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Neuromechanical Alterations Due to Induced Knee Pain and Effusion During Functional Movements

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Doctor of Philosophy

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ABSTRACT

Neuromechanical Alterations Due to Induced Knee Pain and Effusion
During Functional Movements

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Purpose: Examine neuromechanical alterations due to isolated and/or combined knee pain and effusion in functional movements. **Methods:** A 4X3 randomised controlled laboratory study with repeated measures was used. Nineteen, healthy volunteers (age: 22.4 ± 2.4 years) underwent four different treatments (control, effusion, pain, and pain/effusion) with a week wash out period. Ten near-infrared cameras with 43 reflective markers, 12 surface EMG electrodes, and two ground-embedded force platforms were used to record neuromechanical changes during functional movements (walking and drop landing). To induce pain, 5% sodium chloride (1 ml) was injected into the infrapatellar fat pad. To induce effusion, 0.9% sodium chloride (50 ml) was injected into the knee joint capsule. To induce pain/effusion, both injections were employed. No injection was used for the control. Subjects performed walking and a single leg drop landing in three time intervals: precondition (prior to injection), condition (immediate post injection), and postcondition (30 min post injection). To quantify pain perception, the visual analogue scale was measured every two minutes. **Results:** Under pain/effusion treatment, subjects walked slowly with a shorter stride length. Joint moments of plantarflexion, knee extension, knee abduction, and hip abduction were reduced. Subjects also showed a decrease at 20% and 80% of stance phase, and an increase in 50% in vertical ground reaction force (VGRF). Under the same treatment, subjects landed with a less peak VGRF with increased time to peak VGRF, alterations of joint angles (ankle dorsiflexion, knee extension, and hip adduction), and moments (knee extension, knee abduction, and hip abduction). **Conclusions:** Joint pain and effusion cause neuromechanical alterations in the lower extremity during functional movements. These compensatory strategies may alter joint loading, potentially resulting in acceleration of the joint degenerative process. We also recommend use of crutches following injury to avoid modifications of movement strategies.

Key words: arthrogenous muscle response, gait alteration, joint degeneration

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Introduction

Knee joint injuries are common. For example, approximately 80,000 anterior cruciate ligament (ACL) ruptures are seen in the United States annually (39). The estimated prevalence of knee osteoarthritis (OA) is 6.1% in adults aged more than 30 (32) and 12.5% in those aged 45 and above (13). Knee OA often requires total knee arthroplasty (TKA) (89) resulting in 443,008 TKAs from 1990 to 2000 in the United States alone (58). Of all knee joint pathologies, anterior knee pain (AKP) is the most common (59) with a prevalence rate as high as 25% (27). Although diagnoses and etiologies vary, a reduction in quadriceps activation is a common consequence in individuals with knee joint pathologies (29, 52, 76, 107, 112).

Quadriceps dysfunction resulting from a knee joint injury has been termed arthrogenous muscle inhibition (AMI) (82, 105). AMI is a pre- and postsynaptic inhibition of periarticular musculature resulting from surgery, distension, pain, or structural damage of a joint (46, 85, 86). AMI is the body's natural response following a traumatic injury (46). AMI discourages the patient's ability to move the injured joint thus it helps prevent further structural damage (82) and provide time for tissue healing. The presence of AMI, however, may mediate compensatory strategies in the functional kinetic chain of the lower extremity (49, 82, 111). Long term consequences of these abnormalities could modify normal joint loading, eventually resulting in degenerative joint disease (12, 87, 106).

Structural damage and the ensuing inflammatory response are believed to be initiating factors that alter normal afferent input, resulting in AMI (52, 53, 115). Among these factors, pain and joint effusion have been examined as independent contributing factors to AMI. In clinical and laboratory trials, quadriceps AMI has been associated with knee pain (107-109) and

alterations in quadriceps muscle activity during stair ascending (45). Joint effusion has also been shown as an independent cause of quadriceps inhibition (47, 49, 57, 82, 103, 111). Studies observing the effects of experimentally induced knee effusion on lower extremity muscles reported quadriceps inhibition with soleus (49) or hamstring (82, 111) facilitation. These studies reported an increase in knee flexion during walking (111) and an increase in ground reaction forces during a drop landing task (82).

Despite evidence of the consequences of each factor to AMI, the relative or additive contribution of pain and effusion to elicit AMI is still unclear. Since pain and effusion are from different sensory receptors (e.g. nociceptors (14) and Ruffini endings (49)), each stimulus may follow a different pathway. Although each injury model is effective in evaluating pain and effusion stimuli separately, we rarely see pain or effusion alone in knee joint injuries. Introduction of pain and effusion simultaneously in a controlled environment would simulate a condition in which both stimuli are present. The observation of neuromechanical alterations using this combined model may clarify if there is an additive effect with the two stimuli. Additionally, the combined model could potentially help us understand how this additive effect influences AMI and associated lower extremity compensatory strategies.

The purpose of this study is to determine the contributions of AKP, knee joint effusion, and a combination of both stimuli on change in lower extremity neuromuscular activities, kinetics, and kinematics during walking and drop landings. These functional movements demand dynamic joint stability. Dynamic joint stability requires active muscle contraction along with proper sensory feedback and feed-forward controls. When AMI is present in the quadriceps, we expect to observe neuromechanical alterations in the lower extremity.

Methods

Experimental design

This study was a crossover design. The independent variables were treatment (pain, effusion, pain/effusion, and control-no injection) and time (precondition, condition, and postcondition). The dependent variables were subjective pain perception, neuromuscular activities, kinetic, and kinematic data on the lower extremity. The specific dependent variables are as followed:

Neuromuscular activities

Walking: Peak and mean electromyography (EMG) values of each muscle in four equal time intervals (0-25%, 26-50%, 51-75%, 76-100%) during the stance phase in both sides

Drop landing: Peak and mean EMG values of each muscle during the time window from 200 ms before to initial contact; from initial contact to peak knee flexion of the first landing in the ipsilateral side

Muscles: medial gastrocnemius, vastus medialis, vastus lateralis, medial hamstring, gluteus medius, and gluteus maximus

Ground reaction force (GRF)

Walking: Vertical ground reaction force (VGRF) during the stance phase in both sides

Drop landing: Peak VGRF (PVGRF) and time to PVGRF during the stance phase of the first landing in both sides

Joint kinematics

Walking:

(1) Walking speed

(2) Stride length in both sides

(3) Peak joint angles in the sagittal plane (dorsi-flexion, plantar-flexion, knee flexion, hip flexion, and hip extension) and frontal planes (knee abduction, knee adduction, hip abduction, and hip adduction) during the stance phase in both sides

Drop landing:

(1) Peak joint angles in the sagittal plane (dorsi-flexion, plantar-flexion, knee flexion, hip flexion, and hip extension) and frontal plane (knee abduction, knee adduction, and hip adduction) during the stance phase in the ipsilateral side

(2) Hip joint angle in the frontal plane at initial contact in the ipsilateral side

(3) Amount of time between the toe off of the first landing and the initial contact of the second landing

Joint Kinetics

Walking: Peak joint moments in the sagittal (plantar-flexion, knee extension, hip flexion, and hip extension) and frontal plane (knee abduction, knee adduction, and hip abduction) during the stance phase in both sides

Drop landing:

(1) Peak joint moments in the sagittal (plantar-flexion, knee flexion, knee extension, and hip extension) and frontal plane (knee abduction, knee adduction, hip abduction, and hip adduction) during the stance phase in the ipsilateral side

(2)Vertical body stiffness during the stance phase

Participants

Sample size was calculated using an expected change in PVGRF during a single leg drop landing (GRF: N/kg) of 10 and a standard deviation of 7.29 (82). Based on these estimations, 13 subjects in each group were necessary in order to have an 80% chance of detecting a significant difference with p=0.001.

