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Reduction of Risk Factors for ACL Re-injuries using an Innovative Biofeedback Approach: Rationale and Design

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ABSTRACT

Nearly 1 in 60 adolescent athletes will suffer anterior cruciate ligament (ACL) injuries with 90% of these athletes electing to undergo an ACL reconstruction (ACLR) at an estimated annual cost of $3 billion. While ACLR and subsequent rehabilitation allow these athletes to return to sports, they have a 15-fold increased risk of second ACL injuries. The modification of post-operative rehabilitation to improve movement and loading symmetry using visual and tactile biofeedback could decrease the risk factors for sustaining a second ACL injury. Participants included 40 adolescent ACLR patients who were intending to return to full sport participation. This preliminary randomized controlled trial (RCT) examined the changes in knee extension moment symmetry, a known risk factor for second ACL injuries, during landing from a stop-jump task between the following time-points: pre-intervention, immediate post-intervention, and subsequent follow-up 6-weeks post-intervention. Participants met twice per week for six-weeks (12-session). The intervention included bilateral squat biofeedback (visual and tactile); the attention control group attended weekly educational sessions. This RCT enrolled and randomize 40 participants over a two-and-a-half-year period. All participants were greater than 4.5 months post-op from a primary, unilateral ACLR and were released to participate by their treating physician. The findings from this pilot biofeedback RCT will provide critical effect size estimates for use in subsequent larger clinical trials.

Trial registration

ClinicalTrials.gov, NCT03273673.

1. Introduction

Over 200,000 anterior cruciate ligament (ACL) injuries are diagnosed annually in the United States [1,35] at an estimated annual cost of $3 billion [23,29,31]. ACL injury often leads to corrective surgical intervention and rehabilitation, with the goal of restoring joint stability. Most ACL reconstruction (ACLR) patients are adolescents and young adults (15–30 years old) [45] who seek to return to full sports participation. Unfortunately, athletes meet current guidelines for return to sport often have residual muscle imbalances, fear of re-injury, and altered lower extremity mechanics that exist up to two years following surgery and are associated with an increased risk of a second ACL tear [13,15,17,37,52]. Previous studies indicate that 91% [28] of young athletes (mean age: 14.3 years) and 81% [2] of older athletes (mean age: 25.8 years) return to sports following ACL reconstruction. Of those who do return to sport, up to 29% suffer a second ACL tear [38].

Second ACL injuries are a significant problem largely influenced by the failure of current therapeutic approaches to restore symmetry. Current therapeutic interventions and return to sport decisions are based on the time since surgery, typically six to twelve months after surgery, along with achieving full range of motion, optimal isokinetic strength, and acceptable graft stability. Unfortunately, these interventions have

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not been effective at decreasing the incidence of second ACL tears [3–5,17,37].

The assessment of side-to-side symmetry in healthy individuals is common [26,27,46], and more recently studies have shown that movement and loading asymmetries are present following injury and that these asymmetries are present two years post ACL reconstructive surgery [7–9,15,20,21,42–44]. Others have identified movement and load asymmetries as predictors of a second ACL injury [38,39]. Collectively, this work indicates that lower knee extension moment symmetry, as well as increased frontal plane valgus angle, and single limb balance stability are associated with an increased risk for a second ACL injury [39]. Patients with a knee extension moment asymmetry were three times more likely to incur a second ACL injury [39]. Asymmetrical loading and movement patterns are common in 83% of patients following return to full sport participation [16].

The development and use of biofeedback interventions demonstrate the ability to alter loading symmetry with visual feedback during a squatting task, however, the association between altering squatting mechanics and landing mechanics is unknown [33]. It is essential to assess the impact of new therapeutic techniques, such as biofeedback, to determine if improving neuromuscular control will decrease risk factors for second ACL injuries.

This paper describes the design of the Reduction of Risk Factors for ACL Re-injuries using an Innovative Biofeedback Approach (ACL-Biofeedback Trial) preliminary clinical trial. We expect the biofeedback intervention to result in improved knee extension moment symmetry at the immediate post-intervention (IP) visit with the biofeedback (B) group demonstrating improved symmetry when compared to the attention control group (C). This study will provide the foundation for future studies required to shift the post-operative rehabilitation paradigm to include the assessment and restoration of movement and loading symmetry before patients are returned to unrestricted sport participation.

2. Methods/design

2.1. Study design

The ACL-Biofeedback Trial is an assessor-blinded, single-center, 12-week, parallel design randomized controlled trial. Participants are randomized into one of two groups: biofeedback (B) or attention control education (C) (Fig. 1).

2.2. Study sample

The study sample consists of 40 adolescent ACLR patients who are intending to return to full sport participation. Inclusion criteria include: 1) primary, unilateral ACL reconstruction; 2) completion of at least 18 weeks of post-operative physical therapy, 3) willingness to comply with all study procedures, and 4) aged 14–21 years. Exclusion criteria were: 1) history of more than one ACLR, 2) post-operative complications that required additional surgical intervention, 3) live greater than 60 miles from the research lab, 4) any limitations that would prevent the patient from attending the biofeedback training sessions, 5) participating in

