Does Change in Femorotibial Cartilage Thickness Differ Between Acutely Anterior-Cruciate Ligament Injured Knees Treated with and without Reconstructive Surgery

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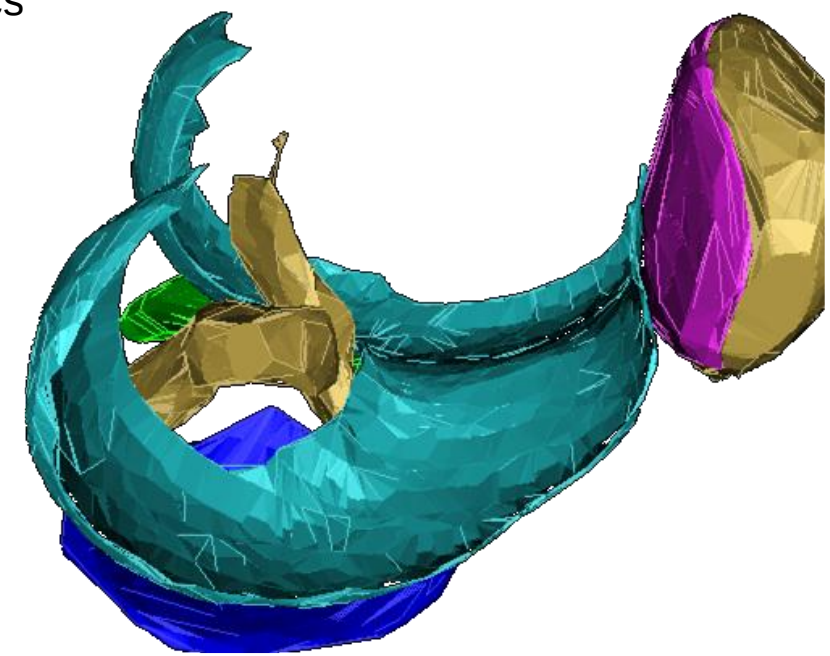
Disclosures

- Wolfgang Wirth: Freelancer for Chondrometrics GmbH, Ainring, Germany; Share-holder of Chondrometrics GmbH, Ainring, Germany; Received consulting fees from Merck Serono S.A.
- Martin Hudelmaier: Part-time employment with Chondrometrics GmbH
- Felix Eckstein: CEO and share-holder of Chondrometrics GmbH, Ainring, Germany; Received consulting fees from Merck Serono S.A., Novartis, Abbvie, and Sanofi Aventis
- Stefan Lohmander & Richard Frobell: No disclosures

Anterior cruciate ligament (ACL) tears

- Common injury in young adults (soccer, skiing)
- ACL injuries associated with elevated risk of developing knee OA
  - » Molecular & cellular changes
  - » Chronic alterations in joint biomechanics
- Model for early OA
  - » Post-traumatic OA
  - » Defined baseline
  - » Healthy knees
  - » Monitor disease onset
  - » Identify biomarkers



The KANON trial

- Comparison of surgical vs. non-surgical treatment in young, active adults with rotational trauma to previously uninjured knee

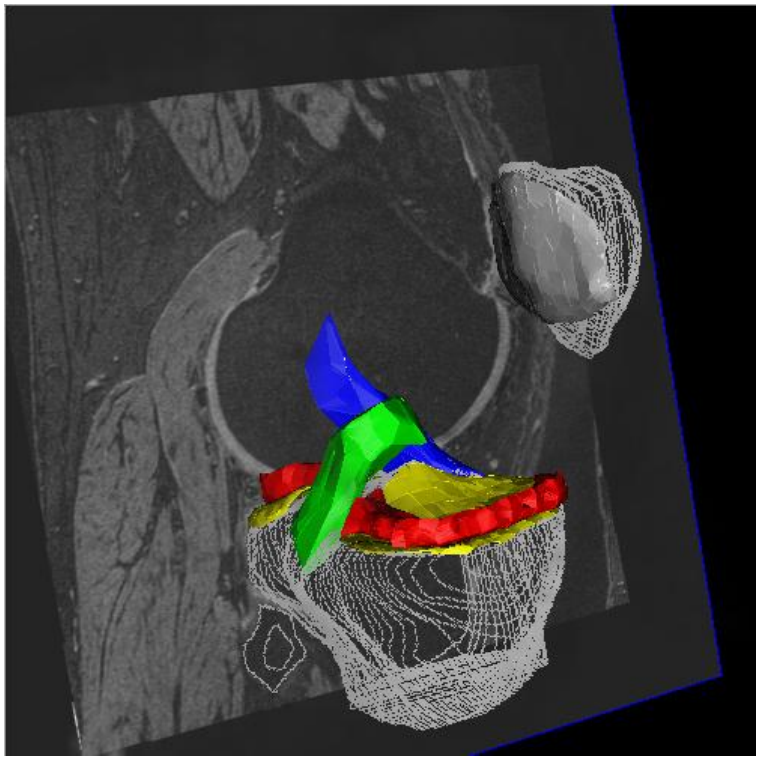
- Randomization to either:
  - » early ACL reconstruction and structured rehabilitation or
  - » structured rehabilitation with optional delayed ACL reconstruction

- Primary objective: Patient reported outcomes (Knee injury and Osteoarthritis Outcome Score, KOOS)

- No significant differences in patient reported outcomes after 2 (Frobell et al. N Engl. J. Med. 2010) and 5 years (Frobell et al. BMJ 2013).