Nineteen, (10 males and 9 females, age: 22± 2 years, height: 1.73 ± 0.1 m, mass: 73 ± 16 kg) healthy subjects volunteered to participate. Exclusion criteria included current pregnancy, history of neuromuscular disorders, lumbar spine or lower extremity surgery, or lower extremity injury within the past six months. All subjects read and signed the informed consent form approved by University's Institutional Review Board.

Data collection and reduction

Neuromuscular activity

Twelve wireless surface EMG electrodes (Trigno Wireless, Delsys Inc., Boston, MA) were used to record neuromuscular activity of the lower extremity (2000 Hz). Electrode locations were shaved, debrided with sandpaper, and cleaned with isopropyl alcohol. The

electrodes were placed on the medial gastrocnemius (MG), vastus medialis (VM), vastus lateralis (VL), medial hamstring (MH), gluteus medius (GM), and gluteus maximus (GX) in both sides. EMG placements were guided by the Surface ElectroMyoGraphy for the Non-invasive Assessment of Muscles (97). EMG during an isometric reference position was recorded to normalize the EMG amplitude. Subjects were asked to squat down until their butt barely touches a barrier (an office desk with height of 0.74 m) and maintain the position for four seconds (Figure 1-a). All EMG signals were band-pass filtered (20-450 Hz), involved a common mode rejection ratio that was greater than 80 dB, and were amplified using a gain of 1000.

Raw EMG data further were smoothed using a root mean square (RMS) algorithm with a 50 ms moving window for walking trials and a 15 ms moving window for drop landing trials. The data for the isometric reference position were treated the same way. For the walking trials, the EMG signals in each muscle were first time-normalized to the stance time: a stance phase on each leg corresponded to 100% (1,000 data points), then normalized again by the isometric reference position. A48 ms fixed delay, from sensor input to analog output, was accounted for all EMG data to harmonise with kinetic and kinematic data.

GRF

GRF data were measured using two-floor-mounted force platforms (AMTI, Watertown, MA) at a sampling rate of 2,000 Hz. Prior to data collection, both force platforms were calibrated to zero. Initial contact on the force platforms was defined as the instant at which the VGRF exceeded 10 N. GRF data were not filtered or normalized in walking and drop landing trials.

Joint kinematics and kinetics

Kinematic data were recorded with Vicon Nexus 1.7 (VICON, Centennial, CO). The movements of the lower extremities were measured using ten high-speed digital video cameras (Vicon MX, Oxford Metrics Ltd, Oxford, UK) at a sampling rate of 200 Hz. Twenty seven single reflective markers were attached on the lower extremity and trunk. Four rigid clusters of four markers each were applied to the mid-lateral thigh and shank on each leg. Single markers were bilaterally placed over the acromion, inferior angle of the scapula, anterior superior iliac spine, greater trochanter, lateral and medial femoral condyle, medial and lateral malleoli, dorsal surface of the mid-foot, toe (between the second and third metatarsal), lateral foot (fifth metatarsal), and heel. Foot markers were attached onto standardized athletic shoes. Single markers were also placed over the C7, T7, and sacrum.

A static standing trial (subjects stood with equal distribution of body weight on each foot) was measured and considered as each subject's neutral body alignment; subsequent kinematic measurements were referenced in relation to this position (Figure 1-b). Subjects performed standing leg motions for each leg in order to estimate the functional hip joint center (44). These motions consisted of three hip flexions and extensions in the sagittal plane and three hip abductions and adductions in the frontal plane.

The spatial coordinates for each reflective marker were determined and tracked using Vicon Nexus and then exported to Visual3D. The coordinates for the walking and drop landing tasks were smoothed using a 4^{th}-order low-pass Butterworth filter with a cut off frequency of 6 (51) and 12 Hz (66), respectively. A static model was first built using the static standing trial. This model was applied to each walking and drop landing trial, in order to calculate joint angle. Joint angles were calculated using a Cardan rotation sequence of flexion-extension and

abduction-adduction. Three-dimensional internal joint moments were then calculated using inverse dynamics which combined the kinematic, GRF, and anthropometric data (62).

Vertical stiffness was calculated by dividing PVGRF by vertical displacement of the center of mass (56) during the first stance during drop landing trials. Vertical displacement of the center of mass was calculated as the distance between the highest and lowest vertical discrete value of center of mass. Center of mass was estimated using the reflective markers on the lower extremity and trunk.

All data were synchronised using Vicon Nexus (VICON, Centennial, CO) and exported into Visual3D (C Motion, Germantown, MD) for analysis. Afterwards, Matlab 7.12 (Mathworks, Natick, MA) software was utilized to reduce and extract the necessary values in the outcomes from Visual3D.

Perceived pain

Subjective pain perception was quantified using a 10 cm VAS (18). Terms "No pain" and "pain as bad as it could possibly be" were placed on each end of scale. Every two minutes throughout each time interval, subjects were asked to mark where their pain level is at the time of measurement.

Treatments

Following the precondition trials (see the testing procedures below), subjects sat on a table and received one of the four treatments. Saline injections were used in each treatment except for the control. A licensed, board certified physician performed all injections on the subject's dominant side. Dominant side was defined as the preferred leg used to kick a ball.

Prior to injection, the needle insertion area was cleaned with povidone-iodine. After removal of the needle, the puncture site was cleaned with an alcohol swab and covered with sterilised gauze.

Control

The control consisted of no injection. Subjects simply sat on a table for five minutes and performed the condition trials at the same time intervals.

Effusion

For anesthetic purpose, sterile lidocaine (1%, 2.0-ml, Hospira, Inc., Lake Forest, IL) was subcutaneously injected using the 25-gauge needle and 3-ml syringe. An 18-gauge needle was inserted into the superolateral knee joint. Sterile saline (0.9% sodium chloride, 50.0-ml, Hospira, Inc., Lake Forest, IL) was injected using a 50-ml syringe (Becton Dickinson Medical Systems Inc, Sandy, UT). An effusion wave and ballotable patella test were performed to ensure that the effusion was within the knee joint capsule (60).

Pain

A 25-gauge needle (Becton Dickinson Medical Systems Inc, Sandy, UT) was inserted into the lateral infrapatellar fad pad. The needle was inserted at an angle of 45 degrees, in an inferior-medial direction, to a depth of 1 cm (15). Sterile hypertonic saline (5% sodium chloride, 1.0-ml, B. Braun medical, Inc., Irvine, CA) was injected using 1-ml syringe (Becton Dickinson Medical Systems Inc, Sandy, UT).

Pain/effusion

To induce a combination of pain and effusion, three injections were performed in the order of 1% lidocaine, 0.9% isotonic saline, and 5% hypertonic saline. The same volume of each saline solution was injected as the volume used for pain and effusion treatments. Effusion was induced first followed by pain due to the limited amount of time for effective pain sensation.

