QUADRICEPS FUNCTION IN ACL RECONSTRUCTED PATIENTS WITH AND WITHOUT KNEE OSTEOARTHRITIS

A Dissertation

Presented to

The Faculty of the Curry School of Education

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by

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ABSTRACT

Post-traumatic quadriceps dysfunction is well-documented following anterior cruciate ligament reconstruction (ACL-R), and is associated with impairments detrimental to joint-specific and global health, including decreased physical activity, accelerated onset of knee joint osteoarthritis, and decreased quality of life. Since articular cartilage degeneration is irreversible, the hallmark for prevention is early detection with thorough evaluation of quadriceps neuromuscular function. Neuromuscular adaptations are theorized to arise from alterations in spinal-mediated and corticospinal pathways, and if unaddressed, may present a limiting factor in recovery from ACL-R. The specific origins of impairment have been theorized as a way to address subtle underlying factors impeding the recovery of quadriceps function following ACL-R. By understanding the temporal nature of neuromuscular adaptations, clinicians and researchers can improve patient care. The focus of manuscript 1 was to *compare quadriceps neuromuscular function* at clinically relevant time points following ACL-R, including patients who experienced post-traumatic knee osteoarthritis. We found that patients early (< 1 year), late (> 2 years), and with osteoarthritis after ACL-R exhibited quadriceps weakness and decreased corticospinal input to the quadriceps compared to healthy individuals. The focus of manuscript 2 was to *identify the relationship between objective measures of quadriceps function and patient-reported outcomes* at clinically relevant time points following ACL-R, including patients who experienced post-traumatic knee osteoarthritis. We found that perceived knee function and global health status were best explained by objective measures of quadriceps function in patients early and with osteoarthritis after ACL-R. Both limb symmetry and unilateral limb performance were meaningful to patients early, and unilateral limb performance was meaningful to patients with osteoarthritis after ACL-R.

Measures of isokinetic quadriceps strength (torque, work, power) consistently demonstrated the strongest relationships with patient-reported outcomes. The focus of manuscript 3 was to *investigate the underlying constructs of lower extremity muscle function* that uniquely describe aspects of quadriceps neuromuscular function in patients after ACL-R. We found that unique constructs of peripheral, central, and combined peripheral and central muscle function are likely to exist in ACL-R patients. Quadriceps function (total work at 90°/sec, active motor threshold, and central activation) of the involved limb was able to discriminate best between ACL-R patients and healthy individuals compared to the uninvolved limb or limb symmetry. It is unclear if early changes in strength, endurance, voluntary activation, and corticospinal excitability perpetuate long-term muscle dysfunction; however, the temporal relationships of these measures may be a contributing factor to long-term outcomes. If left unaddressed, the progressive nature of contributing factors may result in irreversible joint injury.

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APPROVAL OF THE DISSERTATION

This dissertation, "Quadriceps Function in ACL Reconstructed Patients With and Without Knee Osteoarthritis," has been approved by the Graduate Faculty of the Curry School of Education in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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SECTION II: MANUSCRIPT I

CHRONICITY OF QUADRICEPS FUNCTION IN ACL RECONSTRUCTED PATIENTS WITH AND WITHOUT KNEE OSTEOARTHRITIS

ABSTRACT

Context: Central and peripheral neural adaptations from muscular, spinal, and supraspinal regions have been identified following ACL injury and reconstruction and are hypothesized to contribute to post-traumatic muscle dysfunction. Currently, there is limited evidence with regard to the temporal nature of neuromuscular adaptions during early and late term durations after ACL-R, and none that include patients with post-traumatic osteoarthritis. **Objective:** To compare quadriceps neuromuscular function early and late after ACL-R, including patients who experienced post-traumatic knee osteoarthritis. **Design:** Cross sectional. **Setting:** University laboratory. **Patients or Participants:** 102 participants volunteered for this study, including 72 ACL reconstructed patients: *Early* (n = 34, 20M/14F, 9.0 ± 4.3 months post-ACL-R), *Late* (n = 30, 10M/20F, 70.5 ± 41.6 months post-ACL-R), *Osteoarthritis* (n = 8, 2M/6F, 115.9 ± 110.0 months post-ACL-R), and 30 healthy individuals (12M/18F). **Intervention(s):** None. **Main Outcome Measure(s):** Normalized knee extension maximum voluntary isometric contraction (MVIC) torque (Nm/kg), quadriceps fatigue index (% decline), quadriceps central activation ratio (CAR, %), quadriceps spinal reflex excitability (H:M ratio), quadriceps corticospinal excitability (AMT, % 2.0 Tesla) were measured bilaterally. Comparisons were made using two-way analyses of variance to determine the effect of limb and group on MVIC torque, fatigue index, CAR, H:M ratio, and AMT. **Results:** Compared to the healthy control group, MVIC torque was lower among all ACL-R patients ($p < .001$), quadriceps fatigue index ($p = .003$) and CAR ($p < .001$) were lower among *early* ACL-R patients only, and quadriceps AMT was higher among all ACL-R patients ($p < .001$). **Conclusions:** Neuromuscular impairments are present in patients early and late after ACL-R with and without knee osteoarthritis. Quadriceps strength and corticospinal excitability were impaired at all time points compared to healthy individuals, suggesting the role of addressing cortical function following ACL-R.

Word Count: 289

Key Words: corticospinal, neuromuscular, quadriceps activation

INTRODUCTION

Anterior cruciate ligament (ACL) injuries are common among young, active individuals,[1] and present a specific challenge to long-term joint health.[2] ACL reconstruction (ACL-R) remains the recommended treatment in this population;[3] unfortunately, poor outcomes are well documented.[4] As many as one-third of patients will not return to pre-injured levels of activity,[5] and among those who do, prospective data supports the dramatically increased incidence of a second ACL injury to the ipsilateral or contralateral limb within two years of reconstruction.[6] More concerning is the high prevalence of post-traumatic knee joint osteoarthritis, with radiographic signs appearing as early as the first decade in more than one-third of patients following reconstruction.[4] Quadriceps function has been widely studied in response to ACL-R, both as a source of persistent impairment and contributing factor for subsequent joint injury.[7] Post-traumatic quadriceps dysfunction is well described following ACL-R,[8] and is associated with decreased physical activity[9] and increased self-reported global and regional disability.[10] Moreover, quadriceps weakness is reported to be associated with diminished tibiofemoral joint space width,[11] which may contribute to the progression of osteoarthritis.[12] Since articular cartilage degeneration is irreversible, the hallmark for prevention is early detection with thorough evaluation of quadriceps neuromuscular function.

Central and peripheral neural adaptations from muscular, spinal, and supraspinal regions have been identified following ACL injury and reconstruction,[13] and are hypothesized to contribute to post-traumatic muscle dysfunction.[14] The specific origins of impairment have been theorized as a way to address subtle underlying factors impeding the recovery of quadriceps function following ACL-R.[15] Central activation failure of the quadriceps has been identified more than four years following ACL-R[13,16] and in patients with radiographic tibiofemoral osteoarthritis.[17] Neuromuscular adaptations are theorized to arise from alterations in spinal-mediated and corticospinal pathways,[18] and if unaddressed, may present a limiting factor in recovery from ACL injury.[19] Therefore, it may be necessary to assess each of these unique

pathways to build a complete neuromuscular profile following ACL-R in an attempt to identify early and subtle deficits that may lead to persistent muscle dysfunction.

Outcomes following major joint injury and reconstruction often deteriorate with time, suggesting that chronicity plays an important role in identifying those at risk for long term consequences associated with altered neuromuscular function. The nature and magnitude of neural adaptations following peripheral joint injury is reported to change over time. For example, alterations in spinal reflex excitability have been identified in response to a simulated knee joint effusion,[20] suggesting an acute neural response to joint injury mediated at the spinal level. However, spinal-mediated alterations have not been consistently reported in the context of chronic ACL injury.[13,16] For example, researchers have reported no differences in spinal reflex excitability at an average of 2.5 years[16] following ACL-R compared to healthy individuals; whereas, others have observed a bilateral up-regulation at an average of 4 years post-op.[13] In contrast, immediate changes in corticospinal excitability have not been observed in response to a simulated knee joint effusion;[21] yet, deficits have been observed more than 3 years following ACL-R.[13,16] These findings agree with a recent longitudinal study reporting decreased spinal reflex excitability prior to and 2 weeks following ACL-R, and a decrease in corticospinal excitability at 6 months following ACL-R.[15] Collectively, these data provide evidence of the temporal nature of the pathophysiological response to ACL injury and reconstruction, although long-term evaluation is warranted to understand the impact on clinical outcomes. Neuromuscular adaptations appear to be an expected outcome following joint injury. However, these deficits are treatable and present a way for clinicians to detect problems early with the intention of promoting optimal long-term joint health, especially in the prevention of early-onset knee osteoarthritis.

Currently, there is growing evidence of central nervous system adaptations following ACL-R;[13,22] however, the temporal relationship of these adaptations is unclear. It may be possible that a time point exists along the continuum of recovery in which patients with successful and poor outcomes diverge, indicating a critical junction in a targeted rehabilitation process. Previous

models of study have largely classified ACLR patients as a single group of comparison relative to healthy counterparts with widespread time since surgery, which may prevent early detection of impairments or delay early intervention. In an effort to better understand how neuromuscular adaptations progress over time, time from surgery should be considered. There is limited evidence with regard to the specific timing of alterations in neuromuscular function of the quadriceps during early (< 1 year) and late (> 2 years) term durations after ACL-R, and none that include patients with post-traumatic osteoarthritis following ACL-R. Therefore, the purpose of this study was to compare quadriceps neuromuscular function at clinically relevant time points following ACL-R, including patients who experienced post-traumatic knee osteoarthritis.

METHODS

This was a cross-sectional study to investigate patients following ACL-R and healthy controls. Independent variables included one between factor (Group: < 1 year post ACL-R, > 2 years post ACL-R, patients with radiographic evidence of knee osteoarthritis post ACL-R, and healthy matched controls) and one within factor (Limb: involved, uninvolved). Dependent variables included measures of quadriceps neuromuscular function, including knee extension maximal voluntary isometric contraction (MVIC) torque, fatigue index (FI), central activation ratio (CAR), Hoffmann reflex (H-reflex), and active motor threshold (AMT). Quadriceps neuromuscular function was recorded bilaterally, and the order of testing was counterbalanced by limb for each group. Limb dominance was recorded for each participant, and determined by asking which limb would be used to kick a ball. The International Knee Documentation Committee (IKDC) subjective form, Knee Injury and Osteoarthritis Outcome Score (KOOS), and Western Ontario and McMaster Universities Arthritis Index (WOMAC) were used to measure regional patient-reported function.

Participants

A total of 102 subjects volunteered for this study, including 72 ACL reconstructed patients: < 1 year (n = 34), > 2 years (n = 30), osteoarthritis: 9.7 years (range, 10 to 301 months)

(n = 8), and 30 healthy controls between the ages of 15-65. To be eligible, patients must have undergone a primary, unilateral reconstruction with no post-surgical complications. Meniscectomy and meniscal repair were accepted as potential concomitant procedures. Patients were excluded if they had a history of lower extremity injury other than ACL-R within 6 months, multiligament knee injury, lower extremity orthopaedic surgery prior to ACL-R, or concussion within 6 months. Patients with knee osteoarthritis must have had documented radiographic evidence of tibiofemoral or patellofemoral compartment involvement (Kellgren-Lawrence > 1) at a minimum of 12 months post ACL-R. Patients with a diagnosis prior to ACL-R were excluded. A convenience sample of healthy individuals with no history of lower extremity injury within 6 months or prior joint surgery was recruited from the community. All participants were screened for the use of transcranial magnetic stimulation according to the safety and ethical guidelines proposed by the International Federation of Clinical Neurophysiology.[23] Our University's Institutional Review Board for Health Sciences Research approved this study, and all participants provided informed consent prior to enrollment.

Procedures

Testing was conducted during one study visit, which always followed the same order: H-reflex, knee extension MVIC torque, quadriceps CAR, FI, and AMT.

Patient Reported Outcomes

Regional knee function was assessed using the 2000 International Knee Documentation Committee (IKDC) subjective knee form[24] and Knee Injury and Osteoarthritis Outcome Score (KOOS).[25] The KOOS was used to supplement the IKDC in order to assess specific functional domains of pain, symptoms, activities of daily living, sport related function, and quality of life. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is advocated for use among patients with osteoarthritis, and was used to assess pain, stiffness, and function.[26] The combination of measurement tools for regional knee function was used to ensure appropriate assessment for all patients over a long duration of time from ACL-R (range, 4.2 – 301.2 months).

Activity level, fear of movement, and global health perception were quantified using the Tegner Activity Scale,[27] Tampa Scale of Kinesiophobia (TSK),[28] and Veteran's Rand 12-Item Health Survey (VR-12)[29] respectively.

Quadriceps Spinal Reflex Excitability

The H-reflex was used to quantify spinal reflex excitability of the quadriceps as previously described.[30] The area of the greatest bulk over the vastus medialis was cleaned, shaved, and debrided, prior to placement of two 10 mm pre-gelled Ag-AgCl recording electrodes (EL503, BIOPAC Systems, Inc.) in accordance with surface electromyography (EMG) for noninvasive assessment of muscle guidelines.[31] EMG signals were sampled at 2000 Hz, band-pass filtered from 10 to 500 Hz, and processed using AcqKnowledge 4.2 software (BIOPAC Systems, Inc., Goleta, CA). The recording electrodes were outlined to ensure similar placement during corticospinal testing. A ground electrode was placed over the contralateral distal anteromedial tibia. Testing was completed in a quiet, dimly lit room in which participants lied supine with a bolster under the knees to maintain approximately 15° of knee flexion, and hands folded over their chest. Participants wore earplugs (Aero Technologies, Indianapolis, IN) and were instructed to "close your eyes, and clear your mind" during testing. The femoral artery was palpated, and a 4 mm rounded stimulating electrode (EL254, BIOPAC Systems, Inc.) was placed in the inguinal fold over the femoral nerve. A round carbon dispersive electrode was placed under the ipsilateral posterior thigh. A series of 10 ms square wave electrical stimuli ranging 10-200 volts were delivered via stimulator module (STM100A, BIOPAC Systems, Inc.) and current isolation unit (STMISOC, BIOPAC Systems, Inc.) with a minimum of 10 seconds between stimuli. Three maximal Hoffmann reflexes were averaged and normalized to the average of three maximal muscle responses (M-response) to calculate the H:M ratio.[30,32]

Quadriceps Strength and Voluntary Activation

Knee extension MVIC torque and the quadriceps CAR were used to quantify quadriceps strength and voluntary activation. Participants were seated in a Biodex System 3 Dynamometer (Biodex Medical Systems, Inc., Shirley, NY) with the hips and knees flexed to 85° and 90° respectively. Participants completed a standardized acclimatization protocol, in which a series of submaximal trials (25%, 50%, 75% perceived effort) were performed prior to recording three maximal effort trials.[30] Accessory motion was discouraged by having participants cross their arms over their chest, while keeping their head and shoulders back against the rest. To ensure maximal effort, verbal encouragement was provided. Participants were provided with visual feedback via 50-inch LCD monitor, and encouraged to kick harder than each previous trial. Participants rested for a minimum of 60 seconds between trials.

The superimposed burst technique was used as previously described to estimate quadriceps CAR during the third maximal effort trial.[33] A square wave stimulator (S88, GRASS-TeleFactor, W. Warwick, RI) and isolation unit (SIU8T, GRASS-TeleFactor) were used to deliver a supramaximal percutaneous electrical stimulus to the anterior thigh via two 3 x 5 in self-adhesive electrodes applied over the proximal vastus lateralis and distal vastus medialis. Force data were sampled at 125 Hz, low-pass filtered at 10 Hz, and normalized to body mass. A 100 ms epoch was recorded from a stable region of trials 1 and 2, and from immediately prior to the superimposed burst torque of trial 3. The mean MVIC torque from the three MVIC trials was used for analysis, and the MVIC torque from trial 3 was used to calculate the CAR as previously described.[34]

Quadriceps Fatigue Index

Quadriceps fatigue was quantified using a previously described[35] index of torque decline during a 30 second knee extension MVIC. Participants were instructed to kick out as hard as possible, and to maintain the contraction while seated in a Biodex System 3 Dynamometer in a similar fashion to quadriceps strength testing. Participants were prompted to start kicking,

increasing to a maximal effort over three seconds. The 30-second trial began after three seconds, once the participant had achieved their perceived maximal effort. Verbal encouragement and visual feedback were not used to minimize the occurrence of transient aberrant increases in torque, which were observed during pilot testing. Force data were sampled at 125 Hz, low-pass filtered at 15 Hz, and processed using Acqknowledge software. The mean torque was recorded from a series of 1-second epochs, and the greatest torque epoch during the first 5 seconds of the trial was recorded as the maximal torque (T_{Max}). Quadriceps FI was calculated using the area under the force-time curve (AUFC) for the entire contraction period for 0 to 30 seconds, which began at the time point of maximum muscle torque (TPM) (Equation 1).

Equation 1: $$FI = [1 - (AUFC_{TPM\text{-}30} / (T_{Max,0\text{-}5} x (TPM - 30)))] x 100$$

Quadriceps Corticospinal Excitability

Transcranial magnetic stimulation (TMS) was used to quantify quadriceps corticospinal excitability as measured by the AMT. Participants were asked to abstain from caffeine consumption and intense exercise for a minimum of 12 hours prior to testing. Participants were seated in a Biodex System 3 Dynamometer, and asked to rest their hands in their lap while minimizing accessory motion. Two surface EMG electrodes were replaced over the vastus medialis in a similar manner as the Hoffmann reflex testing. Participants wore earplugs and a Lycra swim cap with straight lines drawn vertically in the sagittal and frontal planes to aid in determining the appropriate location for the TMS coil over the primary motor cortex (M1).[36] A 1 cm x 1 cm grid was drawn on the swim cap to improve the precision of stimuli delivered. Motor evoked potentials (MEP) were elicited in the vastus medialis using a magnetic stimulator (Magstim Rapid, MagStim Company, Ltd., Wales, UK) with a 110 mm double-cone coil. MEP signals were sampled at 2000 Hz, and band-pass filtered from 1 to 5000 Hz. The coil was positioned over the contralateral cortical hemisphere in the area of M1, and shifted by 0.5 cm in the anterior, posterior, medial, and lateral directions to identify the optimal stimulating location

(hotspot).[37] The hotspot was defined as the greatest MEP amplitude. A researcher manually positioned the coil for each measurement while standing behind the participant on a 54 cm step. Once the hotspot was determined, the stimulus intensity was sequentially lowered by 5% until no MEP was detected, then increased by 1% until the MEP returned. The AMT was defined as the lowest intensity required to evoke a measurable MEP (> 200 μV) during a tonic contraction.[23] Participants were instructed to maintain an isometric contraction at 5% of their previously determined MVIC, and to relax immediately following each stimulus.[16] Participants were instructed to match solid line depicting 5% of the MVIC that was displayed in real time on an LCD monitor, and to relax between each stimulus.

Statistical Analysis

A sample size estimate was based on the minimal detectable change (MDC_{95}) for each dependent variable, assuming an alpha level of $p \leq .05$ and power of $1\text{-}\beta = 0.80$. The MDC_{95} was calculated as $\sqrt{2}$ x 1.96 x SEM. Accordingly, the MDC_{95} and required sample per group for each dependent variable were: MVIC[38] (47.8 Nm, n = 24), CAR[38] (6.0%, n = 16), fatigue index[39] (11.0%, n = 11), H:M ratio[40] (0.30, n = 11), and AMT[41] (8.4%, n = 14).

All data were assessed for normality prior to analysis. Separate one-factor analyses of variance were used to compare demographics and patient reported outcomes between groups (4 levels). Separate mixed model 2 x 4 (limb x group) analyses of variance were used to assess differences between the involved and uninvolved limbs for each measure of quadriceps function across all groups. In healthy participants, the non-dominant limb was initially treated as the "involved limb." However, 57% of ACL-R limbs were dominant. Therefore, a random number generator was used to re-assign an equal proportion of dominant to non-dominant limbs in the healthy group compared to ACL-R patients (i.e. the dominant limb was now treated as the "involved limb" in 57% of the participants in each group). Separate one-factor analyses of variance were performed to compare groups (at 4 levels) for each limb in the event of significant main effects where appropriate. Dunnett's *post-hoc* comparisons were used to compare each

ACL-R group to the healthy control group. Fisher's LSD *post-hoc* comparisons were used to determine group differences among ACL-R patients only. Planned comparisons between limbs were made using paired sample *t*-tests. Cohen's *d* effect sizes with associated 95% confidence intervals were calculated to determine the magnitude of difference between the involved limb in ACL-R patients and healthy individuals for each outcome measure. Effect sizes with confidence intervals that did not cross zero were considered clinically meaningful.

As an exploratory analysis, bivariate Pearson's product moment correlation coefficients (*r*) were used to assess the relationship between knee extensor MVIC torque and quadriceps CAR in each limb between groups. The level of statistical significance was set a priori at $P \leq .05$. All statistical analyses were performed using SPSS (version 20.0, IBM, Chicago, IL).

RESULTS

Group demographics and patient-reported function data are presented in table 1. Age was significantly different between groups ($F_{3,97} = 36.1$, $p < .001$), indicating that patients with osteoarthritis were older than all other participants ($p < .001$). Group means and standard deviations are presented for MVIC torque, FI, CAR, H-reflex, and AMT (Table 2, Figure 1). Effect sizes demonstrating the magnitude of difference between the involved ACL-R and matched healthy limbs are presented for each dependent variable in figure 2.

Patient Reported Outcomes

Each ACL-R group reported significantly lower knee function compared to healthy controls (group main effect for IKDC, KOOS, and WOMAC, $p < .001$). IKDC and WOMAC scores were higher in ACL-R patients without osteoarthritis compared to those with osteoarthritis, but did not differ between early and late ACL-R groups. Among ACL-R patients, those early after ACL-R reported the highest KOOS scores, followed by the late and osteoarthritis groups.

Quadriceps Spinal Reflex Excitability

H:M ratio was not significantly different by group ($F_{3,176} = 2.5$, $p = .065$) or limb ($F_{1,176} = 0.01$, $p = .916$). Between limb differences were not detected for any group. Effects sizes were

moderate for early (d = 0.45 [-0.03, 0.94]) and late (d = 0.59 [0.09, 1.09]) ACL-R patients, and large for patients with osteoarthritis (d = 0.98 [0.09, 1.87]).

Quadriceps Strength and Voluntary Activation

A significant group main effect ($F_{3,194}$ = 11.6, p < .001) indicated that each ACL-R group demonstrated lower knee extension MVIC torque than healthy controls. A significant limb main effect ($F_{1,194}$ = 5.5, p = .02) indicated that the involved ACL-R limb was weaker in patients early (d = -1.46 [-2.01, -0.91]), late (d = -1.00 [-1.54, -0.46]), and with osteoarthritis (d = -1.75 [-2.62, -0.88]) compared to healthy controls; however, there were no differences between ACL-R patients. Uninvolved limb MVIC torque was lower in the late ACL-R and osteoarthritis groups compared to healthy controls. Patients with osteoarthritis were also weaker in the uninvolved limb compared to patients early after ACL-R. A significant group-by-limb interaction ($F_{3,194}$ = 4.8, p = .003) indicated that the involved limb was weaker than the uninvolved limb in the early and late ACL-R groups (p = .029), but not in patients with osteoarthritis. There was no difference between limbs in the healthy control group.

A significant group main effect ($F_{3,193}$ = 6.8, p < .001) indicated that quadriceps CAR was lower early (d = -1.74 [-2.32, -1.16]), but not late (d = -0.84 [-1.37, -0.31]) after ACL-R, or in patients with osteoarthritis (d = -0.45 [-1.24, 0.33]), compared to healthy controls. CAR was significantly lower in the early compared to late and osteoarthritis groups. CAR did not differ significantly by limb ($F_{1,193}$ = 0.1, p = .711) or group-by-limb ($F_{3,193}$ = 0.4, p = .781). There were no differences between limbs for any group.

Quadriceps Fatigue Index

A significant group main effect ($F_{3,193}$ = 4.9, p = .003) indicated that patients in the early ACL-R group fatigued less than patients in the late ACL-R group and healthy controls (d = -0.95 [-1.47, -0.43]). Quadriceps fatigue was not different between the early ACL-R and osteoarthritis groups. Fatigue index did not differ by limb ($F_{1,193}$ = 0.2, p = .619) or group-by-limb ($F_{3,193}$ = 1.8, p = .147). Planned comparisons between limbs revealed that patients in the early ACL-R group

fatigued significantly less in the involved compared to the uninvolved limb (p = .002). There were no differences between limbs for any other group.

Quadriceps Corticospinal Excitability

A significant group main effect ($F_{3,173}$ = 9.7, p < .001), indicated AMT was higher bilaterally in patients early (d = -0.87 [-1.44, -0.30]), *late* (d = -0.42 [-1.00, 0.15]), and with osteoarthritis (d = -1.56 [-2.46, -0.65]) compared to healthy controls (decreased corticospinal excitability). Patients in the early ACL-R and osteoarthritis groups had a higher AMT compared to the late ACL-R group. AMT did not differ by limb ($F_{1,173}$ = 1.0, p = .319) or group-by-limb ($F_{3,173}$ = 0.2, p = .880). There were no differences between limbs for any group.

Correlations

Involved limb MVIC torque and CAR were correlated early (r = .546, p = .001) and late (r = .486, p = .006) after ACL-R, but not in patients with knee osteoarthritis (r = -.135, p = .750). Uninvolved limb MVIC torque and CAR were correlated late after ACL-R (r = .388, p = .034), but not early (r = .200, p = .257), or in patients with knee osteoarthritis (r = -.020, p = .963).

DISCUSSION

Our results indicate that patients early after ACL-R demonstrated reduced quadriceps strength in the involved limb, and bilateral reductions in fatigue, voluntary activation, and corticospinal excitability compared to healthy controls. Less symmetric quadriceps strength and fatigue indices were also observed in patients early. Patients with and without knee osteoarthritis late after ACL-R demonstrated a bilateral reduction in quadriceps strength and corticospinal excitability compared to healthy controls. Less symmetric quadriceps strength was also observed in patients late after ACL-R, but not in those with knee osteoarthritis. This study was the first to cross-sectionally examine quadriceps neuromuscular function at distinct early and late phases of ACL-R recovery with the inclusion of a post-traumatic osteoarthritic cohort. These data provide supporting evidence of the temporal nature of neuromuscular adaptations after ACL-R.

Early Post-Operative Outcomes

Large magnitude reductions in unilateral quadriceps strength, fatigue, voluntary activation, and corticospinal excitability were observed between 6 and 12 months post ACL-R compared to healthy controls, which is supported by large and clinically meaningful effect sizes. H:M ratio did not statistically differ from healthy limbs; however, a moderate effect size was calculated for the involved limb, suggesting a clinically meaningful up-regulation of spinal reflex excitability. These findings agree with longitudinal data of neural function in patients 6 months after ACL-R.[15] In this study, spinal reflex excitability increased from 2 weeks to 6 months post ACL-R despite not being different from healthy controls. In contrast, corticospinal excitability did not differ from healthy controls by 2 weeks, but was significantly reduced by 6 months after ACL-R. These data suggest a temporal, yet reciprocal relationship between spinal-mediated and cortically driven signaling to muscle, which supports the theoretical attempt to maintain muscle function. The time frame in which neural adaptations manifest is unclear.

Persistent quadriceps weakness is reported to manifest from aberrant sensory information arising from damaged peri-articular tissue.[42] Early after ACL injury and reconstruction, the presence of pain, swelling, and inflammation may stimulate nociceptors and articular mechanoreceptors, theorized to result in an ongoing reflexive inhibition of uninjured musculature due to a net reduction in spinal-mediated excitability.[14] Clinical signs of swelling and inflammation were not observed in our cohort, and only minimal pain was reported (< 1/10 cm). Previous authors[43,44] have used rabbit models to investigate the ongoing influence of ACL injury on sensory input to the central nervous system. In one study,[44] the ACL was transected with or without patellar tendon reconstruction, and sensory information arising from the femoral nerve was measured. After two weeks, a large magnitude (d = 1.15 [0.54, 1.76]) and statistically significant increase in afference of the ACL reconstructed limb was observed compared to control rabbits, suggesting that overload of sensory information transmission may contribute to persistent muscle dysfunction after ACL-R. Continued alterations in sensory integration after ACL-R

despite the resolution of pain and swelling may have contributed to the persistent muscle dysfunction observed in this study. Although spinal reflex excitability was not statistically different from healthy individuals in our study, a clinically meaningful up-regulation was detected, which may have began to occur as clinical signs of injury resolved. If true, this may suggest that persistent sensory aberrations inhibit peripheral musculature via supraspinal, and not only spinal-mediated mechanisms. In support of this, we observed a decrease in corticospinal excitability at each time point after ACL-R, suggesting that alterations in the threshold of neuronal depolarization in the motor cortex may be a mediating factor, contributing to the observed reduction in quadriceps strength and voluntary activation.

Interestingly, the quadriceps fatigued less than healthy control limbs early after ACL-R. Reduced knee extensor fatigue has been observed in patients with quadriceps dysfunction (CAR < 90%) more than 6 months post ACL-R compared to healthy counterparts following 30 minutes of continuous exercise.[45] Previous authors have hypothesized that selective type II fiber atrophy of the injured limb may explain this phenomenon, supporting the role of morphological adaptations in muscle dysfunction after ACL-R.[46] Type II atrophy of the quadriceps has been observed in patients 13 months post ACL-R,[47] which may be an attempt to maintain function during activity, although this finding has been inconsistently reported.[48,49] Muscle atrophy and fiber type were not assessed in the current study. However, atrophy of type II fibers is likely to occur early after ACL injury due to disuse, which may persist through the first year of recovery and explain the observed reduction in quadriceps strength and activation. In contrast, an increase in quadriceps fatigue was observed by two years compared to the early group, which did not differ from healthy controls, which may indicate a partial recovery of type II muscle fibers, if atrophied during early recovery; however, the presence of persistent weakness suggests incomplete morphological recovery. Chronic ACL injury may result in selective type I[48] or a combination of type I and type II fiber atrophy,[49] thereby explaining the long-term persistence of muscle weakness, despite an increase in fatigability. If patients are returning to more activity

beyond the first year from surgery, type II fiber hypertrophy could possibly be explained. Muscle dysfunction during early recovery likely appears to be a product of combined neuromuscular and morphological factors.

Late Post-Operative Outcomes

Large magnitude reductions in quadriceps strength were observed bilaterally late after ACL-R, compared to healthy controls, which is supported by a large and clinically meaningful effect size calculated for the involved limb. Quadriceps CAR was significantly higher in patients late after ACL-R compared to early (90.4% vs. 85.5%), but not statistically different from healthy controls (95.2%) or patients with knee osteoarthritis (92.6%). This could be interpreted as an improvement in voluntary activation over time; however, a large and clinically meaningful effect size was calculated between the involved and matched healthy control limb, suggesting the presence of persistent central activation failure during late recovery beyond what is considered normal. A bilateral reduction in corticospinal excitability was observed compared to healthy individuals; however, the effect size was moderate and the confidence interval crossed zero. Interestingly, a pattern of up-regulated spinal reflex excitability was observed similar to patients early after ACL-R, which was supported by a moderate and clinically meaningful effect size, despite the absence of a statistical difference. The combination of a meaningful increase in spinal reflex and corticospinal excitability may have contributed to the improvement in voluntary activation observed late after ACL-R. Previous authors[13] have identified increased spinal reflex excitability bilaterally at an average of 4 years after ACL-R, which is theorized to be a shunting response to maintain voluntary activation. This could explain the improvement of activation observed, yet may still be inadequate to fully restore quadriceps strength.

Knee Osteoarthritis

Patients with knee osteoarthritis demonstrated reductions in quadriceps strength and corticospinal excitability bilaterally, with large and clinically meaningful effect sizes calculated for the involved limb compared to healthy controls. Quadriceps strength did not differ among

ACL-R patients at any time point in the involved limb, which may reflect an ongoing inhibitory process preventing complete recovery of quadriceps function. Interestingly, both the involved and contralateral limb was weaker in patients with knee osteoarthritis compared to all other ACL-R patients including healthy individuals. The reduction in contralateral limb strength likely contributed to the symmetry observed in this patient group, and may provide a false sense of successful outcomes when based on symmetry alone.

The relationship between quadriceps strength and voluntary activation is hypothesized to have a greater association early after ACL-R,[50] which is not present at 2-15 years.[51] Our data partially support this in that involved limb MVIC torque and CAR were correlated early and late after ACL-R, but not in patients with knee osteoarthritis (figure 3). Patients with knee osteoarthritis demonstrated a bilateral reduction in MVIC torque compared to healthy controls; yet fell within normal limits of healthy voluntary activation. This divergence between quadriceps strength and voluntary activation may suggest that a point along the spectrum from late recovery to the onset of osteoarthritis exists where patients must adapt to use a larger proportion of an already diminished motor neuron pool. This could explain why patients with knee osteoarthritis exhibit relatively high activation despite being significantly weaker than healthy individuals. Patient with knee osteoarthritis also demonstrated the lowest corticospinal excitability coupled with the highest spinal reflex excitability (not statistically significant) compared to healthy individuals, each of large magnitude and clinically meaningful differences. It would appear that a reorganization of the central nervous system may occur in patients with chronic joint degeneration after ACL-R in an effort to maintain adequate muscle activation. A differentiation in organization of the motor cortex has been identified in patients with and without knee osteoarthritis,[52] further highlighting the importance of addressing cortical adaptations early after ACL injury and reconstruction. It remains unclear how improving corticomotor function would influence muscle strength and clinical outcomes; however, the results of this study warrant further investigation in this regard.

Patients with knee osteoarthritis in the current study were older than all other ACL-R and healthy groups. However, age was not significantly correlated with any of the primary outcome measures, and therefore was not controlled for statistically in our analyses. Previous authors have identified age-related alterations in motor unit recruitment patterns.[53] Knee extension strength is reportedly highest between the ages of 25-35, whereas a 15% decline may be expected per decade from 50-70 years.[54] This may be in part due to the known reduction in motor neuron volume, leading to a spatial redistribution of motor unit fibers.[55] The average age of patients with knee osteoarthritis was 45 years old, which ranged from 36-59. The involved osteoarthritic limb demonstrated more than a 38% decline in MVIC torque compared to healthy controls, which appears to exceed the natural response to aging, although this relationship is not clear. Additionally, patients with knee osteoarthritis reported lower activity levels and perceived health status than healthy individuals and ACL-R patients, which may contribute to a decline of neuromuscular function.

Implications

Quadriceps weakness was observed among all patients with a history of ACL-R. It is unclear if early changes in strength, endurance, voluntary activation, and corticospinal excitability perpetuate long-term muscle dysfunction; however, the temporal relationships of these measures may be a contributing factor. While we cannot support this theory due to the cross-sectional design of this study, time from surgery was not correlated with any measure of quadriceps function listed above, suggesting that the underlying cause of persistent muscle dysfunction is multifactorial, and not related to time alone. If left unaddressed, the progressive nature of contributing factors may result in irreversible joint injury. Time is often used as a primary consideration when determining readiness for return to activity;[56] however, previous authors have reported the recovery after ACL-R to be independent of time, which our results support. Therefore, it is possible that the progression of many factors other than time may be driving outcomes after ACL-R.

Limitations

The natural history of neuromuscular outcomes over the long term following ACL reconstruction is unknown, and cannot be elucidated using a cross-sectional study design. To further understand the impact of ACL injury on the natural history of quadriceps neuromuscular function, longitudinal data in injured and uninjured cohorts are warranted. Future long-term studies may better address the natural course of muscle function following ACL reconstruction. Secondly, this study did not match groups by age. Age may influence outcomes after ACL-R; however, no measures of quadriceps function were correlated with age, supporting our decision to include these patients. In order to achieve a realistic case-series, it is reasonable to have age distributions among groups that are different. Future studies may consider matching by age to determine if the same relationships exist. Lastly, we were not able to verify the severity of knee osteoarthritis at the time of enrollment, which likely increased heterogeneity among ACL-R patients with and without known osteoarthritis. Likewise, we could not verify the absence of osteoarthritis in all other ACL-R patients. Radiographic changes are likely to precede the onset of clinical symptoms, which may have inflated the presence of osteoarthritis in patients beyond two years from ACL-R. Future investigations may consider assessment of neuromuscular function based on a clinical diagnosis in addition to radiographic evidence only.

CONCLUSION

Neuromuscular impairments are present in patients early and late after ACL reconstruction with and without knee osteoarthritis. Quadriceps strength and corticospinal excitability were impaired at all time points compared to healthy individuals, suggesting the role of addressing cortical function following ACL-R. Seemingly mal-adaptive strategies appear to have both peripheral and central origins. While time may play a role in the manifestation of specific neuromuscular adaptions following ACL-R, clinical outcomes are multifactorial and not likely influenced by time alone.

Table 1_i. Participant demographics and patient reported outcomes

	Healthy (N = 30)	Early ACL-R (N = 34)	Late ACL-R (N = 30)	Osteoarthritis (N = 8)
Gender [a]	12 M/ 18 F	20 M/ 14 F	10 M/ 20 F	2 M/ 6 F
Age (years)	22.7 ± 4.6	22.5 ± 6.3§	24.9 ± 5.9§	45.4 ± 7.4*†‡
Height (cm)	174.8 ± 11.8	174.1 ± 11.0	171.7 ± 11.8	170.0 ± 9.7
Mass (kg)	75.1 ± 16.2	73.9 ± 16.9	74.9 ± 16.2	85.2 ± 24.8
IKDC	98.2 ± 4.2	81.5 ± 13.4*§	86.4 ± 10.4*§	62.9 ± 15.2*†‡
KOOS Total [b]	98.7 ± 2.5	87.5 ± 9.3*	92.1 ± 6.0*§	76.4 ± 10.8*‡
KOOS Pain	98.6 ± 3.7	90.1 ± 8.3*‡§	94.1 ± 5.8*†§	79.2 ± 8.1*†‡
KOOS Symptoms	98.0 ± 4.1	84.8 ± 12.1*§	86.3 ± 10.1*§	71.4 ± 11.5*†‡
KOOS Activities of Daily Living [b]	99.8 ± 0.7	95.8 ± 6.4*	97.8 ± 3.1*	90.1 ± 9.1*
KOOS Sport [b]	97.8 ± 6.3	76.5 ± 21.1*	88.5 ± 13.7*§	53.8 ± 29.4*‡
KOOS Quality of Life	96.5 ± 9.8	64.5 ± 20.6*‡§	78.1 ± 18.5*†§	49.2 ± 27.4*†‡
WOMAC Total [b]	0.3 ± 0.8	4.9 ± 6.2*	3.2 ± 2.9*	10.9 ± 7.7*
WOMAC Pain [b]	19.8 ± 0.6	19.3 ± 1.0§	19.4 ± 0.9§	17.6 ± 1.4*†‡
WOMAC Stiffness [b]	8.0 ± 0.0	7.0 ± 1.4*	7.0 ± 1.4*	6.5 ± 1.5*
WOMAC Function [b]	67.9 ± 0.3	65.3 ± 4.4*	66.5 ± 2.1*	61.4 ± 6.3*
Tegner: Pre-Injury	NA	8.4 ± 1.4§	8.4 ± 1.1§	6.3 ± 1.5†‡
Tegner: Current	7.2 ± 1.4	6.1 ± 1.9*§	6.9 ± 1.6§	4.3 ± 1.7*†‡
VAS (cm) [b]	0.1 ± 0.2	0.7 ± 0.9*‡	0.2 ± 0.5†§	1.2 ± 0.8*‡
Tampa Scale of Kinesiophobia	28.6 ± 5.8	34.4 ± 5.7*‡	32.1 ± 6.5†§	36.0 ± 6.0*‡
Veteran's Rand 12-Item Health	86.0 ± 7.6	80.4 ± 10.0*§	82.4 ± 6.7§	68.9 ± 14.2*†‡
Time since surgery (months) [b]	N/A	9.0 ± 4.3‡§	70.5 ± 41.6†§	115.9 ± 110.0†‡
Graft type, %				
Patellar tendon	N/A	51.5%	27.6%	37.5%
Hamstring	N/A	42.4%	48.3%	62.5%
Allograft	N/A	6.1%	24.1%	0%
Meniscectomy, %	N/A	35.5%	37.0%	75%
Meniscus repair, %	N/A	19.4%	14.8%	12.5%

Abbreviations: M, male; F, female; IKDC, International Knee Documentation Committee Subjective; KOOS, Knee Injury and Osteoarthritis Outcome Score; WOMAC, Western Ontario and McMaster Universities Arthritis Index

[a] Chi-squared analysis (χ^2)

[b] Non-normally distributed (Kruskal-Wallis Test)

* Different than healthy

† Different than early ACL-R

‡ Different than late ACL-R

§ Different than ACL-R with knee osteoarthritis

Alpha level set at $p \leq .05$

Table 2$_i$. Quadriceps neuromuscular function in ACL-r patients and healthy individuals (means ± SD)

		ACL-R			Healthy		
		Involved Limb	Uninvolved Limb	*p* value [a]	Matched Involved	Matched Uninvolved	*p* value [b]
Knee Extension MVIC Torque (Nm/kg)	Early	1.9 ± 0.6*	2.6 ± 0.7	**< .001**	2.8 ± 0.6	2.7 ± 0.6	.179
	Late	2.2 ± 0.6*	2.3 ± 0.6*	**.029**			
	OA	1.7 ± 0.7*	1.9 ± 0.9*†	.331			
Knee Extension Fatigue Index (%)	Early	14.3 ± 9.7*‡	19.6 ± 9.0*‡	**.002**	22.0 ± 8.0	22.2 ± 8.2	.721
	Late	21.7 ± 7.6	21.1 ± 6.8	.557			
	OA	21.6 ± 6.8	19.7 ± 7.3	.299			
Central Activation Ratio (%)	Early	85.5 ± 11.4*‡§	88.1 ± 9.4*‡§	.060	95.2 ± 5.6	93.8 ± 6.6	.181
	Late	90.5 ± 8.4	91.0 ± 10.3	.696			
	OA	92.6 ± 6.8	92.9 ± 7.6	.902			
Hoffmann Reflex (H:M ratio)	Early	0.19 ± 0.19	0.16 ± 0.15	.147	0.14 ± 0.12	0.14 ± 0.12	.988
	Late	0.21 ± 0.19	0.19 ± 0.16	.164			
	OA	0.26 ± 0.23	0.30 ± 0.32	.666			
Active Motor Threshold (% 2.0 Tesla)	Early	45.8 ± 7.9*‡	45.1 ± 7.4*‡	.600	39.0 ± 4.1	39.0 ± 3.4	.920
	Late	42.8 ± 9.1*§	42.3 ± 9.5*§	.601			
	OA	50.8 ± 7.6*‡	48.3 ± 7.1*‡	.106			

Abbreviations: MVIC, maximal voluntary isometric contraction; OA, knee osteoarthritis

[a] *p* value for difference between limbs in ACL-R patients

[b] *p* value for difference between limbs in healthy controls

* Different than healthy

† Different than early ACL-R

‡ Different than late ACL-R

§ Different than ACL-R with knee osteoarthritis

Alpha level set at $p \leq .05$

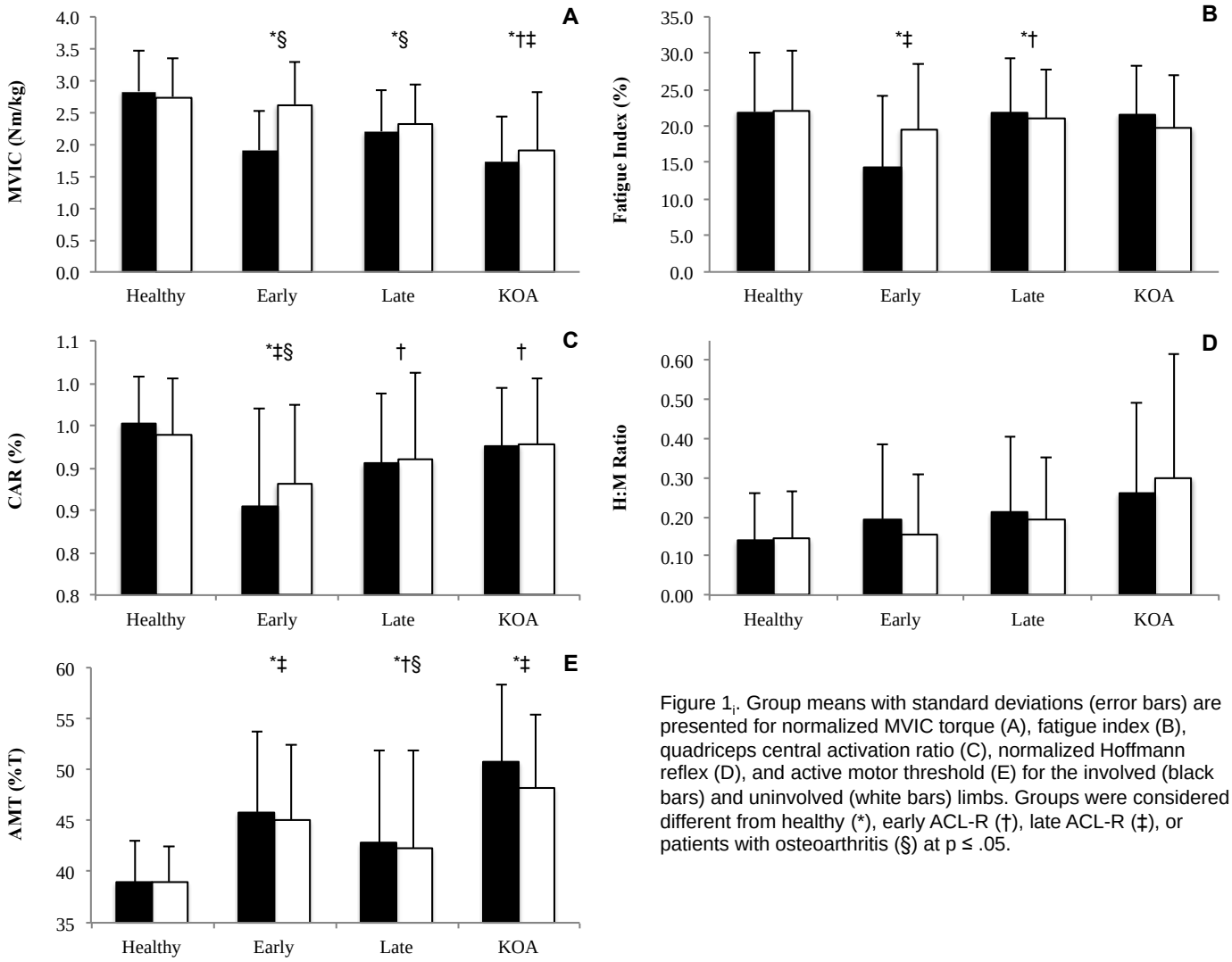

Figure 1$_i$. Group means with standard deviations (error bars) are presented for normalized MVIC torque (A), fatigue index (B), quadriceps central activation ratio (C), normalized Hoffmann reflex (D), and active motor threshold (E) for the involved (black bars) and uninvolved (white bars) limbs. Groups were considered different from healthy (*), early ACL-R (†), late ACL-R (‡), or patients with osteoarthritis (§) at $p \leq .05$.

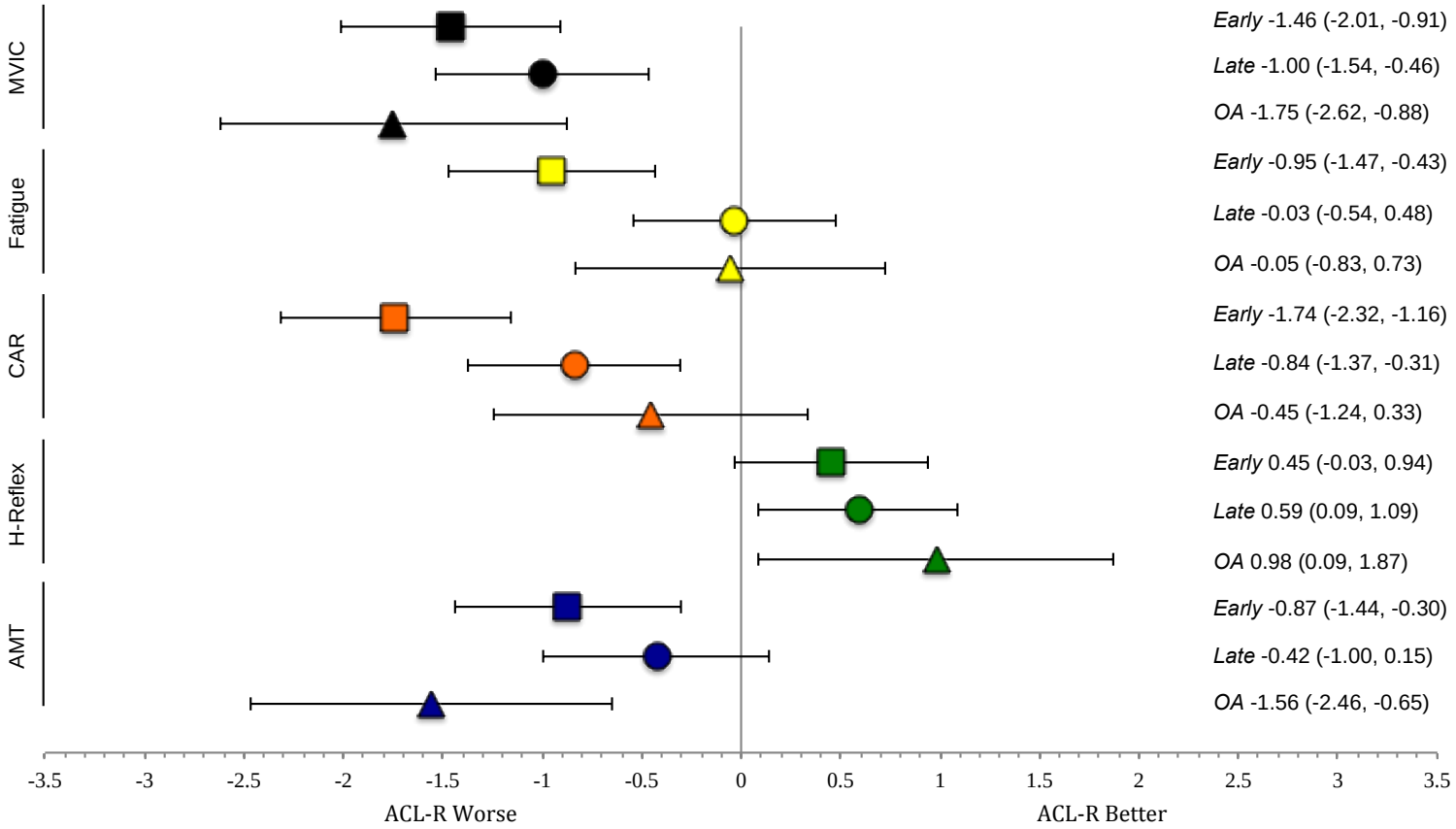

Figure 2$_i$. Cohen's d effect sizes with 95% confidence intervals for involved limb MVIC torque, fatigue index, CAR, H-reflex, and AMT compared to matched health control.

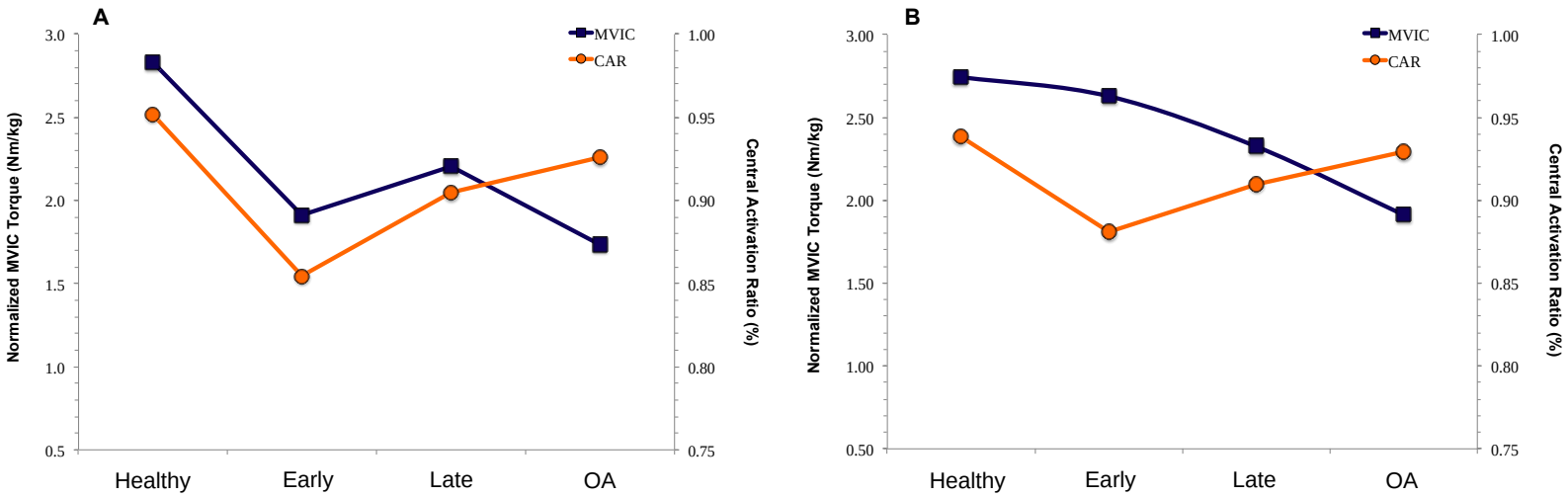

Figure 3$_i$. MVIC torque and quadriceps central activation ratio (CAR) of the involved (A) and uninvolved (B) limb in *healthy*, *early* ACL-R, *late* ACL-R, and ACL-R with *osteoarthritis* (OA) patients.

SECTION II: MANUSCRIPT II

RELATIONSHIP BETWEEN QUADRICEPS FUNCTION AND PATIENT REPORTED OUTCOMES IN ACL RECONSTRUCTED PATIENTS WITH AND WITHOUT KNEE OSTEOARTHRITIS

ABSTRACT

Context: The relationship between quadriceps muscle function and patient-reported outcomes over time after ACL reconstruction (ACL-R) is unclear. Understanding the relationships between muscle function and patient-reported outcomes may help clinicians better understand which factors may be affecting quality of life. **Objective:** To identify the relationship between objective measures of quadriceps function and patient-reported outcomes *early* (< 1 year) and *late* (> 2 years) after ACL-R, including patients who experienced post-traumatic *knee osteoarthritis*. **Design:** Cross sectional. **Setting:** University laboratory. **Patients or Participants:** 72 ACL-R patients were categorized as *early* (n = 34), *late* (n = 30), or *osteoarthritis* (n = 8). **Intervention(s):** None. **Main Outcome Measure(s):** Isokinetic strength (peak torque, total work, average power), maximum voluntary isometric contraction (MVIC) torque, fatigue index, central activation ratio, spinal reflex excitability, and corticospinal excitability were measured bilaterally. The Knee Injury and Osteoarthritis Outcome Score (KOOS) and Veteran's Rand 12-Item Health Survey (VR-12) were used to quantify knee function and global health. Multiple linear (stepwise) regression analyses were used to predict patient reported outcomes in each group. **Results:** *Early* after ACL-R, knee extensor work, AMT symmetry, pain, and activity level explained 67.8% of variance in KOOS ($p < .001$); whereas, knee extensor work, activity level, and pain explained 53.0% variance in VR-12 ($p < .001$). *Late* after ACL-R, age and isokinetic torque symmetry explained 28.9% of variance in KOOS ($p = .004$). In patients with *osteoarthritis*, kinesiophobia and isokinetic torque explained 77.8% of variance in KOOS score ($p = .010$); whereas, activity level explained 86.4% variance in VR-12 ($p = .001$). **Conclusions:** Factors of muscle function that are correlated with patient reported outcomes are different for patients early and late after ACL-R, and in those with knee osteoarthritis. These results support the importance of developing optimal evidence-based assessment strategies to identify impairments early after ACL-R.

Key Words: Isokinetic, limb symmetry, neuromuscular

Word Count: 300

INTRODUCTION

Anterior cruciate ligament (ACL) injury and reconstruction (ACL-R) remains common among young and middle-aged, active individuals.[1] ACL-R not only presents early challenges with regard to functional restoration, but also threatens long-term joint health,[57] return to physical activity,[58] and quality of life.[59] Persistent quadriceps weakness is a particular interst to many clinicians and researchers in this regard given its association with post-traumatic sequelae.[7,10] The causal relationship between long-term quadriceps dysfunction (e.g. muscle weakness and decreased neuromuscular control) and knee joint degeneration has been proposed;[7] however, the natural history of muscle function after ACL-R is not clear in this regard. Deleterious consequences of muscle weakness are commonly thought to develop over a long duration, yet significant joint space narrowing has been observed in patients within 4 years of reconstruction.[11] In a recent investigation, quadriceps weakness has been identified at 20-year follow up,[60] supporting the temporal relationship between muscle function and joint health. As an alarming proportion of individuals may experience degenerative changes within the first and second decade from reconstruction,[4] early identification of modifiable impairments are necessary.

Time from injury is a commonly reported criterion used in return to activity decision-making following ACL-R;[56] however objective evidence-based measures of function are warranted.[61] Recent authors[62] have identified persistent physical impairments beyond the time of return to activity, recommending the inclusion of single-limb functional performance in addition to limb symmetry when making these decisions. While these data suggest that physical recovery from ACL-R may be independent of time, the relationship between physical impairments and perceived function may be in part mediated by time. Previous authors[63] have established the diagnostic utility of both unilateral isometric knee extension torque and symmetric quadriceps central activation as strong indicators of self-reported knee function.[63] Interestingly, symmetric quadriceps strength is reported to explain more variance (R^2 = 0.13 vs. 0.08) in self-reported knee

function than unilateral strength in patients 8.2 months post ACL-R.[64] However, the relationship between unilateral function, limb symmetry, and time after ACL-R is not fully understood.