Objectives

- Does the surgical reconstruction of an acute ACL tear influence the change in femorotibial cartilage thickness over the first five years after the injury?



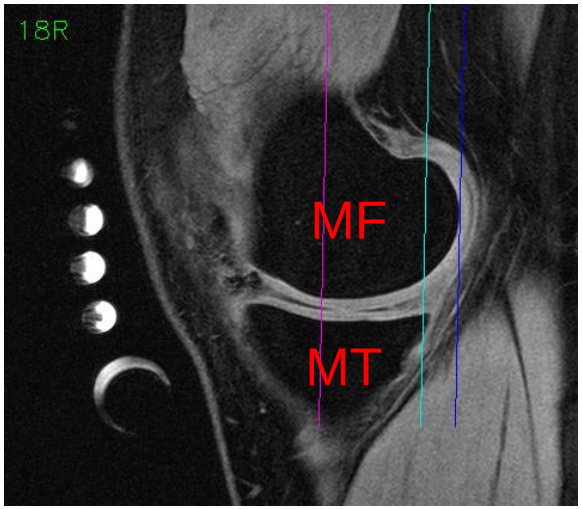
KANON Baseline Characteristics

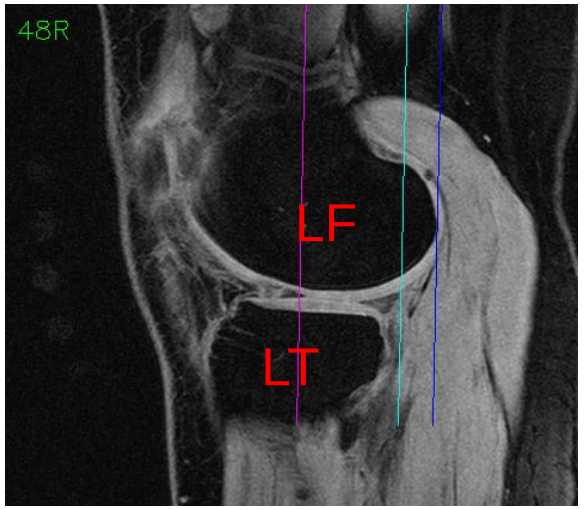
- N=121 young, active adults:
  - » 62 randomized to early ACL reconstruction surgery (3 lost to follow-up)
  - » 59 randomized to structured rehabilitation only with optional delayed ACL reconstruction surgery

	Early ACR reconstruction	Delayed ACL reconstruction	Structured rehabilitation only
N	59	30	29
Age	26.6±5.1 y	25.2±4.5 y	26.4±4.9
Female sex	12 (20%)	11 (37%)	9 (31%)
BMI	24.5±3.2 kg/m^2	23.3±2.0 kg/m^2	24.3±3.1 kg/m^2

MRI

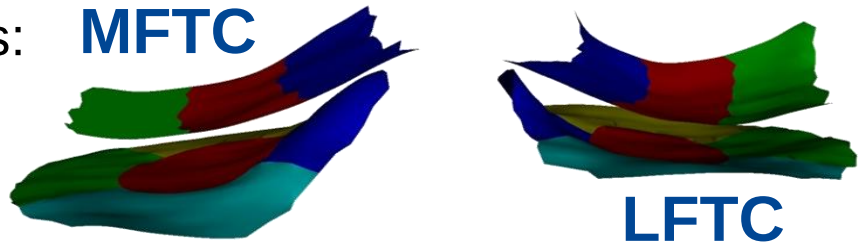
- Sagittal FLASH (1.5T, 0.29mm in-plane, 1.5mm slice spacing)
- Image acquisition at visits:
  - » Recruitment (BL = baseline, n=117)
  - » Year 2 (Y2) follow-up (n=112)
  - » Year 5 (Y5) follow-up (n=112)



