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Short-term contact kinematic changes and longer-term biochemical changes in the cartilage after ACL reconstruction - a pilot study

Guoan Li[1], **Jing-Sheng Li**[1,2], **Martin Torriani**[3], and **Ali Hosseini**[1]

[1] Orthopaedic Bioengineering Research Center, Newton-Wellesley Hospital and Harvard Medical School, Newton, MA, 02462

[2] College of Health and Rehabilitation Sciences, Boston University, Boston, MA, 02215

[3] Division of Musculoskeletal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital and Harvard Medical School

Abstract

Investigation of the development of cartilage degeneration after ACL reconstruction is important for improving current surgical treatment of ACL injuries to prevent long-term knee joint degeneration. This pilot study examined the relationship between the changes in weight-bearing knee contact kinematics 6 months after ACL reconstruction and the biochemical composition changes in the knee cartilage measured using T2 relaxation values 3 years after the surgery in seven patients. The analysis indicated that the change of the knee contact kinematics in short-term after ACL reconstruction is associated with an increase of T2 values of the cartilage in longer follow up times. The data of this study could provide preliminary data to power future studies that use prospective, longitudinal research and large patient populations to establish prognostic biomechanical markers for determination of long-term cartilage degeneration after ACL reconstruction.

Keywords

ACL; ACL reconstruction; Cartilage degeneration; Prognostic marker; Kinematics; Knee

Introduction

ACL reconstruction is a popular treatment for unstable ACL deficient knees. Although satisfactory clinical outcomes regarding the anterior stability of the knee have been

Corresponding Author Guoan Li, Orthopaedic Bioengineering Research Center, Newton-Wellesley Hospital, Newton, MA, 02462. Phone: +1 617 530 0563; gli1@partners.org.

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Guoan Li: research idea, data analysis and interpretation, drafting manuscript
Jing-Sheng Li: research idea, data analysis and interpretation, drafting manuscript
Martin Torriani: data interpretation, assisting in paper writing
Ali Hosseini: data interpretation, assisting in paper writing
All authors have read and approved the final submitted manuscript

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reported[1], recent mid- to long-term follow-up studies have revealed prevalent radiographic knee osteoarthritis (OA) in ACL reconstructed patients [2–18]. It is important to improve current treatment techniques to delay or prevent post-operative cartilage degeneration of ACL reconstruction patients.

Magnetic resonance (MR) imaging is widely used for analysis of early knee OA. Considerable progress has been made to explore biochemical composition changes in cartilage using T1 p or T2 mapping sequences [19–22] Both T1ρ and T2 techniques reported that the superficial layer of the cartilage is more susceptible to early cartilage degenerative changes. The majority of relevant literature assumes that altered kinematics after ACL reconstruction play a crucial role in cartilage degeneration [23-27] However, a paucity of data exists on the quantitative relationship between the post-operative kinematic alteration and cartilage degeneration after ACL reconstruction. This information is necessary for development of biomechanical markers that can predict long-term cartilage degeneration after the surgery.

We previously investigated contact kinematics of the knee after ACL reconstruction[28] and measured T2 relaxation values of the ACL reconstructed and intact contralateral knees[29,39] where patients were investigated for early post-operative contact kinematics and T2 values 3 years after surgery. In this paper, we present a pilot study of a small sample size patient cohort that analyzed the relationship between the contact kinematics of the knee during weight-bearing full extension standing 6 months after ACL reconstruction and the cartilage status measured using T2 relaxation values 3 years after the surgery. Our objective is to provide preliminary data to power future studies that use prospective, longitudinal research and large patient populations to establish prognostic biomechanical markers for determination of long-term cartilage degeneration after ACL reconstruction. We hypothesized that the changed knee joint kinematics at short-term after ACL reconstruction was associated with longer-term cartilage degeneration.

