Overall Avg.	44.5 ± 2.8	43.5 ± 2.2	45.0 ± 3.0	0.010^
Patella	44.3 ± 4.6	43.0 ± 3.5	44.8 ± 3.8	0.084^
MFC	50.4 ± 3.1	50.0 ± 3.1	51.3 ± 4.1	0.078^
MT	39.2 ± 3.6	38.5 ± 2.5	39.2 ± 2.9	0.394
LFC	49.1 ± 4.1	48.0 ± 3.1	49.2 ± 3.3	0.194
LT	39.7 ± 3.4	38.0 ± 3.1	40.2 ± 3.3	0.001*^



Hovis et al., Arthritis and Rheumatism, 2011 Aug;63(8):2248-56

T2 over 4 years



Lin et al. Osteoarthritis Cartilage. 2013 Oct;21(10):1558-66

Clinical Significance

2. T2 shows impact of prevention

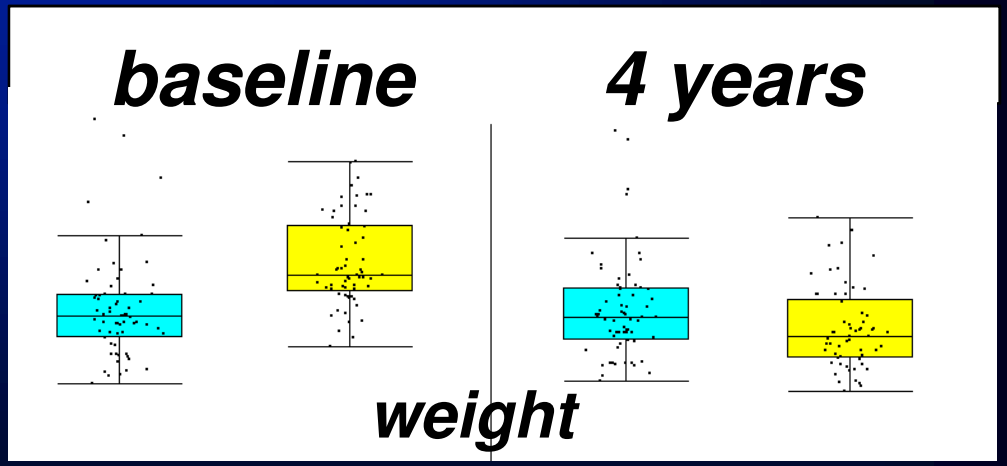
- Weight loss -

Serebrakian et al. J Magn Reson Imaging. 2015 May;41(5):1272-80

127 individuals (71 f, 57 m)
age: 45-70 years
asymptomatic (WOMAC, Pain =0)
with risk factors for OA

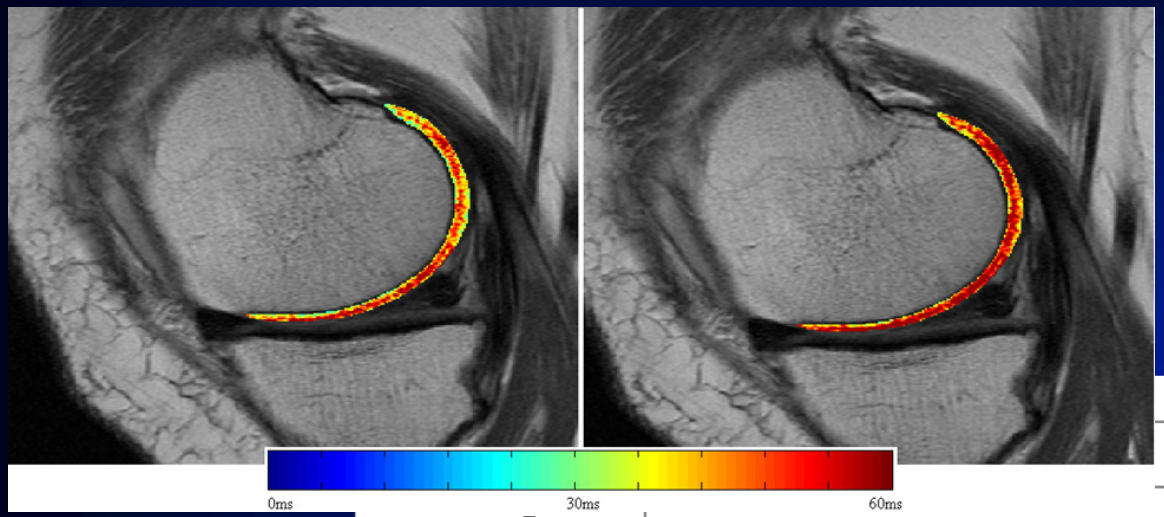
2 groups:
>10% loss of weight over 4 years
No weight change over 4 years