Establishing associations between disease and patient-oriented outcomes is a necessary step in developing evidence-based assessment paradigms. The association between quadriceps muscle function and patient-reported outcomes is widely studied; however, conflicting findings make it difficult for clinical recommendations. For example, isometric knee extension torque has been reported to explain between 7.8 and 61.0% of the variance in self-reported knee function at an average of 3.7[65] and 4.5[10] years post ACL-R respectively. These discrepancies may be in part due to the inclusion of patients at widespread time points after surgery. Risk for secondary or contralateral ACL injury is considerably greater during the two years following reconstruction,[66] making this a clinically relevant time range. However, it is unclear how these relationships may change beyond two years post-op. Understanding the relationships between muscle function and patient-reported outcomes may help clinicians to better understand which factors may be affecting quality of life.

Therefore, the purpose of this study was to identify the relationship between objective measures of quadriceps function and patient-reported outcomes at *early* (< 1 year) and *late* (> 2 years) durations after ACL-R, including patients who experienced post-traumatic *knee osteoarthritis*. We hypothesized that greater unilateral and more symmetric quadriceps function would be associated with improved patient-reported knee function and global health in patients early; whereas, symmetry would be most meaningful late, and unilateral function most meaningful in patients with knee osteoarthritis. Secondly, we aimed to identify which measures of quadriceps function best explained patient-reported function in each patient group, and hypothesized that strength would have the greatest influence on perceived outcomes.

METHODS

This was a cross-sectional study to investigate the influence of time from ACL-R on the relationship between quadriceps muscle function and patient-reported outcomes. Patients were

compared at *early* (< 1 year) and *late* (> 2 years) post-operative durations with and without *knee osteoarthritis*. Predictor variables for patient-reported function included isokinetic knee extension (peak torque, total work, average power) at 90°/sec, knee extension MVIC torque, fatigue index (FI), central activation ratio (CAR), Hoffmann reflex (H-reflex), and active motor threshold (AMT). Dependent variables included regional knee function, measured by the Knee Injury and Osteoarthritis Outcomes Score (KOOS), and global health, measured by the Veteran's Rand 12-Item Health Survey (VR-12).

Participants

72 patients with a history of primary, unilateral ACL-R participated in this study (table 1). Patients with a history of failed reconstruction, multiple ligament knee injury, treatable cartilage lesion, lower extremity joint surgery prior to ACL-R, lower extremity injury within 6 months other than ACL-R, concussion within 6 months, or neurological impairment were excluded from participation. Participants designated to the knee osteoarthritis group must have received a physician diagnosis after ACL-R based on radiographic evidence (Kellgren-Lawrence > 1) in one or more compartment.

Procedures

Participants were asked to refrain from caffeine use and intense exercise within 12 hours of testing.[16] Order of testing was maintained throughout the study, and counterbalanced by limb dominance (i.e. which limb would be used to kick a ball).

Patient-Reported Function

The KOOS[25] has been established as a reliable and valid subjective assessment tool sensitive to detect change in knee function after ACL-R and osteoarthritis. The KOOS includes subdomains of pain, symptoms, activities of daily living, sport related function, and quality like. The total KOOS score was used to quantify 'knee function' in this study. Patient-reported outcomes following ACL-R commonly emphasize regional knee function. However, the impact of ACL injury on global health and quality of life are less represented. The VR-12 is an example

of a 'global health' related quality of life measure that asks questions regarding general health, emotions, physical activity, pain, and personal feelings following injury.[29] The VR-12 is similar to the Short Form-36, which has reported to be responsive to ACL-R,[67] despite its widespread use in a variety of medical conditions. Activity level, pain, and fear of movement, were quantified using the Tegner Activity Scale,[27] visual analog scale (VAS) for pain at rest, and the Tampa Scale of Kinesiophobia (TSK).[28]

Spinal Reflex Excitability

The H-reflex was used to quantify spinal reflex excitability as described.[30,32] The area of greatest bulk over the vastus medialis was shaved, cleaned, and debrided. Two recording surface electromyography (EMG) electrodes were placed according to SENAM guidelines.[31] A ground-recording electrode was placed over the contralateral distal anteromedial tibia. The EMG signal was digitally converted at 2000 Hz via 16-bit data acquisition system (MP150, BIOPAC Systems, Inc., Goleta, CA), band-pass filtered from 10 to 500 Hz, and processed using Acqknowledge software (v. 4.2, BIOPAC Systems, Inc.). A stimulator module (STM100A, BIOPAC Systems, Inc.) and STMISOC current isolation unit were used to deliver an electrical stimulus to the femoral nerve. A dispersive carbon electrode was placed over the ipsilateral posterior thigh. A series of 1-millisecond square wave stimuli were sequentially administered until the maximum H-reflex and muscle response (M-response) were identified. Three maximal H-reflexes were averaged and normalized to the average of three maximal M-responses (H:M ratio) for analysis.

Isokinetic Strength

Isokinetic knee extension peak torque, total work, and average power were assessed at 90° per second using a Biodex multimodal dynamometer (System 3, Biodex Medical Systems, Inc., Shirley, NY). Participants were seated in 85° hip flexion and 90° knee flexion (anatomical reference) for the start of each test. A correction for limb weight was used. Participants were ensured a range of motion arc of 110°. Eight repetitions were completed at each testing speed with 45 seconds of rest between. An explanation of testing was provided, instructing participants

to “kick out and pull back as hard and fast as possible.” Participants were asked to keep their head and shoulders against the seat rest with arms crossed over their chest to minimize aberrant movement.[68] Several repetitions were practiced at each speed to visualize proper technique. Participants were provided real time visual feedback via 50-inch LCD monitor to view progress during testing. Verbal encouragement was provided to ensure maximal effort. Isokinetic peak torque (Nm/kg), total work (J/kg), and average power (W/kg) were normalized to body mass.

Isometric Strength and Quadriceps Central Activation

Participants were seated in the multimodal dynamometer and completed a standardized acclimatization protocol, in which a series of submaximal trials (25%, 50%, 75% perceived effort) were performed prior to recording three maximal effort trials with 60 seconds of rest between trials. A supramaximal percutaneous electrical stimulus was delivered to the quadriceps using the superimposed technique[33] during the third MVIC. Once the MVIC torque had reached a plateau consistent with previous trials, a square wave stimulator (S88, GRASS-TeleFactor, W. Warwick, RI) with isolation unit (SIU8T, GRASS-TeleFactor) was used to manually deliver a 100-millisecond train of 10 square-wave pulses to the thigh via two self-adhesive electrodes (3” x 5”) placed over the proximal vastus lateralis and distal vastus medialis. Real time visual feedback was provided, and verbal encouragement given to ensure maximal effort during testing. Force data were digitally converted at 125 Hz via 16-bit data acquisition system, low-pass filtered at 10 Hz, and processed using Acqknowledge software. The mean torque was calculated from a 100-millisecond epoch during the maximal contraction plateau, or immediately prior to the SIB torque (MVIC 3 only). The MVIC torque epoch recorded from three maximal trials was averaged, and normalized to body mass (Nm/kg) to quantify quadriceps strength. Quadriceps CAR was calculated as previously described.[34]

Quadriceps Fatigue Index

Quadriceps FI was quantified during a 30-second knee extension MVIC task.[35] Participants were instructed to “kick out as hard as possible and to maintain the contraction”

while seated in the dynamometer in a similar fashion to quadriceps strength testing. A researcher prompted participants to start kicking, and the 30-second trial began once the participant had achieved their perceived maximal effort. Verbal encouragement and visual feedback were omitted to minimize the occurrence of transient aberrant increases in torque. Force data were digitally converted at 125 Hz via 16-bit data acquisition system, low-pass filtered at 15 Hz, and processed using Acqknowledge software. The mean torque was recorded during a series of 1-second epochs, and the greatest torque epoch from the first 5 seconds of the trial was recorded as the maximal torque (T_{Max}). The area under the force-time curve (AUFC) for the entire contraction period for 0 to 30 seconds began at the time point of maximum muscle torque (TPM), and was used to quantify fatigue (Equation 1).

Equation 1: $$FI = [1 - (AUFC_{TPM\text{-}30} / (T_{Max,0\text{-}5} x (TPM - 30)))] x 100$$

Corticospinal Excitability

The AMT was used to quantify corticospinal excitability via transcranial magnetic stimulation. Participants were again seated in the dynamometer similar to the aforementioned procedures. Surface EMG electrodes were replaced over the vastus medialis and distal anteromedial tibia for each limb. Participants wore a Lycra swim cap with bisecting lines and a 1 cm x 1 cm grid to aid in the determination of the optimal stimulus location. Motor evoked potentials were elicited in the vastus medialis using a magnetic stimulator (MagStim Rapid, MagStim Company, Ltd., Wales, UK) with 110 mm double-cone coil. The AMT was determined by systematically reducing the stimulus intensity by 5% until a measurable MEP (> 200 μV) could no longer be elicited, then increased by 1% until its return for a minimum of 5 of 10 trials.[23] Real time visual feedback was used to aid participants during a force-matching task at 5% of the MVIC. EMG signals were digitally converted at 2000 Hz via 16-bit data acquisition system, band-pass filtered from 1 to 5000 Hz, and processed using Acqknowledge software.

Limb Symmetry

Unilateral data were assessed using the involved ACL-R limb, and limb symmetry indices (LSI) were calculated for each measure (Equation 2).

Equation 2: $LSI = (Involved / uninvolved) x 100$

Statistical Analysis

Group differences in demographics were assessed using separate one-way analyses of variance or Fisher's exact test. Pearson's product-moment correlations (r) were used to identify the relationship between individual measures of quadriceps function and patient-reported function when normally distributed. Spearman's rank-order correlations (ρ) were used in the event of non-normally distributed data. Correlations were performed within each patient group (*early* ACL-R, *late* ACL-R, ACL-R with *knee osteoarthritis*) for KOOS and VR-12 separately. The absolute value of correlation coefficients was classified as very weak (0.0 – 0.19), weak (0.20 – 0.39), moderate (0.40 – 0.59), strong (0.60 – 0.79), or very strong (0.80 – 1.0).

Separate multiple linear (stepwise) regression analyses were used to predict patient reported outcomes from measures of quadriceps function in each group. Only significantly correlated variables were considered for inclusion as predictors in our regression models. Variables were first assessed for multicollinearity, and those that were very strongly correlated with one another were reduced to only include the variable with the highest correlation. Probability thresholds for variable entry and removal were set at 0.05 and 0.10 respectively. Missing values were replaced with the mean for each respective group. The total R^2, adjusted R^2, and change in R^2 were calculated for each step of the respective analysis. The level of statistical significance was set a priori at $P \leq .05$. All statistical analyses were performed using SPSS (version 20.0, IBM, Chicago, IL).

RESULTS

Patient demographics are presented in table 1. There were no differences in gender, height, or mass between groups ($p > .05$). Patients with knee osteoarthritis were older than those without ($p < .05$).

Correlations

Correlation coefficients are presented for each patient group in table 2. In patients *early* after ACL-R, KOOS scores exhibited strong correlations with isokinetic work, moderate correlations with isokinetic power and torque, isokinetic power and work symmetry, AMT symmetry, MVIC torque, and pain, and weak correlations with isokinetic torque symmetry, activity level, and kinesiophobia. VR-12 was moderately correlated with all measures of unilateral isokinetic strength and symmetry, MVIC torque, and activity level, and weakly correlated with pain and time since surgery.

In patients *late* after ACL-R, KOOS scores exhibited moderate correlations with isokinetic torque symmetry, and weak correlations with isokinetic work and power symmetry, and age. VR-12 was weakly correlated with fatigue index symmetry.

In patients with *knee osteoarthritis* after ACL-R, KOOS scores exhibited strong correlations with all measures of isokinetic strength, MVIC torque, and activity level. VR-12 was very strongly correlated with all measures of isokinetic strength, MVIC torque, and activity level.

Multiple Regression

Regression results are presented for each group in tables 3-5. In patients *early* after ACL-R, normalized isokinetic work, active motor threshold symmetry, pain, and activity level predicted 67.8% of variance in KOOS score ($F_{4, 29} = 18.4$, $p < .001$). Normalized isokinetic work, activity level, and pain predicted 53.0% variance in VR-12 ($F_{3, 30} = 13.4$, $p < .001$).

In patients *late* after ACL-R, current age and peak torque symmetry predicted 28.9% of variance in KOOS score ($F_{2, 27} = 6.9$, $p = .004$). There were no significant predictors for VR-12.

In patients with *knee osteoarthritis* after ACL-R, kinesiophobia and normalized isokinetic torque predicted 77.8% of variance in KOOS score ($F_{2, 5} = 13.2$, $p = .010$). Activity level predicted 86.4% variance in VR-12 ($F_{1, 6} = 37.9$, $p = .001$) (Figure 1).

DISCUSSION

Measures of unilateral quadriceps muscle function and symmetry were correlated with patient-reported function *early* after ACL-R. In patients *late* after ACL-R, weak to moderate correlations were observed for only limb symmetry and patient-reported function. In contrast, unilateral measures of muscle function were strongly correlated with patient-reported function in patients with *knee osteoarthritis*. Knee extension isokinetic strength exhibited the strongest correlations with perceived knee function and global health in each patient group. The results of this study suggest that different factors predict patient reported outcomes at different time points after surgery, and that emphasis placed on a single outcome measure may not be the best strategy in evaluating all patients with ACL-R.

Our results indicate that both unilateral quadriceps function and symmetry are meaningfully associated with patient-reported function early after reconstruction. Improvements in unilateral quadriceps function and symmetry have been associated with improved knee function and lower extremity movement patterns at the time of return to sport.[69,70] Quadriceps strength and performance symmetry ≥ 90% have been suggested as indicators of safe return to activity.[71] For patients within a year after reconstruction, patient-reported outcomes may be best predicted by the combination of isokinetic knee extensor work in the involved limb, pain at rest, active motor threshold symmetry, and current activity level, suggesting that a single measure of muscle function may be insufficient to detect meaningful impairments related to perceived knee function and global health. Patients often experience a rapid decline in quadriceps strength and functional performance early after ACL-R, resulting in large asymmetries.[72] This may be explained in part by early peripheral changes in muscle of the injured limb,[50,51] as well as decreased central drive to muscle,[15] which may result in a functional decline of the contralateral

limb. Bilateral responses to unilateral injury may confound estimates of limb symmetry, and appear to support the additional use of unilateral assessments to identify impairments early after ACL-R. This may explain why the combination of a unilateral measure of peripheral muscle function and bilateral measure of central nervous system function were able to predict knee function in patients early after ACL-R.

We observed a moderate negative correlation between knee function and active motor threshold symmetry in patients early after ACL-R. Unilateral quadriceps isometric strength and corticospinal excitability have been reported to explain 66% of the variance in self-reported knee function.[10] Our results partially agree with these data in that measures of muscle function and patient demographics were able to explain 67.8% of self-reported knee function. Previous authors[22,73] have observed functional reorganization of the brain after ACL-R, with increased activation in attentional and sensory regions, suggestive of an increase in the cortical effort needed to complete a given task. In support of this, decreased corticospinal excitability, as measured by an increase in cortical motor thresholds, has been identified in patients as early as 6 months following ACL-R.[15] Our results suggest that patients with lower bilateral cortical thresholds report improved knee function. In contrast to previous findings, isokinetic knee extensor work and active motor threshold symmetry alone accounted for 46.1% of the variation in knee function, which appear to highlight the importance of additional factors that may influence perceived function in patients early after ACL-R. While the relationship between quadriceps strength and self-reported function is commonly investigated, it is clear that muscle function alone does not dictate clinical outcomes. Based on the findings of this study, activity level, pain, fear of movement or re-injury, and time since surgery should be considered in the context of perceived outcomes within the first year from ACL-R

Weak to moderate correlations were observed between knee function and isokinetic knee extensor strength (peak torque, total work, and average power) symmetry in patients late after ACL-R. Interestingly, no other measure of muscle function was correlated in these patients, with

the exception of fatigue index symmetry and global health; however, no variables were able to explain variance in global health. ACL injury and reconstruction is theorized to alter the natural history of muscle function;[60,74] however, the trajectory of bilateral muscle function after unilateral injury is not clear. Inter-limb asymmetries are reported to be greater early after surgery,[75] which may explain why measures of limb symmetry were correlated with patient-reported function early after ACL-R. Despite the observed relationships between isokinetic strength symmetry and knee function in patients late after ACL-R, peak torque symmetry was the only predictor of knee function, accounting for 12.5% of its variance. Compared to total work, which contributed 39.3% to the predictive ability in patients early after ACL-R, it appears that the relationship between unilateral muscle function and symmetry and patient reported outcomes is diminished beyond two years after ACL-R. It is possible that improved symmetry due to both improved ipsilateral muscle function and deterioration of the contralateral limb may mask persistent impairments. This may provide a false sense of good clinical outcomes and underestimate the presence of sub-clinical impairments, making assessment strategies difficult during this time frame. Beyond measures of muscle function, age was negatively correlated with knee function and accounted for 21.3% of its variance, indicating that younger patients reported improved knee function. Increased age at the time of surgery is a reported predictor of persistent muscle weakness up to 9 months after ACL-R.[76] Although age was able to explain nearly a quarter of the variance in knee function in the current study, the included measures of muscle function do not appear to have good predictive ability for perceived knee function or global health beyond two years in patients without osteoarthritis.

In patients with knee osteoarthritis after ACL-R, strong to very strong correlations between unilateral isokinetic and isometric quadriceps strength with knee function and global health were observed. The increased prevalence of osteoarthritis development in the contralateral limb has been observed at 20 years following unilateral ACL-R.[57] This, in conjunction with the functional decline that may naturally occur over time in the contralateral limb, may help patients

achieve symmetry despite having poor long-term outcomes. In support of this, our results suggest that unilateral muscle function is highly associated with knee function and global health in patients with knee osteoarthritis. Previous authors[9,77] have reported strong correlations between unilateral quadriceps strength and self-reported function in patients with knee osteoarthritis. In further support of the importance of unilateral muscle function in patients with knee osteoarthritis, our results demonstrated that symmetry of muscle function was not correlated with patient-reported outcomes. Quadriceps weakness and activation failure is widely reported in patients with knee osteoarthritis,[78] which may begin to explain why symmetry was not related to patient reported function in our study. Chronic bilateral deficits in voluntary quadriceps activation has been observed in patients with tibiofemoral osteoarthritis compared to healthy individuals.[17] Therefore, symmetry values may be misleading in these patients since bilateral weakness is a possibility, which may explain the lack of observed correlations between patient-reported function and symmetry in the current study.

Beyond objective measure of muscle function, kinesiophobia was strongly correlated with knee function, and current activity level was very strongly correlated with global health in patients with knee osteoarthritis. These data indicate that individuals with less fear of movement were more likely to report higher perceived knee function, and those who were more physically active perceived better health status. The role of physical activity and muscle function is well established. Decreased physical activity, or inactivity, commonly occurs with ageing, and is reported to negatively influence muscle function. Patients with osteoarthritis in this study were 45 years old on average, yet reported lower activity levels than patients with no osteoarthritis, which may have influenced the relationship between physical impairments and perceived function. Interestingly, current activity level was the only predictor of global health in these patients, indicating that this may be an adequate surrogate for objective muscle function relative to perceived health status in patients with knee osteoarthritis. Both kinesiophobia and current activity level contributed to more than half of the variance explained in patient-reported

outcomes, suggesting the need to look beyond traditional clinic or laboratory based measures of muscle strength in this patient population. By including a subset of patients with known osteoarthritis in this study, we were able better understand the long-term relationships between subjective and objective outcomes after ACL-R.

Clinical Implications

The results of this study suggest factors that are important during patient evaluations at different time points following ACL-R. The factors that are correlated with patient reported outcomes are different for patients early after ACL-R (< 1 year), late after ACL-R (> 2 years), and in patients with diagnosed knee osteoarthritis after ACL-R. Unilateral strength and symmetry are important factors early; however, as time progresses, symmetry may not be as useful to identify individuals with poor outcomes. Specifically, measures of isokinetic knee extensor strength appear to best predict patient-reported outcomes after ACL-R relative to other objective measures of muscle function. While very strong associations between unilateral measures of isokinetic and isometric quadriceps strength and patient-reported function were observed in patients with knee osteoarthritis, clinicians must be able to identify impairments early. The results of this study support the importance of developing optimal evidence-based assessment strategies to identify impairments early after ACL-R, and effectively guide patient care.

Limitations

The cross-sectional design of this study does not allow us to make conclusions based on the natural history of the relationship between quadriceps function, demographics, and patient-reported function. Efforts were made to recruit a homogenous sample of patients after ACL-R; however, the purpose of the study was to investigate the relationships between subjective and objective outcomes over time, thus making it difficult to match groups on all demographics. We believe that the sample included in this study is representative of patients after ACL-R given the distribution of gender, graft type, and meniscal involvement. Additionally, we were not able to confirm the absence of osteoarthritis in patients early and late after ACL-R.

CONCLUSION

Involved limb knee extensor work and corticospinal excitability symmetry explained patient outcomes early after ACL-R, suggesting the importance of assessing limb symmetry and unilateral function within the first year after surgery. Isokinetic knee extensor torque symmetry was only able to explain knee function to a lesser degree, making patient assessment beyond two years more challenging when using traditional measures of muscle function. Involved limb isokinetic knee extensor torque was only able to explain knee function in patients with osteoarthritis; however, outcomes were largely influenced by activity level and kinesiophobia in this group. These data support the inclusion of both objective measures of muscle function and patient-reported function when assessing patient outcomes, and suggest factors that are important during patient evaluations at different time points following ACL-R. Clinicians can use the information from this study to formulate an assessment that is specific to patients at different time points after surgery.

Table 1_{ii}. Patient demographics (mean ± standard deviation)

	Group		
	Early (n = 34)	Late (n = 30)	Osteoarthritis (n = 8)
Gender [a]	20 M/ 14 F	10 M/ 20 F	2 M/ 6 F
Age (years)	22.5 ± 6.3‡	24.9 ± 5.9‡	45.4 ± 7.4*†
Height (cm)	174.1 ± 11.0	171.7 ± 11.8	170.0 ± 9.7
Mass (kg)	73.9 ± 16.9	74.9 ± 16.2	85.2 ± 24.8
KOOS total	87.5 ± 9.3†‡	92.1 ± 6.0*‡	76.4 ± 10.8*†
VR-12	80.4 ± 10.0‡	82.4 ± 6.7‡	68.9 ± 14.2*†
Tegner activity scale: current	6.1 ± 1.9‡	6.9 ± 1.6‡	4.3 ± 1.7*†
Visual analog scale for pain (cm)	0.7 ± 0.9†	0.2 ± 0.5*‡	1.2 ± 0.8*†
Tampa Scale of Kinesiophobia	34.4 ± 5.7	32.1 ± 6.5	36.0 ± 6.0
Time since surgery (months)	9.0 ± 4.3†‡	70.5 ± 41.6*‡	115.9 ± 110.0*†

Abbreviations: KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veteran's Rand 12-Item Health Survey

[a] Chi-squared analysis

* Different than early ACL-R

† Different than late ACL-R

‡ Different than ACL-R with osteoarthritis

Alpha level set at $p \leq .05$

Table 2_{ii}. Association between quadriceps function, patient demographics, and patient-reported function

	Correlation Coefficient [a]					
	Early		Late		Osteoarthritis	
	KOOS	VR-12	KOOS	VR-12	KOOS	VR-12
Quadriceps Function						
Peak torque at 90°/s (Nm/kg)	**.522**	**.539**	.261	.000	**.723**	**.809**
Total work at 90°/s (Nm/kg)	**.627**	**.585**	.049	.035	**.659**	**.876**
Average power at 90°/s (Nm/kg)	**.570**	**.529**	.156	-.013	**.730**	**.866**
MVIC torque (Nm/kg)	**.405**	**.414**	.117	.245	**.649**	**.843**
Fatigue index (%)	-.227	-.128	-.124	.156	.009	-.367
Central activation ratio (%)	.165 [a]	.109 [a]	-.063	.118 [a]	.310 [a]	.405 [a]
Hoffmann reflex (H:M)	-.138 [a]	.046 [a]	-.049	-.360	.451	-.200
Active motor threshold (%T)	-.003	-.201	.102	-.152	.465	-.281
LSI peak torque at 90°/s	**.398**	**.460**	**.445**	.105	.424	.136
LSI total work at 90°/s	**.413**	**.493**	**.388** [a]	.105 [a]	.396	.394
LSI average power at 90°/s	**.465**	**.498**	**.380**	-.065	.318	-.135
LSI MVIC torque	.138	.268	.276	.097	-.214	.386
LSI fatigue index	.054	.021	-.013	**-.371**	-.732	-.126
LSI central activation ratio	.133 [a]	.108	.069	.147	.154	.198
LSI Hoffmann reflex	-.292 [a]	-.138 [a]	-.263	.143	.429 [a]	.143 [a]
LSI active motor threshold	**-.448**	.007	.101	.163	-.515 [a]	-.443 [a]
Patient Demographics						
Current Age (years)	-.263	-.119	**-.461**	.015	.061	-.045
Current Activity Level (Tegner)	**.384**	**.515**	.059	.340	.260	**.929**
Pain (VAS)	**-.538**	**-.395**	-.214 [a]	.159 [a]	-.169	-.076
Kinesiophobia (TSK)	**-.381**	-.260	-.300	-.064	**-.771**	-.050
Time since surgery (months)	.178	**.351**	-.130 [a]	-.278 [a]	.111	-.041

Abbreviations: KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veteran's Rand 12-Item Health Survey; MVIC, maximal voluntary isometric contraction; LSI, limb symmetry index; VAS, visual analog scale; TSK, Tampa Scale of Kinesiophobia

[a] Spearman's ρ

Bold indicates significant at $p \leq .05$

Table 3_{ii}. Final regression model in patients early after ACL-R

	KOOS					VR-12			
Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]	Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]
Total work	.393	.374	.393*	.001	Total work	.342	.322	.342*	.006
Pain	.578	.551	.185*	< .001	Activity level	.456	.421	.114*	.003
AMT Symmetry	.646	.610	.068*	.008	Pain	.573	.530	.116*	.008
Activity level	.717	.678	.071*	.011					

Abbreviations: KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veteran's Rand 12-Item Health Survey; AMT, active motor threshold; Adj., adjusted R^2; Δ, change in R^2

[a] *p* value for individual variable in final model

* $p \leq .05$

Table 4_{ii}. Final regression model in patients late after ACL-R

	KOOS					VR-12			
Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]	Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]
Age	.213	.185	.213*	.024	No significant predictors	-	-	-	-
Peak torque symmetry	.338	.289	.125*	.032					

Abbreviations: KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veteran's Rand 12-Item Health Survey; Adj., adjusted R^2; Δ, change in R^2

[a] *p* value for individual variable in final model

* $p \leq .05$

Table 5_{ii}. Final regression model in patients with knee osteoarthritis after ACL-R

	KOOS					VR-12			
Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]	Step/Variable	R^2	Adj. R^2	ΔR^2	*P* value [a]
Kinesiophobia	.595	.527	.595*	.025	Activity level	.864	.841	.864*	.001
Peak torque	.841	.778	.246*	.039					

Abbreviations: KOOS, Knee Injury and Osteoarthritis Outcome Score; VR-12, Veteran's Rand 12-Item Health Survey; Adj., adjusted R^2; Δ, change in R^2

[a] *p* value for individual variable in final model

* $p \leq .05$

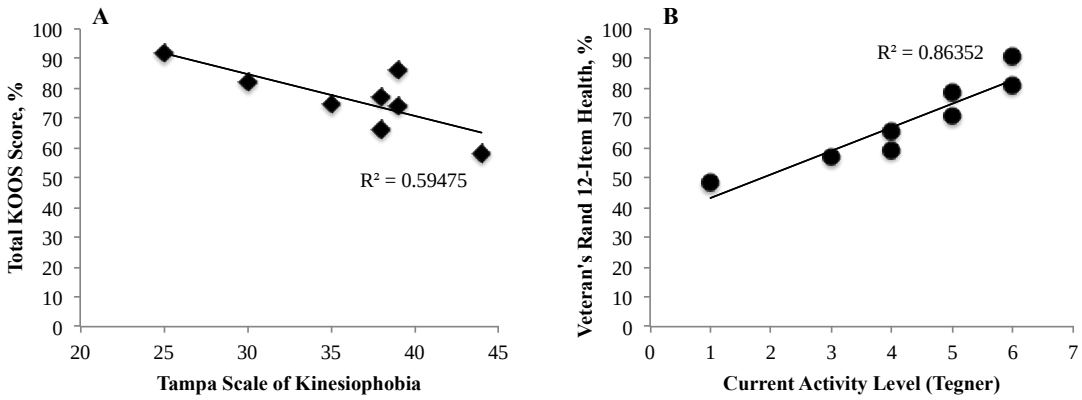

Figure 1_{ii}. Relationship between self-reported knee function and fear of movement (A) and between self-reported global health and current activity level (B).

SECTION II: MANUSCRIPT III

QUADRICEPS AND PATIENT REPORTED FUNCTION IN ACL RECONSTRUCTED PATIENTS: A PRINCIPAL COMPONENT ANALYSIS

ABSTRACT

Context: Assessment of physical function for individuals after ACL reconstruction (ACL-R) is complex and warrants the use of diverse evaluation strategies. By identifying tests that provide the most unique and meaningful information, a clearer understanding of post-traumatic muscle characteristics can be gained while maximizing the efficiency of assessment. **Objective:** To investigate the underlying constructs of quadriceps muscle function that uniquely describes aspects of performance in patients after ACL-R. **Design:** Cross sectional. **Setting:** University laboratory. **Patients or Participants:** 72 patients with a history of primary, unilateral ACL-R, and 30 healthy individuals participated. **Intervention(s):** None. **Main Outcome Measure(s):** Isokinetic strength (peak torque, total work, average power) at 90° and 180°/second, maximal voluntary isometric contraction (MVIC) torque, fatigue index, central activation ratio (CAR), Hoffmann reflex (H:M ratio), and active motor threshold (AMT) were measured bilaterally. Principal component analyses were performed for the involved limb, uninvolved limb, and limb symmetry. Receiver-operator-characteristic curve analyses were conducted to determine the diagnostic utility of each variable. Binary logistic regression was used to predict group membership (ACL-R vs. healthy). **Results:** Three components of peripheral, central, and combined muscle function were identified, which explained 70.7-80.5% of variance among measures of quadricep function. Total knee extensor work at 90°/sec (≥18.4 J.kg), AMT (≥39.5%), and CAR (≥94.7%) of the involved limb were strong predictors of patient status, and correctly classified 83.5% of patients with ACL-R ($p < .001$). **Conclusions:** Unique constructs of peripheral, central, and combined peripheral and central muscle function likely exist in ACL-R patients. Total knee extensor work at 90°/sec, AMT, and quadriceps CAR consistently explained a significant portion of variance in measures of quadriceps function, demonstrated acceptable to excellent diagnostic utility, and predicted group membership with 72.8 to 83.5% accuracy.

Word Count: 282

Key Words: Active motor threshold, isokinetic torque, quadriceps activation

INTRODUCTION

Clinical outcomes following ACL reconstruction (ACL-R) are often evaluated based on impairment and patient-reported function. The use of clinically meaningful tests is an important aspect of return to activity decision-making following ACL-R. Information from a variety of tasks including strength, performance, movement quality and perceived function have been recommended[61,71] while evaluating athletes recovering from ACL-R. Unfortunately, the use of objective measures of function in clinical decision making remains sparse. A recent systematic review[56] identified time since surgery as the most widely cited criterion used to determine readiness for return to activity after ACL-R, with subjective and/or objective criteria being far less utilized. The lack of consensus regarding the most appropriate criteria for releasing patients to activity following ACL-R may contribute to inconsistent reporting of standardized tests, or test batteries.[56,61]

Assessment of physical function and health status for individuals with ACL-R is complex and warrants the use of diverse evaluation strategies. Multimodal assessments of peripheral muscle function (e.g. isokinetic and isometric quadriceps strength) are commonly used to evaluate outcomes after ACL-R. For example, persistent quadriceps weakness is well described,[8,79] and remains a long-term concern in this population. Maximizing both unilateral strength and symmetry is reported to positively influence self-reported knee function after ACL-R.[64] Quadriceps strength symmetry is commonly quantified, and is believed to be an important factor in landing mechanics,[69,80] functional outcomes,[70,81] and perceived function.[63] However, bilateral alterations in quadriceps strength are believed to arise from a centrally mediated response to unilateral peripheral joint injury,[14,18,82] which may confound measures of limb symmetry. For example, bilateral quadriceps activation failure has been identified in patients after ACL-R,[8] suggesting the need to include measures of centrally-mediated muscle function (e.g. voluntary activation, spinal reflex excitability, corticospinal excitability) in assessment batteries. The wealth of data available to clinicians may be overwhelming since there are many possible

measures that may help guide treatment decision-making. By identifying tests that provide the most useful information, clinicians and researchers can utilize a consistent set of measures, and improve the ability to assess patient outcomes with the fewest and most important tests.

Some potential factors in performing large test batteries are the time requirement from clinician and patient, expensive and technically demanding equipment, and the concern for exposing patients to unnecessary risk with extensive testing. In an effort to minimize risk, and maximize the efficiency of an assessment program, we aim to identify tests that provide the most meaningful information about a population of interest. Principal component analysis (PCA) is an analytical technique that can help in this regard by reducing the dimensionality of a larger set of measures to provide a clearer interpretation of underlying constructs that best characterize a given population. By further establishing the diagnostic and predictive abilities of assessment tools to discriminate between patients with and without ACL-R, clinicians and researchers can begin to evaluate the utility of each, and work towards an evidence-based assessment.

Therefore, the purpose of this study was to investigate the underlying constructs of lower extremity muscle function that uniquely describe aspects of performance in ACL-R individuals. We hypothesized that clinically relevant clusters of data would be identified and that each would provide unique and meaningful information. A secondary purpose was to establish clinical thresholds for measures of quadriceps function to classify patients with and without ACL-R.

METHODS

This was a descriptive laboratory study to investigate quadriceps neuromuscular and patient-reported function among ACL-R individuals and healthy controls. Independent variables included group (ACL-R, healthy) and limb (involved, uninvolved). Dependent variables included isokinetic strength (peak torque, total work, average power) at 90° and 180° per second, maximal voluntary isometric contraction (MVIC) torque, fatigue index, central activation ratio (CAR), Hoffmann reflex (H-reflex), and active motor threshold (AMT). The International Knee Documentation Committee (IKDC) subjective knee evaluation form,[24] Knee Injury and

Osteoarthritis Outcome Score (KOOS),[25] and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[26] were used to quantify regional knee function. The Tampa Scale of Kinesiophobia (TSK)[28] and Veteran's Rand 12-Item Health Survey (VR-12)[29] were used to quantify psychological function. The Tegner Activity Scale[27] and Godin Leisure-Time Exercise questionnaire[83] were used to quantify activity related function.

Participants

A total of 102 individuals volunteered for this study, including 72 patients with a history of primary, unilateral ACL-R and 30 healthy individuals between the ages of 15 and 65 (table 1). Patients were excluded if they had a lower extremity joint surgery prior to ACL-R, multiple ligament reconstruction, history of graft failure, contralateral knee surgery, lower extremity injury within 6 months, concussion within 6 months, neurological disorder, or were currently taking a centrally acting medication[23] at the time of enrollment. Graft type and meniscal involvement were reported descriptively, but not used to determine eligibility. Healthy participants were excluded if they reported a lower extremity joint injury requiring care within 6 months or history of concussion. Our University's Institutional Review Board for Health Sciences Research approved this study, and all participants provided informed consent prior to enrollment.

Procedures

All testing was performed bilaterally during a single study visit. Participants were asked to refrain from caffeine use and intense exercise within 12 hours prior to participation.[16] Testing always occurred in the following sequence: H-reflex, isokinetic strength, MVIC torque, CAR, fatigue index, and AMT. Limb dominance was determined by asking participants which limb would be used to kick a ball. The order of testing was counterbalanced by limb dominance to account for a potential learning effect.

Spinal Reflex Excitability

The H-reflex was used as previously described[30] to quantify spinal-mediated inhibition of the quadriceps. The area of greatest bulk over the vastus medialis was shaved, cleaned, and

debrided. Two recording surface electromyography (EMG) electrodes were placed according to SENAM guidelines.[31] A ground-recording electrode was placed over the contralateral distal anteromedial tibia. The EMG signal was digitally converted at 1000 Hz via 16-bit data acquisition system (MP150, BIOPAC Systems, Inc., Goleta, CA), band-pass filtered from 10 to 500 Hz, and processed using Acqknowledge software (v. 4.2, BIOPAC Systems, Inc.). A stimulator module (STM100A, BIOPAC Systems, Inc.) and STMISOC current isolation unit were used to deliver an electrical stimulus to the femoral nerve. A dispersive carbon electrode was placed over the ipsilateral posterior thigh. A series of 1-millisecond stimuli were sequentially administered until the maximum H-reflex and muscle response (M-response) were identified. The average of three maximal responses was recorded for each measure, and the H-reflex was normalized the M-response (H:M ratio) for final analysis. Strong within-session reliability ($ICC_{3,k}$ = 0.987) has been reported when using the average of three measures.[30]

Isokinetic Strength

Isokinetic peak torque, total work, and average power were assessed at 90° and 180° per second using a Biodex multimodal dynamometer (System 3, Biodex Medical Systems, Inc., Shirley, NY). Participants were seated in 85° hip flexion and 90° knee flexion (anatomical reference) for the start of each test. A correction for limb weight was used. Participants were ensured a range of motion arc of 110°. Eight repetitions were completed at each testing speed with 45 seconds of rest between. An explanation of testing was provided, instructing participants to "kick out and pull back as hard and fast as possible." Participants were asked to keep their head and shoulders against the seat rest with arms crossed over their chest to minimize aberrant movement.[68] Several repetitions were practiced at each speed to visualize proper technique. Participants were provided real time visual feedback via 50-inch LCD monitor to view progress during testing. Verbal encouragement was provided to ensure maximal effort. Data were normalized to body mass for peak torque (Nm/kg), total work (J/kg), and average power (W/kg).

Knee Extension MVIC Torque and Voluntary Activation

Participants were seated in the multimodal dynamometer and completed a standardized acclimatization protocol, in which a series of submaximal trials (25%, 50%, 75% perceived effort) were performed prior to recording three maximal effort trials with 60 seconds of rest between trials. A supramaximal percutaneous electrical stimulus was delivered to the quadriceps using the superimposed technique[33] during the third MVIC. Once the MVIC torque had reached a plateau consistent with previous trials, a square wave stimulator (S88, GRASS-TeleFactor, W. Warwick, RI) with isolation unit (SIU8T, GRASS-TeleFactor) was used to manually deliver a 100-millisecond train of 10 square-wave pulses to the thigh via two self-adhesive electrodes (3" x 5") placed over the proximal vastus lateralis and distal vastus medialis. Real time visual feedback was provided, and verbal encouragement given to ensure maximal effort during testing. Force data were digitally converted at 125 Hz via 16-bit data acquisition system, low-pass filtered at 10 Hz, and processed using Acqknowledge software. A 100-millisecond epoch was recorded during a stable region from MVIC 1 and 2, and immediately prior to the resultant superimposed burst torque (T_{SIB}) of MVIC 3. MVIC torque (T_{MVIC}) were normalized the body mass (Nm/kg). The central activation ratio (CAR) was used to quantify voluntary activation (Equation 1).[34]

Equation 1: $CAR = T_{MVIC} / (T_{MVIC} + T_{SIB})$

Fatigue Index

Quadriceps fatigue was quantified during a 30-second knee extension MVIC task.[35] Participants were instructed to "kick out as hard as possible and to maintain the contraction" while seated in the dynamometer in a similar fashion to quadriceps strength testing. Participants were prompted to start kicking, and the 30-second trial began once the participant had achieved their perceived maximal effort. Verbal encouragement and visual feedback were omitted to minimize the occurrence of transient aberrant increases in torque. Force data were digitally converted at 125 Hz via 16-bit data acquisition system, low-pass filtered at 15 Hz, and processed

using Acqknowledge software. The mean torque was recorded during a series of 1-second epochs, and the greatest torque epoch from the first 5 seconds of the trial was recorded as the maximal torque (T_{Max}). The fatigue index was calculated as the area under the force-time curve (AUFC) for the entire contraction period for 0 to 30 seconds, which began at the time point of maximum muscle torque (TPM) (Equation 2).

Equation 2: $$FI = [1 - (AUFC_{TPM\text{-}30} / (T_{Max,0\text{-}5} x (TPM - 30)))] x 100$$

Corticospinal Excitability

Active motor threshold (AMT) was used to quantify corticospinal excitability via transcranial magnetic stimulation. Participants were again seated in the dynamometer similar to the aforementioned procedures. Surface EMG electrodes were replaced over the vastus medialis and distal anteromedial tibia for each limb. Participants wore a Lycra swim cap with bisecting lines and a 1 cm x 1 cm grid to aid in the determination of the optimal stimulus location. Motor evoked potentials were elicited using a magnetic stimulator (MagStim Rapid, MagStim Company, Ltd., Wales, UK) with 110 mm double-cone coil. The AMT was determined by systematically reducing the stimulus intensity by 5% until a measurable MEP (> 200 μV) could no longer be elicited, then increased by 1% until its return for a minimum of 5 of 10 trials.[23,84] Real time visual feedback was used to aid participants during a force-matching task at 5% of the MVIC. EMG signals were digitally converted at 2000 Hz via 16-bit data acquisition system, band-pass filtered from 1 to 5000 Hz, and processed using Acqknowledge software.

Limb Symmetry

Limb symmetry indices (LSI) were calculated for each dependent variable of quadriceps function in the ACL-R group (Equation 3) and healthy control group (Equation 4). The ACL-R limb was identified as the dominant limb in 57% of ACL-R patients. Therefore, a random number generator was used to randomly assign 57% of the healthy control dominant limbs as the "matched ACL-R limb" for analysis.

Equation 3: $LSI_{ACL\text{-}R} = ACL\text{-}R\lim b / contralteral\lim b$

Equation 4: $LSI_{CON} = MatchedACL\text{-}R\lim b / matchedcontralteral\lim b$

Statistical Analysis

Criteria to determine the appropriate sample size when using PCA is variable, with recommended subject-to-variable ratios ranging 3:1 to 20:1. In the current study, PCA was performed on a sample of 72 ACL-R patients using 11 variables per model, which resulted in a 6.5:1 subject-to-variable ratio. Although no absolute threshold for minimum sample size exists, 50 samples are generally considered a minimum. The Kaiser-Meyer-Olkin (KMO) measure was used to verify that our sample was adequate, where a value greater than 0.5 indicates adequate sample size.

All normally distributed data were compared between groups using independent *t*-tests, and non-normally distributed data were compared using Mann-Whitney U tests. Gender was compared between groups using a Chi-squared test.

PCA was performed via principal component extraction on ACL-R patients only. Separate analyses were conducted for quadriceps function and patient-reported function. Data were analyzed with and without varimax rotations in an attempt to uncover simple structure. Both theoretical and empirical evidence were considered when deciding on the number of components to retain in the final model. Separate analyses were conducted using data from the (1) involved limb, (2) uninvolved limb, and (3) limb symmetry indices. Missing values were replaced with the grand mean from ACL-R patients. The decision to retain a component was made if the unrotated component exceeded an eigenvalue of 1.0, met Horn's parallel analysis and minimum scree requirement, and explained an appreciable percentage of total variance ($\geq 5\%$). Individual variables within each component were initially retained if they explained a minimum of 10% of the variance (loaded ≥ 0.3). Bivariate Pearson product-moment correlations (r) were conducted among variables that met these criteria to determine the presence of multicollinearity ($r \geq 0.9$) or

lack of association ($r < 0.3$) within each component. Variables were retained based on strength of loading, redundancy in variance explained, the ability to distinguish between healthy and ACL reconstructed patients (based on *p* value and Cohen's *d* effect size), and diagnostic utility.

Receiver operator characteristic (ROC) curve analyses were conducted to determine the diagnostic utility of each variable. The area under the ROC curve (AUC) represents the ability of a diagnostic tool to correctly assign a patient to an appropriate diagnostic category, and was used to evaluate each variable, where an AUC of 0.5 = no discrimination, 0.7 – 0.8 = acceptable discrimination, 0.8 – 0.9 = excellent discrimination, and > 0.9 = outstanding discrimination. Cut-off values that maximized both sensitivity and specificity were visually selected as thresholds to classify group membership (ACL-R vs. healthy) for all retained variables.

Binary logistic regression was used to predict group membership (ACL-R vs. healthy) using the combination of variables with the greatest discriminatory value in each retained component. Included variables were entered into a regression model for the involved limb, uninvolved limb, and limb symmetry. All variables entered into each model were retained to determine the predictive ability of each test battery. Missing values were replaced with the grand mean for ACL-R patients. The accuracy of classification, sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio was calculated for each model. The level of statistical significance was set a priori at $p \leq .05$. All statistical analyses were performed using SPSS (version 20.0, IBM, Chicago, IL).

RESULTS

Between Group Comparisons

Demographics and patient-reported function are presented in table 1. Groups did not significantly differ by gender, age, height, or mass ($p > .05$). Means and standard deviations for measures of quadriceps function are presented in table 2.

Principal Component Analysis

PCA for the involved limb revealed a three-component solution that explained 80.5% of the cumulative variance (table 3). Component one accounted for 59.1% variance, and included all measures of isokinetic strength and knee extension MVIC torque, which were strongly correlated with one another ($r > 0.7$). Component two accounted for 10.7% variance, and included the H:M ratio, and AMT, which were weakly correlated ($r = -.168$, $p = .177$). Component three accounted for 10.7% variance, and included CAR and fatigue index, which were weakly correlated ($r = .083$, $p = .486$).

PCA for the uninvolved limb revealed a two-component solution that explained 70.7% of the cumulative variance (table 4). Component one accounted for 56.1% variance, and included all measures of isokinetic torque and knee extension MVIC torque, which were strongly correlated with one another ($r > 0.7$). Component two accounted for 14.6% variance and included AMT, H:M ratio, CAR, and fatigue index, which were weakly correlated with one another ($r < 0.3$).

PCA for limb symmetry revealed a three-component solution that explained 78.9% of the cumulative variance (table 5). Component one accounted for 54.0% variance, and included all measures of isokinetic strength and knee extension MVIC torque, which were strongly correlated with one another ($r > 0.7$). Component two accounted for 14.9% variance, and included fatigue index and CAR, which were moderately correlated ($r = -.311$, $p = .008$). Factor three accounted for 10.0% variance, and included AMT and H:M ratio, which were weakly correlated ($r = .041$, $p = .751$).

PCA for patient reported function revealed a two-component solution that explained 70.7% of the cumulative variance among variables (table 6). Component one accounted for 43.7%, and included IKDC, KOOS, WOMAC, and TSK. Component two accounted for 27.0% variance, and included the Godin, Tegner, and VR-12.

Receiver Operator Characteristic Curve (Discriminatory Value)

Involved limb total work at 90°/sec, AMT, and CAR yielded the highest discriminatory ability for each respective factor (table 3). Cut-off values of 18.4 J/kg (sensitivity: 0.83, specificity: 0.77), 39.5% (sensitivity: 0.77, specificity: 0.62), and 94.7% (sensitivity: 0.71, specificity: 0.69) were established to discriminate between groups for each respective variable.

Uninvolved limb total work at 90°/sec and AMT yielded the highest discriminatory ability for each respective factor (table 4). Cut-off values of 18.9 J/kg (sensitivity: 0.61, specificity: 0.80) and 41.5% (sensitivity: 0.68, specificity: 0.78) were established to discriminate between groups for each respective variable.

Limb symmetry indices for peak torque at 180°/sec, CAR, and AMT had the highest discriminatory ability for each respective factor. Cut-off values of 0.93 (sensitivity: 0.78, specificity: 0.83), 1.01 (sensitivity: 0.72, specificity: 0.48), and 1.02 (sensitivity: 0.67, specificity: 0.53) were established to discriminate between groups for each respective variable.

Logistic Regression (Predictive Value)

Regression results are presented in table 7. Involved limb, total work at 90°/sec, AMT, and CAR explained 49.0% (Nagelkerke R^2) of the variance in the presence of ACL-R, and correctly classified 83.5% of ACL-R cases; χ^2 (3) = 35.6, $p < .001$.

Uninvolved limb total work at 90°/sec and AMT explained 22.0% (Nagelkerke R^2) of the variance in the presence of ACL-R, and correctly classified 72.8% of ACL-R cases; χ^2 (2) = 14.8, $p = .001$

Limb symmetry indices of peak torque at 180°/sec, CAR, and AMT explained 30.9% (Nagelkerke R^2) of the variance in the presence of ACL-R, and correctly classified 79.5% of ACL-R cases; χ^2 (3) = 19.6, $p < .001$.

DISCUSSION

The results of this study support our hypothesis that individual constructs of peripheral and central nervous system function describe unique aspects of lower extremity function and

performance in ACL-R patients. Based on discriminatory and predictive ability, we propose a rationale for a reduced test battery that can be considered when making decisions about return to activity in ACL-R individuals. Identifying objective and clinically useful test batteries are essential to develop evidence-based assessments. By taking into account the ability to differentiate between individuals with and without pathology using a multimodal approach, clinicians and researchers can begin to advance patient care.

Patient-Reported Outcomes and Quadriceps Function

Identifying individual subjective and objective tests that differentiate individuals with and without ACL-R may be helpful to determine which are most important to optimize patient assessment. In the current study, ACL-R patients demonstrated a reduction in all measures of patient-reported function compared to healthy controls. Patients with higher self-reported knee function may be more likely to present with higher unilateral and more symmetric quadriceps strength, with individuals reporting IKDC scores greater than 89.9 being 3 times more likely to achieve 90% limb symmetry.[64] Patients in the current study reported an average IKDC score of 81.5, which may have negatively influenced quadriceps strength and neuromuscular function. Our results not only indicate that ACL-R patients demonstrated large magnitude deficits in quadriceps strength (isokinetic and isometric) compared to healthy controls, but that large asymmetries (≥ 15%) persisted, which may place individuals at a greater risk for joint degeneration.[81]

Bilateral central activation failure (> 10%) and decreased corticospinal excitability was also observed in ACL-R patients compared to healthy controls. Symmetric quadriceps activation > 99.2% has been reported to be a strong indicator of good patient-reported function.[63] Patients in the current study demonstrated very symmetric quadriceps activation despite reporting lower patient-reported function than healthy controls, which suggests this relationship is less true in the presence of clinically meaningful activation failure.

Involved Limb

PCA suggested three unique constructs of peripheral, central, and combined peripheral and central muscle function, which conceptually agree with prior theory. Isometric strength assessment is commonly used to evaluate patients after ACL-R; however, isokinetic function explained the greatest variance among all strength measures in this study. Total knee extensor work at 90°/sec demonstrated the largest magnitude difference between ACL-R patients and healthy controls, and was the best indicator of group membership. Threshold values of knee extensor MVIC torque based on patient-reported function have been established in ACL-R patients.[63] However, the information gained from this study adds to the current body of literature by establishing a highly sensitive and specific threshold of knee extensor work (18.4 J/kg) to discriminate between ACL-R and healthy individuals, which accounted for 91.6% of variance in peripheral muscle function. Although isokinetic torque, work, and power were strongly correlated, it is clear that assessment strategies may benefit by including more than isometric strength. As a whole, peripheral muscle function explained nearly 60% of the variance among all measures of quadriceps function, suggesting this is a highly influential physiological construct to evaluate patients with ACL-R.

Interestingly, H:M ratio and AMT loaded separately from CAR and fatigue index on the involved limb. A clear distinction between the two components was present; however CAR and AMT also loaded to a lesser degree on components one and three respectively. These finding suggest that each combination of measures represent unique, yet interrelated constructs of central and combined peripheral and central muscle function. Spinal reflex excitability may reflect a purely centrally mediated construct, separate from voluntary movement, as it is recorded statically. In contrast, AMT is recorded during voluntary movement, and therefore encompasses a peripheral component, which could explain its secondary loading. AMT demonstrated the greatest magnitude difference between ACL-R patients and healthy controls, and best discriminative ability among measures of central muscle function. Thresholds for AMT have not

been established previously, however, our results indicated that an AMT ≥ 40% is moderately sensitive and specific to discern patients with and without ACL-R. Quadriceps CAR loaded highest on combined peripheral and central muscle function, demonstrating the largest magnitude difference between groups, and best discriminatory value. A threshold of 86.4% for unilateral CAR has been reported to determine good patient-reported function;[63] however, the higher threshold of 94.7% reported in this study may result in an improved diagnostic ability. Interestingly, fatigue loaded with CAR and not other measures of peripheral muscle function. Short duration fatiguing protocols are believed to induce fatigue via peripheral mechanisms. However fatigue in the presence of maximal effort tasks may be more reflective of central fatigue that can originate at spinal or supraspinal levels,[85] which could explain its relationship with CAR. Regardless, each of these components explained 10.7% of the variance among all measures of quadriceps function, suggesting a meaningful role of centrally mediated constructs.

Uninvolved Limb

PCA suggested that peripheral (isokinetic strength and knee extension MVIC torque) and combined peripheral and central (AMT, H:M ratio, CAR, and fatigue index) muscle function characterize the uninvolved limb. Persistent deficits in muscle function have been identified in patients at early, mid, and long-term evaluation after ACL-R. The fact that our analysis suggested different constructs for each limb supports the notion that inter-limb differences remain present after ACL-R. Regression analysis in the uninvolved limb was able to classify group membership with 72.8% accuracy; however, quadriceps function of the involved limb resulted in greater classification accuracy (83.5%).

Limb Symmetry

The results of this study indicate that symmetry of quadriceps neuromuscular function contributes meaningful information to understanding patients after ACL-R. Symmetric peripheral muscle function (isokinetic strength and knee extensor MVIC torque) explained the largest amount of variance among measures of quadriceps function at 54%, followed by combined (CAR

and fatigue index) at 14.9%, and central muscle function (AMT and H:M ratio) at 10.0%. However, isokinetic and isometric quadriceps strength were the only tests that differed between limbs in ACL-R patients and also maintained acceptable diagnostic utility (AUC $\geq$ 0.7). Limb symmetry indices are often used as surrogates of physical impairments, activity limitations, and overall function.[71] Symmetrical quadriceps strength of 80-90% is commonly advocated;[56] however, symmetry of quadriceps neuromuscular function (i.e. spinal and corticospinal excitability) has been examined to a lesser degree. Determining readiness for return to activity after ACL-R is a complex decision that may benefit by including tests that can identify impairments in multiple constructs of muscle function.

Clinical Recommendations

This was an exploratory analysis conducted to examine the redundancy in information provided, magnitude of group differences, diagnostic, and predictive ability of a given measure(s) of quadriceps function, which may aid the clinician or researcher in selecting the most appropriate test, or test battery in the assessment of ACLR patients. All measures of quadriceps function explained a meaningful degree of variance, and may be considered in assessment paradigms. Isokinetic testing consistently predicted the greatest variance; however, standardized protocols following ACL-R are lacking.[86] The results of this study suggest that unique, but interrelated constructs of peripheral and centrally mediated muscle function exist in patients with ACL-R. These data appear to support the incorporation of quadriceps neuromuscular function into the test battery, suggesting that strength alone may be insufficient to evaluate clinical outcomes. The authors provide the following three clinical recommendations that may stem from the findings of this study:

- The test battery should include a component of isokinetic knee extensor strength, voluntary activation, and corticospinal excitability.
- From a practical standpoint, knee extension MVIC torque should be assessed because quadriceps central activation ratio is assessed isometrically.

- Measures of unilateral quadriceps function and symmetry demonstrated relatively good predictive ability, however, using data from the involved limb may be most meaningful in this population.

Limitations

This was an exploratory analysis, and not confirmatory; therefore, further validation of the proposed test battery is needed. PCA does not account for measurement error and as a result may overestimate the variance explained. Patients with a history of ACL-R in this study spanned a large age range 15-65. While the distribution of age may improve the generalizability of our findings to larger patient populations, this likely increased the heterogeneity among the included sample. To combat this, only patients with primary, unilateral ACL reconstructions were enrolled. Quadriceps neuromuscular function is likely to change over time after ACL-R. The specific thresholds and predictive abilities of tests, or test batteries, may therefore differ based on the time from surgery. The fact that our group was nearly 4 years removed form ACL-R on average, would likely provide a conservative estimate.

CONCLUSION

Unique constructs of peripheral, central, and combined peripheral and central muscle function are likely to exist in ACL-R patients. The results of this study highlight the redundancy in strength estimates, most notably among strength tests. Total isokinetic knee extensor work at 90°/sec, quadriceps CAR, and AMT consistently explained a significant portion of variance in measures of quadriceps function, demonstrated acceptable to excellent diagnostic utility, and predicted group membership with 72.8 to 83.5% accuracy. Measures of the involved limb appear to have greater diagnostic and predictive ability than the uninvolved limb or limb symmetry.

