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Biomechanical Outcomes 1 Year After Acl Reconstruction And Meniscus Surgery

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BIOMECHANICAL OUTCOMES 1 YEAR AFTER ACL RECONSTRUCTION AND MENISCUS SURGERY

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By

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ABSTRACT

Post-traumatic osteoarthritis (PTOA) is a long-term outcome following anterior cruciate ligament reconstruction (ACLR) surgery. PTOA is defined by pain limitations during movement and the degeneration of articular cartilage. This study aimed to investigate side-to-side differences in arthrokinematics and quantitative magnetic resonance imaging (qMRI) in patients who underwent ACLR with meniscal surgery. Nine participants who had undergone ACLR surgery with meniscal repair and/or partial meniscectomy were included in this study. Arthrokinematic analysis was performed during walking and jogging activities. qMRI measurements, including $T1\rho$ and $T2^*$ relaxation times, were assessed to evaluate cartilage composition. qMRI measurements were acquired with patients laying supine in the MR scanner without an external load applied, as is performed normally, and while a MR-compatible device applied an axial load equivalent to 50% of body weight. The results showed posterior shifts in contact locations during walking, increased cartilage overlap during walking and jogging, and higher sliding velocities in the posterior direction in the injured knee compared to the uninjured knee. The qMRI analysis revealed increased $T1\rho$, decreased loaded $T2^*$ relaxation times and the higher effect of load in the injured knees. These findings contribute to our understanding of the effects of ACLR surgery on arthrokinematics and cartilage composition.

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و در آخر، میخواهم از خانواده‌ام بابت تحمل فاصله و اجازه دادن به من برای پیگیری رویاهایم سپاسگزاری کنم. در زندگی‌ام فقط یک وظیفه دارم و آن این است که شما را به خوشحالی برسانم و به خاطر می‌گیرم و این را قول می‌دهم.

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1.1 POST-TRAUMATIC OSTEOARTHRITIS

Anterior cruciate ligament (ACL) tear is among the most prevalent and serious injuries affecting the youthful athletic community (1; 2). With the advent of novel surgical techniques and rehabilitation, athletes can now undergo ligament reconstruction procedures that effectively restore joint stability. While patients regain their physical abilities shortly after the surgery, previous studies illustrate long-term consequences of ACL reconstruction (ACLR) surgery on their knees. Post-traumatic osteoarthritis, which is the result of degeneration of articular cartilage, is the most concerning long-term repercussion that patients suffer after the ACLR.

Osteoarthritis (OA) stands as the primary cause of mobility limitations among elderly individuals in the United States (3). The prevalence of OA has been steadily increasing, with a rise of 6 million adults affected between 1995 and 2005. It is projected that by 2030, the total number of OA cases will reach 67 million (4). Moreover, People who experience OA following ACLR generally encounter this condition 15-20 years earlier compared to individuals without a previous traumatic knee injury (5). Thus, there is an urgent need for targeted therapies aimed at reducing the incidence of post-traumatic osteoarthritis (PTOA) (5)

In 2004, Lohmander et al. evaluated 67 ACL-injured women soccer players, and they found that 34 of the patients (50 %) developed osteoarthritis within 12 years after the surgery (6) . Two years later in 2006, Seon et al reported that 43 % of their participants (43 ACL reconstructed patients) demonstrated the signs of radiographic osteoarthritis within 8-13 years after the surgery (7). In 2010, Oistad found out that within 182 of their subjects who had undergone ACLR and meniscal lesion, 80% developed osteoarthritis 10-15 years after the incidence (8). Moreover, Stephan G. Bodkin et al, performed a study on 10,516 ACLR participants, and they announced that 12% of the total population suffered from the degenerative osteoarthritis only 5 years after the surgery (9). Therefore, the clarity of the articular cartilage's degeneration as a long-term consequence of ACLR, specifically when combined with meniscal surgery, has drawn the attention of orthopedic clinicians and researchers.

Although previous studies presented evidence of long-term changes in kinematics and cartilage morphology resulting from the ACLR surgery (6; 8) , the immediate presence and timing of these alterations following surgery remain uncertain primarily due to the constraints of conventional imaging methods. Thus, the mechanism that initiates and drives this degenerative process has yet to be found.

1.2 MECHANISMS CONTRIBUTING TO THE DEVELOPMENT OF POST-TRAUMATIC OSTEOARTHRITIS (PTOA)

To advance therapeutic interventions for PTOA, it is crucial to gain a comprehensive understanding of its initiation and progression. The sequence of post-traumatic osteoarthritis (PTOA) commences with an initial ACL tear. Following this, patients undergo ACL reconstruction surgery, aimed at restoring joint stability. Nevertheless, despite regaining joint stability, patients may experience the onset of osteoarthritis in the affected joint after a period of 5-20 years. The hypothesis of this study is that after the surgery, patients experience alteration to their arthrokinematics (the way the two main components of the knee joint, the femur and tibia, articulate) during their routine physical activities such as walking and jogging (Figure 1). Thereafter, the abnormal arthrokinematics in the injured knee will cause the articular cartilage to encounter atypical loading patterns. Eventually, abnormal mechanical environment produces changes in cartilage thickness and degradation of articular cartilage.

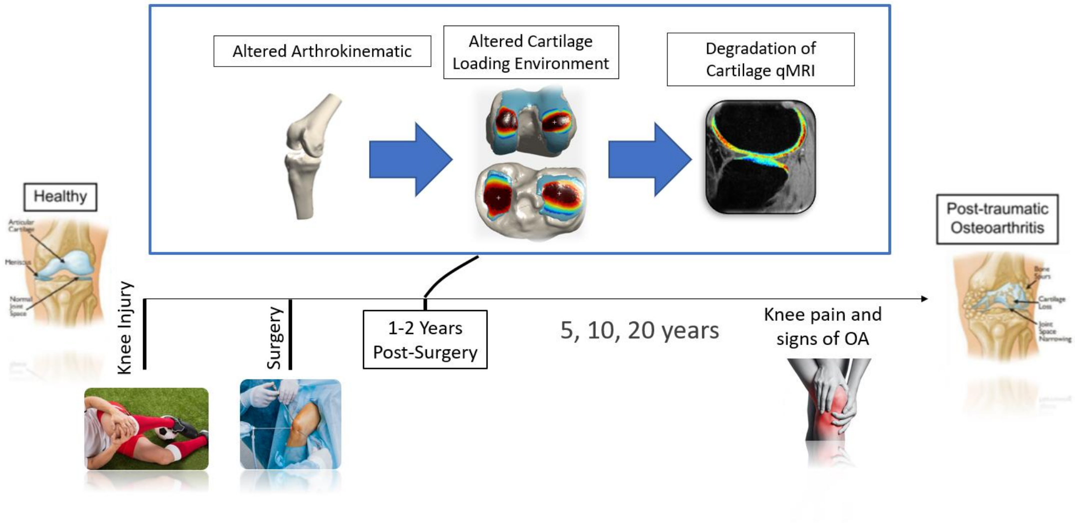

Figure 1. The hypothesis of this study: PTOA timeline

There is a growing focus on the utilization of model-based tracking (MBT) combined with high-speed dual fluoroscopic imaging for capturing biomechanical outcomes. MBT offers significant advantages, including accurate tracking with small bias and precision less than one degree and one mm. By incorporating subject-specific tissue models, MBT enables the measurement of cartilage contact mechanics. This technique is a substantial improvement over traditional kinematic and kinetic analyses that rely on optical marker tracking (10).

