Knee OA: Scope of the Problem

- Need for early identification in knee osteoarthritis (OA)
  - since it is too late once structural changes occur
  - because current management ineffective at long-term symptom modification or any disease modification\(^3,4\)
  - to develop sub-group specific preventative interventions
  - depends on ability to detect early biochemical changes
  - using promising quantitative MR imaging techniques\(^3,4\)

1. Zhang et al. 2008
3. Mosher et al. 2004
4. Li et al. 2007
**BACKGROUND**

Knee OA: MR Imaging Biomarkers

**PURPOSE**

- Balancing external
- Collagen integrity = important for
- Weakness progression
- Young healthy
- Patterns
- Imbalance
- T1 - T1 Relaxation Times

**Knee OA: Risk Factors**

- Articular & Meniscal
- Cartilage T1ρ/T2
- Relaxation Times

Association of MR relaxation times with risk factors in young healthy adults

2. Mosher et al. Semin Musculoskel Rad 2004
4. Li et al. Magn Res Imag 2010
5. Kumar et al. 2011
6. Pan et al. 2011
7. Pan et al. 2011
8. Barrios et al. 2010
9. Miyazaki et al. 2002
10. Koo et al. 2010
Subjects

<table>
<thead>
<tr>
<th>n</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>25 (42 knees)</td>
</tr>
<tr>
<td>BMI</td>
<td>25 (42 knees)</td>
</tr>
</tbody>
</table>

- Physically active
- No knee pain
- No h/o knee trauma, surgery

Mechanical Axis (Alignment)

- Standard weight-bearing long limb radiographs
- Internal angle
  - Center of femur head to center of the knee
  - Center of the knee to the center of talar dome
  - **Smaller angle = greater varus**
  - Available from 27 knees
**Quantitative MRI of Cartilage**

- 3 Tesla MRI with 8 channel T/R knee coil

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Parameters</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sagittal 3D fat-saturated high-resolution SPGR</td>
<td>TR/TE = 15/6.7 ms, FA = 18, FOV = 14 cm, matrix = 512 x 512, ST = 1 mm, BW = 31.25 kHz, NEX = 1</td>
<td>Articular Cartilage Thickness</td>
</tr>
<tr>
<td>$T_{1p}/T_2$ quantification</td>
<td>TSL = 0/10/40/80 ms, prep TE = 0/13.7/27.3/54.7 ms, FOV = 14 cm, matrix = 256 x 128, time of recovery = 1.2 sec, ST = 4 mm</td>
<td>$T_{1p}/T_2$ Relaxation times</td>
</tr>
</tbody>
</table>

$S(TSL) \propto \exp(-TSL/\frac{T_{1p}}{T_2})$

**METHODS**

**Quantitative MRI of Thigh Muscle**

- 3 Tesla MRI with 8 channel T/R knee coil

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Parameters</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midthigh Axial T1-W</td>
<td>TE/TR = 6.41/800, slice thickness = 10 mm, matrix = 384 x 1932, ETL = 2, bandwidth = 150 kHz, NEX = 4</td>
<td>Quadriceps and Hamstrings Cross-sectional Area</td>
</tr>
</tbody>
</table>

- Mid-thigh
- Mean of 4 slices

- Quads M:L ratio
- Overall M:L Ratio
METHODS

Walking Patterns

Peak Flexion Moment
Sagittal knee Moment
(Also: Sagittal Rate of Loading)

Peak KAM
Frontal knee Moment
(Also: KAM Impulse, Frontal ROL)

% Stance Phase

METHODS

Statistics

- Mechanical Axis and Cartilage Parameters
  - Pearson’s correlations

- Muscle morphology, Loading and Cartilage Parameters
  - Generalized Estimating Equations (GEE)
  - Accounting for age, BMI, gender, walking speed and data from both knees
RESULTS & DISCUSSION