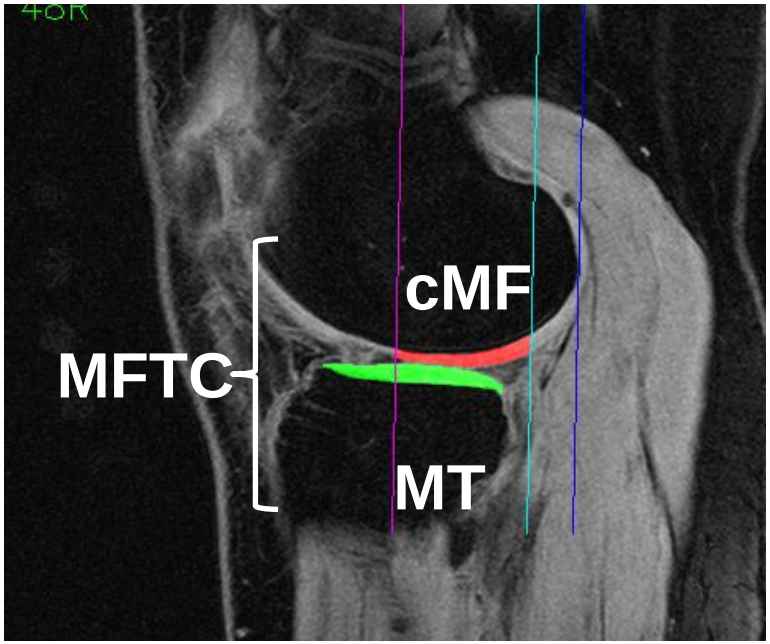


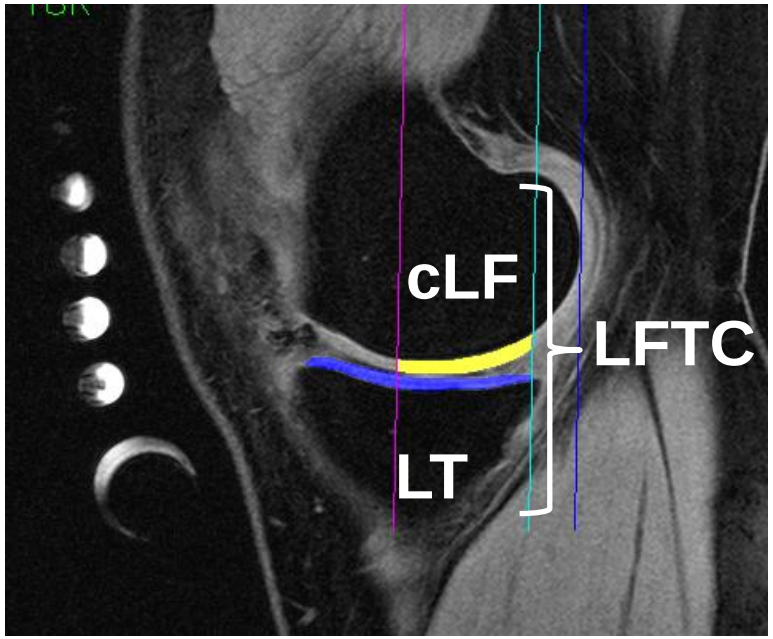
Quantitative cartilage analysis

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



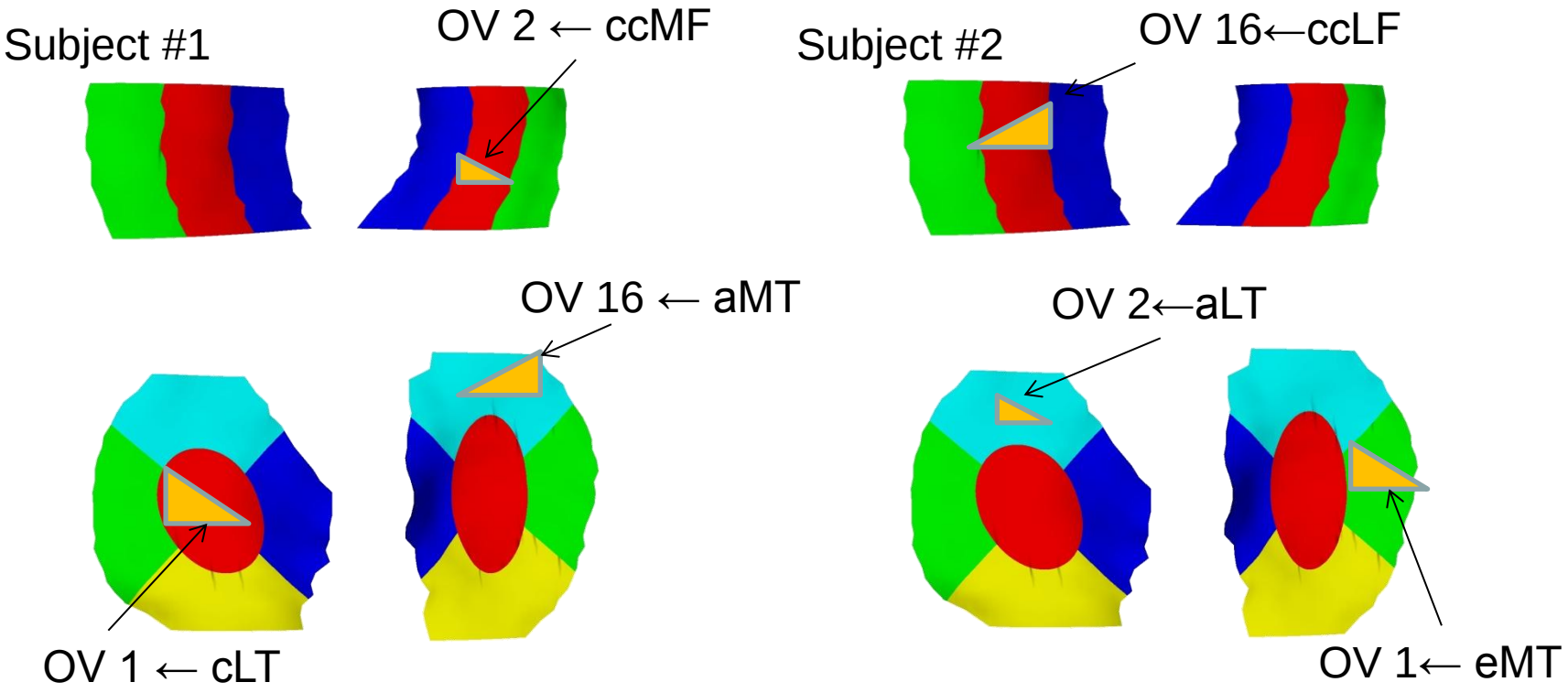
- Computation of cartilage thickness in cartilage plates and subregions
- **FTJ = MFTC + LFTC**