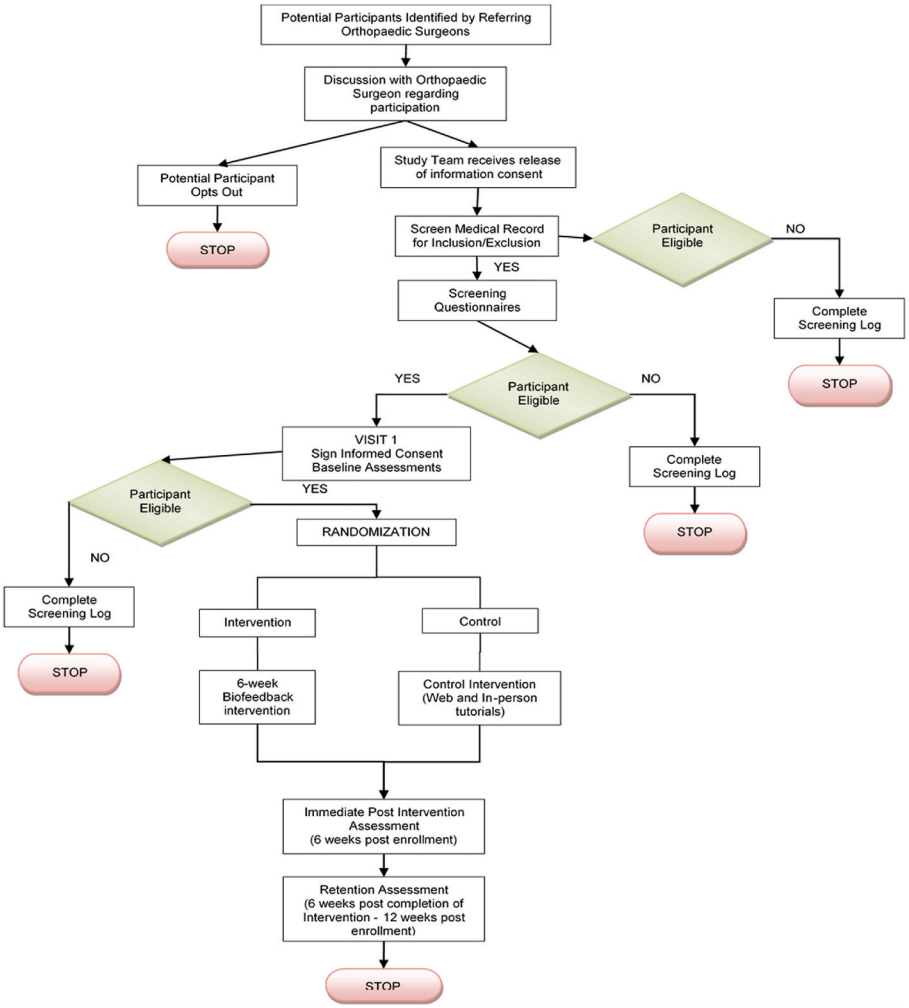

Fig. 1. Participant eligibility and screening flow chart.

another ACL intervention outside of standard post-operative physical therapy and 6) knee extension moment limb symmetry index (LSI) greater than or equal to 90% at the time of the initial study assessment. A full list of all inclusion and exclusion criteria are provided in Table 1.

The study protocol was reviewed and approved by the Human Research Protection Program at Virginia Tech (Human Protocol: IRB# 17-007). Informed consent was obtained from all study participants.

2.3. Interventions

2.3.1. Biofeedback

The 6-week biofeedback training program focused on improving loading and movement symmetry during bilateral squatting in biweekly intervention sessions on non-consecutive days (12 sessions). The biofeedback training program was designed to provide sensory (visual and tactile) feedback to the participant to heighten awareness of asymmetrical movement strategies (e.g. load shift, decreased movement symmetry) and neuromuscular control during a squat. The two exercises that were completed during the biofeedback training program were a visual feedback squat and a resisted squat (tactile feedback). Each of these tasks was completed 30 (3 sets of 10 repetitions) times per session. We provided a 20 s rest between trials, and a 10-min break between the visual and tactile feedback exercises to decrease the effects of fatigue. Prior to the biofeedback intervention session, each participant completed a 5-min warmup on a stationary bicycle.

Visual Feedback: The simplest way to provide biofeedback during a squat is through visual feedback of load. Under this approach, participants were asked to stand on force plates, which measure the ground reaction forces (load) beneath each foot. Shoulder width for each participant was measured as the distance between acromioclavicular joints. This distance was measured on the force plates and 2 pieces of tape were placed this distance apart (one on each force plate) and participants were asked to stand with one heel on each piece of tape. Stance width was recorded on the data collection sheet and then entered in the REDCap [24,25] database so that this distance could be used during each subsequent training and testing session and foot position could be measured and marked prior to participant arrival. Participants faced a projection screen that displayed 2 bar graphs of the vertical ground reaction force, depicting each foot's load. Participants were asked to stand with their feet shoulder width apart (one foot on each force plate) with their hands in front on them with the shoulder flexed to 90° for counterweight. The foot width was standardized to ensure that foot placement was consistent for both the squatting trials and during the biofeedback training. The participants were asked to squat until their thighs were parallel with the ground or until their heels begin to come off the ground, whichever occurred first. A stool was placed behind the participant (Fig. 2) and was set to the height where the participant's thighs were parallel to the ground if they sat down (stool was placed at the height of the popliteal fold), so that the participant would know the deepest position they have to achieve. If the participant was able to achieve a squat position where the thigh was parallel to the floor they were instructed to squat until they barely touch down on the bench and then slowly stand back up without transferring any weight to the bench (Fig. 2). Participants were asked to stand on the force plates and transfer weight between their feet and watch the visual biofeedback during bilateral squatting to see the change in load beneath each foot. After completing the practice bilateral squat, participants completed all subsequent squats with the goal of keeping the bars level on the graph or maintaining an LSI $\geq$90% (symmetric load on both feet) (Fig. 2). This process was completed a total of 30 times (3 sets of 10 repetitions each) during each of the training sessions with the same goal each time of maintaining the bars at an equal level. During all squatting tasks, participants were instructed to squat to the pace of a metronome that is set at 30 beats per minute and the participants were asked to complete one squat every two beats.

Tactile Feedback: The second set of exercises at each biofeedback session was a series of resisted squats. Participants were asked to squat while an external force was applied to the side of the knee (Fig. 3) requiring the participant to work against this resistance to maintain balance and complete the squat. The band was placed on the surgical limb of each patient and was pulled at approximately a 45-degree angle toward the contralateral side. Pulling the participant toward the non-operative limb (one that is typically displaying higher loads) required the participant to pull toward the surgical limb and maintain good frontal plane knee position by resisting frontal plane valgus. A handheld dynamometer (Rolyan Smart Handle, Performance Health, Warrenville, IL) was used to maintain a consistent load across trials and sessions. The clinician who completed the biofeedback session set this load based on their clinical judgement. This is a typical exercise utilized in the clinic to aid in equal weight bearing and active hip abduction. The squat position that was used during these exercises was the same as the squat position used in the visual biofeedback task and during the biomechanical testing. The participants were asked to stand with their feet at the same standard width as described in the visual feedback section and squat until they contacted the stool that was positioned behind them during the biofeedback session. Participants were asked to complete 30 tactile feedback squats (3 sets of 10 squats) during each of the biofeedback sessions.

