PROLONGED SUBREGIONAL FEMOROTIBIAL CARTILAGE INCREASE AFTER ACUTE ANTERIOR CRUCIATE LIGAMENT TEAR - FIVE YEAR FOLLOW UP DATA AFTER INJURY

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Introduction: An anterior cruciate ligament (ACL) tear is a serious and common knee injury, mainly affecting young active adults. In the long term, the risk of OA development in the injured joint is increased, due to the acute joint trauma and the chronic unfavorable mechanical conditions in the injured joint. Little is known about the structural changes in cartilage immediately following the injury or over longer follow up periods. The purpose of this study was to use validated quantitative MRI technology (1), to determine the rate of change in subregional cartilage thickness (2) in the femorotibial joint both in the early phase after ACL injury (2 year follow up after ACL rupture), and in the intermediate phase after ACL injury (2 year to 5 year follow up after ACL rupture).

<u>Methods</u>: 121 young active adults (mean age 26.1 years) with an acute ACL tear in a previously uninjured knee were included in a randomized control trial (3), comparing rehabilitation plus early ACL reconstruction (n=62) with rehabilitation plus the option of having a delayed ACL reconstruction if needed (n=59). Sagittal MR images (3D/WATSc sequence) with 3.0 mm slice thickness (1.5 mm slice spacing) and 0.29 mm in-plane resolution (TR=20 ms, TE =7.8ms, FA = 25°) were acquired using a 1.5T Philips Gyroscan Intera magnet and a CP knee coil. Baseline images were acquired within 5 weeks of an ACL tear; and 2 and 5 year follow up images were acquired in 107 of the 121 participants. The mean cartilage thickness over the entire subchondral bone area (ThC.tAB) was assessed by manual segmentation of the cartilage thickness change was determined in 16 femorotibial subregions (1), 8 medial and 8 lateral, 5 tibial and 3 femoral, respectively. In the present analysis, MRI results were not unblinded for treatment group, because we aimed to explored "early" and "later" cartilage changes in acutely ACL injured knees, independent of treatment. In this exploratory study, paired t-tests were used to study whether changes between ACL injury and 2 year follow up (early phase), and between 2 year and 5 year follow up (later phase) were significantly different from zero, without correction for multiple testing.

<u>Results:</u> In the total femorotibial joint (FTJ), the mean cartilage thickness significantly increased between ACL injury and 2 year follow up (+0.7 %), and increased further between 2 and 5 year follow up (+1.2 %; Table 1). The cartilage thickness increase in the medial femorotibial compartment (MFTC) was greater than that in the lateral femorotibial compartment (LFCT) and was statistically significant in MFTC but not in LFTC. Between ACL injury and 2 year follow-up, the most marked increase in subregional cartilage thickness was observed in the central subregion of the lateral weight-bearing femur (2.7%; p<0.001) and in the external subregion of the medial weight-bearing femur (2.0%; p=0.021). The most marked decrease in subregional cartilage thickness was seen in the posterior aspect of the lateral (-4.2%; p<0.001) and in the posterior aspect of the medial tibia (-1.4%; p=0.043). Amongst the 16 femorotibial subregions, 6 showed a significant increase, 2 a significant decrease, and 8 no significant change over the 2 years. Between 2 year and 5 year-follow-up, the greatest increase in subregional cartilage thickness was again seen in the external subregion of the medial weight-bearing femur (2.6%; p<0.001) and in the anterior subregion of the medial tibia (2.4%; p<0.001). However, no further significant increase was noted in the central aspect of the lateral weight-bearing femur. The only subregion showing a small (but non-significant) decrease in cartilage thickness (-0.5%) was the posterior aspect of the lateral tibia. Amongst the 16 subregions, 8 showed significant increases, none a significant decrease, and 8 no significant change between 2 and 5 year follow up.

		Mean Change µm	Standardized response mean	95% CI-Intervall Lower - Upper		t-Test 2-tailed
	FTJ	58.3	0.195	1.0	115.5	0.046
	MFTC	48.6	0.294	16.9	80.3	0.003
ACL injury→Year 2	LFTC	9.7	0.054	-24.7	44.0	0.579
	FTJ	95.1	0.408	50.4	139.8	p<0.000
	MFTC	69.7	0.535	44.8	94.7	p<0.000
Year 2→Year 5	LFTC	25.4	0.179	-1.9	52.6	0.068

Table 1: Change in cartilage thickness in the total femorotibial joint (FTJ) and in the medial (MFTC) and lateral femorotibial compartment (LFTC) between ACL injury and 2 year follow-up, and between 2 year and 5 year follow-up after ACL injury

Discussion and Conclusions: These results extend previous short term follow-up findings after ACL injury (4,5). They confirm that an increase (rather than a decrease) in overall mean femorotibial cartilage thickness is observed after ACL injury, and that this increase predominates in the medial femorotibial compartment. This increase in cartilage thickness does not appear to represent a short-term phenomenon after the ACL injury, but becomes even more evident between 2 and 5-year follow up after ACL tear. The external subregion of the medial weight-bearing femur has been previously shown to display an increase (and the posterior lateral tibia a decrease) in cartilage thickness in knees with early radiographic OA knees (6). These subregional changes may hence provide the first evidence of femorotibial cartilage pathology in OA. Future studies will explore to what extent these findings predict clinical and structural (radiographic) outcomes and whether the between-subject variability of these changes can be predicted using molecular biomarker obtained after the injury.

References

- 1. Wirth W, and Eckstein F. IEEE Trans.Med.Imaging 2008,27: 737-744
- 2. Eckstein F et al.. Magn Reson Med 1996, 1: 89-96
- 3. Frobell RB et al. *N Engl J Med* 2010; 4:331-342
- Frobell RB et al. Osteoarthritis Cartilage 2009; 2:161-167
 Frobell RB et al. J Bone Joint Surg Am 201;12:1096-1103
- 6. Frobell RB et al. Arthritis Care Res 2010; 11:1612-1623