Ordered values of subregional changes

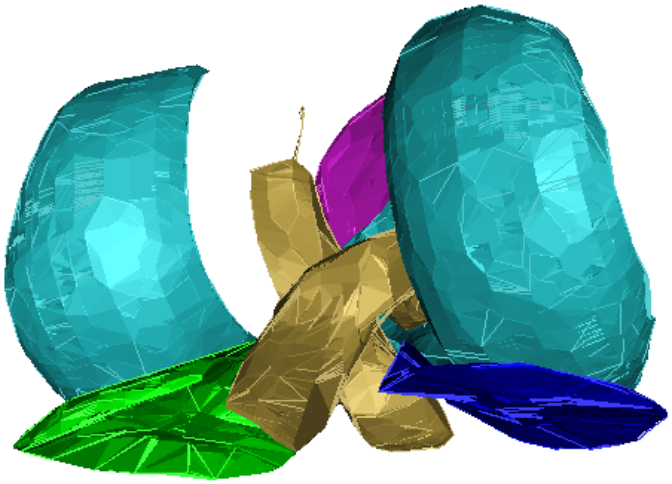
- Sorting of changes observed in the 16 subregions within each knee in ascending order (Buck et al. Arthritis Rheum. 2009)



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

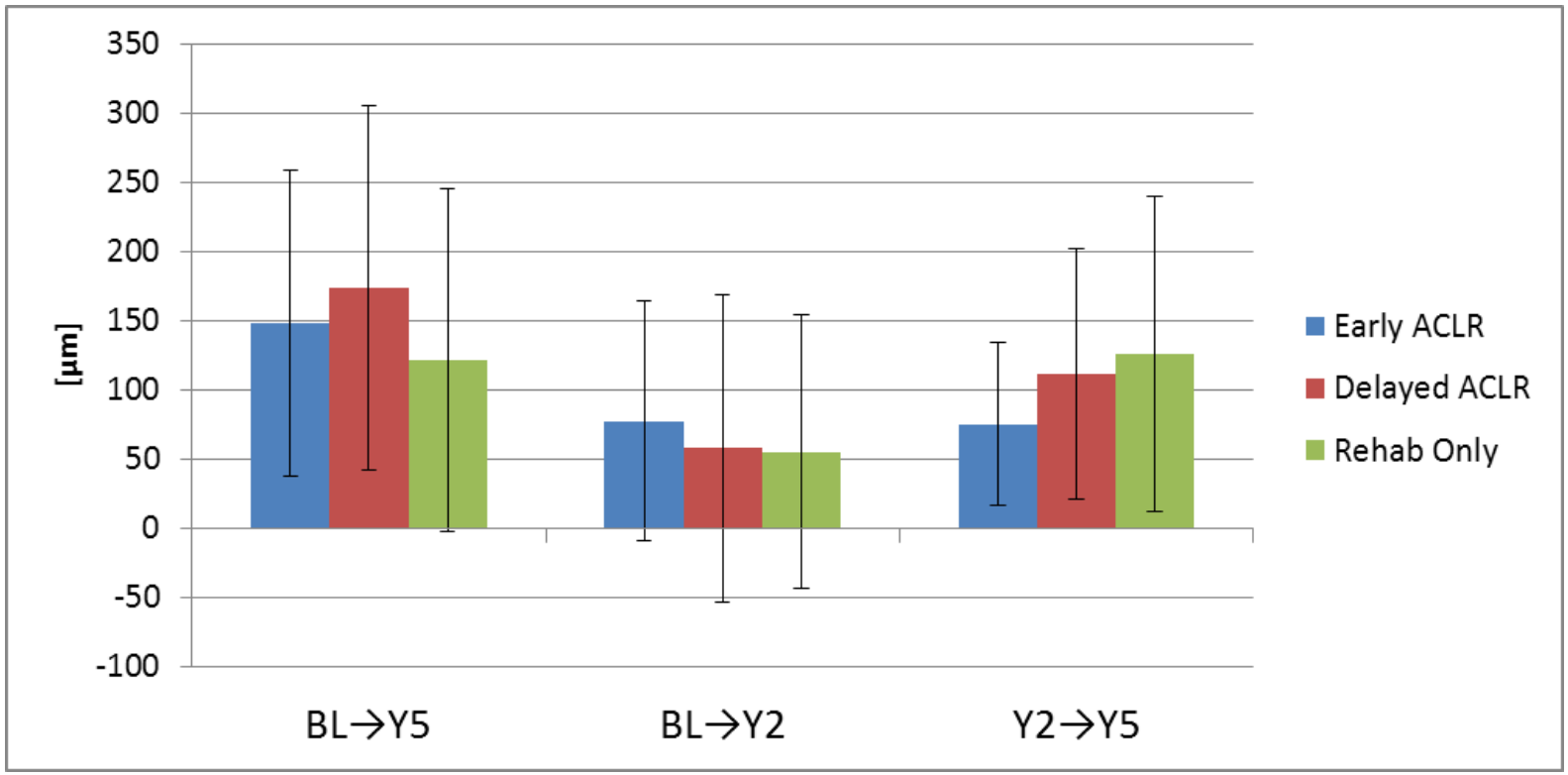
Statistical analysis

- Primary outcome: Change in entire femorotibial joint (**FTJ**)
- Secondary outcomes:
  - » Ordered value 1 (**OV 1**)
  - » Ordered value 16 (**OV 16**)
  - » Medial femorotibial compartment (**MFTC**)
  - » Lateral femorotibial compartment (**LFTC**)
- Observation periods:
  - » Baseline → Year 5 (**BL→Y5**)
  - » Baseline → Year 2 (**BL→Y2**)
  - » Year 2 → Year 5 (**Y2→Y5**)
- As-treated analysis:
  - » Early ACL reconstruction
  - » Delayed ACLR
  - » Rehabilitation only (no ACL reconstruction)
- T-test (crude analysis)
- Analysis of covariance (analysis with adjustment for age, sex & BMI)



Entire femorotibial joint (FTJ)

- Increase in cartilage thickness observed over the entire 5 years
- No significant differences between treatment groups (crude/adjusted p≥0.38 / p ≥ 0.39)

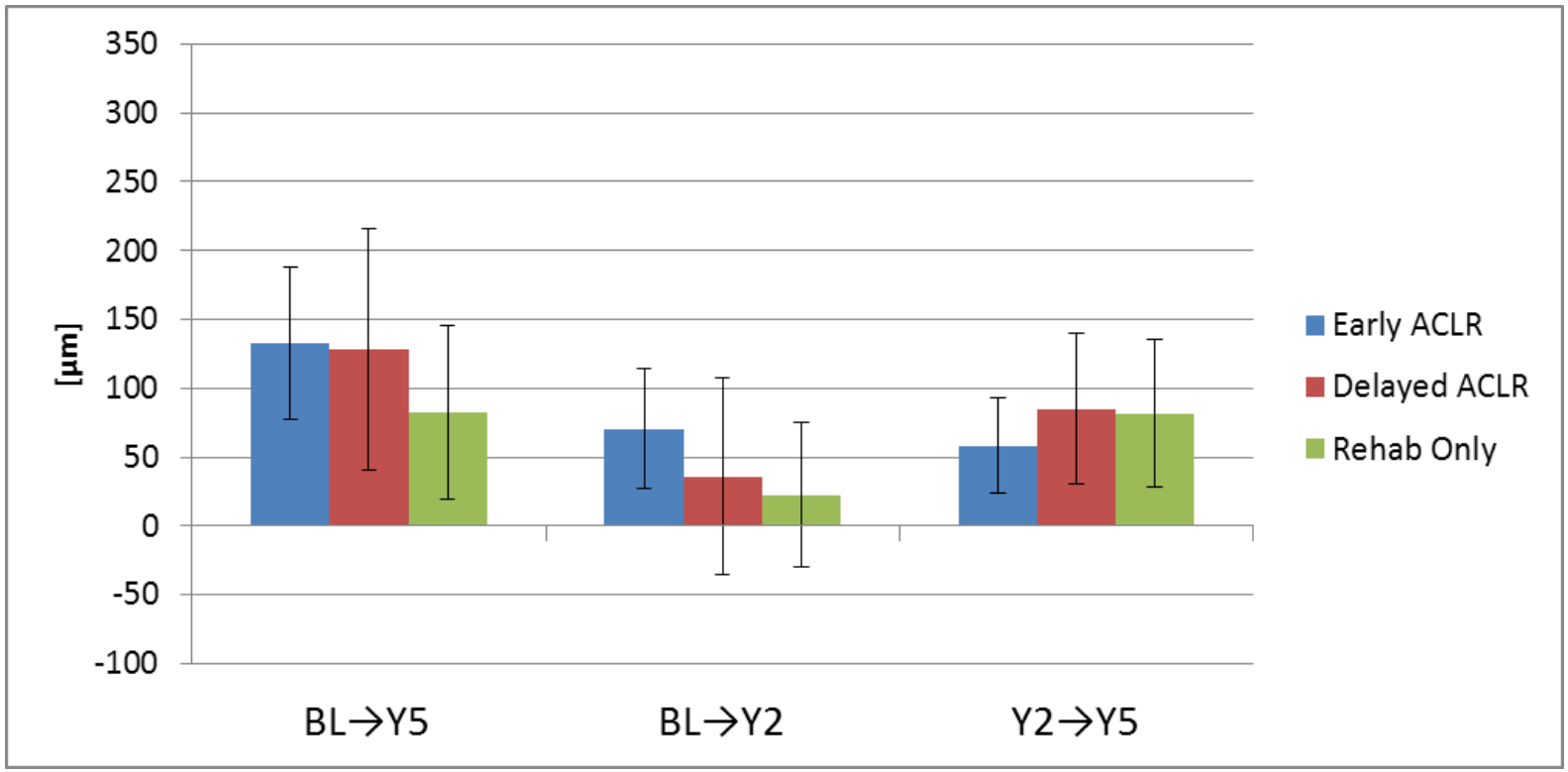


(n=59/27/26) (n=58/27/27) (n=58/25/24)