Table 1
Full list of trial Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
Primary, unilateral ACL reconstruction	History of more than one ACLR
No pain in the contralateral leg	post-operative complications that required additional surgical intervention
Completion of at least 18 weeks of post-operative physical therapy	Hospitalization for any reason other than the ACLR in the last 3 months
Within 6 weeks of being ready to be released	Currently pregnant or planning to become pregnant
Willingness to comply with all study procedures and availability for the duration of the study	Plans for additional surgical procedures in the next 12 months
Aged 14–21 years	Live greater than 60 miles from the research lab
	Any limitations that would prevent the patient from attending the biofeedback training sessions
	Motor neuron diseases, Parkinson's disease, multiple sclerosis
	Severely impaired hearing or speech
	No access to a telephone
	Participating in another ACL intervention outside of standard post-operative physical therapy
	Attending post-operative physical therapy more than 2 times per week
	Inability to understand or speak English
	Self-reported medical problem that would prohibit participation in the study
	Health condition or personal issue judged by a study team or primary physician to make the patient inappropriate for study participation
	Knee extension moment limb symmetry index (LSI) greater than or equal to 90%

2.3.2. Attention Control

The 6-week attention control program focused on providing educational information to the participants related to the clinical and sports expectations as they are released to return to sport. These participants were asked to meet 6 times, once a week, during the 6-week intervention period. Three of these visits were completed in person and three were completed using an online educational module (6 sessions in total). The online sessions were completed in week 1, week 3, and week 5, while the in-person sessions were completed during week 2, week 4, and week 6. The content of these sessions focused on providing information on ACL

Fig. 2. Participant completing the visual feedback training.

Fig. 3. Participant completing the tactile feedback intervention.

reconstruction, athlete expectation as they return to sport, incidence, and risk factors for second ACL injuries, as well as some suggestions on the gradual progression back into sport. A short quiz was administered at the completion of each educational session to assess understanding of the content from each session.

2.4. Trial conduct

2.4.1. Recruitment

An 18-month recruitment period was used to recruit the target sample of 40 adolescent (between the ages of 14 and 21) participants for this study, who had a primary ACL reconstruction by one of the referring physicians. The predominant recruitment strategy was through referral from the treating orthopaedic surgeon. At weekly meetings, all recruitment activities and the number of participants referred, recruited, and randomized were reviewed.

We used the electronic medical record to identify all patients who had an ACLR within the last 4 months or who were scheduled to have an ACLR with any of the referring orthopaedic surgeons. The clinic schedule for each of the five referring physician was reviewed weekly to screen post-operative ACLR patients who meet the age (between 14 and 21) and time since surgery (approximately 4 months) inclusion criteria on a weekly basis and the patient was added to the potential study participant list. This list was generated for each referring orthopaedic surgeon and included identifying information about the patient, the scheduled appointment time and ACLR operative date. The patient, and the parents if the patient was a minor, of all potential participants was approached by the treating orthopaedic surgeon or member of the surgeon's clinical staff. If the patient was interested in participating in the study and the referring physician believed that the patient was medically ready to participate in the study, the surgeon completed and signed a release to participate form (available upon request to the first author) and asked the patient (and parent if the patient is a minor) to sign a release of information form. These two signed forms were returned to the study team as a referral to participate in the study. Once the release of information form was received the medical record was reviewed to

ensure that the potential participant met all inclusion and exclusion criteria for the study except for the knee extension moment limb symmetry index (LSI) being greater than or equal to 90% which was assessed at the initial study assessment (baseline) and served as the final enrollment criterion. All potential participants were contacted within one week of receiving the referral by a member of the study team to inform the potential participant as to whether they were eligible to participate in the study or not. If the patient was eligible and interested in participating an additional screening questionnaire was competed over the phone to ensure eligibility and answer any questions from potential participants and their parents before the first assessment visit is scheduled.

2.4.2. Techniques to improve adherence and retention

Participant retention began with the recruitment process. Based on medical records and release of information consent forms from the treating physician, only those patients who do not actively opt out were contacted by phone to receive follow-up information about the study and assess their interest in participating. Once enrolled in the study, all participants were contacted by the study team to schedule each measurement time point (baseline, 6 weeks and 12 weeks). In addition, based on group randomization the participants were in contact with the study team either two times a week for six weeks (Biofeedback Group) or once a week for six weeks (Attention Control). Participants who decide to withdraw from study were encouraged to complete the study assessments. The reason for any missed intervention sessions as well as assessment sessions were recorded for future analysis to improve planning for subsequent clinical trials. All successful and unsuccessful attempts to contact participants were documented within the participant's study record. Additionally, alternate phone numbers were requested from participants to aid in locating the participant. Participant recruitment and retention statistics were collected and monitored on a regular basis such that any problems or negative trends could be identified early, and appropriate measures taken and/or procedures modified.

2.5. Measurements

2.5.1. Screening and follow-up visits

Those who were eligible after completing the final screening questionnaire signed informed consent and complete the baseline assessment (BA). All 40 participants were measured at baseline and all those who meet the final inclusion criteria completed assessments at 6- and 12-weeks (Fig. 1 and Table 2). The 6-week assessment was the immediate post-intervention (IP) and the 12-week assessment was the retention visit (RV).