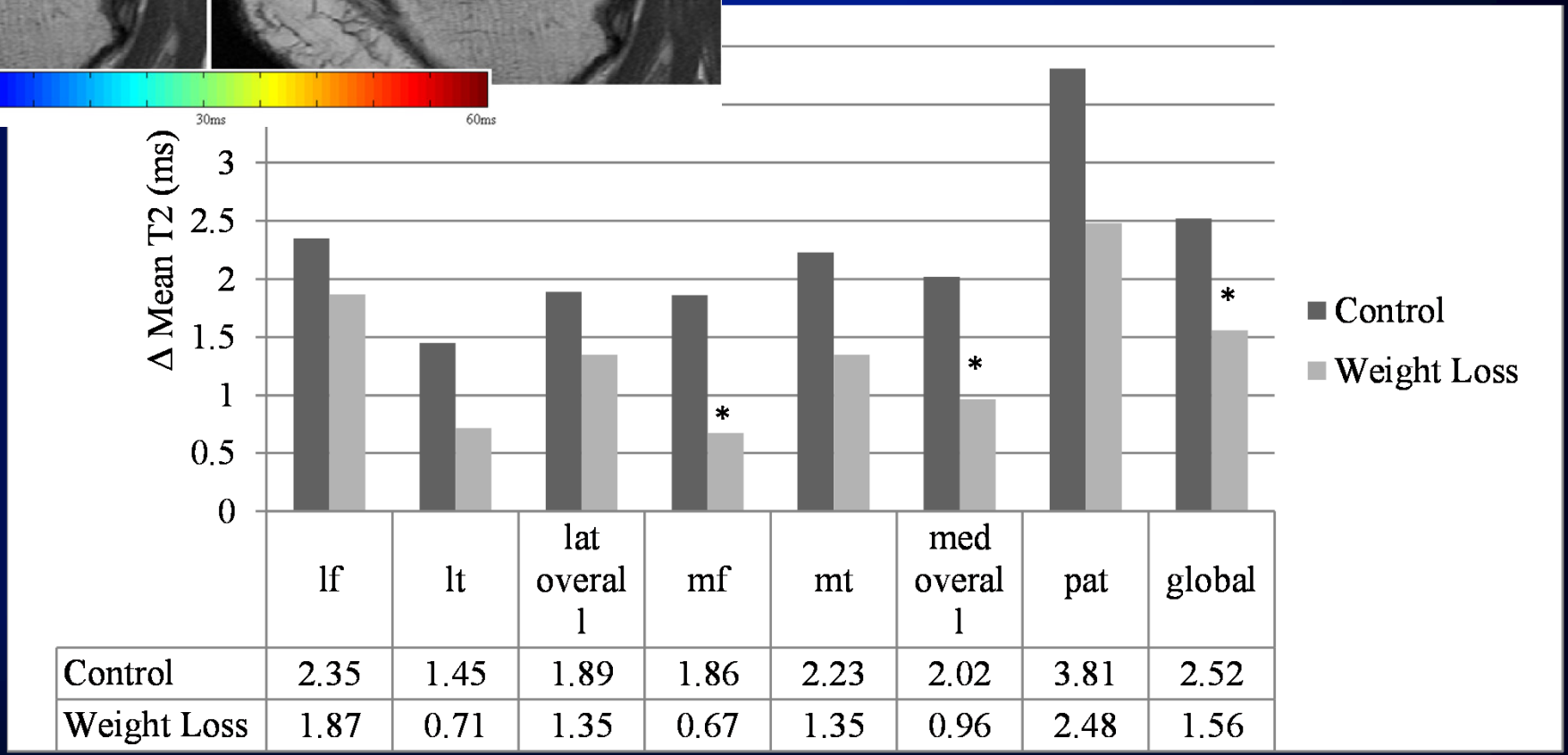
MRI
T2 relaxation time



Serebrakian et al. J Magn Reson Imaging. 2015 May;41(5):1272-80

Individuals with weight loss show less progression of T2





	lf	lt	lat overall	mf	mt	med overall	pat	global
Control	2.35	1.45	1.89	1.86	2.23	2.02	3.81	2.52
Weight Loss	1.87	0.71	1.35	0.67	1.35	0.96	2.48	1.56

Serebrakian et al. J Magn Reson Imaging. 2015 May;41(5):1272-80

Compositional Imaging of Joint Tissues

- What is the rationale?
- What techniques are available?
- What tissues and what joints can we examine?
- What have clinical studies shown?