Materials and Methods

Patients

Seven patients (sex: 3M, 4F; age: 20–43 years; height: 65–72 inches; BW: 150–190 lbs; BMI: 23.6–27.4 kg/m^2) with a unilateral ACL injured knee were investigated with the IRB approval. This patient group was a sample of convenience obtained from our previous study.These patients were diagnosed with no other ligamentous injuries and gross cartilage or meniscus damage (confirmed by MRI and arthroscopy) that required surgery, and no history of contralateral knee injury or symptoms. All patients underwent ACL reconstruction within 6 weeks after injury. Written consent was obtained from all subjects before participation in the study.

Contact kinematics

Both knees were scanned using a 3-Tesla MR scanner (MAGNETOM Trio, Siemens, Malvern, PA) before ACL reconstruction. The MR images were used to construct 3 dimensional (3D) models of the knee, including the femur, tibia, patella and their cartilage

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surfaces. All patients then performed a step-up motion (14 cm high) before and 6 months after surgery using both knees. The step-up motion was chosen because it represents a strenuous motion of the knee during daily life activity. The knee motion was imaged using a dual fluoroscopic imaging system (DFIS) with a frame rate of 30 Hz (**Fig. 1A**). In this study, we only analyzed the knee kinematics at the end of the step-up motion after a standing position had been achieved.

The fluoroscopic images were imported into solid modeling software (Rhinoceros, Robert McNeel and Assoc, Seattle, WA) to construct a virtual DFIS based on the positions of the actual DFIS setup. The knee positions along the motion path were reproduced using a 2D-3D matching method that has been previously validated with an error of 0.08 mm and a repeatability of <0.38° in measurement of the position and orientation of the knee, respectively [32–34]. To analyze the tibiofemoral cartilage contact locations, the cartilage models of the femur and tibia were mapped to the corresponding bony models at each knee position. The cartilage contact area at a given knee position was determined by overlapping of the tibial and femoral cartilage surfaces, where the centroid of the overlapping area was defined as the cartilage contact location [35] A contact axis was defined by connecting the medial and lateral contact locations. The position of the midpoint of the contact axis was defined as the contact location in the tibial coordinate system (**Fig. 1B**) [28,36] The tibial long axis (**z**) was selected parallel to the posterior wall of the tibial shaft. The medial-lateral axis (**x**) of the coordinate system was defined as a line connecting the centroids of the two circles fit to the medial and lateral tibial plateau surfaces [36] The anterior-posterior axis (**y**) was perpendicular to the other two axes. The angle between the contact axis and the **x**-axis was used to describe the internal(+)/external(−) rotation of the contact axis.

To compare the contact kinematics between the ACL reconstruction and intact contralateral knees, only the data corresponding to the full weight-bearing, single-legged standing position (representing the knee position at the end of the step-up motion) was analyzed, since the ACL mainly functions at low flexion angles [37,38] The changes in cartilage contact kinematics at the standing position 6 months after ACL reconstruction was calculated by subtracting the cartilage contact data of the intact contralateral knee measured before surgery [39]

T2 Mapping

At least three years (36–39 months) after ACL reconstruction, both knees of each patient were scanned using a 3T MR scanner. A multiple-TE fast-spin echo sagittal pulse sequence (a repetition time: 1700 ms; ten echo times: 10.6, 21.2, 31.8, 42.4, 53.0, 63.6, 74.2, 84.8, 95.4, 106 ms; matrix: 384×384; field of view: 18 × 18 cm; slice thickness: 3.0 mm; slice gap: 0 mm; number of slices: 26–30; bandwidth: 250 Hz/pixel; and total scan time: 11 min per knee) was used for T2 relaxometry images [29] Both knees were scanned using the same imaging parameters at the same session.