Following recruitment and the completion of informed consent, each participant completed a biomechanical assessment in the Kevin P. Granata Biomechanics Lab at Virginia Tech. All participants were asked to wear form fitting shorts and a shirt, and a standard pair of athletic shoes (Nike Pegasus, Nike Inc, Beaverton, CO) to use during testing (Fig. 4). Previous literature has shown that differences in footwear can alter the ground reaction forces [34,36]. Patients warmed up by riding a stationary bike at a comfortable pace for 5 min. After the warm-up, patients had retro-reflective markers attached on their skin to track segmental motion during both squatting and landing (Fig. 4). Three-dimensional coordinate data were collected using a 10–camera motion capture system at a sampling rate of 240 Hz (Qualisys, Gothenburg, Sweden) and 43 retroreflective markers in a modified Helen-Hayes marker set (Fig. 4) [45]. Ground-reaction forces were collected using a series of force plates at a sampling rate of 1920 Hz (AMTI, Watertown, Massachusetts). In-shoe plantar force was collected using size appropriate, loadsol® sensors sampling at 100 Hz (Novel Electronics, St. Paul, Minnesota). The loadsol® is a single sensor insole that was used to monitor real-time plantar load during each task for future analysis and clinical applications. Each participant was asked to complete a standing trial followed by a series of bilateral squatting and landing trials.

Table 2
Data collection visits.

Description	Baseline	Follow-up	
	Initial Biomechanical Assessment	Biomechanical Assessment 2 Week 6	Biomechanical Assessment 3 Week 12
Informed Consent	X		
Randomization (Following Baseline)	X		
Participant Demographics	X		
Height and Weight	X	X	X
Maximum Vertical Jump Height	X		
Tegner Physical Activity	X	X	X
ACL-RSI	X	X	X
KSES	X	X	X
Multidimensional LOC	X	X	X
TSK-11	X	X	X
Stop-Jump Assessment	X	X	X
Visual Analog Pain (previous 2 weeks)	X	X	X
Adverse Events	X	X	X
Serious Adverse Events	X	X	X

Squatting trial: With their feet shoulder width apart (one foot on each force plate) and their hands in front of them for counterweight, participants completed 15 bilateral squats. Stance width was standardized to ensure that foot placement was consistent for both the squatting trials and during the biofeedback training. Participants were asked to squat down until their thighs were parallel with the ground or until their heels began to come off the ground (Fig. 5). The squat assessment was completed so that the exact same setup and protocol was used for the biofeedback training program and obtained a baseline measure of skill during a squat.

Landing trial: The stop-jump task was selected based on its game-like nature. The stop-jump task is a good simulation of a basketball jump-shot or heading a soccer ball and therefore could produce loads and movements that are closely related to those seen during game play [41]. Participants were asked to complete 10 trials of a vertical stop-jump task. During the vertical stop-jump task, participants ran straight forward for up to 5 steps took off on 1 foot, landed on 2 feet (one foot on each force plate), and took off again on 2 feet [15,16,18,19]. Prior to testing, maximum jump height was determine using a Vertec vertical jump tester (Power Systems, Knoxville, TN). During testing, a ball was hung above the force plates at 75% of the participant's maximum jump height to provide a target during jumping (Fig. 6). Participants were instructed to jump up and tap the ball and then come down bilaterally on the two force plates. No instructions were provided on how to land or what to do with their arms to initiate the jump. The stop-jump task was used to determine if the biofeedback intervention was effective at decreasing second ACL risk factors. Participants could practice the task between 3 and 5 times until they are comfortable with the movement. A minimum of 5 min of rest was provided between conditions to minimize the effects of fatigue.

Data Reduction: Knee kinematics and kinetics were computed using Visual 3D (C-Motion, Bethesda, Maryland) and the 3D marker coordinate and ground reaction force data from the embedded force plates. Hip joint center locations were estimated based on the work of Bell et al. [6], and the knee and ankle joint center locations were estimated as the

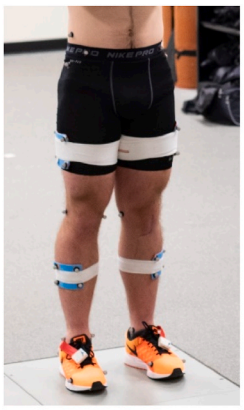

Table 2: Data Collection Visits

Description	Baseline	Follow-Up	
	Initial Biomechanical Assessment	Biomechanical Assessment 2 Week 6	Biomechanical Assessment 3 Week 12
Informed Consent	X		
Randomization (Following Baseline)	X		
Participant Demographics	X		
Height and Weight	X	X	X
Maximum Vertical Jump Height	X		
Tegner Physical Activity	X	X	X
ACL-RSI	X	X	X
KSES	X	X	X
Multidimensional LOC	X	X	X
TSK-11	X	X	X
Stop-Jump Assessment	X	X	X
Visual Analog Pain (previous 2 weeks)	X	X	X
Adverse Events	X	X	X
Serious Adverse Event	X	X	X

Fig. 4. Motion Capture set up and marker set used for data collection at each assessment visit.

Fig. 5. Testing setup for squatting assessments.

Fig. 6. Setup for the landing assessments. A) landing from the stop-jump followed by (B) a jump to a target.

midpoint between medial and lateral femoral epicondyle and malleoli markers, respectively. Kinematic and kinetic data during motion was low-pass filtered using a fourth-order recursive Butterworth filter with a cutoff frequency of 7 and 100 Hz, respectively. Knee joint angles and moments were computed during the descending phase of each bilateral squat and the landing phase of each stop jump, with flexion set as the

first and ab/adduction set as the second rotation in the Cardan rotation sequence. The descending phase of each squat was defined between the first frame when the pelvis center of mass exceeds 5 cm per second and the instant when the pelvis reaches its lowest vertical position. The landing phase of each stop jump was defined between the first frame when the vertical ground reaction force exceeded 25 N (for each limb) and ended when the pelvis reached its lowest vertical position. Peak internal knee extension moment symmetry (primary outcome measure) was computed during each trial using the limb symmetry index (Equation (1)) and averaged across trials for the bilateral squatting and landing tasks. The Limb Symmetry Index (LSI) is calculated as shown in Equation (1) with Sx indicating the value on the surgical limb and NSx indicating the value on the non-surgical limb.

$$\boldsymbol{LSI} = \boldsymbol{ABS}\left[\frac{\mathbf{Sx} - \mathbf{NSx}}{0.5(\mathbf{Sx} + \mathbf{NSx})}\right] \quad (1)$$

Peak vertical ground reaction force symmetry, ground reaction force impulse symmetry, peak knee flexion angle symmetry, peak flexion angle, peak knee abduction angle, and knee ab/adduction range of motion (secondary outcome measures) was computed during each trial and averaged across trials for both the landing and bilateral squatting tasks.