Furthermore, quantitative magnetic resonance imaging (qMRI) has garnered significant attention in the assessment of early-onset osteoarthritis disease onset and progression. In particular, qMRI parameters such as T1ρ and T2*, which are correlated with water content and proteoglycan content of the cartilage, have proven valuable in evaluating the matrix composition of articular cartilage. The advantage of using qMRI is that changes in cartilage composition can occur before morphological changes, which have traditionally been relied upon to measure PTOA-related changes. Both qMRI and MBT approaches demand substantial personnel, time, technical expertise, and financial resources. As a result, there is a limited understanding of the relationship between arthrokinematic outcome metrics obtained through MBT and compositional metrics derived from qMRI measurements.

Therefore, this study aims to accomplish two objectives: first, to evaluate outcome metrics related to arthrokinematics through MBT 1-2 years after surgery, and second, to assess qMRI metrics of cartilage composition at the same timeframe.

CHAPTER 2 METHODOLOGY

2.1 PARTICIPANTS

A total of 9 participants, comprising 5 males and 4 females, with an average age of 26 ± 5 years (ranging from 18 to 35 years), were included in the study. The participants had an average BMI of 24.5 ± 3.6 kg/m^2 (ranging from 18.6 to 29.5 kg/m^2). The average time since surgery was 1.4 ± 0.3 years (ranging from 1.0 to 1.96 years). All participants provided written informed consent prior to their involvement in the study. Each participant in the study underwent ACLR using an ipsilateral bone-patellar tendon-bone autograft. In addition, they received either a meniscus repair or partial meniscectomy procedure, as indicated in Table 1. Furthermore, all participants reported having an uninjured contralateral limb, which was confirmed through MR scanning and assessment by a board-certified musculoskeletal fellowship trained radiologist.

2.2 COMPUTED TOMOGROPHY

Bilateral computed tomography (CT) images were obtained using an iCT SP imaging system (Philips Eindhoven, Netherlands). The CT acquisition parameters were configured to include a slice thickness of 0.67 mm, 120 KVp and an in-plane resolution of 0.195 mm per pixel. The field of view (FOV) for the images was set at 300 mm.

Table 1.Participant and meniscal injury (treatment) characteristics

Subject	*Sex*	*Injured Knee*	*Meniscus injury Compartment*
S01	Male	Left	Medial complex tear (repaired)
S02	Male	Right	Medial longitudinal tear (repaired)
S03	Female	Left	Medial longitudinal tear (repaired); Lateral complex tear (repaired)
S04	Male	Left	Medial complex tear (repaired + resected)
*S05**	Female	Left	Medial complex tear (repaired); Lateral complex tear (repaired)
S07	Male	Right	Medial RAMP lesion; Lateral root tear (resected); Lateral complex tear (repaired)
*S08***	Female	Right	Medial tear (resected)
S09	Female	Right	Medial longitudinal tear (repaired + resected); Medial ramp lesion (repaired); Lateral complex tear (repaired + resection)
S10	Female	Right	Lateral complex tear (repaired + resected)
S11	Female	Left	Medial oblique undersurface tear (repaired)
S12	Male	Left	Medial meniscus buckethandel repair and partial meniscectomy

** Subject withdrawn due to scheduling conflicts*

***Subject withdrawn due to Incidental MR findings*

2.3 MAGNETIC RESONANCE IMAGING (MRI)

For the MR scanning session, the subject's left knee was off-weighted 15 minutes before any image acquisitions. Bilateral scans were performed on all participants. Initially, proton density (for clinical assessment) and T1ρ images of the left knee were captured while the subject was lying down in an unloaded position. Following this, T1ρ and T2* images of the left knee were obtained while applying a compressive load equivalent to 50% of the subject's body weight using an MRI loading device (**Figure 2**). The same process was repeated for the right knee, except for the off-weighting since the participants' right knee remained non-weightbearing during the scanning of the left knee. T1ρ measurements were performed using a three-dimensional (3D) magnetization prepared angle modulated partitioned k-space spoiled gradient echo snapshots (3D MAPSS) sequence. T2* measurements were conducted using a 3D gradient echo sequence with a spiral-out k-space and stack of spirals trajectory sampling strategy.

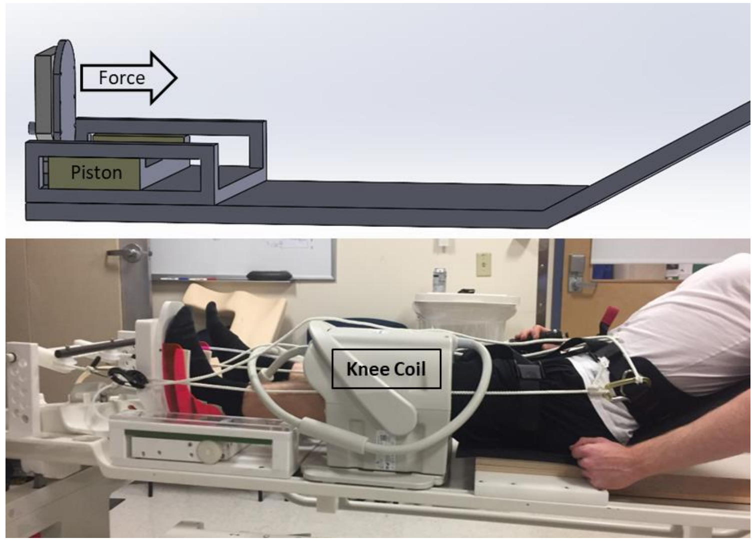

Figure 2. The pneumatic-controlled MRI loading device applies a superiorly directed force to the plantar aspect of the foot. Researchers control the air pressure in two pistons, which applies a superiorly directed force to the foot. To secure the participants during the scanning process, a climbing harness attached to the pelvis and the frictional force exerted by the angled back rest are used in combination. This ensures the participants' stability and limits any unwanted movement during the imaging procedure.