For quantification of the T2 relaxation time, the MR images were imported into OsiriX software (Pixmeo Sarl, Bernex, Switzerland). Six compartments of the articular cartilage of the knee were investigated: medial femoral condyle (FM), lateral femoral condyle (FL), medial tibial plateau (TM), lateral tibial plateau (TL), trochlear grove (Tro), and patella

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(Pat). The femoral condyle cartilage was divided into five sub-compartments (**Fig. 2A**) (FM1 or FL1, FM2 or FL2, FM3 or FL3, FM4 or FL4, and FM5 or FL5); the tibial plateau into three sub-compartments (TM1 or TL1, TM2 or TL2, and TM3 or TL3); and the patellar and femoral trochlear cartilage evenly into three regions in coronal plane (medial, central and lateral regions) [30] Further, each region was evenly divided into superficial and deep zones since the cartilage could respond to early degeneration differently along the thickness direction [29] (**Fig. 2B**). The change of T2 value at each region was calculated by subtracting the T2 value of the contralateral knee from that of the ACL reconstruction knee. A higher T2 value of the ACL reconstruction knee compared to the intact contralateral knee indicates early biochemical composition changes of the cartilage In this study, we aimed to investigate the superficial weight-bearing cartilage layer of the tibiofemoral joint by combining FM2 with FM3, FL2 with FL3, TM1 with TM2, and TL1 with TL2.

Statistical analysis

An ANOVA was used to compare the contact kinematics and cartilage T2 values between the ACL reconstruction and intact contralateral knees. A General Linear Model [40,41] was used to test the relationship between the changes in the cartilage contact kinematics 6 months after ACL reconstruction (independent variables) and the cartilage T2 value changes 3 years post-operatively (dependent variables). The output variables were r^2 (representing how close the data are to the fitted regression line), β (representing the weight of change in kinematic variable values in response to T2 variable) and SE (the standard deviation of the estimate of β). Significant difference was set when $p<0.05$.

Results

Six months after surgery, no statistically significant difference in contact kinematics was observed between the ACL reconstruction and intact contralateral knees among this small patient cohort ($p>0.08$) (**Table 1**). Three years after surgery, no statistically significant differences in cartilage T2 values were observed between the ACL reconstructed and intact contralateral knees in this patient cohort ($p>0.06$) (**Table 2**).

Overall, there is no statistically significant correlation between the changes in the contact locations in anterior-posterior and medial-lateral directions 6 months and the changes in T2 values of the cartilage 3 years after ACL reconstruction in this small patient cohort ($p>0.11$) (**Table 3**). For example, the increased T2 values of the medial femoral and tibial cartilage were not significantly associated with the anteior-posterior contact location changes after ACL reconstruction (r^2=0.26, β=−1.4, p=0.24; r^2=0.30, β=−0.67, p=0.20); the lateral trochlea and medial patellar cartilage were not significantly correlated with the anterior-posterior contact location changes (r^2=0.43, β=6.76, p=0.11; r^2=0.04, β=1.94, p=0.19).

The increased T2 values of the femoral cartilage were not significantly associated with reduced internal (increased external) rotation angle of the contact axis (ΔAIE) for the medial side (ΔFM: r^2=0.51, β=−0.64, p=0.07), but were significantly associated for the lateral side (AFL: r^2=0.64, β=−0.47, p=0.03) (**Fig. 3**). No significant correlations were observed for the tibial cartilage (r^2=0.41, β=−0.26, p=0.12; r^2=0.22, β=−0.31, p=0.28, respectively for the medial (ΔTM) and lateral (ΔTL) sides). The increased T2 value of the medial trochlea

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(ΔMed Tro) was correlated with the reduced internal (increased external) rotation angle of the contact axis (ΔAIE) (r^2=0.71, β=−1.02, p=0.02). The T2 value increase of the lateral patellar cartilage (ΔLat Pat) was not significantly correlated with the external rotation angle change of the contact axis (r^2=0.34, β=−0.72, p=0.17).

Discussion

This pilot study examined the relationship of longer-term cartilage biochemical composition changes and short-term contact kinematics of the knee after ACL reconstruction using a small sample size patient cohort. The data indicated that for weight-bearing regions of the knee cartilage, there was an association between the contact kinematics changes during the weight-bearing single-legged standing 6 months and the changes in the T2 relaxation values 3 years after ACL reconstruction. The data only partially supported our hypothesis that the changed knee joint kinematics at short-term after ACL reconstruction was associated with longer-term cartilage degeneration.