Testing Procedures

Subjects also completed the demographic information. Subjects' height and mass were measured. Subjects performed several trials of drop landings for familiarization. This helped ensure a consistent drop height between sessions. Qualified subjects came back a week later for data collection.

Each subject experienced all four treatments (control, effusion, pain, and pain/effusion) in each session with a week wash-out period in between sessions. Each session consisted of three time intervals (precondition, condition, and postcondition). During each time interval, three trials of functional movements (walking trials first followed by drop landing trials) were recorded. Order of the treatments was randomized using Latin Square designs (24).

Upon arrival in the laboratory, subjects were asked to wear standardized spandex shorts and shirts, socks, and athletic shoes during data collection. EMG electrodes and reflective markers were attached. Subject's isometric reference position, static standing video, and standing leg motions were recorded. Subjects performed the precondition trials (three successful trials of walking and drop landings). Afterwards, subjects sat on the table and received one of the treatments (pain, effusion, pain/effusion, control). Two minutes after the injection, subjects were asked to stand up. Subjects spent a minute in a standing position. Subjects then performed the condition trials. Data collection was terminated if the subject complained of intolerable pain and/or fainting, or did not begin condition trial within eight minutes following injection. Subjects sat on the table (same position as injection) and rested for 20-25 minutes before the postcondition trials. Resting time prior to the postcondition measurement was dependent up on the length of time taken to complete the condition measurements.

Walking

Subjects completed three successful walking trials at a self selected walking speed. A successful walking trial constituted each foot fully landing on each force platform. For each successful trial, one gait cycle for each side was collected.

Drop landing

Subjects performed a drop landing task from a 30 cm height wooden box. The box was placed 20 cm away from the near edge of the force platform. Three successful trials were collected in each time interval. A successful trial was defined as the subjects dropping down (not step or jump down) on their dominant leg onto the force platform followed by an immediate vertical jump as determined visually by the assessor (34, 35, 95). Subjects were instructed not to touch the ground with the contralateral side and to maintain balance after the second landing for two seconds (93). The first landing was used for analysis.

Statistical analyses

For perceived pain a 4×24 mixed model analysis of variance (ANOVA) was performed to test for differences in treatment over time.

For neuromechanical measurements during walking and drop landing, means for each subject were computed from three trials at each time interval for each treatment.

For neuromuscular activities during walking, twelve separate 4×3×2×4 mixed model analysis of covariances (ANCOVAs; covariate: walking speed) were performed to test differences in treatment over time on each leg during different time windows in the stance phase. For walking speed a 4×3 mixed model ANOVAs was performed to test for differences in treatment over time. For stride length a 4×3×2 mixed model ANOVA was performed to test for

differences in treatment over time on each leg. For joint angles and moments during walking, sixteen separate 4X3X2 mixed model ANCOVAs (covariate: walking speed) were performed to test for differences in treatment over time on each leg. For VGRF in the stance phase, functional data analyses were performed to compare the VGRF data as functions rather than discrete values. This required registering, or time normalizing, where we warped the peaks and unloading in the VGRF.

Similar statistical analyzes were performed for the measurements recorded during drop landing trials. For neuromuscular activities, twelve separate 4×3×2×2 mixed model ANOVAs were performed to test differences in treatment over time on each leg during different time windows in the stance phase. For the PVGRF, time to PVGRF, vertical stiffness, joint angles, and joint moment, twenty four separate 4×3 mixed model ANOVAs were performed to test differences in treatment over time.

Subjects were blocked on all statistical analyzes. In order to avoid the type I error, Bonferroni type adjustment for multiple comparisons with the significant level as ≤ 0.001 were used for all tests. All data except VGRF during walking were analyzed using SAS 9.2 (SAS Institute Inc., Cary, NC). R 2.14.0 was used to analyze VGRF data during walking.

Results

Pain perception

We found a treatment by time interaction ($F_{69,1242}=12.36$, $p<0.0001$) for perceived pain (Figure 2). Compared to control treatment, subjects immediately felt knee pain after saline injections for effusion ($p<0.0001$), pain ($p<0.0001$), and pain/effusion ($p<0.0001$). Compared to

the control treatment, saline injection for effusion, pain, and pain/effusion resulted in knee pain for six minutes ($p<0.0001$), ten minutes ($p<0.0001$), and 16 minutes ($p=0.0001$), respectively. During the painful time period for the effusion treatment, knee pain intensity was noted to be lower when compared to those subjects who received the pain and pain/effusion treatment ($p<0.0001$).

Walking

Neuromuscular activities

Peak and mean EMG values of during walking trials are presented in Table 1-a through h). We did not find any treatment, time, side, or time window effect in the peak and mean EMG values during the stance phase during walking. The peak EMG data, F statistics $_{6,108}$ ranged from 0.3 to 0.95 with p values between 0.52 and 0.99. For the mean EMG data, F statistics $_{6,108}$ were ranged from 0.47 to 1.13 with p values between 0.31 and 0.97.

Walking speed

Summary data of walking speed and stride length during walking trials are presented in Figure 4-a. We found a treatment by time interaction in walking speed ($F_{6,108}=7.46$, $p<0.0001$). Compared to precondition ($p<0.0001$) and postcondition ($p<0.0005$) measurements, subjects for pain/effusion walked slower during condition measurements. Compared to the control ($p<0.0003$) and pain ($p<0.0005$) treatment, subjects for pain/effusion walked slower during condition measurement. There was a trend towards slower walking speed between the precondition and condition measurement under the effusion treatment ($p=0.002$).

Stride length

We did not find a treatment by time by side interaction in stride length ($F_{6,108}$=1.96, p=0.08). However, there was a treatment by time interaction ($F_{6,108}$=5.58, p<0.0001: Figure 4-b). Subjects for the pain/effusion treatment walked in a shorter stride length during condition measurements than they did during precondition (ipsilateral side: p<0.0001; contralateral side: p<0.0001) and postcondition measurements (ipsilateral side: p<0.0001; contralateral side: p<0.0009).

Joint angles

Summary data of joint angles during walking trials are presented in Table 1-i.

For ankle angles, we did not find a treatment by time by side interaction in ankle dorsi-flexion ($F_{6,108}$=0.84, p=0.54) and ankle plantar-flexion ($F_{6,108}$=1.43, p=0.21).

For knee angles, we did not find a treatment by time by side interaction in, knee flexion ($F_{6,108}$=1.19, p=0.32), knee abduction ($F_{6,108}$=1.08, p=0.38), and knee adduction ($F_{6,108}$=1.00, p=0.43).

For hip angles, we did not find a treatment by time by side interaction in hip extension ($F_{6,108}$=0.80, p=0.57), hip flexion ($F_{6,108}$=0.37, p=0.9), and hip abduction ($F_{6,108}$=1.01, p=0.42), but found a trend in hip adduction ($F_{6,108}$=2.20, p=0.05). Compared to the precondition, condition measurements under the pain/effusion treatment showed a decrease in hip adduction angle on the ipsilateral side (p=0.002: Figure 4-c). Compared to the condition, postcondition measurements under the pain/effusion treatment showed an increase in hip adduction angle on the contralateral side (p=0.004).

VGRF

Plots containing 95% confidence interval bands in comparisons between each time interval under each treatment are presented in Figure 3.