Table 1_{iii}. Participant demographics and patient-reported outcomes (mean ± standard deviation)

	ACL-R (n = 72)	Healthy (n = 30)	P value
Gender [a]	32 M, 40 F	12 M, 18 F	.680
Age (years) [b]	26.0 ± 9.3	22.7 ± 4.6	.351
Height (cm)	172.6 ± 11.2	174.8 ± 11.8	.396
Mass (kg)	75.6 ± 17.7	75.1 ± 16.2	.910
IKDC	81.5 ± 14.1	98.2 ± 4.2	**< .001**
KOOS Total [b]	88.2 ± 9.4	98.7 ± 2.5	**< .001**
KOOS Pain	90.5 ± 3.7	98.6 ± 3.7	**< .001**
KOOS Symptoms	83.9 ± 12.0	98.0 ± 4.1	**< .001**
KOOS Activities of Daily Living [b]	96.01 ± 6.0	99.8 ± 0.7	**< .001**
KOOS Sport [b]	79.0 ± 21.9	97.8 ± 6.3	**< .001**
KOOS Quality of Life	68.5 ± 22.3	96.5 ± 9.8	**< .001**
WOMAC [b]	4.9 ± 5.7	0.3 ± 0.8	**< .001**
WOMAC Pain [b]	19.2 ± 1.1	19.8 ± 0.6	**.003**
WOMAC Stiffness [b]	7.0 ± 1.4	8.0 ± 0.0	**< .001**
WOMAC Function [b]	65.3 ± 4.1	67.9 ± 0.3	**< .001**
VAS: involved (cm) [b]	0.6 ± 0.8	0.1 ± 0.2	**< .001**
VAS: uninvolved (cm) [b]	0.1 ± 0.2	0.0 ± 0.1	.063
Tegner: pre-injury	8.1 ± 1.4	N/A	N/A
Tegner: current	6.3 ± 1.9	7.2 ± 1.4	**.008**
Godin leisure-time exercise	59.1 ± 25.6	75.5 ± 29.7	**.011**
Tampa Scale of Kinesiophobia	33.6 ± 6.1	28.6 ± 5.8	**< .001**
Veteran's Rand 12-Item Health [b]	79.9 ± 10.1	86.0 ± 7.6	**.005**
Time since surgery (months)	46.5 ± 58.0	N/A	N/A
Graft type	Patellar (40.0%) Hamstring (47.1%) Allograft (12.9%)	N/A	N/A

Abbreviations: M, male; F, female; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Score; WOMAC, Western Ontario and McMaster Universities Arthritis Index; VAS, visual analog scale

[a] Chi-squared

[b] Mann-Whitney U

Alpha level set at $p \leq .05$

Table 2$_{iii}$. Quadriceps neuromuscular function in ACL-R patients and healthy individuals (mean ± standard deviation)

	Group					
	ACL-R			Healthy		
	Involved	Uninvolved	Limb Symmetry	Matched Involved	Matched Uninvolved	Limb Symmetry
Peak torque (90°/s) (Nm/kg)	1.7 ± 0.5*	2.1 ± 0.5	0.82 ± 0.19 †	2.2 ± 0.4	2.2 ± 0.6	1.29 ± 1.64
Peak torque (180°/s) (Nm/kg)	1.3 ± 0.4*	1.6 ± 0.4	0.83 ± 0.16 †	1.7 ± 0.3	1.7 ± 0.3	1.01 ± 0.15
Total work (90°/s) (J/kg)	14.7 ± 4.5*	18.0 ± 4.5*	0.82 ± 0.16 †	20.1 ± 3.4	20.5 ± 3.6	1.00 ± 0.18
Total work (180°/s) (J/kg)	11.5 ± 3.5*	13.9 ± 3.7*	0.84 ± 0.16 †	15.8 ± 2.9	15.8 ± 3.2	1.02 ± 0.22
Average power (90°/s) (W/kg)	1.6 ± 0.5*	2.0 ± 0.5*	0.83 ± 0.17 †	2.2 ± 0.4	2.2 ± 0.4	1.00 ± 0.22
Average power (180°/s) (W/kg)	2.1 ± 0.6*	2.6 ± 0.7*	0.84 ± 0.17 †	2.9 ± 0.6	2.9 ± 0.6	1.02 ± 0.21
MVIC torque (Nm/kg)	2.0 ± 0.6*	2.4 ± 0.7*	0.85 ± 0.20 †	2.8 ± 0.6	2.7 ± 0.6	1.04 ± 0.14
Fatigue index (%)	18.2 ± 9.2	20.2 ± 7.9	1.98 ± 7.96 †	21.8 ± 8.1	22.2 ± 8.2	0.76 ± 6.19
Central activation ratio (%)	88.4 ± 10.1*	89.8 ± 9.6*	0.99 ± 0.08	95.2 ± 5.6	93.8 ± 6.7	1.02 ± 0.06
Hoffmann reflex (H:M)	0.21 ± 0.19*	0.18 ± 0.17	1.27 ± 0.89	0.14 ± 0.12	0.14 ± 0.12	1.11 ± 0.66
Active motor threshold (%T)	45.2 ± 8.6*	44.3 ± 8.4*	0.99 ± 0.15	39.0 ± 4.1	39.0 ± 3.4	1.01 ± 0.12

* Different from healthy

† Different between limbs

Alpha level set at $p \leq .05$

Table 3_{iii}. Principal component analysis using involved limb measures of quadriceps function

Variable	Component [a]			Criteria for Retention		
	1	2	3	Different from healthy (*p*)	Magnitude of difference (*d*)	Diagnostic ability (AUC)
Average power (180°/s)	.971			.001	1.33	.812
Peak torque (180°/s)	.967			.001	1.33	.806
Average power (90°/s)	.967			.001	1.50	.833
Total work (90°/s)	.957			.001	1.59	.847
Total work (180°/s)	.954			.001	1.48	.832
Peak torque (90°/s)	.954			.001	1.25	.826
MVIC torque	.863			.001	1.33	.821
Hoffmann reflex		.813		.047	0.58	.590
Active motor threshold		.687		.001	1.51	.730
Central activation ratio			.752	.000	1.21	.731
Fatigue index			.629	.056	0.44	.635

Principal component analysis was used as the method of extraction
Variables listed in order of strength of loading
Missing data replaced: H:M (n = 4), AMT (n = 2)
[a] Factor matrix coefficients following Varimax rotation with Kaiser normalization
KMO = .822; Bartlett's $\chi^2(55) = 917.5$, $p < .001$
1 – Eigenvalue = 6.5, % variance = 59.1
2 – Eigenvalue = 1.2, % variance = 10.7
3 – Eigenvalue = 1.2, % variance = 10.7
Cumulative variance = 80.5%

Table 4_{iii}. Principal component analysis using uninvolved limb measures of quadriceps function

Variable	Component [a]		Criteria for Retention		
	1	2	Different from healthy (*p*)	Magnitude of difference (*d*)	Diagnostic ability (AUC)
Average power (180°/s)	.957		.028	0.50	.631
Peak torque (180°/s)	.956		.086	0.33	.592
Total work (90°/s)	.952		.008	0.69	.684
Total work (180°/s)	.948		.018	0.59	.650
Peak torque (90°/s)	.947		.105	0.17	.632
Average power (90°/s)	.937		.018	0.50	.663
MVIC torque	.814		.031	0.50	.626
Active motor threshold		.696	.005	1.56	.732
Hoffmann reflex		.632	.311	0.33	.547
Central activation ratio		.571	.019	0.60	.640
Fatigue index		.569	.264	0.24	.580

Principal component analysis was used as the method of extraction

Variables listed in order of strength of loading

Missing data replaced: H:M (n = 4), AMT (n = 3)

[a] Factor matrix coefficients following Varimax rotation with Kaiser normalization

KMO = .804; Bartlett's $\chi^2(55) = 819.3$, $p < .001$

1 – Eigenvalue = 6.2, % variance = 56.1

2 – Eigenvalue = 1.6, % variance = 14.6

Cumulative variance = 70.7%

Table 5_{iii}. Principal component analysis using limb symmetry measures of quadriceps function

Variable	Component [a]			Criteria for Retention		
	1	2	3	Between limb difference (*p*)	Magnitude of difference (*d*)	Diagnostic ability (AUC)
Average power (180°/s)	.956			.001	0.66	.778
Total work (180°/s)	.949			.001	0.67	.787
Peak torque (180°/s)	.947			.001	0.75	.808
Average power (90°/s)	.944			.001	0.77	.743
Total work (90°/s)	.934			.001	0.75	.774
Peak torque (90°/s)	.928			.001	0.82	.746
MVIC torque	.717			.001	0.60	.776
Fatigue index		.812		.038	0.35	.529
Central activation ratio		.745		.087	0.15	.610
Active motor threshold			.948	.279	0.10	.558
Hoffmann reflex			.321	.137	0.11	.530

Principal component analysis was used as the method of extraction
Variables listed in order of strength of loading
Missing data replaced: H:M (n = 6), AMT (n = 3)
[a] Factor matrix coefficients following Varimax rotation with Kaiser normalization
KMO = .877; Bartlett's $\chi^2(55) = 849.9$, $p < .001$
1 – Eigenvalue = 5.9, % variance = 54.0
2 – Eigenvalue = 1.6, % variance = 14.9
3 – Eigenvalue = 1.1, % variance = 10.0
Cumulative variance = 78.9%

Table 6_{iii}. Principal component analysis using patient-reported outcomes

Variable	Component [a]		Criteria for Retention		
	1	2	Different from healthy (*p*)	Magnitude of difference (*d*)	Diagnostic ability (AUC)
KOOS Total	.934		.001	4.28	.919
IKDC Subjective	.860		.001	3.99	.923
WOMAC Total	.858		.001	5.74	.822
Tampa Scale of Kinesiophobia	.542		.001	0.86	.707
Godin Leisure-Time Activity		.866	.004	0.55	.647
Tegner Activity Scale		.757	.006	0.66	.654
Veteran's Rand 12-Item Health Survey		.623	.018	0.79	.677

Principal component analysis was used as the method of extraction

Variables listed in order of strength of loading

[a] Factor matrix coefficients following Varimax rotation with Kaiser normalization

KMO = .771; Bartlett's $\chi^2(21) = 299.4$, $p < .001$

1 – Eigenvalue = 3.0, % variance = 43.7

2 – Eigenvalue = 1.9, % variance = 27.0

Cumulative variance = 70.7%

Table 7_{iii}. Results from logistic regression analyses to predict group membership

	Involved Limb [a]	Uninvolved Limb [b]	Limb Symmetry [c]
Accuracy of classification (%)	83.5	72.8	79.5
Sensitivity (%)	91.4	91.3	97.1
Specificity (%)	57.1	17.4	15.8
Positive predictive value (%)	87.7	75.9	80.7
Negative predictive value (%)	66.7	40.0	60.0
Positive likelihood ratio	2.13	1.11	1.15
Negative likelihood ratio	0.15	0.50	0.18
R^2	.490	.220	.309
P value	< .001	.001	< .001

[a] Model includes: total work at 90°/sec*, AMT†, and CAR*

[b] Model includes: total work at 90°/sec*, and AMT*

[c] Model includes: peak torque symmetry at 180°/sec*, CAR symmetry, and AMT symmetry

* Significant at $p \leq .05$

† Significant at $p \leq .10$

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SECTION III: APPENDICES

APPENDIX A

The Problem

Significance

Knee joint injuries remain common among athletic and recreationally active populations. Unfortunately, early mal-adaptations throughout the central nervous system can occur following injury, resulting in long-term consequences with regard to joint health and decreased quality of life. Anterior cruciate ligament injuries present a specific challenge to joint health in this regard and continue to constitute a large portion of major knee joint injuries in young, active populations. Post-traumatic muscle dysfunction is well described following ACL reconstruction,[1] and is linked to a sequelae of impairments detrimental to global and joint-specific health, including decreased physical activity,[2-5] increased risk of re-injury,[6] and an accelerated onset of post-traumatic knee joint osteoarthritis.[7-11] Strong evidence exists supporting the causal link between ACL-R and early post-traumatic articular cartilage joint degeneration.[9,12-14] Since articular cartilage degeneration is irreversible, the hallmark for prevention is early detection.

The ability of the central nervous system to reorganize, adapt, and compensate is theorized to be a compensatory mechanism, thereby preserving global functional capabilities in the presence of peripheral injury.[15] Regional brain activity has been studied using functional MRI imaging, demonstrating central re-organization of the somatosensory cortex in patients with a recent history of ACL injury[16] and reconstruction.[17] Central and peripheral neural adaptations have been identified following ACL injury, and hypothesized to contribute to post-traumatic muscle impairments.[18,19] Such changes may arise from peripheral (muscle), spinal (spinal cord), or supraspinal (cerebral cortex) regions. At a muscular level, morphologic changes will manifest as gross weakness or atrophy,[1] which is problematic due to the high potential for altered

biomechanics leading to excessive loading transmitted through lower extremity joints.[20] At the spinal region, changes in reflex excitability of lower extremity musculature have been identified in patients with joint injury.[21] Currently, the best way to measure central nervous system changes originating from supraspinal centers is to assess corticospinal excitability, which is defined as excitability of the portion of the cerebral cortex responsible for initiating motor commands to skeletal muscle.[22] Transcranial magnetic stimulation (TMS) provides a method of assessing excitability of the pre-motor area of the cerebral cortex.[22] TMS produces a small, but powerful field of magnetic energy that depolarizes neural tissue to initiate action potentials.[22] When a TMS device is placed over the scalp, superficial to the pre-motor area, action potentials are conveyed to the associated skeletal muscles resulting in a motor evoked potential (MEP). Although neuromuscular adaptations are inevitable following joint injury, they present a modifiable source of dysfunction in the prevention of post-traumatic knee joint osteoarthritis.

Despite evidence suggesting that the central nervous system is significantly involved in mediating neuromuscular function following joint injury, there is a paucity of literature concerning intervention strategies directly targeting supraspinal centers. The corticospinal tract is the major descending pathway from the motor cortex to α- and γ-motor neurons,[23] making this an important construct to study in response to peripheral injury. Theoretically, a Gaussian shaped curve of corticospinal excitability would occur over the course of recovery following injury. However, in cases of incomplete sensorimotor recovery, corticospinal excitability may not return to pre-injury levels, resulting in a reduction of clinical outcomes. A point of interest to clinicians is the theoretical high-risk zone, where individuals with good and poor outcomes diverge, indicating a critical junction in a targeted rehabilitation process (Figure A1). The figure below depicts theoretical changes that occur at supraspinal centers over time following knee joint trauma.

To date, there is limited evidence with respect to specific neuromuscular adaptations within the central nervous system following ACL reconstruction (ACL-R),[24] and no information regarding the temporal relationship of these factors following ACL injury through the development of post-traumatic joint degeneration. Current models of study have classified ACL-R patients as a single group of comparison relative to healthy counterparts (Figure A2). Exclusion of multiple time groupings may prevent early detection of impairments, delaying early intervention. In an effort to better understand how early state changes manifest over time, it is imperative that time from injury be considered in study design. Additionally, the inclusion of an end-stage model of disability is lacking in this regard.

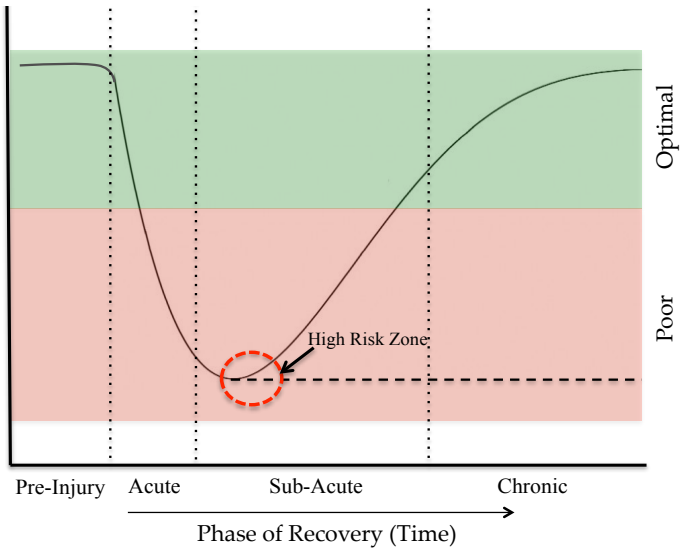


Figure A1. Theoretical model depicting the temporal relationship between quadriceps function and clinical outcomes following ACL reconstruction

In an effort to effectively combat the detrimental plastic changes that may occur if left untreated, it is imperative for clinicians to identify impairments early in this continuum

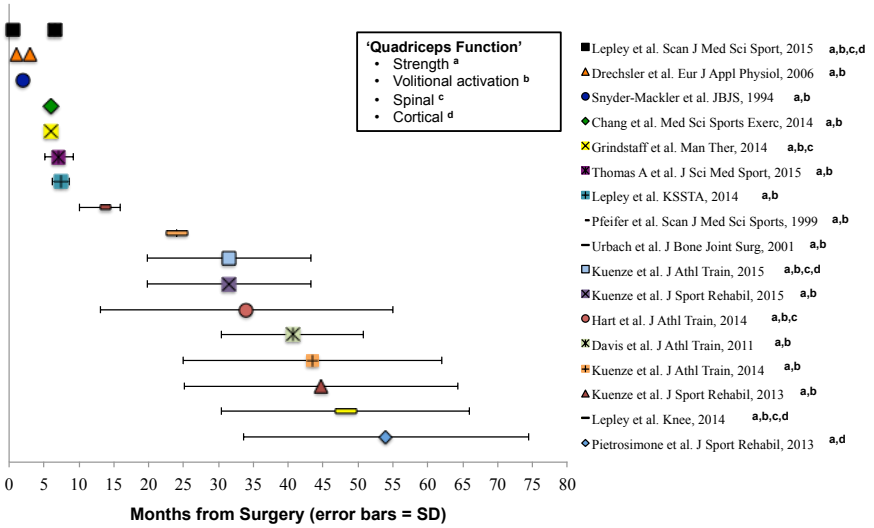


Figure A2. Summary of studies that include a minimum of one measure of quadriceps neuromuscular function in addition to muscle strength in patients after ACL reconstruction. Point estimates indicate mean time from surgery, with error bars indicating standard deviation or range of time since surgery.

(Figure A3). Furthermore, it becomes necessary to identify characteristics of patients with poor clinical outcomes (e.g. osteoarthritis) to explore the relevance of early sensorimotor changes. Therefore, the current study will use a cross-sectional design to compare differences in sensorimotor function among patients following ACL reconstruction at various phases of recovery through the development of post-traumatic joint degeneration.

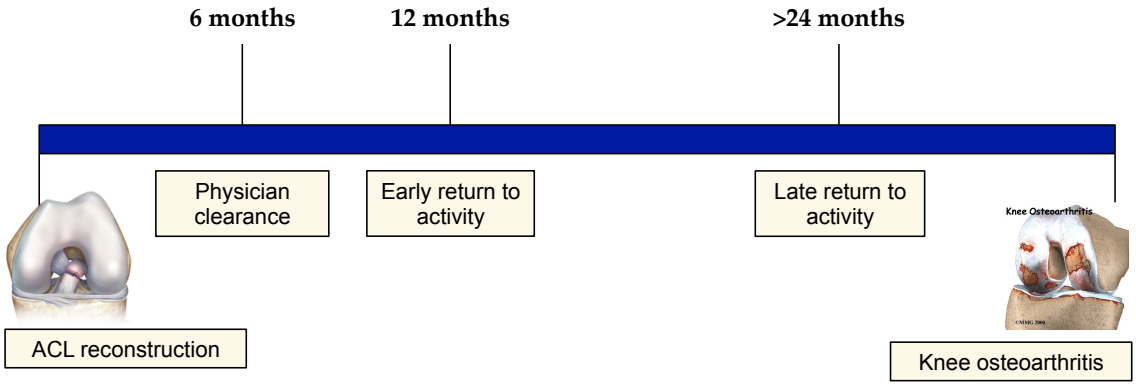


Figure A3. Represents the potential continuum of ACL reconstruction through the development of cartilage degeneration (sub-optimal outcomes)

Specific Aims

The overall purpose of this study was to describe quadriceps muscle function over the course of recovery following ACL reconstruction (ACL-R) through development of post-traumatic osteoarthritis. This study included three specific aims to achieve this purpose. The primary aim of this study was to assess quadriceps neuromuscular function in patients after ACL-R with regard to chronicity (*early*: 6-12 months, *late*: 2-10 years, and in those who experience post-traumatic knee *osteoarthritis*). Quadriceps function was assessed bilaterally via isometric and isokinetic knee extensor strength, quadriceps fatigue, spinal reflex excitability using the Hoffmann reflex, and corticospinal excitability using TMS to evaluate multiple regions of the central and peripheral nervous system. The purpose of this aim was to identify unique neurophysiological factors that distinguish ACL reconstructed patients with regard to time from surgery. The secondary aim of this study was to compare the relationships between measures of quadriceps function and patient reported function at clinically relevant phases after ACL-R. This aim provided information regarding the associations of unilateral and limb symmetry estimates of performance with perceived knee function and global health in patients *early*, *late*, and with knee *osteoarthritis* after ACL-R. This data will be used to assess the predictive capabilities of quadriceps function in determining clinical outcomes. The tertiary aim of this study was to identify unique constructs, or subgroupings, of muscle function that best characterize this patient population via principal component analysis. Within each construct, or component, relationships between individual variables will be assessed, and redundancy among measures will be identified, eliminating those that do not contribute unique information within this patient population. This analysis will identify important constructs of muscle function and maximize the efficiency of the assessment model in patients after ACL-R.

Research Question(s) and Experimental Hypotheses

Manuscript 1: Chronicity of Quadriceps Function in ACL Reconstructed Patients With and Without Knee Osteoarthritis

Research Question

Do peripheral (strength/fatigue/activation), spinal (spinal-reflexive excitability), and supraspinal (corticospinal excitability) measures of quadriceps function differ at clinical relevant phases (*early*: 6-12 months, *late*: 2-10 years, knee *osteoarthritis*) of post-operative recovery between ACL reconstructed patients with and without knee osteoarthritis and healthy matched controls?

Research Hypothesis

- Quadriceps strength, fatigue, activation, spinal-reflexive excitability, and corticospinal excitability will be worse in patients early after ACL-R, and in those with knee osteoarthritis, and will return to healthy values in patents late after ACL-R with no osteoarthritis.

Statistical Analysis

Separate mixed model 2 x 4 (limb x group) analyses of variance will be used to assess differences between the involved and uninvolved limbs for each measure of quadriceps function across all groups. Dunnett's *post hoc* tests will be used to identify the exact location of group differences between ACL-R patients and healthy controls if main effects are observed. Fischer's LSD post hoc tests will be used to identify group differences between ACL-R patients only. Separate models will be performed for the subjective data and the objective data (injured side vs. matched healthy control side; contralateral side vs. matched healthy control side; injured side vs. uninjured side). Finally as an exploratory analysis, side-to-side ratios (involved/uninvolved) will be calculated for an additional analysis to determine group differences in data when normalized within subject. Cohen's *d* effect sizes with 95% confidence intervals will be

calculated to assess the magnitude of difference between ACL-R patients and healthy controls. Alpha will be set at $p \leq .05$, with $1\text{-}\beta = 0.80$.

Manuscript 2: Relationship between quadriceps function symmetry and patient-reported outcomes in ACL reconstructed individuals with and without knee osteoarthritis

Research Question 1

Does unilateral quadriceps function or limb symmetry better explain patient reported outcomes early and late after ACL reconstruction in patients with and without knee osteoarthritis?

Research Hypothesis 1

- Limb symmetry will be most meaningful in patients early after ACL reconstruction
- Unilateral quadriceps function will be most meaningful in patients late after ACL reconstruction with and without osteoarthritis.

Research Question 2

Which measures of quadriceps function explain the greatest portion of variance in patient-reported function in patients early, late, and with osteoarthritis after ACL reconstruction?

Research Hypothesis 2

- Isokinetic strength (peak torque, total work, and average power) will explain the greatest variance in patient-reported function in each group.

Statistical Analysis

Simple bivariate correlations will be used to identify relationships among objective measures of quadriceps function and patient-reported outcomes. These coefficients will be calculated in separate analyses per group. We will perform a multiple linear stepwise regression analysis to identify the variance explained in patient-reported outcomes specific to knee (KOOS) and global health (VR-12) using (1) quadriceps

function: isokinetic knee extensor strength (peak torque, total work, average power), knee extension MVIC torque, quadriceps fatigue index, quadriceps central activation ratio, Hoffmann reflex, active motor threshold, and (2) demographics: current patient age, time since surgery, pain, current activity level, and kinesiophobia.

Manuscript 3: Quadriceps and Patient Reported Function in ACL Reconstructed Patients: A Principal Component Analysis

Research Question

Which groupings of variables, or underlying constructs, representative of quadriceps, can be used to uniquely characterize ACL reconstructed patients?

Research Hypothesis

- Constructs related to (1) peripheral muscle function: quadriceps isokinetic strength, MVIC torque, fatigue index and (2) central muscle function: quadriceps central activation ratio, spinal-reflexive excitability, corticospinal excitability, will uniquely identify four distinct factors.

Statistical Analysis

A principal component analysis (PCA) will be performed using all dependent variables separately for the involved limb, uninvolved limb, and limb symmetry indices among ACL-R patients only. Simple bivariate correlations will be used to determine the relationship between variables that load onto like components to identify those that provide unique information with regard to this patient population. Receiver operator characteristic curve analyses will be used to establish thresholds for retained variables to discriminate between patients with and without ACL reconstruction. Finally, retained variables will be entered into a binary logistic regression model for the involved limb, uninvolved limb, and limb symmetry values to determine the ability to predict group membership.

Independent Variables

Group

1. Early ACL reconstruction (6-12 months)
2. Late ACL reconstruction (2-10 years)
3. Osteoarthritis after ACL reconstruction
4. Healthy controls

Limb

1. Involved
2. Uninvolved

Dependent Variables

Patient Reported Outcomes

1. International Knee Documentation Committee (IKDC) Subjective Knee Joint Evaluation
2. Knee Injury and Osteoarthritis Outcome Score (KOOS)
3. Pain and Activity Rating Scale (VAS)
4. Tegner Activity Scale
5. Godin Leisure-Time Questionnaire
6. Tampa Scale of Kinesiophobia (TSK)
7. Veterans Rand 12-Item Health Survey (VR-12)
8. Marx Activity Scale

Peripheral Muscle Function

1. Normalized isokinetic knee extension peak torque (Nm/kg), total work (J/kg), and average power (W/kg) @ 90°/second and 180°/second
2. Normalized knee extension maximal voluntary isometric contraction torque (Nm/kg)
3. Quadriceps fatigue index (%)

Central Muscle Function

1. Quadriceps central activation ratio (%)

2. Normalized quadriceps Hoffmann reflex (H:M ratio)
3. Quadriceps active motor threshold (% MSO)

Inclusion Criteria

Healthy Controls

- 15-65 years old
- No prior knee injury
- No recent hip or ankle injury (last 6 weeks)
- BMI less than 35
- No history or immediate family history of seizures or epilepsy

ACL Reconstruction

- 15-65 years old
- No recent hip or ankle injury (last 6 weeks)
- History of ACL injury and/or reconstruction
- BMI less than 35
- No history or immediate family history of seizures or epilepsy

ACL Reconstruction with Osteoarthritis

- 15-65 years old
- Diagnosed tibiofemoral or patellofemoral osteoarthritis (Kellgren-Lawrence grade 2-4)
- No recent hip, knee, or ankle injury (last 6 weeks)
- History of ACL reconstruction (revision accepted)
- BMI less than 35
- No history or immediate family history of seizures or epilepsy

Exclusion Criteria

Healthy Controls

- Currently experiencing knee pain

- History of knee joint injury or surgery
- Current neuropathy (numbness and tingling)
- Known muscular abnormality
- History of skull fracture
- History of neurological disorders including poorly controlled migraine headaches, seizure disorder, history or immediate family history of seizures and/or epilepsy and taking medications that lower seizure threshold
- History of subdural hematoma or epidural hematoma
- Implanted biomedical device (active or inactive implants (including device leads), including deep brain stimulators, cochlear implants, and vagus nerve stimulators)
- Conductive, ferromagnetic or other magnetic-sensitive metals implanted in their head or within 30 cm of the treatment coil. Examples include cochlear implants, implanted electrodes/stimulators, aneurysm clips or coils, stents, bullet fragments, jewelry and hair barrettes.
- History of cardiopulmonary disorder
- Pregnant women
- Significant activity change 48 hours prior to enrollment

ACL Reconstruction

- Multiple ligament reconstruction or a history of graft failure
- Serious surgical complication following ACL reconstruction
- Chondral resurfacing procedure (microfracture or OATS procedure)
- History of cardiopulmonary disorder
- Current symptoms of meniscal injury or failed meniscal repair
- Current neuropathy (numbness and tingling)
- Known muscular abnormality

- History of skull fracture
- History of neurological disorders including poorly controlled migraine headaches, seizure disorder, history or immediate family history of seizures and/or epilepsy
- Taking medications that lower seizure threshold
- History of subdural hematoma or epidural hematoma
- History of neurological disorders
- Implanted biomedical device (active or inactive implants (including device leads), including deep brain stimulators, cochlear implants, and vagus nerve stimulators)
- Conductive, ferromagnetic or other magnetic-sensitive metals implanted in their head or within 30 cm of the treatment coil. Examples include cochlear implants, implanted electrodes/stimulators, aneurysm clips or coils, stents, bullet fragments, jewelry and hair barrettes
- Pregnant women
- Significant activity change 48 hours prior to enrollment

ACL Reconstruction with Osteoarthritis

- Diagnosis of osteoarthritis prior to ACL reconstruction
- Less than 1 year from ACL reconstruction
- Prior knee replacement (partial or total)
- Knee surgery on the contralateral limb
- Multiple ligament reconstruction
- Chondral resurfacing procedure (microfracture or OATS procedure)
- Recent knee surgery within 6 months
- History of cardiopulmonary disorder
- Current neuropathy (numbness and tingling)
- Known muscular abnormality

- History of skull fracture
- History of neurological disorders including poorly controlled migraine headaches, seizure disorder, history or immediate family history of seizures and/or epilepsy
- Taking medications that lower seizure threshold
- History of subdural hematoma or epidural hematoma
- History of neurological disorders
- Implanted biomedical device (active or inactive implants (including device leads), including deep brain stimulators, cochlear implants, and vagus nerve stimulators)
- Conductive, ferromagnetic or other magnetic-sensitive metals implanted in their head or within 30 cm of the treatment coil. Examples include cochlear implants, implanted electrodes/stimulators, aneurysm clips or coils, stents, bullet fragments, jewelry and hair barrettes
- Pregnant women
- Significant activity change 48 hours prior to enrollment

Procedures

1. Obtained informed consent
2. Screening (TMS questionnaire)
3. Patient-reported function questionnaires
    a. International Knee Documentation Committee Subjective Knee Evaluation
    b. Knee Injury and Osteoarthritis Outcome Score
    c. Pain and Activity Rating Scale
    d. Tegner Activity Scale
    e. Godin Leisure-Time Exercise Questionnaire
    f. Tampa Scale of Kinesiophobia
    g. Veterans Rand 12-Item Health Survey

4. Bilateral Hoffmann reflex
5. Bilateral quadriceps isokinetic strength
6. Bilateral quadriceps central activation ratio
7. Bilateral quadriceps fatigue index
8. Bilateral quadriceps active motor threshold

Assumptions

- The obtained measures are valid and reliable
- Participants responded truthfully to questionnaires
- Participants provided maximal effort during strength assessment(s)
- The quadriceps central activation ratio (CAR) was representative of force generated by activated motor units recruited volitionally when compared to the maximal capacity of the muscle
- The transcutaneous electrical stimulation utilized during the quadriceps superimposed burst technique was sufficient to activate all quadriceps muscle tissue not active during a maximal voluntary isometric contraction
- Participants were fully relaxed during quadriceps Hoffmann reflex testing.
- Surface electromyography adequately represented the true activation of the quadriceps muscle during active contractions
- The quadriceps Hoffmann reflex was representative of quadriceps motorneuron pool excitability
- The area of the pre-motor cortex stimulated during quadriceps active motor threshold testing was the optimal location for stimulation resulting in the largest magnitude response in the target muscle
- Participants were assessed in a non-fatigued state
- Participants did not have caffeine within 6 hours prior to being assessed

- Participants were not taking medications that could alter spinal or corticospinal excitability
- Participants with no diagnosis of knee osteoarthritis truly did not have arthritic changes at the time of enrollment
- Participants with diagnosed knee osteoarthritis did not have arthritic changes prior to ACL-R

Delimitations

- Physically active individuals between the ages of 15-65 years
- Primary, unilateral and uncomplicated ACL reconstruction
- Time from ACL reconstruction: (1) 6-12 months, (2) 2-10 years, (3) diagnosed osteoarthritis after ACL-R
- Knee osteoarthritis (Kellgren Lawrence ≥ grade 2) with a history of unilateral ACL reconstruction

Limitations

- Cross-sectional design does not allow for conclusions regarding the natural history of post-traumatic neuromuscular function of the quadriceps
- Healthy controls were not age matched to the osteoarthritis patient group
- Unable to confirm severity of arthritis at time of enrollment in patients with arthritis
- Unable to verify absence of arthritis in patients with no diagnosis of osteoarthritis
- Heterogeneous sample with regard to age, gender, graft type, and meniscal involvement
- Principal component analysis may overestimate the variance explained among measures of quadriceps neuromuscular function

Operational Definitions

1. ***Active motor threshold*** – The TMS intensity that produces a positive MEP measured locally at the target muscle in at least 5 out of 10 trials during an active contraction, measuring 5% of maximal effort.[25]
2. ***Arthrogenic muscle inhibition*** – Presynaptic, ongoing reflex inhibition of musculature surrounding a joint after distension or damage to structures of that joint.[26]
3. ***Cortical plasticity*** – The capacity of the nervous system to modify its organization. Such changes can occur as a consequence of many events, including normal development, the (re)acquisition of skills (learning/ relearning), after damage to the nervous system and as a result of sensory deprivation.[27]
4. ***Corticospinal excitability*** – The ability of corticospinal neurons within the primary motor cortex to be activated in response to input from sensory centers, the pre-motor cortex, the spinal cord, and the basal ganglia.[28] The intensity of input signal require to evoke excitation of the area related to the quadriceps in the primary motor cortex is commonly measured using the active motor threshold via transcranial magnetic stimulation.[29]
5. ***Chronicity*** – Refers to time from injury/ surgery or progression of condition.
6. ***H:M ratio*** – A representation of the motorneuron pool available to be recruited (H_{max}) compared to the entire motorneuron pool (M_{max}). The ratio can be interpreted as the proportion of the motorneuron pool available for recruitment at a given time.[30]
7. ***Hoffmann reflex (H-reflex)*** – An electrically induced reflex analogous to the mechanically induced spinal stretch reflex,[30] which provides an estimate of alpha motoneuron excitability when presynaptic and intrinsic excitability remain constant. The H-reflex is elicited via direct electrical stimulation of the peripheral nerve that results in preferential depolarization of Ia afferent fibers at low stimulus intensities. The maximum H-reflex (Hmax) represents the maximum number of motorneurons that can be activated in a given state of condition.

8. ***Limb symmetry*** – The comparison of within participant, between-limb performance on a given outcome measure that is represented as a unit-less ratio. This limb symmetry index (LSI) is represented as: ACL-R LSI = Injured Limb/ Uninjured Limb or Healthy LSI = Non-Dominant Limb/ Dominant Limb.
9. ***Motor evoked potential*** – Artificial depolarization of cortical neurons via electromagnetic stimulation over the motor cortex.
10. ***Motorneuron pool excitability*** – The percentage of the total motorneuron pool that can be achieved at rest or during active contraction in response to an applied stimulus, which is commonly estimated using the Hoffmann reflex and expressed as the H_{max}:M_{max} ratio.[30]
11. ***Motor threshold*** – The TMS intensity that produces a positive MEP measured locally at the target muscle in at least 5 out of 10 trials.[25]
12. ***Muscle response (M response)*** – The efferent arc of the H-reflex pathway, resulting from action potentials generated by the alpha motoneurons traveling along efferent fibers, until they reach the neuromuscular junction and produce a twitch response in the electromyograph.[30] The maximal M response (M_{max}) represents activation of the entire motorneuron pool, and is commonly used as a normalization factor for the maximal Hoffmann reflex (H_{max}).[31]
13. ***Neuromuscular Control*** – Any of the aspects surrounding nervous system control over muscle activation, and the factors contributing to task performance. The unconscious activation of dynamic restraints occurring in preparation for and in response to joint motion and loading for the purpose of maintaining and restoring functional joint stability.[23]
14. ***Post-traumatic osteoarthritis*** – Diagnosed Kellgren-Lawrence Grade 2 or higher tibiofemoral osteoarthritis with possible patellofemoral compartment involvement, secondary to joint trauma.

15. ***Proprioception*** – The afferent information arising from 'proprioceptors' located in the 'proprioceptive field', the area of the body screened from the environment by the surface cells, which contained receptors specifically adapted for the changes occurring inside the organism independent of the interoceptive field.[32]
16. ***Quadriceps activation (QA)*** – The proportion of motor neuron pool that can be volitionally activated during a force-based task.[1]
17. ***Quadriceps central activation ratio (CAR)*** – A ratio of the maximal voluntary isometric force (F_{MVIC}) to the total force generated when a supramaximal percutaneous electrical stimulus is superimposed during a maximal voluntary isometric contraction (F_{SIB}),[1] commonly expressed as: CAR = [F_{MVIC}/ (F_{MVIC} + F_{SIB})] a 100. A CAR of 1.0 indicates complete activation, whereas a CAR of less than 1.0 indicates central activation failure or inhibition.[33]
18. ***Quadriceps inhibition (QI)*** – A reduction in central motor drive to the quadriceps musculature, which results in a decreased ability to generate maximal volitional activation of the muscle, commonly expressed as: QI = 1-CAR.[33]
19. ***Sensorimotor Control*** – The dynamic interaction between sensation of sensory information, the integrating of information in the central nervous system and motor output to perform voluntary movements and postural control.[34]
20. ***Sensorimotor System*** – The sensory, motor, and central integration and processing components involved in maintaining joint homeostasis during bodily movements (functional joint stability).[35]
21. ***Somatosensory*** – All mechanoreceptive, thermoreceptive, and pain information arising from the periphery.[36]
22. ***Spinal reflexive excitability*** – Refers to the magnitude of alpha motoneuron excitability when presynaptic and intrinsic excitability remain constant. This will be synonymous to H:M ratio.

23. ***Superimposed burst technique (SIB)*** – Application of a train of percutaneous supramaximal electrical stimuli to the quadriceps musculature during a maintained voluntary contraction,[37] used to quantify the extent of voluntary activation failure of a muscle.[38]
24. ***Transcranial magnetic stimulation*** – A method for studying the relationship between brain activity and physical function through the use of electromagnetic stimulation of the motor cortex to generate a motor evoked potential which can be measured over the targeted muscle via electromyography.[29]
25. ***Voluntary activation failure*** – The inability to produce all available force of a muscle despite maximal conscious effort.[39]

Innovation

Athletic trainers are situated as primary health care providers able to identify early risk factors for poor outcomes following joint injuries, such as ACL tears and reconstruction. The process of joint degeneration following trauma is irreversible, making it imperative that clinicians and researchers alike continue to make strides in optimizing patient care following injury. Despite evidence suggesting that the central nervous system is significantly involved in mediating neuromuscular function following joint injury, there is a paucity of literature concerning intervention strategies directly targeting supraspinal centers. The lack of such studies raises the question: *are current rehabilitative efforts comprehensive enough to address the neuromuscular impairments observed in response to ACL injury and reconstruction? How is peripheral, spinal, and supraspinal input modulated over time following joint injuries?* To optimize patient care, these questions must be addressed. Understanding the natural history of neuromuscular modulation from peripheral, spinal, and supraspinal centers is a necessary step in answering this gap of knowledge. Examining the inter-relationships of these sources of neuromuscular modulation from a temporal perspective is paramount in developing evidence based treatment strategies. In a continuing shift towards evidence-based practice, researchers and clinicians must gain a more comprehensive understanding of underlying pathophysiologic mechanisms of neuromuscular adaptations following knee joint injuries. Gaining insight with regard to the neuromuscular adaptations that occur throughout the spectrum of disability, from injury to development of degenerative changes, will provide information paramount to develop optimal strategies for early treatment and active prevention of poor outcomes in active individuals who suffer joint injuries. Understanding the temporal relationship of neural mechanisms involved in mediating neuromuscular function following a common knee joint injury is a necessary step to validate patient-specific interventions. Central reorganization is a naturally occurring phenomenon following injury; therefore, evaluating supraspinal sources of neuromuscular impairment across a spectrum of disability will provide insight into the naturally occurring

adaptive responses that take place following injury, specifically plastic changes within the primary motor cortex. It is imperative that clinicians identify impairments along the continuum of injury and disability to combat unwanted plastic changes, detrimental to long-term joint health. Exploring the lesser understood role of supraspinal excitability and centrally mediated changes over time will help clinicians understand how to most effectively treat patients, and may provide a missing link in current practice.

Long-term benefits to the proposed study have both *clinical* and *research* implications. Clinically, information gained from this study can be used to understand how different patient populations adapt following injury from a neurophysiologic perspective. Clinicians must understand how individuals adapt over time to truly understand and predict the effects of therapeutic interventions. Pairing the proposed neurophysiologic observations with patient reported outcomes would establish the connection between neuromuscular adaptations and quality of life following injury. Having these data may allow clinicians to predict outcomes, and intervene at earlier points in order to avoid permanent detrimental changes in neuromuscular function. This information will provide a crucial dataset for identifying early changes following ACL injury. The data from this study will be used for future, larger scale applications to study how these regions mediate neuromuscular function over time following various knee injuries. Although the proposed study utilizes a cross-sectional design, it will be used to provide insight moving forward with longitudinal observations.

APPENDIX B

Literature Review

INTRODUCTION

Knee joint injuries remain common among athletic and recreationally active populations. Unfortunately, early mal-adaptations throughout the central nervous system can occur following injury, resulting in long-term consequences with regard to joint health and decreased quality of life. Anterior cruciate ligament (ACL) injuries present a specific challenge to joint health in this regard and continue to constitute a large portion of major knee joint injuries in young, active populations. Post-traumatic muscle dysfunction is well described following ACL reconstruction,[1] and is linked to a sequelae of impairments detrimental to global and joint-specific health, including decreased physical activity,[2-5] increased risk of re-injury,[6] and an accelerated onset of post-traumatic knee joint osteoarthritis.[7-11] Strong evidence exists supporting the causal link between ACL-R and early post-traumatic articular cartilage joint degeneration.[9,12-14] Since articular cartilage degeneration is irreversible, the hallmark for prevention is early detection. Neuromuscular adaptations are inevitable following joint injury, but present a modifiable source of dysfunction in the prevention of post-traumatic knee joint osteoarthritis. To date, there is limited evidence with respect to changes within the central nervous system following ACL reconstruction (ACL-R),[24] and no information regarding the temporal relationship of these changes following ACL injury through the development of post-traumatic joint degeneration.

EPIDEMIOLOGY OF ANTERIOR CRUCIATE LIGAMENT INJURY

Epidemiologic data regarding the incidence of ACL injury and reconstruction has been widely studied, however, remains considerably variable, as it is often based on expert opinion and limited electronic databases. Several studies have examined trends over time in the ACL injury. In 2007, Hootman et al.[40] reported a 1.3% annual increase in ACL injuries from 1988-2004 using data from the NCAA Injury Surveillance System collected from 15 sports. Approximately 5,000 ACL injuries were reported to this system during this time, with an average annual occurrence of 313. ACL rupture remains common in sports,[41] and reconstruction is often recommended to facilitate return to sport.[42] In the United States, the incidence of ACL reconstruction (ACLR) was reported to rise from 86,687 (32.9 per 100,1000 person years) in 1994 to 129,836 (43.5 per 100,000 person years) in 2006.[43] Varying incident is reported, however, similar trends in rate of reconstruction have been reported in the United States. In 2009, Lyman et al[44] reported a 22% increase in ACLR from 1997 to 2006 using data from hospital admissions in New York State. The decision to undergo ligament reconstruction following ACL rupture is multifactorial and patient specific. Within an active population, ACLR is often selected in an attempt to prevent further injury.

RISK FOR INJURY

A multitude of factors, both internal and external, may contribute to risk of ACL injury. Within an active population, ACL ruptures remain one of the most common knee injuries.[45]

Sex

The relationship between patient sex and risk for ACL injury has been widely studied in a sports medicine context. Data is somewhat conflicting regarding the number of ACL injuries sustained by male and female counterparts. Higher incidence rates for ACL injury has been identified in males relative to female counterparts using data from a population-based study.[46] However, when comparing rates of injury within sport, a 2007 meta-analysis revealed an increased occurrence among female athletes, citing a 3 times greater incidence in soccer and

basketball specifically.[47] A variety of suggested risk factors including environmental factors, anatomical indices, hormonal influences, and biomechanical factors have been reported to contribute to ACL injuries in females.[48-50]

Age

The number of ACL reconstructions in young, active populations has continued to increase over the past several decades.[44] In patients younger than 20 years, the average number of ACLRs increased from 12.2 to 18.0 per 100,000 person-years between 1996 and 2006. Additionally, this age group comprised a greater proportion of all ACL injuries compared to patients in their 2nd, 3rd, or 4th decade of life.[43] Although the cause of this increase is unknown, it is possible that an increase in sport participation or duration of athletic activities throughout the year may contribute to this finding.

Sport

Epidemiologic studies using large electronic data capture systems have provided valuable insight on injury rates by sport. In collegiate athletics, the NCAA Injury Surveillance System (ISS) has been used to obtain these data. Data from 15 sports were obtained between 1988 and 2004. ACL injury rates have been reported as highest in football, women's gymnastics, women's soccer, and women's basketball.[40] These data support evidence of increased risk for ACL injury in soccer and basketball, specifically among female athletes. Because these sports mimic the cutting tasks associated with ACL injury, research among such athletes has been a specific interest in sports medicine. Prodromos et al. 2007[47] reported combined injury rates for female soccer and basketball players at 0.3 per 1,000 exposures, which they equate to an approximate 5% annual risk for injury. Similarly, previous data has reported a 4.4% 1-year incidence of ACL injury in this population.[51]

RISK FOR RE-INJURY AND POST-TRAUMATIC KNEE OSTEOARHTRITIS

Mitigating the risk for re-injury is a primary concern for health care practitioners when making rehabilitative and return to activity decisions. The greatest predictor for future injury is a

history of previous injury, and unfortunately, not all risk factors for secondary injury can be modified. It is however important for clinicians to be aware of risk factors, internal and external, that may be considered by varying members of the sports medicine team.

Early (ACL Reconstruction – Return to Play at 2-15 Years)

Graft Type

Many studies have compared short and long-term outcomes among graft types, most notably among patellar tendon and hamstring tendon grafts. In 2011, a systematic review[52] examined clinical outcomes in ACL deficient patients with patellar tendon and hamstring autografts. From nineteen studies reporting follow up data 2-8.5 years post ACLR, the authors of this review concluded that there is insufficient evidence to support the clinical benefit of either graft choice. In partial support of this finding, a recent prospective analysis of patients 15 years following ACLR, no differences in incidence of further ACL injury were noted between those with patellar tendon (8%) or hamstring tendon (17%) autograft.[53] Although graft type was not associated with graft injury, a 2.6 increase in odds of contralateral ACL rupture was observed among patients with patellar tendon (26%) graft compared to hamstring (12%). Additional consideration and debate has been given with regard to use of single- and double-bundle grafts. A recent comparative study of over 16,000 patients revealed no difference in rate of ACL revision between those with single and double-bundle hamstring autograft.[54]

Gender, Age, Race, Ethnicity

Gender influence on injury rates is a debated topic in musculoskeletal research. Much of the literature examining risk of primary ACL injury indicates women are at an increased risk for injury. For the same reasons, women remain susceptible to re-injury, and have been cited as having a higher rate of ACL graft rupture than men.[55] Within an athletic context, female soccer players are more likely than men to sustain second ACL injury (20% vs. 5.5%).[56] Additionally, women have been reported to be at greater risk for contralateral ACL injury at 12 and 24 months following return of sport.[57,58] In contrast, a recent prospective analysis of patients 15 years after

ACLR, reported that men were 3.2 times more likely to sustain and ACL graft rupture than women.[53] Although this conflicts with previous data, this finding may be a product of men returning to higher-level activities than female counterparts. These findings are corroborated by a prior systematic review, concluding insufficient evidence to determine superiority in graft bundle.[59]

Age at time of injury and subsequent surgery has been identified as a factor related to risk of re-injury with conflicting evidence. Data from the Swedish national ACL register identified age at the time of surgery (< 16 years) as a significant predictor of ACL revision at 5 years.[60] A retrospective analysis of high-level athletes ranging 16-53 years of age, did not find an association between age and re-injury rates.[61] Although a significant association was not found, athletes under 18 years of age demonstrated a re-injury rate of 8.7%, whereas, only 2.6% of those 18-25 years sustained a second injury. Interestingly, Leys et al[53] reported that graft rupture was not associated with age less than 18; however, young individuals were 4.1 times more likely to sustain a contralateral injury.

Race and ethnicity have been linked with risk of ACL injury, although evidence is lacking. In a retrospective study[62] of female athletes in the Women's National Basketball Association, White European Americans (WEA) were determined to be 6.55% more likely to sustain a primary ACL injury than non-White European American players (African American, Hispanic, Asian). Furthermore, this study noted that WEA injury rates were greater (0.45 per 1,000 exposures) compared to overall ACL injury rates in the WNBA (0.20 per 1,000 exposures). Although the cause is not clear, Shelbourne et al[63] reported that the intercondylar notch width measured during flexed weight bearing radiographs were significantly wider among African Americans than White European American counterparts, which may partially explain the increased incidence of ACL injuries among non-White European Americans.

Time

Incidence of a second ACL injury in the first 12 months following reconstruction in a young, active population has been reported as 15 times greater than a previously uninjured cohort,[57] and 6 times greater at 24 months.[58] Nearly 30% of athletes sustained a second ACL injury within 24 months of return to sport (~21% contralateral, 9% ipsilateral). Secondary injury data within 24 months of reconstruction appear to highlight the importance of continued rehabilitative efforts following ACL injury. Timing is commonly used as a primary criterion in return to sport decision-making. A lack of association between time from surgery and persistent functional deficits has been identified in athletes after ACLR,[64] supporting the inclusion of more objective criterion when making return to play decisions. A 2010 retrospective analysis of 298 patients four years post ACLR revealed that athletes returning to competition within seven months from surgery were at a greater risk of re-injury than those returning at a later time (15.3% vs. 5.2%).[61]

Late (Late Stage Return to Play – Osteoarthritis)

Concomitant Injury

National data from the Swedish national ACL register reported 5-year post-operative rates of revision (4.3%) and contralateral ACL reconstruction (3.8%) among nearly 21,000 patients.[60] This study further identified concomitant injury at the time of ACL rupture as a significant risk factor for secondary ACL reconstruction, including operative and non-operative meniscus, articular cartilage, and collateral ligament injuries. Of note, surgically treated meniscus injuries were identified in 78.8% and 79.1% of all patients who sustained a revision or contralateral ACL reconstruction respectively. Due to the high prevalence of meniscal injuries at the time of ACL rupture, early articular cartilage degeneration in this population is a concern. A 2009 systematic review[65] aimed to identify the impact of meniscal injury at time of ACL reconstruction on the development of osteoarthritis. This review concluded that patients who underwent partial meniscectomy at the time of ACL reconstruction were at a significantly greater

risk for developing radiographic evidence of osteoarthritis at 5-10 year follow up, whereas, inconsistent findings were reported for those who underwent meniscal repair.

Muscle Function

Persistent quadriceps weakness and central activation failure are widely reported following knee joint injury.[1] Post-traumatic muscle dysfunction is linked to a sequelae of impairments detrimental to global and joint-specific health, including decreased physical activity,[3,4] increased risk of re-injury,[6] and an accelerated onset of knee joint osteoarthritis.[10,66] Strong evidence exists supporting the causal link between ACL-R and early post-traumatic articular cartilage joint degeneration.[9,12-14] Central and peripheral neural adaptations accompany these consequences, and are established as an underlying contributor to muscle impairment.[19] Quadriceps dysfunction is reported to manifest via altered excitability from spinal and cortical regions.[67,68] The diminished ability to activate otherwise healthy peri-articular muscular tissue in the presence of joint pathology is termed arthrogenic muscle inhibition (AMI), and is proposed as a neural phenomenon responsible for limiting the progression of rehabilitation.[26] Following injury, this arthrogenic response can manifest as an ongoing reflex inhibition due to aberrant sensory information arising from mechanoreceptors located in peri-articular structures, which the central nervous system (CNS) interprets as inhibitory.[26,69] Inhibition of surrounding musculature may therefore result from transmission of aberrant afferent stimuli, and has been examined following artificial joint effusion,[70] pain,[71] and structural damage.[68]

Post-Traumatic Osteoarthritis

ACL rupture and subsequent reconstruction have been linked with early onset of articular cartilage degeneration. Specifically, medial compartment and patellofemoral joint osteoarthritis (OA) have been identified in patients following ACLR. In a recent systematic review of ACLR individuals, the authors concluded that there is insufficient evidence to suggest that ACL is adequate to prevent knee OA. This review identified radiographic signs of OA in 44% of all ACLR patients (n = 2,500). The prevalence of OA varied by isolated ACL rupture (42%) and

presence of meniscus injury (52%). When further stratified by study design, retrospective studies reported 39% (n = 1,455), whereas, prospective studies demonstrated a 56% occurrence of OA (n = 1,099) during 3.9 – 35 years follow up.[72] Although much attention has been given to the development of tibiofemoral OA in the medial compartment, the prevalence of patellofemoral joint OA has been reported to range 11-90% (median 36%) within 2-15 years from surgery.[2,73]

CLINICAL OUTCOMES

Clinical outcomes are comprised of impairment-based and patient-oriented factors, including joint stability, muscle function, activity level, and self-reported function.

Short-Term (0-2 years)

Return to pre-injury activity levels following ACL reconstruction is a common goal among active individuals. In an updated systematic review of 4,837 ACL reconstructed patients, 81% returned to some form of sporting activity, whereas, 65% returned to pre-injury activity levels, and only 55% returned to competitive levels of sport.[74] These data highlight the difficulties in returning to high-level sporting activities following ACL-R, which presents a specific challenge to young, active patients pursuing high-level athletics. The inability to return to specific activities is likely multifactorial. Symmetry of hopping performance, and contextual factors of younger age, male gender, playing an elite sport, and having a positive psychological response increased the change of return to pre-injury levels of sport.[75] Impairment-based knee function has yielded considerably positive results following ACL-R, making, the psychological response to injury a recent topic of study in this regard. A positive psychological response to measures of readiness to return to sports participation (ACL-Return to Sport after Injury Scale) and fear of re-injury (Tampa Scale of Kinesiophobia) prior to and early after ACL-R significantly classified return to pre-injury activity level in a cohort of 187 athletes.[76]

Medium (2-10 years)-Long-Term (10+ years)

In a cohort of 314 ACL reconstructed individuals at a mean of 39.6 months from surgery were surveyed to determine the proportion of people participating in pre-injury activity levels and

competitive sport.[77] 45% were identified as playing sport at pre-injury levels, and only 29% were playing competitive sport. Additionally, early return to activity at 12 months was not predictive of activity level at 39 months in this sample, suggesting that people who return early may not maintain sports participation. Interestingly, a lack of association between high satisfaction and increased activity levels has been observed following ACL-R. In a retrospective review of 29 skeletally immature patients, 41% returned to pre-injury activity levels, despite reporting a mean satisfaction score of 9 (range, 4-10) and Lysholm score of 91 (range, 61-100) at 2 years.[78]

PROBLEMS PATIENTS ARE FACED WITH FOLLOWING ACL RECONSTRUCTION

Sources of Sensorimotor Dysfunction

The resulting inhibition of surrounding musculature that occurs following ACL injury may has been theorized to result from transmission of aberrant afferent stimuli, and has been examined in the presence of artificial joint effusion[70], inflammation[79], pain[71], and/ or structural damage. Reduced quadriceps muscle function has been reported to manifest as altered excitability at the spinal and cortical level[67,68], including reduced volitional activation[1], torque[80], and electromyographic activity[81] among individuals with artificial and true knee joint pathology.

Peripheral receptors

The location of sensory nerves has been suggested to be of particular importance to clinicians when treating arthrogenic muscle inhibition following joint injury.[26] Somatosensory information originating from peripheral receptors is reported to influence motor function via projections to spinal motoneurons, as well as supraspinal structures.[82] Specifically, sensory nerves innervating knee joint terminating in specialized mechanoreceptors have been theorized to play a primary role in modulating inhibition.[83] It has been established that articular mechanoreceptors play a significant role in regulating afferent signals to the central nervous system, and appear to be sensitive to change in the presence of joint damage,[84] making the neurophysiological response of these receptors a clinical interest.

Spinal

Research to date has largely focused on spinal mechanisms of AMI.[19] The Hoffmann reflex (H-reflex) is a common neurophysiologic test used in sports medicine research to assess modulation of monosynaptic reflex activity in the spinal cord.[30] The H-reflex can be viewed as analogous to the mechanically induced stretch reflex. However, in this instance, the muscle spindles are bypassed by stimulating a mixed nerve directly. As a mixed nerve is stimulated, action potential volleys are sent in opposing directions along the afferent (spinal cord) and efferent (muscle) pathways. At lower stimulus intensities, the H-reflex can be mapped until reaching its peak amplitude as measured by surface EMG. As the stimulus intensity is increased, an opposing volley (antidromic) essentially masks the H-reflex, leaving behind the muscle response, or M-response. The H-reflex is interpreted within the context of sports medicine research as an estimate of alpha motoneuron pool excitability, or the proportion of alpha motoneurons available for use when normalized to the maximal M-response (H:M ratio).[30] This measure has been extensively used to assess the motoneuron pool of the quadriceps[85] and soleus[21] musculature in healthy and injured cohorts, as well as the neural response following musculoskeletal injury. Although useful information can be gained from this measurement, it may be limited to monosynaptic synapses at the spinal level, and may miss a piece of the puzzle in regard to complete neurophysiologic assessment following joint injury. As this measurement is conventionally performed in a completely static state, due to inherent confounding during dynamic movement, it has the potential to bypass descending input from supraspinal centers. This provides a clearer interpretation of the measurement, but does not represent the complete neurophysiologic state of the individual.

