EARLY DETECTION OF CHANGES IN ARTICULAR CARTILAGE MORPHOLOGY: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Introduction

• **Problem:** Cartilage changes are complex and non-uniform in nature. Segmentation is difficult and standard average measurements of cartilage thickness are no sensitive enough to capture the complex behavior.

  Watson PJ, Carpenter TA, Hall LD, Tyler JA. *Cartilage swelling and loss in a spontaneous model of osteoarthritis visualized by magnetic resonance imaging.* 1996.
  Buck, R, *et. al.* *Osteoarthritis may not be a one-way-road of cartilage loss e comparison of spatial patterns of cartilage change between osteoarthritic and healthy knees,* O&C, 2010
Introduction

**Solution:** Advanced image segmentation with advanced quantification.

**Atlas Based Segmentation**

Voxel to Voxel mapping and quantification

Use more than average statistics

- Atlas-Based Segmentation

- Cartilage Segmentation & Registration
  - Pelletier; JP, Martel-Pelletier; J, Raynauld J, *et. al.* “Evaluating disease progression using magnetic resonance imaging”, US. Patents 2003, 2005
Atlas-Based Segmentation

- Generate Atlas
- Register and Segment Each MRI to the Atlas (ITK registration modules)
- Postprocess the segmentation to match underlying MRI information.
- Visually score the quality of the segmentation.
- Use the registration data to map each segmentation to the atlas space
- Subtract each mapped segmentation to compute change in cartilage thickness
Objective

• To evaluate the sensitivity of an atlas based standardized measurement method to detect changes in articular cartilage thickness in subjects with potential OA symptoms but no baseline radiological evidence of OA.
Material & Methods

• OAI progression cohort
  – Participants were chosen, if they had a body mass index (BMI) >25 kg/m², a mJSN OARSI grade 1–3 in one knee, no or less mJSN in the contra-lateral knee, and no (or less than medial) lateral JSN in both knees. In addition, the participants displayed chronic pain in both knees (most days of a month within the last 12 months), or had occasional pain in one knee (pain in past 12 months but not most days of a month) in combination with a definite osteophyte.
  – OAI DESS Images from Data Release 0.C.2, 1.C.2, 3.C.1
    • Only subjects that had complete observations (n=138)
  – Segmented using an Atlas Based Segmentation Algorithm
    • Subjects with large segmentations errors at either the tibia or femur bone segmentations at any time point were removed from the analysis (n=9)
    • 129 analyzed subjects
  – Subjects with Central Assessment KL scores lower than 2 were selected for this analysis (n=23)
Patient specific thickness map

Thickness map in the atlas-space
Change Measurement: Difference maps
Quantification

• Once the change at each cartilage thickness between baseline and the follow-up, the following measures are done:
  – Mean
  – Standard Deviation
  – Median
  – Skewness
  – Kurtosis
  – Percentiles: 5%, 25%, 75%, 95%
Cross-Validation on low KL (KL<2)

CHM Reference

VS to CHM

\[ y = 1.1407x + 0.3087 \]

\[ R^2 = 0.6722 \]

ATLAS to CHM

\[ y = 0.9024x - 3.0733 \]

\[ R^2 = 0.7282 \]
Results

Standardized Thickness Maps

Baseline

12 Month

24 Month
Average Change Results

Average Change of the Entire Tibia and Femur Cartilage

- $d = -0.01 \text{mm}$
  - $p = 0.53$
  - $SRM = -0.19$

- $d = -0.02 \text{mm}$
  - $p = 0.002$
  - $SRM = -0.41$

- $d = -0.00 \text{mm}$
  - $p = 0.66$
  - $SRM = -0.02$
Standard Deviation of Change

Standard Deviation of the Entire Tibia and Femur Cartilage

- \( d = 0.02 \text{mm} \)
- \( p = 0.085 \)
- \( \text{SRM} = 0.45 \)

- \( d = 0.02 \text{mm} \)
- \( p = 0.02 \)
- \( \text{SRM} = 0.41 \)

- \( d = 0.02 \text{mm} \)
- \( p = 0.002 \)
- \( \text{SRM} = 0.46 \)
Lower 5% Change