2.6. Patient reported outcomes

2.6.1. Tegner physical activity

The Tegner Physical Activity questionnaire assesses the current level of physical activity at the time when the instrument is completed. The Tegner [48] has adequate test–retest reliability (ICC = 0.82–0.97) [10,11,30,40], and acceptable validity [10,11].

2.6.2. ACL-Return to Sport after Injury (ACL-RSI)

The ACL-RSI is a 12-question measurement of an athlete's emotions, confidence in performance, and the patient's risk appraisal for returning to unrestricted physical activity following ACL reconstruction with each question being on a 0–10 scale with 0 indicating not at all confident to 10 extremely confident [53]. The ACL-RSI has high internal consistency (α = 0.960) [53] in previous work as well as the current study (α = 0.942).

2.6.3. Knee self-efficacy scale (K-SES)

The Knee Self-Efficacy Scale is a 22-question assessment that seeks to assess an individual's perceived ability to accomplish a task, not the actual ability to complete the task. Each question is rated on a scale on a 0 to 10 scale with 0 indicating that the participant is not certain at all and 10 being very certain. The internal consistency of the K-SES is 0.94 for the total test in previous studies [49] as well as the current study (α = 0.970). The K-SES has excellent test–retest validity with an intraclass correlation coefficient of 0.75 [49].

2.6.4. Multidimensional health locus of control scale (MHLC)

The multidimensional health locus of control scale is an 18-question assessment to determine if ACLR patients believe that they, as opposed to external, outside forces (e.g., parents, coaches, doctors), have control over their recovery and eventual return to activity [47]. Each question is answered on a scale from 1 to 6 with 1 being strongly disagree and 6 being strongly agree. The results of the MHLC are reliable (Cronbach alpha between 0.60 and 0.75) and good test–retest stability (coefficients from 0.60 to 0.70) [51]. The internal consistency of the MHLC for this study was moderate (α = 0.754).

2.6.5. Tampa scale for Kinesiophobia (TSK-11)

The TSK-11 is an 11-question assessment of an individual's fear of movement as it relates to the potential for re-injury as well as perceptions of pain changes that occur with physical activity [50,53,54]. Each question is answered on a scale from 1 to 4 with 1 being strongly disagree and 4 being strongly agree. The higher the score on the TSK-11, the greater the pain-related fear of movement or re-injury. The TSK-11 score has good internal consistency (α = 0.88) in previous research and good test-retest reliability (ICC = 0.81 and 0.93) [22,54]. The internal consistency for the TSK-11 was lower in the current study (α = 0.605) than was previously reported.

2.6.6. Adverse event collection and reporting

All adverse events (AEs) had their relationship to study intervention assessed by the trial medical director who examined and evaluated the participant based on temporal relationship and his clinical judgment. The degree of certainty about causality was determined to be related, probably related, or not related by the trial medical director.

The trial medical director and the principal investigator in consultation will be responsible for determining whether an AE is expected or unexpected. All AEs and SAEs were captured on the appropriate report form within the REDCap database. The study team recorded all reportable events with start dates occurring any time after informed consent was obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. All AEs and/or laboratory abnormalities identified in the protocol as critical to participant safety were reported to the NIAMS and the safety officer. All AEs experienced by a participant during the time frame specified in the protocol were reported. Study team members who became aware of any adverse event related to the study notified the principal investigator immediately who then notified of the Virginia Tech IRB within 24-h of a study-related death, within 5 business days for any another serious adverse event, and within 10 business days of a protocol deviation/violation, or other unanticipated problem. All AEs and protocol deviations were reported to the study's NAIMS safety officer on a biannual basis, or as requested. All SAEs were reported to the study's safety officer within 48 h of the event being made known to the investigator.

2.6.7. Randomization

A 1:1 block randomization with block size unknown to investigators and staff was utilized to ensure equal accrual to each study arm. Participants were allocated in one of the two study arms, with randomization stratified according to gender, age (young: 14–17 years old, older: 18–21 years old) and activity level (mild activity: Tegner score 1–3, moderate activity: Tegner 4–7, or vigorous activity: Tegner 8–11) to ensure that the groups were balanced in these respects. All participants continued with any other usual medical care they receive for their ACLR.

Eligible participants were randomized following the first biomechanical assessment (Baseline), during which informed consent was obtained. After the Baseline biomechanical assessment, participants were scheduled for their first study visit (biofeedback intervention or control in-person education session) at this time each participant was informed about the research arm to which they were assigned. Randomization was based on a computer-generated sequence maintained by the project statistician and implemented in the randomization module in REDCap [24,25] where the randomization assignment was entered and stored. As this is an assessor blinded trial, no participant unblinding procedures were necessary.

2.6.8. Data management

Data were uploaded to a web-based REDCap software program that is validated and meets HIPAA compliance rules [24,25]. New data were inspected for completeness and queried for programmed logic checks and out-of-range values. Only participants who completed a release of information form had their data entered and stored in REDCap. REDCap was used for tracking referral and recruitment of participants and the collection of all patient outcome measures throughout the study. The person responsible for data collection worked with the project manager to track participant enrollment, outcome form completion and prompts for email and telephone reminders and appointment scheduling.

Clinical data were entered into REDCap [24,25], a 21 CFR Part 11-compliant data capture system provided by Virginia Tech under a fully executed technology control plan with the Office of Export and Secure Research Compliance. The data system included password protection and internal quality checks, such as automatic range checks, to identify data that appeared inconsistent, incomplete, or inaccurate.

Reducing measurement bias: To reduce the possibility of bias, the biofeedback intervention was completed by a single individual (clinician – Athletic trainer) and the biomechanical assessments was completed by a second individual who was masked to the participant's group assignment (research technician). The research technician was trained to complete the biomechanical assessment using a standard set of directions. The clinician completed the intervention using a standard set of instructions to decrease between participant variability and provide consistent feedback to each participant. The intervention instructor was trained by the clinical rehabilitation expert (DSBW) in proper technique and instruction.