2.4 MOTION CAPTURE DATA COLLECTION

Each participant actively participated in three distinct activities: standing, walking, and jogging. These activities were performed while simultaneously recording full-body optical marker locations, high-speed dual fluoroscopic images, and ground reaction forces (GRFs).

The full-body marker locations were captured using a ten-camera motion capture system (VICON) operating at a frequency of 125 Hz. This system allowed for precise tracking of the markers placed on the participant's body throughout the activities.

High-speed dual fluoroscopic images were acquired using a well-established and validated system (10). The images had dimensions of 1024 × 1024 pixels and were captured at a frame rate of 250 frames per second. The emitter parameters were configured to 125 kV and 5 mA.

To measure GRFs exerted during the activities, a force plate (AMTI) was embedded beneath the field of view (FOV) of the dual fluoroscopic imaging system (DFIS) **(Figure 3).** The GRFs were sampled at a rate of 1000 Hz, providing finely sampled data on the forces experienced by the participants during each activity.

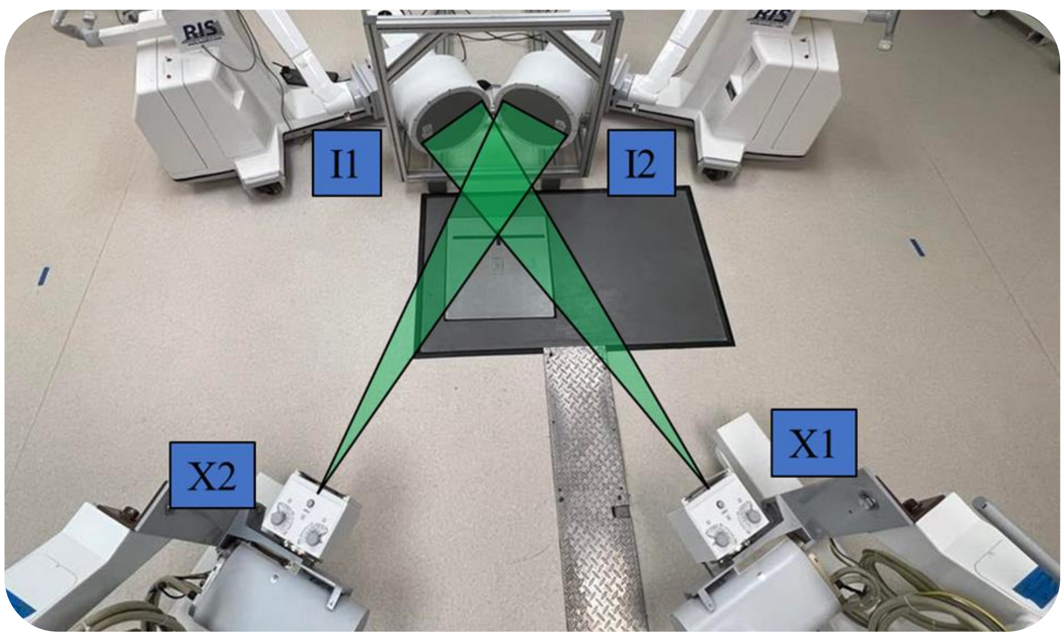

Figure 3. Dual fluoroscopic imaging system and a force plate embedded beneath it. The intersection of two green areas represents the trackable field of view.

Given the limited and non-adjustable FOV of the DFIS, the dynamic activities were performed in both directions along the lab's walkway. This approach ensured that the knees were properly centered within the FOV for optimal imaging. The sequence of the activities started with the left knee followed by the right knee.

Except for the standing activity, the dynamic activities were repeated three times. The initial trial was always performed with the left side to ensure the capture of at least one successful trial. A successful trial was defined as one in which both main components of the knee were clearly visible within the FOV of the DFIS at heel strike. For each activity and each limb, the trial that captured the largest percentage of the gait cycle within the FOV of the DFIS was selected for subsequent post-processing and analysis.

2.5 ARTHROKINEMATIC ANALYSIS

Patient-specific 3D bone models were constructed from the CT scans by using a semi-automatic segmentation process (Seg3D v2.4.4, University of Utah). The anatomical coordinate system, bone poses and knee joint 6 DOF kinematics were measured by a previously validated system for all the activities for both injured and uninjured joints. Heel strike and the peak load of the loading phase of gait were detected by force plate data for each trial. Subsequently, the bone poses were resampled using linear interpolation to generate a set of 100 evenly spaced poses between the instances of heel strike and maximum loading. In addition, bone and cartilage models were segmented from T1ρ MR images and the surface models were smoothened and meshed with an edge length of 0.75 mm (MeshLab v2012.12, Visual Computing Lab). Afterwards, MR bone models were registered to its corresponding CT bone models for the MR-to-CT transformation matrix to be obtained. The transformation matrix was used for MR cartilage-to-CT bone registration.

This study assessed three arthrokinematic outcome measures to compare the disparities between injured and uninjured joints through MATLAB (The MathWorks Inc., Natick, MA) software. These measures included: 1) Weighted contact centroids 2) the sliding velocity of centroids and 3) the volume of overlap between two cartilages.

Initially, cartilage models were converted into point clouds, each point of which represents a segmented cartilage pixel. At 50% and 20% of the heel strike to max loading interval for the walk and jog activities, respectively, cartilages' weighted contact points were assessed with the following steps. At first, for the tibia and femur to be in the same coordinate system, the tibia was transformed into the femoral coordinate system at each frame. Secondly, at each frame, to find the center of contact, the distance between every femoral cartilage's surface point with its closest tibial cartilage's surface point in sagittal plane and in perpendicular direction was measured. All the points outside of a 3mm threshold of the other cartilage model were excluded. Lastly, using a continuous weighting algorithm, the overlap points were given a weight of 3 and the other points were given a weight as a function of their distance:

$$Wieght(n) = [dist(n) - 3]^2$$

where n is the pixel's number and dist(n) represents the sagittal distance from the closest point from the other cartilage.

Registering the left tibia to the right tibia, left-to-right transformation matrix was extracted to transform the centroid of the left tibia to the right one to be able to compare the contact location of the injured knee with the uninjured knee. Subsequently, for each participant, the anterior-posterior and medial-lateral positions of the contact points of the injured knee were compared to the uninjured knee.