- What is required to apply it in clinical practice?

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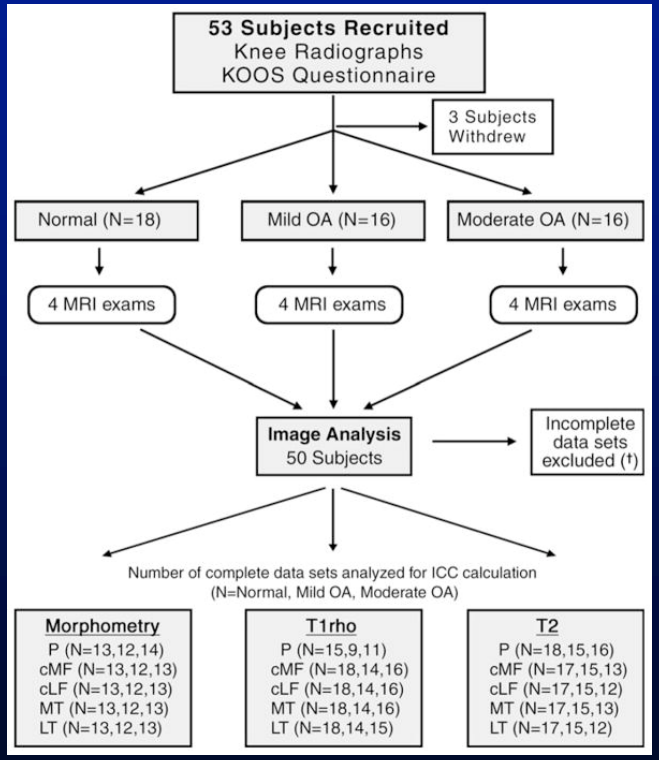
Requirements for clinical practice

- **Reproducibility between different MR scanners and vendors**
- **Automated segmentation**
- **Age and gender adjusted reference databases**

Mosher T et al. Radiology. 2011 Mar;258(3):832-42
Schneider E et al. Osteoarthritis Cartilage. 2013 Jan;21(1):110-6
Tama-Pena JG et al. IEEE Trans Biomed Eng. 2012 Apr;59(4):1177-86
Joseph et al. Osteoarthritis Cartilage. 2015 Feb 11. [Epub ahead of print]

