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

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Background/Motivation

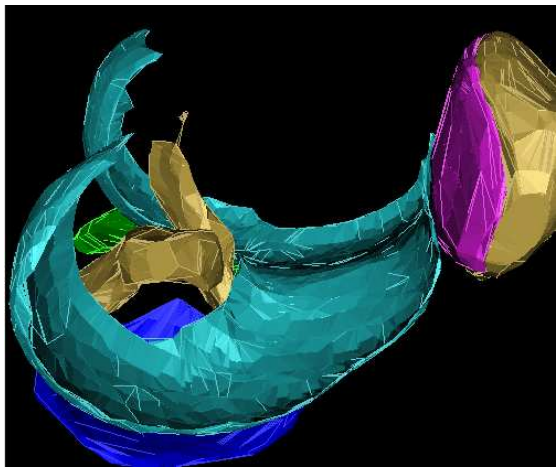
- KANON study (Frobell et al., NEJM 2010 & Abstract #1):
  - » Randomized, controlled trial
  - » 121 young, active adults with rotational trauma to previously uninjured knee
  - » Primary objective: Comparison of the clinical outcome between surgical and non-surgical treatments of acute ACL disruptions

➢ Association between ACL injury and onset of OA

NanoDiaRA

- Quantitative analysis of cartilages from KANON study funded as part of NanoDiaRa project (EU 7th framework programme for research)
- “Development of Novel Nanotechnology Based Diagnostic Systems for Rheumatoid Arthritis and Osteoarthritis” (http://nanodiara.eu)

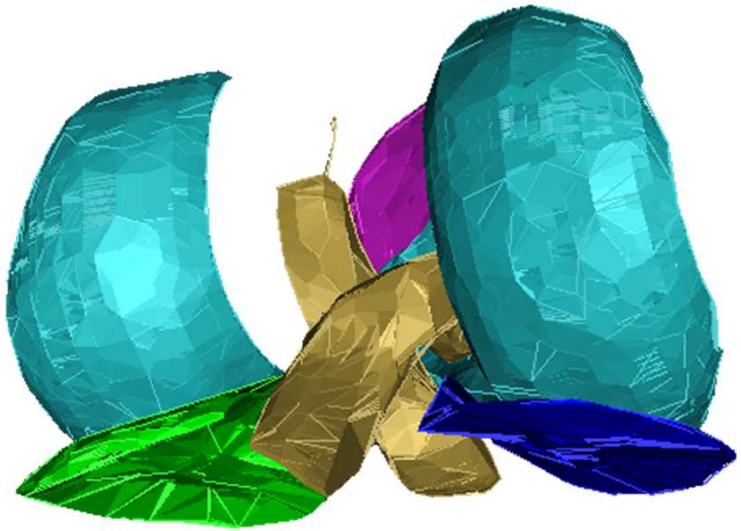
➢ Establish a model of human knee OA to test imaging, molecular and other markers for predicting OA onset and progression



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

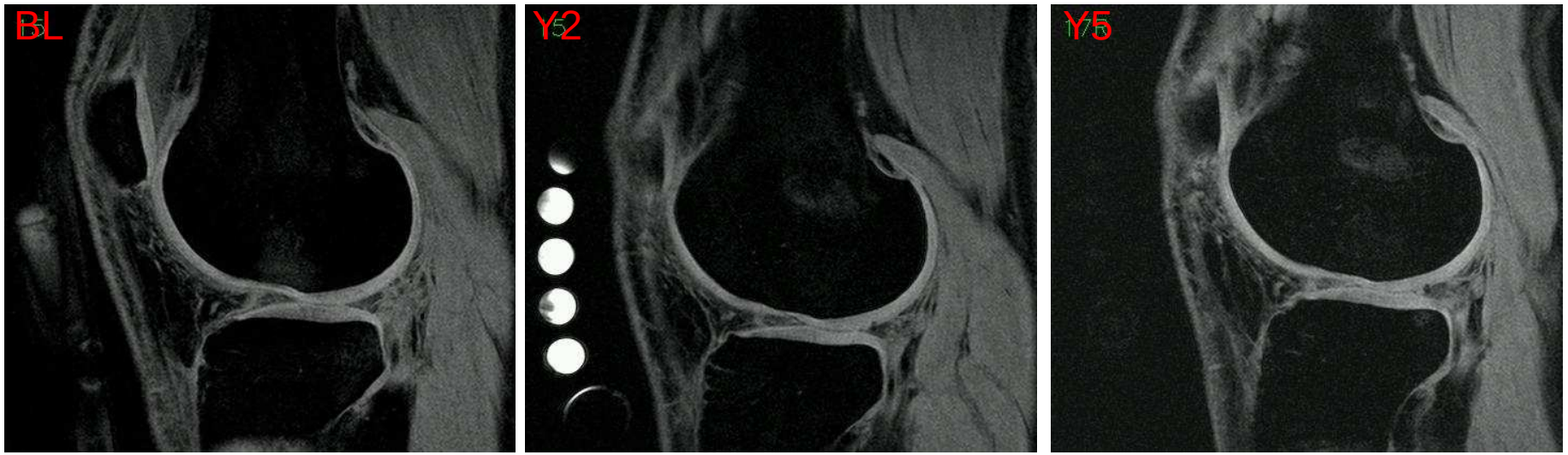
- Random treatment assignment of 121 subjects:
  - » Structured rehabilitation and early surgical ACL reconstruction
  - » Structured rehabilitation with optional delayed ACL reconstruction