Then, the differences in AP and ML positions of the contact points (injured - uninjured) as a percentage of the plateau's ML width and AP length were reported. The second arthrokinematic outcome metric, the sliding velocity of weighted centroid, was measured with the following steps at 50% and 20% of the loading phase for walk and jog, respectively. Firstly, the cartilage's centroid velocities were measured by using the central difference method (11). Subsequently, the femoral cartilage's centroid velocity was converted to the tibial coordinate system. Then by subtracting the tibial centroids' velocities by the femoral centroids' velocities, the sliding velocity was defined as the AP and ML relative centroids' velocities (tibial - femoral) (12).

Cartilage overlapping volume was also assessed by the numbers of overlap points by the voxel size of MR images at 50% and 20 % of the loading phase for walk and jog, respectively.

2.6 QMRI ANALYSIS

From each cartilage, three sagittal slices centered at 20% and 80% of the width of tibial plateau (**Figure 3)** were picked and segmented for each compartment representing the load-bearing regions of cartilages during stance for all three scans (T1ρ, T1ρ loaded, and the T2* loaded) (13). The contact regions of cartilage were selected as the ROIs for each compartment. All spin lock image volumes were registered to the one that the segmentation was done on. Thereafter, for each segmented pixel within the ROI, a mono-exponential function was fitted to the signal's intensity to measure relaxation times for all the three scans.

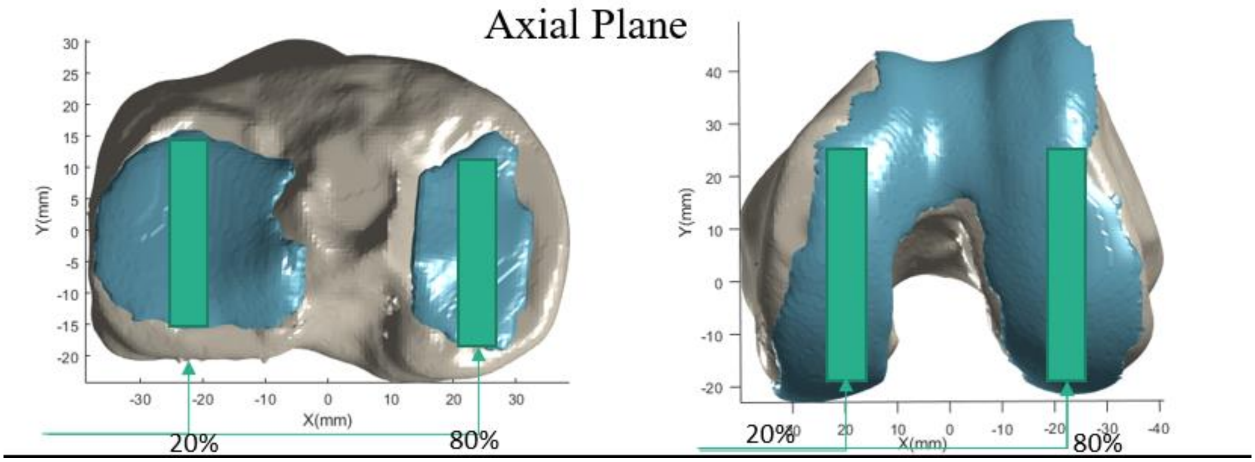

Figure 4. Region of interests in each compartment for measuring quantitative values

Finally, the mean of the relaxation times from all the pixels within a region of interest (ROI) was computed and utilized as the representative T1ρ or T2* relaxation time for that particular ROI.

Based on the findings from our previous repeatability analysis in healthy knees, we introduced a systematic bias of 3.4 ms and 2.5 ms to the left region of interests (ROIs) for the T1ρ and T2* measurements, respectively.

2.7 STATISTICAL ANALYSIS

To evaluate the first aim of this study which was the arthrokinematic changes after the surgery, the contact locations of injured knee were compared to the uninjured knee and projected on the right limb to be able to determine the AP and ML differences. Thereafter, the AP and ML differences were normalized over tibial AP length and ML length, respectively. For relative velocity, the injured knee's sliding velocity was subtracted by the uninjured one. In addition, the difference of the overlap points between the injured and uninjured knee was measured as the changes in overlap volume and the average of all the subjects' overlap points for injured and uninjured knees was determined.

To quantify the second aim of qMRI changes after ACLR+M, the average of relaxion time for each compartment was measured as the qMRI value for that compartment. Following that, the qMRI value of the injured limb was subtracted by the value of its corresponding compartment on the uninvolved joint. This process was done for both T1ρ unloaded, T1ρ loaded and T2* loaded scans to assess the qMRI differences of injured knee from the uninjured one. To compare the effect of load on cartilage composition on both involved and uninvolved joints, the qMRI values of the T1ρ loaded scan was subtracted by T1ρ unloaded values and then averaged over all the patients.

As the recruitment of participants for this study is still ongoing, no statistical tests have been conducted. Consequently, all the analyses performed in this study are descriptive.

CHAPTER 3 RESULTS

3.1 ARTHROKINEMATICS

3.1.1 Contact Centroids

A posterior shift of contact locations was observed in the medial compartment for 8 out of 9 subjects, ranging from 0% to -19% (**Table 2**), at the 50% loading phase of walking. Additionally, all patients displayed a greater difference in anterior-posterior (AP) compared to the medial-lateral (ML). In the lateral compartment, 7 subjects exhibited a larger side-to-side difference in the AP than the ML, while 6 of them demonstrated more posterior contact locations. (**Figure 4**).

In contrast, during the jog activity, subjects did not exhibit any consistent variations in the locations of their weighted centroids between the injured and uninjured joints.

3.1.2 Overlapping Volume

For both activities and in both compartments, six of the nine subjects exhibited an increase in overlapping volume in their injured knee compared to their uninvolved knee. In addition, there was an increase in the average of overlap volume in injured knee versus uninjured knee for both activities **(Figures 4 and 5).**

Table 2. Arthrokinematic results for all patients at 50% of the loading phase for walk and 20% for jog. Mediolateral (ML) and anteroposterior (AP) contact locations are expressed as differences between injured limb and uninjured limb over the ML and AP width of tibial plateau. The overlap outcome is measured as the number of overlap pixels (injured - uninjured). ML and AP velocities are represented as the injured-uninjured centroids' relative velocities (mm/s). The metrics demonstrated consistent side-to-side differences were highlighted.