Reproducibility

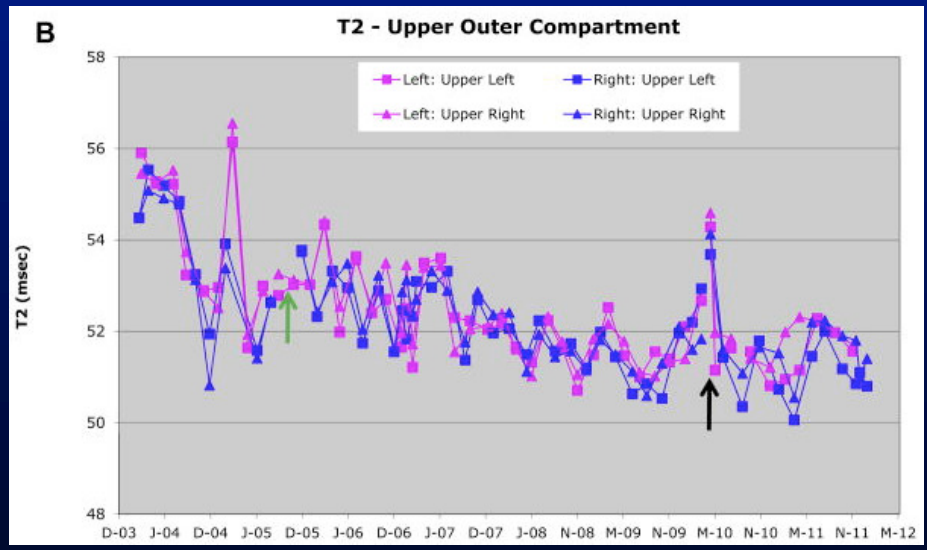
- **Reproducibility different MR scanners and vendors**
- **Analysis of MR Image Biomarker Reproducibility in ACRIN-PA 4001 Multicenter Trial**
- **Three 3-T Magnetom Trio (Siemens) and two 3-T Achieva magnets (Philips) phased-array knee coils, used in 50 subjects**
- **Good to high reproducibility for T2**
- **Relatively large precision errors for T1rho, better at the patella**



Mosher T. Radiology. 2011 Mar;258(3):832-42

Reproducibility

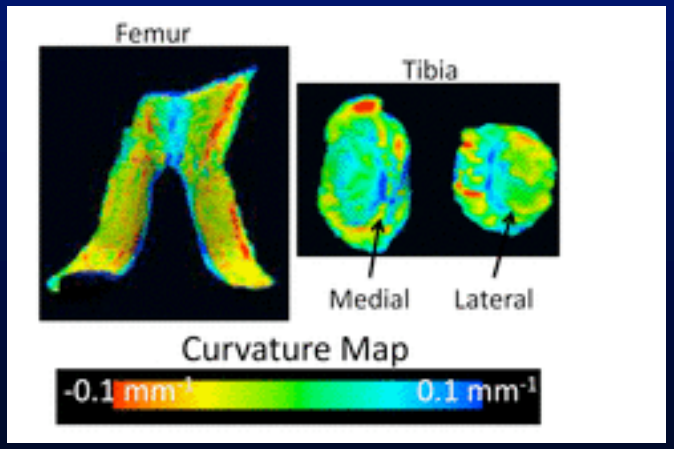
- **Reproducibility of different MRI scanners in the OAI over eight years**
- **Good stability and reproducibility**
- **T2 relaxation time reproducibility varied from 1.5% to 5.3%**
- **seasonal fluctuations observed at two sites**
- **coil signal uniformity and signal level varied significantly over time**

