Acute Anterior Cruciate Ligament Injury Causes Cartilage Thickness Increase Over Two and Five Years

W. Wirth¹, F. Eckstein¹, L.S. Lohmander², M. Hudelmaier¹, R.Frobell²

¹Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany; ²Orthopedics, Clinical Sciences Lund, Lund University, Lund, Sweden
Background/Motivation

- **KANON study** (Frobell et al., NEJM 2010 & Abstract #1):
  - Randomized, controlled trial
  - 121 young, active adults with rotational trauma to previously uninjured knee
  - Primary objective: Comparison of the clinical outcome between surgical and non-surgical treatments of acute ACL disruptions

- Association between ACL injury and onset of OA
Quantitative analysis of cartilages from KANON study funded as part of NanoDiaRa project (EU 7\textsuperscript{th} framework programme for research)

“Development of Novel Nanotechnology Based Diagnostic Systems for Rheumatoid Arthritis and Osteoarthritis” ([http://nanodiara.eu](http://nanodiara.eu))

- Establish a model of human knee OA to test imaging, molecular and other markers for predicting OA onset and progression
Objectives

To determine:

- Rate of change in femorotibial cartilage thickness over 2 and over 5 years after ACL injury
- Percentage of knees showing a significant increase or decrease in cartilage thickness over 2 and 5 years
Subject Characteristics

- Random treatment assignment of 121 subjects:
  - Structured rehabilitation and early surgical ACL reconstruction
  - Structured rehabilitation with optional delayed ACL reconstruction

- Demographics at baseline (BL):
  - 24% female participants
  - Age: 26 ± 5 years
  - BMI: 24.2 ± 3.0 kg/m²

- 107 of 121 subjects with complete MRI data
MR Imaging

- Sagittal FLASH (0.29mm IPR, 1.5mm slice spacing)
- 1.5T Philips Intera
- Image acquisition at visits:
  - Recruitment (BL = baseline)
  - Year 2 (Y2) follow-up
  - Year 5 (Y5) follow-up
Cartilage segmentation & computation

- Manual segmentation of cartilages:
  - Medial and lateral tibia (MT/LT)
  - Central 75% of the medial and lateral femoral condyle (cMF/cLF)

- Computation of cartilage thickness in cartilage plates and subregions

\[ FTJ = MFTC + LFTC \]
Ordered values

- Sorting of changes observed in the 16 subregions within each knee in ascending order (*Buck et al. Arthritis Rheum. 2009*)

Subject #1: OV 1 ← cLT, OV 2 ← ccMF, OV 16 ← aMT

Subject #2: OV 16 ← ccLF, OV 2 ← aLT, OV 1 ← cLT, OV 1 ← eMT

- Quantitative analysis of ordered values 1-16 (OV 1 – OV 16)
Pogression definition

- Changes larger than the changes observed in healthy knees likely to be „real“ progression
- Distribution of one-year changes observed in OAI healthy reference cohort (n=112)
- Mean change ± 2 SD of change

<table>
<thead>
<tr>
<th></th>
<th>Increase</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTJ</td>
<td>289 µm</td>
<td>-256 µm</td>
</tr>
<tr>
<td>MFTC</td>
<td>153 µm</td>
<td>-161 µm</td>
</tr>
<tr>
<td>LFTC</td>
<td>149 µm</td>
<td>-143 µm</td>
</tr>
</tbody>
</table>
- Large variability of changes between BL and Y2 and between BL and Y5

![Graph showing changes in total joint cartilage thickness](attachment:graph.png)
Average change in joint and compartments

- Significant increase over 2 and 5 years in entire FTJ
- Significant increase over 2 and 5 years in MFTC
- Greater increase over 5 than over 2 years

![Graph showing average change in joint and compartments]

- N=107
- Error bars represent 95% CIs
- 
  *: p<0.05; **: p<0.01; ***: p<0.001 (paired t-test)
Change in ordered values

- OV 1 (subregion with largest decrease within each knee) similar for intervals BL→Y2 and BL→Y5
- OV 16 (subregion with largest increase within each knee) greater for BL→Y5 than BL→Y2

***: p<0.001 (Wilcoxon test)

N=107

Error bars represent 95% CIs
Percentage of knees showing progression

- Increase more frequent than decrease in cartilage thickness
- Percentage of knees with decrease similar over 2 and 5 years
- Percentage of knees with increase over 5 higher than over 2 years
- Decrease more frequent in LFTC than MFTC
- Percentage of knees with increase similar for MFTC and LFTC

N=107
Conclusions

- Significant increase in cartilage thickness over 2 and 5 years
- Increase in cartilage thickness greater over 5 than over 2 years

- Percentage of knees with decrease in cartilage thickness similar over 2 and 5 years
- Proportion of knees with significant increase higher over 5 than over 2 years

- Decrease in cartilage thickness observed predominantly in lateral but not the medial femorotibial compartment
- Long-term outcome of
  - Knees with increase?
  - Knees with decrease?
The KANON was funded by: Swedish Research Council, the Medical Faculty of Lund University, Region Skåne, Thelma Zoegas Fund, Stig & Ragna Gorthon Research Foundation, Swedish National Centre for Research in Sports, Crafoord foundation, Tore Nilsson research fund, and Pfizer Global Research.

The image analysis was funded by NanoDiaRA (NMP4-LA-2009-228929)