		Medial					*Lateral*				
	Subject	Pos ML	Pos AP	Overlap	ML Vel	AP Vel	Pos ML	Pos AP	Overlap	ML Vel	AP Vel
Walk at 50% HS-ML	01	-7%	-14%	1323	-40	-20	-4%	-4%	-1158	-44	8
	02	1%	-4%	2684	-9	-7	-7%	-9%	887	-14	41
	03	0%	0%	-158	-6	-25	1%	-2%	-130	-4	-21
	04	-1%	-7%	2751	8	-32	-1%	-2%	1061	9	-20
	07	3%	-6%	535	48	61	2%	2%	639	51	18
	09	-3%	-10%	352	37	32	-5%	-6%	197	44	-23
	10	-1%	-4%	179	3	-5	-2%	7%	1305	4	-9
	11	0%	-19%	-305	-65	26	-3%	-12%	-661	-62	-25
	12	-7%	-12%	-1926	-31	-32	-5%	3%	-352	-38	55
Jog at 20% HS-ML	01	-2%	0%	401	-15	-19	6%	-1%	-779	-19	22
	02	1%	-3%	2256	59	-34	-7%	11%	4539	62	-141
	03	2%	1%	447	31	-4	3%	-3%	919	33	-3
	04	8%	4%	2668	-1	4	3%	-4%	-2340	24	-90
	07	7%	0%	-110	-40	60	11%	-8%	795	-36	54
	09	-3%	-5%	1146	60	-29	-5%	2%	605	63	-69
	10	-4%	-14%	-283	14	-5	-6%	2%	-575	19	-17
	11	1%	-6%	1509	-29	10	0%	-4%	567	-26	21
	12	9%	6%	-1261	-23	-16	11%	-6%	660	-36	59

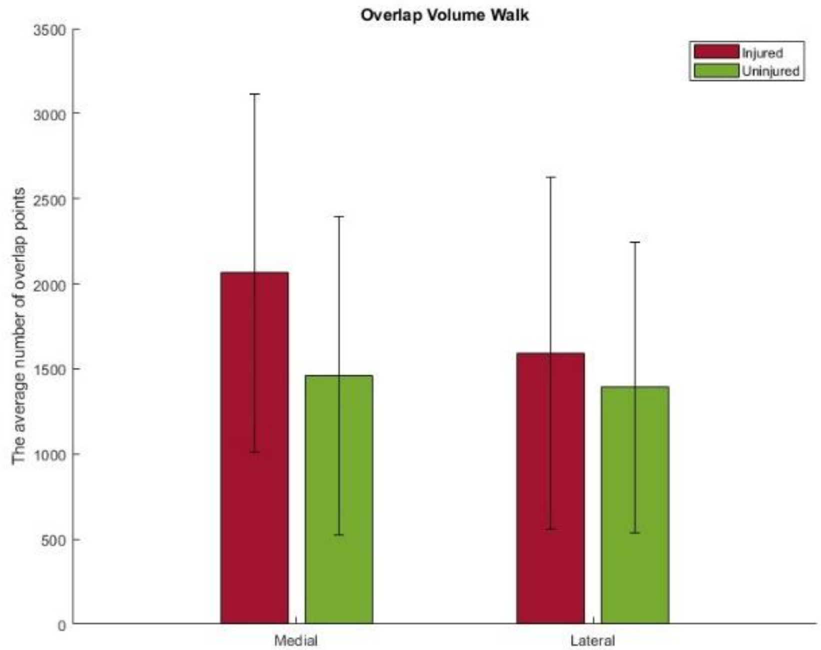

Figure 5. The average of overlap points for each compartment for both injured and uninjured joints for the walk activity at 50% the loading phase

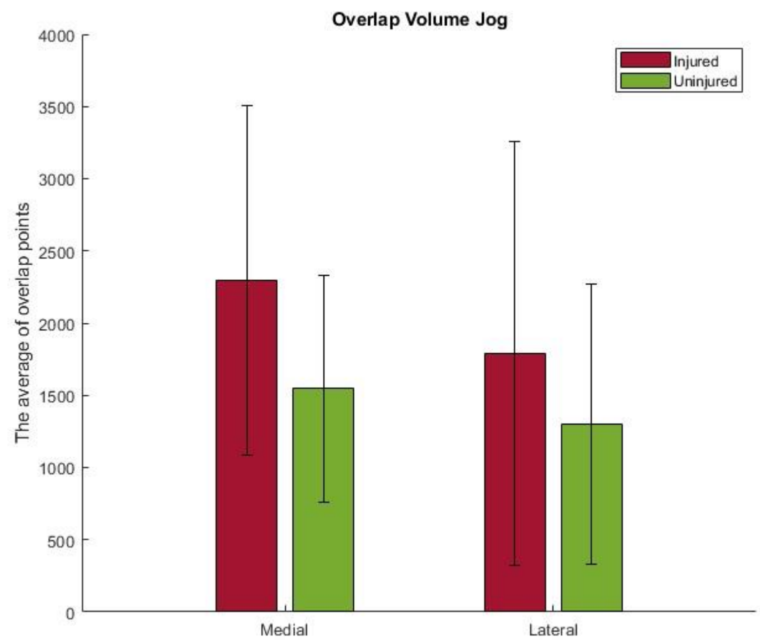

Figure 6. The average of overlap points for each compartment for both injured and uninjured joints for the jog activity at 20% the loading phase

3.1.3 Sliding Velocity

For both the walk and jog activities, six subjects displayed an increase in AP centroids' relative velocity in the posterior direction in the medial compartment.