- Demographics at baseline (BL):
  - » 24% female participants
  - » Age: 26 ± 5 years
  - » BMI: 24.2 ± 3.0 kg/m^2

- 107 of 121 subjects with complete MRI data

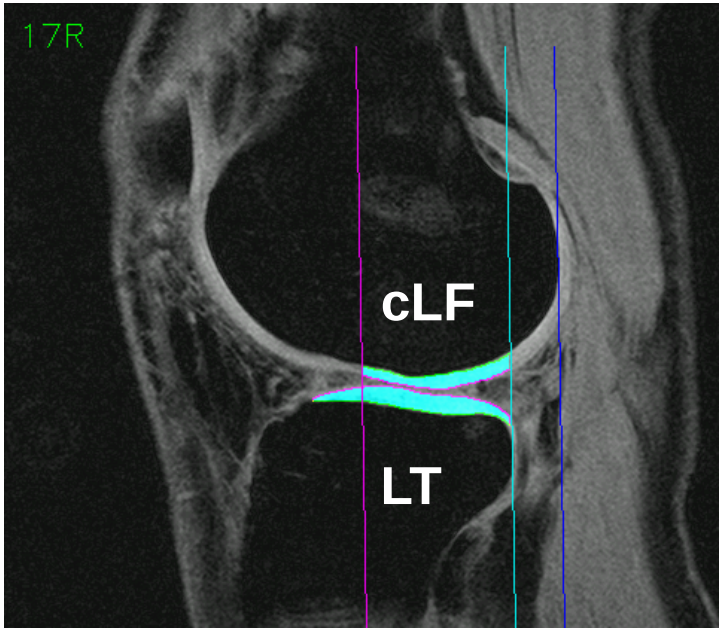
MR Imaging

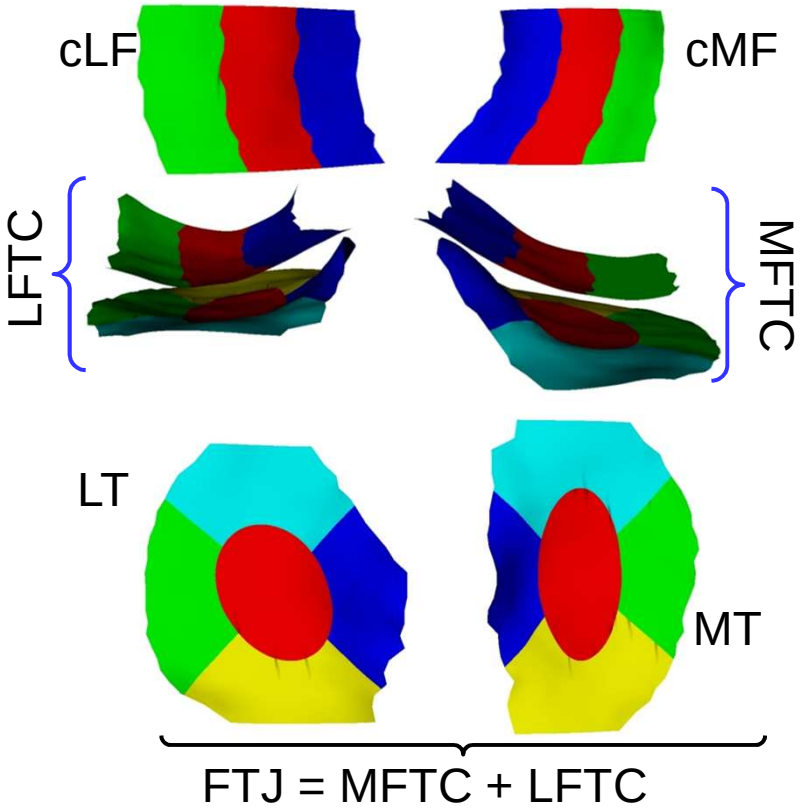
- Sagittal FLASH (0.29mm IPR, 1.5mm slice spacing)
- 1.5T Philips Intera
- Image acquisition at visits:
  - » Recruitment (BL = baseline)
  - » Year 2 (Y2) follow-up
  - » Year 5 (Y5) follow-up