When compared to precondition walking, subjects demonstrated reduced ipsilateral VGRF during condition measurements at around 20 and 80% under the pain/effusion treatment. In the same comparison, subjects walked with an increased ipsilateral VGRF ranging between 40 and 55%, and 90% and 100% of stance (Figure 3-j). While subjects walked with a reduced ipsilateral VGRF ranging between 90% and at the end of stance, it was also noted that they demonstrated an increased contralateral VGRF in the same portion of stance (Figure 3-v).

Joint moments

For ankle joint moments, we found a treatment by time by side interaction in plantar-flexion moment ($F_{6,108}$=5.54, p<0.0001: Figure 4-d). Compared to the precondition (p<0.0001) and postcondition measurements (p=0.0007), condition measurements under the pain/effusion treatment showed a decrease in ankle plantar-flexion moment on the ipsilateral side. In condition measurements subjects under pain/effusion treatment walked with less of a plantar-flexion moment than they did under the control (p<0.0001) and pain treatment (p=0.0008) on the ipsilateral side.

For knee joint moments, we found a treatment by time by side interaction in knee extension moments ($F_{6,108}$=4.49, p=0.0004: Figure 4-e) and knee abduction moments ($F_{6,108}$=8.62, p<0.0001: Figure 4-f) but not in knee adduction moments ($F_{6,108}$=0.96, p=0.45). Compared to the precondition measurements, condition measurement under the pain/effusion treatment had a decrease in knee extension moment on the ipsilateral side (p<0.0008) and an increase in knee extension moment on the contralateral side (p<0.0001). Compared to the precondition

(p<0.0001) and postcondition (p<0.0001) measurements, condition measurements under the pain and pain/effusion treatment had a decrease in knee abduction moment on the ipsilateral side. Compared to the postcondition measurements, condition measurements under the pain treatment had a decrease in knee abduction moment on the ipsilateral side. (p=0.0002)

For hip moments, we found a treatment by time by side interaction in hip abduction moments ($F_{6,108}$=6.32, p<0.0001: Figure 4-g) but not in hip extension moments ($F_{6,108}$=0.45, p=0.84: Table 1-j). Compared to the precondition (p<0.0001) and postcondition measurements (p<0.0001), condition measurements under the pain/effusion treatment had a decrease in hip abduction moment on the ipsilateral side. Compared to the precondition measurements, postcondition measurements under the pain/effusion treatment had an increase in hip abduction moment on the contralateral side (p=0.0007).

Drop landing

Neuromuscular activities

We did not find a treatment, time, side, or time window effect (from 200 ms before to initial contact; from initial contact to peak knee flexion) in the peak EMG values in the stance phase during drop landing (Table 2-a through d). For the peak EMG data, F statistics $_{6,108}$ ranged from 0.18 to 0.96 with p values between 0.52 and 0.99. For the mean EMG data, F statistics $_{6,108}$ ranged from 0.2 to 0.94 with p values between 0.18 and 0.94.

Joint angles

Summary data of peak joint angles during drop landing trials are presented in Table 2-f. Except the frontal plane hip angle at initial contact on the force platform, all angles are the peak angles during drop landing.

For ankle joint angles, we found a treatment by time interaction in peak ankle dorsi-flexion ($F_{6,108}$=7.02, p<0.0001: Figure 5-a) but not in peak plantar-flexion ($F_{6,108}$=2.43, p=0.03). Compared to the precondition measurements of each treatment, condition measurements subjects under the effusion (p<0.0001), pain (p<0.0001), and pain/effusion treatments (p<0.0001) landed with a less ankle dorsi-flexion.

For knee joint angles, we found a treatment by time interaction in peak knee flexion ($F_{6,108}$=4.51, p=0.0004: Figure 5-b) but not in peak knee abduction ($F_{6,108}$=0.97, p=0.45) and adduction ($F_{6,108}$=1.66, p=0.14). Compared to the precondition and postcondition measurements, condition measurements under the effusion (p<0.0001), pain (p<0.0001), and pain/effusion (p<0.0001) demonstrated less peak knee flexion during drop landing.

For hip joint angles, we found a treatment by time interaction in hip angle at initial contact in the frontal plane ($F_{6,108}$=6.43, p<0.0001: Figure 5-c), but not in peak hip extension ($F_{6,108}$=1.95, p=0.08) and flexion ($F_{6,108}$=0.63, p=0.7). A trend towards a decrease existed in peak hip adduction during stance ($F_{6,108}$=2.94, p=0.01: Figure 5-d). Compared to the precondition measurements, subjects touched the force platform with an increase in hip

abduction angle under the effusion (p=0.0005) and pain/effusion (p<0.0001) treatment in the condition measurements.

PVGRF and time to PVGRF

We found a treatment by time interaction in PVGRF ($F_{6,108}$=9.10, p<0.0001: Figure 5-e). During condition measurements subjects under the effusion (p=0.0002) and pain/effusion treatments (p<0.0001) landed with less of a PVGRF than they did under the control. During condition measurements subjects under the pain/effusion treatment landed with less of a PVGRF than they did under the control (p<0.0001) and pain treatment (p<0.0001). During postcondition measurements, subjects under the pain/effusion treatment landed with less of a PVGRF than they did under the control (p<0.0001).

Vertical stiffness

We did not find a treatment by time interaction in the vertical stiffness ($F_{6,108}$=1.81, p<0.1: Table 2-f) but found a trend in the time to PVGRF ($F_{6,108}$=2.92, p<0.01: Figure 5-f). Compared to the control, the amount of time to PVGRF increased under the effusion (p=0.003) and pain/effusion (p=0.001) treatment.

Joint moments

For peak ankle joint moments, we did not find a treatment by time interaction in plantar-flexion ($F_{6,108}$=1.10, p=0.37: Table 2-g).

For knee joint moments, we found a treatment by time interaction in knee extension moment ($F_{6,108}$=14.88, p<0.0001: Figure 5-g) and knee abduction moment ($F_{6,108}$=5.63, p<0.0001: Figure 5-h) but not in knee flexion moment ($F_{6,108}$=1.78, p=0.11: Table 2-g) and adduction moment ($F_{6,108}$=1.53, p=0.17: Table 2-g). During condition measurements, subjects under the pain/effusion treatment landed with less of a knee extension moment than did the control

(p<0.0001). During postcondition measurements, subjects under the effusion (p=0.0009) and pain/effusion treatment (p=0.0005) landed with a smaller knee extension moment than the control. Compared to the precondition (p<0.0001) and postcondition (p=0.0004) measurements, subjects under the pain/effusion treatment landed with a decreased knee abduction moment in the condition measurement.

For hip joint moments, we found a treatment by time interaction in hip abduction moment ($F_{6,108}$=6.84, p<0.0001: Figure 5-i) but not in hip extension ($F_{6,108}$=1.96, p=0.08: Table 2-g), and adduction ($F_{6,108}$=0.69, p=0.66: Table 2-g). Compared to the precondition measurements, condition measurements under the effusion (p<0.0001) and pain/effusion (p<0.0001) treatment landed with less hip abduction moment.

For the time between toe off of the first landing and the initial contact of the second landing, we did not find a treatment by time interaction ($F_{6,108}$=1.42, p=0.22: Table 2-h).