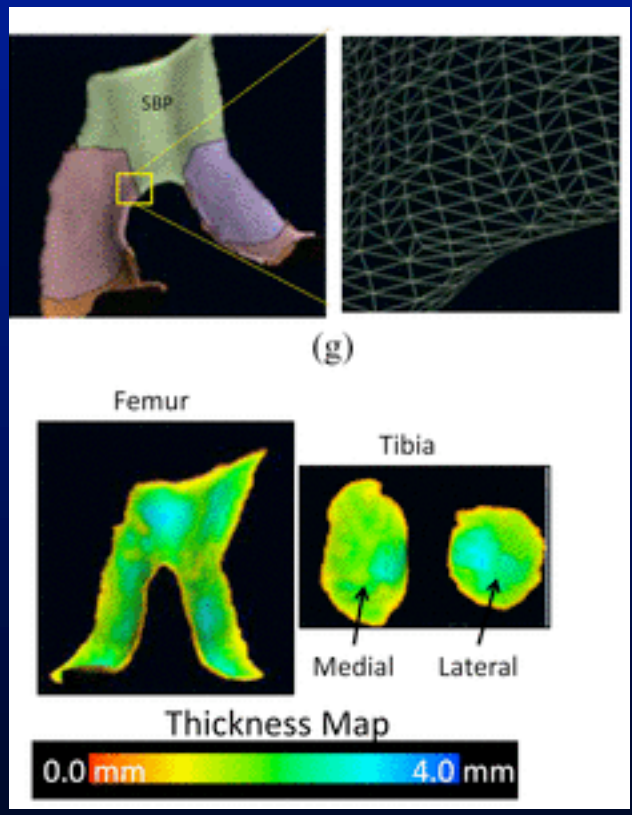


Schneider E et al. Osteoarthritis Cartilage. 2013 Jan;21(1):110-6

Segmentation

- **Automated segmentation**
- **Required to reduce post-processing time and improve reproducibility**
- **Limited number of studies**
- **So far no standard algorithm**

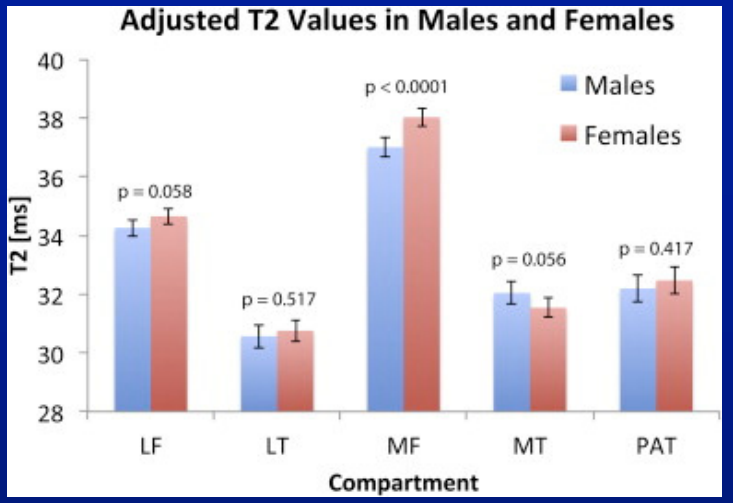


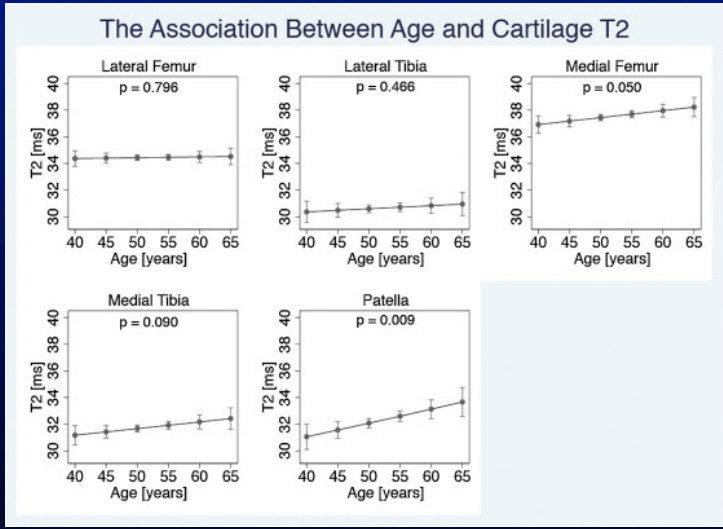


Tama-Pena JG et al. IEEE Trans Biomed Eng. 2012 Apr;59(4):1177-86

Normative Databases

- Age and gender adjusted ‘normative” reference databases
- So far only for T2 measurements
- Relatively limited impact of age and gender but high impact of BMI





Joseph et al. Osteoarthritis Cartilage. 2015 Feb 11. [Epub ahead of print]

Summary and Conclusions - 1

I. Compositional imaging allows to analyze **cartilage quality** before cartilage is lost

II. most information available on **T2 measurements** – **T1rho** may be superior and was suggested by AF for new ACL study

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Summary and Conclusions - 2

III. Hyaline cartilage, menisci, knee and hip

IV. **Differentiating, predicting, monitoring** but not diagnosing OA

V. Future requirements: Standardization, automated post-processing

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Thank you
for your attention
email: tmlink@radiology.ucsf.edu