Mean change ± 95% confidence intervals

Medial femorotibial compartment (MFTC)

- FTJ increase driven by increase in MFTC
- No significant differences between treatment grups (crude/adjusted p≥0.19 / p ≥ 0.20)

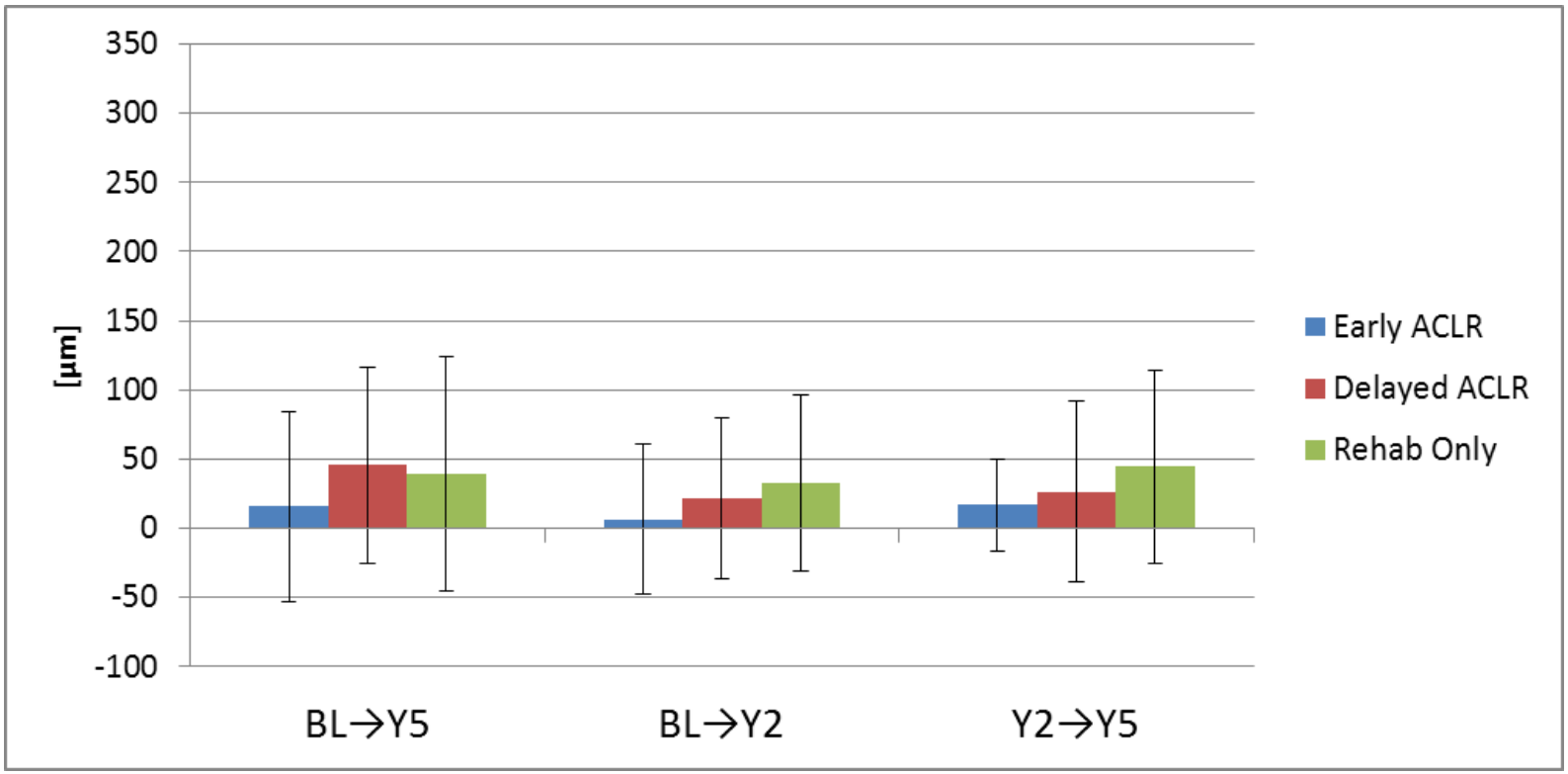


(n=59/27/26) (n=58/27/27) (n=58/25/24)

Mean change ± 95% confidence intervals

Lateral femorotibial compartment (LFTC)