Cartilage segmentation & computation

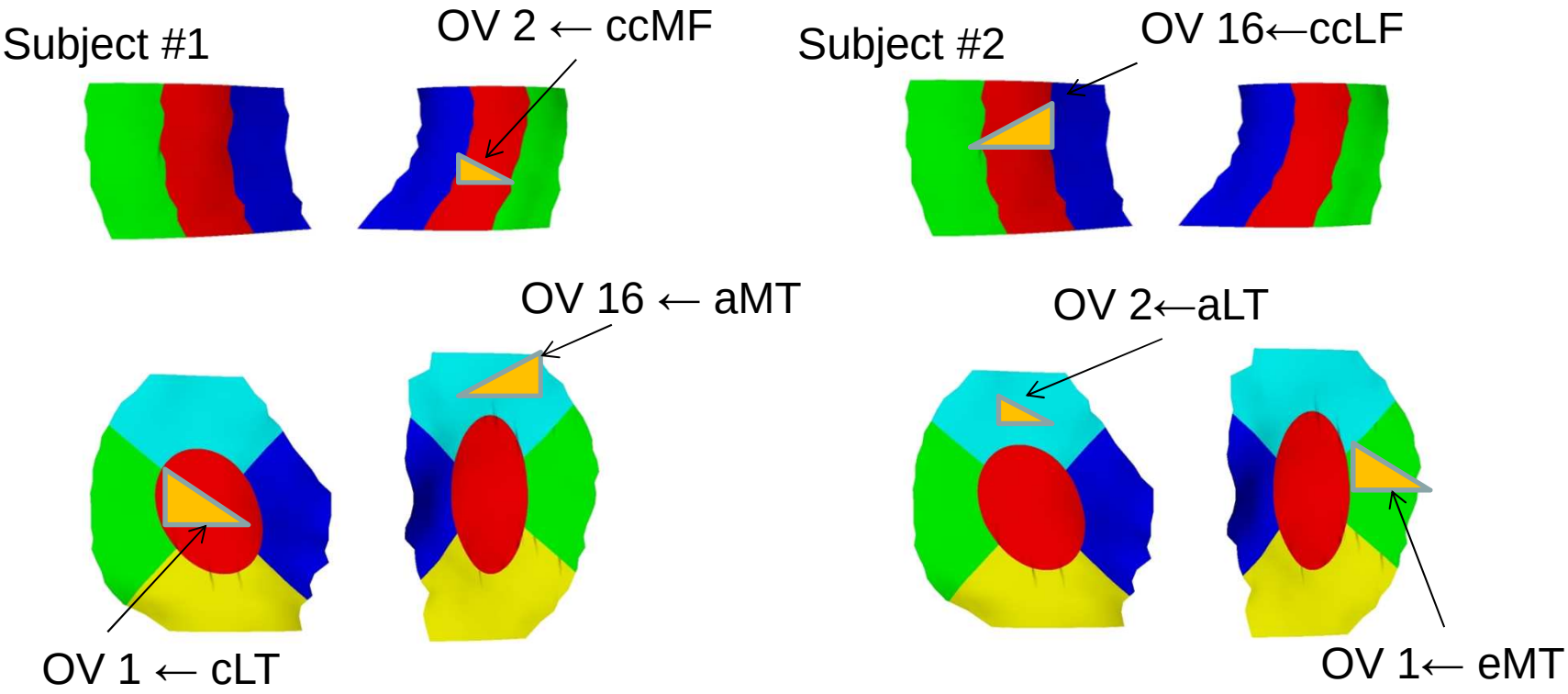
- Manual segmentation of cartilages:
  - » Medial and lateral tibia (MT/LT)
  - » Central 75% of the medial and lateral femoral condyle (cMF/cLF)
- Computation of cartilage thickness in cartilage plates and subregions