Discussion

Pain perception

Knee effusion (50-ml of 0.9% sodium chloride injection) increased perceived pain, and subjects felt pain for six minutes (average pain intensity: 1.9 cm in the VAS). Our subjects began walking trials two minutes after the injection of fluid into the joint capsule. Since the measurements of walking and drop landing took approximately five to eight minutes, an increased pain perception under the effusion treatment during this time period may confound the results. The minimal amount of volume injected into the knee joint to induce quadriceps inhibition has been suggested as 20-30-ml for the VM and 50-60-ml for the VL (57). A high

volume saline injection (>80-ml) may stimulate nociceptors (111). We thought that 2-ml of lidocaine injected subcutaneously with 50-ml of sodium chloride injected into the joint capsule was an appropriate volume not only to alter neuromechanics but also to prevent knee pain from the activation of the receptor specific to tissue stretch and pressure (e.g. Ruffini endings). Previously, experimental effusion produced no pain (103, 111, 114). Most subjects in our study described the sensation by saying "My knee feels tight". "Tightness" is one of the terms describing pain in the McGill pain questionnaire (91). Many of them may have interpreted the tightness as pain. Previously, the McGill pain questionnaire showed a score of less than 1out of 78 possible points (48). Therefore, we speculate that there was little stimulation of the nociceptors under the effusion treatment.

The pain model (1-ml of 5% sodium chloride injection) induced knee pain for ten minutes. An average pain perception over this time period was 3.0 cm as measured by a VAS. This is similar to the previous reports in pain duration (approximately 10 minutes) (14) and intensity (2.58 – 3.20 cm in VAS) (42, 43). Exact mechanisms and neural pathways of pain induction due to the use of 5% sodium chloride are unclear. 5% sodium chloride could have caused chemical irritation within the infrapatellar fat pad, causing nociceptor activation (group III and/or IV) (4), resulting in an increase of pain perception. Hyperosmolarity of the sodium chloride may also stimulate release of substance P (37). These support the idea that neural pathways in 5% sodium chloride injection are consistent with musculoskeletal pain. It should be noted that cognitive processes such as emotion, depression, past experience, cultural background, or motivation may also affect pain perception, and while pain intensity was controlled on the sensory level, these factors may have affected pain perception in our subjects as well.

We employed experimental knee pain and effusion models to test the single and combined effects on two different afferent pathways. For the pain perception, a combination of pain and effusion treatment did not induce a higher intensity of pain compared to the isolated pain but produced a longer painful period (16 minutes). This may suggest that the interaction of afferent fibers specific to sensation of pain (nociceptors) and tissue distention (e.g.: Ruffini endings) produces an additive effect in terms of pain duration. Ruffini endings (group III) are low-threshold and slow adapting articular mechanoreceptors located in the skin, joint capsules, and ligaments (92). It could be speculated that interaction of stimulation in nociceptor and Ruffini endings may further decrease pain tolerance, resulting in a longer painful period.

Walking

Neuromuscular activities

We observed that the isolated pain, and combined effusion and pain stimulus did not change neuromuscular activity in the lower extremity. Recent data reported that induced knee pain immediately reduced quadriceps activation (isometric and isokinetic measurements) (43). Previously, however, the use of non-steroidal anti inflammatory drugs was noted to reduce knee pain, but did not change quadriceps activation in patients with clinical knee pain (107). This suggests that quadriceps inhibition may be associated with pain but that other factors (e.g.: tissue damage, effusion, and inflammation) independently or combined with pain, may also contribute to inhibition.

In addition to pain, it has been well established that knee joint effusion causes quadriceps inhibition (47, 49, 84, 85, 111). Previously, knee joint effusion resulted in quadriceps inhibition and hamstring facilitation during walking (111). This reverse relationship between quadriceps

and hamstrings has also been observed in dynamic (single leg drop landing (82)) and static (the H-reflex (49)) contractions. Many have suggested that activation of Ruffini endings in the knee joint capsule stimulate the Ib inhibitory interneurons, resulting in quadriceps inhibition (57, 103). Based on the previous reports, we expected to see a similar effect with both isolated effusion and combined effusion and pain stimuli, however but we observed no changes.

Speculating, the lack of differences in neuromuscular activity may be due to the various compensatory strategies used in different individuals under each treatment. This variation in neuromuscular adaptations include changes in walking speed, step length, and joint kinematics and kinetics; different onset and magnitude in voluntary withdrawal and involuntary physiological motor responses; and muscle fiber recruitment patterns. For example, some subjects may have decreased plantar-flexion angle during the first 50% of stance while others increased it during the same time period, showing no changes. Another example, the activation of the fast twitch fibers may have reduced while the recruitment of the slow twitch fibers increased to compensate the activation deficits in the same muscle, resulting in no difference in the net motor unit activity (31). While these ideas are purely speculative, the variability in EMG data between subjects does support the general idea. More data are needed to determine specific neuromuscular strategies used during painful and/or effused movements.

The EMG data were normalized by isometric reference position (Figure 1-a). Quadriceps (VM and VL) and gastrocnemius (GA) are the primary musculature to maintain this position. Comparatively, the MH and GM are relatively relaxed during the isometric reference position used in this study. If the reference value is small (MH and GM), then any small change in the reference data would produce large changes in the reported ratios; ultimately adding variability

to the EMG data. Lastly, the inherent instability of the EMG signals and cross talk may have increased variability as well, lending to our failure to demonstrate statistical differences.

Walking speed and stride length

Slower walking speeds have previously been reported in patients with knee OA (1, 68, 116). The average walking speed of our subjects in the control during the condition measurement was 1.32 (0.08) m/s. Our subjects walked at 1.22 (0.13) m/s in the pain/effusion treatment during the condition measurement. Previous reports show that chronic knee OA patients walked at 1.3 (0.3) m/s (16). Our subjects only demonstrated a decreased walking speed in the pain/effusion treatment as compared to the control. Patients' overall health, joint pain, joint effusion, quadriceps activation, and alignment of the lower extremity are all potential factors in changing walking speed (99). Based on our data, the induction of isolated pain or isolated knee joint effusion does not appear to have altered walking speed. However, when both pain and effusion stimuli are present in the knee joint, walking speed decreased. This may suggest that joint pain and effusion elicit a summative effect in relation to walking speed.

Decreased stride length has also been reported in patients with knee OA (1, 5, 6, 68, 74). The average stride lengths of our subjects under the control and pain/effusion treatment were 1.49 (0.09) m and 1.40 (0.11) m, respectively. Prior research has shown that healthy subjects had an average stride length of 1.45 (0.12) m compared to knee OA patients with an average of 1.42 (0.13) m. Like walking speed, stride length in patients with knee OA was closer to what was observed under the control in the current study as compared to the values noted under the pain/effusion treatment.

Since knee joint pain and effusion are common in the acute stage of knee joint injury, it is likely that knee joint injury would immediately modify gait mechanics due to changes in walking

speed, resulting in alterations in VGRF and joint loading (88). In addition, stride length has a direct proportional relationship with joint moment (2). Clinicians should be aware that a slower walking speed and/or shorter stride length following a knee joint injury could be an indication of neuromechanical alterations in the lower extremity. Thus, joint pain and effusion should be treated in both the acute stage of knee joint injury and found in chronic condition.