The results of this pilot study revealed interesting implications for future investigation of post-operative cartilage degeneration after ACL reconstruction. While marginal correlations emerged between the short-term contact location changes and longer-term cartilage biochemical composition changes in this small sample size patient cohort, we found that the reduced internal (increased external) rotation of the contact axis 6 months after ACL reconstruction were correlated with the increased T2 values 3 years after the surgery. An increased internal rotation of the contact axis compared to the intact contralateral knee corresponds to less changes in T2 values, and we therefore speculate that this could be beneficial for maintenance of the cartilage after the surgery. For example, at the patellofemoral cartilage, a reduced internal contact axis rotation angle (increased internal tibial rotation) was shown to correspond to increased T2 values in the medial patellofemoral cartilage. This is consistent with the biomechanics observation that an increased internal tibial rotation is associated with an increase of the contact pressure at the medial compartment of the patellofemoral joint [42].

One of the primary goal of ACL reconstruction is to restore anterior stability of the knee. The data of this pilot study indicate that to prevent long-term changes in cartilage biochemical composition, more biomechanics research, such as during dynamic gait, is necessary to understand how kinematics changes after the surgery could affect the long-term cartilage homeostasis,althogh other factors besides biomechanical ones could also play a role. For example, the correlation analyses implied that for knees having similar contact kinematics of the intact contralateral knees at 6 months after ACL reconstruction (i.e.,ΔIE~0 in **Fig. 3**), their cartilage could experience higher T2 values in certain regions than the contralateral knees 3 years after the surgery. Previous in-vitro cadaveric studies indicated that contemporary ACL reconstructions could restore normal knee stability, but the graft forces were larger than the intact ACL [43] We therefore speculate that the increased ACL graft forces could be beneficial for restoration of knee stability, but could also increase the cartilage contact force [44] In addition, altered muscle strength[45] and different ACL reconstruction techniques[46] could also cause changes of the kinematics and consequently the cartilage contact loadings of the ACL reconstruction knees. We speculate that eventually,

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these factors could be a biomechanical cause for long-term cartilage degeneration. Therefore, more prospective, longitudinal studies using larger patient cohorts are warranted to determine if there is a threshold for restoration of knee kinematics after the surgery that corresponds to minimal changes in biochemical compositions of the cartilage long-term after ACL reconstruction.

Diagnosis of early cartilage biochemical composition changes is critical for prevention or treatment of post-operative cartilage degeneration. While T1ρ and T2 mapping are sensitive and feasible to detect early biochemical composition changes in the cartilage, this indicates that the cartilage has already lost some structural integrity and has started to degenerate. It would be ideal if there is a biomarker that could predict cartilage biochemical composition changes before it is initiated. This pilot study implies that an early detection of altered tibiofemoral contact kinematics of the knee after ACL reconstruction compared to the intact contralateral side might serve as a prognostic marker of long-term cartilage biochemical composition changes. With such a predictive tool, early intervention could be developed, such as patient-specific muscle training and rehabilitation regimen, to improve the knee joint contact biomechanics to potentially impede long-term cartilage degeneration.

This is a pilot study that investigated the correlation between the contact kinematic changes in short-term (at weight-bearing, full extension of the knee) and cartilage biochemical composition changes in longer-term after ACL reconstruction using a small sample size patient cohort. There are several limitations when interpreting these data. The correlation analysis was based on a patient cohort of 7. A sample analysis using the data of Table 1 indicated that to detect a statistically significant change in contact axis rotation angles after ACL reconstruction with 80% power, 44 patients would be needed. Therefore, future studies should include a large patient population in a prospective, longitudinal investigation to confirm the association between longer-term cartilage biochemical composition changes and short-term kinematics measurements of the knee after ACL reconstruction. We only analyzed the knee kinematics at the weight-bearing, single-legged standing position and corresponding weight-bearing contact locations of the cartilage due to the retrospective nature of the study. To evaluate the cartilage of the entire knee, the knee kinematics during functional daily activities, such as gait, jumping, etc., that include various flexion angles and loading ranges should be investigated. Our early study only used T2 relaxation values to examine the cartilage biochemical composition changes. Future studies should also use other validated techniques, such as T1ρ sequence, cartilage thickness change, to detect cartilage degeneration. Despite these various limitations, the results of this pilot study provide insights for designing future research for prediction of long-term cartilage degeneration using short-term knee kinematics after ACL reconstruction.