Ordered values

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



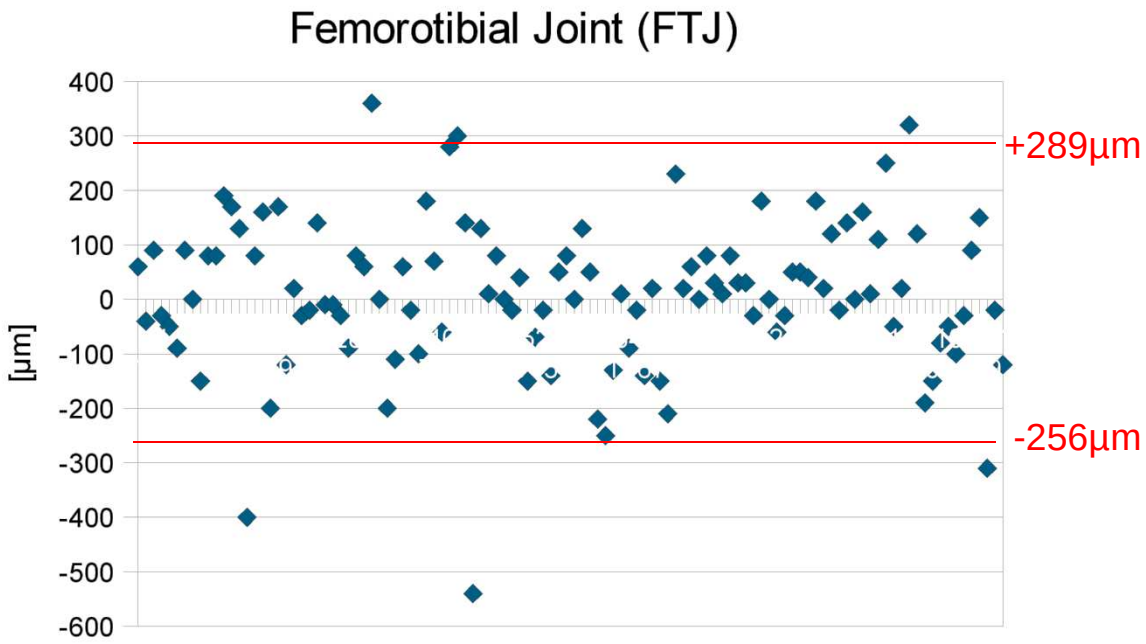
- Quantitative analysis of ordered values 1-16 (OV 1 – OV 16)

