In vivo diffusion tensor imaging (DTI) of articular cartilage as a biomarker for osteoarthritis

Jose G. Raya¹, Annie Horng², Olaf Dietrich², Svetlana Krasnokutsky³, Luis S. Beltran¹, Maximilian F. Reiser², Michael Recht¹, Christian Glaser¹,²

¹ Department of Radiology, New York University Langone Medical center
² Department of Clinical Radiology, University of Munich
³ Department of Rheumatology, New York University Langone Medical Center

INTRODUCTION

• Diffusion of water molecules in cartilage → Cartilage integrity
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- Proteoglycan (PG) and collagen different imprint in diffusion
  1. PG → isotropic distributed → mean diffusivity (MD)
  2. Collagen architecture → fractional anisotropy (FA)

INTRODUCTION

- Validation of DTI in OA samples
- Histology reference standard (OARSI score)

- n=43 samples with early cartilage damage (OARSI 0 (14), 1 (11), 2 (12) 3-4 (6))

- Correlation DTI with OARSI score (P<0.05)

- ACCURACY = 95% to detect cartilage damage (random → accuracy=50%)

- ACCURACY = 75% to stage cartilage damage (random → accuracy=25%)

Raya JG et al. Radiology (accepted)

INTRODUCTION

- Diffusion of water molecules in cartilage → Cartilage integrity
- Proteoglycan (PG) and collagen different influence in diffusion
  1. PG → isotropic distributed → mean diffusivity (MD)
  2. Collagen → anisotropic → fractional anisotropy (FA)
- But in vivo DTI of the articular technically challenging
  1. Short T2 ≈ 30 ms
  2. High resolution ≤ 0.6 mm
  3. Complex knee anatomy → $B_0$ $B_1^+$ Inhomogeneity
- Failure of standard diffusion sequences → New sequences
INTRODUCTION: Line Scan Diffusion Imaging sequence

Advantages of the LSDI:
1. SE-based → insensitive to $B_0$ and $B_1^+$ inhomogeneity
2. No phase encoding → insensitive to motion artifacts
3. Short TR → much faster than SE

Disadvantages of the LSDI:
1. Low SNR → Use of 7 T + 28 Ch receive coil

OBJECTIVE

To assess the value of in vivo DTI of articular cartilage for the early diagnosis of OA as compared with the T2 relaxation time.

Raya JG et al. Radiology 2012;262:550-559
METHODS: Experimental design

SUBJECTS
1. **16 asymptomatic volunteers** (age 30.7±2.3 y) 10 scanned twice
   exclusion: knee pain, surgery or trauma
2. **10 OA subjects** (mean age 61.2±8.3 y) from NYU-HJD OA knee cohort
   inclusion: intact cartilage surface + signal alteration in T2w TSE fs

7 T (Siemens) and 1 Ch transmit, 28 Ch receive knee coil (QED)

IMAGE PROTOCOL
1. High-resolution T2*-weighted fat-saturated GRE
   (TE/TR=9.2/40 ms, Matrix=256×256×192, isotropic voxel size=0.5 mm³, flip angle = 15°, fat-saturation, acquisition time=10 min)
2. LSDI sequence
   (TE/TR/TReff=46/180/2890 ms, Matrix=256×128, in-plane=0.6×0.6 mm², b-values=5, 450 s/mm², 6 directions, fat-saturation, acquisition time=14 min)
3. Multislice Multiecho spin-echo sequence
   (TE/TR=16/3500 ms, Matrix=256×128, ETL=6, fat-saturation, acquisition time=10 min)

METHODS: Image processing

1. Cartilage segmentation (MSME) and parameter calculation (MD, FA,T2)
2. MRI parameter profiles

<table>
<thead>
<tr>
<th>Bone-cartilage interface (0) → articular surface (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD (10⁻³ mm²)</td>
</tr>
<tr>
<td>0  0.5  1  1.2</td>
</tr>
<tr>
<td>Mean, STD Test-retest reproducibility Root mean square of the Coefficient of variation</td>
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### RESULTS: Asymptomatic volunteer

<table>
<thead>
<tr>
<th>FLASH</th>
<th>MD ($10^{-3}$ mm$^2$/s)</th>
<th>FA</th>
<th>$T_2$ (ms)</th>
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<tbody>
<tr>
<td>![Image](131x538 to 489x666)</td>
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</tr>
<tr>
<td>0</td>
<td>2.50</td>
<td>0.50</td>
<td>35</td>
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<tr>
<th>Global</th>
<th>Layers</th>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
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<tbody>
<tr>
<td>MD ($10^{-3}$ mm$^2$/s)</td>
<td>DEEP</td>
<td>SUP</td>
<td>1.00</td>
<td>0.89</td>
<td>1.20</td>
<td>1.08</td>
</tr>
<tr>
<td>FA</td>
<td></td>
<td></td>
<td>0.45</td>
<td>0.52</td>
<td>0.35</td>
<td>0.43</td>
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P<0.001 NON-SIGNIFICANT

### RESULTS: Test-retest reproducibility

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<tr>
<td>MD</td>
<td>DEEP</td>
<td>SUP</td>
<td>8.1%</td>
<td>7.4%</td>
<td>9.5%</td>
<td>10.7%</td>
</tr>
<tr>
<td>FA</td>
<td>9.7%</td>
<td>7.7%</td>
<td>15.4%</td>
<td>15.3%</td>
<td>13.0%</td>
<td>13.2%</td>
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### RESULTS: Asymptomatic volunteer

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#### PROFILES

Distance from the bone-cartilage interface to the articular surface.

### RESULTS: OA subject 1

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#### PROFILES

Distance from the bone-cartilage interface to the articular surface.
RESULTS: Asymptomatic vs. OA

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<th>Specificity</th>
<th>Threshold</th>
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<tbody>
<tr>
<td>MD</td>
<td>90%</td>
<td>81%</td>
<td>1.20×10⁻³ mm²/s</td>
</tr>
<tr>
<td>FA</td>
<td>80%</td>
<td>88%</td>
<td>0.25</td>
</tr>
<tr>
<td>T2</td>
<td>60%</td>
<td>68%</td>
<td>29 ms</td>
</tr>
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* P <0.01 (Wilcoxon test)

+ Outlier

LIMITATIONS

- Small number of patients, patient selection criteria
- Only 5 slices were acquired (SAR)
- Difference in age between asymptomatic and OA
- Test-retest reproducibility only in asymptomatic subjects
In vivo DTI of the articular cartilage is feasible

Comparison between asymptomatic and OA subjects
1. MD was significantly increased in OA (P<0.01)
2. FA was significantly decreased in OA (P<0.01)
3. T2 showed no difference between asymptomatic and OA
   - Reduced dynamic of T2 at 7T
   - DTI is sensitive to earlier degeneration

Diagnostic value of MRI parameters
1. MD and FA has specificity and sensitivity 80–90%
2. T2 had lower specificity and sensitivity 60–68%

DISCUSSION AND CONCLUSION

OUTLOOK: DTI OF ALL KNEE COMPARTMENTS
OUTLOOK: DTI OF CARTILAGE REPAIR

T2 (ms)  MD (×10⁻³ mm²/s)  FA

8 Months

16 Months

OUTLOOK: DTI AT 3T
Radial spin echo diffusion (RAISED) sequence
(Resolution=0.6×0.6×3 mm³, acquisition time 17:30 min, b=0, 400 s/mm²)

b = 1 s/mm²  b = 400 s/mm²