Conclusion

Despite the small sample size, several relationships between changes in contact kinematics and T2 values were identified in this study. For example, for knees having similar contact kinematics of the intact contralateral sides at 6 months after ACL reconstruction, their cartilage could still experience higher T2 values in certain regions than the contralateral sides 3 years after the surgery. These observations could provide the basis for future studies that use prospective, longitudinal research and large patient cohorts to further explore these novel, yet preliminary, findings.

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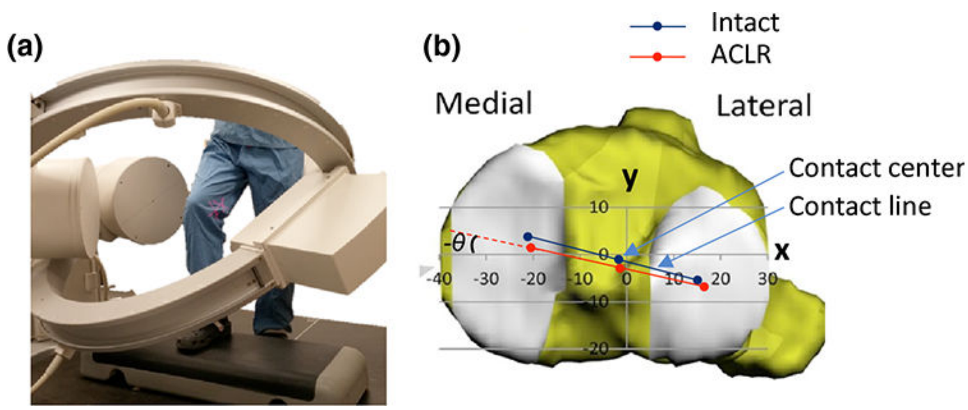

Fig. 1.
(A) The step-up activity captured using a dual-fluoroscopic imaging system; (B) coordinate system on the tibial plateau showing the contact axis, location of contact center and rotation of the contact axis. ACLR is abbreviation of ACL reconstruction.

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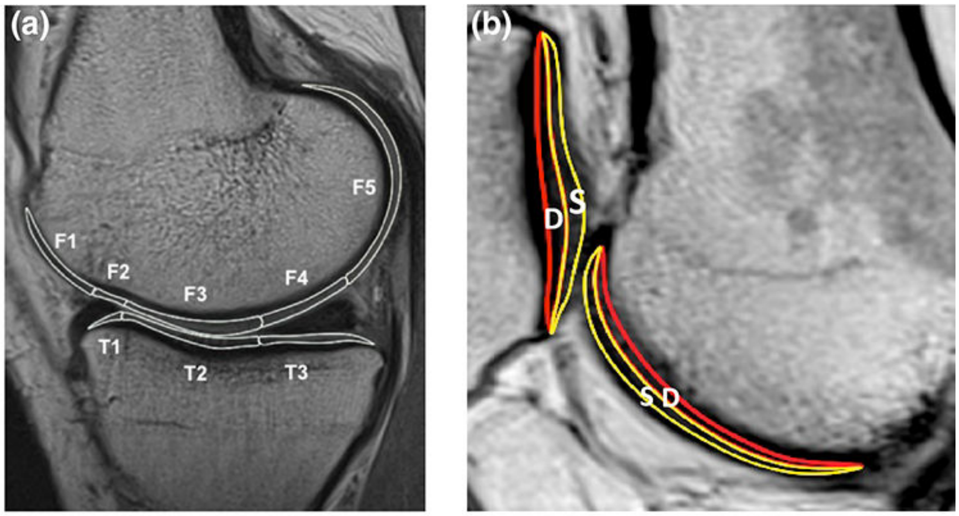

Fig. 2.