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

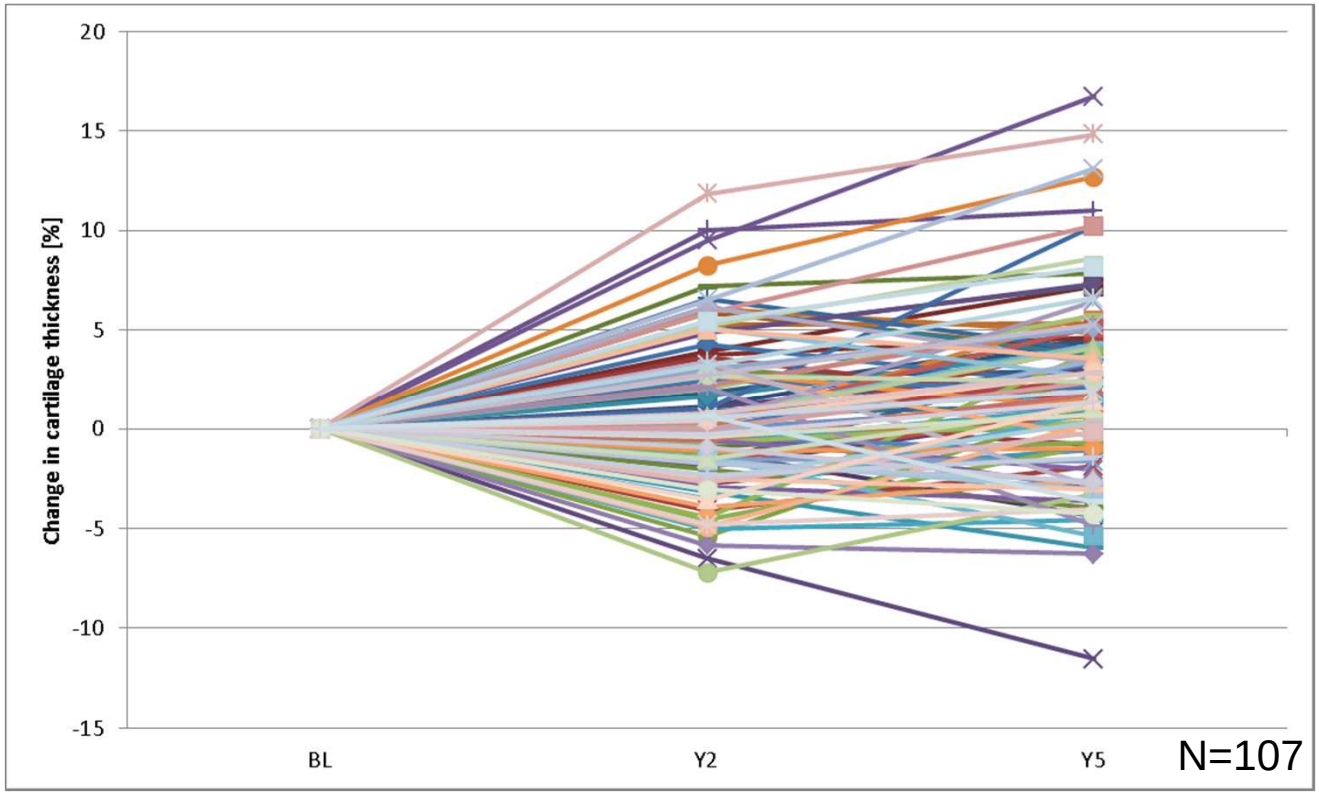
- Thresholds:

	Increase	Decrease
FTJ	289µm	-256µm
MFTC	153µm	-161µm
LFTC	149µm	-143µm



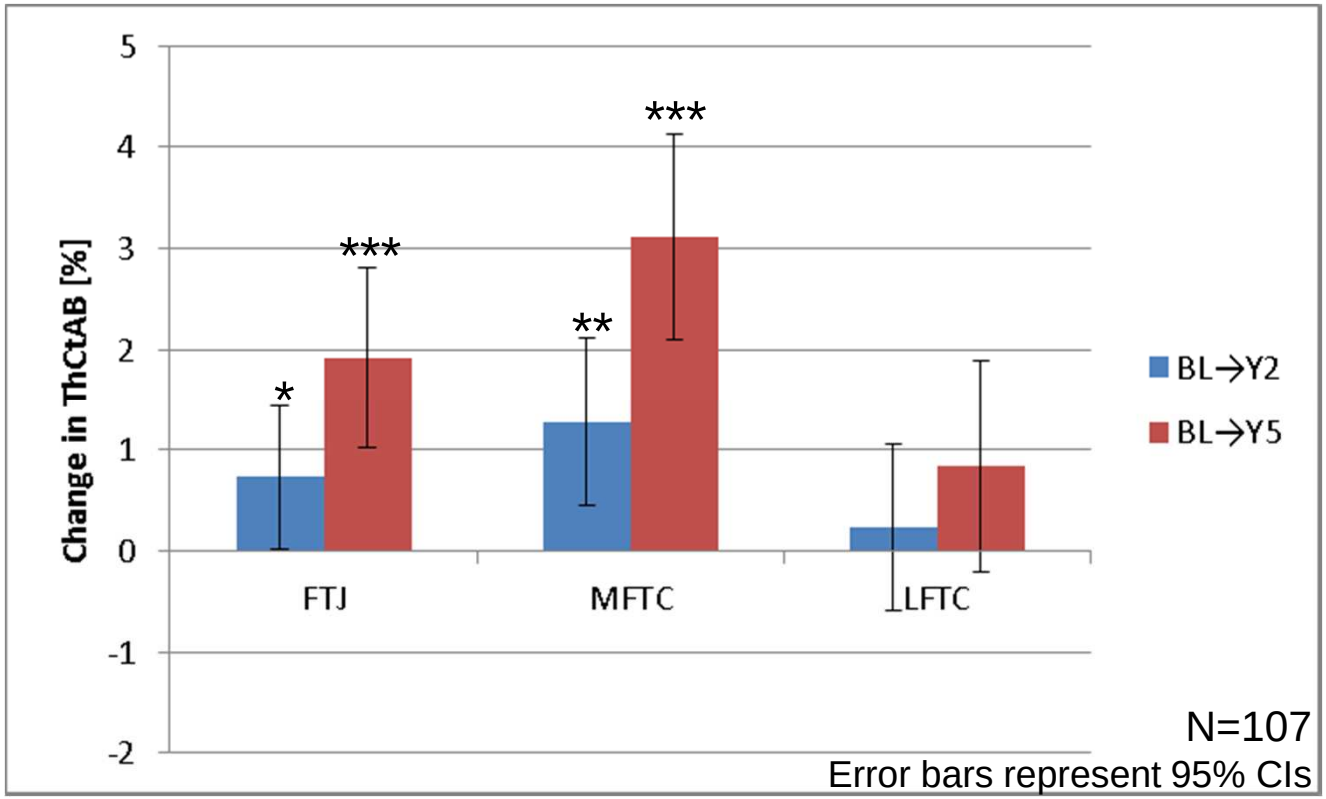
Individual changes in total joint cartilage thickness