Alignment and qMRI

<table>
<thead>
<tr>
<th>Correlation</th>
<th>Lateral Cartilage</th>
<th>Medio-lateral Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T_{1p}$</td>
<td>$T_2$</td>
</tr>
<tr>
<td>r</td>
<td>0.357</td>
<td>0.489</td>
</tr>
<tr>
<td>p</td>
<td>0.067</td>
<td>0.010</td>
</tr>
</tbody>
</table>

*↑ Varus related to ↑ medio-lateral ratio of cartilage $T_2$
  - collagen in medial compartment more disorganized compared to lateral
  - Changes evident as early as 3rd decade

RESULTS & DISCUSSION

Loading & $T_{1p}/T_2$ Relaxation Times

**Cartilage**

<table>
<thead>
<tr>
<th>MR variable</th>
<th>Predictors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT, Global T1p</td>
<td>Peak Sag Moment</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FT, PF, Global T2</td>
<td>Peak Sag Moment</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Meniscus**

<table>
<thead>
<tr>
<th>MR variable</th>
<th>Predictors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial, M: L T1p</td>
<td>Peak KAM</td>
<td>0.001 – 0.031</td>
</tr>
<tr>
<td>M: L T2</td>
<td>Frontal ROL</td>
<td>0.002</td>
</tr>
</tbody>
</table>

↑ loading associated with ↓ thickness and ↓ PG and ↑ collagen density of cartilage

↑ loading associated with relatively ↓ PG and ↓ collagen density in medial compared to lateral meniscus
**RESULTS & DISCUSSION**

**Muscle CSA & T1ρ/T2 Parameters**

<table>
<thead>
<tr>
<th>Cartilage</th>
<th>MR variable</th>
<th>Predictors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TF, PF, Global T2</td>
<td>Quads Hams Ratio</td>
<td>0.007-0.045</td>
</tr>
<tr>
<td></td>
<td>Medial T1ρ, T2</td>
<td>Quads M:L Ratio</td>
<td>0.052-0.057</td>
</tr>
</tbody>
</table>

**Meniscus**

<table>
<thead>
<tr>
<th>MR variable</th>
<th>Predictors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial T1ρ</td>
<td>Quads M:L Ratio</td>
<td>0.002</td>
</tr>
<tr>
<td>M:L Ratio T1ρ</td>
<td>Quads M:L Ratio</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**RESULTS & DISCUSSION**

**Muscle CSA & Walking Patterns**

<table>
<thead>
<tr>
<th>Gait variable</th>
<th>Predictors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak KAM</td>
<td>Q: H ratio, Quads M:L Ratio</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>KAM impulse</td>
<td>Quads M:L Ratio</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Frontal ROL</td>
<td>Q: H Ratio</td>
<td>0.002</td>
</tr>
</tbody>
</table>

↑ imbalance related to ↑KAM, KAM impulse and frontal ROL
- ↑ imbalance related to walking patterns that predispose to knee OA
- ? mechanism by which muscle imbalance impacts cartilage health
CONCLUSIONS

• T1ρ and T2 relaxation times are sensitive to mechanical loading
  – could be used in interventional and clinical studies.
• Malalignment and KAM are associated with medio-lateral imbalances of cartilage composition
  – as early as 3rd decade, which could progress to OA.
• Impact of loading more pronounced on the meniscus than articular cartilage
  – ? Meniscus degenerates first
• Muscle imbalance is related to walking patterns known to predispose to OA as well as higher MR relaxation times
  – importance of targeted muscle balance training in addition to strengthening

FUTURE STUDIES

• From this dataset
  – Association of spatial distribution of T1ρ and T2 relaxation times and texture parameters to OA risk factors
  – Focus on weight-bearing cartilage regions

• In people with knee OA and matched controls
  – Cross-sectional analysis of risk factors with cartilage morphology, T1ρ and T2 relaxation times
  – Longitudinal analysis of relationship of walking patterns, muscle activation patterns, strength changes with cartilage degradation

• General questions
  – Meniscus relaxation times and biochemical correlation
Thank You

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- NIH- NIAMS R01AR046905-11A1

http://www.radiology.ucsf.edu/research/centers/translation-study-osteoarthritis