Joint angles

In the current study, there was a trend towards a decreased ipsilateral hip adduction angle under the pain/effusion treatment (p=0.004). Similar results were observed in patients with AKP (28). During the stance phase, a decrease in hip adduction angle can occur due to either femoral abduction on a stationary pelvis, or from the elevation of the contralateral pelvis. Additionally, elevation of the contralateral pelvis can be caused by a lateral trunk shift towards ipsilateral side. Visual inspection of the data revealed that, subjects tended to shift their trunks to the ipsilateral side. Unfortunately, trunk motion in the frontal plane was not analyzed and thus cannot be included in the results. Therefore, we are uncertain if an ipsilateral trunk shift caused a decrease in hip adduction. In speculation, subjects may have moved the trunk to the ipsilateral side in an attempt to alter knee joint loading characteristics and relieve pain and/or pressure. This would have resulted in the elevation of the contralateral pelvis, resulting in the observed decreased in hip adduction. We also speculate that this compensatory mechanism affected the hip abductor muscles that stabilize or control the pelvis in the frontal plane, resulting in a decrease of hip abduction moment.

Alterations in joint angles have been previously reported in patients with AKP (80, 88), knee OA (9, 74, 77), and experimentally induced knee effusion (111). Although we expected to observe alterations in joint angles, no such alterations existed. These findings are surprising

because there was a 10.1% reduction in walking speed and a 4.7% decrease in stride length. As walking speed was used as a covariate in all statistical tests, it is logical to think that altered stride length would also demonstrate kinematic changes. With reduction of walking speed and stride length, one would expect to see changes in the hip joint angle in the frontal (61) and/or sagittal plane (65) as these are thought to be influential kinematic variables. In the current study, there was no difference noted in sagittal plane hip angle, however there was a trend towards decreased ipsilateral hip adduction angle under the pain/effusion treatment (p=0.004). As previously discussed, these kinematic alterations might elevate the contralateral hip. This may have altered the hip range of motion in the sagittal plane, resulting in no observed difference in the hip extension and flexion angles.

Variability in the characteristics of measurements may be an additional explanation. The data reduction process has more calculations in joint angles, which has greater chance to create measurement error and/or variability. While stride length with small variability showed differences, greater variability in the joint angles may hamper to detect statistical differences. We believe that our study design (within subject comparisons) minimized this issue, but measurement error and variability could have possibly contributed.

VGRF

VGRF data are commonly reported to describe gait adaptations in patients with AKP (88), ACL deficiency (70), meniscectomy (110), and knee OA (116). Discreet values of the peak impact, unloading, and peak push-off values are typically reported during walking (22, 110). However, a functional analysis was used to detect changes in VGRF throughout the stance phase in the current study. This allowed us to determine where differences existed as well as the magnitude. We observed a decrease in VGRF at around 20 and 80% of stance, and an increase in

VGRF ranging between 40 and 55% of stance under the pain/effusion treatment. The VGRF at the first 20%, ranging between 40 and 55 %, and 80% during stance phase could be considered as the peak impact, unloading, and peak push-off VGRF, respectively (22, 33).

Our data are consistent with many previous studies that have reported a reduced impact PVGRF (first 50% of stance phase) in patients with AKP (88) and knee OA (110, 116). These studies are in general agreement that reduced GRF was likely from the joint unloading mechanism to reduce joint pain (110, 116). In addition, altered VGRFs are likely associated with a decreased knee extension moment although we did not observe any change in the neuromuscular activity in quadriceps. Therefore, alterations in VGRF may provide additional support for studies reporting quadriceps inhibition. It should be noted that self-selected walking speed was not used as a covariate in the statistical analyzes of VGRF data. Since there is a positive relationship between VGRF and walking speed (64, 116), alterations in VGRF in the current study may be related to reduced walking speed (88).

An increase in ipsilateral VGRF ranging between 40 and 55% of stance was observed under the pain/effusion treatment. During the mid stance phase of normal gait, full knee extension typically occurs and the direction of the VGRF passes over the knee joint center resulting in unloading VGRF (104). In the current study, the peak impact, unloading, and peak push-off VGRF were not identifiable in three subjects under the pain/effusion treatment. A retrospective review of these subjects' kinematics and GRF data revealed that these subjects did not fully extend their knees during the mid stance phase. The direction of the GRF did not move over the knee joint center but stayed posterior to the knee joint. While the joint unloading mechanism caused reduced VGRF at 20 and 80% of stance, increased VGRF during the mid-stance may have been a compensatory strategy to maintain upright posture during walking.

Under the pain/effusion treatment, ipsilateral VGRF was also reduced at the end of stance phase. This could be associated with decreased ipsilateral plantar-flexion moments, which we observed in this study and are reported elsewhere (3). Contralateral VGRF at the end of stance was noted to increase under the pain/effusion treatment. This alteration could be a compensatory strategy to decrease the amount of time for the contralateral swing and increase amount of time for the contralateral stance to help unload the ipsilateral side, thus maintaining functional gait patterns.

Joint moments

The peak ankle plantar-flexion moment decreased due to pain/effusion. Little data are available regarding alterations of ankle joint moment in patients with knee joint injury. Using a knee effusion model, previous research has shown that the quadriceps was inhibited while the soleus was facilitated with measurements of the H-reflex (49). The soleus facilitation was interpreted as a compensatory response to quadriceps inhibition, possibly to maintain the functional kinetic chain of the lower extremity (49). Since the H-reflex assesses motoneuron pool excitability with the subjects' position completely controlled (83), it allows for the elimination of the voluntary or intentional withdrawal response. Since the soleus is one the plantar-flexors, we hypothesized that the plantar-flexor moment would increase, but our results contradict the previous findings that the soleus was facilitated by knee joint effusion (49). This could suggest that the subjects' intentional withdrawal response (deactivation of the ankle plantar-flexors) dominated the alteration of the motoneuronpool excitability (facilitation of the solues). We believe that the subjects' voluntary withdrawal of the ankle plantar-flexors resulted from the intention of unloading the joint in the ipsilateral side.

The peak knee extension moment was reduced under both the effusion and pain/effusion treatment but not under pain treatment. A trend toward decreased knee extension moment existed under the effusion treatment (p=0.002). Unfortunately, we did not observe any neuromuscular activity changes in the quadriceps (VM and VL). However, a reduction in the knee extension moment during walking can be interpreted as a modification that was adjusted to decrease or avoid quadriceps contraction thus minimizing knee joint loading (63). This phenomenon has been termed "quadriceps avoidance" (17) and is reported in individuals with ACL deficiency (17, 63, 67, 113). This response is thought to decrease anterior translation of the tibia, thus preventing the knee joint from "giving way" (17, 82). A decreased knee extension moment has also been observed in knee OA patients as compared to normal subjects (6, 54, 63). However, this protective mechanism causes quadriceps weakness which has been blamed as a risk factor for re-injury (46). We speculate that quadriceps inhibition may be a key to modifying/adapting gait patterns, and finally a factor in accelerating degenerative joint disease (100). Clinicians should attempt to reverse quadriceps inhibition to avoid potential alterations of normative movement patterns at the knee joint as well as other joints, instead of considering it a protective response.