- Large variability of changes between BL and Y2 and between BL and Y5



Average change in joint and compartments

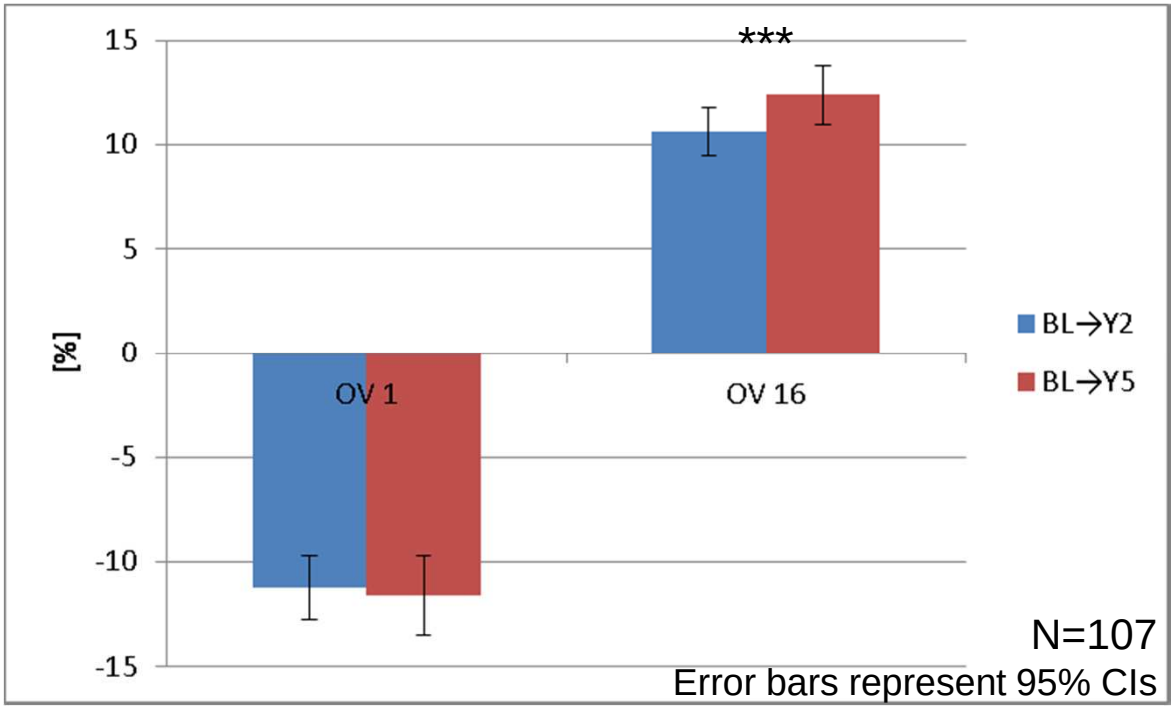
- Significant increase over 2 and 5 years in entire FTJ
- Significant increase over 2 and 5 years in MFTC
- Greater increase over 5 than over 2 years



*: p<0.05; **: p<0.01; ***: p<0.001 (paired t-test)