2.7. Statistical considerations

2.7.1. Statistical analyses

The results from all descriptive statistics were calculated and reported as percentages as well as means and standard deviations as appropriate for the measure. For inferential tests, the p-value and confidence intervals for statistical significance (Type I error) were reported along with an indication as to whether a two or one-tailed test was performed. Checks for the assumption of normality were performed prior to additional statistical procedures. If this assumption was not met, then corrective procedures were applied such as transformation or nonparametric tests as appropriate.

All preliminary analyses were based on the Modified Intention-to-Treat (ITT) method in which each participant was included independent of adherence. Per-Protocol analyses was completed in which a subset of the participants in the full analysis (ITT) set who complied with the protocol sufficiently to ensure that these data would be likely to represent the effects of study intervention according to the underlying scientific model (participants who completed at least 75% of the study intervention visits).

2.7.2. Primary aim

The primary aim of this study was to determine the impact of an innovative biofeedback training program on decreasing risk factors for second ACL injuries in adolescent athletes. Based on previous work, the primary outcome measure, a surrogate for second ACL injury risk, was the knee extension moment limb symmetry index (LSI) at the six-week visit (immediately post-intervention). Secondary outcomes were vertical ground reaction force, and frontal plane knee range of motion symmetry. Symmetry between the operative and non-operative limbs in this study was determined by calculating the LSI.

For the primary aim of this pilot study, a mixed effects model will be used to determine if a clinical (LSI>90%) and/or statistical difference exists between the pre- and the two post-intervention time points (efficacy and durability) for the primary outcome of interest (knee extension moment LSI). Post-hoc testing will be completed for any variable that is determined to be statistically different.

2.7.3. Secondary aims

The secondary aim of this preliminary clinical trial will assess the rates of recruitment, retention, and adherence. No hypothesis tests will be performed. For each of the outcome measures the between session analysis will allow us to calculate test-retest reliability. The use of correlations will allow us to compute criterion and predictive validity. Study retention will be defined as a participant who attends each of the biomechanical testing session (baseline, immediately following intervention (intervention)/6 weeks after baseline (control), and then 6 weeks after training (intervention) or 12 week after the baseline (control). Proportion retention will be computed by dividing the number of retained participants at the end of the intervention by the total number of patients randomized into the study. Adherence to the intervention will be defined as a participant who attends at least 75% of the biofeedback training sessions during the six weeks of the intervention. Proportion adherence will be computed by dividing the number of sessions attended by the total number training sessions (n = 12).

2.7.4. Sample-size calculations

This was a pilot study, with the purpose of discerning parameter estimates for use in powering a subsequent multi-center clinical trial. To estimate statistical power for this pilot design, we considered a comparison of outcomes by group across time. Previous studies have not examined the knee extension moment limb symmetry index, therefore the difference in knee joint position and the knee extension moment were employed as proxy variables to estimate statistical power for this pilot design. We considered a comparison of outcomes between pre- and post-intervention [18,19] and side-to-side differences in ACL-R patients. (Table 3) [16].

Using 2-sided testing between groups based on previous results, we needed 14 patients overall randomized at 1:1 ratio assuming 80% power to detect a significant difference in the knee extension moment between the groups with $\alpha = 0.05$ [14]. Therefore, with recruitment of 40 participants (goal of retaining 30 participants through study completion), we were adequately powered to declare significance. Thus, while not the primary purpose of this experiment, we were adequately powered to declare significance between groups.

3. Discussion

The high rate of ACL re-injury implies that in many cases current post-operative interventions fail to restore adequate knee motion and neuromuscular control to decrease re-injury risk. Many patients cleared to return to sport following ACL reconstruction demonstrate residual muscle weakness, imbalances, and asymmetrical movement and loading patterns [32,38,39,43,44,48,50]. Previous interventions improve strength and joint range of motion while failing to assess and modify lower extremity movement deficits. Although the American Academy of Orthopaedic Surgeons' ACL return to sport guidelines state a need for restoration of movement, they do not provide or reference objective assessment measures or criteria for release [3,17,37]. Following ACL reconstruction and clinical release to return to sports, most patients have residual limb asymmetries during jumping and landing [12,15,32,43,44]. The primary risk factors for second ACL injuries, based on previous prospective work, include asymmetrical frontal plane knee range of motion and knee extension moment during bilateral landing [39]. Thus, to decrease the risk for second ACL injuries, there is a pressing need to evaluate novel, clinically relevant interventions that improve lower extremity movement patterns and restore movement and loading symmetry prior to release to return to full sport participation.

This novel biofeedback intervention may be an alternative approach

Table 3
Sample Size Calculations (N = sample size per group).

	Pre-intervention	Post-intervention	Sample Size
Peak Knee Extension Moment [9]	3.7 ± 0.9	2.4 ± 0.5	N = 7
Peak Knee Flexion [21]	88.8 ± 8.0	105.0 ± 5.6	N = 5
	Control	**Intervention**	**Sample Size**
Knee Flexion Angle [21]	83.5 ± 20.5	103.8 ± 16.3	N = 15
Vertical ground reaction force [21]	2.0 ± 0.4	1.6 ± 0.3	N = 14

to current rehabilitation protocols to decrease the risk of second ACL injury. The results of this pilot clinical trial will also provide effect size estimates for the planning of a subsequent larger clinical trial.