5 Percentile Change by KL by Visit at the Tibia Femoral Cartilage

- 12M.1: d=-0.07mm, p=0.058, SRM=-0.48
- 24M.1: d=-0.07mm, p=0.001, SRM=-0.54
- 12M.2: d=-0.07mm, p=0.058, SRM=-0.48
- 24M.2: d=-0.04mm, p=0.02, SRM=-0.32
- 12M.3: d=-0.07mm, p=0.058, SRM=-0.48
- 24M.3: d=-0.07mm, p=0.058, SRM=-0.48

Time:KL GROUP
### Some Statistics: (KL<2)
#### 12 month and 24 month changes

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Stat</th>
<th>Entire Femur</th>
<th>Tibia + Femur</th>
<th>mWB</th>
<th>WB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average</strong></td>
<td>Annual Change</td>
<td>-0.01</td>
<td>-0.02</td>
<td>0.01</td>
<td>-0.02</td>
</tr>
<tr>
<td></td>
<td>Standard Dev.</td>
<td>0.06</td>
<td>0.10</td>
<td>0.15</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>SRM</td>
<td>-0.17</td>
<td>-0.21</td>
<td>0.08</td>
<td>-0.10</td>
</tr>
<tr>
<td></td>
<td>proportion</td>
<td>57%</td>
<td>52%</td>
<td>52%</td>
<td>61%</td>
</tr>
<tr>
<td><strong>5%</strong></td>
<td>Annual Change</td>
<td><strong>-0.09</strong></td>
<td>-0.12</td>
<td>-0.08</td>
<td><strong>-0.29</strong></td>
</tr>
<tr>
<td></td>
<td>Standard Dev.</td>
<td>0.11</td>
<td>0.28</td>
<td>0.36</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td>SRM</td>
<td><strong>-0.82</strong></td>
<td>-0.43</td>
<td>-0.22</td>
<td>-0.58</td>
</tr>
<tr>
<td></td>
<td>proportion</td>
<td>65%</td>
<td>65%</td>
<td>65%</td>
<td><strong>70%</strong></td>
</tr>
<tr>
<td><strong>Standard Deviation</strong></td>
<td>Annual Change</td>
<td><strong>0.05</strong></td>
<td>0.05</td>
<td>0.06</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Standard Dev.</td>
<td>0.05</td>
<td>0.11</td>
<td>0.14</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>SRM</td>
<td><strong>0.90</strong></td>
<td>0.48</td>
<td>0.43</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>proportion</td>
<td>65%</td>
<td>52%</td>
<td>61%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Annual Change were computed using a generalized least squares models with time and JSN as covariates in a covariance structure grouped by subject and time as a continuous covariate. Residuals adjusted to reflect segmentation accuracy.
Limitations

• Atlas dependent results:
  – Male Atlas vs. Female Atlas?
    • We selected a female subject from the progression cohort to create the atlas.
    – Random noise: It similar to having different observers
• Automated segmentations has lower cartilage segmentation reliability on advanced OA stages KL>2
• We still need to estimate scan-rescan performance and comparisons to expert segmentations
• Small number of subjects (n=23)
  – Discrepancies in their KL scores.
    • Site score >2, central readings < 2?
• Only three time points
  – Are the trends constant?
Conclusions

• Although is not superior to human observer, fully automated Atlas-based segmentation is a viable option to segment all knees from the OAI cohort with KL<=2.

• Atlas referenced analysis enhance the ability to study differences in populations.

• This small pilot study suggest that automated segmentations coupled with statistical analysis of difference map can be useful in the detection of cartilage changes subjects with early radiological OA and frequent pain symptoms.
Acknowledgements

- Santiago Gonzalez
- The OAI for all the imaging and clinical data
Thanks
Validation

• Accuracy
  – Visual Inspection and compare OARSI 2009 and dependent on the OA stage.
  • In this population between 67% (Trochlea) to 83% (WB) in paired accuracy (No errors at both baseline and follow-up).

Reproducibility
  ▪ Scan-Rescan Analysis
    ▪ Similar performance to human observer
  ▪ Comparisons to Felix Eckstein Segmentations and VirtualScopics Segmentations
  ▪ Association to KL scores and JSN see poster section
  ▪ Comparisons of change Edited vs. Automated on 17 subjects r>=0.5
  ▪ Bone Changes see poster section