Corticospinal

Although afferent signals project to the spinal cord directly, joint afferents are known to have extensive supraspinal projections to the cerebral cortex as well.[86] Supraspinal influence on descending cortical output following injury is often neglected within the context of

musculoskeletal research, specifically of the lower extremity, and has only begun to be better understood over the last decade. Cortical excitability has been researched in this regard following knee joint injuries.[24,87] As descending pathways do have widespread projections within the spinal cord, there remains a great potential to influence AMI. Transcranial magnetic stimulation (TMS) provides a method of assessing excitability of the pre-motor area of the cerebral cortex.[22] TMS produces a small, but powerful field of magnetic energy that depolarizes neural tissue to initiate action potentials.[22] When a TMS device is placed over the scalp, superficial to the pre-motor area, action potentials are conveyed to the associated skeletal muscles resulting in a motor evoked potential (MEP). By stimulating the cortical neurons corresponding to quadriceps activity in the contralateral primary motor cortex, a motor evoked action potential can be detected via surface electromyography. When stimulated during minimal volitional activity of the involved musculature, this measurement is termed active motor threshold (AMT), and has been used as a primary indicator of corticospinal excitability in individuals following knee joint injury.[88]

TMS is a non-invasive tool used to measure neural conduction and processing time, activation thresholds, facilitation and inhibition in the primary motor cortex, and neural connections.[22] Since its original description in 1985, single pulse TMS has been widely used to study motor, visual, and somatosensory systems, as well as sensorimotor integration and cognition in patients with a variety of diagnosed disease processes.[22] It has since emerged in sports medicine research as an intervention and assessment tool primarily in the upper extremity.[89] Several authors have used TMS to measure cortical excitability in the lower extremities of varied cohorts.[24,87,90,91] Our research laboratory has demonstrated the ability to successfully and reliably utilize this technique in the treatment[90] and assessment[91,92] of lower extremity muscular dysfunction. However, to date there is minimal evidence of the role of cortical excitability in neuromuscular recovery at various points in time following knee joint injury.

SENSORIMOTOR ADAPTATIONS TO JOINT INJURY

Musculoskeletal injuries are common among athletic and recreationally active populations. Joint injuries specifically constitute a clinically important subgroup in these patient populations, presenting long-term consequences to joint health. Impairments in neuromuscular function and decreased self-reported quality of life have been reported in patients after ankle, knee, and hip joint injury. Strong evidence supports the link between lower extremity joint injury and early post-traumatic articular cartilage joint degeneration.[9,12,13,93] Since articular cartilage degeneration is irreversible, the hallmark for prevention is early detection. Therefore, understanding the current knowledge base surrounding the neuromuscular adaptations that occur following joint injury is paramount.

Within the broad scope of the sensorimotor system, a term used to describe the sensory, motor, and central integration and processing components involved in maintaining joint homeostasis during bodily movements[35], neuromuscular impairment has been purported to influence gross motor output, and should be of extreme interest to sports medicine clinicians. To effectively evaluate the neuromuscular function of an individual in this capacity, clinicians must have a comprehensive understanding of the neural adaptations that occur following injury. It is imperative that health care professionals continue to make efforts, from clinical practice to laboratory-based research, to identify objective evidence of persistent dysfunction following injury. This review will attempt to provide a link between clinicians and researchers from a measurement perspective in regard to neuromuscular changes following lower extremity joint injury.

Measures of Neuromuscular and Sensorimotor Function

The evolution of measurement techniques used to identify neuromuscular impairments following injury will be explored. Common clinical and laboratory-based measurement techniques used in current practice will be examined, with a specific focus on the application and interpretation of results. Within the literature, clear descriptions of measurement techniques and

perspective on clinical interpretation related to lower extremity neuromuscular function are lacking. Therefore, the purpose of this review is to provide a detailed overview of the techniques used to evaluate neuromuscular function with specific regard to bridging the gap between common clinical and research specific measures of lower extremity function after joint injury.

Use of Clinical and Laboratory Measures

A variety of measurement techniques are commonly utilized in clinical practice to assess sensorimotor impairments following joint injury. Such measures provide valuable insight to gross functional impairments, which aid clinicians in assessing the progress of patients throughout the rehabilitation process. Many of the clinical assessment techniques utilized in practice have been validated using instrumented tools commonly used in the research setting. In addition, the ability of clinicians and researchers to reliably assess patients using these techniques and measurement tools has been established in most cases.

Laboratory based measurements are a vital component in sports medicine research, and beneficial supplement to clinical practice. Such tests are not meant to replace clinical measures, but to compliment them, in order to provide a comprehensive approach to clinical care. Oftentimes, there may be a lack of interpretation in regard to the clinical relevance of laboratory-based measures, which can subsequently hinder the incorporation of such measures into clinical practice. The following section will attempt to provide an interpretation of commonly used clinically and laboratory measures in sports medicine research, while placing an emphasis on clinical relevance. Additionally, techniques and pitfalls associated with these measures will be highlighted.

POSTURAL CONTROL

Postural control is a multi-system process that relies on feedback from the somatosensory, visual, and vestibular input, and is a necessary component of daily function.[94,95] Postural control, or balance, has been widely studied in musculoskeletal and cognitive injury research. These easy to use tests provide useful information to clinicians, and present good

alternatives to more expensive laboratory based measures. Whereas static measures provide useful information in regard to postural control, they may not be challenging enough to detect impairments during physical activity[96], and caution should be made when interpreting results. Numerous modifications have been described in the literature, making scoring and comparisons with other studies difficult. Results should be compared within individuals, ideally from pre-injury data under the same testing conditions when possible.

Clinical Measures

Balance Error Scoring System (BESS)

The Balance Error Scoring System (BESS) is a clinically useful tool originally developed as a cost-effective objective assessment used in the evaluation of postural stability following concussion.[95,97,98] As classically described, the BESS consists of 6 different conditions: double-leg stance (hands on the hips with feet together), single-leg stance (standing on non-dominant leg with hands on hips), and a tandem stance (heel-to-toe with non-dominant foot behind) on a firm and foam surface, with the eyes closed and shoes removed.[95,99,100] This test is designed to detect gross balance deficits as noted by errors during each stance over a 20 second time epoch. Errors are defined as opening the eyes during stance, lifting the hands from hips, stepping, falling out of position, lifting the forefoot or heel, abducting the hip greater than 30 degrees or failing to return to the starting position in 5 seconds.[99] Each error is given 1 point, with a maximum allowable number of 10 per stance. Once all 6 trials are completed, the total number of points per stance is summed, allowing for a maximum of 60 points. Point totals exceeding 10 in a given position, or 60 overall are considered a failed trial.

Deficits in postural stability are multi-factorial and common after joint injury. It is important not only to have an easy to use clinical tool, but a test that will be valid, reliable, and sensitive to change. The intra-rater[97,101], inter-rater[95,97,102], and test-retest[103,104] reliability have been extensively examined. Although the BESS has been demonstrated to be sensitive enough to detect subtle postural changes, the reliability of this test is varied in the literature.[99] Valovich McLeod et

al.[101] reported an intra-rater reliability ranging 0.87 to 0.98; however, a more recent review has reported 0.74 for total BESS scores.[97] Large ranges of inter-rater reliability from 0.57-0.96[95,97,102] have been described for total BESS score, with test-retest reliability consistently lower between 0.64-0.67.[103,104] Finnoff et al.[97] reported acceptable intra-rater reliability with firm single leg, firm tandem, and foam double leg, and inter-rater reliability for the firm single leg stance only. Additionally, a learned effect has been observed[101], which has influenced how the test is administered. Broglio et al.[103] demonstrated an increase in reliability when averaging three BESS trials within a given session, or twice if performed over multiple days. Furthermore, muscle fatigue has led to confounding results by increasing errors immediately after exercise.[105] Therefore, it is recommended to wait a minimum of 20 minutes following exercise to administer the BESS.[106] A modified version of the BESS was developed. Hunt et al.[107] described a modified version of the BESS using single-leg and tandem leg stance on firm and foam surfaces. Using this protocol, reliability was measured at 0.88 when averaging three trials. Due to the purported learning effect, the first trial was excluded from further analysis, reducing reliability slightly to 0.84. A subsequent analysis of one trial alone further reduced the reliability to 0.74. An additional investigation of a modified protocol by Clark et al.[108], using 6 conditions: single-leg dominant, single-leg non-dominant, and tandem on firm and foam surfaces, demonstrated fair test-retest and inter-rater reliability of 0.74 and 0.61 respectively. The results of these studies further support the recommendation for multiple trials when using either the original or modified BESS.

Beyond its use as a valid assessment tool for postural stability following sports related concussion, the BESS has been demonstrated to be a valid measure of assessing postural sway in individuals with functional ankle instability[98], and sensitive to changes following fatigue[105], neuromuscular training[102], ankle bracing[109,110], and varied training backgrounds.[111] Additionally, subcategories of the BESS have been correlated with force plate measures, which are commonly used in the assessment of postural control following musculoskeletal injury.[95] According to the presented literature, the BESS can be a valuable tool used in adjunct with other clinical and

laboratory measurements in the assessment of sensorimotor impairment following musculoskeletal joint injury.

Romberg Positional Stance

Vestibular and somatosensory input are two of three peripheral modalities that influence static and dynamic postural control[95], an aspect of sensorimotor control paramount in coordinated movement. Although vestibular dysfunction is not at the forefront of clinical sports medicine, a variety of clinical assessment techniques have been utilized to identify balance deficits in a variety of pathologic populations. Romberg's Test is a commonly used assessment tool described in the early 19th century as a patient reported symptom to detect the loss of coordination due to a decrease in sensory input.[112-114] This simple test may offer an important clue to the presence of vestibular dysfunction[115], multiple sclerosis[116], Parkinson's disease[117], chronic low back[118] and neck pain[119], chronic ankle instability, and ACL injury.[120] During the Romberg Test, the patient is asked to stand upright with feet close together, and arms at the side, in an anatomic position.[113] A trial is initiated by having the individual stand still on a firm surface with the eyes open for a period of time, typically 10-30 seconds. During this time, the clinician will qualitatively note any deviations in movement. The individual's eyes are then closed, and the stance task is repeated, again noting any deviations in movement. The task can be altered by observing any postural abnormalities while having the individual look directly ahead and follow the clinician's finger as it moves rapidly from left to right or up and down.[121] Variations have included a narrowed stance, tandem stance, balance on foam surfaces, use of footwear, alterations in hand placement, and external perturbations.[113] Of recent, a modified Romberg Test of Standing Balance on Firm and Compliant Surfaces has been developed to identify isolated vestibular dysfunction.[122] This modification includes 4 test conditions, adding double limb stance with the eyes open and closed on a compliant surface to the originally described protocol.[122,123] In addition to noting the degree of sway, the source (e.g. ankles, hips, entire body) should be recorded. To make appropriate observations, the clinician should stand directly in front of the individual being testing with arms

extended to either side for support if necessary. A positive test, or Romberg's Positive, is determined if there is significant imbalance or worsening of balance with the eyes closed.[121]

Early descriptions of Romberg's Test have led to developments in modern posturography[113], and variations of the test are currently utilized in a variety of medical disciplines.[124,125] Within the realm of clinical sports medicine practice, studies assessing static postural control are most commonly reported with respect to ankle injuries.[126] Although instrumented force plate measures have become the gold standard when assessing postural control, versions of Romberg's Test have been employed in clinical practice. In a 2008 systematic review, McKeon and Hertel reported that increased risk of sustaining an acute ankle sprain as noted by decreased postural control could be detected using a modified Romberg's test in conjunction with force plate measures.[126] As decreased postural control has been demonstrated following ankle sprains, and linked with chronic ankle instability, the use of Romberg's Test during sensorimotor assessment following injury is warranted. Caution should be used when interpreting the results of this test, and ideally paired with baseline values; however, this may serve as a simple estimate of neuromuscular ability following lower extremity joint injury.

Star Excursion Balance Test (SEBT)

Dynamic balance is paramount in successfully completing athletic-related activities, and is frequently affected by musculoskeletal injury. Measures of dynamic postural control can be used to screen high-risk individuals or an assessment tool following injury as a means of identifying persisting dysfunction or return to play decisions. The Star Excursion Balance Test (SEBT) has been widely researched with regard to dynamic postural control. The SEBT was originally described as a rehabilitative tool[127], and has multiple clinically relevant uses. The SEBT is a series of single-limb squats performed in eight directions on a flat surface using designated lines on the ground spread in 45° angles.[128] The non-stance limb is used to reach in each direction: anterior, anteromedial, anterolateral, medial, lateral, posterior, posteromedial, and posterolateral, which are named in orientation to the stance limb. The goal of the task is maintain

a stable base of support with the stance limb with the foot flat of the floor surface, while reaching as far as possible with the non-stance limb.[128] Athletic tape or a grid is commonly employed to measure reach distance; however, commercially available tools have been reported and may serve to improve the efficiency of the test.[129] While reaching, the participant must touch down lightly with the distal most aspect of the reach limb lightly and return to the starting standing position. Should the reach limb rest of the floor surface, touch down hard, or lose balance, the trial is failed and should not be taken into consideration.[128,130] The limb reach distance of 3 trials is typically averaged and normalized to limb length as measured from anterior superior iliac spine to medial malleolus, and expressed as a percentage of limb length.[130] Normalization is most commonly performed using true limb length, and serves to standardize values for comparison between individuals.

Given that individuals unfamiliar with the task often perform poorly during initial trials, researchers have investigated the learning effect of the SEBT. An early investigation[131] noted a plateau in reach distance after 7 trials, and therefore recommended participants perform 6 practice trials in each direction of the SEBT before recording. However, a more recent examination[132] has recommended only 4 practice trials, which has been supported by follow up investigation.[133] Although the accepted practice session has been reduced over time, the time necessary to complete testing in all 8 directions has led researchers to examine whether all directions serve a discrete purpose. In 2006, Hertel et al.[134] demonstrated redundancy in participant performance in each of the 8 reach directions, which later led to the recommendation that only 3 reach directions: anterior, posteromedial, and posterolateral be performed.[135] In a recent systematic review, Gribble et al.[96] summarized all supported performance recommendations. Of note, clinicians are encouraged to conduct testing with the participant's shoes off, to use 4 practice trials prior to testing[132], to use video instruction when available, to control the order of testing, to standardize the position of the stance limb while minimizing movement of the foot and trunk during reach[136],

maintain the participant's hands on hips[136], and to normalize reach distance to limb length of the stance leg.[130]

To further support its clinical use, strong intra-rater reliability using the SEBT has been reported. Kinzey and Armstong[109] first reported intra-rater reliability of the SEBT, at a range of 0.67 to 0.87, whereas Hertel et al.[131] later noted an increase, from 0.81 to 0.96 ($ICC_{2,k}$). The SEBT has also been demonstrated as a reliable measure between clinicians, with inter-rater reliability ranging 0.35 to 0.84 and 0.81 to 0.93.[127] Although 0.35 is not an acceptable level of reliability, this value was determined on the first day of a two-day testing session, and has been attributed to a learning effect.[127] Beyond the established reliability of this tool, it has demonstrated validity as a dynamic test to predict risk of lower extremity injury[129,137], to identify dynamic balance deficits following a variety of lower extremity injuries[134], and to detect postural responses to neuromuscular training programs in healthy and injured individuals.[96,102,138]

In light of the available evidence, the SEBT can be considered a highly representative non-instrumented dynamic balance test for physically active individuals.[96] The SEBT combines sagittal, frontal, and transverse moments, while allowing for an easy to use, and cost-effect approach to the neuromuscular assessment. Although this is a widely utilized assessment tool, caution should be made when interpreting results. With conflicting evidence of varied effects based on sport, sex, age, foot type, time of day, and body height, efforts should be made to standardize between session trials. Furthermore, the SEBT should be used in conjunction with other clinical assessment tools, and not solely relied upon when assessing sensorimotor function.

Laboratory Measures

Forceplate

Postural control deficits have been widely observed following lower extremity injury.[139-146] Such impairments are commonly assessed in research settings via changes in balance and distribution of pressure about the foot. Instrumented measures using force plate and pressure mat calculations are useful in describing these impairments with high precision. Although these

measures have been largely studied among individuals with chronic ankle impairments, such data are not limited to those suffering from distal joint injuries.

Traditional force plate measures including average center of pressure (COP) excursion velocity and area have been used to describe changes in postural control following injury[126] and rehabilitative programs.[147] These measurements are calculated during a single limb balance task, and provide information in regard to how quickly the foot is moving, and the size of area covered during movement, with higher values of each indicating poorer performance. A more recent approach to characterizing postural control is a time-to-boundary (TTB) analysis.[148-150] TTB is a spatiotemporal analysis of COP data points that quantifies the theoretical amount of time an individual has to make a postural correction in order to maintain postural stability.[148-150] In this instance, lower values are considered pooper outcomes, indicating less time to make postural corrections. Wide, albeit acceptable levels of reliability, have been reported using traditional ($ICC_{2,1} = 0.35 – 0.80$), and TTB ($ICC_{2,1} = 0.34 – 0.87$) measures of postural stability between sessions.[150] Understanding how well an individual can respond to changes in postural demands is a primary point of concern for clinicians when determining readiness for activity progression following injury.

Alterations in the distribution of plantar pressures have been observed following acute and chronic[151-154] lower extremity joint injury. Most notably, the shift towards a more laterally based COP has been observed during gait pattern among those with a history of chronic ankle instability. Researchers have used pressure mats and instrumented insoles to identify shifts in these pressures following injury. Utilizing, or understanding, the interpretation of such instrumented measures may aid clinicians in identifying sensitive changes during this process.

FUNCTIONAL TASKS

Clinical Measures

Landing Error Scoring System (LESS)

Non-contact ACL injuries remain a major concern in sport and carry with them long-term sequelae.[155,156] The high prevalence of ACL injuries have led to a vast amount of research related to faulty movement patterns, ACL risk and prevention, and ACL loading characteristics.[51,157-161] The available evidence has demonstrated an inter-relationship between these factors, specifically between lower extremity movement patterns and ACL loading.[162] Such data has led to a relatively consistent list of ACL risk factors and the development of subsequent prevention programs. Isolated and combined patterns of knee valgus, internal rotation, and decreased flexion have been traditionally labeled as high-risk movement patterns for non-contact ACL injury.[162,163] Additionally, faulty movements distal and proximal to knee joint have been related to lower extremity injury risk.[160] In light of the importance placed on optimal movement patterns during sport, and the ability to correct faulty movement patterns efforts have been made to establish clinically relevant tools to identify high-risk individuals.

The Landing Error Scoring System (LESS) is a qualitative assessment tool used to identify gross movement pattern dysfunction. Padua et al.[160] developed this tool as an inexpensive method of providing a standardized functional movement assessment. The LESS uses two off-the-shelf video cameras to record motion in the sagittal and frontal planes during a jump landing maneuver. Each camera is set 136 inches from the landing area facing each plane, and 48 inches from the floor. To perform this task, the individual must jump with both feet from a 30 cm high box to a distance of 50% of their height away from the box. The individual is instructed to jump from a neutral position with feet shoulder width apart and toes pointing forward, and perform a maximal vertical jump immediately upon landing. Evaluator instruction during testing is minimal, with feedback provided only to insure the task is performed correctly. Several practice trials are commonly allowed, with the average of three trials taken.[160,164,165]

LESS scores are simply reflective of gross observable movement errors during a jump-landing task, with higher scores indicative of high-risk biomechanics.[160] Trials are scored in the sagittal and frontal planes, on a 17-item scale. Scoring is broken down into several sets of items: (1) lower extremity and trunk position at time of initial ground contact, (2) positioning of the feet at initial ground contact, (3) lower extremity and trunk motion between initial ground contact and maximum knee flexion, and (4) overall sagittal plane motion and general perception of landing quality. Total scores can be dichotomized into excellent (≤ 4), good (> 4 to ≤ 5), moderate (> 5 to ≤ 6) and poor (> 6) landing techniques.[160] In the absence of an injured extremity, the dominant limb is focused on for scoring purposes. Padua et al. has reported good inter-rater and excellent intra-rater reliability of 0.84 and 0.91 respectively.[160] Authors employing large-body screening interventions have demonstrated excellent inter-rater reliability ($ICC_{2,1} = 0.835$) between expert and novice raters in scoring the LESS, which further supports its use in a variety of clinical settings.[166]

In addition to the LESS, researchers have used 2D video analysis to measure frontal plane motion during other common athletic tasks. The use of 2D video analysis has been validated[167] and demonstrated to be a reliable measure of lower extremity dynamic knee valgus.[168] Although simple video analysis is inherently useful beyond the scope of the described LESS criteria, the LESS is recognized as the most commonly used valid assessment tool to identify dynamic movement error. In 2009, Padua et al.[160] validated the LESS against the gold standard of 3D motion capture analysis. However, in cases in which 2D video cameras are unavailable and/or immediate feedback is warranted, a real-time version of the LESS (LESS-RT) has been explored. In 2011, Padua et al.[165] reported on the inter-rater reliability of the LESS-RT, ranging 0.72-0.81. In this modified version, individuals complete 4 trials of the previously reported jump-landing maneuver, and are evaluated on 10 jump-landing characteristics by two raters in the frontal and sagittal planes. Despite showing promising evidence of clinical implementation, the LESS-RT has yet to be validated to the same extent as the original LESS.

As the development of clinical tools to predict injury, or risk of injury, attempts to become more sophisticated, a variety of field-based algorithms have recently been described. With the demonstrated link between increased knee abduction moments (KAM) during landing, specifically in females[169], efforts have focused on prevention programs to reduce knee valgus. In 2012, Myer et al.[170] described a field-based measurement used to predict high knee abduction moments in female athletes who may be at greater risk of injury. This algorithm utilized a jump-landing task similar to the LESS, taking into account measures of body mass, tibia length, quadriceps to hamstrings ratio, knee valgus motion, and knee flexion ROM. The described algorithm accounted for 78% of the variance in KAM during landing, and was able to successfully predict high KAM with 85% sensitivity and 93% specificity. Although algorithms may aid clinicians in the absence of more sophisticated measurement instruments, caution should be taken when applying them to larger populations. Authors have questioned the utility of such measures, conducting a large, prospective study that found the probability of high knee abduction moments was not associated with noncontact ACL injury in at risk female high school and collegiate athletes, or matched healthy individuals.[171] Such field-based assessments can be easily implemented within clinical practice; however, extrapolation of predicted kinetics should be interpreted with caution.

Although follow up examination of the LESS has demonstrated an inability of the test to predict ACL injury[172], it has been shown to detect kinematic changes linked with ACL injury risk factors.[159] The primary aim of the LESS is to identify faulty movement patterns during the early landing phase, in which individuals are at higher risk for injury. The LESS specifically identifies high-risk patterns previously linked with ACL injury from a gross perspective. Traditionally, scores have been used as a screening assessment to implement prevention programs for large athletic cohorts.[157,159,166] However, given the nature of its intent, the LESS may be a beneficial assessment tool along the spectrum of rehabilitation following a lower extremity joint injury. Furthermore, implementing the LESS into return to play criteria would inherently serve clinicians

well, providing them an additional criterion for progression. With specific recommendations including quantification of muscle strength, stability, neuromuscular control, and function following ACL reconstruction[156], the LESS may be a valuable tool used throughout the rehabilitative process.

Step-Down Tests

Step-down tasks are commonly used in clinical practice to assess lower extremity movement patterns and general quality of movement.[173] The lateral and frontal step-down are useful tasks that pose a challenge to the strength and neuromuscular control of the lower extremity, which can be useful as an assessment tool before and after injury occurs.[174] With the demonstrated link between poor dynamic stability, specifically in the frontal and transverse planes, and increased risk of lower extremity injury[51,169], it remains highly important for clinicians to employ easy to use tests to identify neuromuscular dysfunction.

Step-down tasks may be used to identify poor dynamic alignment in the frontal and transverse planes, including excessive pelvic drop, hip adduction and internal rotation, knee valgus, and foot pronation.[175,176] These tasks essentially utilize a controlled, eccentric single limb squat with the addition of a contralateral heel touch. Individuals being tested are asked to stand naturally in single limb support with hands on the waist on a raised box in the range of 20-31 cm in height.[177,178] Some authors have recommended using a height that allows for participants to achieve 60 degrees of knee flexion on the stance limb.[179] Participants are then asked to slowly lower the opposite foot at a self-selected pace to lightly touch the floor with the heel, and return to the previously standing position.[173] Practice trials have been reported used to familiarize participants with the task. Multiple trials (i.e. 5-6) are performed when assessing the quality of movement. Trials are scored based on 5 criteria: 1) Arm strategy, 2) Trunk movement, 3) Pelvis plane, 4) Knee position, and 5) Steady stance.[177,179] For a more detailed description of grading criteria, refer to Piva et al.[177] Possible scores may range 0-7, with higher scores indicating poorer quality of movement. Some authors[177] have dichotomized scores into ranges, indicating good (0-

1), medium (2-3), and poor (4+) quality; however, the risk of lower extremity injury per category remains unknown.

Given the prevalence of step-down tasks in clinical practice, authors have attempted to assess the reliability in healthy cohorts. Acceptable intertester reliability of 0.67 has been demonstrated with the lateral step-down task, using the aforementioned scoring criteria.[177] However, when using a global qualitative approach to observing quality of movement, authors[178,180] have reported lower intertester and intratester reliability. To improve the accuracy of qualitative observations during these tasks, simply strategies, such as marking the tibial tuberosity to facilitate visualization can be employed.[179] Although less clinically applicable, 3D motion capture has been used as a supplement to quantify movement patterns during step-down tasks.

When deciding whether to incorporate step-down tests from a screening (pre or post injury) or rehabilitative perspective, clinicians should consider the joint forces created, and the specific biomechanical components to be assessed. Greater patellofemoral joint reaction forces have been described in both frontal and lateral step-down tasks as compared to those stepping up.[181] Understanding the kinematic influence on joint reaction forces will help guide clinicians when implementing this these tasks. Additionally, the lateral step-down task has been reported to be a more useful tool when assessing neuromuscular control of the hip, whereas a drop-vertical jump may detect greater frontal plane changes at knee.[173] Although step-down tasks may be used to assess gross lower extremity quality of movement, appropriate caution should be taken when making clinical decisions.

Single Limb Hop Tests

Criterion-based measures are important pieces of the rehabilitation process.[156,182] From a functional perspective, this becomes extremely relevant when making return to play decisions. The clinician is often faced with the task of matching an appropriate task, based on difficulty and functionality, to an individual following an injury. Some dynamic tests may not challenge the participant enough to adequately identify deficiencies. In late stages of rehabilitation, dynamic

tasks should be difficult enough to identify neuromuscular adaptations that an individual will likely experience during sport. Additionally, using such tasks during early phases of rehabilitation may be useful in predicting functional outcomes after non-operative injuries. Single-leg hop tests have been commonly used to evaluate functional performance specifically after ACL injury or reconstruction.[183]

Single-leg hop tests are commonly used in a rehabilitative setting as measures of function and impairment[183]; however, these tests encompass a variety of tasks, making comparisons between individuals or groups difficult at times. Several more commonly used hop tests have been described by Noyes et al.[182], and include the single hop for distance, triple hop for distance, crossover hop for difference, and 6-meter timed hop.[184] Albeit others have been described, such as the hop and stop[185], stair hop[186], and vertical jump tests[187], the focus of this review will remain on those previously mentioned given their demonstrated reliability and prevalence in functional testing.[184,188,189]

The goal of the single, triple and crossover hop tests is to achieve maximum hop distance moving forward while maintaining a controlled landing strategy on the ipsilateral limb.[184] During the timed hop test, the goal is to hop as quickly as possible over a 6-meter distance.[184] In each test, participants should not be instructed to restrict arm movement, and should maintain the final landing for a minimum of 2 seconds to verify jump distance. A loss of balance, additional hop, or touching down of the contralateral limb is considered a failed trial. Measurements are be made from the great toe to the rear of the foot upon landing using a tape measure. Raw scores are recorded in centimeters based on the maximum hop distance achieved, and normalized to limb length when making comparisons between individuals.[190] Scores are most commonly reported in context of limb symmetry as a percentage.[156,182,183] Limb symmetry has been described as an important prognostic factor after injury, with higher hop symmetry indices being predictive of knee function following ACL reconstruction.[191] The limb symmetry index (LSI) is commonly used in functional assessments following injury, and can be described as: [(involved

score/uninvolved score) x 100%]. A LSI of ≥ 85 has been described as 'normal' limb symmetry[182]; however, recent evidence suggests normal values are greater than 90 (cite).

To enhance its use in clinical practice, authors have extensively studied the reliability of hop tests, reporting intraclass coefficients from 0.66 to 0.99.[190,192,193] Good to excellent test-retest reliability has been demonstrated in the single-leg, triple-leg, and cross-over hop test.[190] Early investigations of reliability may be underestimated due to a learning effect that has been described in more recent investigations. Previous authors[192] have recommended three practice trials be used for the four mentioned hop tests, which has been corroborated by follow up study.[190] However, due to its complexity, a fourth practice trial has been recommended when performing the crossover hop test.[190] Gender may also be considered when determining how much practice to include prior to testing, as limited evidence has demonstrated that males require less practice than their female counterparts when performing the single-leg timed hop test.[190] Despite these claims, familiarity and complexity of the task should be used to determine the quantity of practice trials, with a minimum of three practice trials included.

Hop tests have are used ubiquitously in clinical practice as a measure of functional ability following injury. Function is an important outcome to patient satisfaction after injury, and has specifically been reported on following ACL reconstruction. In an attempt to move towards evidence-based practice, it is important that patient oriented outcomes, such as self-reported function, are included in clinical care. Hop tests have been used in such a manner, and continue to help clinicians understand functional capabilities. They have been reported as sensitive tests, able to detect difference between limbs after lower extremity injury, helping to identify limb asymmetries. Additionally, hop tests have been able to predict strength and power in healthy individuals. Furthermore, these tests have been researched in a variety of populations, owing to the generalizability of results within athletic cohorts. Although hop tests may partially fill a gap between mid-stage rehabilitation and return to sport, they should be used in conjunction with

other clinical and laboratory measures to capture neuromuscular performance in a comprehensive manner.

Laboratory Measures

Kinematic/ Kinetic Measures

Gait adaptations have been observed in individuals following an induced knee joint effusion[20], ACL tear[194,195], and ACL reconstruction.[196] Compensatory movement strategies in the sagittal plane, most notably reduced knee flexion angles evident by a decrease in external knee extension moment, has been observed following ACL injury.[194,197] These adaptations have been theorized to be the result of decreased muscle strength[198] distal and proximal to the injured joint. Additionally, muscular imbalances have been reported as a possible contributor to a quadriceps avoidance pattern.[199] The combination of decrease muscular strength and reduced joint angles results in a less effective mechanism of load absorption during activity while preserving functional mobility. The reduced ability to dissipate loads, results in greater forces directed through the joints of the lower extremity. Researchers have employed a variety of motion analysis techniques in order to capture kinematic and kinetic adaptations before and after joint injury.

Three-dimensional motion analysis has been largely utilized in sports medicine research to measure gait related kinematics. In doing so, camera-based systems such as Vicon, are routinely used. Camera-based systems require the use of numerous retro reflective markers placed along body segments of interest, which can be detected during motion. This form of motion capture allows researchers and clinicians to utilize a large space, able to accommodate a variety of physical tasks. However, this system relies on maintaining visualization of placed markers. Therefore, marker security, participant clothing and body composition become important considerations during the set up process.

In contrast to conventional camera-based systems, electromagnetic motion capture allows for an alternative method of measuring gait related kinematics. These systems operate by projecting a spherical electromagnetic field, which detect sensors placed on body segments. In

contrast to the previously mentioned system, sensors placed on the body are not free, but connected to a central unit. Additionally, any functional tasks completed are limited to the projected field, which is typically in the range of 10 meters. Although this system may utilize a smaller area in which to complete a given task, electromagnetic systems are portable, and can be used to measure kinematics during filed based activities.

Although a variety of methodological considerations exist when performing 3D motion capture analysis, many of the common kinematic measures obtained have been reported to be reliable. In a 2009 systematic review of studies examining the inter-session and inter-assessor reliability of three-dimensional kinematic gait analysis, McGinley et al.[200] reports high reliability indices (CMC = 0.83 to 0.99) at the hip, knee, and ankle in the sagittal plane. Additionally, the least amount of errors were found in pelvic rotation, pelvic obliquity, and hip abduction. However, low reliability and increased errors were reported to occur during hip and knee transverse plane motion. Despite the observed decrease in reliability in the transverse plane, this review ultimately concluded that clinically acceptable errors are possible in gait analysis.

MUSCLE STRENGTH AND ACTIVATION

Clinical Measures

Hand-Held Dynamometry

Force based measures are commonly used in clinical practice during the evaluation and rehabilitation process. In the clinical setting, force based measures are almost exclusively limited to manual resistance and hand held dynamometry testing. Although, clinics may have isokinetic testing available, this will be discussed in later sections in more detail.

Hand-held dynamometry (HHD) is a commonly used clinical measure to quantify isometric strength. In addition to its use clinically in sports medicine practice, HHD has been used to examine muscle strength in a variety of pathologic cohorts, including cerebral palsy[201], spinal cord injury[202], and traumatic brain injury.[203] With questionable reliability of such measures reported in these cohorts, recommendations have been developed to improve the validity and

reliability of HHD measurements within healthy and athletic populations.[204,205] Although hand-held dynamometry has demonstrated good intra-rater reliability, its use has been limited in its inability to produce reliable data between testers (ICC = 0.11 – 0.28), due to varying counter pressure applied.[206] Additionally, the subject strength or mechanical advantage over the tester may confound results. In response to poorly observed reliability between examiners, authors[206] have recommended the use of a novel, resistance-enhanced dynamometer to standardize force production. These authors have reported strong intra-examiner (0.91 – 0.94), inter-examiner (0.98), inter-session (0.91 – 0.92), and intra-session (0.93 – 0.99) reliability using this approach. Although such recommendations may enhance the reliability of hand held measures, they may not always be practical.

Despite previous reports questioning the reliability of standard hand-held dynamometry, more recent authors[204] have cited acceptable reliability between sessions (ICC = 0.62 – 0.92), between testers (ICC = 0.65 – 0.87), and within tester (ICC = 0.77 – 0.97) when using a systematic approach to measure lower extremity strength in young, healthy individuals. Furthermore, this study provided evidence that the level of tester experience had little to no bearing on the intratester reliability.

While acceptable values have been reported, the use of HHD is indicated in early stages of recovery following injury, and is not recommended as a primary strength measurement in healthy, strong individuals.[204,203] Despite its inherent limitations, HHD presents a viable option in quantitative strength assessment following injury. Its portability, generalizability between clinicians and easy of use make this an attractive tool in sports medicine practice.[204,207]

Laboratory Measures

Maximal Voluntary Isometric Contraction (MVIC)

Instrumented force based measures are commonly utilized for clinical and research purposes in the evaluation of strength following joint injuries. These data are conventionally used as criteria for return to play decision-making, and are often heavily relied upon as objective

measures.[156] With the established link between decreased muscle strength following joint injury and poor outcomes[67,208], multimode dynamometry is widely used to assess persistent weakness. Strength assessments are conventionally performed bilaterally, with the uninjured limb serving as a reference standard. In certain cases, this method may serve as an adequate comparison; however, the presence or past history of injury to the contralateral limb may hinder its use in this capacity. Furthermore, authors have demonstrated evidence of bilateral neuromuscular deficits following acute unilateral joint injury.[24,209] To contribute to this notion, these deficits have been cited to persist into chronic phases of healing, becoming a plastic central nervous system adaption is left untreated.[1] Therefore, in addition to using force-based measures in isolation, researchers have begun to explore more advance techniques of neuromuscular assessment following joint injury.[87]

Instrumented force based estimates of torque have demonstrated strong reliability when repeated within and between sessions in the lower extremity. Authors have reported intraclass correlation coefficients of ranging 0.93 – 0.96. Although isokinetic dynamometry may not provide all information necessary to the clinician's decision-making process following injury, it will provide a substantial estimate of persistent asymmetries between limbs.

Estimates of Volitional Muscle Activation

Voluntary activation failure is a common occurrence following lower extremity joint injuries, resulting from the inability of the central nervous system to provide maximal descending input to a muscle during volitional contraction.[33,89,210] Quadriceps central activation failure is common following knee joint injury[1,26,67,211,212] and has been described as a significant predictor of post-traumatic osteoarthritis if left untreated.[1,26,93,213] Furthermore, neural changes in the musculature of the lower leg have been observed in the presence of chronic ankle joint injury. Given the nature of these consequences to manifest as irreversible degenerative changes with long-term joint health implications, it is important to have valid estimates of central activation in this context.

Interpolated Twitch Technique (ITT)

The interpolated twitch is a technique commonly employed to estimate skeletal muscle activation during voluntary effort.[214] Originally described by Merton[215], the ITT came to light under the hypothesis that the force produced by voluntary effort is limited by the capacity of the central nervous system. It was this thought that led to the notion of using a supramaximal exogenous agent, electrical stimulation, to recruit inhibited motor units in an attempt to estimate true muscle activation. The ITT was the first technique popularized in this context. Developments in this technique have demonstrated an inability to fully activate all muscle fibers in healthy individuals, which have propagated its investigation in musculoskeletal research since.

The ITT requires the delivery of a supramaximal exogenous agent with the ability to excite inhibited musculature that cannot be volitionally activated.[216,217] This technique involves direct stimulation of the nerve trunk innervating the muscle being studied (e.g. femoral nerve; quadriceps) via focal stimulating electrode, or intramuscular nerve branches of an active muscle during voluntary contraction (e.g. quadriceps muscle belly).[214] Delivery of a 200 V single or doublet electrical pulse generates a transient twitch response, which provides an estimate of muscle activation, or percent inhibition.[217] In this instance, the size of the resultant twitch is indicative of the degree of inhibition present, with greater twitches indicating more inhibition. Stimuli are delivered with the muscle in an active and relaxed state. The resultant twitch generated during each state can be used to estimate voluntary activation as a percentage using the linear equation: [1-(superimposed twitch/control twitch)] x 100. In this instance the superimposed twitch refers to the stimulus being delivered in concert with a voluntary muscular contraction, and the control twitch being that obtained in a resting state.

Although equations such as these may provide useful insight to neuromuscular capacity, evidence has demonstrated a non-linear relationship between evoked and voluntary force.[216,218,219] This finding has led researchers to question the validity of using such ratios and to rather extrapolate the evoked-voluntary force relationship, and estimate ‘true activation.’ For more

information on this technique, refer to Shield and Zhou.[214] Reliability of the ITT has improved with methodological advances. Authors have reported acceptable intraclass correlation coefficients in the biceps brachii (0.858 [95% CI 0.61 – 0.98]) using a single electrical pulse[220], and soleus musculature (0.52 to 0.84) using a doublet stimulus.[221] However, improvements in reliability (ICC ≥ 0.74) have consistently been noted when paired with a voluntary contraction greater than 40% of MVIC.[218,221,222]

Technological advances have improved the sensitivity of the ITT over time. Despite these advances, a number of limitations of this measure persist. The greatest limitation is the assumption that a percutaneously delivered supramaximal stimulus will recruit all motor units (MU) unable to be volitionally recruited, and likewise that the control twitch measured in a resting state provides an estimate of the complete motor neuron pool.[214,217,218,223-225] Although this technique has demonstrated the ability to recruit MUs beyond those which can be recruited volitionally, we cannot distinctly state that complete activation occurs. Authors have attributed the inability to maximally recruit MUs to the antidromic volleys that occur when stimulating a mixed motor nerve, and have postulated that these factors result in a net overestimation of muscle activation.[226] Additional limitations including participant discomfort, impedance from subcutaneous tissue, and the observed non-linear relationship between evoked and voluntary forces force researchers and clinicians to interpret results with caution.[214,218]

Although limitations to this measure exist, it has been utilized in a variety of sports medicine research to estimate muscle activation during and after bouts of fatigue, maximum force production capability, to evaluate the influence of resistance training. Additionally, the ITT and similar measures have been employed to evaluate patients following joint injury and subsequent disuse.[214] Despite the inherent limitations of this technique, valuable information in regard to gross muscle activation relative to one's maximal potential may still be gained. Measurements should be interpreted with caution, but not discounted.

Superimposed Burst Technique (SIB)

The superimposed burst technique (SIB), likewise to the ITT, requires a percutaneously delivered supramaximal agent to provide an estimate of volitional muscle activation. Since it's early descriptions, the SIB technique has become increasingly popular in musculoskeletal research.[33]

In contrast to the ITT, the SIB technique however provides a train, or burst, of electrical stimuli via two stimulating electrodes directly over the quadriceps musculature at the proximal lateral and distal medial during a maximal voluntary knee extension task. By superimposing a supramaximal stimulus in this fashion, a transient twitch in force production is generated, indicating the maximal capacity of the motoneuron pool. The percent of volitional muscle activation can then be estimated and expressed as a ratio. The central activation ratio (CAR) is an equation commonly used to estimate maximal volitional activation of the quadriceps musculature.[33,38] Conventionally, the SIB technique is used in this manner to deliver a supramaximal percutaneous electrical stimulus to the quadriceps musculature during a maximal voluntary isometric knee extension task (T_{MVIC}).[33,227] The resultant torque (T_{SIB}) from this technique can be interpreted as a theoretical representation of the complete motoneuron pool.[33] Therefore, CAR measurements of 1.0, or 100% if expressed as a percentage, are indicative of complete volitional activation ($CAR = T_{MVIC}/[T_{MVIC} + T_{SIB}] \times 100$).[33,38]

Despite early beliefs that maximal recruitment of all motoneurons was possible, researchers have since demonstrated an inability to maximally activate all muscle fibers during voluntary effort. Through these observations and CAR studies, 0.95, or 95%, activation has been deemed fully activated.[228] This value is somewhat arbitrary however, as other authors have reported values between 0.84 and 0.99. Despite these data, debate in regard to normative CAR values in healthy individuals has remained prevalent, with methodological variations the likely culprit for these differences.

Although methodological variations persist within this measurement, acceptable levels of reliability have been established. The superimposed burst technique has been recognized as a reliable measure of quadriceps activation in the open chain position, with inter-session intraclass correlation coefficients ($ICC_{2,k}$) ranging 0.80 to 0.86.[229,230] Even greater within session reliability has been demonstrated in young healthy individuals ($ICC_{2,1} = 0.94$). It is likely that a variety of factors, including verbal encouragement, task instruction, and joint angle during testing play a significant role in CAR values. Additionally, the SIB technique has been reported to overestimate muscle activation when compared to the gold standard of MRI based studies. Despite the various considerations clinicians and researchers must take into account, the SIB serves as a viable option to estimate volitional muscle activation before and after joint injury.

CENTRAL NERVOUS SYSTEM EXCITABILITY

Estimates of Spinal Reflex Excitability

Hoffmann Reflex (H-Reflex)

Research to date has largely focused on spinal mechanisms of muscle inhibition following joint injury.[231] The Hoffmann reflex (H-reflex) is a common neurophysiologic test used in sports medicine research to assess modulation of monosynaptic reflex activity in the spinal cord.[30] The H-reflex can be viewed as analogous to the mechanically induced stretch reflex. However, in this instance, the muscle spindles normally activated are bypassed by stimulating a mixed nerve directly. As a mixed nerve is stimulated, action potential volleys are sent in opposing directions along the afferent (spinal cord) and efferent (muscle) pathways. At lower stimulus intensities, the H-reflex can be mapped until reaching its peak amplitude as measured by surface EMG. As the stimulus intensity is increased, an opposing volley (antidromic) essentially masks the H-reflex, leaving behind the muscle response, or M-response. The H-reflex is interpreted within the context of sports medicine research as an estimate of alpha motoneuron pool excitability, or the proportion of alpha motoneurons available for use when normalized to the maximal M-response (H_{max}:M_{max}), which represent the total motoneuron pool available.[30]

This measure has been extensively used to assess the motoneuron pool of the quadriceps[85,232,233] and soleus[21,234,235] musculature in healthy and injured cohorts, as well as the neural response following musculoskeletal injury. Although useful information can be gained from this measurement, it may be limited to monosynaptic synapses at the spinal level, and may miss a piece of the puzzle in regard to complete neurophysiological assessment following joint injury. As this measurement is conventionally performed in a completely static state, due to inherent confounding during dynamic movement, it has the potential to bypass descending input from supraspinal centers. This provides a clearer interpretation of the measurement by limiting pre-synaptic inhibition, but does not likely represent the complete neurophysiologic state of the individual.

The H-reflex has been widely used in sports medicine research to identify the state of excitability along the spinal tract following musculoskeletal injuries[21], effects of therapeutic modalities[236], and pain.[237] Additionally, the H-reflex has been used to examine the effects of exercise training[173] and performance of motor tasks[238] in healthy and injured individuals. Albeit useful information may be gained from this neurophysiologic technique, it carries with it many inherent methodological considerations. This measure is extremely sensitive to the influence of pre-synaptic inhibition from supraspinal centers of the body.[30,239] Therefore, subject positioning, lighting, time of day, and stress may each affect H-reflex values. Additionally, considerations in regard to the specific instrumentations such as stimulation setup, duration, and intensity make this technique difficult to reproduce between studies.[30] However, strong intersession ($ICC_{3,1} = 0.97$) and intrasession ($ICC_{2,1} = 0.97$) reliability has been reported in the quadriceps[240], where this measure is typically taken. Additionally, strong and acceptable levels of reliability have been demonstrated for the H:M ratio between sessions in the soleus ($ICC_{2,1} = 0.97$), peroneals ($ICC_{2,1} = 0.97$) and tibialis anterior ($ICC_{2,1} = 0.78$).[241] In addition to these factors, the greatest limitation of the H-reflex measure is that is an electrically induced reflex, and not one that occurs naturally in the human body.

Despite this limitation, it can provide insight to the neural pathways from peripheral areas of the body to the spinal cord following injury. However, caution should be taken when interpreting H-reflex measures. If care is taken to obtain valid measurements, the H-reflex can provide information about the state of neuromuscular function following injury.

Volitional Wave (V Wave)

The volitional wave (V-wave) is an electrophysiological variant of the H-reflex,[242,243] which provides insight in regard to descending neural drive during maximal voluntary effort.[244] The V-wave can be essentially detected following the disappearance of the H-reflex during volitional muscle contraction, as descending cortical stimuli supersede the antidromic action potentials of the muscle response. The combined measures of H-reflex and V-wave may provide a more comprehensive understanding of neural adaptations following injury and intervention.[245]

The V-wave is consistently reported within the literature as a proportion of the maximal muscle response (M_{max}).[244-249] This relationship is thought to represent the level of efferent αMN output (neural drive), or ability to volitionally activate a proportion of the entire αMN pool, while also reflecting reflex excitability.[249] Changes in M-wave peak-to-peak amplitude have been reported during volitional activation, changes in the length-tension relationship, and contraction mode.[244,250] For this reason, authors have also reported V-wave measurements relative to the M-wave obtained via supramaximal exogenous electrical stimulus during maximal voluntary contraction (M_{sup}), while standardizing type of contraction and joint angles.[244,250] Adding to the complexity of obtaining accurate data with this measurement is the ability to stabilize the lower limb during MVIC. For this reason, researchers have employed novel approaches, with the subject seated in a semi-reclined, supine position.[249] However, these approaches may interfere with testing procedures, namely the stimulating electrode. To obtain accurate data, it becomes important to develop a protocol in which an MVIC can be obtained without interfering with testing procedures.

Current research efforts have utilized the $V:M_{sup}$ ratio as an outcome measure in the evaluation endurance training,[245] resistance training programs,[245,251] and neuromuscular electrical stimulation[252] in the ankle plantar flexors. Inclusion of the motor evoked V-wave represents an interesting compliment to the H-reflex in that it reflects neural changes at the spinal and supraspinal levels.[245] Understanding and quantifying neuromuscular modulation at the spinal and supraspinal are useful measurements in assessing neuromuscular alterations following joint injury. As measurements are oftentimes repeated over time in intervention studies, it is necessary to demonstrate high reliability. To this point, there is only limited evidence demonstrating the test-retest reliability of the V:M or $V:M_{sup}$ in the soleus (ICC = 0.86).[249]

Nerve Conduction

Nerve conduction studies have been utilized in sports medicine practice to evaluate pain, sensation, and motor capabilities following injury. Nerve conduction measures are used as diagnostic tools used to examine the electrical functioning of peripheral nerves.[253] Additionally, these measures can provide information about the relationship with sensorimotor capacities that influence mobility. Nerve conduction studies are performed by placing electrodes percutaneously to directly stimulate peripheral nerves with an electrical stimulus. From this electrical stimulus, information regarding the path and strength of the resultant afferent action potential can be gained.[253] Conventional nerve conduction measures include velocity, latency, amplitude, and duration. Conduction velocity describes the speed of an impulse along its axon upon stimulation, which represents how well an electrical impulse is conducted. Latency refers to the time from stimulation of a nerve to the beginning of depolarization. The amplitude of an action potential is the sum of all amplitudes from individual action potentials following a stimulus, with greater amplitude signifying a stronger response.[253] From these measurements, clinicians can gain a comprehensive assessment of the action potential morphology, and identify sensorimotor impairments.

Impairments in peripheral nerve conduction measurements have been observed following lateral ankle sprains[254-256], and knee joint injuries. Additionally, traditional therapeutic modalities, such as cryotherapy, have been reported to impact nerve conduction properties via changes in skin temperature. Understanding how peripheral nerve characteristics can be altered may aid clinicians in the assessment and treatment of individuals following injury.

Estimates of Corticospinal Excitability

Transcranial Magnetic Stimulation (TMS)

TMS is a non-invasive tool used to measure neural conduction and processing time, activation thresholds, facilitation and inhibition in the primary motor cortex, and neural connections.[22] Since its original description in 1985, single pulse TMS has been widely used to study motor, visual, and somatosensory systems, as well as sensorimotor integration and cognition in patients with a variety of diagnosed disease processes.[22] It has since emerged in sports medicine research as an intervention and assessment tool primarily in the upper extremity.[257] Several authors have used TMS to measure cortical excitability in the lower extremities of varied cohorts.[24,87,90,229,258]

Although afferent signals project to the spinal cord directly, joint afferents are known to have extensive supraspinal projections to the cerebral cortex as well.[86] Supraspinal influence on descending cortical output following injury is often neglected within the context of musculoskeletal research, specifically of the lower extremity, and has only begun to be better understood over the last decade. Currently, the best way to measure neuromuscular changes at the supraspinal level is to assess cortical excitability, which is defined as excitability of the portion of the cerebral cortex responsible for initiating motor commands to skeletal muscle.[22]

Transcranial magnetic stimulation (TMS) provides a method of assessing excitability of the pre-motor area of the cerebral cortex.[22] TMS produces a small, but powerful field of magnetic energy that depolarizes neural tissue to initiate action potentials.[22] When a TMS device is placed over the scalp, superficial to the pre-motor area, action potentials are conveyed to the associated

skeletal muscles resulting in a motor evoked potential (MEP). By stimulating the cortical neurons corresponding to quadriceps activity in the contralateral primary motor cortex, a motor evoked action potential can be detected via surface electromyography.[259,260] When stimulated during minimal volitional activity of the involved musculature, this measurement is termed active motor threshold (AMT), and has been used as a primary indicator of corticospinal excitability in individuals following knee joint injury.[88] In sports medicine research, the amplitude and transmission time of MEP's have been used to detect subtle neuromuscular deficiencies in patients with mild traumatic brain injury[261], patients with ankle[262] and knee[90] joint injury, and in individuals who are fatigued due to continuous exercise.[89]

Although TMS protocols widely vary in the literature with respect to coil type and placement, measures of interest, and technique to obtain measurements, acceptable levels of reliability have been established. Reliability of TMS measures has primarily been established in the upper extremities[263]; however more recent researchers have begun to look at the hip[258], knee, and ankle[264] musculature with success.

In contrast to assessment technique requiring an electrical stimulus, TMS relies on a magnetic pulse of energy, thereby reducing patient discomfort during testing. Additionally, this technique may provide unique information regarding the influence of descending neural drive to peripheral musculature following injury, not achieved by other techniques. Understanding sensorimotor adaptations at supraspinal centers may allow for a more comprehensive assessment approach, fostering early intervention strategies.

CONCLUSION

Sensorimotor deficits occur after joint injury due to alterations in transmission of neural signal to the central nervous system. Lasting impairments likely manifest from a combination of peripheral, spinal, and supraspinal centers. As sensorimotor impairments and resulting neuromuscular deficits are the result of disruption to a multifaceted biological system, comprehensive assessment techniques appear to be warranted. Identifying impairments will provide information to develop optimal strategies for early treatment and active prevention of poor outcomes in active individuals who suffer joint injuries. Future research should use such an approach to identify changes over time in and effort to maximize patient care. Clinical and laboratory based assessment tools can be used in concert to provide clinicians with a comprehensive understanding of sensorimotor impairments following lower extremity joint injury.

APPENDIX C

Additional Methods

Table C1. Informed Consent form

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Parents' or Guardians' Permission for Your Child to Be in a Research Study

Agreement of a Child to Be in a Research Study
Age 15 to <18

In this form "you" means the child in the study *and* the parent or guardian.
- ✓ If you are the parent or guardian, you are being asked to give permission for your child to be in this study.
- ✓ If you are the child, you are being asked if you agree to be in this study.

In this form "we" means the researchers and staff involved in running this study at the University of Virginia.

Participant's Name_____

Principal Investigator: Joseph Hart, PhD, ATC
Box 400407
Charlottesville, VA 22904-4407
Telephone: (434) 924-6187

Sponsor: Eastern Athletic Trainers' Association (EATA)
Mid-Atlantic Athletic Trainers' Association (MAATA)

What is the purpose of this form?
This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this form.

Who is funding this study?
This study is being partially funded by the Eastern Athletic Trainers' Association (EATA) and Mid-Atlantic Athletic Trainers' Association (MAATA). The EATA and MAATA are providing funds for some of the equipment being used in this study.

Why is this research being done?
The purpose of this study is to compare muscle strength and functional ability at different time points after ACL reconstruction. This information will be useful to identify the changes that naturally take place after this surgery, and help clinicians understand how to treat patients in the most effective way.

You are being asked to be in this study, because you (1) have had a knee injury involving your ACL, (2) have had your ACL surgically reconstructed, (3) have had your ACL surgically reconstructed and have knee arthritis, (4) or you are healthy and have not had a serious lower body injury.

Up to 83 people will be in this study at UVA.

How long will this study take?
Your participation in this study will require 1 study visit that will last about 2 hours. You may be able to participate in several additional visits if you are eligible.

What will happen if you are in the study?
Summary
- If you choose to participate in this study, and provide consent, you will be asked to come to the Exercise and Sport Injury Laboratory (EASIL) in Memorial Gymnasium.
- Prior to the testing session you will be asked questions about your medical history and previous knee history to determine your eligibility.
- This study will involve collecting information about your health, knee injury, and activity level from the following questionnaires: International Knee Documentation Committee Knee Joint Evaluation (IKDC), Knee Injury and Osteoarthritis Outcomes Score (KOOS), Tegner Activity Scale, Pain and Activity Rating (VAS), Godin Leisure-Time, Tampa Scale of Kinesiophobia, and Veterans Rand 12-Item Health Survey.
- This study will involve testing how well your thigh muscles work while you contract and relax, using several techniques referred to as the Hoffmann reflex, superimposed burst technique, and transcranial magnetic stimulation.

Please note: All the procedures in this study are for research purposes only.

CONSENT and SCREENING (will take about 5 minutes to complete):
Visit 1 only:
If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:
- Review of consent form

- Review of inclusion and exclusion criteria
- Review of your medical history
- Examine the function of your knee and thigh muscles

If these criteria show you are eligible, you can begin study procedures immediately, or return at your earliest convenience.

STUDY PROCEDURES (will take about 1 hour and 45 minutes):
Visit 1 only (Required)

Questionnaires; about 15 minutes to complete (visit 1 only)
During this study, you will be asked to fill out some questionnaires. These questionnaires include an International Knee Documentation Committee Subjective Knee Joint Evaluation (IKDC), Tegner Activity Rating, Godin Leisure-Time Questionnaire, Tampa Scale of Kinesiophobia, and Veterans Rand 12-Item Health Survey (VR-12), and will ask about:
- How you are feeling
- Your lifestyle habits
- Daily activities
- Your knee function
- Your pain during activities
- Your current level of pain

Hoffmann Reflex; about 30 minutes
- Three small sticky pads will be placed on your thigh to measure your muscle activity during testing.
- You may need to have the hair shaved from your skin where the pads will be placed. Another small pad will be placed over the front of your thigh to deliver a small amount of electrical energy through your skin to the nerve being tested.
- The electrical energy will make your thigh muscles twitch suddenly and may cause some minor discomfort (like being snapped with a rubber band).
- The electrical energy will be delivered multiple times. There will be about 10 seconds between each delivery of energy.
- This will be performed on both legs.

Superimposed Burst Technique; about 30 minutes
- You will be asked to stand near the testing chair and two self-adhesive electrodes will be applied to your thigh.
- One of the electrodes will be placed above your knee and the other will be given to you to place below your hips so that it lies flat when you are sitting. These electrodes will be used to deliver a small electrical current to your thigh muscles.
- You will be secured into the chair near where the electrodes are applied so that we can easily collect information about the force you are producing with your leg that has the electrodes on it.

- Your hips will be secured, as will your shoulders and testing thigh with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device designed to measure how much force you can produce.
- You will be asked to kick and pull your leg as hard and fast as you can several times (isokinetic testing)
- You will then be asked to extend your leg as hard as you can and hold it for five seconds. While you are kicking out an electrical charge will be delivered to your thigh. This stimulus feels similar to a static electric shock that you could get from walking across a carpet in a dry room and then touching a doorknob, although the voltage is lower.
- You will be asked to perform this one to three times to verify the measurement.
- You will be allowed up to three minutes of rest between each repetition if applicable.
- This will be performed on both legs.

Fatigue Test; about 20 minutes
- You will be secured into a stationary chair so that we can easily collect information about the force you are producing with your leg.
- Your hips will be secured, as will your shoulders and testing thigh with Velcro straps. Your ankle will be secured to a padded strap below the chair. This strap is connected to a device designed to measure how much force you can produce.
- You will be asked to kick out as hard as you can several times in order to estimate your maximum force production. We will create a line to reference 60% of this value.
- You will then be asked to kick out at 60% of your maximum effort and hold for 30 seconds to measure motor fatigue. You will be instructed to watch the numbers on the computer screen that represent the amount of force output, and will be given verbal feedback to help keep you at the targeted amount of force for the 30 seconds of motor fatigue testing. This will be repeated three times, with 2 minutes of rest in between trials.
- This will be performed on both legs

Transcranial Magnetic Stimulation; about 45 minutes
- You will be fitted with a non-latex swim cap and asked to sit comfortably in a chair. The purpose of the swim cap is to mark (with an ink pen) certain points or features of your head that will be used to determine the best areas of magnetic coil placement for stimulation.
- You will be given a pair of disposable earplugs to wear during the testing; the purpose of the earplugs is to limit the clicking sound that comes from the magnetic stimulation coil.
- Next, the skin over the muscles on your leg will be cleaned with an alcohol pad over the areas where surface electrodes will be put in place. Cleansing these areas is necessary to remove any oils, lotions, and dry skin that may interfere with the recording of an electrical response. Four adhesive disposable electrodes will be applied to these areas.
- A device will be placed against your head, resting against the swim cap; this device is a magnetic stimulator that is capable of delivering a non-painful stimulus through the scalp and underlying skull. This magnetic response is detected by the brain as an electrical potential and will be recorded by the electrodes placed on your thigh. The magnetic impulse used to stimulate the brain causes an audible "click" associated with the

magnetic stimulating coil, and a brief muscle contraction (similar to a muscle "twitch") in the muscles of your thigh or leg, which will feel like what is felt during standard medical reflex testing. Otherwise there is no or a minimal chance of discomfort associated with the testing.