Authors' Contributions

RMQ conceived the study, participated in its design and coordination, and drafted the manuscript. ATP helped coordinate the intervention and assessment visits and completed the biomechanical testing. TKM participated in its design, coordinated participant recruitment coordination, and is the medical director of the trial. JS participated in its design, coordinated statistical analyses and data management. TO participated in its design and coordinated patient compliance and adherence protocols. SPM participated in study design and served as the senior clinical trialist. DSBW participated in its design, trained all clinical personnel for the biofeedback intervention, and aided in the development of the attention control educational materials. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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References

[1] Acl injury: does it require surgery?. http://orthoinfo.aaos.org.
[2] C.L. Ardern, N.F. Taylor, J.A. Feller, K.E. Webster, Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors, Br. J. Sports Med. 48 (21) (2014) 1543–1552.
[3] S.D. Barber-Westin, F.R. Noyes, Factors used to determine return to unrestricted sports activities after anterior cruciate ligament reconstruction, Arthroscopy 27 (12) (2011) 1697–1705.
[4] S.D. Barber-Westin, F.R. Noyes, Objective criteria for return to athletics after anterior cruciate ligament reconstruction and subsequent reinjury rates: a systematic review, Physician Sportsmed. 39 (3) (2011) 100–110.
[5] S.D. Barber, F.R. Noyes, R.E. Mangine, J.W. McCloskey, W. Hartman, Quantitative assessment of functional limitations in normal and anterior cruciate ligament-deficient knees, Clin. Orthop. Relat. Res. (255) (1990) 204–214.
[6] A.L. Bell, R.A. Brand, D.R. Pedersen, Prediction of hip joint centre location from external landmarks, Hum. Mov. Sci. 8 (1) (1989) 3–16.
[7] D.R. Bell, K.A. Pfeiffer, L.A. Cadmus-Bertram, et al., Objectively measured physical activity in patients after anterior cruciate ligament reconstruction, Am. J. Sports Med. 45 (8) (2017) 1893–1900.
[8] S.G. Bodkin, L.V. Slater, G.E. Norte, J. Goetschius, J.M. Hart, Acl reconstructed individuals do not demonstrate deficits in postural control as measured by single-leg balance, Gait Posture 66 (2018) 296–299.
[9] H. Bookbinder, L.V. Slater, A. Simpson, J. Hertel, J.M. Hart, Single-leg jump performance before and after exercise in healthy and anterior cruciate ligament reconstructed individuals, J. Sport Rehabil. (2019) 1–7.
[10] K.K. Briggs, M.S. Kocher, W.G. Rodkey, J.R. Steadman, Reliability, validity, and responsiveness of the lysholm knee score and tegner activity scale for patients with meniscal injury of the knee, J Bone Joint Surg Am 88 (4) (2006) 698–705.
[11] K.K. Briggs, J. Lysholm, Y. Tegner, et al., The reliability, validity, and responsiveness of the lysholm score and tegner activity scale for anterior cruciate ligament injuries of the knee: 25 Years later, Am. J. Sports Med. 37 (5) (2009) 890–897.
[12] R.J. Butler, B. Dai, W.E. Garrett, R.M. Queen, Changes in landing mechanics in patients following anterior cruciate ligament reconstruction when wearing an extension constraint knee brace, Sport Health 6 (3) (2014) 203–209.
[13] T.L. Chmielewski, D. Jones, T. Day, et al., The association of pain and fear of movement/reinjury with function during anterior cruciate ligament reconstruction rehabilitation, J. Orthop. Sports Phys. Ther. 38 (12) (2008) 746–753.
[14] J. Cohen, Statistical Power Analysis for the Behavioral Sciences, second ed., L. Erlbaum Associates, Hillsdale, N.J., 1988.
[15] B. Dai, R.J. Butler, W.E. Garrett, R.M. Queen, Anterior cruciate ligament reconstruction in adolescent patients: limb asymmetry and functional knee bracing, Am. J. Sports Med. 40 (12) (2012) 2756–2763.
[16] B. Dai, R.J. Butler, W.E. Garrett, R.M. Queen, Using ground reaction force to predict knee kinetic asymmetry following anterior cruciate ligament reconstruction, Scand. J. Med. Sci. Sports 24 (6) (2014) 974–981.
[17] S.L. Di Stasi, D. Logerstedt, E.S. Gardinier, L. Snyder-Mackler, Gait patterns differ between acl-reconstructed athletes who pass return-to-sport criteria and those who fail, Am. J. Sports Med. 41 (6) (2013) 1310–1318.
[18] A.V. Dowling, J. Favre, T.P. Andriacchi, Inertial sensor-based feedback can reduce key risk metrics for anterior cruciate ligament injury during jump landings, Am. J. Sports Med. 40 (5) (2012) 1075–1083.
[19] H.M. Ericksen, A.C. Thomas, P.A. Gribble, S.C. Doebel, B.G. Pietrosimone, Immediate effects of real-time feedback on jump-landing kinematics, J. Orthop. Sports Phys. Ther. 45 (2) (2015) 112–118.
[20] K.R. Ford, S.J. Minning, G.D. Myer, et al., Landing adaptations following isolated lateral meniscectomy in athletes, Knee Surg. Sports Traumatol. Arthrosc. 19 (10) (2011) 1716–1721.
[21] K.R. Ford, L.C. Schmitt, T.E. Hewett, M.V. Paterno, Identification of preferred landing leg in athletes previously injured and uninjured: a brief report, Clin. Biomech. 31 (2016) 113–116.
[22] S.Z. George, C. Valencia, J.M. Beneciuk, A psychometric investigation of fear-avoidance model measures in patients with chronic low back pain, J. Orthop. Sports Phys. Ther. 40 (4) (2010) 197–205.
[23] L.Y. Griffin, M.J. Albohm, E.A. Arendt, et al., Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the hunt valley ii meeting, January 2005, Am. J. Sports Med. 34 (9) (2006) 1512–1532.
[24] P.A. Harris, R. Taylor, B.L. Minor, et al., The redcap consortium: building an international community of software platform partners, J. Biomed. Inf. 95 (2019) 103208.
[25] P.A. Harris, R. Taylor, R. Thielke, et al., Research electronic data capture (Redcap)–a metadata-driven methodology and workflow process for providing translational research informatics support, J. Biomed. Inf. 42 (2) (2009) 377–381.
[26] W. Herzog, P.J. Conway, B.J. Willcox, Effects of different treatment modalities on gait symmetry and clinical measures for sacroiliac joint patients, J. Manip. Physiol. Ther. 14 (2) (1991) 104–109.
[27] W. Herzog, B.M. Nigg, L.J. Read, E. Olsson, Asymmetries in ground reaction force patterns in normal human gait, Med. Sci. Sports Exerc. 21 (1) (1989) 110–114.
[28] J. Kay, M. Memon, R.G. Marx, et al., Over 90 % of children and adolescents return to sport after anterior cruciate ligament reconstruction: a systematic review and meta-analysis, Knee Surg. Sports Traumatol. Arthrosc. 26 (4) (2018) 1019–1036.
[29] J. Koh, Computer-assisted navigation and anterior cruciate ligament reconstruction: accuracy and outcomes, Orthopedics 28 (10 Suppl) (2005) s1283–1287.
[30] R. Letchford, V. Sparkes, R.W. van Deursen, Assessing participation in the acl injured population: selecting a patient reported outcome measure on the basis of measurement properties, Knee 22 (3) (2015) 262–269.
[31] E. Linko, A. Harilainen, A. Malmivaara, S. Seitsalo, Surgical versus conservative interventions for anterior cruciate ligament ruptures in adults, Cochrane Database Syst. Rev. (2) (2005) CD001356.
[32] S.W. Mayer, R.M. Queen, D. Taylor, et al., Functional testing differences in anterior cruciate ligament reconstruction patients released versus not released to return to sport, Am. J. Sports Med. 43 (7) (2015) 1648–1655.
[33] R. McGough, K. Paterson, E.J. Bradshaw, A.L. Bryant, R.A. Clark, Improving lower limb weight distribution asymmetry during the squat using nintendo wii balance boards and real-time feedback, J. Strength Condit Res. 26 (1) (2012) 47–52.
[34] P.J. McNair, R.N. Marshall, Kinematic and kinetic parameters associated with running in different shoes, Br. J. Sports Med. 28 (4) (1994) 256–260.
[35] K. Miyasaka, D. Daniel, M. Stone, The incidnece of knee ligament injuries in the general population, Am. J. Knee Surg. 4 (1991) 3–8.
[36] B.M. Nigg, H.A. Bahlsen, S.M. Luethi, S. Stokes, The influence of running velocity and midsole hardness on external impact forces in heel-toe running, J. Biomech. 20 (10) (1987) 951–959.
[37] R.M. Palmieri-Smith, A.C. Thomas, E.M. Wojtys, Maximizing quadriceps strength after acl reconstruction, Clin. Sports Med. 27 (3) (2008) 405–424.
[38] M.V. Paterno, M.J. Rauh, L.C. Schmitt, K.R. Ford, T.E. Hewett, Incidence of contralateral and ipsilateral anterior cruciate ligament (acl) injury after primary acl reconstruction and return to sport, Clin. J. Sport Med. 22 (2) (2012) 116–121.
[39] M.V. Paterno, L.C. Schmitt, K.R. Ford, et al., Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport, Am. J. Sports Med. 38 (10) (2010) 1968–1978.
[40] E.W. Paxton, D.C. Fithian, M.L. Stone, P. Silva, The reliability and validity of knee-specific and general health instruments in assessing acute patellar dislocation outcomes, Am. J. Sports Med. 31 (4) (2003) 487–492.
[41] A.T. Peebles, L.C. Dickerson, K.E. Renner, R.M. Queen, Sex-based differences in landing mechanics vary between the drop vertical jump and stop jump, J. Biomech. 105 (2020) 109818.
[42] A.T. Peebles, T.K. Miller, J.T. Moskal, R.M. Queen, Hop testing symmetry improves with time and while wearing a functional knee brace in anterior cruciate ligament reconstructed athletes, Clin. Biomech. 70 (2019) 66–71.
[43] A.T. Peebles, K.E. Renner, T.K. Miller, J.T. Moskal, R.M. Queen, Associations between distance and loading symmetry during return to sport hop testing, Med. Sci. Sports Exerc. 51 (4) (2019) 624–629.
[44] K.E. Renner, C.T. Franck, T.K. Miller, R.M. Queen, Limb asymmetry during recovery from anterior cruciate ligament reconstruction, J. Orthop. Res. 36 (7) (2018) 1887–1893.
[45] P. Renstrom, A. Ljungqvist, E. Arendt, et al., Non-contact acl injuries in female athletes: an international olympic committee current concepts statement, Br. J. Sports Med. 42 (6) (2008) 394–412.