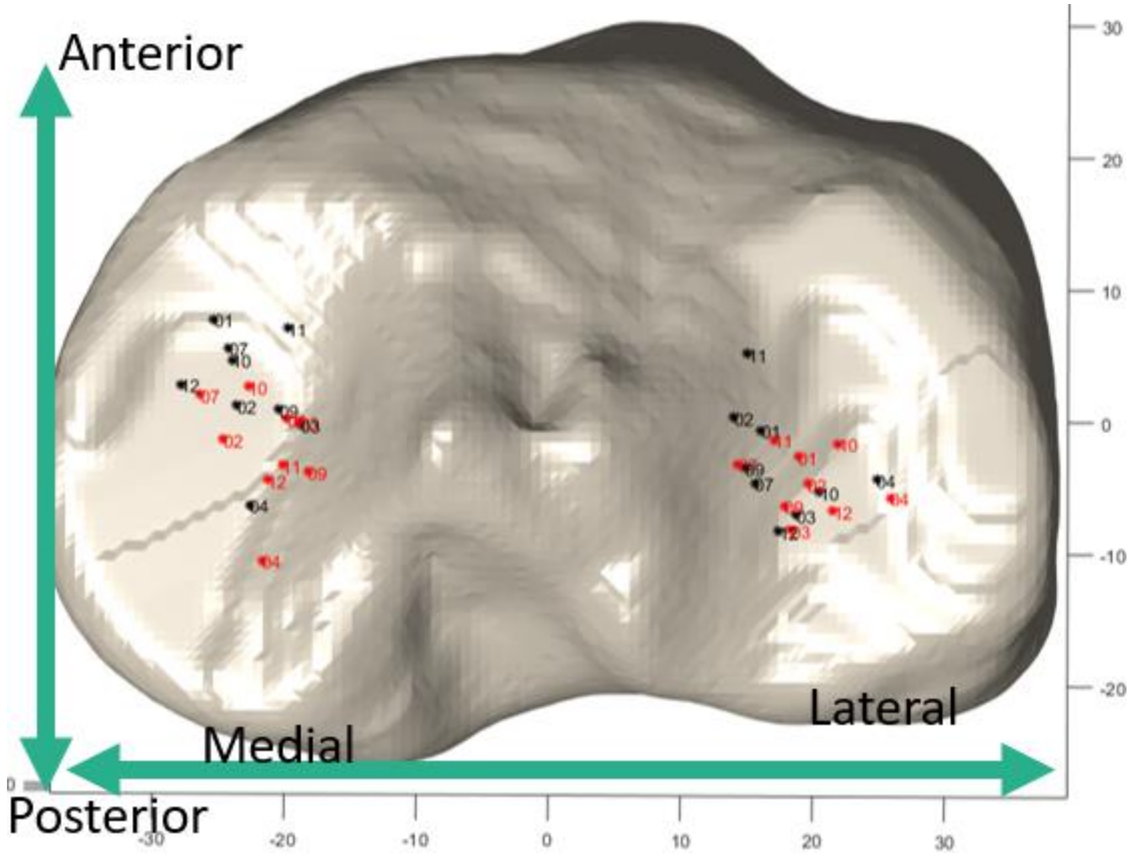

Figure 7. The contact points at 50% heel strike to midstance for the walk activities are displayed. In each compartment, the contact locations are indicated for the uninjured knee (represented in black) and the injured knee (represented in red).

3.2 QUANTITATIVE MRI

The qMRI outcome metrics are reported in **Table 3.** There was no metric that consistently exhibited a discernible alteration between the injured and uninjured limbs for all the patients. However, on average, there was an increase in the T1ρ of the injured knees compared to the uninjured limbs (**Figure 5**). Moreover, on average, there was a decrease in T2* loaded relaxation times from uninjured to injured knees (**Figure 6**). For tibial compartments, there was a decrease in the average of the effect of load in T1ρ relaxion times for both injured and uninjured knees, while there was an increase in the femoral compartments. Injured knees exhibited a larger effect of load in magnitude in all the ROIs compared to the uninjured knees (**Figure 7**).

Table 3.QMRI outcomes for each subject are measured as the difference between the relaxation times (ms) for the injured and uninjured conditions. The measurements are taken for the medial (Med) and lateral (Lat) compartments of both the tibia (Tib) and femur (Fem). The specific QMRI outcomes are T1ρ loaded (T1ρLD), T1ρ unloaded (T1ρUL), and T2* loaded (T2*LD).

	Subject	*Med-Tib*	*Lat-Tib*	*Med-Fem*	*Lat-Fem*
T1ρLD	01	7.34	4.11	5.09	3.75
	02	-9.57	-2.05	4.04	8.45
	03	-13.27	-7.75	16.34	21.24
	04	5.18	-4.25	14.37	9.10
	07	-1.95	-0.51	4.28	-0.20
	09	-11.86	-4.33	0.38	1.70
	10	4.34	-2.22	-2.24	7.07
	11	9.60	7.02	-4.08	-2.09
	12	-11.45	0.64.	-1.85	-4.15
	01	7.11	1.69	-3.22	0.73

T1ρUL	02	-0.85	-3.75	-0.62	5.88
	03	1.60	4.88	10.53	8.13
	04	17.79	3.48	-3.53	-6.82
	07	-5.07	-1.25	3.77	3.31
	09	-7.28	-6.58	13.45	6.66
	10	9	-4.82	-5.3	9.36
	11	3.77	1.51	7.26	1.80
	12	-5.41	0.42	4.27	13.06
*T2*LD*	01	-11.15	-8.30	-18.01	-5.28
	02	-10.38	-5.62	-5.54	-11.84
	03	5.03	5.61	-1.84	7.94
	04	4.47	-5.61	6.61	4.05
	07	-1.20	-2.23	6.07	-0.18
	09	-12.34	-5.49	-14.92	-6.19
	10	36.73	0.97	-10.42	-27
	11	1.90	-0.51	-18.14	-14.16
	12	-2.4	4.89	8.32	7.86

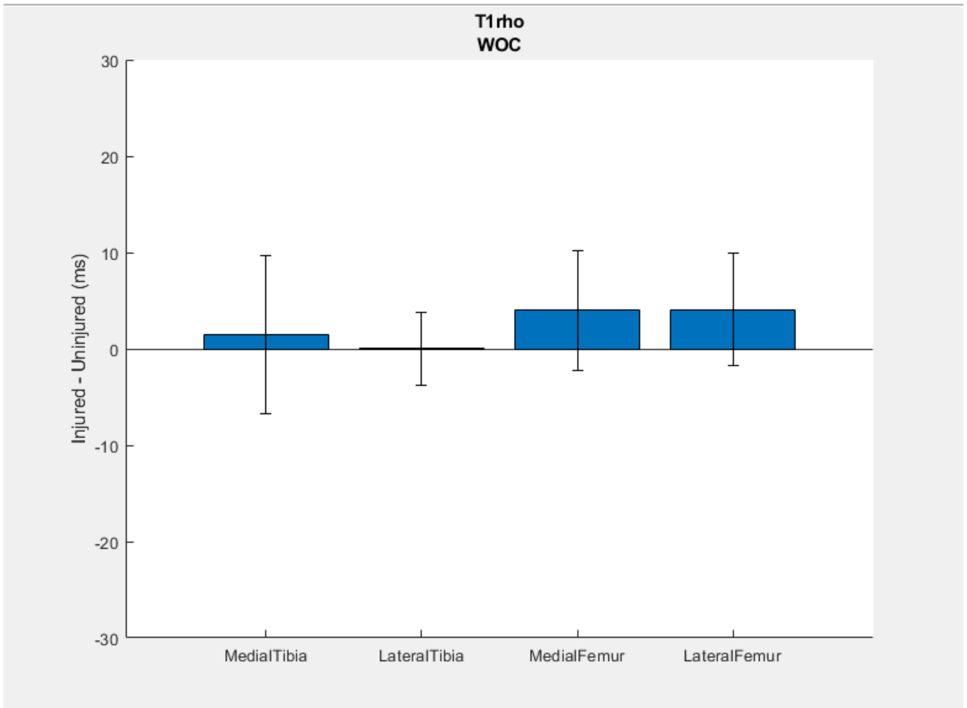

Figure 8. The average difference and standard deviations in T1 unloaded relaxion between injured and uninjured for each compartment.