- There is a minimal risk for obtaining a mild headache following the application of the TMS, if such event occurs, it can be cured by taking over the counter headache medication. The audible "click" from the magnetic stimulator will not harm your ears, but earplugs are required for your comfort and safety.
- Several measurements will be taken while you are seated. The intensity of the magnetic pulse will be gradually increased until a maximum electrical response is detected and recorded. You will not experience any discomfort despite the increased intensity of the stimulation. Once the best response is detected and recorded, a mark will be made on the swim cap using an ink pen. These markings will be used as reference points for future test sessions. Once these measurements are recorded, you may remove the swim cap (which will be saved for your subsequent testing sessions).
- This will be performed on both legs.

Visit 2 **(Non-required). Those who have an ACL injury, but have not had surgery will not be eligible for the hop tests due to safety considerations***

Hop Tests; about 10 minutes

- You will be asked to lie down on a treatment table so that the length of your leg can be measured.
- You will then be asked to hop as far as you can on each leg multiple times in different directions. The distance you hop will be measured along a tape measure.
- You will be given 5 practice hop trials in order to practice before testing begins.
- Once testing begins, three hop trials will be measured.
- This will be performed on both legs.

Gait Analysis; about 30 minutes

- You will be asked to stand upright with your shoes and socks off.
- Your skin will be cleaned, similar to the EMG, where each of the sensors will be placed on your legs and back.
- Eight sensors will be placed on your legs and back using double-sided tape and athletic wrap before testing begins.
- You will be given a pair of shoes to put on for testing. If we do not have a pair that fits, you will be allowed to use the shoes you are wearing.
- You will be asked to walk approximately 10 yards at a comfortable speed back and fourth 5-10 times.
- You will be asked to crouch down 5-10 times with both legs and with one leg at a time.
- You will be asked to step off of a box and land in a crouched position 5-10 times with both legs and with one leg at a time.
- You will be asked to crouch down and jump straight up 5-10 times with both legs and with one leg at a time.
- You will be given time to rest between each task.

Follow Up Visits

You may be eligible to return for additional visits every 6 months if enrolled in this study before you are 2 years from the time of your knee surgery. No additional study visits will be available once you are 2 years from the time of your surgery. If you return for additional study visits, the same study procedures as your last completed visit will be repeated each time. At a minimum, this will include the required portion of study procedures.

If you want to know about the results before the study is done:

During the study you are having an investigational test done. The purpose of the test is not to diagnose any disease or abnormality you may have. Because the test is investigational there is no way for the study leader to understand if the results are "normal" or "abnormal". However, if any test results are concerning, your study leader will let you know.

In addition, as the research moves forward, your study leader will keep you informed of any new findings about the research itself that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks and side effects related to the study procedures include:

Likely

- You may experience a mild, short - lasting muscle soreness after testing.

Less Likely

- You could experience minor, short - lasting skin irritation where the self-adhesive electrodes have been placed.
- Risk of temporary discomfort from electrical stimulation during superimposed burst and Hoffmann-reflex testing.
- You may experience a mild, transient headache after receiving the transcranial magnetic stimulation.

Rare but serious

- You may produce a seizure if you have a history of epilepsy or other seizure disorder.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

This study provides no benefit to individuals. It poses minimal risk of breach of Protected Health Information that will be minimized by following institutional and federal confidentiality regulations.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include physical therapy as prescribed by your treating physician.
If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

For subjects with ACL injury:
If you have had an injury to your ACL, you will be paid $20 for finishing this study.
You should get your payment about 4-6 weeks after finishing the study by check. The income may be reported to the IRS as income.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

For healthy subjects:
If you are a healthy participant, you will not be compensated for finishing the study.

Will being in this study cost you any money?

All of the procedures in this study will be provided at no cost to you or your health insurance. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader, Dr. Joe Hart, can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to please notify Dr. Joe Hart in writing at 210 Emmet Street South, P.O. Box 400407, Charlottesville, VA 22904-4407. Please note that any information already obtained from you may continue to be used by the investigators of this study.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information. If required for this study, this may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- People who pay for the study: EATA, MAATA, including insurance companies
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. We ask them to protect your privacy. However, they may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished

Express a concern about the study

Joe Hart, PhD, ATC
Human Services, Curry School of Education
PO Box 400407
Charlottesville, VA 22904-4407
Telephone: (434) 924-6187

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908
Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?
Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Consent From Impartial Witness
If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the subject and the subject had the opportunity to ask any questions he/she had about the study. I also agree that the subject freely gave their informed consent to participate in this trial.

IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Person Obtaining Consent
By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Parental/ Guardian Permission
By signing below you confirm you have the legal authority to sign for this child.

PARENT/GUARDIAN (SIGNATURE)	PARENT/GUARDIAN (PRINT NAME)	DATE

Consent From Impartial Witness
If this consent form is read to the parent(s) because the parent(s) is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The parent may place an X on the Parent Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the parent(s) guardian(s) and the parent(s)/guardian(s) had the opportunity to ask any questions he/she had about the study. I also agree that the parent(s)/guardian(s) freely gave their informed consent for their child to participate in this trial.

IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Person Obtaining Parental/Guardian Permission
By signing below you confirm that you have fully explained this study to the parent/guardian, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING PARENTAL/ GUARDIAN PERMISSION (SIGNATURE)	PERSON OBTAINING PARENTAL/GUARDIAN PERMISSION (PRINT NAME)	DATE

Assent from Child
Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

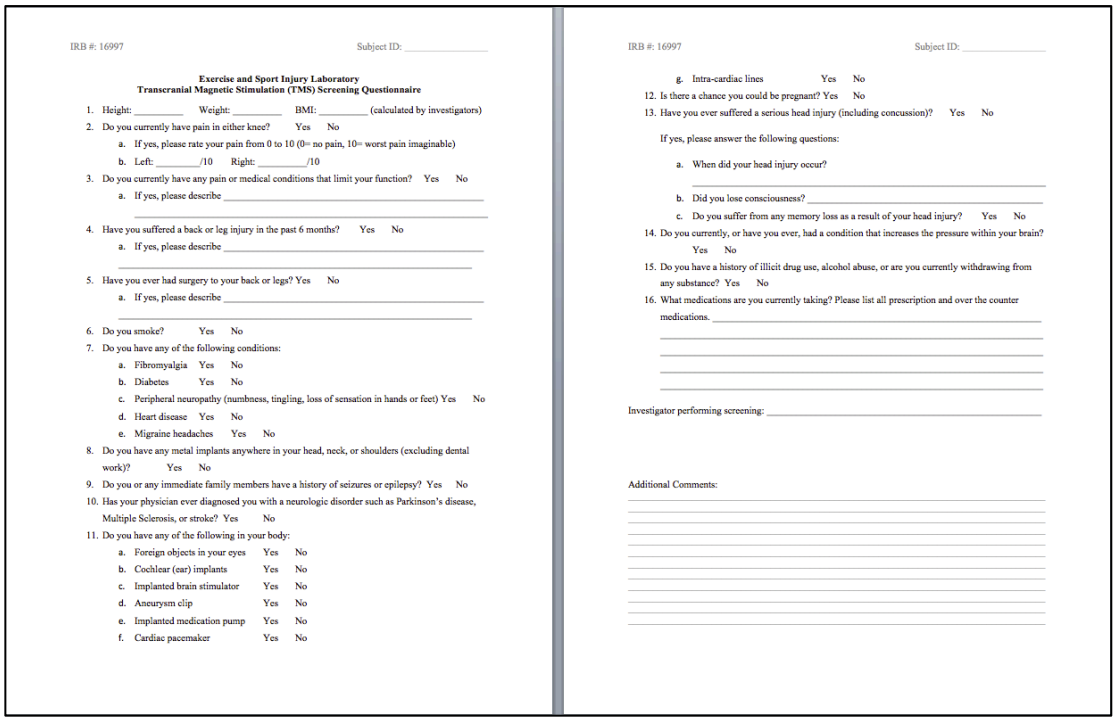
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

Person Obtaining Assent of the Child (less than 18 years of age)
Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

By signing below you confirm that the study has been explained to the child (less than 18 years of age), all questions have been answered and the child has voluntarily agreed to participate.

PERSON OBTAINING ASSENT (SIGNATURE)	PERSON OBTAINING ASSENT (PRINT)	DATE

Table C2. Transcranial Magnetic Stimulation Screening Form



IRB #: 16997 Subject ID: _____

Exercise and Sport Injury Laboratory
Transcranial Magnetic Stimulation (TMS) Screening Questionnaire

1. Height: _____ Weight: _____ BMI: _____ (calculated by investigators)
2. Do you currently have pain in either knee? Yes No
   a. If yes, please rate your pain from 0 to 10 (0= no pain, 10= worst pain imaginable)
   b. Left: _____/10 Right: _____/10
3. Do you currently have any pain or medical conditions that limit your function? Yes No
   a. If yes, please describe _____
4. Have you suffered a back or leg injury in the past 6 months? Yes No
   a. If yes, please describe _____
5. Have you ever had surgery to your back or legs? Yes No
   a. If yes, please describe _____
6. Do you smoke? Yes No
7. Do you have any of the following conditions:
   a. Fibromyalgia Yes No
   b. Diabetes Yes No
   c. Peripheral neuropathy (numbness, tingling, loss of sensation in hands or feet) Yes No
   d. Heart disease Yes No
   e. Migraine headaches Yes No
8. Do you have any metal implants anywhere in your head, neck, or shoulders (excluding dental work)? Yes No
9. Do you or any immediate family members have a history of seizures or epilepsy? Yes No
10. Has your physician ever diagnosed you with a neurologic disorder such as Parkinson's disease, Multiple Sclerosis, or stroke? Yes No
11. Do you have any of the following in your body:
    a. Foreign objects in your eyes Yes No
    b. Cochlear (ear) implants Yes No
    c. Implanted brain stimulator Yes No
    d. Aneurysm clip Yes No
    e. Implanted medication pump Yes No
    f. Cardiac pacemaker Yes No

IRB #: 16997 Subject ID: _____

    g. Intra-cardiac lines Yes No
12. Is there a chance you could be pregnant? Yes No
13. Have you ever suffered a serious head injury (including concussion)? Yes No

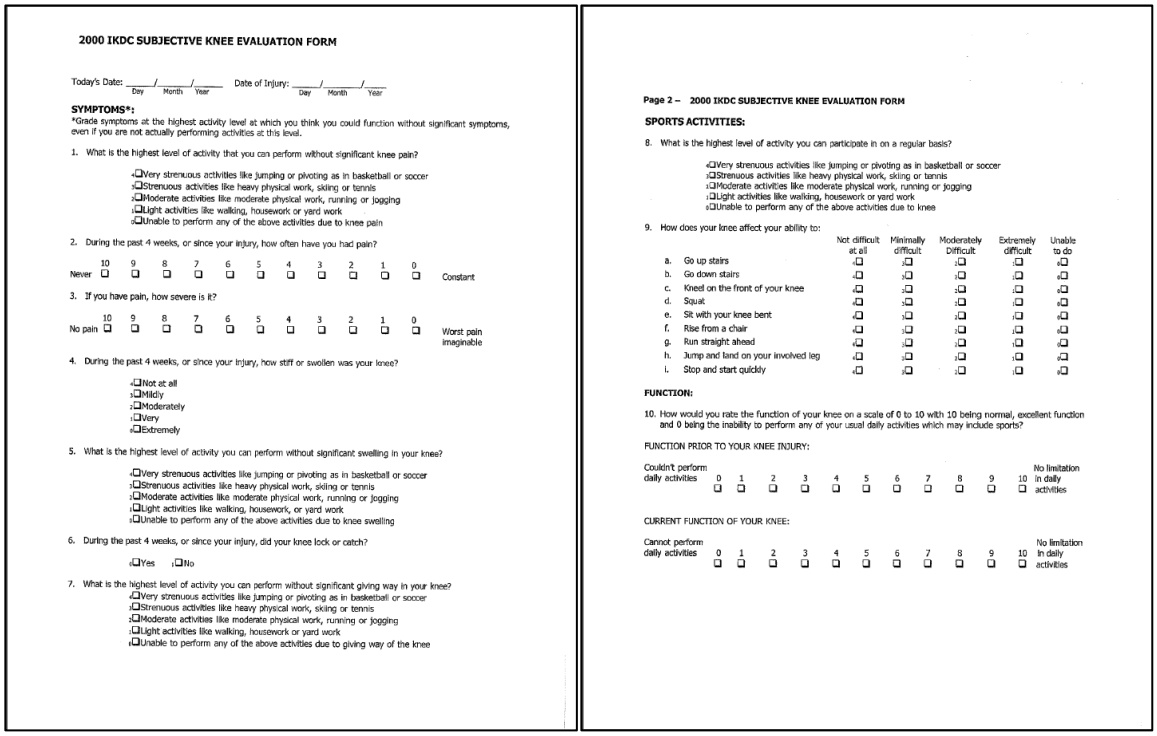
    If yes, please answer the following questions:

    a. When did your head injury occur?
    b. Did you lose consciousness? _____
    c. Do you suffer from any memory loss as a result of your head injury? Yes No
14. Do you currently, or have you ever, had a condition that increases the pressure within your brain? Yes No
15. Do you have a history of illicit drug use, alcohol abuse, or are you currently withdrawing from any substance? Yes No
16. What medications are you currently taking? Please list all prescription and over the counter medications. _____

Investigator performing screening: _____

Additional Comments:

Table C3. International Knee Documentation Committee (IKDC) Subjective Knee Evaluation



2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

Today's Date: _____/_____/_____ (Day / Month / Year) Date of Injury: _____/_____/_____ (Day / Month / Year)

SYMPTOMS*:

*Grade symptoms at the highest activity level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?

   - ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   - ☐ Strenuous activities like heavy physical work, skiing or tennis
   - ☐ Moderate activities like moderate physical work, running or jogging
   - ☐ Light activities like walking, housework or yard work
   - ☐ Unable to perform any of the above activities due to knee pain

2. During the past 4 weeks, or since your injury, how often have you had pain?

	10	9	8	7	6	5	4	3	2	1	0	
Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Constant

3. If you have pain, how severe is it?

	10	9	8	7	6	5	4	3	2	1	0	
No pain	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Worst pain imaginable

4. During the past 4 weeks, or since your injury, how stiff or swollen was your knee?

   - ☐ Not at all
   - ☐ Mildly
   - ☐ Moderately
   - ☐ Very
   - ☐ Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?

   - ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   - ☐ Strenuous activities like heavy physical work, skiing or tennis
   - ☐ Moderate activities like moderate physical work, running or jogging
   - ☐ Light activities like walking, housework, or yard work
   - ☐ Unable to perform any of the above activities due to knee swelling

6. During the past 4 weeks, or since your injury, did your knee lock or catch?

   ☐ Yes ☐ No

7. What is the highest level of activity you can perform without significant giving way in your knee?

   - ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   - ☐ Strenuous activities like heavy physical work, skiing or tennis
   - ☐ Moderate activities like moderate physical work, running or jogging
   - ☐ Light activities like walking, housework or yard work
   - ☐ Unable to perform any of the above activities due to giving way of the knee

Page 2 – 2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?

   - ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   - ☐ Strenuous activities like heavy physical work, skiing or tennis
   - ☐ Moderate activities like moderate physical work, running or jogging
   - ☐ Light activities like walking, housework or yard work
   - ☐ Unable to perform any of the above activities due to knee

9. How does your knee affect your ability to:

		Not difficult at all	Minimally difficult	Moderately Difficult	Extremely difficult	Unable to do
a.	Go up stairs	☐	☐	☐	☐	☐
b.	Go down stairs	☐	☐	☐	☐	☐
c.	Kneel on the front of your knee	☐	☐	☐	☐	☐
d.	Squat	☐	☐	☐	☐	☐
e.	Sit with your knee bent	☐	☐	☐	☐	☐
f.	Rise from a chair	☐	☐	☐	☐	☐
g.	Run straight ahead	☐	☐	☐	☐	☐
h.	Jump and land on your involved leg	☐	☐	☐	☐	☐
i.	Stop and start quickly	☐	☐	☐	☐	☐

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

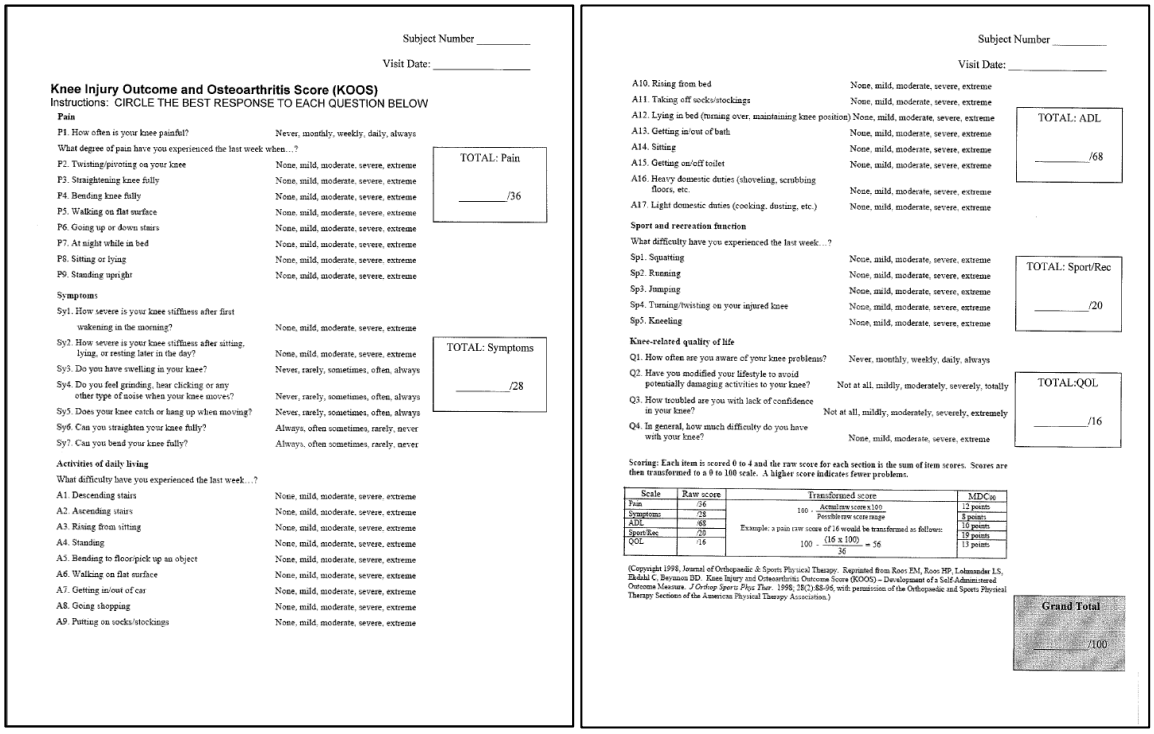
FUNCTION PRIOR TO YOUR KNEE INJURY:

	0	1	2	3	4	5	6	7	8	9	10	
Couldn't perform daily activities	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	No limitation in daily activities

CURRENT FUNCTION OF YOUR KNEE:

	0	1	2	3	4	5	6	7	8	9	10	
Cannot perform daily activities	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	No limitation in daily activities

Table C4. Knee Injury and Osteoarthritis Outcome Score (KOOS)



Subject Number _____

Visit Date: _____

Knee Injury Outcome and Osteoarthritis Score (KOOS)

Instructions: CIRCLE THE BEST RESPONSE TO EACH QUESTION BELOW

Pain

P1. How often is your knee painful?	Never, monthly, weekly, daily, always
What degree of pain have you experienced the last week when…?	
P2. Twisting/pivoting on your knee	None, mild, moderate, severe, extreme
P3. Straightening knee fully	None, mild, moderate, severe, extreme
P4. Bending knee fully	None, mild, moderate, severe, extreme
P5. Walking on flat surface	None, mild, moderate, severe, extreme
P6. Going up or down stairs	None, mild, moderate, severe, extreme
P7. At night while in bed	None, mild, moderate, severe, extreme
P8. Sitting or lying	None, mild, moderate, severe, extreme
P9. Standing upright	None, mild, moderate, severe, extreme

TOTAL: Pain

_____/36

Symptoms

Sy1. How severe is your knee stiffness after first wakening in the morning?	None, mild, moderate, severe, extreme
Sy2. How severe is your knee stiffness after sitting, lying, or resting later in the day?	None, mild, moderate, severe, extreme
Sy3. Do you have swelling in your knee?	Never, rarely, sometimes, often, always
Sy4. Do you feel grinding, hear clicking or any other type of noise when your knee moves?	Never, rarely, sometimes, often, always
Sy5. Does your knee catch or hang up when moving?	Never, rarely, sometimes, often, always
Sy6. Can you straighten your knee fully?	Always, often sometimes, rarely, never
Sy7. Can you bend your knee fully?	Always, often sometimes, rarely, never

TOTAL: Symptoms

_____/28

Activities of daily living

What difficulty have you experienced the last week…?	
A1. Descending stairs	None, mild, moderate, severe, extreme
A2. Ascending stairs	None, mild, moderate, severe, extreme
A3. Rising from sitting	None, mild, moderate, severe, extreme
A4. Standing	None, mild, moderate, severe, extreme
A5. Bending to floor/pick up an object	None, mild, moderate, severe, extreme
A6. Walking on flat surface	None, mild, moderate, severe, extreme
A7. Getting in/out of car	None, mild, moderate, severe, extreme
A8. Going shopping	None, mild, moderate, severe, extreme
A9. Putting on socks/stockings	None, mild, moderate, severe, extreme
A10. Rising from bed	None, mild, moderate, severe, extreme
A11. Taking off socks/stockings	None, mild, moderate, severe, extreme
A12. Lying in bed (turning over, maintaining knee position)	None, mild, moderate, severe, extreme
A13. Getting in/out of bath	None, mild, moderate, severe, extreme
A14. Sitting	None, mild, moderate, severe, extreme
A15. Getting on/off toilet	None, mild, moderate, severe, extreme
A16. Heavy domestic duties (shoveling, scrubbing floors, etc.	None, mild, moderate, severe, extreme
A17. Light domestic duties (cooking, dusting, etc.)	None, mild, moderate, severe, extreme

TOTAL: ADL

_____/68

Sport and recreation function

What difficulty have you experienced the last week…?	
Sp1. Squatting	None, mild, moderate, severe, extreme
Sp2. Running	None, mild, moderate, severe, extreme
Sp3. Jumping	None, mild, moderate, severe, extreme
Sp4. Turning/twisting on your injured knee	None, mild, moderate, severe, extreme
Sp5. Kneeling	None, mild, moderate, severe, extreme

TOTAL: Sport/Rec

_____/20

Knee-related quality of life

Q1. How often are you aware of your knee problems?	Never, monthly, weekly, daily, always
Q2. Have you modified your lifestyle to avoid potentially damaging activities to your knee?	Not at all, mildly, moderately, severely, totally
Q3. How troubled are you with lack of confidence in your knee?	Not at all, mildly, moderately, severely, extremely
Q4. In general, how much difficulty do you have with your knee?	None, mild, moderate, severe, extreme

TOTAL:QOL

_____/16

Scoring: Each item is scored 0 to 4 and the raw score for each section is the sum of item scores. Scores are then transformed to a 0 to 100 scale. A higher score indicates fewer problems.

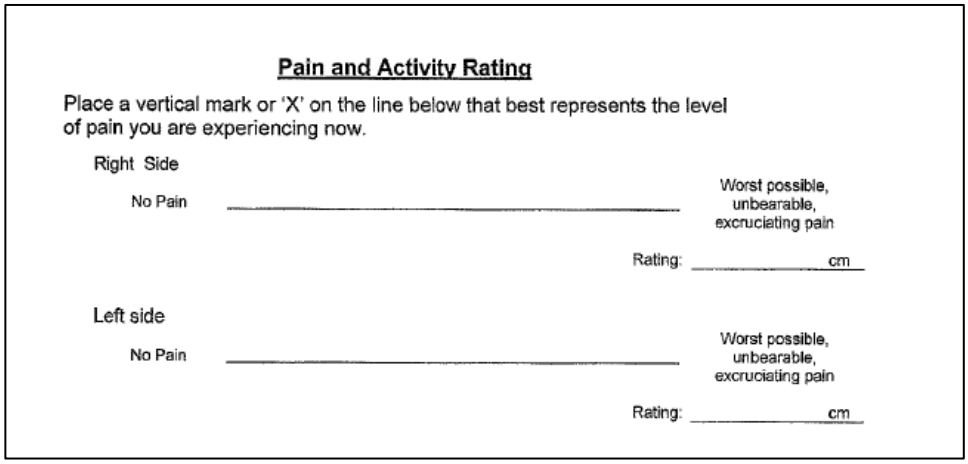
Scale	Raw score	Transformed score	MDC95
Pain	/36	$100 - \frac{\text{Actual raw score} \times 100}{\text{Possible raw score range}}$	12 points
Symptoms	/28		8 points
ADL	/68		10 points
Sport/Rec	/20	Example: a pain raw score of 16 would be transformed as follows:	19 points
QOL	/16	$100 - \frac{(16 \times 100)}{36} = 56$	13 points

(Copyright 1998, Journal of Orthopaedic & Sports Physical Therapy. Reprinted from Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS) – Development of a Self-Administered Outcome Measure. *J Orthop Sports Phys Ther.* 1998; 28(2):88-96, with permission of the Orthopaedic and Sports Physical Therapy Sections of the American Physical Therapy Association.)

Grand Total

_____/100

Table C5. Visual Analog Scale (VAS) for Pain at Rest



Pain and Activity Rating

Place a vertical mark or 'X' on the line below that best represents the level of pain you are experiencing now.

Right Side

No Pain _____ Worst possible, unbearable, excruciating pain

Rating: _____ cm

Left side

No Pain _____ Worst possible, unbearable, excruciating pain

Rating: _____ cm

Table C6. Tegner Activity Level Scale

TEGNER ACTIVITY SCALE

Please indicate in the spaces below the HIGHEST level of activity that you participated in BEFORE YOUR INJURY and the highest level you are able to participate in CURRENTLY.

BEFORE INJURY: Level_____ CURRENT: Level_____

Level 10	Competitive sports- soccer, football, rugby (national elite)
Level 9	Competitive sports- soccer, football, rugby (lower divisions), ice hockey, wrestling, gymnastics, basketball
Level 8	Competitive sports- racquetball or bandy, squash or badminton, track and field athletics (jumping, etc.), down-hill skiing
Level 7	Competitive sports- tennis, running, motorcars speedway, handball Recreational sports- soccer, football, rugby, bandy, ice hockey, basketball, squash, racquetball, running
Level 6	Recreational sports- tennis and badminton, handball, racquetball, down-hill skiing, jogging at least 5 times per week
Level 5	Work- heavy labor (construction, etc.) Competitive sports- cycling, cross-country skiing, Recreational sports- jogging on uneven ground at least twice weekly
Level 4	Work- moderately heavy labor (e.g. truck driving, etc.)
Level 3	Work- light labor (nursing, etc.)
Level 2	Work- light labor Walking on uneven ground possible, but impossible to back pack or hike
Level 1	Work- sedentary (secretarial, etc.)
Level 0	Sick leave or disability pension because of knee problems

All information in this Worksheet is **Confidential.**

Table C7. Godin Leisure-Time Exercise Questionnaire

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

	Times Per Week
a) **STRENUOUS EXERCISE** **(HEART BEATS RAPIDLY)** (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	_____
b) **MODERATE EXERCISE** **(NOT EXHAUSTING)** (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	_____
c) **MILD EXERCISE** **(MINIMAL EFFORT)** (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	_____

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

OFTEN	SOMETIMES	NEVER/RARELY
1. ☐	2. ☐	3. ☐

Table C8. Tampa Scale for Kinesiophobia (TSK)

TAMPA SCALE FOR KINESIOPHOBIA

(MILLER , KORI AND TODD 1991)

	CIRCLE THE NUMBER THAT BEST DESCRIBES YOUR BELIEF FOR EACH STATEMENT BELOW:	STRONGLY AGREE	DISAGREE	AGREE	STRONGLY AGREE
1	I'm afraid that I might injury myself if I exercise	1	2	3	4
2	If I were to try to overcome it, my pain would increase	1	2	3	4
3	My body is telling me I have something dangerously wrong	1	2	3	4
4	My pain would probably be relieved if I were to exercise	1	2	3	4
5	People aren't taking my medical condition seriously enough	1	2	3	4
6	My accident has put my body at risk for the rest of my life	1	2	3	4
7	Pain always means I have injured my body	1	2	3	4
8	Just because something aggravates my pain does not mean it is dangerous	1	2	3	4
9	I am afraid that I might injure myself accidentally	1	2	3	4
10	Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening	1	2	3	4
11	I wouldn't have this much pain if there weren't something potentially dangerous going on in my body	1	2	3	4
12	Although my condition is painful, I would be better off if I were physically active	1	2	3	4
13	Pain lets me know when to stop exercising so that I don't injure myself	1	2	3	4
14	It's really not safe for a person with a condition like mine to be physically active	1	2	3	4
15	I can't do all the things normal people do because it's too easy for me to get injured	1	2	3	4
16	Even though something is causing me a lot of pain, I don't think it's actually dangerous	1	2	3	4
17	No one should have to exercise when he/she is in pain	1	2	3	4

Reprinted from:
Pain, Fear of movement/(re) injury in chronic low back pain and its relation to behavioral performance, 62, Vlaeyen, J., Kole-Snijders A., Boeren R., van Eek H., 371. Copyright (1995) with permission from International Association for the Study of Pain.

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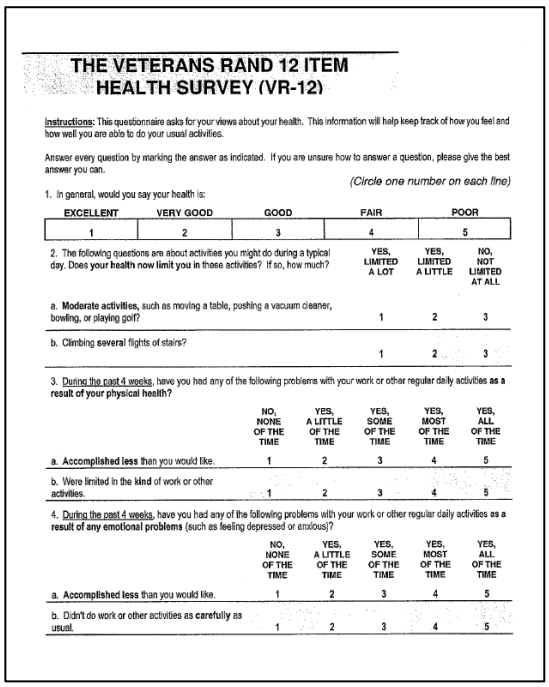
Table C9. The Veterans Rand 12-Item Health Survey (VR-12)



THE VETERANS RAND 12 ITEM HEALTH SURVEY (VR-12)

Instructions: This questionnaire asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure how to answer a question, please give the best answer you can.

(Circle one number on each line)

1. In general, would you say your health is:

EXCELLENT	VERY GOOD	GOOD	FAIR	POOR
1	2	3	4	5

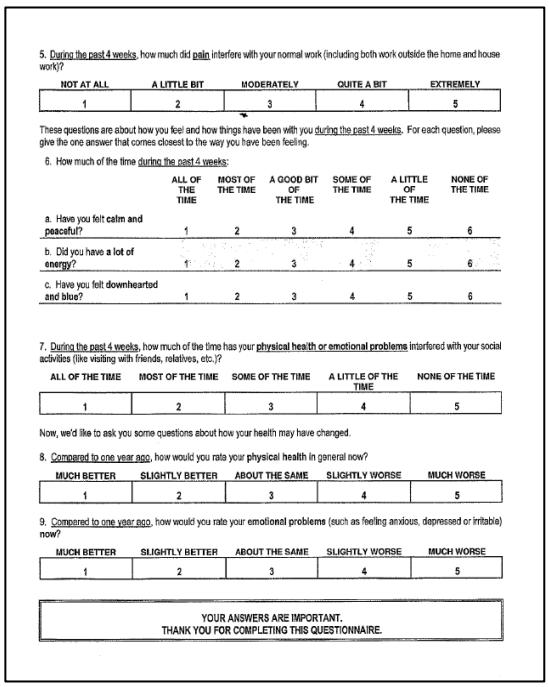
2. The following questions are about activities you might do during a typical day. Does **your health now limit you in** these activities? If so, how much?	YES, LIMITED A LOT	YES, LIMITED A LITTLE	NO, NOT LIMITED AT ALL
a. **Moderate activities,** such as moving a table, pushing a vacuum cleaner, bowling, or playing golf?	1	2	3
b. Climbing **several** flights of stairs?	1	2	3

3. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health?**

	NO, NONE OF THE TIME	YES, A LITTLE OF THE TIME	YES, SOME OF THE TIME	YES, MOST OF THE TIME	YES, ALL OF THE TIME
a. **Accomplished less** than you would like.	1	2	3	4	5
b. Were limited in the **kind** of work or other activities.	1	2	3	4	5

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	NO, NONE OF THE TIME	YES, A LITTLE OF THE TIME	YES, SOME OF THE TIME	YES, MOST OF THE TIME	YES, ALL OF THE TIME
a. **Accomplished less** than you would like.	1	2	3	4	5
b. Didn't do work or other activities as **carefully** as usual.	1	2	3	4	5



5. During the past 4 weeks, how much did **pain** interfere with your normal work (including both work outside the home and house work)?

NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY
1	2	3	4	5

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

6. How much of the time during the past 4 weeks:

	ALL OF THE TIME	MOST OF THE TIME	A GOOD BIT OF THE TIME	SOME OF THE TIME	A LITTLE OF THE TIME	NONE OF THE TIME
a. Have you felt **calm and peaceful?**	1	2	3	4	5	6
b. Did you have **a lot of energy?**	1	2	3	4	5	6
c. Have you felt **downhearted and blue?**	1	2	3	4	5	6

7. During the past 4 weeks, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

ALL OF THE TIME	MOST OF THE TIME	SOME OF THE TIME	A LITTLE OF THE TIME	NONE OF THE TIME
1	2	3	4	5

Now, we'd like to ask you some questions about how your health may have changed.

8. Compared to one year ago, how would you rate your **physical health** in general now?

MUCH BETTER	SLIGHTLY BETTER	ABOUT THE SAME	SLIGHTLY WORSE	MUCH WORSE
1	2	3	4	5

9. Compared to one year ago, how would you rate your **emotional problems** (such as feeling anxious, depressed or irritable) now?

MUCH BETTER	SLIGHTLY BETTER	ABOUT THE SAME	SLIGHTLY WORSE	MUCH WORSE
1	2	3	4	5

YOUR ANSWERS ARE IMPORTANT.
THANK YOU FOR COMPLETING THIS QUESTIONNAIRE.

Table C10. Overall Study Procedures

1. Attend study visit at Memorial Gymnasium (#224B)
    a. Obtain informed consent (Table C1)
    b. Complete screening and intake form (Table C2)
        i. Assess eligibility criteria
        ii. Obtain subject body mass (kg)
        iii. Obtain subject height (cm)
        iv. Determine limb dominance – "leg used to kick a ball"
        v. Determine involved (injured) limb in ACL subjects
        vi. Determine involved (non-dominant) limb in healthy subjects
        vii. Determine order of limb testing – counterbalanced per group
    c. Complete patient reported outcome measures (Tables C3-C9)
    d. Assess quadriceps Hoffmann reflex[a] (Table C12)
    e. Assess quadriceps isokinetic torque[b] (Table C13)
    f. Assess quadriceps MVIC torque and central activation ratio[b] (Table C14)
    g. Assess quadriceps fatigue index[b] (Table C15)
    h. Assess quadriceps active motor threshold (Table C16)
    i. [a] Study procedure(s) repeated in the contralateral limb immediately following completion of the starting limb
    j. [b] Study procedure(s) repeated in the contralateral limb after each test has been completed in the starting limb
    k. Dismiss subject from the study

Figure C1. Study Flowchart

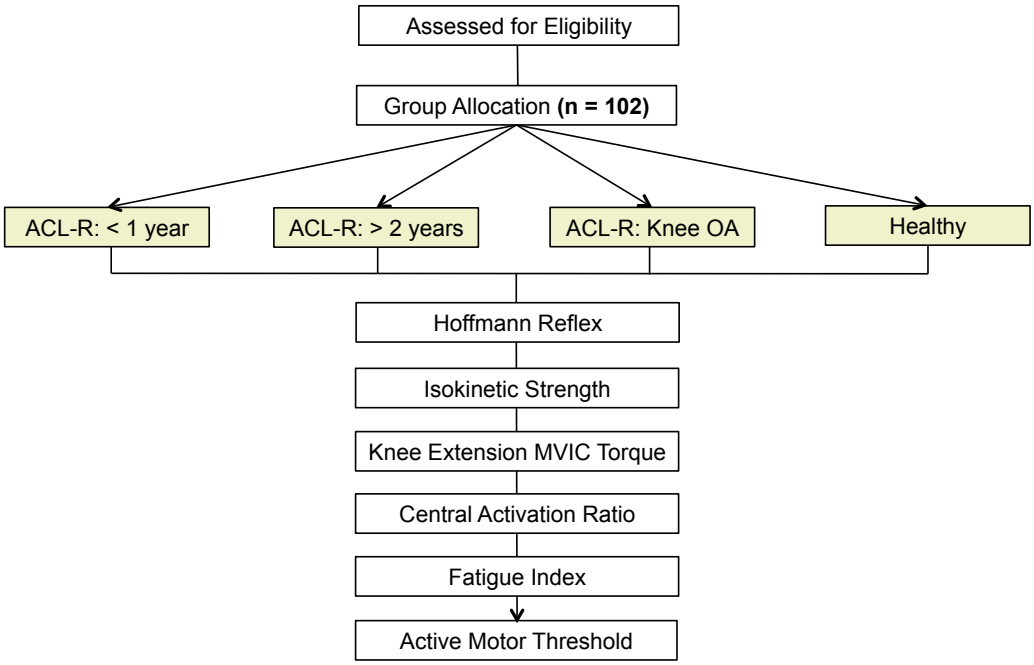


Figure C1. Flow chart of study procedures. Each measure was recorded bilaterally, with limb counterbalanced within each group.

Table C11. Patient Reported Outcome Measures

1. Subjects will complete subjective measures in a quiet room under supervision once determined to be eligible
2. All subjects will complete 7 subjective measures:
    a. International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form (Table C3)
    b. Knee Injury and Osteoarthritis Outcome Score (KOOS) (Table C4)
    c. Visual Analog Scale (VAS) for Pain at Rest (Table C5)
    d. Tegner Activity Level Scale (Table C6)
    e. Godin Leisure-Time Exercise Questionnaire (Table C7)
    f. Tampa Scale for Kinesiophobia (TSK) (Table C8)
    g. Veterans Rand 12-Item Health Survey (VR-12) (Table C9)

Table C12. Quadriceps Hoffmann Reflex Setup and Procedures

1. Biopac Setup
    a. Connect UIM100C, STM100C, and EMG100C to the MP150 unit
    b. Connect STMISOC to the STM100C via output jack
    c. Connect MP150 to the computer using a LAN wire
    d. Turn on MP150 unit and the computer
    e. STM100C Settings
        i. Source = OUT0
        ii. Level = 100%
        iii. Polarity = POS
        iv. Current = DC
    f. EMG100C Settings
        i. Gain = 1000
        ii. Filter = Off
        iii. LP = 5 kHz
        iv. HP = 1.0 Hz
    g. STMISOC Settings
        i. Voltage Monitor = 0.5 V
        ii. Voltage Switch = Voltage (1:10) 200 V Max
    h. Plug active and dispersive electrodes into the STMISOC

2. Acqknowledge Setup
    a. Open Acqknowledge 4.2.0 for Windows and select the attached MP150 unit
    b. MP150 | Setup Channels | Analog menu
        i. Channel 1
            1. Sample Rate = 2000 Hz
            2. Label = QUAD
            3. Check all boxes associated with this channel
        ii. Channel 2
            1. Sample Rate = 2000 Hz
            2. Label = STIM
            3. Check all boxes associated with this channel
    c. MP150 | Set Up Acquisition
        i. Change menus to “Record” and “Append”
        ii. Sample Rate = 2000 Hz
        iii. Acquisition Length = 79 msec
    d. MP150 | Set Up Stimulator
        i. Click square wave icon
        ii. Duration = Output Once
        iii. Stimulator Sample Rate = 2000 Hz
        iv. Seg #1 Width = 3.0 msec
        v. Seg #2 Width = 1.0 msec
        vi. Seg #3 Width = 0.0 msec
        vii. Seg #4 Width = 0.0 msec
        viii. Seg #5 Width = 33.5 msec
    e. MP150 | Show Manual Control
        i. Analog Outputs: Out 1 = 0.0
        ii. Analog Outputs: Out 2 = 10.0
        iii. Open data journal and stimulator window
    f. Click start button to confirm proper setup

3. Subject Preparation (Figure C2)
    a. Position the subject supine on the testing table
    b. Place small half foam bolster under subjects' knees
    c. Identify the bulk of vastus medialis during manually resisted isometric knee extension contraction
        i. Shave the area
        ii. Debride skin with an abrasive pad or gauze
        iii. Clean with isopropyl alcohol
    d. Place two surface EMG electrodes in the prepared area
        i. Parallel with muscle fiber orientation
        ii. Interelectrode distance of 2.0 cm
    e. Identify an area on the distal anteromedial tibia for the ground (reference) electrode
        i. Shave the area
        ii. Debride skin with an abrasive pad or gauze
        iii. Clean with isopropyl alcohol
    f. Place one surface EMG electrode in the prepared area
    g. Attach the leads from the EMG100C unit to the active and ground (reference) electrodes
        i. Proximal active electrode = Red lead
        ii. Distal active electrode = White lead
        iii. Ground (reference) electrode = Black lead
    h. Drape the subject
    i. Liberally gel the stimulating and dispersive electrodes
    j. Palpate the inguinal fold and locate the femoral pulse
    k. Move slightly lateral and place the active stimulating electrode over the femoral nerve
    l. Place the dispersive electrode on the posterior thigh near the gluteal fold
    m. Instruct the subject to remain calm and relaxed, and to close their eyes throughout testing, while keeping their arms at their side
    n. Turn off the lights and any additional unnecessary electronics in the testing area
    o. Confirm appropriate setup and begin testing procedures

4. Data Collection (Figure C2)
    a. Confirm that the data window, stimulator window, and data journal are open in the AcqKnowledge software
    b. Change the measurement tools within the data window to confirm that P-P and delta T are available
    c. Change the Seg #2 Level in the stimulator window to 2.0
    d. Click the start button in the data window to trigger a stimulus (or CTL + space)
        i. Monitor for subject motor response or discomfort throughout testing
    e. Progressively increase the stimulus by 0.5 V until an H-reflex is measured
        i. Highlight the EMG response within the data window and measure the P-P amplitude (confirm location of EMG response using delta T)
        ii. Save this value to the data journal
    f. Allow at least 10 seconds between stimuli
    g. After the first measureable H-reflex, continue to progressively increase stimulation intensity by 0.2 V
    h. Continue to change the stimulus intensity by 0.1 V increments or decrements to identify the maximum P-P EMG measurement

        i. Repeat measurement and recording steps e.i-e.ii above
    i. Confirm the maximum recorded H-reflex value and complete 3 trials at the corresponding stimulus intensity
    j. After recording maximum H-reflex, progressively increase the stimulus intensity by 0.5 V until a measurable M response is present, and a measureable H-reflex is no longer present
    k. Record the value for the M response in the data journal (confirm location of EMG response using delta T)
    l. After the first measureable M response, continue to progressively increase stimulation intensity by 0.2 V
        i. Repeat measurement and recording steps e.i-e.ii above
    m. Confirm the maximum recorded M response value, and complete 3 trials at the corresponding stimulus intensity
    n. Repeat procedures on contralateral limb
    o. Save the data file and remove the testing equipment from the subject

5. Data Processing
    a. Open the data file
    b. Transform | Digital Filters | FIR | Bandpass
        i. Low Frequency Cutoff | Fixed At | 10 Hz
        ii. High Frequency Cutoff | Fixed At | 500 Hz
        iii. Number of Coefficients | Optimize for sample rate and cutoff
        iv. Check the box next to Filter entire waveform
    c. Transform | Digital Filters | FIR | Bandstop
        i. Low Frequency Cutoff | Fixed At | 59.5 Hz
        ii. High Frequency Cutoff | Fixed At | 60.5 Hz
        iii. Number of Coefficients | Optimize for sample rate and cutoff
        iv. Check the box next to Filter entire waveform
    d. Start processing at the first maximum H-reflex trial
    e. Highlight the EMG response
    f. Measure the P-P amplitude and record in the data journal
        i. Repeat this procedure for the 3 recorded maximum trials
    g. Locate the 3 maximum M-wave trials
    h. Highlight the EMG response
    i. Measure the P-P amplitude and record in the data journal
        i. Repeat this procedure for the 3 recorded maximum trials
6. Save file

Figure C2. Quadriceps Hoffmann Reflex

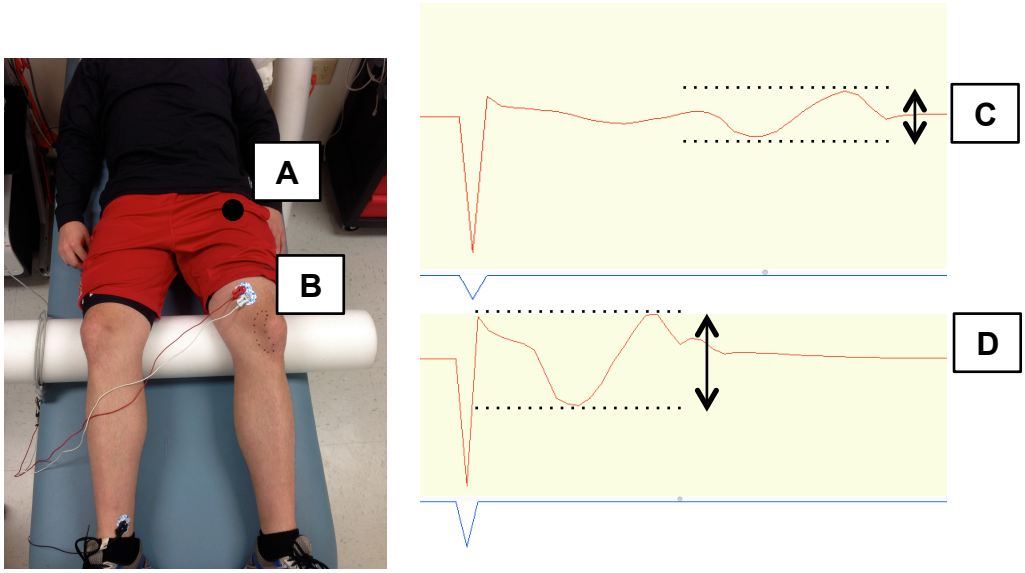


Figure C2. Represents Hoffmann reflex procedures, including (A) stimulating electrode placed over the femoral nerve and (B) recording surface EMG electrodes placed over the vastus medialis. Data were processed by recording the peak-peak amplitude for maximal H-reflex (C) and maximal M response (D).

Table C13. Quadriceps Isokinetic Torque Setup and Procedures

1. Biodex Setup
    a. Turn on the Biodex System 3
    b. Allow time for calibration and attach the desired knee attachment
    c. Position the back of the Biodex chair at 80 degrees
    d. Confirm the Biodex arm is perpendicular to the floor using a handheld dynamometer
    e. Select isokinetic mode and press the start button
    f. Press the computer control button

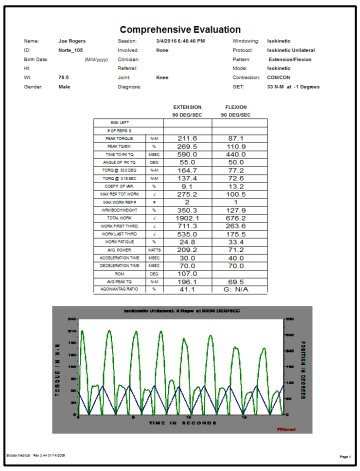
2. Computer Setup
    a. Open Biodex System 3 software
    b. File | Setup – Confirm simulation mode is turned off
    c. Select the "patient" icon
    d. Add patient | enter the appropriate demographics
    e. Select the "protocol" icon
    f. Click protocol definition
    g. Select isokinetic unilateral | knee extension/flexion | con/con: test: 90/90, 180/180 (ACL-R Ortho Protocol) | close
    h. Select the "range of motion" icon
    i. Click on the appropriate side (i.e. left, right)
    j. Click define new range of motion | clear
    k. Extend subjects' test limb to a neutral position (0 degrees) | press black "hold" button on Biodex unit | click "Away" on computer | press black "hold" button
    l. Flex subjects' test limb to 70 degrees | press black "hold" button on Biodex unit | click "Toward" on computer | press black "hold" button again | press "continue"
    m. Flex subjects' test limb to 90 degrees | press black "hold" button on Biodex unit | click "position" on computer | press black "hold" button again
    n. Extend subjects' test limb to a neutral position (0 degrees) | ask subject to relax the leg | press black "hold" button on Biodex unit | click "limb weight" on computer | press black "hold" button
    o. Click the start button to begin testing

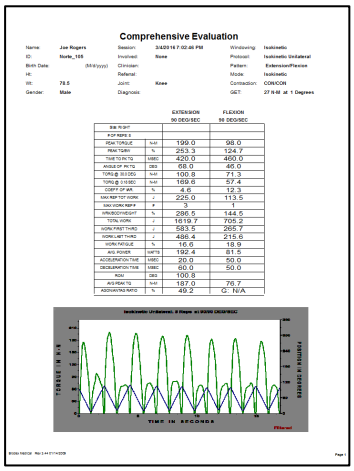
3. Subject Preparation (Figure C3)
    a. Position the subject in the dynamometer chair in an upright seated posture
        i. Knees flexed to 90 degrees
        ii. Hips flexed to 80 degrees
        iii. Restrain the subject using the lap strap
        iv. Engage the ankle strap 2 cm proximal to the lateral malleolus
    b. Provide instructions on proper knee extension testing technique
        i. "Sit up straight"
        ii. "Do not lift your backside out of the seat"
        iii. "Do not rotate or arch your back"
        iv. "Do not grip the handles on the dynamometer"
        v. "Cross your arms across your chest"
        vi. "Concentrate on kicking out and pulling back as hard and as fast as you can using only your thigh muscles"

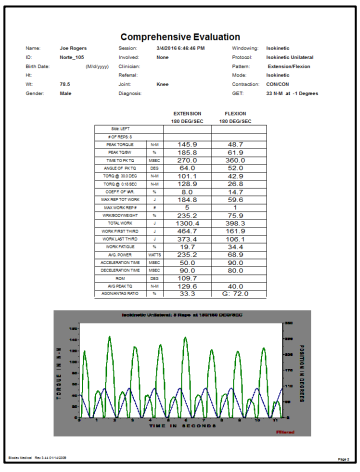
4. Data Collection
    a. Click the start button to begin testing
    b. Subject will perform 2-4 practice trials
    c. Subject will complete 8 repetitions (full extension + full flexion = 1 repetition) at 90 degrees/ second
    d. Subject will rest for 30 seconds
    e. Subject will perform 2-4 practice trials
    f. Subject will complete 8 repetitions (full extension + full flexion = 1 repetition) at 180 degrees/ second
    g. Click the continue button on the screen following testing

5. Data Processing
    a. Open the data file
    b. Select the "report" icon
        i. Under "choose options" click on "window isokinetic data" and "use metric units"
        ii. Under "choose report" click on "comprehensive evaluation"
        iii. Click print preview
    c. Select print screen (prtscn) on keyboard
    d. Open Microsoft Word
    e. Paste (CTL + V) report in Word
        i. Repeat for each report: 4 total (involved and uninvolved limb at 90 and 180 degrees/ second)
    f. Save Word document with prefix "Isokinetic_"
    g. Record quadriceps peak torque, total work, and average power in data spreadsheet

Figure C3. Isokinetic Torque







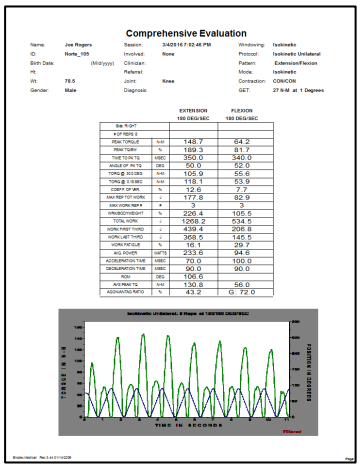


Figure C3. Patients' lower extremities were secured to a stationary dynamometry at the shank approximately 2 cm proximal to the lateral malleolus with knee flexed to 90 degrees. Peak torque (Nm/kg), total work (j/kg), and average power (W/kg) were recorded at 90 and 180 degrees per second from the isokinetic report (above).

Table C14. Quadriceps Superimposed Burst Technique Setup and Procedures

1. Biodex Setup
    a. Turn on the Biodex System 3
    b. Allow time for calibration and attach the desired knee attachment
    c. Set the away limit to 0 degrees
    d. Set the toward limit to > 90 degrees
    e. Select isometric mode and press the start button
    f. Confirm the Biodex arm is perpendicular to the floor using a handheld dynamometer
    g. Position the back of the Biodex chair at 80 degrees
    h. Connect the Biodex output wire to the MP150 (Force – channel 2)

2. AcqKnowledge Setup
    a. Open AcqKnowledge 4.2.0 for Windows and select the attached MP150 unit
    b. Select MP150 | Acquire
        i. Change the menus to “record” and “append”
        ii. Change the sampling rate to 2000 Hz
        iii. Change the Acquisition Length to 30 seconds
        iv. Exit the menu
    c. Select MP150 | Setup Channels
        i. Click the Analog tab
        ii. Label Channel 2 = Force
        iii. Click the Acquire, Plot, and Values boxes
        iv. Changes the sampling rate to 125 Hz
        v. Exit the menu
    d. Click the start icon to confirm data acquisition and graphical representation
    e. Save the data file

3. GRASS S48 Stimulator Setup
    a. Turn the stimulator on
    b. Confirm proper SIU8T stimulation isolator connection
        i. Do not turn this unit on until ready to deliver a stimulus
    c. Confirm isolation unit settings (SIU8T)
        i. Constant Voltage = Low
        ii. Polarity = Normal
        iii. Stimulus Intensity = 20
    d. Confirm stimulator settings
        i. Train Rate = 1.0 TPS
        ii. Train Duration = 10.0 ms
        iii. Stim Rate = 10.0 PPS
        iv. Delay = 1.0 ms
        v. Duration = 6.0 ms
        vi. Volts = Max
        vii. Output = On
        viii. Stim Mode = Single
    e. Connect electrode wires to the stimulation isolation unit (SIU8T)

4. Subject Preparation (Figure C4)
    a. Place self-adhesive carbon impregnated electrodes over the proximal vastus lateralis and distal vastus medialis

b. Position the subject in the dynamometer chair in an upright seated posture
    i. Knees flexed to 90 degrees
    ii. Hips flexed to 80 degrees
    iii. Restrain the subject using the lap strap
    iv. Engage the ankle strap 2 cm proximal to the lateral malleolus
c. Provide instructions on proper knee extension testing technique
    i. "Sit up straight"
    ii. "Do not lift your backside out of the seat"
    iii. "Do not rotate or arch your back"
    iv. "Do not grip the handles on the dynamometer"
    v. "Cross your arms across your chest"
    vi. "Concentrate on kicking out using only your quadriceps muscle – ramp up over 2 seconds, hold steady for 3 seconds, and relax"
d. Allow the subject practice trials at 25%, 50%, 75% and 100% of their perceived maximum effort contraction
e. Confirm maximal effort and appropriate plateau in at least 2 practice trials at 100% effort before testing

5. Data Collection
    a. Turn on the stimulus isolation unit (SIU8T)
    b. Confirm the stimulus intensity setting on the GRASS S48 stimulator
    c. Click the start button within the AcqKnowledge 4.2.0 window
    d. The subject should complete a maximal knee extension contraction that matches or exceeds the torque output achieved during practice trials
    e. Trigger a single stimulation pulse using the GRASS S48 stimulator when a plateau is reached at the maximal force output value
        i. If no plateau is reached, abort the contraction
    f. Instruct the subject to relax
    g. Click the stop button within the AcqKnowledge 4.2.0 window
    h. Repeat steps b-g two additional times for a total of three trials
        i. Allow at least 30 seconds between trials
    i. Save the data file

6. Data Processing (Figure C4)
    a. Open the data file
    b. Change the measurement tools to the desired options
        i. Delta T
        ii. Min/Max depending on limb tested
        iii. Mean
    c. Click Transform | Digital Filters | FIR | Low Pass
        i. Frequency cutoff = 10 Hz
        ii. Rate of Coefficients = Optimized for sampling rate and cutoff
        iii. Click filter entire waveform
        iv. Close the window
    d. Highlight the 100 ms epoch immediately prior to the superimposed burst stimulus
        i. Record the Mean voltage value
    e. Highlight the superimposed burst epoch in the data window
        i. Record the Min/Max value
    f. Repeat for subsequent trials
    g. Do not save before closing the data file

Figure C4. Superimposed Burst Technique and Quadriceps Central Activation Ratio Calculation

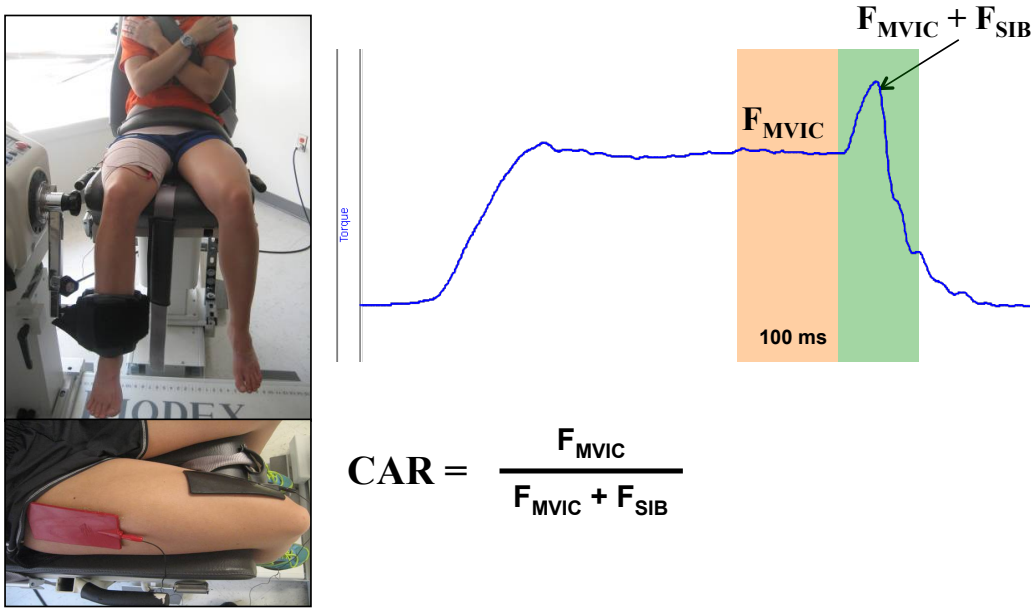


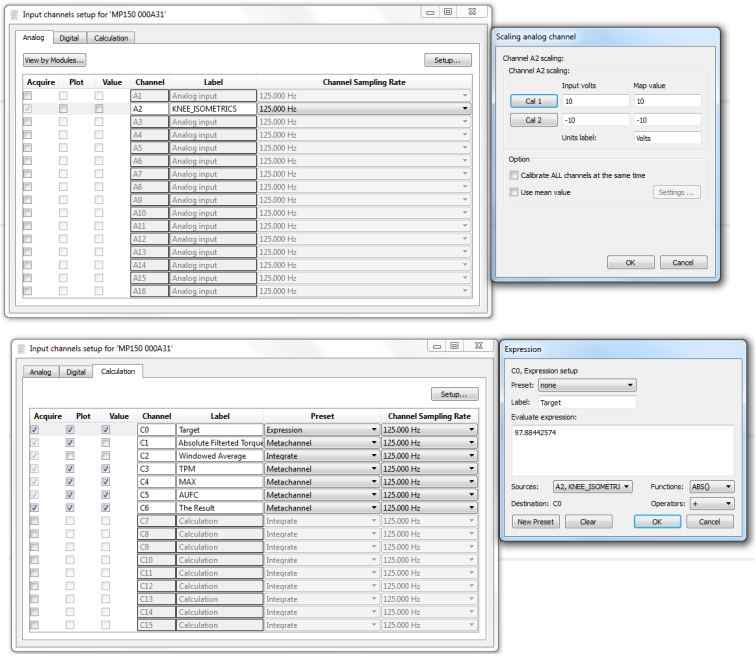
Figure C4. The superimposed burst technique was used to measure quadriceps activation. Adhesive electrodes were applied to the anterior thigh over the proximal vastus lateralis and distal vastus medialis. Participants provided a maximal knee extension force, and an electrical stimulus was applied through the stimulating electrodes. The central activation ratio (CAR) was calculated from a 100 ms mean MVIC force (F_{MVIC}) and the resulting superimposed burst force (F_{SIB}) using the equation above. Mean MVIC was recorded from a 100 ms epoch approximately 1 second into each trial, and averaged across a minimum of two trials. A third MVIC trial obtained during the superimposed burst technique was used in the final averaged torque value. All force data were converted to a torque and normalized to body mass (Nm/kg).