(A) The cartilage of femur and tibia is divided into the sub-compartments with regard to the anterior and posterior horns of the meniscus. The femoral condyle has five sub-compartments (F-1, 2, 3, 4, 5) and the tibia plateau has three sub-compartments (T-1, 2, 3). (B) The articular cartilage is divided into the superficial and deep zones. S; superficial zone, D; deep zone

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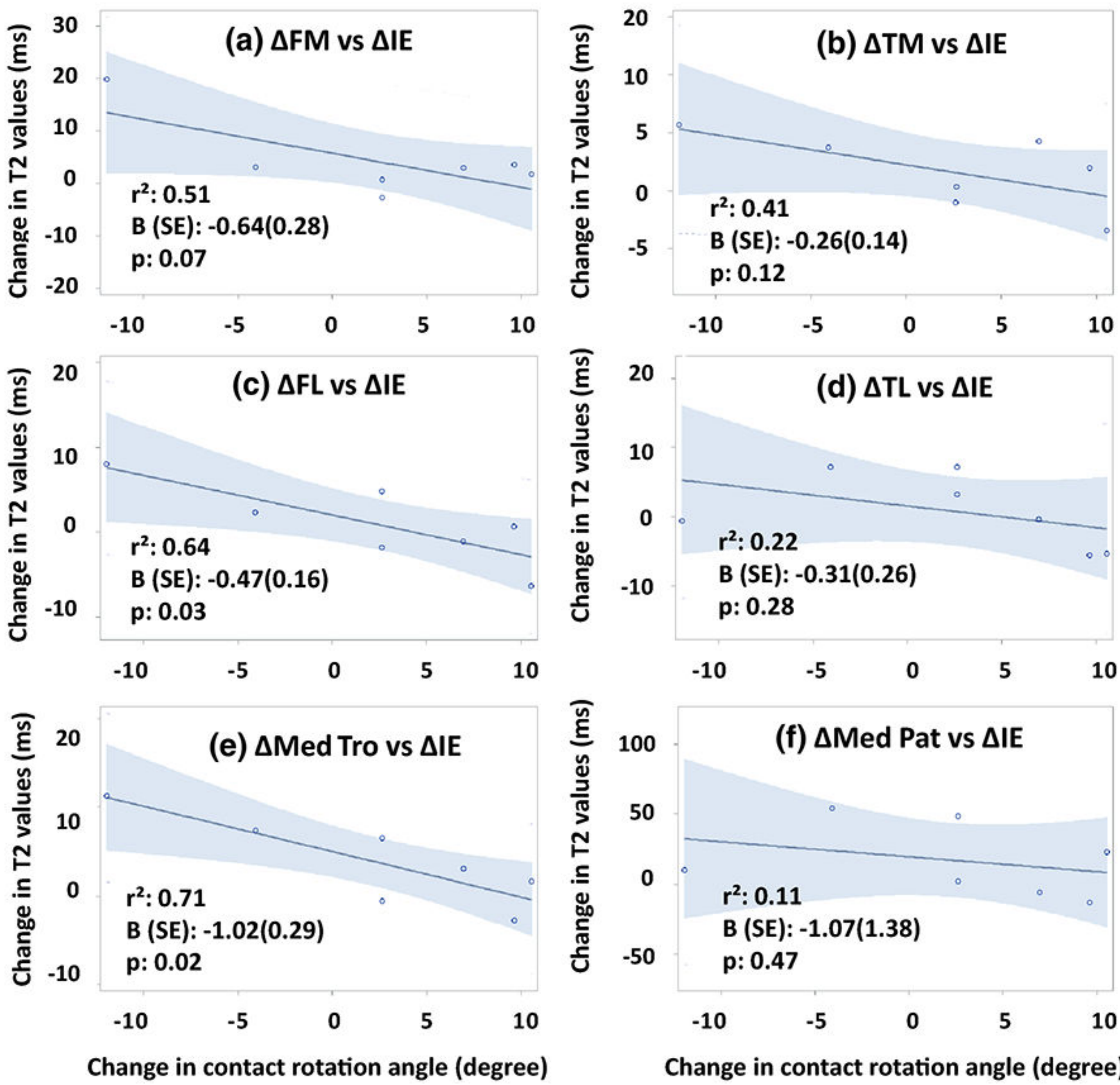

Fig. 3.