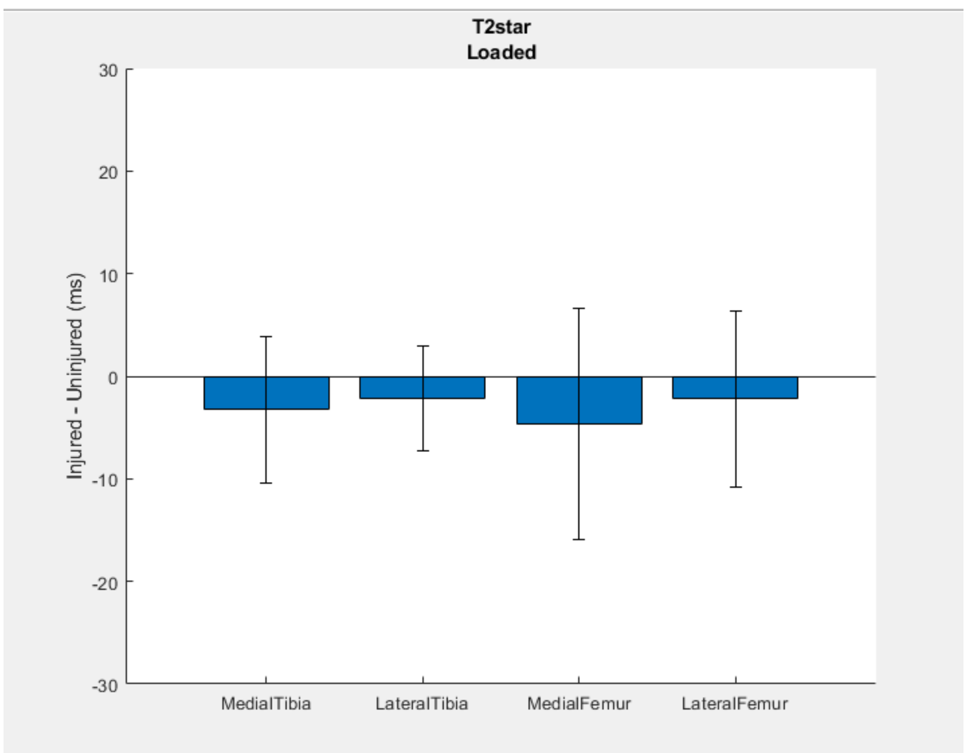

Figure 9. The average difference and standard deviations in T1 unloaded relaxion between injured and uninjured for each compartment.

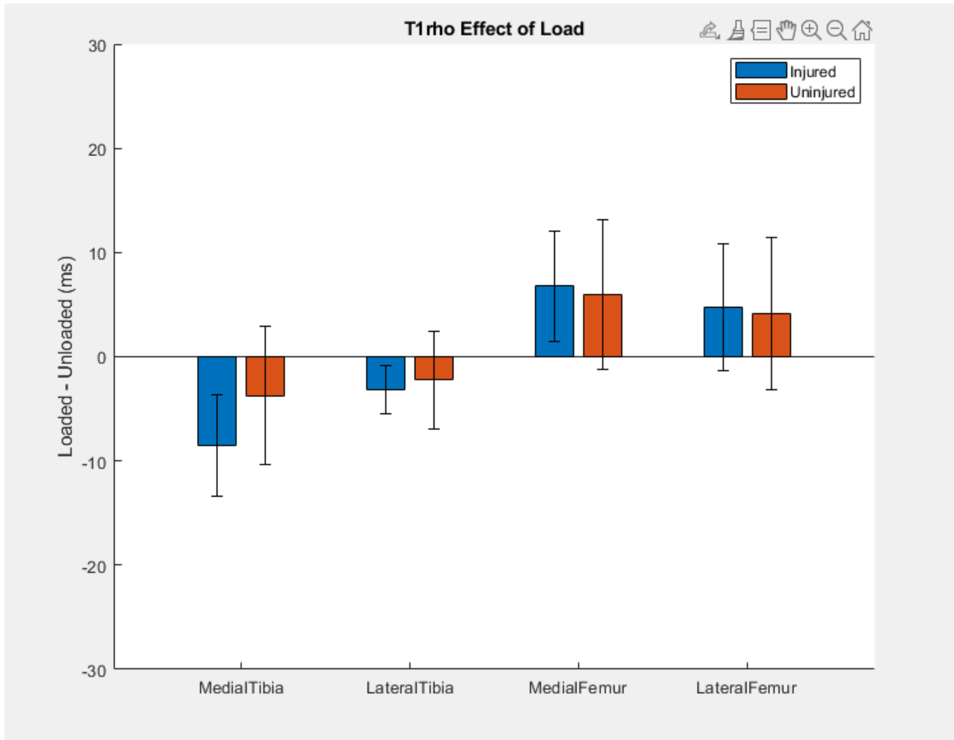

Figure 10. The average effect of load for injured and uninjured knees.

CHAPTER 4 DISCUSSION

The hypothesis of this study was that the ACLR+M surgery will affect the arthrokinematics (aim 1) and quantitative MRI (aim 2) of patients' surgical limb shortly after the surgery. Our arthrokinematic results at this timepoint, 1-2 years after the surgery, report: *i)* posterior shift of contact points for the injured knees at 50% loading phase in walk activity*, ii)* increased overlap for injured knees at 50% and 20% of the loading phase for the walk and jog activities, respectively, and *iii)* increase in the centroids' velocities toward the posterior direction. In other words, the anterior translation of the tibia in injured knees is observed as the posterior shift of the contact locations. Moreover, increased overlap between the cartilage layers illustrates more contact in injured knees versus the uninjured knees, and increased AP relative centroids' velocities in the posterior direction demonstrate the larger anterior sliding velocity of the tibia relative to the femur.