The knee extension moment was increased in the contralateral side under the pain/effusion treatment. Diminishing ipsilateral knee extension can modulate the excitability of reflex pathways to the contralateral knee extensors (30). When a knee joint is flexed by an unexpected noxious stimulus, an appropriate response would be to extend the contralateral side (10). This is called the crossed extensor reflex (11). Excitation of the Ib interneuron is thought to be the major contributor to quadriceps inhibition on the ipsilateral side (40). Activation of the Ib afferents may interact with interneurons, resulting in facilitation of excitatory post-synaptic

potentials of the contralateral quadriceps (69). An increase in the contralateral knee extension moment is a compensatory mechanism to maintain balance and assist the ipsilateral knee joint during flexion while walking.

Peak internal knee abduction moment was reduced for the ipsilateral side. Medial compartment knee compression force during walking is nearly 2.5 times greater than the lateral compartment (94), which may partially explain why medial tibiofemoral OA is more common than lateral tibiofemoral OA (54). Internal knee abduction moment reflects joint load distribution between the medial and lateral compartment of the tibiofemoral joint (55). Numerous researchers (6, 9, 50, 75, 98) have reported a decreased knee abduction moment for medial knee OA patients, which results in an increased varus angle (75, 78), and an increased medial compartment joint load (94). Contrarily, reduced a knee abduction moment may decrease medial compartment load, due to related lateral trunk movement to the ipsilateral side (77), which decreases the horizontal distance between the center of mass and knee joint center. Because abnormal joint loading patterns are a key factor in joint degeneration, either of aforementioned situations could promote medial compartment articular cartilage degeneration.

The pain/effusion treatment was noted to reduce ipsilateral hip abduction moment, which has also been reported in individuals with knee OA (19, 77). The hip abduction moment is associated with the GM activation, possibly suggesting that the knee joint pain and effusion immediately produced GM inhibition. However, this should be carefully interpreted because we did not detect any neuromuscular activity change in the GM. Reduced hip abduction may be due to changes in postural alignment. For example, a position with an increase in the ipsilateral hip adduction angle, coupled with a trunk shifting towards the ipsilateral side during the stance phase, may require less activation in GM to maintain functional gait. Subjects could have also shifted

their body weight to the contralateral side to unload or minimise joint pressure, we speculate that a decrease in the hip abduction moment may be an intentional gait adaptation due to the alterations of the knee extension and abduction moments. However, combining a reduction in the hip abduction moment with a decreased knee abduction moment may place patients in the position where a higher impact force may be transferred through the medial compartment at the knee joint. Hip abductor weakness would lead to pelvic drop in the contralateral side during swing phase (21). The body center of mass then moves towards the contralateral side, resulting in an increase in joint loading across the medial compartment (21). Iliotibial tightness over time may cause hip abductor weakness (36), which may increase compressive force in the medial compartment. These mechanical alterations are consistent with the idea that factors associated with acute joint injury (e.g.: pain and effusion) could lead to altered knee joint loading, which could ultimately contribute to chronic joint disease.

We also observed an increase in contralateral hip abduction moment in the postcondition measurements. This is consistent with the previous report (6) and can be interpreted as compensation for the decreased ipsilateral hip abduction moment as it assists ipsilateral swing and unloading during walking. Interestingly, we did not observe the alteration of the contralateral hip abduction moment in the condition measurements but did in the postcondition measurements. Compared to the hip in the frontal plane, the contralateral knee extension moment immediately increased as opposed to a reduction in the ipsilateral knee extension moment. The contralateral hip seems to adapt slower to an alteration of the hip abduction moment. It is plausible that the joint movements in the sagittal plane are the primary contributors to human bipedal forward locomotion, thus the body may attempt to maintain functional gait without an alteration in contralateral hip motion. It is speculated that the

increased contralateral hip abduction moment may lead to more adaptations in other joints along the kinetic chain over time.

Gait adaptations

Level walking is the most common activity of daily living. Following knee joint injury, patients modify their normal gait pattern. Using experimentally induced knee joint effusion and pain, our subjects showed immediate gait deviations. Reduced ipsilateral knee extension moment and knee abduction moment are the first responses noted due to the induced pain/effusion stimulus. A decreased ipsilateral knee extension moment is likely related to the observed increase in contralateral knee extension moment. Decreased ipsilateral knee abduction likely alters knee joint loading characteristics, including the medial compartment. Ipsilateral peak ankle plantar-flexion and hip abduction moments were also altered due to pain/effusion. We theorize that these modifications indicate a voluntary withdrawal, in an attempt to unload the ipsilateral knee. Reduced hip abduction moment moves the center of mass towards the contralateral side, placing additional force to the medial compartment at the knee joint. However, this may relieve medial compartment joint pressure depending on the trunk motion. Either case an abnormal joint loading pattern, potentially accelerating joint degeneration (9, 77, 98). As a result of reduced ipsilateral hip abduction moment, contralateral hip abduction moment increases to maintain body posture and assist with the ipsilateral swing phase of gait. Since we added walking speed as covariate for all statistical analyzes in joint moments, we are confident that potential effects of walking speed in joint moments were controlled.

Gait adaptations observed in this study are consistent with the idea that pain and/or effusion, as an independent factor in joint injury, could lead degenerative changes in the joint

and potentially chronic joint disease. More data are needed to bridge changes observed in this study to degenerative joint disease.

Drop landing

Neuromuscular activity

With knee joint effusion, reduced quadriceps and increased hamstring neuromuscular activity have been reported during a single leg drop landing (82). Since we used a knee effusion model, we expected to observe similar results. Additionally, neuromechanical alterations (knee extension moments and dorsi-flexion moments) were observed in the current study. We did not, however, observe any change in the peak and mean values of lower extremity neuromuscular activity. Similar to the walking trials, the lack of difference observed in the neuromuscular activity may also be due to similar reasons such as variation in compensatory strategies, normalization process, and inherent instability of EMG measurements.

PVGRF and time to peak VGRF

The measurement of PVGRF during drop landing can indicate the amount of force absorbed by the body (96). Interestingly, our subjects landed with a reduced PVGRF under the effusion and pain/effusion treatment. The previous reports of changes of the PVGRF during a single leg drop landing have varied. In pre- and post-measurement studies, the PVGRF was decreased in the fatigued group (71, 101). There was no difference of the PVGRF in between healthy controls and patients with ACL deficiency (73) and ACL reconstruction (25). Artificial knee effusion caused an increase in the PVGRF in healthy subjects (82). The inconsistency in PVGRF change, during drop landing, was one of the reasons that we employed the controlled injury models. Among those previous data, it would be parallel to compare our results to those

that used the knee effusion model. Our results are in contradiction to the previous study reporting an increase in the PVGRF by artificial knee joint effusion (82).

Several factors may explain why our subjects showed a reduction in the PVGRF under the effusion and pain/effusion treatment. First of all, we observed changes in joint angles: a decrease in dorsi-flexion angle, knee flexion, and hip adduction. Compared to a normal landing technique, the stiffer landing of the lower extremity has previously shown to increase the PVGRF during drop landing (height of 32 cm; current study: 30 cm) (117). Contrarily, our subjects landed with a more erected posture causing a decrease of the PVGRF. This may suggest that the energy from the imposed force to the body may have not been dissipated by the lower extremity or the subjects have tried to avoid absorption of the impact force using their lower extremity. Additionally, the amount of time between the toe off of the first landing and the initial contact of the second landing was not different among the treatments at any time interval. This may suggest that the secondary vertical jump did not affect the alterations in the PVGRF. Therefore, we believe that trunk shifting towards the ipsilateral side may have been strategy used by subjects to absorb the energy, resulting in a decrease in the PVGRF. It is unfortunate that the trunk motions were not analyzed but this is indirectly supported by decreased ipsilateral hip adduction. We also observed a trend towards an increase in the amount of time to PVGRF under the effusion (p=0.003) and pain/effusion (p=0.001) treatment. These results also support the idea that trunk lateral shifting delayed the time to PVGRF, potentially dissipating forces over a longer period of time.