Table C15. Quadriceps Fatigue Index Setup and Procedures

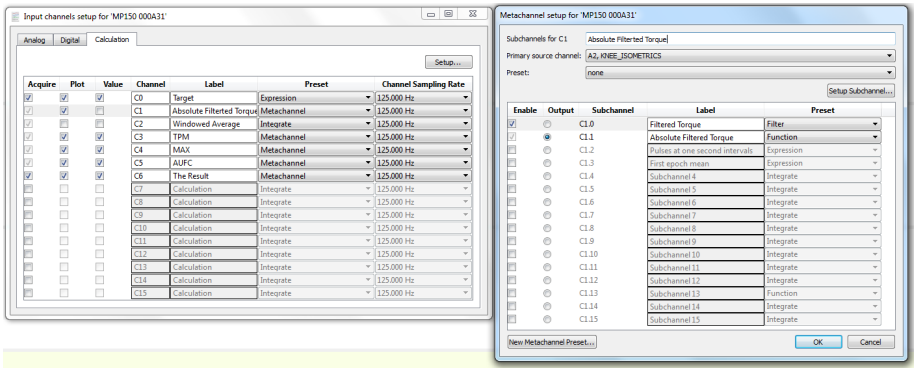
1. Biodex Setup
    a. Turn on the Biodex System 3
    b. Allow time for calibration and attach the desired knee attachment
    c. Set the away limit to 0 degrees
    d. Set the toward limit to > 90 degrees
    e. Select isometric mode and press the start button
    f. Confirm the Biodex arm is perpendicular to the floor using a handheld dynamometer
    g. Position the back of the Biodex chair at 80 degrees
    h. Connect the Biodex output wire to the MP150 (Force – channel 2)

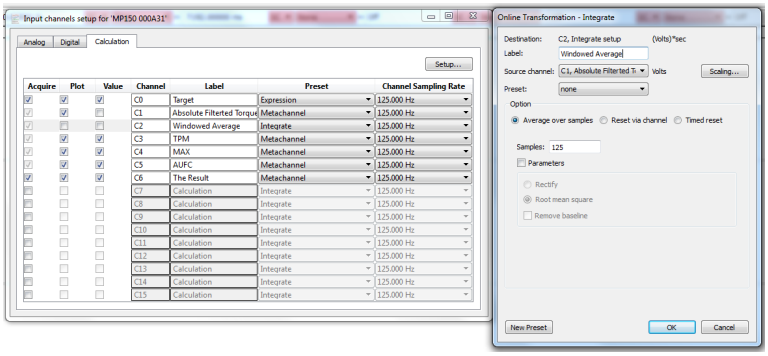
2. AcqKnowledge Setup
    a. Open AcqKnowledge 4.2.0 for Windows and select the attached MP150 unit
    b. Select MP150 | Acquire
        i. Change the menus to “record” and “append”
        ii. Change the sampling rate to 2000 Hz
        iii. Change the Acquisition Length to 30 seconds
        iv. Exit the menu
    c. Select MP150 → Setup Channels
        i. Click the Analog tab
        ii. Label Channel 1 → Force
        iii. Click the Acquire, Plot, and Values boxes
        iv. Changes the sampling rate to 125 Hz
        v. Exit the menu
    d. Take the following steps to set up fatigue index protocol

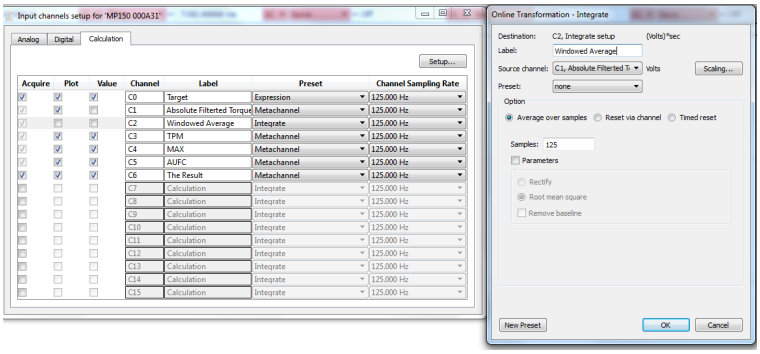
        Label variables under the ANALOG and CALCULATION tabs. Set force channel as source for TARGET

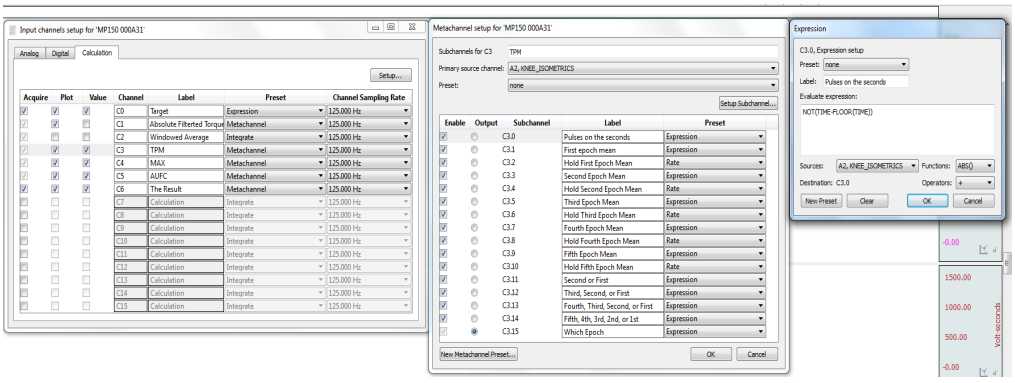


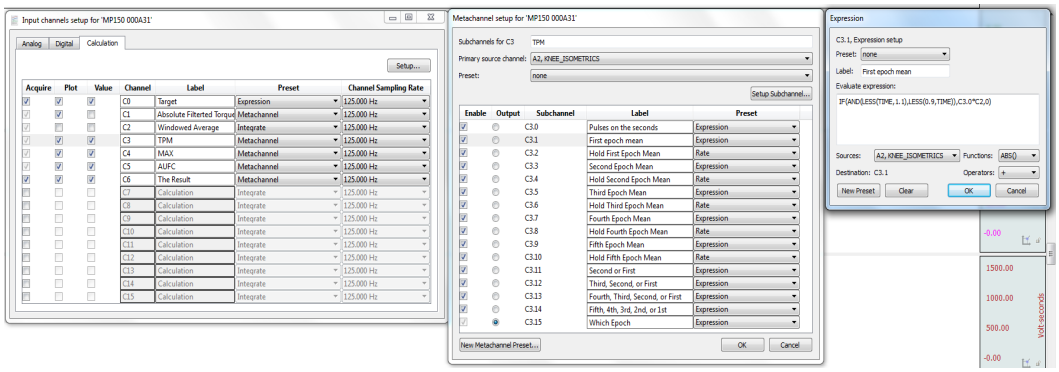
Continue down list of labels (images on left) – For each variable, select the label box|click SETUP|set up according to image on right







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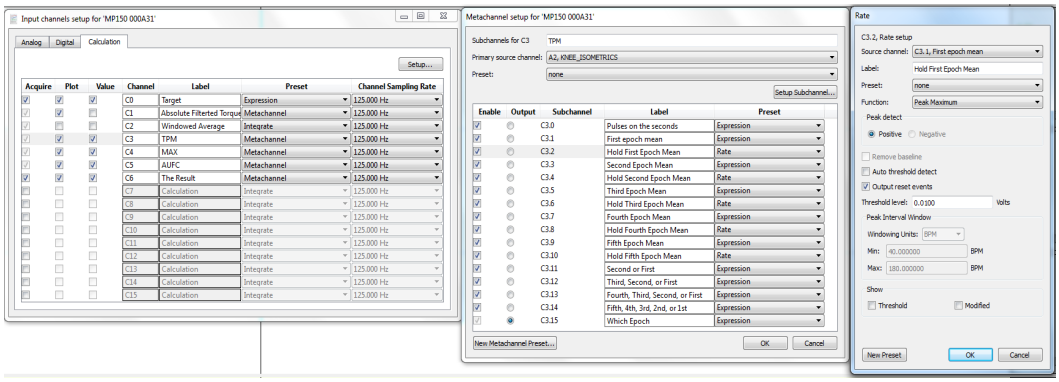
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3 TPM
Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.1, Expression setup
Preset: none
Label: First epoch mean
Evaluate expression:
IF(AND(LESS(TIME,1.1),LESS(0.9,TIME)),C3.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.1
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds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Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
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C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
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Subchannels for C3 TPM
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Enable
Output
Subchannel
Label
Preset
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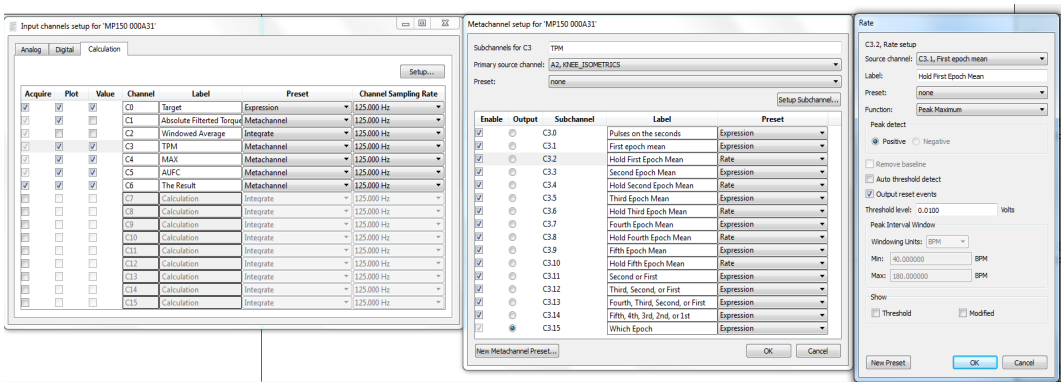
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.2, Rate setup
Source channel: C3.1, First epoch mean
Label: Hold First Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
BPM
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel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C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
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Subchannels for C3 TPM
Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
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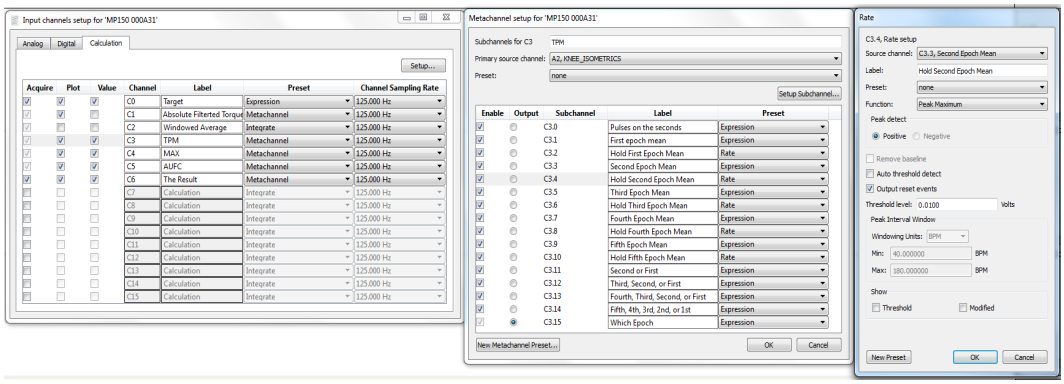
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.2, Rate setup
Source channel: C3.1, First epoch mean
Label: Hold First Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
BPM
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel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C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
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Subchannels for C3 TPM
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Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
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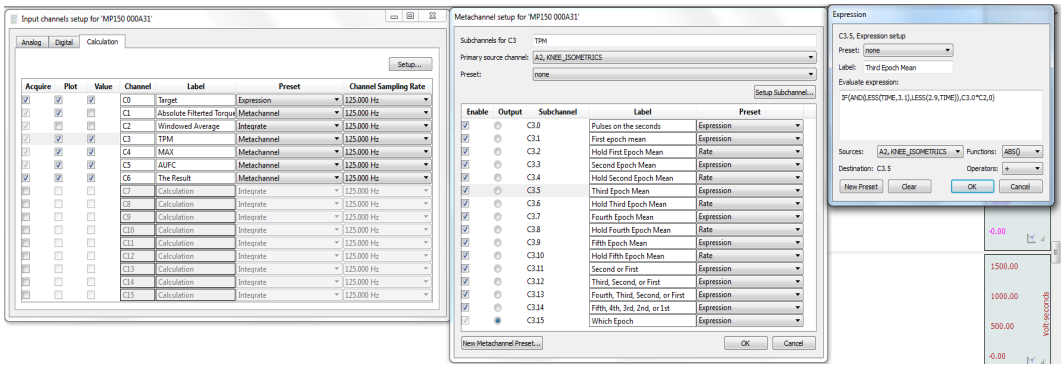
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.4, Rate setup
Source channel: C3.3, Second Epoch Mean
Label: Hold Second Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
BPM
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel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Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
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C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
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Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
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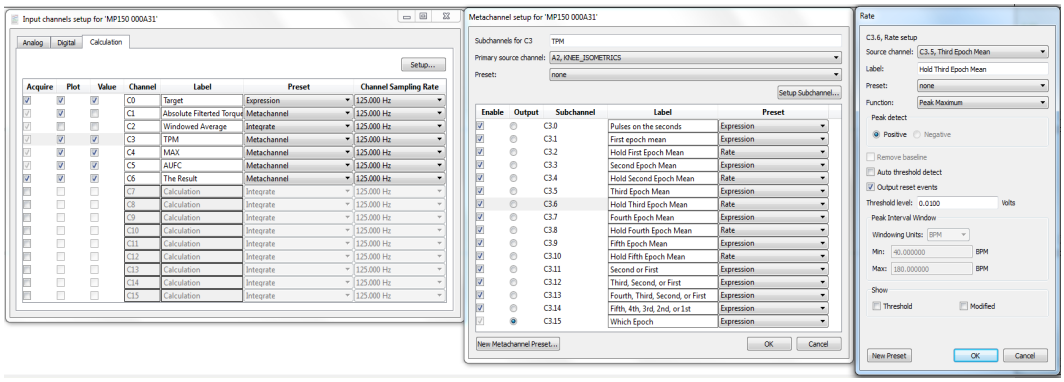
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.5, Expression setup
Preset: none
Label: Third Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,3.1),LESS(2.9,TIME)),C3.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.5
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds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C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
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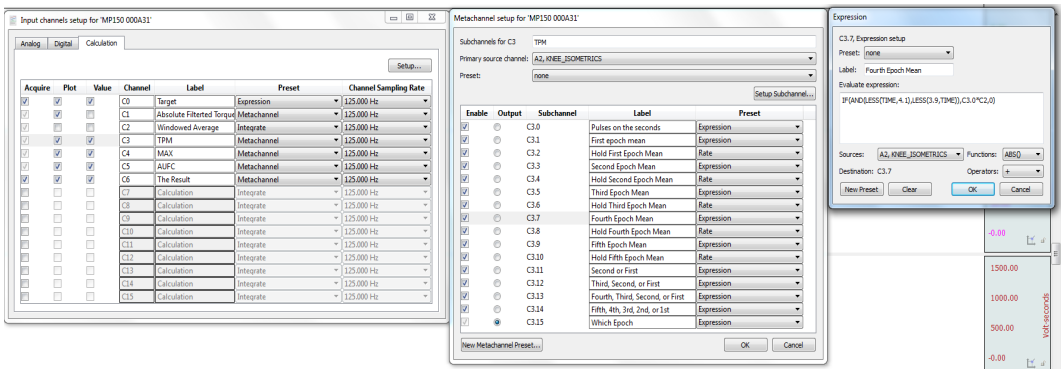
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3 TPM
Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.6, Rate setup
Source channel: C3.5, Third Epoch Mean
Label: Hold Third Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel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Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
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C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
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C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3 TPM
Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.7, Expression setup
Preset: none
Label: Fourth Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,4.1),LESS(3.9,TIME)),C3.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.7
Operators: +
New Preset
Clear
OK
Cancel
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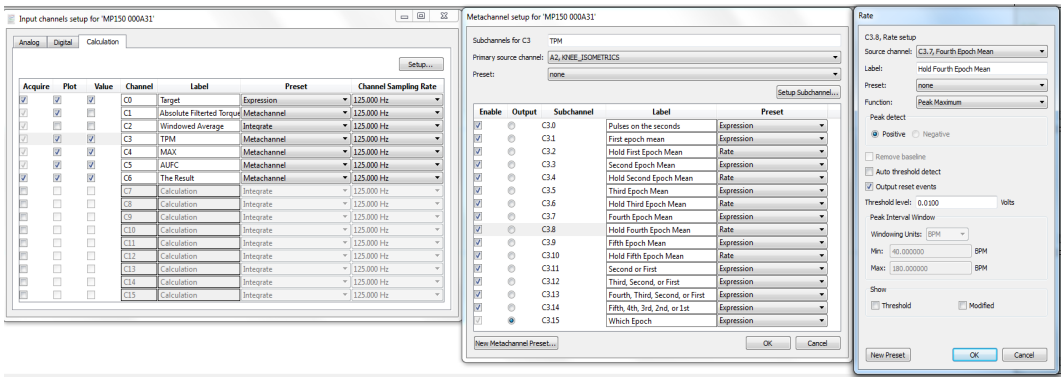
1000.00
500.00
-0.00
Volt-seconds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Analog
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Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
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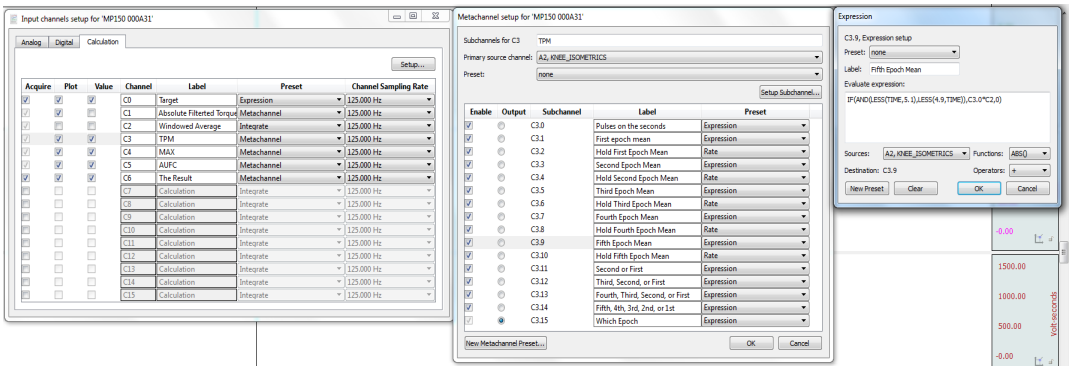
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3 TPM
Primary source channel: A2, KNEE_ISOMETRICS
Preset: none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.8, Rate setup
Source channel: C3.7, Fourth Epoch Mean
Label: Hold Fourth Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel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Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
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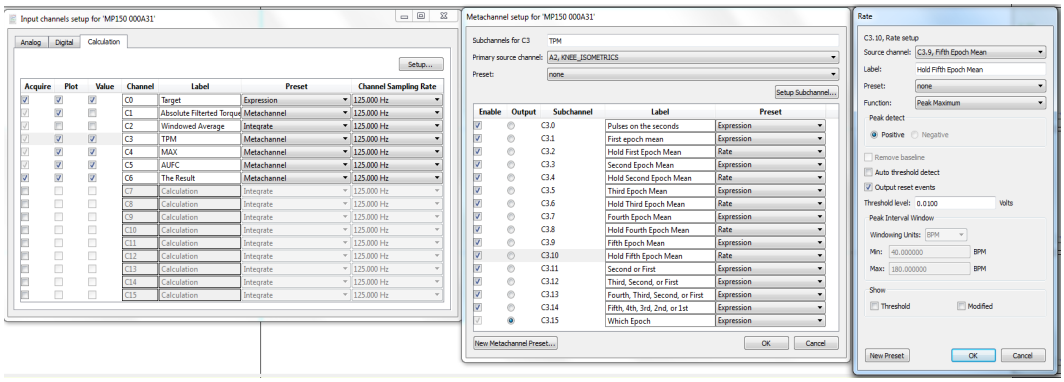
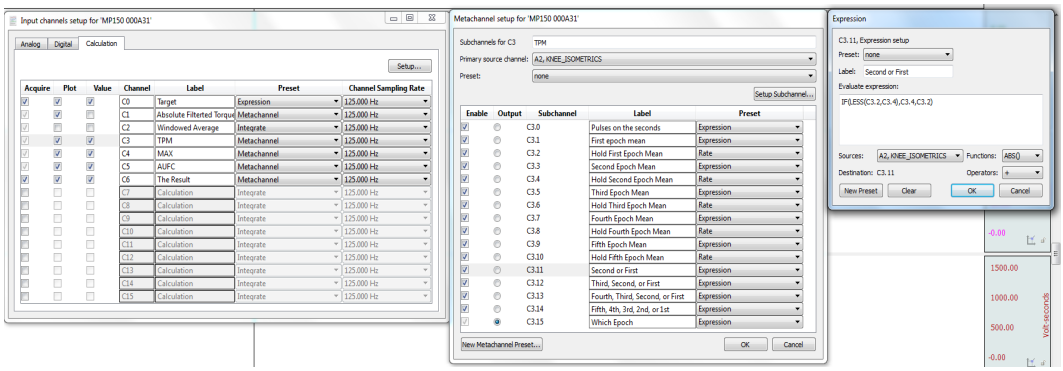
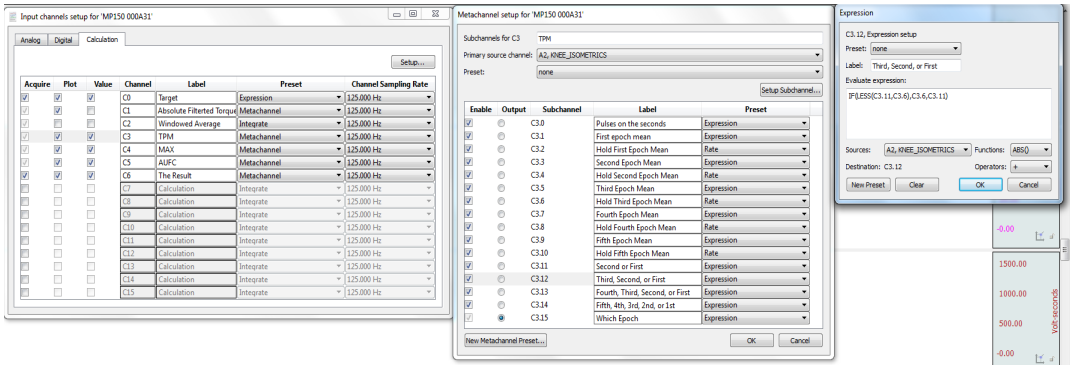
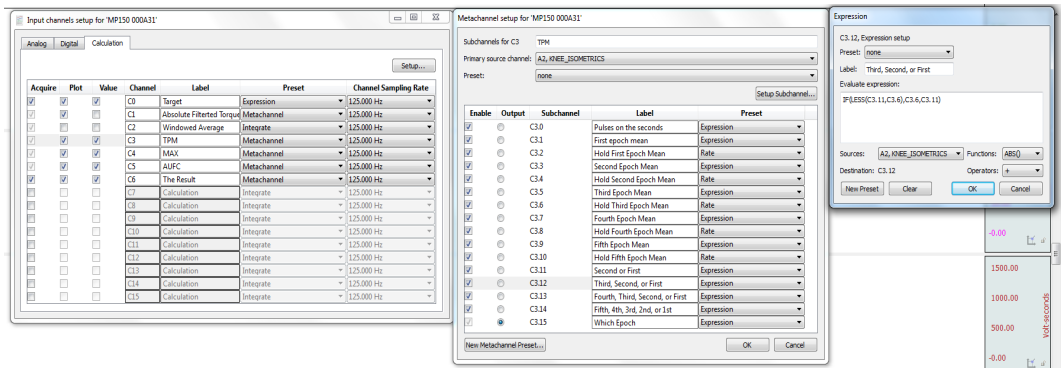
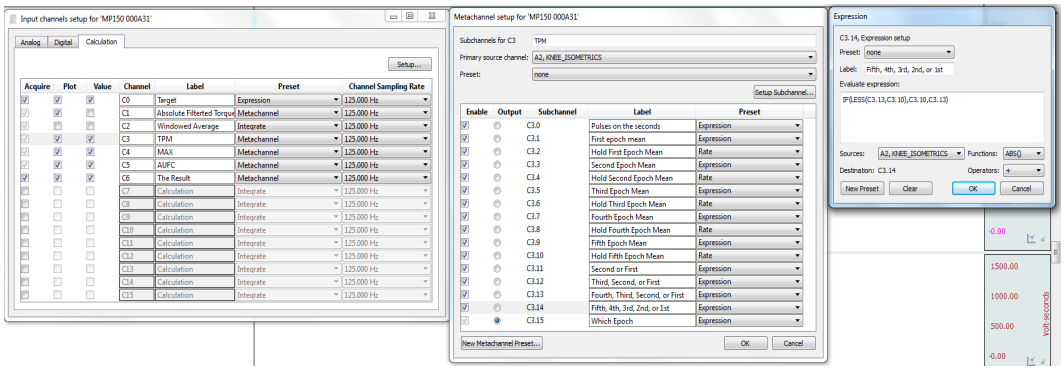
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.9, Expression setup
Preset:
none
Label:
Fifth Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,5.1),LESS(4.9,TIME)),C3.0*C2,0)
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination: C3.9
Operators:
+
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

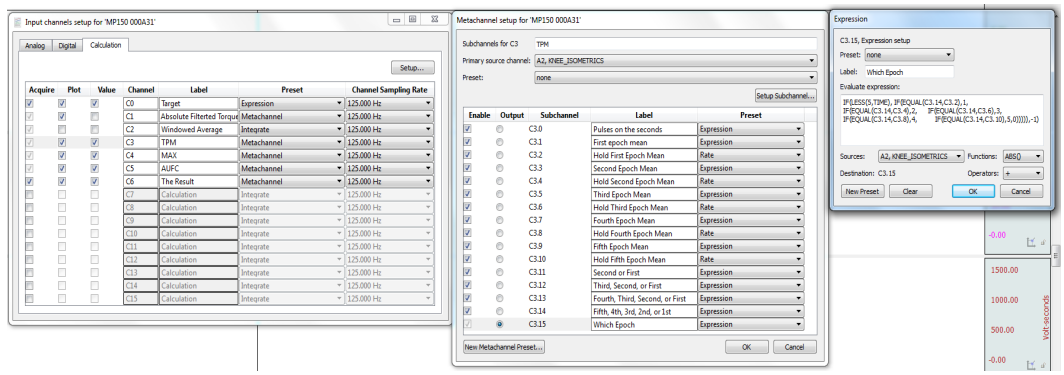

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Rate
C3.10, Rate setup
Source channel:
C3.9, Fifth Epoch Mean
Label:
Hold Fifth Epoch Mean
Preset:
none
Function:
Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level:
0.0100
Volts
Peak Interval Window
Windowing Units:
BPM
Min:
40.000000
BPM
Max:
180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel

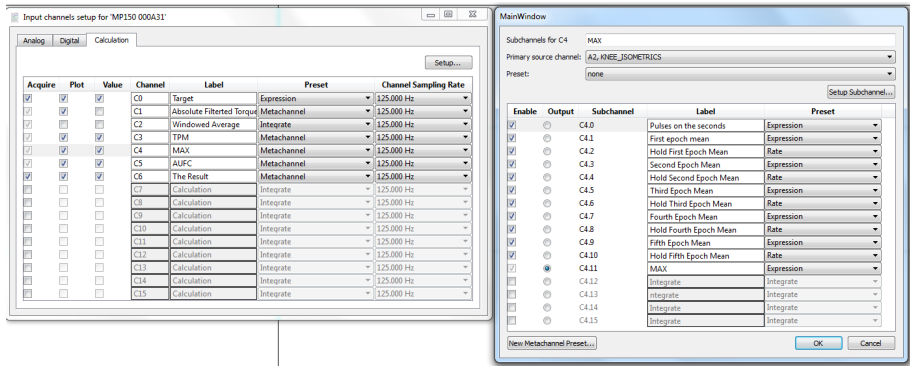

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.11, Expression setup
Preset:
none
Label:
Second or First
Evaluate expression:
IF(LESS(C3.2,C3.4),C3.4,C3.2)
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination: C3.11
Operators:
+
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

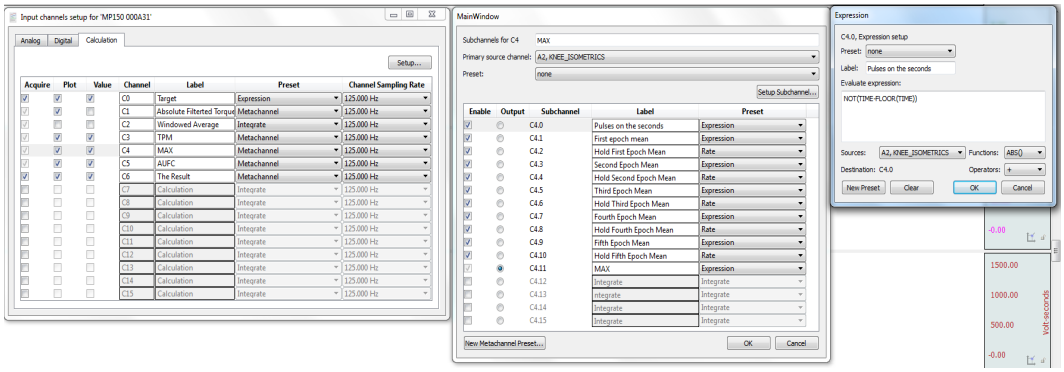

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.12, Expression setup
Preset:
none
Label:
Third, Second, or First
Evaluate expression:
IF(LESS(C3.11,C3.6),C3.6,C3.11)
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination: C3.12
Operators:
+
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

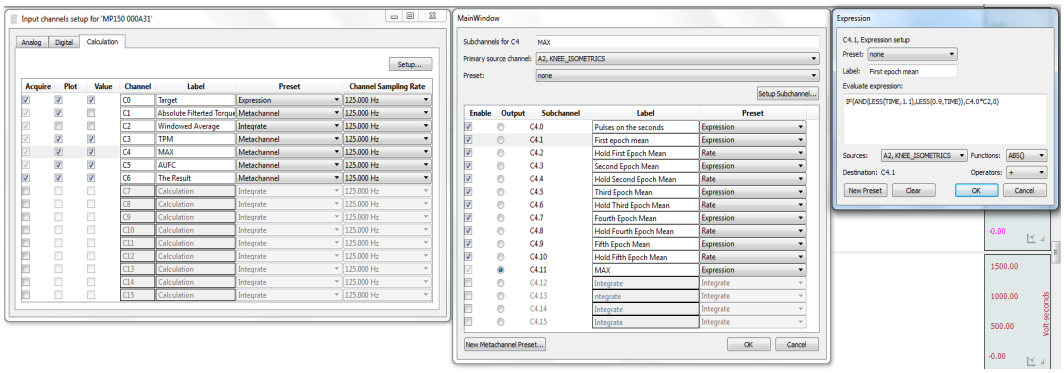

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.12, Expression setup
Preset: none
Label: Third, Second, or First
Evaluate expression:
IF(LESS(C3.11,C3.6),C3.6,C3.11)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.12
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.14, Expression setup
Preset: none
Label: Fifth, 4th, 3rd, 2nd, or 1st
Evaluate expression:
IF(LESS(C3.13,C3.10),C3.10,C3.13)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.14
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
Metachannel setup for 'MP150 000A31'
Subchannels for C3
TPM
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C3.0 Pulses on the seconds Expression
C3.1 First epoch mean Expression
C3.2 Hold First Epoch Mean Rate
C3.3 Second Epoch Mean Expression
C3.4 Hold Second Epoch Mean Rate
C3.5 Third Epoch Mean Expression
C3.6 Hold Third Epoch Mean Rate
C3.7 Fourth Epoch Mean Expression
C3.8 Hold Fourth Epoch Mean Rate
C3.9 Fifth Epoch Mean Expression
C3.10 Hold Fifth Epoch Mean Rate
C3.11 Second or First Expression
C3.12 Third, Second, or First Expression
C3.13 Fourth, Third, Second, or First Expression
C3.14 Fifth, 4th, 3rd, 2nd, or 1st Expression
C3.15 Which Epoch Expression
New Metachannel Preset...
OK
Cancel
Expression
C3.15, Expression setup
Preset: none
Label: Which Epoch
Evaluate expression:
IF(LESS(S_TIME), IF(EQUAL(C3.14,C3.2),1,
IF(EQUAL(C3.14,C3.4),2, IF(EQUAL(C3.14,C3.6),3,
IF(EQUAL(C3.14,C3.8),4, IF(EQUAL(C3.14,C3.10),5,0)))))),-1)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C3.15
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 ntegrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate Integrate
C4.13 Integrate Integrate
C4.14 Integrate Integrate
C4.15 Integrate Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.0, Expression setup
Preset: none
Label: Pulses on the seconds
Evaluate expression:
NOT(TIME-FLOOR(TIME))
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C4.0
Operators: +
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
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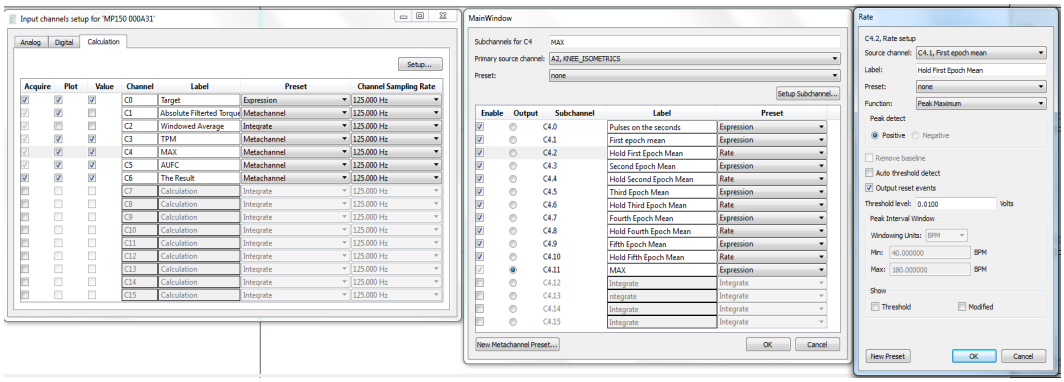
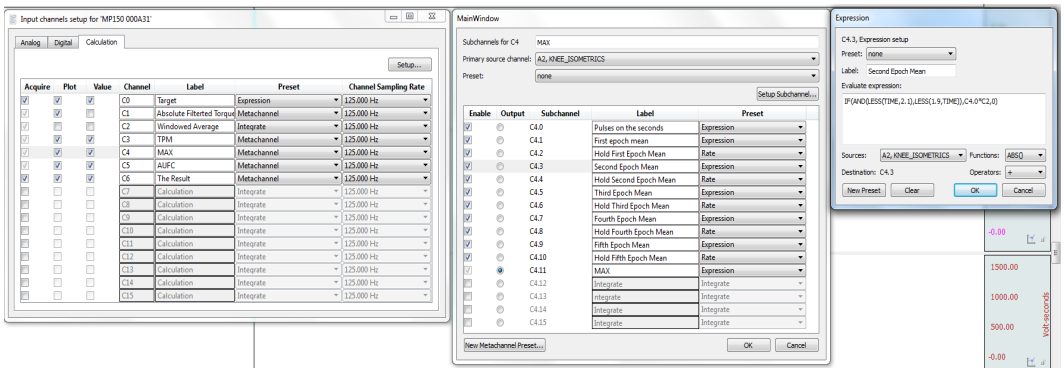
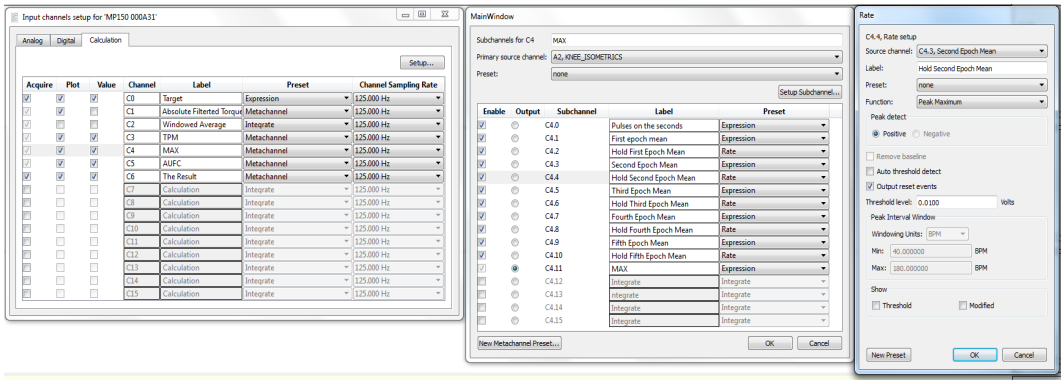
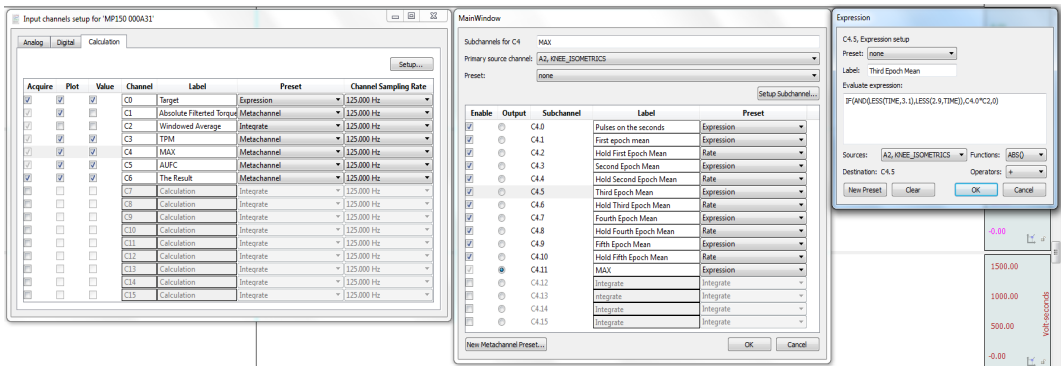
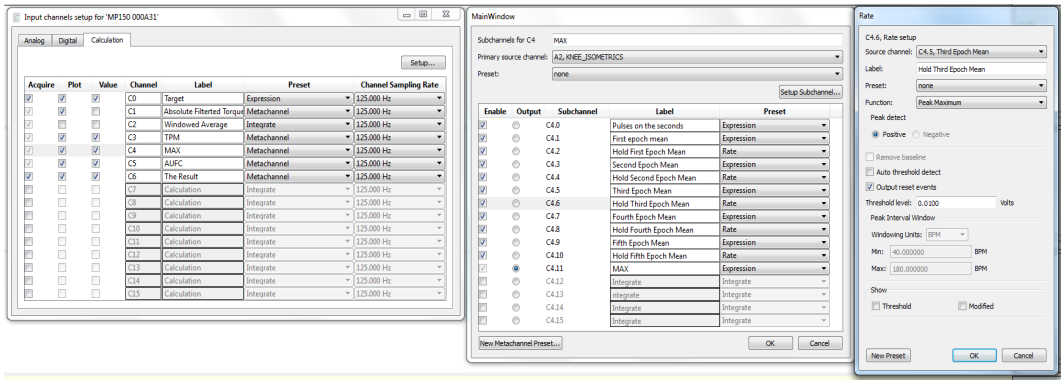
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate Integrate
C4.13 Integrate Integrate
C4.14 Integrate Integrate
C4.15 Integrate Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.1, Expression setup
Preset: none
Label: First epoch mean
Evaluate expression:
IF(AND(LESS(TIME,1.1),LESS(0.9,TIME)),C4.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C4.1
Operators: +
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

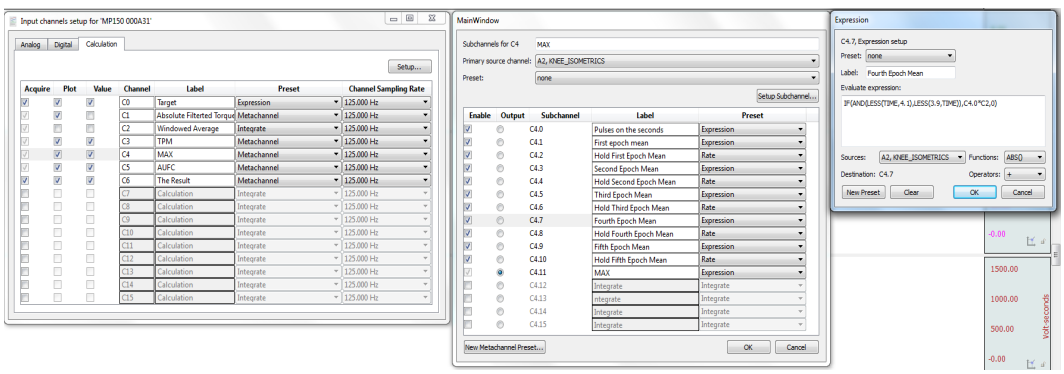

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate Integrate
C4.13 Integrate Integrate
C4.14 Integrate Integrate
C4.15 Integrate Integrate
New Metachannel Preset...
OK
Cancel
Rate
C4.2, Rate setup
Source channel: C4.1, First epoch mean
Label: Hold First Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000 BPM
Max: 180.000000 BPM
Show
Threshold
Modified
New Preset
OK
Cancel

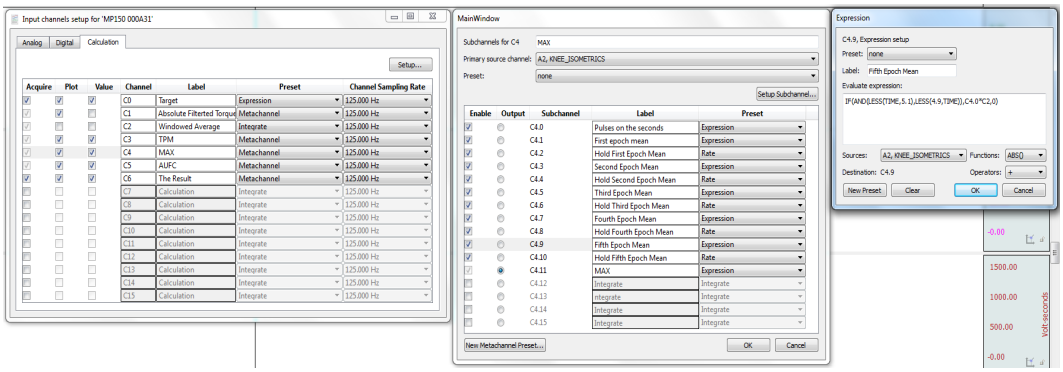

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate Integrate
C4.13 Integrate Integrate
C4.14 Integrate Integrate
C4.15 Integrate Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.3, Expression setup
Preset: none
Label: Second Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,2.1),LESS(1.9,TIME)),C4.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C4.3
Operators: +
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

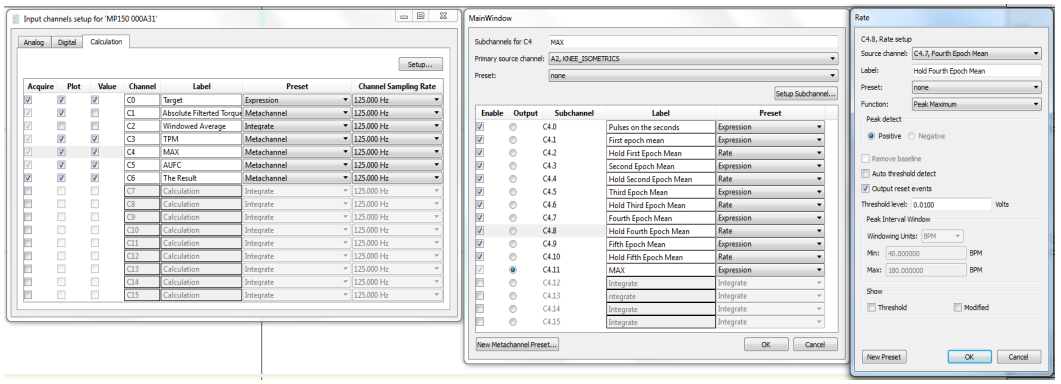

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Rate
C4.4, Rate setup
Source channel:
C4.3, Second Epoch Mean
Label:
Hold Second Epoch Mean
Preset:
none
Function:
Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level:
0.0100
Volts
Peak Interval Window
Windowing Units:
BPM
Min:
40.000000
BPM
Max:
180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel

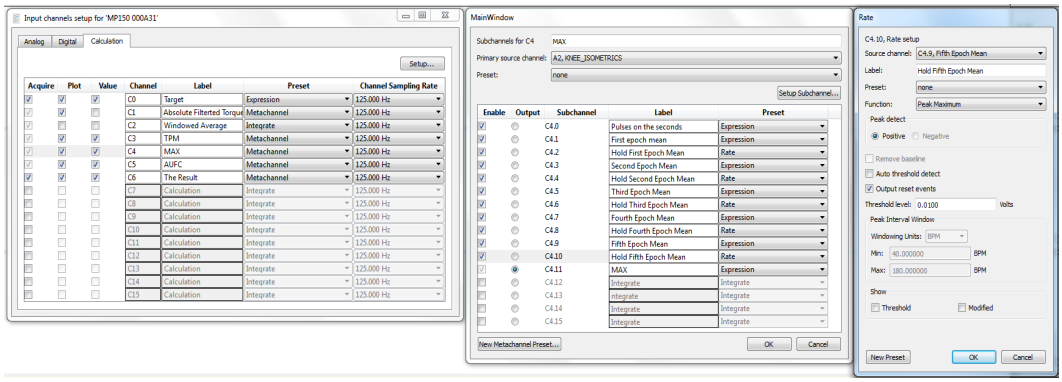

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.5, Expression setup
Preset:
none
Label:
Third Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,3.1),LESS(2.9,TIME)),C4.0*C2,0)
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination:
C4.5
Operators:
+
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

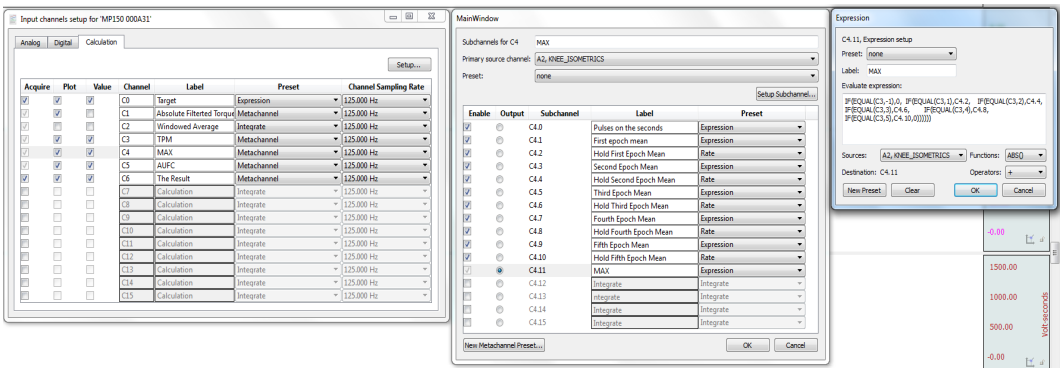

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Rate
C4.6, Rate setup
Source channel:
C4.5, Third Epoch Mean
Label:
Hold Third Epoch Mean
Preset:
none
Function:
Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level:
0.0100
Volts
Peak Interval Window
Windowing Units:
BPM
Min:
40.000000
BPM
Max:
180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel

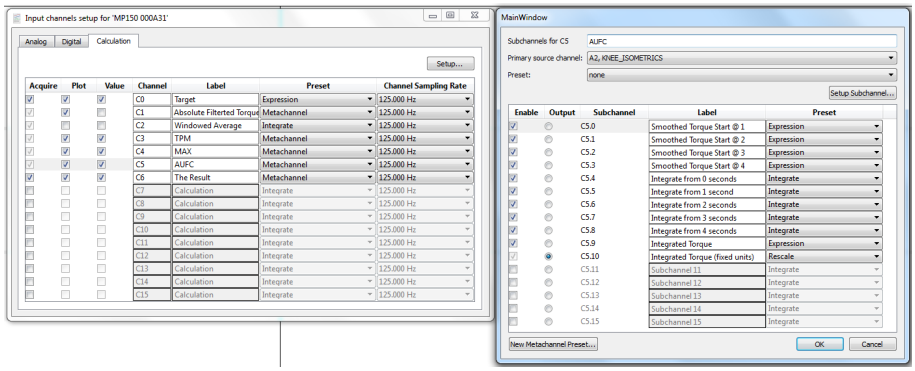

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.7, Expression setup
Preset:
none
Label:
Fourth Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,4.1),LESS(3.9,TIME)),C4.0*C2,0)
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination:
C4.7
Operators:
+
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

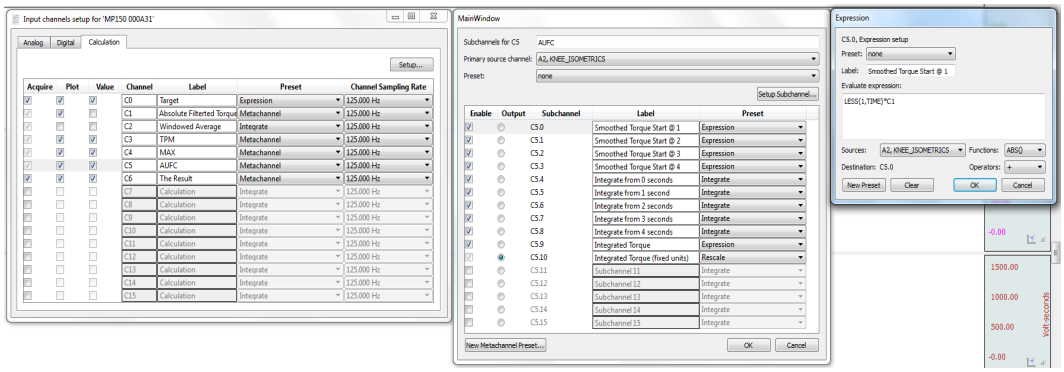

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.9, Expression setup
Preset: none
Label: Fifth Epoch Mean
Evaluate expression:
IF(AND(LESS(TIME,5.1),LESS(4.9,TIME)),C4.0*C2,0)
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C4.9
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

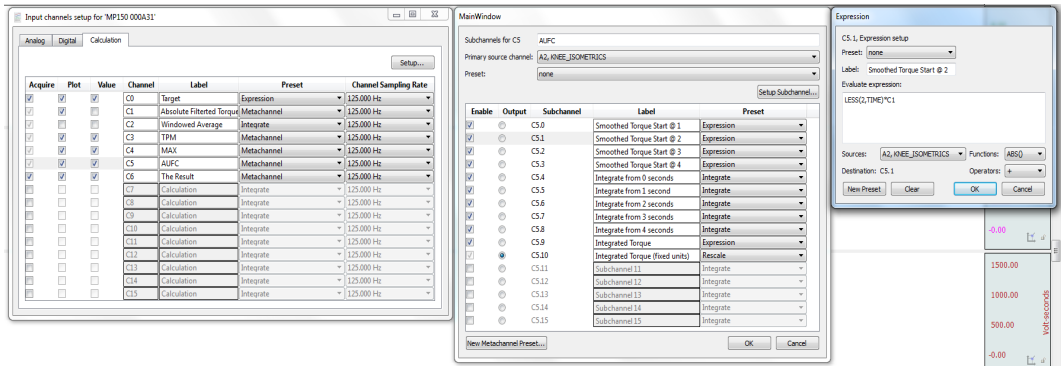

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Rate
C4.8, Rate setup
Source channel: C4.7, Fourth Epoch Mean
Label: Hold Fourth Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
BPM
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel

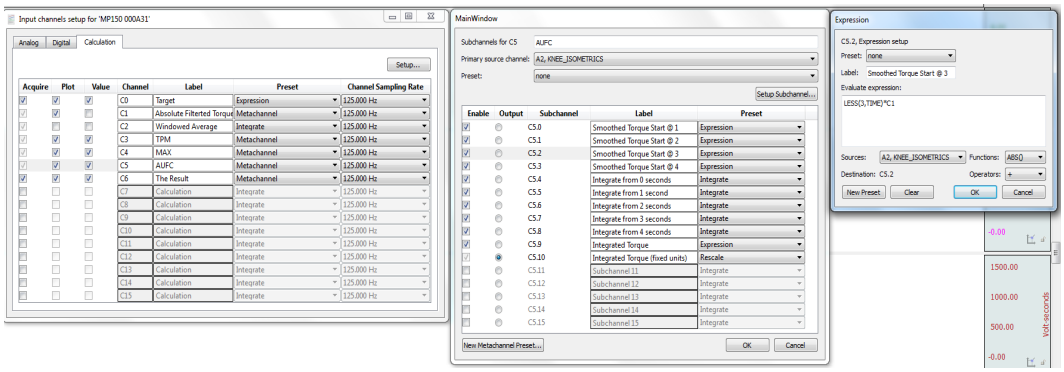

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Rate
C4.10, Rate setup
Source channel: C4.9, Fifth Epoch Mean
Label: Hold Fifth Epoch Mean
Preset: none
Function: Peak Maximum
Peak detect
Positive
Negative
Remove baseline
Auto threshold detect
Output reset events
Threshold level: 0.0100
Volts
Peak Interval Window
Windowing Units: BPM
Min: 40.000000
BPM
Max: 180.000000
BPM
Show
Threshold
Modified
New Preset
OK
Cancel