[46] R.O. Robinson, W. Herzog, B.M. Nigg, Use of force platform variables to quantify the effects of chiropractic manipulation on gait symmetry, J. Manip. Physiol. Ther. 10 (4) (1987) 172–176.
[47] T.P. Ross, L.T. Ross, S.D. Short, S. Cataldo, The multidimensional health locus of control scale: psychometric properties and form equivalence, Psychol. Rep. 116 (3) (2015) 889–913.
[48] Y. Tegner, J. Lysholm, Rating systems in the evaluation of knee ligament injuries, Clin. Orthop. Relat. Res. 198 (1985) 43–49.
[49] P. Thomee, P. Wahrborg, M. Borjesson, et al., A new instrument for measuring self-efficacy in patients with an anterior cruciate ligament injury, Scand. J. Med. Sci. Sports 16 (3) (2006) 181–187.
[50] D.A. Tripp, W. Stanish, A. Ebel-Lam, B.W. Brewer, J. Birchard, Fear of reinjury, negative affect, and catastrophizing predicting return to sport in recreational athletes with anterior cruciate ligament injuries at 1 Year postsurgery, Sport, Exercise, and Performance Psychology 1 (S) (2011) 38–48.
[51] K.A. Wallston, The validity of the multidimensional health locus of control scales, J. Health Psychol. 10 (5) (2005) 623–631.
[52] K.E. Webster, J.A. Feller, Exploring the high reinjury rate in younger patients undergoing anterior cruciate ligament reconstruction, Am. J. Sports Med. 44 (11) (2016) 2827–2832.
[53] K.E. Webster, J.A. Feller, C. Lambros, Development and preliminary validation of a scale to measure the psychological impact of returning to sport following anterior cruciate ligament reconstruction surgery, Phys. Ther. Sport 9 (1) (2008) 9–15.
[54] S.R. Woby, N.K. Roach, M. Urmston, P.J. Watson, Psychometric properties of the tsk-11: a shortened version of the tampa scale for kinesiophobia, Pain 117 (1–2) (2005) 137–144.