Change in ordered values

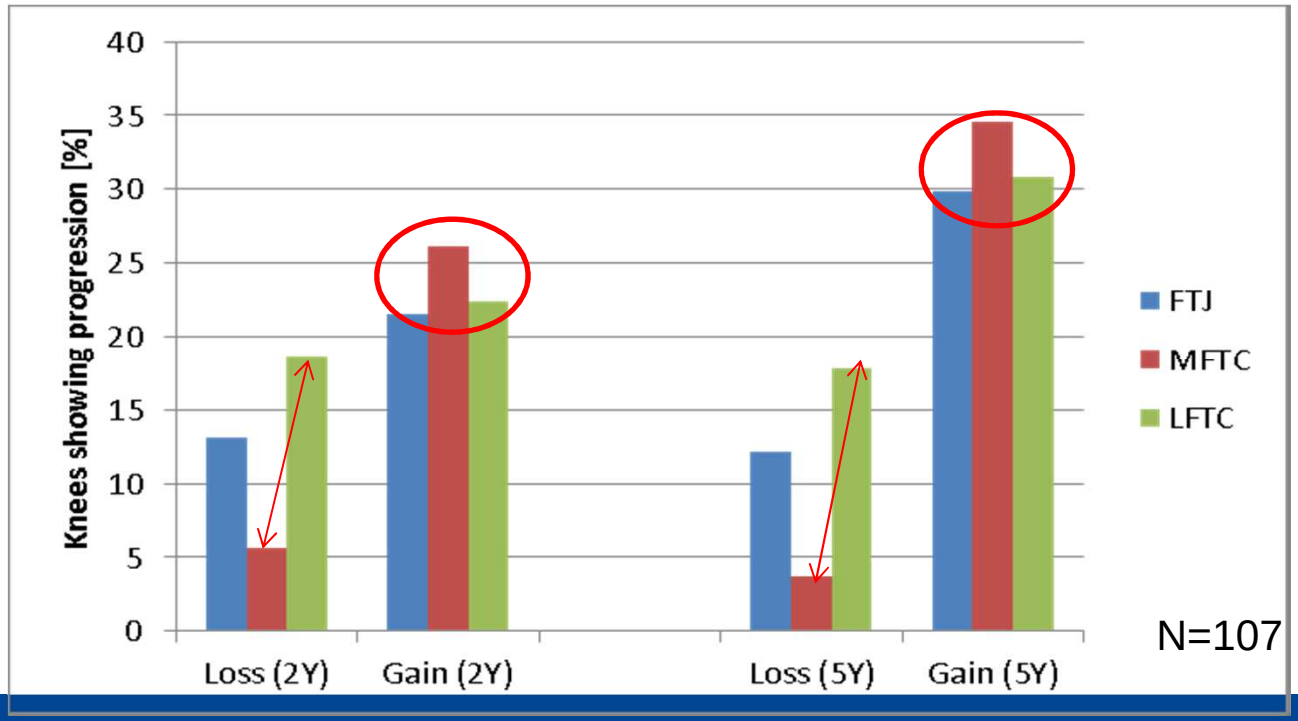
- OV 1 (subregion with largest **de**crease within each knee) similar for intervals BL→Y2 and BL→Y5
- OV 16 (subregion with largest **in**crease within each knee) greater for BL→Y5 than BL→Y2



***: p<0.001 (Wilcoxon test)

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 increse similar for MFTC and LFTC

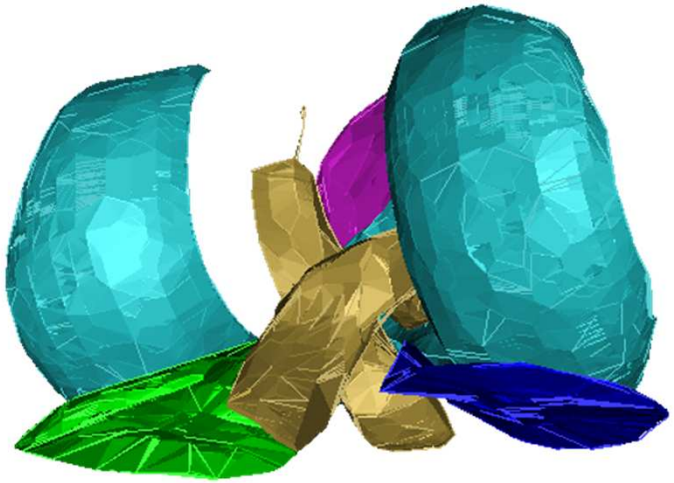


Conclusions

- 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 thickeness 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?



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