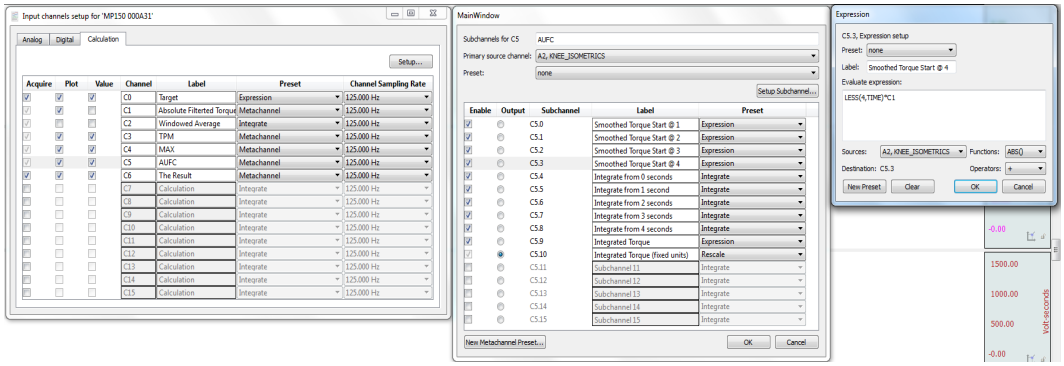

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C4
MAX
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C4.0 Pulses on the seconds Expression
C4.1 First epoch mean Expression
C4.2 Hold First Epoch Mean Rate
C4.3 Second Epoch Mean Expression
C4.4 Hold Second Epoch Mean Rate
C4.5 Third Epoch Mean Expression
C4.6 Hold Third Epoch Mean Rate
C4.7 Fourth Epoch Mean Expression
C4.8 Hold Fourth Epoch Mean Rate
C4.9 Fifth Epoch Mean Expression
C4.10 Hold Fifth Epoch Mean Rate
C4.11 MAX Expression
C4.12 Integrate
C4.13 Integrate
C4.14 Integrate
C4.15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C4.11, Expression setup
Preset: none
Label: MAX
Evaluate expression:
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C4.11
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

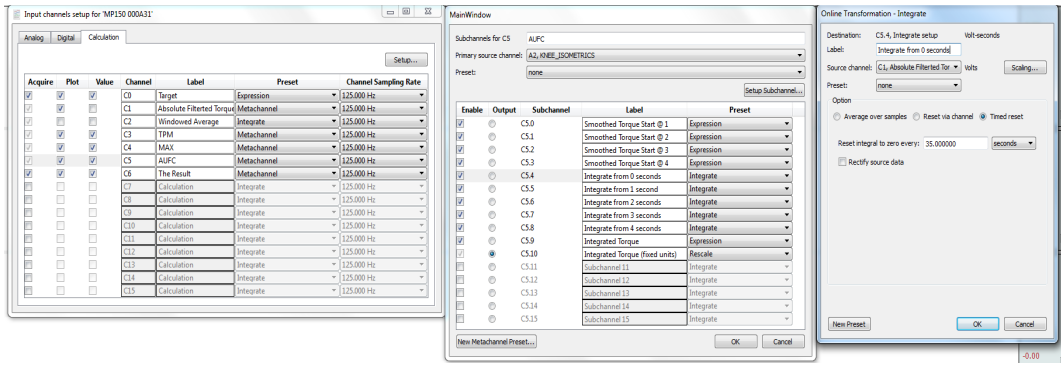

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filterted Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel

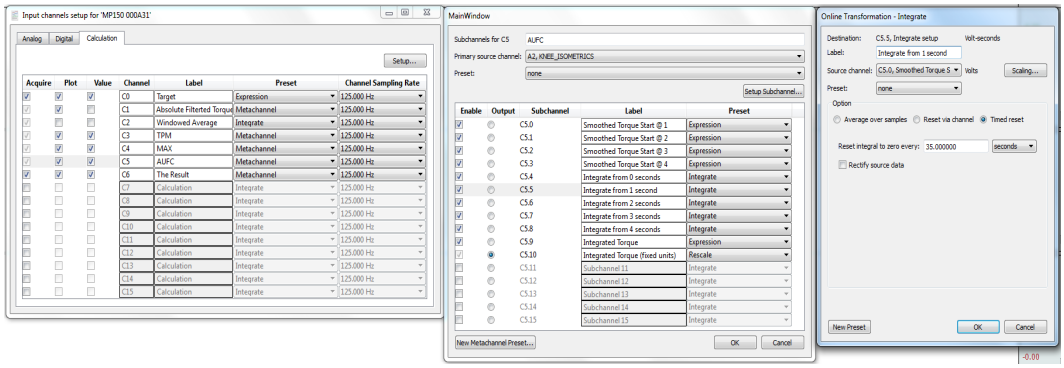

Input channels setup for 'MP150 000A31'
MainWindow
Expression
C5.0, Expression setup
Preset: none
Label: Smoothed Torque Start @ 1
Evaluate expression:
LESS(1,TIME)*C1
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C5.0
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

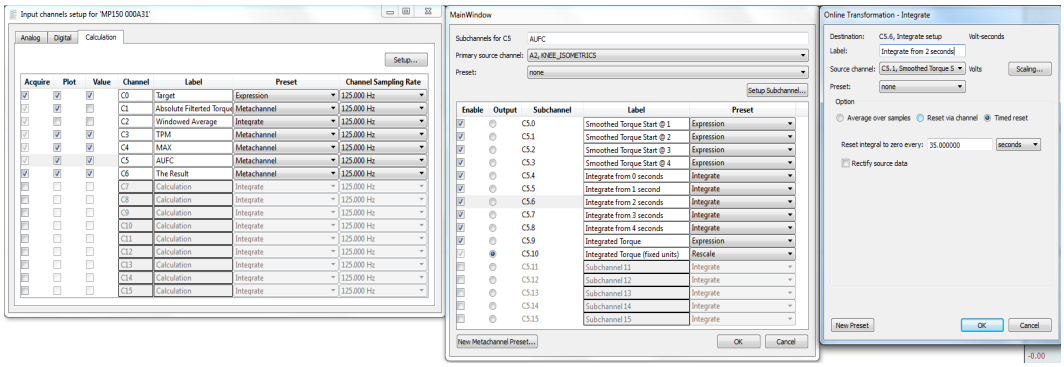

Input channels setup for 'MP150 000A31'
MainWindow
Expression
C5.1, Expression setup
Preset: none
Label: Smoothed Torque Start @ 2
Evaluate expression:
LESS(2,TIME)*C1
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C5.1
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

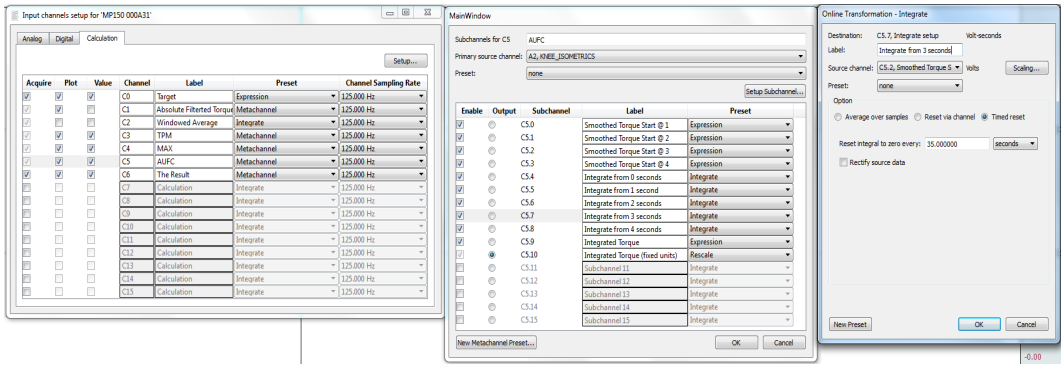

Input channels setup for 'MP150 000A31'
MainWindow
Expression
C5.2, Expression setup
Preset: none
Label: Smoothed Torque Start @ 3
Evaluate expression:
LESS(3,TIME)*C1
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C5.2
Operators: +
New Preset
Clear
OK
Cancel
1500.00
1000.00
500.00
-0.00
Volt-seconds

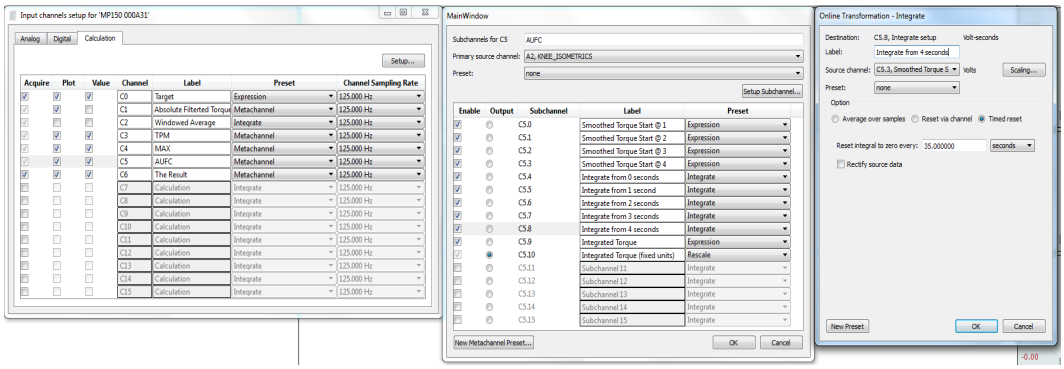

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C5.3, Expression setup
Preset: none
Label: Smoothed Torque Start @ 4
Evaluate expression:
LESS(4,TIME)*C1
Sources: A2, KNEE_ISOMETRICS
Functions: ABS()
Destination: C5.3
Operators: +
New Preset
Clear
OK
Cancel
-0.00
1500.00
1000.00
500.00
-0.00
Volt-seconds

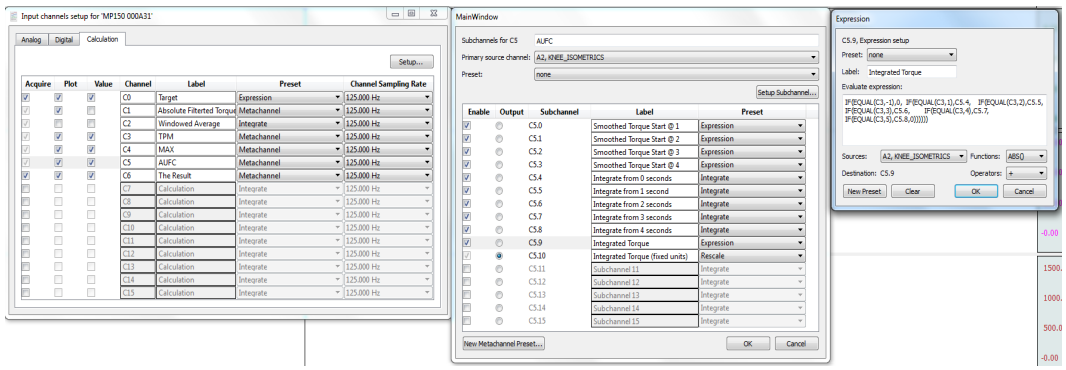

Input channels setup for 'MP150 000A31'
MainWindow
Online Transformation - Integrate
Destination: C5.4, Integrate setup
Volt-seconds
Label: Integrate from 0 seconds
Source channel: C1, Absolute Filtered Tor
Volts
Scaling...
Preset: none
Option
Average over samples
Reset via channel
Timed reset
Reset integral to zero every: 35.000000
seconds
Rectify source data
New Preset
OK
Cancel
-0.00

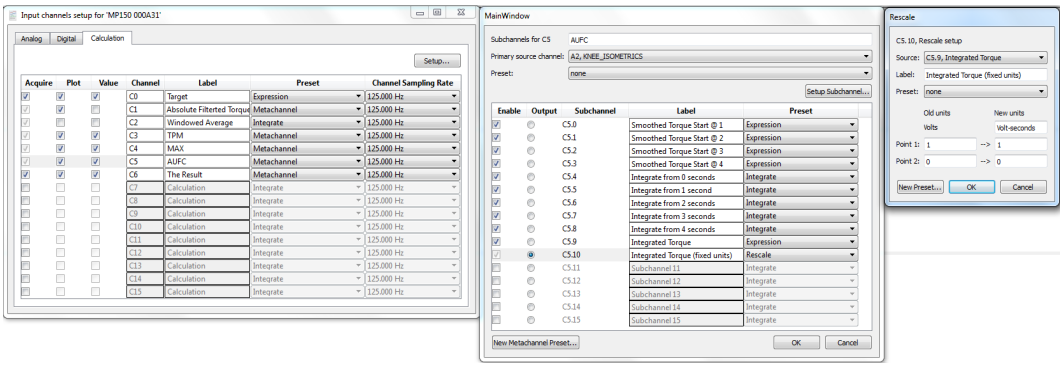

Input channels setup for 'MP150 000A31'
MainWindow
Online Transformation - Integrate
Destination: C5.5, Integrate setup
Volt-seconds
Label: Integrate from 1 second
Source channel: C5.0, Smoothed Torque S
Volts
Scaling...
Preset: none
Option
Average over samples
Reset via channel
Timed reset
Reset integral to zero every: 35.000000
seconds
Rectify source data
New Preset
OK
Cancel
-0.00

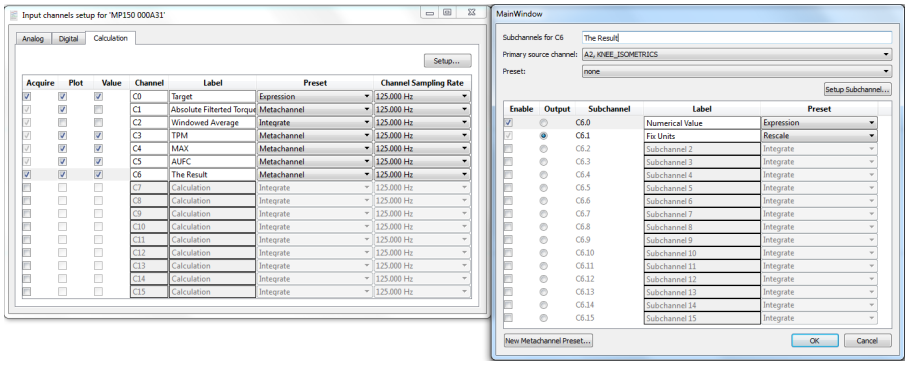

Input channels setup for 'MP150 000A31'
MainWindow
Online Transformation - Integrate
Destination: C5.6, Integrate setup
Volt-seconds
Label: Integrate from 2 seconds
Source channel: C5.1, Smoothed Torque S
Volts
Scaling...
Preset: none
Option
Average over samples
Reset via channel
Timed reset
Reset integral to zero every: 35.000000
seconds
Rectify source data
New Preset
OK
Cancel
-0.00

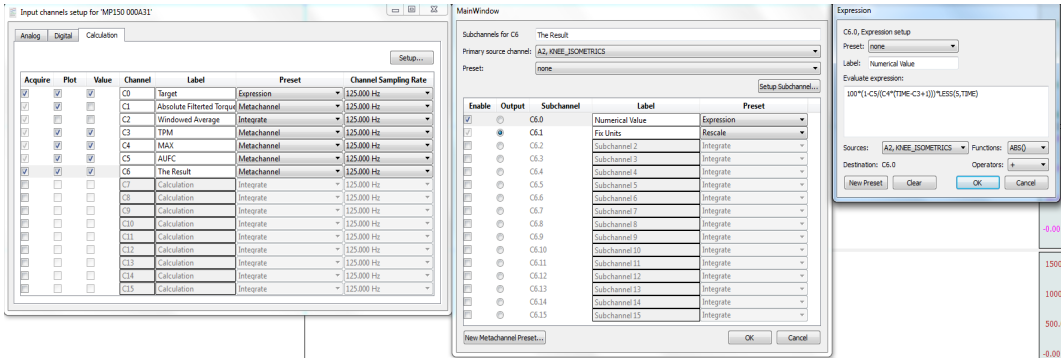

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel
Online Transformation - Integrate
Destination: C5.7, Integrate setup
Volt-seconds
Label: Integrate from 3 seconds
Source channel: C5.2, Smoothed Torque S...
Volts
Scaling...
Preset: none
Option
Average over samples
Reset via channel
Timed reset
Reset integral to zero every: 35.000000
seconds
Rectify source data
New Preset
OK
Cancel
-0.00

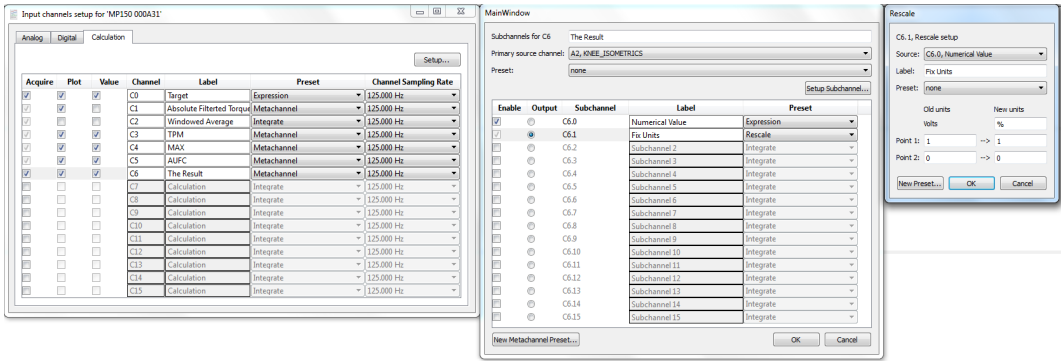

Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel
Online Transformation - Integrate
Destination: C5.8, Integrate setup
Volt-seconds
Label: Integrate from 4 seconds
Source channel: C5.3, Smoothed Torque S...
Volts
Scaling...
Preset: none
Option
Average over samples
Reset via channel
Timed reset
Reset integral to zero every: 35.000000
seconds
Rectify source data
New Preset
OK
Cancel
-0.00


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel
Expression
C5.9, Expression setup
Preset: none
Label: Integrated Torque
Evaluate expression:
IF(EQUAL(C3,-1),0, IF(EQUAL(C3,1),C5.4, IF(EQUAL(C3,2),C5.5,
IF(EQUAL(C3,3),C5.6, IF(EQUAL(C3,4),C5.7,
IF(EQUAL(C3,5),C5.8,0))))))
Sources:
A2, KNEE_ISOMETRICS
Functions:
ABS()
Destination: C5.9
Operators:
+
New Preset
Clear
OK
Cancel
-0.00
1500.
1000.
500.0
-0.00


Input channels setup for 'MP150 000A31'
Analog
Digital
Calculation
Setup...
Acquire
Plot
Value
Channel
Label
Preset
Channel Sampling Rate
C0 Target Expression 125.000 Hz
C1 Absolute Filtered Torque Metachannel 125.000 Hz
C2 Windowed Average Integrate 125.000 Hz
C3 TPM Metachannel 125.000 Hz
C4 MAX Metachannel 125.000 Hz
C5 AUFC Metachannel 125.000 Hz
C6 The Result Metachannel 125.000 Hz
C7 Calculation Integrate 125.000 Hz
C8 Calculation Integrate 125.000 Hz
C9 Calculation Integrate 125.000 Hz
C10 Calculation Integrate 125.000 Hz
C11 Calculation Integrate 125.000 Hz
C12 Calculation Integrate 125.000 Hz
C13 Calculation Integrate 125.000 Hz
C14 Calculation Integrate 125.000 Hz
C15 Calculation Integrate 125.000 Hz
MainWindow
Subchannels for C5
AUFC
Primary source channel:
A2, KNEE_ISOMETRICS
Preset:
none
Setup Subchannel...
Enable
Output
Subchannel
Label
Preset
C5.0 Smoothed Torque Start @ 1 Expression
C5.1 Smoothed Torque Start @ 2 Expression
C5.2 Smoothed Torque Start @ 3 Expression
C5.3 Smoothed Torque Start @ 4 Expression
C5.4 Integrate from 0 seconds Integrate
C5.5 Integrate from 1 second Integrate
C5.6 Integrate from 2 seconds Integrate
C5.7 Integrate from 3 seconds Integrate
C5.8 Integrate from 4 seconds Integrate
C5.9 Integrated Torque Expression
C5.10 Integrated Torque (fixed units) Rescale
C5.11 Subchannel 11 Integrate
C5.12 Subchannel 12 Integrate
C5.13 Subchannel 13 Integrate
C5.14 Subchannel 14 Integrate
C5.15 Subchannel 15 Integrate
New Metachannel Preset...
OK
Cancel
Rescale
C5.10, Rescale setup
Source:
C5.9, Integrated Torque
Label:
Integrated Torque (fixed units)
Preset:
none
Old units
Volts
New units
Volt-seconds
Point 1:
1
-->
1
Point 2:
0
-->
0
New Preset...
OK
Cancel







e. Click the start icon to confirm data acquisition and graphical representation
f. Save the data file

3. Data Processing (Figure C5)
    a. Open file
    b. Minimize force data window
    c. Select “Result” from the left column
    d. Highlight the right most portion of the result
    e. Record value

Figure C5. Fatigue Index Output

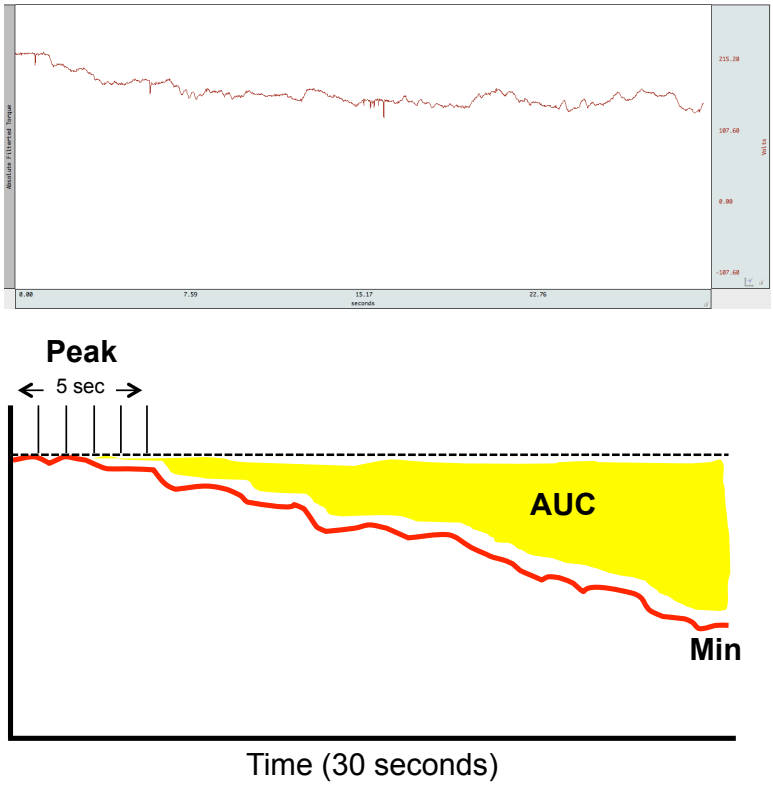


Figure C5. Represents a 30-second knee extension MVIC fatiguing task. Patients performed a knee extension MVIC force at 90 degrees of knee flexion, and attempted to maintain for 30 seconds. The mean torque was recorded from a series of 1-second epochs, and the greatest torque epoch during the first 5 seconds of the trial was recorded as the maximal torque (T_{Max}). Quadriceps FI was calculated using the area under the force-time curve (AUFC) for the entire contraction period for 0 to 30 seconds, which began at the time point of maximum muscle torque (TPM). Fatigue index was calculated as FI = [1-($AUFC_{TPM-30}$/($T_{Max,0-5}$ x (TPM-30)))] x 100.

Table C16. Transcranial Magnetic Stimulation Setup and Procedures

1. Biopac System Setup
    a. Connect an UIM100C and EMG100C to the MP150 unit
    b. Connect the MP150 to the computer using a LAN wire
    c. Turn on the MP150 unit and the computer
    d. EMG100C settings
        i. Gain = 1000
        ii. Filter = Off
        iii. LP = 5 kHz
        iv. HP = 1.0 Hz

2. Magstim Rapid Setup
    a. Insert the footswitch connector in the "Foot Switch" port on the back of the Magstim device
    b. Insert the Magstim output cable to the "Trigger Out" port on the back of the Magstim device, and to channel 3 of the UIM100C
    c. Connect the output cable of the Booster Module Plus to the front of the Booster Module device and back of the Magstim device
    d. Connect the stimulating coil to the Magstim device using the port on the front of the machine
    e. Turn the main power switch located on the front of the Booster Module device to the ON position
    f. Turn the Magstim device on using the ON/OFF button on the front panel
        i. The Unit Power Status Indicator should remain lit throughout the testing session
    g. Press the green RUN button to charge the unit and illuminate the ready indicator

3. AcqKnowledge 4.2.0 Setup (TMS Template)
    a. Open AcqKnowledge 4.2.0 for Mac and select the attached MP150 unit (Laptop used for this)
    b. MP150| Setup Channels| Analog menu
        i. Channel 1
            1. Sample Rate = 125 Hz
            2. Label = Torque
            3. Check all boxes associated with this channel
        ii. Channel 2
            1. Sample Rate = 2000 Hz
            2. Label = MEP
            3. Check all boxes associated with this channel
        iii. Channel 3
            1. Sample Rate = 125 Hz
            2. Label = TMS
            3. Check all boxes associated with this channel
    c. MP150| Set Up Acquisition
        i. Change menus to "Record" and "Append"
        ii. Sample Rate = 2000 Hz
        iii. Acquisition Length = 80 msec
    d. Open the data journal and graph window
    e. Click the start button to confirm proper setup

4. AcqKnowledge 4.2.0 Setup (Torque_TMS Template)
    a. Open AcqKnowledge 4.2.0 for Windows and select the attached MP150 unit
    b. MP150| Setup Channels| Analog menu
        i. Channel 2
            1. Sample Rate = 200 Hz
            2. Label = Force
            3. Check all boxes associated with this channel
    c. MP150| Setup Channels| Calculation menu
        i. Channel 0
            1. Label = C0 – Expression
            2. Preset = Expression
            3. Sample Rate = 200 Hz
        ii. Setup (C0 – Expression)
            1. Preset = None
            2. Label = C0 – Expression
            3. Evaluate Expression = <<Insert voltage = 5% MVIC>>
            4. Sources = A2, Force
            5. Functions = ABS()
            6. Operators = +
        iii. Setup (C1 – Math)
            1. Preset = None
            2. Label = C1 – Math
            3. Source 1 = A2, Force
            4. Operation = a
            5. Source 2 = K, Constant
            6. Constant = 0.05
    d. MP150| Set Up Acquisition
        i. Change menus to “Record” and “Append”
        ii. Sample Rate = 200 Hz
        iii. Acquisition Length = 10 min
    e. Open the data journal and graph window
    f. Click the start button to confirm proper setup

5. Subject Preparation (Figure C6)
    a. Identify the vastus medialis during isometric knee extension
        i. Shave the area
        ii. Debride with an abrasive pad
        iii. Clean with isopropyl alcohol
    b. Place 2 EMG electrodes in the prepared area
        i. Parallel to the muscle fiber orientation
        ii. Interelectrode distance of 2 cm
    c. Identify an area on the distal anteromedial tibia for the ground electrode
        i. Shave the area
        ii. Debride with an abrasive pad
        iii. Clean with isopropyl alcohol
    d. Place 1 EMG electrode in the prepared area
    e. Position the subject in the dynamometer chair in an upright seated posture
        i. Knees flexed to 90 degrees
        ii. Hips flexed to 80 degrees
        iii. Restrain the subject using the lap strap
        iv. Engage the ankle strap 2 cm proximal to the lateral malleolus

f. Attach the leads from the EMG100C unit to the active and reference electrodes
    i. Proximal active = Red lead
    ii. Distal active = White lead
    iii. Reference = Black lead
g. Place a pre-marked nylon swim-cap on the subject's head
    i. Marked with two perpendicular lines from:
        1. Left tragi to right tragi
        2. External occipital protuberance to midline near the midline
    ii. Marked with dots in a grid pattern – 1 cm apart
h. Provide earplugs for the subject to be worn throughout testing
i. Ask the subject to relax, breathe normally, fold hands in lap, and keep head back against the headrest.
    i. Subjects were asked to "kick" to a red line, indicating 5% MVIC, then to relax the leg after the stimulus was delivered
j. Turn off the lights and any additional unnecessary electronics

6. Data Collection Procedures (Figure C6)
    a. Position the stimulating coil over the contralateral homunculus of the testing limb near the central sulcus
        i. Tape piece of paper under central curve of stimulating coil with vertical line drawn extending to the superior and inferior border
        ii. Move coil in 0.5-1 cm increments, aligning the drawn line with a dot on the swim cap
        iii. The homunculus should correspond the area near the cross of the perpendicular lines on the swim-cap
    b. Set the Magstim output to 60%
    c. Click the START button within the Acqknowledge software (on each computer)
    d. Depress the Magstim footswitch
    e. Press and hold the trigger on the stimulating coil
    f. Review the data for motor response in the EMG (MEP) channel
        i. If positive for motor response
            1. Record MEP amplitude in journal, noting the corresponding location from the vertex (i.e. -6, -2)
            2. Repeat stimulus in radius around this point
            3. Continue until the maximum MEP amplitude has been found, and a 1-cm radius around this point has been assessed
            4. Decrease the stimulation intensity by 5%, and re-stimulate
            5. When no response is observed, increase the stimulation intensity by 1% and repeat stimulus until MEP is detected
            6. Wait at least 10 seconds between stimulations
        ii. If negative for motor response, re-position and repeat at same stimulus intensity
            1. Continue until 1-cm radius has been stimulated
            2. If no response, increase stimulus intensity by 5%, and re-stimulate
    g. Continue to decrease the stimulus intensity until MEP is measured
        i. Once confirmed, deliver 10 stimulations
        ii. If positive for MEP in at least 50% of trials, end testing
        iii. If negative for MEP in at least 60% of trials, increase stimulus intensity 1% and test again.

7. Data Processing
    a. During testing, record the peak-to-peak amplitude (P-P), time from stimulus artifact to onset of MEP (delta T), and time for each MEP in the journal of AcqKnowledge – coordinates should be documented when searching for the ideal coil position, or "hotspot," during subsequent testing
    b. Record the active motor threshold (AMT) as the intensity required for 50% success during 10 consecutive trials
    c. Record P-P, Delta T, and time for MEPs detected at 120%, 130%, and 140% MEP
        i. Record the stimulus intensity at each percentage
        ii. Record a minimum of five acceptable trials

Figure C6. Transcranial Magnetic Stimulation Procedures

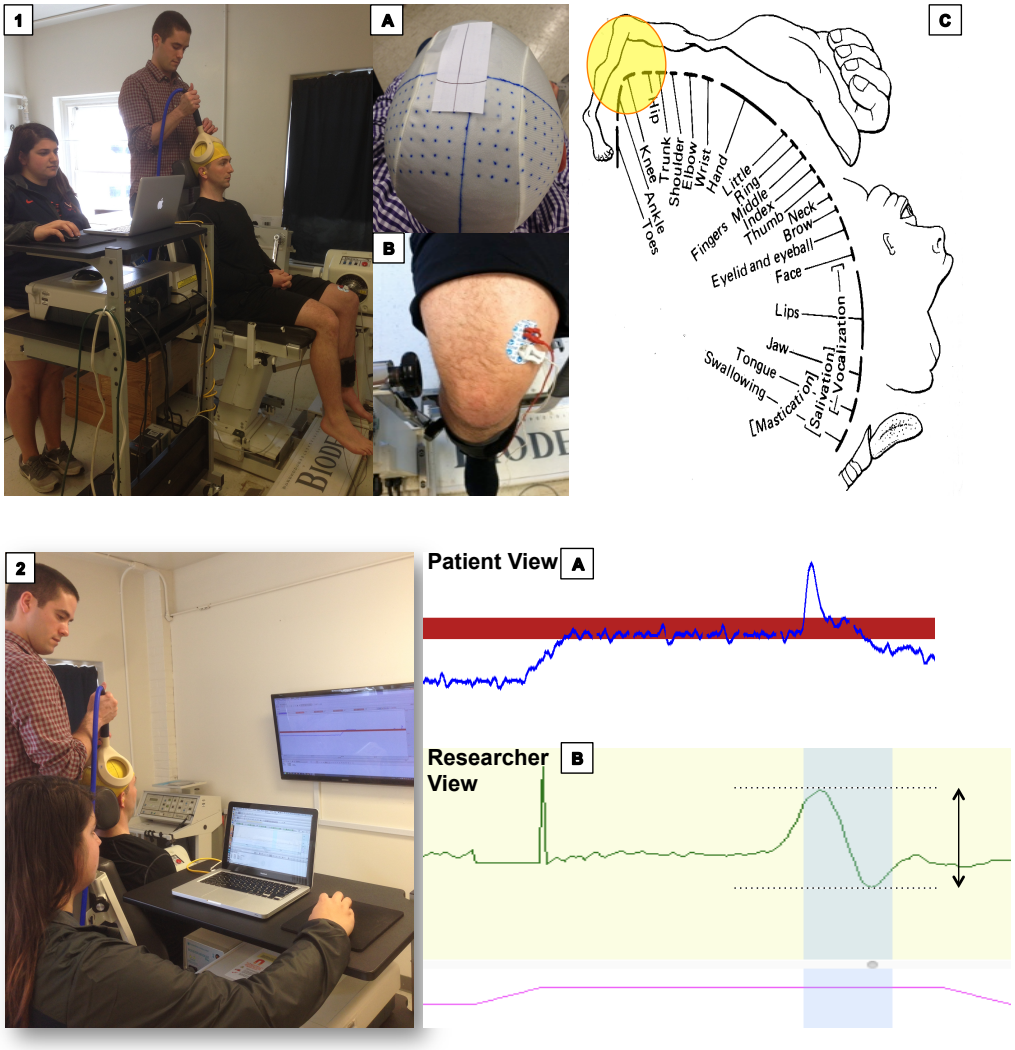


Figure C6. Image 1 illustrates TMS setup, including (A) swim cap to use a grid for optimal coil placement, (B) surface EMG electrode placement over the vastus medialis, and (C) location of stimulus over the motor cortex as depicted by the motor homunculus. Image 2 illustrates the (A) 5% MVIC force matching task performed by the patient, and (B) recording of peak-peak motor evoked potential. Stimulus intensity was reduced until a MEP was no longer detectable. The lowest intensity able to elicit a measurable MEP was recorded as the active motor threshold.

Table C17. Sample Size Estimate

Outcome	Minimal Detectable Change (MDC)	Expected Variance (SD)	Sample Estimate	Source
MVIC (N)	47.8	± 59.1	24	Park and Hopkins, 2013
Fatigue (%)	11.0	± 9.0	11	Poulsen, 2015
CAR (%)	6.0	± 6.0	16	Park and Hopkins, 2014
H:M ratio	0.30	± 0.22	11	Hopkins and Waggie, 2003
AMT (%)	8.4	± 8.0	14	Luc, 2013

APPENDIX D

Additional Results

MANUSCRIPT I

Table D1. ANOVA comparison of group and limb for normalized knee extension MVIC torque

Dependent Variable: MVIC

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	24.092[a]	7	3.442	8.353	.000
Intercept	732.679	1	732.679	1778.177	.000
Group_Small_Stack	14.376	3	4.792	11.630	.000
Limb	2.269	1	2.269	5.508	.020
Group_Small_Stack * Limb	5.962	3	1.987	4.823	.003
Error	79.936	194	.412		
Total	1254.001	202			
Corrected Total	104.028	201			

a. R Squared = .232 (Adjusted R Squared = .204)

Table D2. Post hoc analyses from ANOVA comparison of group and limb for normalized knee extension MVIC torque

Dependent Variable: MVIC

	(I) Group_Small_Stack	(J) Group_Small_Stack	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
LSD	Healthy	6-12 month	.5032*	.11421	.000	.2780	.7285
		2-10 year	.5094*	.11769	.000	.2773	.7415
		OA	.8998*	.18562	.000	.5337	1.2659
	6-12 month	Healthy	-.5032*	.11421	.000	-.7285	-.2780
		2-10 year	.0062	.11370	.957	-.2181	.2304
		OA	.3966*	.18311	.032	.0354	.7577
	2-10 year	Healthy	-.5094*	.11769	.000	-.7415	-.2773
		6-12 month	-.0062	.11370	.957	-.2304	.2181
		OA	.3904*	.18530	.036	.0249	.7559
	OA	Healthy	-.8998*	.18562	.000	-1.2659	-.5337
		6-12 month	-.3966*	.18311	.032	-.7577	-.0354
		2-10 year	-.3904*	.18530	.036	-.7559	-.0249
Dunnett t (2-sided)[b]	6-12 month	Healthy	-.5032*	.11421	.000	-.7753	-.2311
	2-10 year	Healthy	-.5094*	.11769	.000	-.7898	-.2290
	OA	Healthy	-.8998*	.18562	.000	-1.3420	-.4576

Based on observed means.
The error term is Mean Square(Error) = .412.

*. The mean difference is significant at the

b. Dunnett t-tests treat one group as a control, and compare all other groups against it.

Table D3. Between limb comparisons of normalized knee extension MVIC torque per group

Group_Small_Stack			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Healthy	Pair 1	Norm_MVIC_Torque_Inv - Norm_MVIC_Torque_Un	.08702	.34571	.06312	-.04206	.21611	1.379	29	.179
6-12 month	Pair 1	Norm_MVIC_Torque_Inv - Norm_MVIC_Torque_Un	-.71558	.55245	.09474	-.90834	-.52282	-7.553	33	.000
2-10 year	Pair 1	Norm_MVIC_Torque_Inv - Norm_MVIC_Torque_Un	-.12192	.29003	.05295	-.23022	-.01362	-2.303	29	.029
OA	Pair 1	Norm_MVIC_Torque_Inv - Norm_MVIC_Torque_Un	-.18086	.48965	.17312	-.59022	.22849	-1.045	7	.331

Table D4. ANOVA comparison of group and limb for quadriceps fatigue index

Dependent Variable: Fatigue

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1484.459[a]	7	212.066	3.090	.004
Intercept	56713.668	1	56713.668	826.366	.000
Group_Small_Stack	1001.253	3	333.751	4.863	.003
Limb	17.025	1	17.025	.248	.619
Group_Small_Stack * Limb	372.213	3	124.071	1.808	.147
Error	13245.635	193	68.630		
Total	95313.823	201			
Corrected Total	14730.094	200			

a. R Squared = .101 (Adjusted R Squared = .068)

Table D5. Post hoc analyses from ANOVA comparison of group and limb for quadriceps fatigue index

Dependent Variable: Fatigue

	(I) Group_Small_Stack	(J) Group_Small_Stack	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	Upper Bound
LSD	Healthy	6-12 month	5.1158*	1.48073	.001	2.1953	8.0363
		2-10 year	.6770	1.52549	.658	-2.3317	3.6858
		OA	1.4239	2.39971	.554	-3.3091	6.1569
	6-12 month	Healthy	-5.1158*	1.48073	.001	-8.0363	-2.1953
		2-10 year	-4.4388*	1.46735	.003	-7.3328	-1.5447
		OA	-3.6919	2.36318	.120	-8.3529	.9691
	2-10 year	Healthy	-.6770	1.52549	.658	-3.6858	2.3317
		6-12 month	4.4388*	1.46735	.003	1.5447	7.3328
		OA	.7469	2.39148	.755	-3.9699	5.4637
	OA	Healthy	-1.4239	2.39971	.554	-6.1569	3.3091
		6-12 month	3.6919	2.36318	.120	-.9691	8.3529
		2-10 year	-.7469	2.39148	.755	-5.4637	3.9699
Dunnett t (2-sided)[b]	6-12 month	Healthy	-5.1158*	1.48073	.002	-8.6430	-1.5886
	2-10 year	Healthy	-.6770	1.52549	.950	-4.3108	2.9567
	OA	Healthy	-1.4239	2.39971	.893	-7.1401	4.2923

Based on observed means.
The error term is Mean Square(Error) = 68.630.

*. The mean difference is significant at the

b. Dunnett t-tests treat one group as a control, and compare all other groups against it.

Table D6. Between limb comparisons of quadriceps fatigue index per group

Group_Small_Stack			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Healthy	Pair 1	Fatigue_Inv - Fatigue_Un	-.41663	6.22494	1.15594	-2.78447	1.95121	-.360	28	.721
6-12 month	Pair 1	Fatigue_Inv - Fatigue_Un	-5.20853	8.90125	1.52655	-8.31432	-2.10274	-3.412	33	.002
2-10 year	Pair 1	Fatigue_Inv - Fatigue_Un	.65618	6.04112	1.10295	-1.59961	2.91197	.595	29	.557
OA	Pair 1	Fatigue_Inv - Fatigue_Un	1.84308	4.64721	1.64304	-2.04208	5.72825	1.122	7	.299

Table D7. ANOVA comparison of group and limb for quadriceps central activation ratio

Dependent Variable: CAR

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	.181[a]	7	.026	3.149	.004
Intercept	114.572	1	114.572	13922.128	.000
Group_Small_Stack	.168	3	.056	6.817	.000
Limb	.001	1	.001	.137	.711
Group_Small_Stack * Limb	.009	3	.003	.361	.781
Error	1.588	193	.008		
Total	166.211	201			
Corrected Total	1.770	200			

a. R Squared = .103 (Adjusted R Squared = .070)

Table D8. Post hoc analyses from ANOVA comparison of group and limb for quadriceps central activation ratio

Dependent Variable: CAR

	(I) Group_Small_Stack	(J) Group_Small_Stack	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	Upper Bound
LSD	Healthy	6-12 month	.0715*	.01621	.000	.0396	.1035
		2-10 year	.0320	.01670	.057	-.0009	.0650
		OA	.0143	.02628	.588	-.0376	.0661
	6-12 month	Healthy	-.0715*	.01621	.000	-.1035	-.0396
		2-10 year	-.0395*	.01607	.015	-.0712	-.0078
		OA	-.0573*	.02588	.028	-.1083	-.0062
	2-10 year	Healthy	-.0320	.01670	.057	-.0650	.0009
		6-12 month	.0395*	.01607	.015	.0078	.0712
		OA	-.0177	.02619	.499	-.0694	.0339
	OA	Healthy	-.0143	.02628	.588	-.0661	.0376
		6-12 month	.0573*	.02588	.028	.0062	.1083
		2-10 year	.0177	.02619	.499	-.0339	.0694
Dunnett t (2-sided)[b]	6-12 month	Healthy	-.0715*	.01621	.000	-.1102	-.0329
	2-10 year	Healthy	-.0320	.01670	.147	-.0718	.0078
	OA	Healthy	-.0143	.02628	.915	-.0769	.0483

Based on observed means.
The error term is Mean Square(Error) = .008.

*. The mean difference is significant at the

b. Dunnett t-tests treat one group as a control, and compare all other groups against it.

Table D9. Between limb comparisons of quadriceps fatigue index per group

Group_Small_Stack			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Healthy	Pair 1	CAR_Inv - CAR_Un	.01331	.05220	.00969	-.00654	.03317	1.373	28	.181
6-12 month	Pair 1	CAR_Inv - CAR_Un	-.02628	.07879	.01351	-.05377	.00122	-1.945	33	.060
2-10 year	Pair 1	CAR_Inv - CAR_Un	-.00478	.06627	.01210	-.02952	.01997	-.395	29	.696
OA	Pair 1	CAR_Inv - CAR_Un	-.00273	.06042	.02136	-.05324	.04778	-.128	7	.902

Table D10. ANOVA comparison of group and limb for normalized quadriceps Hoffmann reflex

Dependent Variable: HM

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	.251[a]	7	.036	1.221	.293
Intercept	4.656	1	4.656	158.790	.000
Group_Small_Stack	.216	3	.072	2.454	.065
Limb	.000	1	.000	.011	.916
Group_Small_Stack * Limb	.022	3	.007	.253	.859
Error	5.161	176	.029		
Total	11.487	184			
Corrected Total	5.411	183			

a. R Squared = .046 (Adjusted R Squared = .008)

Table D11. Post hoc analyses from ANOVA comparison of group and limb for normalized quadriceps Hoffmann reflex

Dependent Variable: HM

	(I) Group_Small_Stack	(J) Group_Small_Stack	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	Upper Bound
LSD	Healthy	6-12 month	-.0340	.03259	.298	-.0983	.0303
		2-10 year	-.0605	.03328	.071	-.1261	.0052
		OA	-.1372*	.05527	.014	-.2462	-.0281
	6-12 month	Healthy	.0340	.03259	.298	-.0303	.0983
		2-10 year	-.0264	.03079	.392	-.0872	.0343
		OA	-.1031	.05380	.057	-.2093	.0030
	2-10 year	Healthy	.0605	.03328	.071	-.0052	.1261
		6-12 month	.0264	.03079	.392	-.0343	.0872
		OA	-.0767	.05423	.159	-.1837	.0303
	OA	Healthy	.1372*	.05527	.014	.0281	.2462
		6-12 month	.1031	.05380	.057	-.0030	.2093
		2-10 year	.0767	.05423	.159	-.0303	.1837
Dunnett t (2-sided)[b]	6-12 month	Healthy	.0340	.03259	.609	-.0435	.1116
	2-10 year	Healthy	.0605	.03328	.179	-.0188	.1397
	OA	Healthy	.1372*	.05527	.039	.0056	.2687

Based on observed means.
The error term is Mean Square(Error) = .029.

*. The mean difference is significant at the

b. Dunnett t-tests treat one group as a control, and compare all other groups against it.

Table D12. Between limb comparisons of normalized quadriceps Hoffmann reflex per group

			Paired Differences							
						95% Confidence Interval of the Difference				
Group_Small_Stack			Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)
Healthy	Pair 1	HM_Inv - HM_Un	-.00028	.08727	.01820	-.03802	.03746	-.015	22	.988
6-12 month	Pair 1	HM_Inv - HM_Un	.02957	.11048	.01984	-.01096	.07009	1.490	30	.147
2-10 year	Pair 1	HM_Inv - HM_Un	.02434	.09167	.01702	-.01053	.05921	1.430	28	.164
OA	Pair 1	HM_Inv - HM_Un	-.03864	.20631	.08423	-.25515	.17788	-.459	5	.666

Table D13. ANOVA comparison of group and limb for quadriceps active motor threshold

Dependent Variable: AMT

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1725.564[a]	7	246.509	4.399	.000
Intercept	251555.698	1	251555.698	4489.207	.000
Group_Small_Stack	1632.479	3	544.160	9.711	.000
Limb	55.999	1	55.999	.999	.319
Group_Small_Stack * Limb	37.476	3	12.492	.223	.880
Error	9694.171	173	56.036		
Total	350316.000	181			
Corrected Total	11419.735	180			

a. R Squared = .151 (Adjusted R Squared = .117)

Table D14. Post hoc analyses from ANOVA comparison of group and limb for quadriceps active motor threshold

Dependent Variable: AMT

						95% Confidence Interval	
	(I) Group_Small_Stack	(J) Group_Small_Stack	Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
LSD	Healthy	6-12 month	-6.5778*	1.47148	.000	-9.4822	-3.6735
		2-10 year	-3.7025*	1.50642	.015	-6.6758	-.7292
		OA	-10.1163*	2.24474	.000	-14.5469	-5.6857
	6-12 month	Healthy	6.5778*	1.47148	.000	3.6735	9.4822
		2-10 year	2.8753*	1.35212	.035	.2066	5.5441
		OA	-3.5385	2.14425	.101	-7.7707	.6938
	2-10 year	Healthy	3.7025*	1.50642	.015	.7292	6.6758
		6-12 month	-2.8753*	1.35212	.035	-5.5441	-.2066
		OA	-6.4138*	2.16837	.004	-10.6937	-2.1339
	OA	Healthy	10.1163*	2.24474	.000	5.6857	14.5469
		6-12 month	3.5385	2.14425	.101	-.6938	7.7707
		2-10 year	6.4138*	2.16837	.004	2.1339	10.6937
Dunnett t (2-sided)[b]	6-12 month	Healthy	6.5778*	1.47148	.000	3.0837	10.0720
	2-10 year	Healthy	3.7025*	1.50642	.040	.1254	7.2796
	OA	Healthy	10.1163*	2.24474	.000	4.7860	15.4466

Based on observed means.
The error term is Mean Square(Error) = 56.036.

*. The mean difference is significant at the

b. Dunnett t-tests treat one group as a control, and compare all other groups against it.

Table D15. Between limb comparisons of quadriceps active motor threshold per group

Group_Small_Stack			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Healthy	Pair 1	AMT_MSO_Inv - AMT_MSO_Un	-.10526	4.53253	1.03983	-2.28987	2.07935	-.101	18	.920
6-12 month	Pair 1	AMT_MSO_Inv - AMT_MSO_Un	.75000	8.00403	1.41493	-2.13576	3.63576	.530	31	.600
2-10 year	Pair 1	AMT_MSO_Inv - AMT_MSO_Un	.48276	4.91078	.91191	-1.38520	2.35072	.529	28	.601
OA	Pair 1	AMT_MSO_Inv - AMT_MSO_Un	2.50000	3.81725	1.34960	-.69130	5.69130	1.852	7	.106

Figure D1. Quadriceps function limb symmetry for healthy (◆), early ACL-R (■), late ACL-R (O), and ACL-R with osteoarthritis (Δ). Point estimates represent mean values with associated 95% confidence intervals.

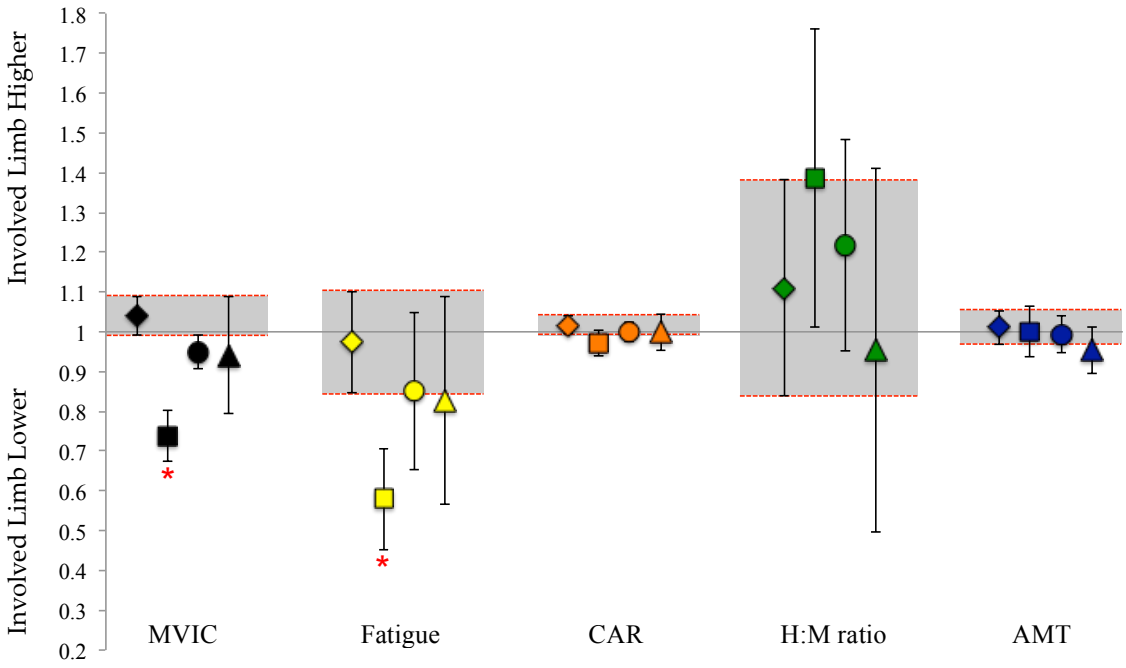


Figure D2. Cohen's *d* effect sizes with 95% confidence intervals comparing subjective outcomes in each ACL reconstructed group to healthy controls. Negative values indicate that ACL reconstructed patients reported worse values than healthy controls.