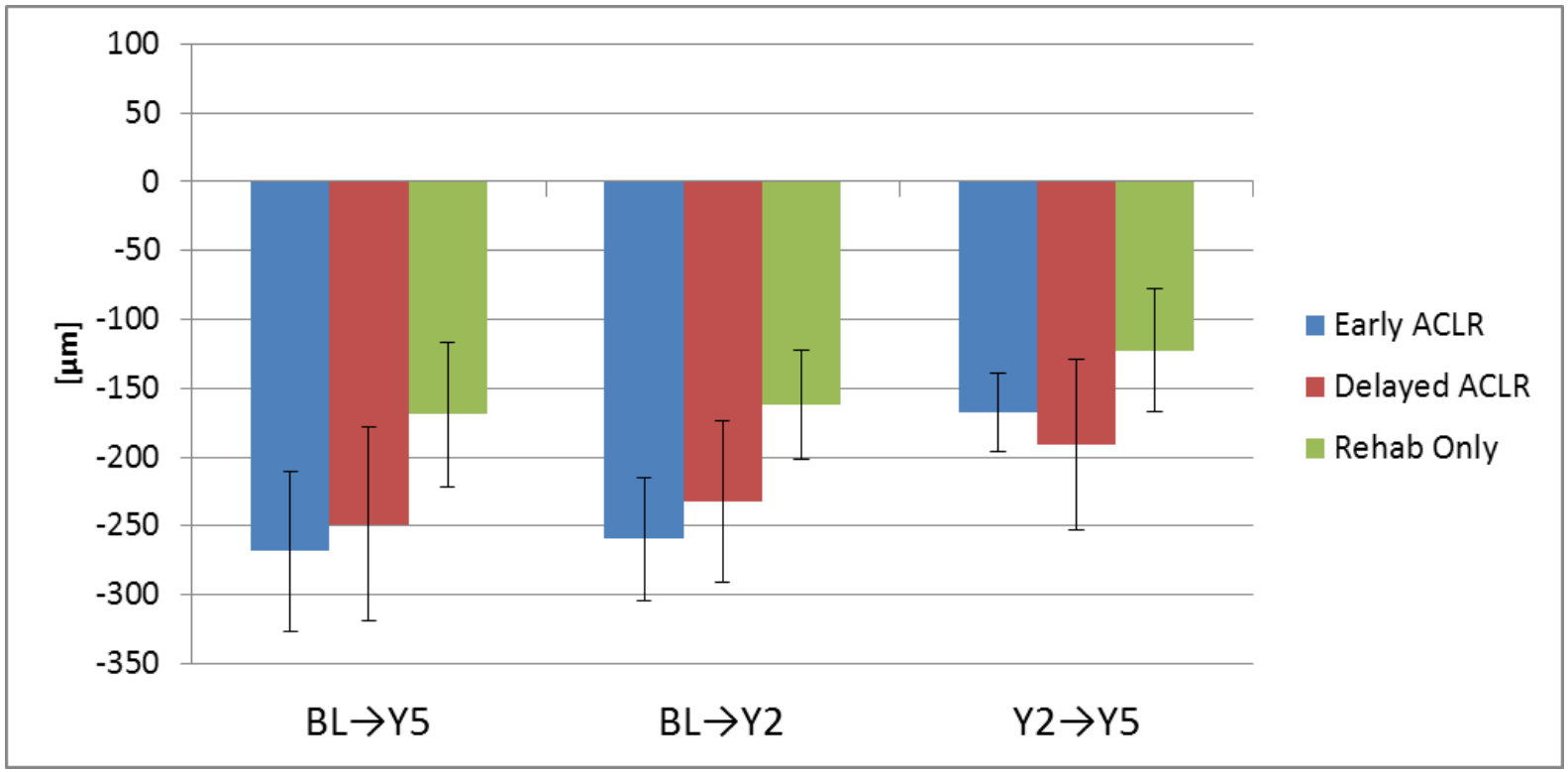
- Small magnitude of change
- No significant differences between treatment grups (crude/adjusted p≥0.41 / p ≥ 0.42)



Mean change ± 95% confidence intervals

Ordered value 1

- OV 1 ↓ for early ACLR than rehabilitation only (BL→Y5: crude/adjusted p=0.04/0.03; BL→Y2: crude/adjusted p=0.007/0.005)
- OV 1 ↓ for delayed ACLR than rehabilitation only (BL→Y2: p=0.04/0.04)