Correlations between the changes of T2 values of individual cartilage sub-compartments 3 years after ACL reconstruction and changes in the contact rotation angles at 6 months after ACL reconstruction.

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Table 1.

Contact locations and rotations of the intact contralateral knees (Intact) measured pre-operatively and of the ACL reconstruction knees (ACLR) at 6 months after surgery. The changes in contact locations and rotations at 6 months after ACL reconstruction were calculated.

	AP Position		ΔAP	ML Position		ΔML	IE Rotation		ΔIE
	Intact	ACLR		Intact	ACLR		Intact	ACLR	
Ave	−0.81	−2.90	−2.08	−3.09	−1.88	1.22	−14.92	−12.29	2.34
Std	1.61	3.01	2.44	2.90	2.64	2.23	5.01	6.70	7.44
p	0.08			0.23			0.41		

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Table 2.

The change in T2 values of individual cartilage sub-compartments at 3 years after ACL reconstruction compared to intact contralateral side.

	Tibiofemoral weightbearing area				**Trochlea**			**Patella**		
	ΔFM	ΔTM	ΔFL	ΔTL	ΔMed	ΔCen	ΔLat	ΔMed	ΔCen	ΔLat
Ave	4.20	1.64	0.94	0.83	7.59	14.07	3.36	16.90	−2.69	0.52
Std	6.69	2.98	4.33	4.93	9.02	14.80	25.21	24.31	12.37	9.17
p	0.17	0.23	0.62	0.70	0.07	0.06	0.99	0.15	0.50	0.93

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Table 3.

Correlation coefficients between the changes of T2 values of individual cartilage sub-compartments 3 years after ACL reconstruction of the intact contralateral side and changes in contact locations and contact rotations at 6 months after ACL reconstruction.

		Tibiofemoral weightbearing area				Trochlea			Patella		
		ΔFM	**ΔTM**	**ΔFL**	**ΔTL**	**ΔMed**	**ΔCen**	**ΔLat**	**ΔMed**	**ΔCen**	**ΔLat**
ΔAP	r^2	0.26	0.30	0.00	0.21	0.04	0.02	0.43	0.04	0.07	0.04
	β (SE)	−1.40 (1.05)	−0.67 (0.46)	−0.04 (0.80)	0.92 (0.80)	−0.72 (1.62)	0.89 (2.68)	6.76 (3.49)	1.94 (4.37)	−1.32 (2.19)	−0.79 (1.64)
	p	0.24	0.20	0.96	0.30	0.68	0.75	0.11	0.19	0.75	0.11
ΔML	r^2	0.00	0.00	0.14	0.35	0.12	0.01	0.11	0.23	0.44	0.16
	β (SE)	−0.11 (1.34)	−0.04 (0.60)	−0.72 (0.81)	−1.31 (0.80)	−1.38 (1.70)	−0.73 (2.95)	−3.82 (4.76)	−5.18 (4.30)	−3.67 (1.86)	−1.64 (1.69)
	p	0.94	0.95	0.42	0.16	0.45	0.81	0.46	0.28	0.11	0.38
ΔIE	r^2	0.51	0.41	0.64	0.22	0.71	0.27	0.12	0.11	0.26	0.34
	β (SE)	−0.64 (0.28)	−0.26 (0.14)	−0.47 (0.16)	−0.31 (0.26)	−1.02 (0.29)	−1.03 (0.76)	−1.15 (1.42)	−1.07 (1.38)	−0.85 (0.64)	−0.72 (0.45)
	p	0.07	0.12	0.03	0.28	0.02	0.24	0.45	0.47	0.24	0.17