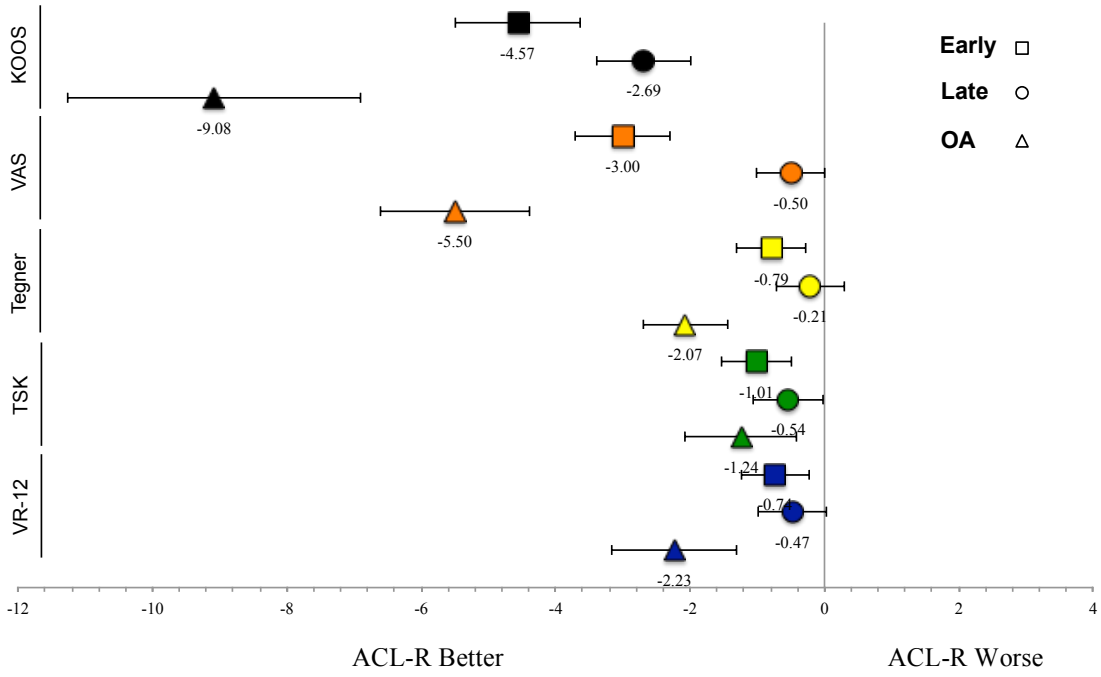


Figure D3. Pearson's *r* or Spearman's ρ correlation coefficients between measures of involved limb quadriceps function and time since surgery in ACL reconstructed patients

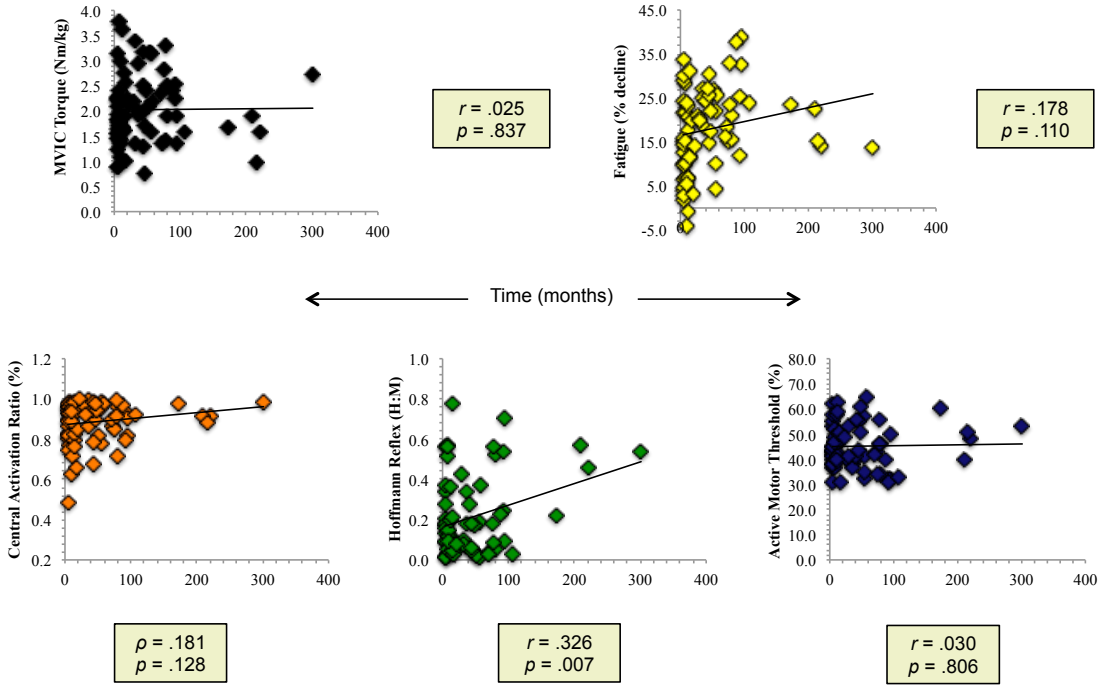


Figure D4. Pearson's *r* or Spearman's ρ correlation coefficients between measures of involved limb quadriceps function and age in ACL reconstructed patients

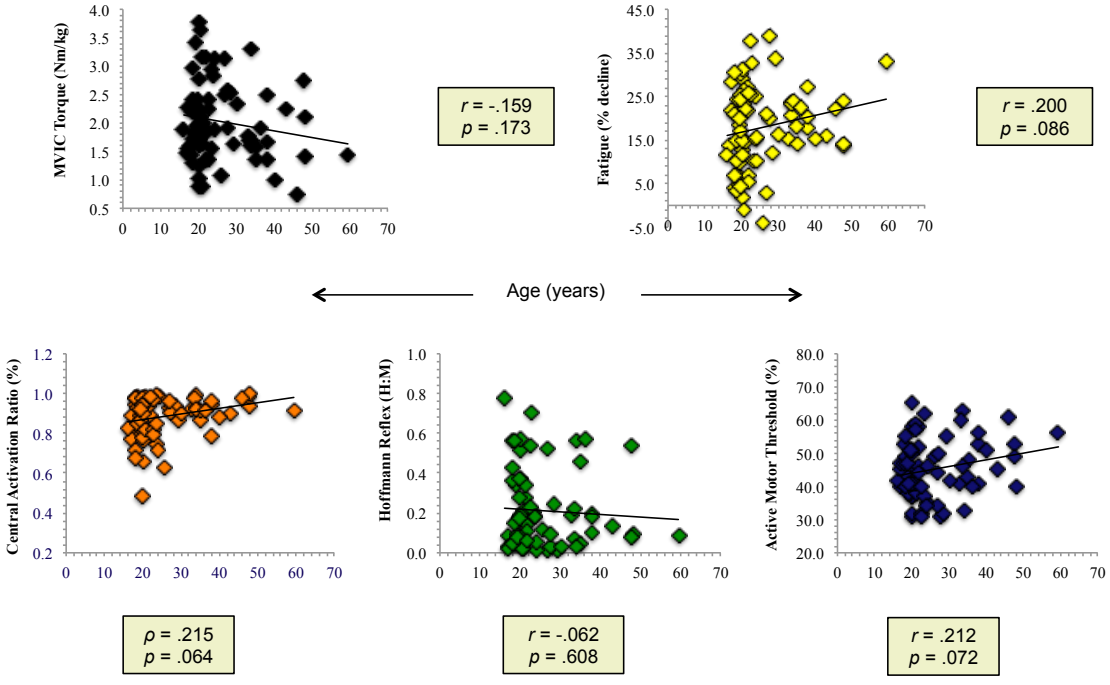


Figure D5. Independent *t* tests comparing measures of involved limb quadriceps function between male and female ACL reconstructed patients

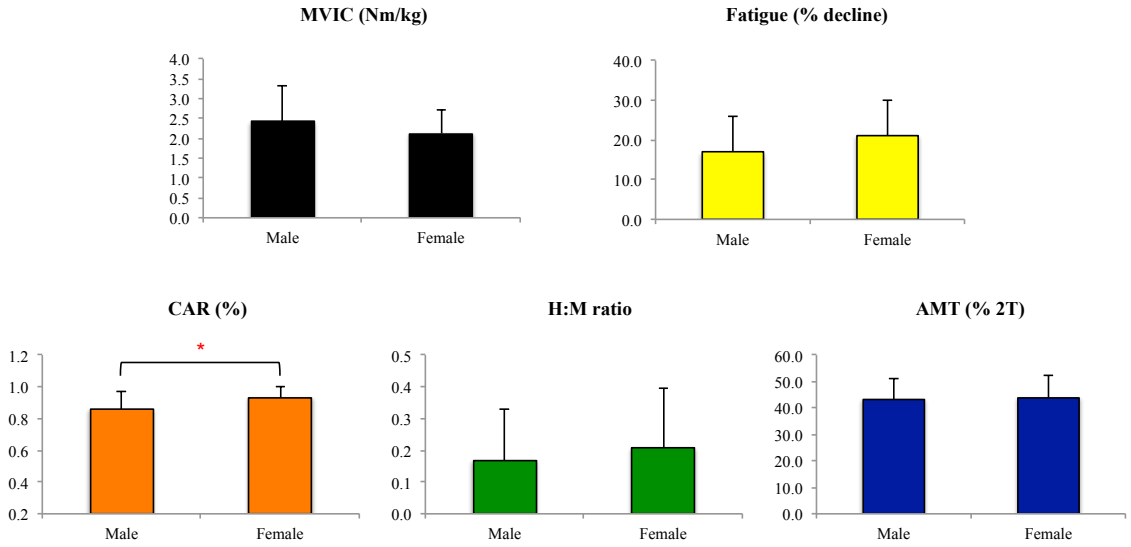
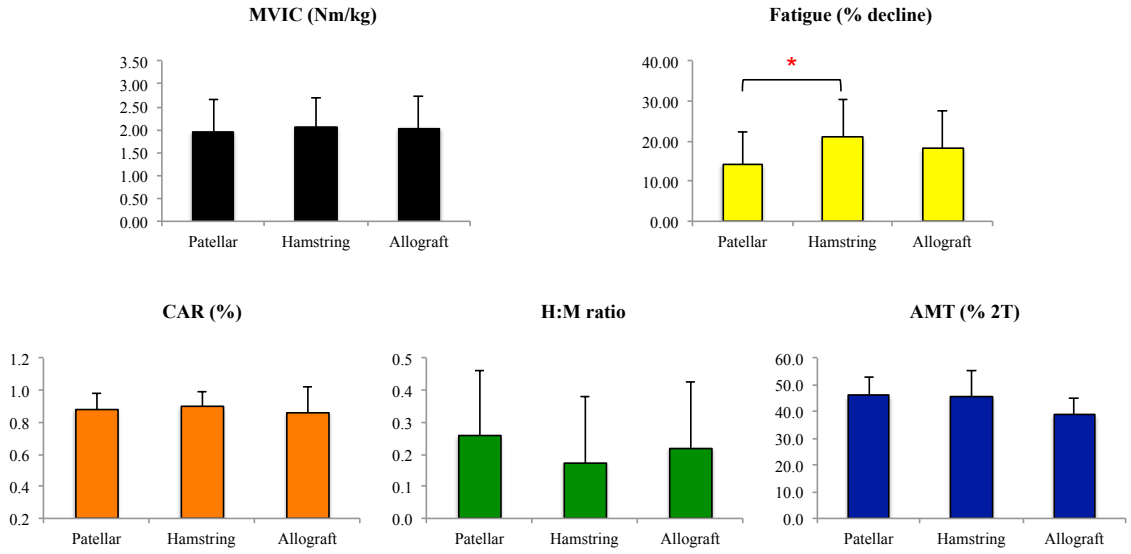


Figure D6. ANOVA comparison of graft type for measures of involved limb quadriceps function in ACL reconstructed patients



MANUSCRIPT II

Table D16. Multiple regression model summary to predict knee function (KOOS) in ACL reconstructed patients per group

						Change Statistics				
Group_Small_Stack	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	R Square Change	F Change	df1	df2	Sig. F Change
6-12 month	1	.627[a]	.393	.374	7.34833	.393	20.711	1	32	.000
	2	.760[b]	.578	.551	6.22644	.185	13.570	1	31	.001
	3	.813[c]	.662	.628	5.66695	.084	7.423	1	30	.011
	4	.841[d]	.708	.668	5.35390	.046	4.611	1	29	.040
	5	.867[e]	.752	.708	5.01759	.044	5.018	1	28	.033
2-10 year	1	.445[f]	.198	.169	5.45797	.198	6.899	1	28	.014
OA	1	.771[g]	.595	.527	7.45126	.595	8.806	1	6	.025
	2	.917[h]	.841	.778	5.10887	.246	7.763	1	5	.039

a. Predictors: (Constant), Norm_Work_Ext_90_Inv

b. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv

c. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv

d. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv, LSI_AMT

e. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv, LSI_AMT, Tegner_Current

f. Predictors: (Constant), LSI_Peak_Torque_Ext_90

g. Predictors: (Constant), Tampa

h. Predictors: (Constant), Tampa, Norm_Torque_Ext_90_Inv

Table D17. ANOVA to predict knee function (KOOS) in ACL reconstructed patients per group

Group_Small_Stack	Model		Sum of Squares	df	Mean Square	F	Sig.
6-12 month	1	Regression	1118.334	1	1118.334	20.711	.000[b]
		Residual	1727.933	32	53.998		
		Total	2846.267	33			
	2	Regression	1644.443	2	822.221	21.208	.000[c]
		Residual	1201.825	31	38.769		
		Total	2846.267	33			
	3	Regression	1882.836	3	627.612	19.543	.000[d]
		Residual	963.431	30	32.114		
		Total	2846.267	33			
	4	Regression	2015.005	4	503.751	17.574	.000[e]
		Residual	831.262	29	28.664		
		Total	2846.267	33			
	5	Regression	2141.333	5	428.267	17.011	.000[f]
		Residual	704.934	28	25.176		
		Total	2846.267	33			
2-10 year	1	Regression	205.524	1	205.524	6.899	.014[g]
		Residual	834.104	28	29.789		
		Total	1039.628	29			
OA	1	Regression	488.912	1	488.912	8.806	.025[h]
		Residual	333.128	6	55.521		
		Total	822.040	7			
	2	Regression	691.537	2	345.769	13.248	.010[i]
		Residual	130.503	5	26.101		
		Total	822.040	7			

a. Dependent Variable: KOOS_Total

b. Predictors: (Constant), Norm_Work_Ext_90_Inv

c. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv

d. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv

e. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv, LSI_AMT

f. Predictors: (Constant), Norm_Work_Ext_90_Inv, VAS_Inv, Norm_Torque_Ext_90_Inv, LSI_AMT, Tegner_Current

g. Predictors: (Constant), LSI_Peak_Torque_Ext_90

h. Predictors: (Constant), Tampa

i. Predictors: (Constant), Tampa, Norm_Torque_Ext_90_Inv

Table D18. Multiple regression coefficients to predict knee function (KOOS) in ACL reconstructed patients per group

Group_Small_Stack	Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
			B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
6-12 month	1	(Constant)	66.090	4.867		13.580	.000	56.176	76.003
		Norm_Work_Ext_90_Inv	1.496	.329	.627	4.551	.000	.826	2.165
	2	(Constant)	72.356	4.461		16.220	.000	63.258	81.454
		Norm_Work_Ext_90_Inv	1.304	.283	.546	4.601	.000	.726	1.882
		VAS_Inv	-4.465	1.212	-.437	-3.684	.001	-6.937	-1.993
	3	(Constant)	72.960	4.066		17.944	.000	64.656	81.264
		Norm_Work_Ext_90_Inv	3.548	.863	1.487	4.111	.000	1.785	5.310
		VAS_Inv	-4.650	1.105	-.456	-4.207	.000	-6.907	-2.393
		Norm_Torque_Ext_90_Inv	-20.495	7.522	-.987	-2.725	.011	-35.857	-5.132
	4	(Constant)	84.960	6.781		12.528	.000	71.091	98.830
		Norm_Work_Ext_90_Inv	3.201	.831	1.342	3.851	.001	1.501	4.901
		VAS_Inv	-4.142	1.071	-.406	-3.869	.001	-6.332	-1.952
		Norm_Torque_Ext_90_Inv	-17.920	7.207	-.863	-2.486	.019	-32.660	-3.180
		LSI_AMT	-11.528	5.369	-.226	-2.147	.040	-22.509	-.548
	5	(Constant)	82.608	6.442		12.824	.000	69.413	95.803
		Norm_Work_Ext_90_Inv	2.556	.831	1.071	3.078	.005	.855	4.258
		VAS_Inv	-4.359	1.008	-.427	-4.324	.000	-6.424	-2.294
		Norm_Torque_Ext_90_Inv	-13.952	6.983	-.672	-1.998	.056	-28.255	.352
		LSI_AMT	-12.977	5.073	-.255	-2.558	.016	-23.369	-2.586
		Tegner_Current	1.122	.501	.234	2.240	.033	.096	2.148
2-10 year	1	(Constant)	72.308	7.594		9.522	.000	56.752	87.864
		LSI_Peak_Torque_Ext_90	20.970	7.984	.445	2.627	.014	4.616	37.324
OA	1	(Constant)	126.959	17.236		7.366	.000	84.784	169.134
		Tampa	-1.404	.473	-.771	-2.967	.025	-2.562	-.246
	2	(Constant)	99.127	15.474		6.406	.001	59.350	138.904
		Norm_Torque_Ext_90_Inv	13.524	4.854	.526	2.786	.039	1.047	26.000
		Tampa	-1.089	.344	-.598	-3.170	.025	-1.972	-.206

a. Dependent Variable: KOOS_Total

Table D19. Multiple regression model summary to predict global health (VR-12) in ACL reconstructed patients per group

Group_Small_Stack	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
						R Square Change	F Change	df1	df2	Sig. F Change
6-12 month	1	.585[a]	.342	.322	8.23706	.342	16.653	1	32	.000
	2	.675[b]	.456	.421	7.61075	.114	6.483	1	31	.016
	3	.757[c]	.573	.530	6.85845	.116	8.174	1	30	.008
OA	1	.929[d]	.864	.841	5.67072	.864	37.961	1	6	.001
	2	.972[e]	.944	.922	3.98033	.080	7.178	1	5	.044

a. Predictors: (Constant), Norm_Work_Ext_90_Inv

b. Predictors: (Constant), Norm_Work_Ext_90_Inv, Tegner_Current

c. Predictors: (Constant), Norm_Work_Ext_90_Inv, Tegner_Current, VAS_Inv

d. Predictors: (Constant), Tegner_Current

e. Predictors: (Constant), Tegner_Current, VAS_Inv

Table D20. ANOVA to predict global health (VR-12) in ACL reconstructed patients per group

Group_Small_Stack	Model		Sum of Squares	df	Mean Square	F	Sig.
6-12 month	1	Regression	1129.876	1	1129.876	16.653	.000[b]
		Residual	2171.174	32	67.849		
		Total	3301.049	33			
	2	Regression	1505.420	2	752.710	12.995	.000[c]
		Residual	1795.629	31	57.924		
		Total	3301.049	33			
	3	Regression	1889.897	3	629.966	13.393	.000[d]
		Residual	1411.152	30	47.038		
		Total	3301.049	33			
OA	1	Regression	1220.711	1	1220.711	37.961	.001[e]
		Residual	192.942	6	32.157		
		Total	1413.653	7			
	2	Regression	1334.438	2	667.219	42.114	.001[f]
		Residual	79.215	5	15.843		
		Total	1413.653	7			

a. Dependent Variable: VR_12

b. Predictors: (Constant), Norm_Work_Ext_90_Inv

c. Predictors: (Constant), Norm_Work_Ext_90_Inv, Tegner_Current

d. Predictors: (Constant), Norm_Work_Ext_90_Inv, Tegner_Current, VAS_Inv

e. Predictors: (Constant), Tegner_Current

f. Predictors: (Constant), Tegner_Current, VAS_Inv

Table D21. Multiple regression coefficients to predict global health (VR-12) in ACL reconstructed patients per group

Group_Small_Stack	Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
			B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
6-12 month	1	(Constant)	58.872	5.455		10.792	.000	47.760	69.985
		Norm_Work_Ext_90_Inv	1.504	.368	.585	4.081	.000	.753	2.254
	2	(Constant)	51.969	5.724		9.080	.000	40.296	63.642
		Norm_Work_Ext_90_Inv	1.192	.362	.464	3.297	.002	.455	1.930
		Tegner_Current	1.847	.725	.358	2.546	.016	.368	3.326
	3	(Constant)	56.411	5.387		10.472	.000	45.410	67.412
		Norm_Work_Ext_90_Inv	.983	.334	.383	2.943	.006	.301	1.665
		Tegner_Current	2.105	.660	.408	3.190	.003	.758	3.453
		VAS_Inv	-3.853	1.348	-.351	-2.859	.008	-6.606	-1.101
OA	1	(Constant)	35.301	5.814		6.071	.001	21.074	49.528
		Tegner_Current	7.912	1.284	.929	6.161	.001	4.770	11.054
	2	(Constant)	24.553	5.723		4.291	.008	9.843	39.264
		Tegner_Current	8.861	.969	1.041	9.149	.000	6.372	11.351
		VAS_Inv	5.653	2.110	.305	2.679	.044	.229	11.077

a. Dependent Variable: VR_12

Figure D7. Pearson's *r* correlation coefficients between total KOOS score and pain at rest, kinesiophobia, and activity level in patients early after ACL reconstruction

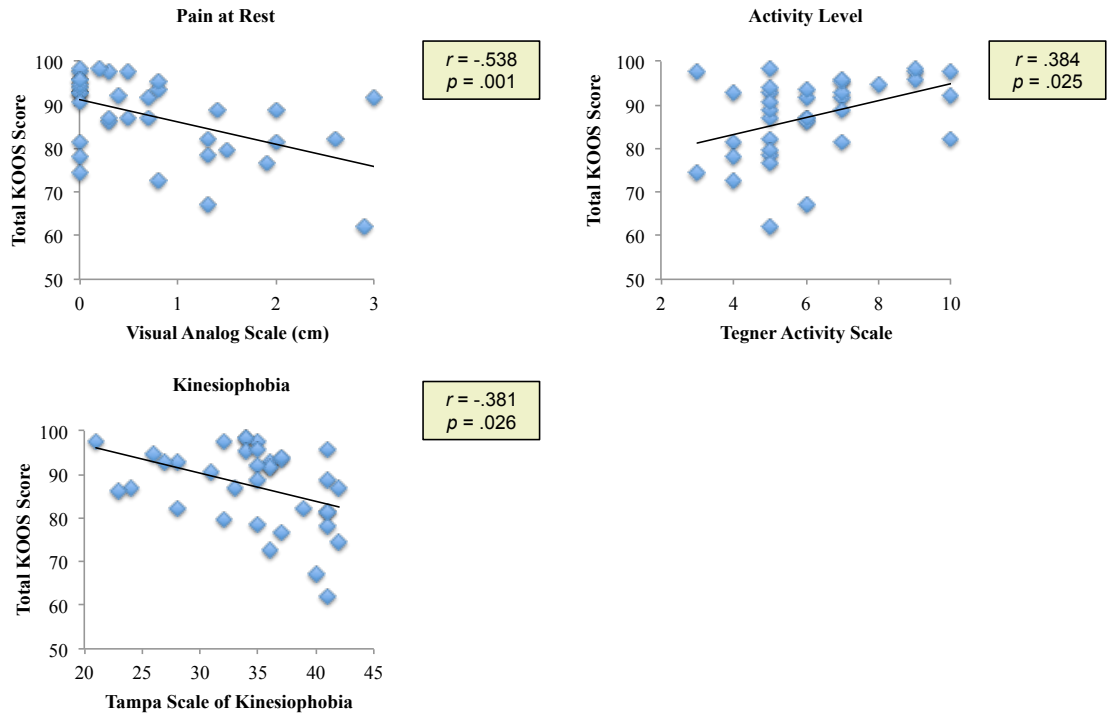


Figure D8. Pearson's *r* correlation coefficients between total VR-12 score and activity level, pain at rest, and time since surgery in patients early after ACL reconstruction

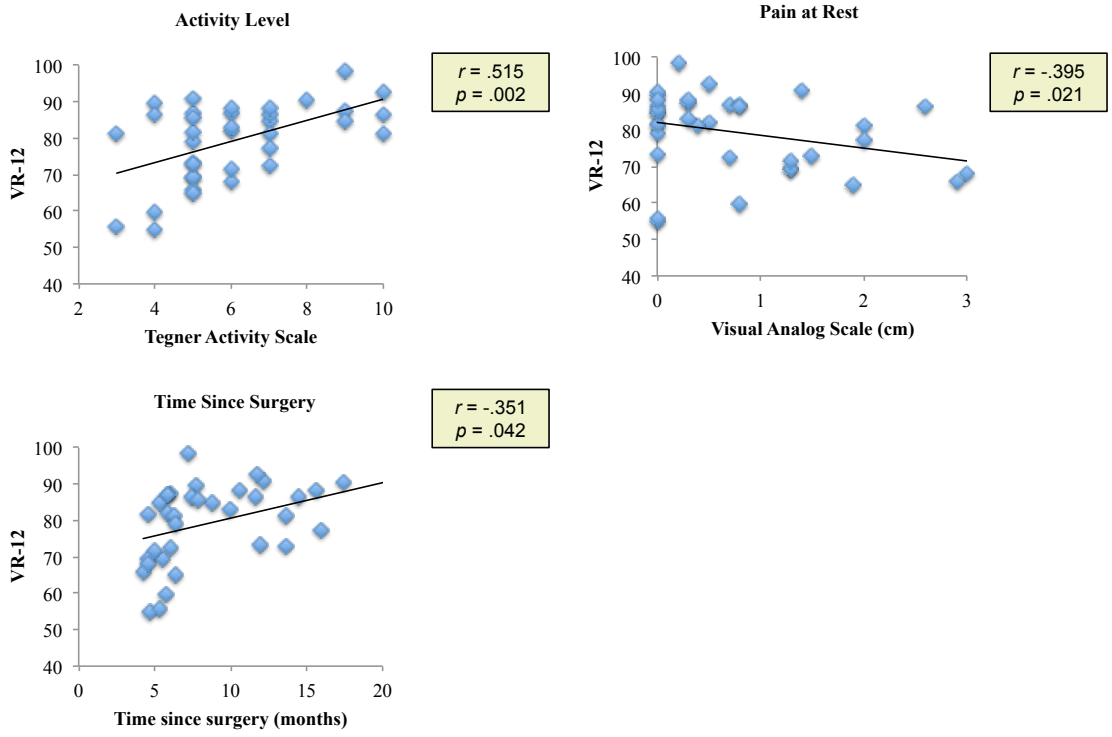


Figure D9. Pearson's *r* correlation coefficients between total KOOS score and age in patients late after ACL reconstruction

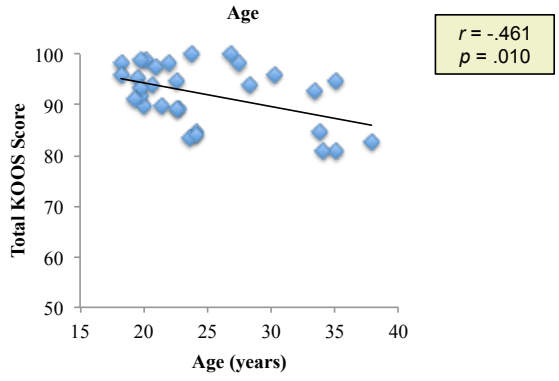


Figure D10. Normalized knee extension MVIC torque for the involved and uninvolved limbs

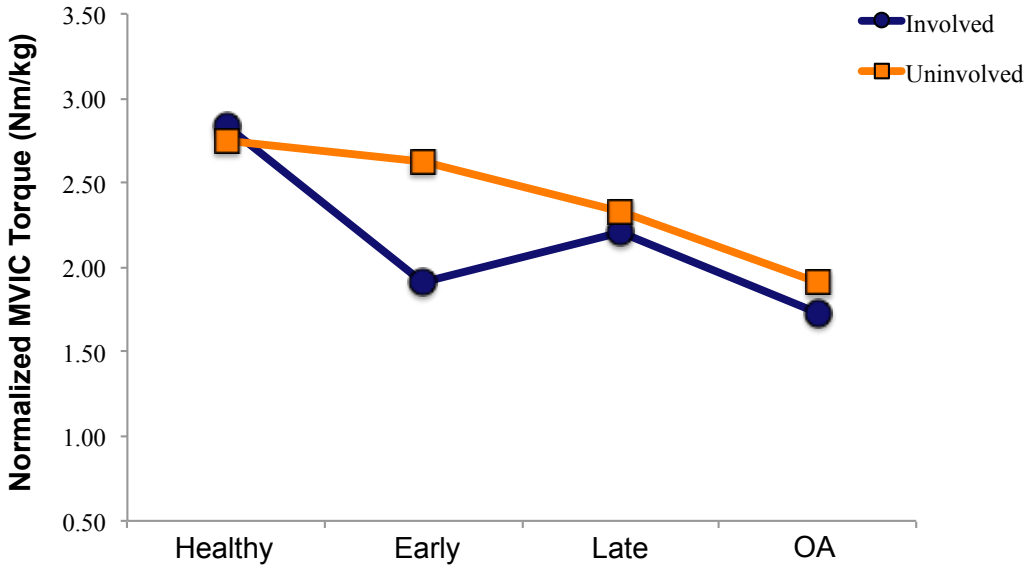


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Table D22. Paired *t* tests comparing the involved to uninvolved limb among ACL reconstructed patients

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Norm_Torque_Ext_90_Inv - Norm_Torque_Ext_90_Un	-.38646	.44967	.05299	-.49212	-.28079	-7.292	71	.000
Pair 2	Norm_Torque_Ext_180_Inv - Norm_Torque_Ext_180_Un	-.27746	.29404	.03465	-.34655	-.20836	-8.007	71	.000
Pair 3	Norm_Work_Ext_90_Inv - Norm_Work_Ext_90_Un	-3.35121	3.32211	.39151	-4.13187	-2.57056	-8.560	71	.000
Pair 4	Norm_Work_Ext_180_Inv - Norm_Work_Ext_180_Un	-2.39828	2.53354	.29858	-2.99363	-1.80293	-8.032	71	.000
Pair 5	Norm_Power_Ext_90_Inv - Norm_Power_Ext_90_Un	-.35730	.38387	.04524	-.44750	-.26710	-7.898	71	.000
Pair 6	Norm_Power_Ext_180_Inv - Norm_Power_Ext_180_Un	-.43173	.49010	.05776	-.54689	-.31656	-7.475	71	.000
Pair 7	Norm_MVIC_Torque_Inv - Norm_MVIC_Torque_Un	-.40881	.53436	.06298	-.53438	-.28324	-6.492	71	.000
Pair 8	Fatigue_Inv - Fatigue_Un	-1.98139	7.96471	.93865	-3.85301	-.10977	-2.111	71	.038
Pair 9	CAR_Inv - CAR_Un	-.01470	.07184	.00847	-.03159	.00218	-1.737	71	.087
Pair 10	HM_Inv - HM_Un	.02107	.11356	.01398	-.00684	.04899	1.507	65	.137
Pair 11	AMT_MSO_Inv - AMT_MSO_Un	.84058	6.40456	.77102	-.69796	2.37912	1.090	68	.279

Table D23. Paired *t* tests comparing the matched 'involved' to matched 'uninvolved' limb among healthy controls

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Norm_Torque_Ext_90_Inv – Norm_Torque_Ext_90_Un	.01977	.46513	.08492	-.15391	.19345	.233	29	.818
Pair 2	Norm_Torque_Ext_180_Inv – Norm_Torque_Ext_180_Un	.01105	.20665	.03773	-.06612	.08821	.293	29	.772
Pair 3	Norm_Work_Ext_90_Inv – Norm_Work_Ext_90_Un	-.39151	2.74990	.50206	-1.41834	.63532	-.780	29	.442
Pair 4	Norm_Work_Ext_180_Inv – Norm_Work_Ext_180_Un	-.06395	2.19357	.40049	-.88304	.75514	-.160	29	.874
Pair 5	Norm_Power_Ext_90_Inv – Norm_Power_Ext_90_Un	-.04185	.32865	.06000	-.16457	.08087	-.697	29	.491
Pair 6	Norm_Power_Ext_180_Inv – Norm_Power_Ext_180_Un	.00606	.39882	.07281	-.14286	.15498	.083	29	.934
Pair 7	Norm_MVIC_Torque_Inv – Norm_MVIC_Torque_Un	.08702	.34571	.06312	-.04206	.21611	1.379	29	.179
Pair 8	Fatigue_Inv – Fatigue_Un	-.41663	6.22494	1.15594	-2.78447	1.95121	-.360	28	.721
Pair 9	CAR_Inv – CAR_Un	.01331	.05220	.00969	-.00654	.03317	1.373	28	.181
Pair 10	HM_Inv – HM_Un	-.00028	.08727	.01820	-.03802	.03746	-.015	22	.988
Pair 11	AMT_MSO_Inv – AMT_MSO_Un	-.10526	4.53253	1.03983	-2.28987	2.07935	-.101	18	.920

Table D24. Independent *t* tests comparing the involved ACL reconstructed limb to matched healthy limb

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference Lower	Upper
Norm_Torque_Ext_90_Inv	Equal variances assumed	1.282	.260	5.686	100	.000	.58165	.10229	.37870	.78459
	Equal variances not assumed			6.178	65.984	.000	.58165	.09415	.39367	.76962
Norm_Torque_Ext_180_Inv	Equal variances assumed	.159	.691	5.486	100	.000	.42667	.07778	.27236	.58098
	Equal variances not assumed			5.652	58.131	.000	.42667	.07549	.27558	.57777
Norm_Work_Ext_90_Inv	Equal variances assumed	2.600	.110	6.026	100	.000	5.47563	.90865	3.67290	7.27837
	Equal variances not assumed			6.722	70.431	.000	5.47563	.81464	3.85106	7.10020
Norm_Work_Ext_180_Inv	Equal variances assumed	1.813	.181	5.816	100	.000	4.20915	.72367	2.77341	5.64490
	Equal variances not assumed			6.243	64.055	.000	4.20915	.67419	2.86233	5.55598
Norm_Power_Ext_90_Inv	Equal variances assumed	.400	.529	5.559	100	.000	.55268	.09943	.35542	.74994
	Equal variances not assumed			5.778	59.325	.000	.55268	.09565	.36130	.74406
Norm_Power_Ext_180_Inv	Equal variances assumed	.295	.588	5.436	100	.000	.75554	.13898	.47981	1.03126
	Equal variances not assumed			5.558	57.094	.000	.75554	.13594	.48333	1.02775
Norm_MVIC_Torque_Inv	Equal variances assumed	.005	.941	5.865	100	.000	.81958	.13973	.54235	1.09681
	Equal variances not assumed			5.933	55.751	.000	.81958	.13813	.54284	1.09632
Fatigue_Inv	Equal variances assumed	1.077	.302	1.935	100	.056	3.74540	1.93570	-.09498	7.58578
	Equal variances not assumed			2.050	62.073	.045	3.74540	1.82697	.09343	7.39738
CAR_Inv	Equal variances assumed	9.752	.002	3.426	99	.001	.06818	.01990	.02869	.10767
	Equal variances not assumed			4.321	89.241	.000	.06818	.01578	.03683	.09954
HM_Inv	Equal variances assumed	5.435	.022	-1.647	91	.103	-.06878	.04177	-.15175	.01418
	Equal variances not assumed			-2.019	68.014	.047	-.06878	.03407	-.13678	-.00079
AMT_MSO_Inv	Equal variances assumed	11.456	.001	-3.167	89	.002	-6.15714	1.94401	-10.01984	-2.29444
	Equal variances not assumed			-4.510	71.081	.000	-6.15714	1.36530	-8.87941	-3.43488

Table D25. Independent *t* tests comparing the uninvolved ACL reconstructed limb to matched healthy limb

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Norm_Torque_Ext_90_Un	Equal variances assumed	.002	.967	1.635	100	.105	.17542	.10731	-.03747	.38831
	Equal variances not assumed			1.491	45.190	.143	.17542	.11764	-.06149	.41233
Norm_Torque_Ext_180_Un	Equal variances assumed	.163	.687	1.732	100	.086	.13816	.07976	-.02007	.29640
	Equal variances not assumed			1.824	61.170	.073	.13816	.07574	-.01328	.28961
Norm_Work_Ext_90_Un	Equal variances assumed	2.003	.160	2.705	100	.008	2.51592	.93026	.67031	4.36153
	Equal variances not assumed			2.956	66.947	.004	2.51592	.85120	.81690	4.21495
Norm_Work_Ext_180_Un	Equal variances assumed	.724	.397	2.411	100	.018	1.87482	.77763	.33203	3.41761
	Equal variances not assumed			2.573	63.165	.012	1.87482	.72865	.41881	3.33084
Norm_Power_Ext_90_Un	Equal variances assumed	.622	.432	2.402	100	.018	.23723	.09878	.04126	.43320
	Equal variances not assumed			2.453	56.951	.017	.23723	.09673	.04354	.43093
Norm_Power_Ext_180_Un	Equal variances assumed	.035	.852	2.235	100	.028	.31775	.14217	.03569	.59981
	Equal variances not assumed			2.296	57.747	.025	.31775	.13838	.04073	.59477
Norm_MVIC_Torque_Un	Equal variances assumed	.460	.499	2.188	100	.031	.32374	.14795	.03022	.61727
	Equal variances not assumed			2.307	61.349	.024	.32374	.14032	.04318	.60430
Fatigue_Un	Equal variances assumed	.295	.589	1.123	99	.264	1.97347	1.75673	-1.51226	5.45920
	Equal variances not assumed			1.108	50.315	.273	1.97347	1.78117	-1.60356	5.55050
CAR_Un	Equal variances assumed	5.228	.024	2.059	99	.042	.04017	.01951	.00146	.07887
	Equal variances not assumed			2.400	74.335	.019	.04017	.01674	.00682	.07351
HM_Un	Equal variances assumed	2.817	.097	-1.018	89	.311	-.04019	.03949	-.11865	.03827
	Equal variances not assumed			-1.205	53.863	.233	-.04019	.03335	-.10707	.02668
AMT_MSO_Un	Equal variances assumed	12.828	.001	-2.905	90	.005	-5.24638	1.80591	-8.83412	-1.65863
	Equal variances not assumed			-4.263	87.144	.000	-5.24638	1.23066	-7.69239	-2.80036

Table D26. Independent *t* tests comparing limb symmetry indices between ACL reconstructed patients and healthy controls

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
LSI_Peak_Torque_Ext_90	Equal variances assumed	6.359	.013	2.410	100	.018	.47080	.19538	.08317	.85843
	Equal variances not assumed			1.565	29.326	.128	.47080	.30077	-.14404	1.08564
LSI_Peak_Torque_Ext_180	Equal variances assumed	1.007	.318	5.232	100	.000	.17893	.03420	.11108	.24678
	Equal variances not assumed			5.418	58.799	.000	.17893	.03303	.11284	.24502
LSI_TotalWork_Ext_90	Equal variances assumed	.750	.389	4.745	100	.000	.17494	.03687	.10179	.24809
	Equal variances not assumed			4.570	50.191	.000	.17494	.03828	.09806	.25182
LSI_TotalWork_Ext_180	Equal variances assumed	.045	.833	4.533	100	.000	.17795	.03926	.10007	.25584
	Equal variances not assumed			3.958	41.884	.000	.17795	.04496	.08721	.26869
LSI_Avg_Power_Ext_90	Equal variances assumed	.159	.691	4.241	100	.000	.16878	.03979	.08983	.24773
	Equal variances not assumed			3.816	44.082	.000	.16878	.04423	.07964	.25792
LSI_Avg_Power_Ext_180	Equal variances assumed	.287	.593	4.493	100	.000	.17606	.03918	.09832	.25379
	Equal variances not assumed			4.122	45.656	.000	.17606	.04272	.09006	.26206
LSI_MVIC	Equal variances assumed	5.845	.017	4.804	100	.000	.18939	.03943	.11117	.26761
	Equal variances not assumed			5.558	77.169	.000	.18939	.03408	.12154	.25724
LSI_Fatigue_Diff	Equal variances assumed	.733	.394	-.740	99	.461	-1.22093	1.65078	-4.49643	2.05457
	Equal variances not assumed			-.823	66.175	.414	-1.22093	1.48419	-4.18406	1.74220
LSI_CAR	Equal variances assumed	1.210	.274	1.803	99	.074	.03089	.01713	-.00310	.06489
	Equal variances not assumed			2.076	72.073	.041	.03089	.01488	.00122	.06056
LSI_HM	Equal variances assumed	.451	.504	-.797	87	.428	-.16190	.20313	-.56565	.24185
	Equal variances not assumed			-.917	51.361	.364	-.16190	.17661	-.51640	.19260
LSI_AMT	Equal variances assumed	.050	.824	.509	86	.612	.01949	.03831	-.05667	.09564
	Equal variances not assumed			.589	36.413	.560	.01949	.03310	-.04761	.08658

Table D27. Total variance explained by measures of involved ACL reconstructed limb quadriceps function

	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
Component	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	6.519	59.263	59.263	6.519	59.263	59.263	6.509	59.175	59.175
2	1.200	10.912	70.176	1.200	10.912	70.176	1.192	10.836	70.011
3	1.160	10.547	80.723	1.160	10.547	80.723	1.178	10.712	80.723
4	.908	8.250	88.973						
5	.636	5.781	94.754						
6	.229	2.085	96.838						
7	.183	1.665	98.503						
8	.085	.769	99.272						
9	.036	.327	99.599						
10	.033	.298	99.897						
11	.011	.103	100.000						

Extraction Method: Principal Component Analysis.

Table D28. Component (A) and rotated component (B) matrices for involved ACL reconstructed limb quadriceps function

	Component		
	1	2	3
Norm_Power_Ext_180_Inv	.970		
Norm_Torque_Ext_180_Inv	.967		
Norm_Power_Ext_90_Inv	.967		
Norm_Work_Ext_90_Inv	.957		
Norm_Torque_Ext_90_Inv	.952		
Norm_Work_Ext_180_Inv	.952		
Norm_MVIC_Torque_Inv	.872		
HM_Inv		.674	-.517
CAR_Inv	.319	.658	.369
Fatigue_Inv		.457	.441
AMT_MSO_Inv			.744

Extraction Method: Principal Component Analysis.

a. 3 components extracted.

	Component		
	1	2	3
Norm_Power_Ext_180_Inv	.971		
Norm_Torque_Ext_180_Inv	.967		
Norm_Power_Ext_90_Inv	.967		
Norm_Work_Ext_90_Inv	.957		
Norm_Work_Ext_180_Inv	.954		
Norm_Torque_Ext_90_Inv	.954		
Norm_MVIC_Torque_Inv	.863		
HM_Inv		.813	
AMT_MSO_Inv		-.687	.336
CAR_Inv	.301		.752
Fatigue_Inv			.629

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 5 iterations.

Table D29. Total variance explained by measures of uninvolved ACL reconstructed limb quadriceps function

	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
Component	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	6.274	57.034	57.034	6.274	57.034	57.034	6.169	56.083	56.083
2	1.508	13.708	70.742	1.508	13.708	70.742	1.613	14.659	70.742
3	.912	8.290	79.032						
4	.855	7.775	86.807						
5	.701	6.370	93.177						
6	.349	3.175	96.352						
7	.183	1.667	98.019						
8	.107	.970	98.989						
9	.064	.578	99.567						
10	.034	.308	99.875						
11	.014	.125	100.000						

Extraction Method: Principal Component Analysis.

Table D30. Component (A) and rotated component (B) matrices for uninvolved ACL reconstructed limb quadriceps function

	Component	
	1	2
Norm_Torque_Ext_180_Un	.956	
Norm_Power_Ext_90_Un	.955	
Norm_Power_Ext_180_Un	.952	
Norm_Work_Ext_90_Un	.952	
Norm_Work_Ext_180_Un	.944	
Norm_Torque_Ext_90_Un	.935	
Norm_MVIC_Torque_Un	.830	
AMT_MSO_Un		.662
HM_Un		-.642
CAR_Un		-.566
Fatigue_Un	-.308	.530

Extraction Method: Principal Component Analysis.

a. 2 components extracted.

	Component	
	1	2
Norm_Power_Ext_180_Un	.957	
Norm_Torque_Ext_180_Un	.956	
Norm_Work_Ext_90_Un	.952	
Norm_Work_Ext_180_Un	.948	
Norm_Torque_Ext_90_Un	.947	
Norm_Power_Ext_90_Un	.937	
Norm_MVIC_Torque_Un	.814	
AMT_MSO_Un		-.696
HM_Un		.632
CAR_Un		.571
Fatigue_Un		-.569

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 3 iterations.

Table D31. Total variance explained by limb symmetry measures of quadriceps function in ACL reconstructed patients

	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
Component	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	6.529	59.358	59.358	6.529	59.358	59.358	5.945	54.045	54.045
2	1.148	10.441	69.799	1.148	10.441	69.799	1.638	14.891	68.936
3	1.006	9.142	78.941	1.006	9.142	78.941	1.101	10.005	78.941
4	.939	8.534	87.475						
5	.694	6.308	93.784						
6	.287	2.612	96.396						
7	.232	2.107	98.503						
8	.082	.749	99.252						
9	.045	.407	99.659						
10	.025	.226	99.884						
11	.013	.116	100.000						

Extraction Method: Principal Component Analysis.

Table D32. Component (A) and rotated component (B) matrices for limb symmetry measures of quadriceps function in ACL reconstructed patients

	Component		
	1	2	3
LSI_TotalWork_Ext_90	.962		
LSI_Avg_Power_Ext_90	.957		
LSI_Peak_Torque_Ext_180	.955		
LSI_Avg_Power_Ext_180	.948		
LSI_Peak_Torque_Ext_90	.945		
LSI_TotalWork_Ext_180	.942		
LSI_MVIC	.839		
LSI_HM			
LSI_Fatigue_Diff	-.370	.745	
LSI_CAR	.404	-.622	
LSI_AMT			.938

Extraction Method: Principal Component Analysis.

a. 3 components extracted.

	Component		
	1	2	3
LSI_Avg_Power_Ext_180	.956		
LSI_TotalWork_Ext_180	.949		
LSI_Peak_Torque_Ext_180	.947		
LSI_Avg_Power_Ext_90	.944		
LSI_TotalWork_Ext_90	.934		
LSI_Peak_Torque_Ext_90	.928		
LSI_MVIC	.717	.472	
LSI_Fatigue_Diff		-.812	
LSI_CAR		.745	
LSI_AMT			.948
LSI_HM			.321

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 4 iterations.

Figure D11. Receiver operator characteristic (ROC) curves using measures of involved limb quadriceps function to determine group membership

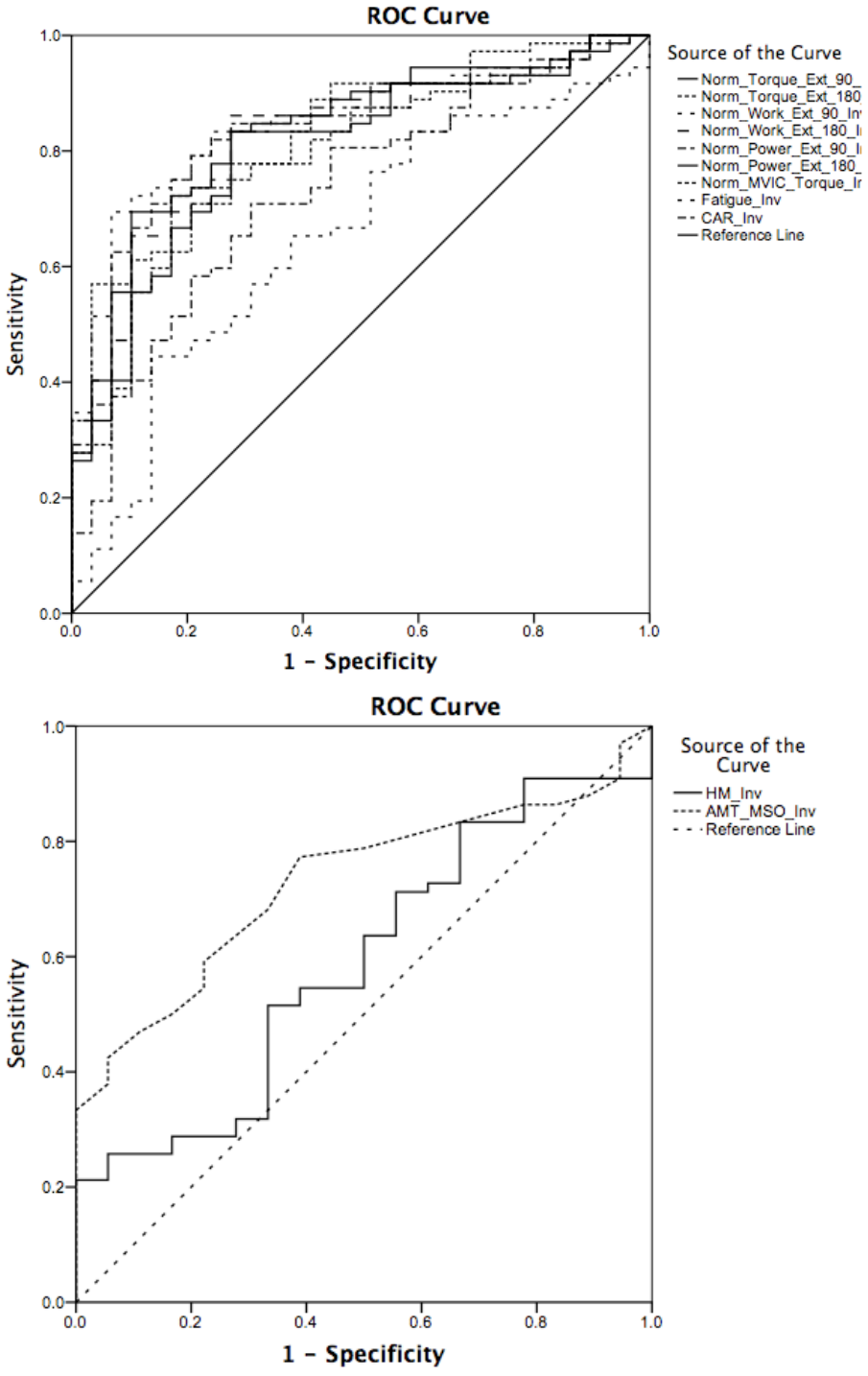

Table D33. Area under the receiver operator characteristic (ROC) curve for measures of involved limb quadriceps function to determine group membership

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Norm_Torque_Ext_90_Inv	.828	.043	.000	.744	.912
Norm_Torque_Ext_180_Inv	.802	.047	.000	.709	.894
Norm_Work_Ext_90_Inv	.848	.039	.000	.771	.925
Norm_Work_Ext_180_Inv	.829	.043	.000	.744	.913
Norm_Power_Ext_90_Inv	.833	.042	.000	.750	.917
Norm_Power_Ext_180_Inv	.807	.046	.000	.716	.898
Norm_MVIC_Torque_Inv	.821	.042	.000	.739	.903
Fatigue_Inv	.649	.060	.019	.533	.766
CAR_Inv	.731	.054	.000	.626	.836

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
HM_Inv	.589	.072	.248	.448	.731
AMT_MSO_Inv	.729	.057	.003	.617	.840

The test result variable(s): AMT_MSO_Inv has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figure D12. Receiver operator characteristic (ROC) curves using measures of uninvolved limb quadriceps function to determine group membership

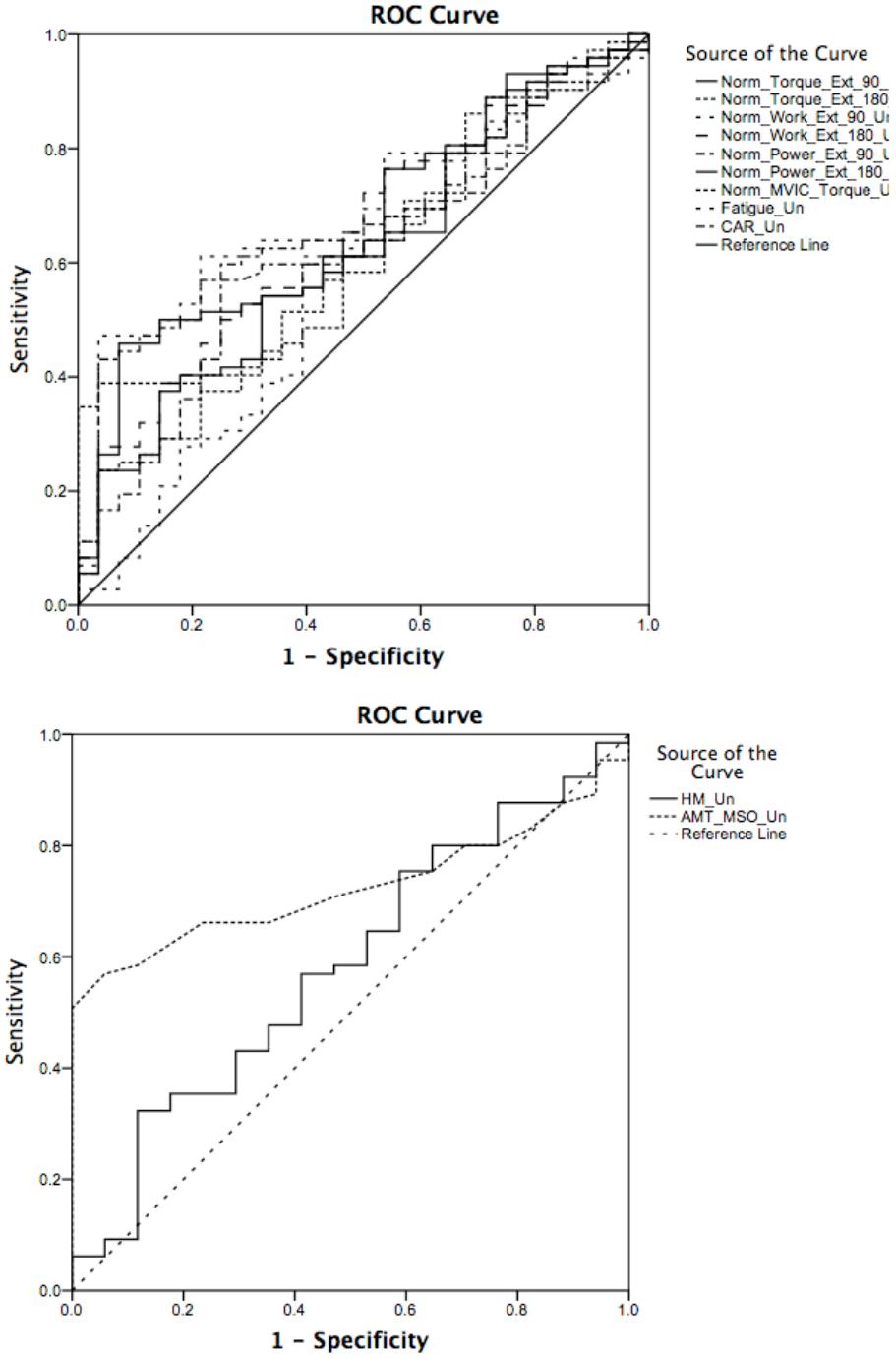

Table D34. Area under the receiver operator characteristic (ROC) curve for measures of uninvolved limb quadriceps function to determine group membership

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Norm_Torque_Ext_90_Un	.654	.057	.017	.542	.766
Norm_Torque_Ext_180_Un	.593	.061	.149	.473	.713
Norm_Work_Ext_90_Un	.685	.054	.004	.578	.791
Norm_Work_Ext_180_Un	.651	.058	.020	.537	.765
Norm_Power_Ext_90_Un	.661	.056	.012	.552	.770
Norm_Power_Ext_180_Un	.633	.060	.039	.515	.752
Norm_MVIC_Torque_Un	.636	.057	.035	.524	.748
Fatigue_Un	.581	.067	.211	.450	.711
CAR_Un	.629	.060	.045	.512	.747

The test result variable(s): Norm_Power_Ext_90_Un has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
HM_Un	.583	.077	.295	.432	.733
AMT_MSO_Un	.725	.053	.004	.621	.830

The test result variable(s): AMT_MSO_Un has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figure D13. Receiver operator characteristic (ROC) curves using limb symmetry measures of quadriceps function to determine group membership

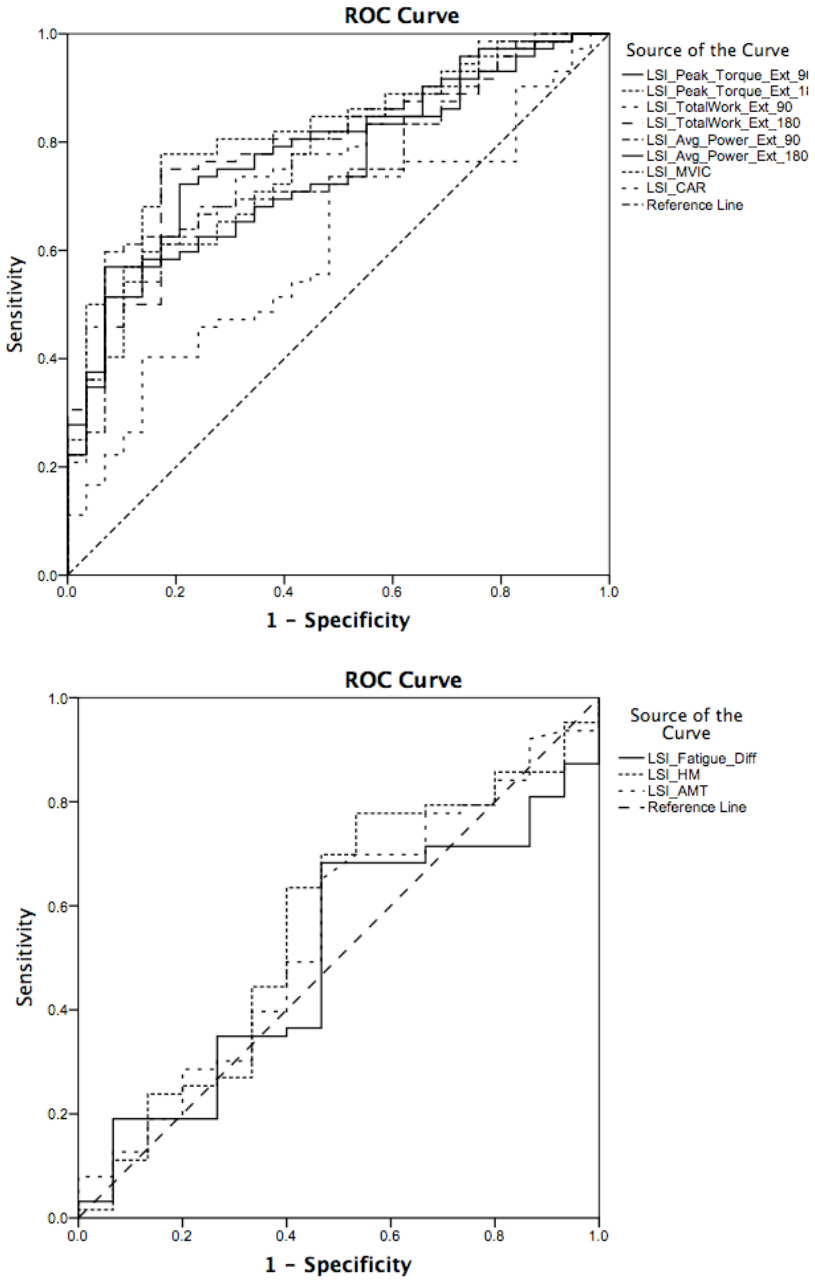

Table D35. Area under the receiver operator characteristic (ROC) curve for limb symmetry measures of quadriceps function to determine group membership

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
LSI_Peak_Torque_Ext_90	.752	.050	.000	.655	.850
LSI_Peak_Torque_Ext_180	.808	.046	.000	.718	.898
LSI_TotalWork_Ext_90	.773	.048	.000	.680	.867
LSI_TotalWork_Ext_180	.788	.047	.000	.697	.880
LSI_Avg_Power_Ext_90	.750	.050	.000	.652	.848
LSI_Avg_Power_Ext_180	.780	.047	.000	.688	.872
LSI_MVIC	.776	.047	.000	.683	.869
LSI_CAR	.610	.059	.084	.495	.726

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
LSI_Fatigue_Diff	.503	.080	.975	.346	.659
LSI_HM	.565	.086	.436	.397	.733
LSI_AMT	.548	.083	.564	.385	.711

The test result variable(s): LSI_AMT has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Table D36. Binary logistic regression results to predict group membership using measures of involved limb quadriceps function

		Chi-square	df	Sig.
Step 1	Step	34.418	3	.000
	Block	34.418	3	.000
	Model	34.418	3	.000

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	63.899[a]	.315	.477

a. Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

	Observed		Predicted ACL		Percentage Correct
			No	Yes	
Step 1	ACL	No	12	9	57.1
		Yes	7	63	90.0
	Overall Percentage				82.4

a. The cut value is .500

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	Norm_Work_Ext_90_Inv	-.236	.081	8.449	1	.004	.790	.674	.926
	CAR_Inv	-9.328	5.747	2.634	1	.105	.000	.000	6.930
	AMT_MSO_Inv	.120	.059	4.073	1	.044	1.127	1.003	1.266
	Constant	9.090	5.533	2.699	1	.100	8865.549		

a. Variable(s) entered on step 1: Norm_Work_Ext_90_Inv, CAR_Inv, AMT_MSO_Inv.

Table D37. Binary logistic regression results to predict group membership using measures of uninvolved limb quadriceps function

		Chi-square	df	Sig.
Step 1	Step	14.781	2	.001
	Block	14.781	2	.001
	Model	14.781	2	.001

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	88.689[a]	.148	.220

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

			Predicted		
			ACL		Percentage Correct
	Observed		No	Yes	
Step 1	ACL	No	4	19	17.4
		Yes	6	63	91.3
	Overall Percentage				72.8

a. The cut value is .500

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Norm_Work_Ext_90_Un	-.148	.062	5.614	1	.018	.862	.763	.975
	AMT_MSO_Un	.105	.042	6.144	1	.013	1.110	1.022	1.206
	Constant	-.338	1.999	.029	1	.866	.713		

a. Variable(s) entered on step 1: Norm_Work_Ext_90_Un, AMT_MSO_Un.

Table D38. Binary logistic regression results to predict group membership using limb symmetry measures of quadriceps function

		Chi-square	df	Sig.
Step 1	Step	19.638	3	.000
	Block	19.638	3	.000
	Model	19.638	3	.000

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	72.178[a]	.200	.309

a. Estimation terminated at iteration number 6 because parameter estimates changed by less than .001.

			Predicted		
			ACL		Percentage Correct
	Observed		No	Yes	
Step 1	ACL	No	3	16	15.8
		Yes	2	67	97.1
	Overall Percentage				79.5

a. The cut value is .500

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	LSI_Peak_Torque_Ext_180	-8.767	2.693	10.601	1	.001	.000	.000	.031
	LSI_CAR	-5.466	4.892	1.248	1	.264	.004	.000	61.702
	LSI_AMT	-.314	2.249	.019	1	.889	.730	.009	60.027
	Constant	15.189	5.723	7.044	1	.008	3950785.36		

a. Variable(s) entered on step 1: LSI_Peak_Torque_Ext_180, LSI_CAR, LSI_AMT.

APPENDIX E

Back Matter

Recommendations for future research

1. Examine the natural history of post-traumatic lower extremity neuromuscular function following ACL reconstruction using a prospective longitudinal study design.

2. Does quadriceps neuromuscular function differ between patients with a clinical diagnosis (WOMAC score) of knee osteoarthritis compared to those with radiographic evidence?

3. Do early mal-adaptive patterns of quadriceps neuromuscular function influence long-term patient outcomes?

4. Which treatment strategy, or strategies, is most effective to treat specific neuromuscular impairments (i.e. muscle weakness, central activation failure, reflex inhibition, decreased corticospinal drive)?

5. Does early treatment of measured neuromuscular impairments influence patient outcomes? Can a minimally clinically important difference be established for common estimates of neuromuscular function (i.e. knee extensor torque, central activation, spinal reflexive excitability, corticospinal excitability)?

6. Does a threshold of time from surgery exist in which patients become less responsive to known treatment strategies for neuromuscular impairments?

7. What are the cutoff values for common estimates of neuromuscular function to discriminate between healthy individuals and ACL reconstructed patients with and without knee osteoarthritis?

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