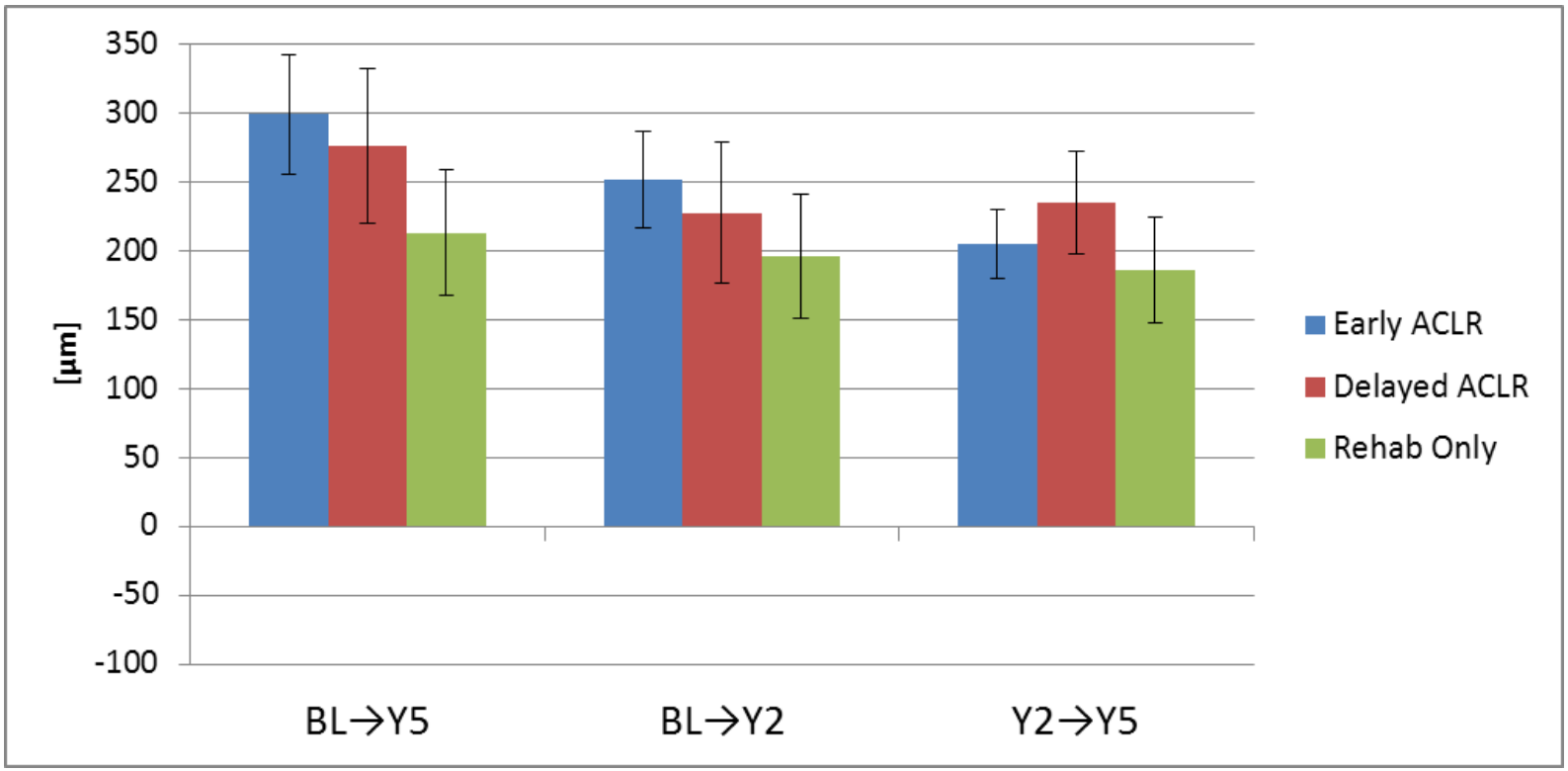


(n=59/27/26) (n=58/27/27) (n=58/25/24)

Mean change ± 95% confidence intervals

Ordered value 16

- OV 16 ↑ for early ACLR than rehab only (BL→Y5:crude/adjusted p=0.02/0.01, *BL→Y2:crude/adjusted p=0.06/0.08*)
- OV 16 tended to be greater for delayed ACLR than rehabilitation only (*BL→Y5: crude/adjusted p=0.07/0.08*)

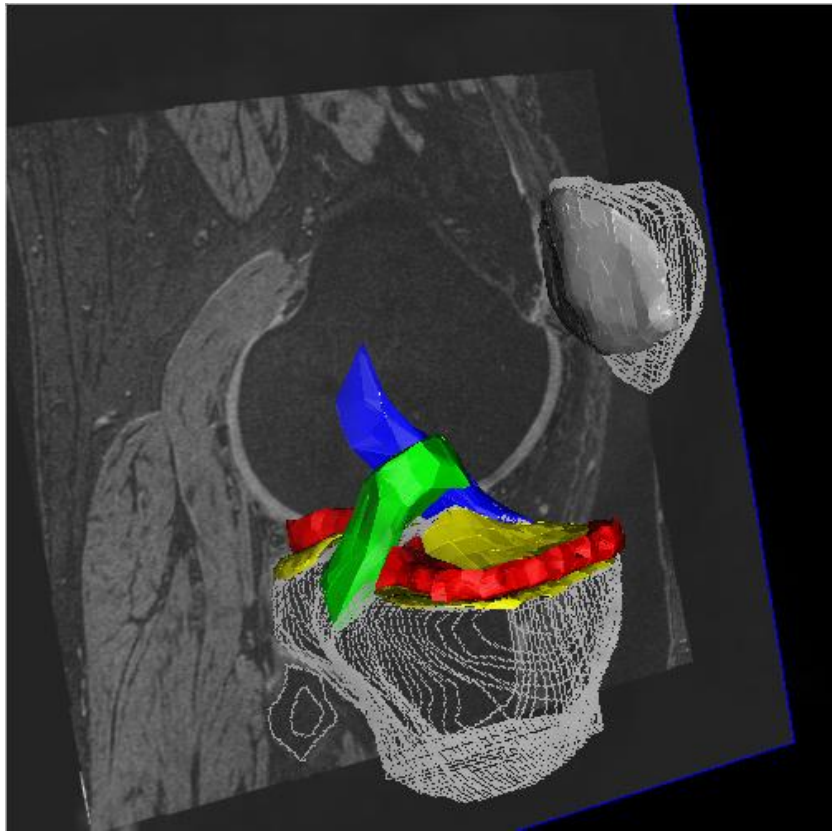


(n=59/27/26) (n=58/27/27) (n=58/25/24)

Mean change ± 95% confidence intervals

Conclusions

- No significant differences observed for primary outcome (FTJ) between treatment groups
- No significant differences observed for MFTC / LFTC
- Greater magnitude of subregional cartilage thickness changes (both decrease and increase) after ACL reconstruction surgery
- Surgical ACL reconstruction may induce greater magnitudes of subregional cartilage thickness changes



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