Current State of the Art in Compositional Imaging of Joint Tissues

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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?
Compositional Imaging of Joint Tissues

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Analyzing the cartilage matrix

Glycosaminoglycans
Collagen

Link
Cartilage Imaging
Springer 2011
Rationale:

Morphological MRI shows irreversible changes
Morphology
Compositional MRI

Early matrix abnormality before cartilage loss

May be reversible

Disease course may be modified
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

Mosher TJ et al. Arthritis Rheum. 2004 Sep;50(9):2820-8
T2 mapping

T2 map - 30 yo volunteer
Before and after marathon
T1rho quantifies macromolecules
In particular glycosaminoglycans

Regatte et al.; J Magn Reson Imaging 2006; 23:547-553
T1rho-relaxation time is higher in OA patients than in normals and increases with degree of disease.
T1rho higher in patients with cartilage defects

Li et al. MRM 2005; 54: 929-936
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
**dGEMRIC** – requires exercise after Gd injection

- **GAG loss**
- **90 min post injection - 60 min scan with varying TI**
- **T1-w + Gd-DTPA**
- **fs iw**
**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

Sodium $T_2$ $T_1p$

Pre-season

Post-season

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
GagCEST MRI

PD fs

$^{23}$Na

CEST

Location of Repair Surgery

Ratio gagCEST Native/Repair

Ratio Sodium Native/Repair

Courtesy Prof. Siegfried Trattnig

Schmitt et al RADIOLOGY 2011
Jul;260(1):257-64
Compositional Imaging of Joint Tissues

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Tissues and Joints

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

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

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
Tissues and Joints

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

Nishii et al. Radiology. 2010 Sep;256(3):955-65
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
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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

**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

T1 rho and T2 predict cartilage loss

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. Adjusted OR per 1 SD increase in T2:

- Lat fem: 2.17
- Lat tib: 2.23
- Med fem: 1.9
- Med tib: n.s.
- Pat: 3.39
Clinical Significance

2. T2 and T1rho show effect of intervention
   - reversible cartilage changes after running -

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
Marathon runners

Controls

T2-Measurements

Marathon runners

Controls

T1rho- Measurements

Clinical Significance

2. T2 shows effect of intervention
   - Physical activity -
**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)

_Hovis et al., Arthritis and Rheumatism, 2011 Aug;63(8):2248-56_
## T2 cross-sectional – 3 exercise levels

<table>
<thead>
<tr>
<th>T2 Values</th>
<th>E₁ (n=26)</th>
<th>E₂ (n=50)</th>
<th>E₃ (n=56)</th>
<th>p value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Avg.</td>
<td>44.5 ± 2.8</td>
<td>43.5 ± 2.2</td>
<td>45.0 ± 3.0</td>
<td>0.010^</td>
</tr>
<tr>
<td>Patella</td>
<td>44.3 ± 4.6</td>
<td>43.0 ± 3.5</td>
<td>44.8 ± 3.8</td>
<td>0.084^</td>
</tr>
<tr>
<td>MFC</td>
<td>50.4 ± 3.1</td>
<td>50.0 ± 3.1</td>
<td>51.3 ± 4.1</td>
<td>0.078^</td>
</tr>
<tr>
<td>MT</td>
<td>39.2 ± 3.6</td>
<td>38.5 ± 2.5</td>
<td>39.2 ± 2.9</td>
<td>0.394</td>
</tr>
<tr>
<td>LFC</td>
<td>49.1 ± 4.1</td>
<td>48.0 ± 3.1</td>
<td>49.2 ± 3.3</td>
<td>0.194</td>
</tr>
<tr>
<td>LT</td>
<td>39.7 ± 3.4</td>
<td>38.0 ± 3.1</td>
<td>40.2 ± 3.3</td>
<td>0.001*^</td>
</tr>
</tbody>
</table>

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T2 over 4 years

Clinical Significance

2. T2 shows impact of prevention
   - Weight loss -

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
Individuals with weight loss show less progression of T2

Compositional Imaging of Joint Tissues

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Requirements for clinical practice

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

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

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

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
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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R01 AR046905
Thank you for your attention

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