Our results are compatible with previous studies that evaluated kinematic alteration after ACL surgery and cartilage contact mechanics (14). In 2017, Kaiser et al. reported anterior tibial translation seen in the ACLR knees in an MRI-based study on 18 subjects 4 years after the surgery, which is consistent with this study (15). Furthermore, the study conducted by Anderst et al. also reported significantly greater anterior translation of the tibia in patients who underwent ACLR+M at 24 years after the surgery, which aligns with the findings of the present study (16). Moreover, this study reported that on average, there is an increase in contact volume in injured knees, which is compatible with a dual-fluoroscopic imaging study conducted by Anderst et al. in 2018 which revealed a larger contact area in ACLR knees (16). Nonetheless, by utilizing the point clouds of the cartilage models, we quantified the contact volume, encompassing both area and contact depth. This analysis offers us a deeper comprehension of the contact mechanics involved in articular cartilages.

As far as the author is aware, no previous studies have examined the changes in sliding velocity on ACLR patients. However, in 2013, Beveridge et al. conducted a study on sheeps, and they discovered a correlation between cartilage damage and tibifemoral centroid velocity (12). Moreover, in their *in vitro* experiments, Nickel et al. established a correlation between tractional force and an elevation in relative surface velocity (18; 19). Hence, the determination of sliding velocity provides insights into the distinct shear forces experienced by injured and uninjured knees, which could potentially contribute to the degeneration of articular cartilage.

However, at 50% and 20% of the HS-to-ML for walk and jog, respectively, there is not a large contact path between two consecutive frames compared to some particular gait events such as heel strike, max loading and hoof-off. Therefore, it is highly suggested to measure the sliding velocities at the heel strike, max loading and hoof-off gait points of interest in the future works.

Our qMRI's findings are in line with previous research as well. Specifically, we observed an increase in T1ρ values in ACLR knees, which is consistent with prior studies. T1ρ values are known to be negatively correlated with proteoglycan content. Therefore, our results suggest that ACLR joints exhibit a decrease in proteoglycan content. In 2019, Pfeiffer also reported a decrease in T1ρ values in ACLR subjects at 6 months post-surgery. This indicates a similar trend of T1ρ values in ACLR knees showing a decrease after the surgical intervention (19). In addition to that, this study also found a decrease in loaded T2* values in ACLR joints compared to the uninvolved knees. Since T2* values are correlated with collagen matrix degredation, a decrease in T2* relaxtion times describe a decrease in collagen matrix degredation in the injured knee. This could indicate the articular cartilage's healing process following the trauma. In simpler terms, the remodeling of the articular cartilage leads to an improvement in its matrix. In addition, T2* is also correlated with the water content of cartilage, a decrease in T2* values suggest a reduction in water content. Therefore, the observed decrease in T2* values in the injured knees indicates a decrease in water content within the cartilage under the applied 50% body weight load. To this date, the previous studies have only reported the T2* values without applying any load and they reported a considerable decrease in T2* after ACLR (20). Thus, the effect of load on cartilage's T2* values has yet to be determined.

Lastly, the present study showed the effect of load on T1ρ relaxion. The results highlight the larger absolute effects of the compressive load on T1ρ values. Moreover, on average, our results report a decrease in T1rho relaxtion times after applying load in the tibial compartments and increase in femoral compartments in both injured and uninjured knees. The variation in T1ρ values indicate significant alterations in the fluid movement within the femoral and tibial cartilage.

Nonetheless, this study has certain limitations. Firstly, the number of subjects is relatively small, with only 9 patients recruited to date, and the recruitment process is still ongoing. Secondly, due to the incomplete recruitment, no statistical analysis has been conducted on the dataset yet.

CHAPTER 5 CONCLUSIONS AND FUTURE WORK

The primary objective of this study was to investigate the side-to-side changes in arthrokinematic and quantitative magnetic resonance imaging (qMRI) outcome metrics. Various medical imaging modalities combined with image processing tools were employed to test the hypothesis of this study. The significant contribution of this research lies in the development of methodologies to measure arthrokinematic and qMRI outcome metrics and in examining the effects of ACL reconstruction surgery on patients' arthrokinematics (contact points, sliding velocity and overlap) and qMRI outcomes (T1rho loaded, T1rho unloaded, and T2* loaded). Our initial results point to a conclusion of anterior translation of the tibia, higher sliding velocity and larger contact volume in surgical limb in our arthrokinematic results, and also our qMRI measurement highlight an increase in T1rho values, decrease in T2* under load and the higher effect of load in the injured knee.

Furthermore, to establish a connection between the findings and the progression of the disease, it is strongly recommended to employ the MOAKS score in future research. By examining the correlation between changes in arthrokinematics and qMRI results with articular cartilage damage scores, a conclusive inference can be made regarding the origin of these changes from the disease.

To date, this study has conducted arthrokinematic analysis on only two activities for the initial nine subjects, namely walking and jogging. Additionally, three more activities—landing, lunging, and pivoting—have been collected. Moreover, the study is currently recruiting participants. Furthermore, the study includes two timepoints, with the second timepoint occurring one year after the first one. The amalgamation of data from these two timepoints and five activities will ultimately enhance our understanding of the biomarkers that contribute to the degenerative process of osteoarthritis following ACL reconstruction surgery. Specifically, the following suggestions are proposed for future research:

- Perform qMRI and arthrokinematic analysis on the new participants.
- Conduct arthrokinematic analysis on the remaining activities at the first timepoint.
- Calculate sliding velocity and overlap at heel strike and maximum loading.
- Conduct qMRI and arthrokinematic analysis at the second timepoint.
- Compare the findings from the first timepoint to those from the second timepoint.

By addressing these areas, a more comprehensive understanding of the subject matter can be achieved in future studies. "Initially, conducting a side-to-side comparison of arthrokinematic metrics between different activities will demonstrate whether the side-to-side differences are activity-dependent. By comparing the arthrokinematic metrics of timepoint one and timepoint two, it can be determined if the loading environment is changing. Additionally, by comparing the results of the timepoint one and timepoint two, an increase in qMRI metrics would suggest the progression of OA. Finally, to corroborate the hypothesis of this study, it is important to establish correlations between the side-to-side differences in arthrokinematics and qMRI metrics. This analysis will help determine whether individuals who exhibit greater differences in arthrokinematics at timepoint one also demonstrate larger qMRI differences at timepoint two, which provides support for the hypothesis that the progression of post-traumatic osteoarthritis (PTOA) is caused by the altered loading environment following ACLR+M surgery.

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