Length-tension relationships in the activation of the plantar-flexors may be considered a factor to reduce the PVGRF. The gastrocnemius and the Achilles tendon slack when the peak knee flexion angle increases during stance. This is not the optimum position for the

gastrocnemius to generate full force according to the length–tension relationship (90). In a previous study, landing technique with decreased knee flexion showed slightly lower PVGRF than the normal knee bent landing technique (96). Unfortunately, this idea is not supported by the neuromuscular activity data in the current study. For the gastrocnemius, however, stiffer landing posture may have been a better position to eccentrically absorb the impact force in the current study.

Finally, subjects may have changed their dropping technique to drop from a different height due to the saline injections, resulting in decreased PVGRF. Subjects were instructed to drop from the box without bending the leg used to support their mass while on the box. The assessors visually verified that subjects did not bend the support leg prior to dropping from the box. While the landing was controlled as much as possible, we admit that the landing techniques under the different treatments may have varied slightly. However, we believe that varied landing techniques caused minimal effects.

Vertical stiffness

Stiffness has been calculated as the ratio between the PVGRF and the maximal vertical displacement of the center of body mass during drop landing (20). To date, there is little whole body stiffness data to make a comparison with our calculations. Previous data in whole body stiffness during a single leg hopping activity ranging between 2000 – 8000 N/m in children (6.1±1.2 yrs) (38). This range is six times less than the range in the current study (8000 – 48000 N/m). The big differences in stiffness values may be due to the performed activity in our study and subjects' age. Our subjects (22.4 ±2.4 yrs) performed a higher velocity activity (landing from a box at a height of 30 cm) while the children performed several hops on the ground (38). Our subjects, under the effusion and pain/effusion treatment, landed with decreased knee flexion

and ankle dosiflexion angle, but stiffness was not different. This may be due to large variations in stiffness values and/or reduced PVGRF.

Joint angles

Subjects landed with a more extended knee under the effusion and pain/effusion treatment as compared to the control. Previously, a decreased knee flexion angle was reported in healthy subjects with artificial knee effusion (82) and in patients with ACL reconstruction (25). A stiffer landing posture may be associated with a decreased knee extension moment. The greater the knee flexion angle becomes after landing requires increased eccentric contraction of the quadriceps. Since the knee extension moment was reduced, subjects may have been dependent on the straightened lower extremity alignment and bony architecture rather than eccentric contraction of the quadriceps.

There was a decrease in ankle dorsi-flexion angle under the effusion, pain, and pain/effusion treatment compared to the control. Combined with decreased knee flexion angle, decreased dorsi-flexion angle allowed the subjects to balance using the lower extremity alignment (more straightened leg) rather than contracting the lower extremity musculature, especially quadriceps. There has been sufficient evidence to support quadriceps weakness with AKP (81) and knee joint effusion (49, 82). Although there was no change observed in neuromuscular activity in the quadriceps, we speculate that the quadriceps inhibition by saline injections resulted in decreased dorsi-flexion and knee flexion.

Subjects were instructed to drop down on the ipsilateral foot followed by an immediate vertical jump. The peak hip abduction occurred at initial contact and at toe off from a jump. Since the results from either movement confound each other, the hip angle in the frontal plane at initial contact would be more appropriate to compare. Subjects touched the force platform with

an increase in hip abduction angle under the effusion and pain/effusion condition. Subjects may have intentionally tried to stretch the ipsilateral limb to prepare for landing, resulting in increased hip abduction. This may have been due to hesitance to land on the ipsilateral side. We also observed a trend towards a decreased ipsilateral hip adduction angle under the pain/effusion treatment (p=0.002) as compared to the control. Upon closer review of the kinematic data, an increase in ipsilateral adduction of the femur was less common in most subjects. As discussed for walking trials, this alteration more likely occurs due to the lateral trunk shifting towards the ipsilateral side, resulting in an elevation of the contralateral pelvis.

Joint moment alterations and injury risk

Landing from a jump is a common and essential movement in most physical activities. Lower extremity neuromechanical changes due to a knee joint injury alters the normal landing strategies, resulting in an injury. For example, a prospective study (79) tracking two seasons of professional handball players reported that a non-contact mechanism of injury occurred in 95% of all ACL ruptures. Non-contact ACL injuries have been reported most commonly in the last 15 minutes of the first half and in the last 30 minutes of the second half of soccer games (41). Therefore, fatigue has been thought to be a factor in increasing the risk of non-contact ACL ruptures. Neuromechanical modifications during drop landing due to fatigue include: a decrease in the PVGRF (71, 101); and landing with a more straightened leg (101). Our data are in general agreement with those previously reported with fatigue, thereby supporting the idea that knee joint pain and effusion stimuli may increase the risk of non-contractile injuries.

Even though we did not observe any neuromuscular changes, a reduction in the ipsilateral knee extension moment could have resulted from quadriceps inhibition under the effusion and pain/effusion treatment. This is consistent with the previous research using artificial knee

effusion (82). Knee extensors are believed to serve as the major energy absorbers (25, 26), suggesting that decreased knee extension moment may reduce knee joint stability during dynamic landing from a jump. Sufficient evidence provides that quadriceps dysfunction exists in patients with ACL injuries (23, 102, 112). A decrease in knee extension moment due to quadriceps inhibition may decrease the capability of the quadriceps to provide as an active restraint in the knee joint stability (7). A reduced knee extension moment was observed during walking in the current study, which supports the previous reports in patients with knee OA (6, 54). Immediate joint pain and effusion appear to produce quadriceps inhibition not only during walking but also during single leg drop landing. As discussed in walking, we believe that quadriceps inhibition triggered other neuromechanical modifications during drop landing. Therefore, it is apparent that the key factor in early rehabilitation following a knee joint injury/surgery will be to reverse quadriceps inhibition and/or restore quadriceps function.

There was a trend towards a decrease in peak internal knee abduction moment in the condition measurement compared to the precondition (P=0.002) and postcondition (P=0.02). This finding is consistent with the walking trials in the current study, suggesting that a decrease in knee abduction moment may affect normal joint loading due to trunk motion. As discussed earlier, we assume that subjects shifted their trunks towards to the ipsilateral side. Speculatively, this compensatory motion changes the center of mass shifting to the ipsilateral side, resulting in a reduction in joint stress on the medial compartment due to a reduction in external knee adduction moment. Again, since an abnormal joint loading is a major factor, either adaptation will cause joint degeneration at the knee joint.

Cadeveric (72) and computer model (8) studies suggest that knee joint loading changes in either direction of the frontal plane (abduction and/or adduction) can increase tension of the ACL.

This suggests that the combination of a reduced knee extension moment and a reduced knee abduction moment could potentially increase the risk of ACL injury.

Assumptions and limitations

We assumed that joint sizes and the ability to absorb the sterile saline (infrapatellar fat pad and knee joint capsule) were similar. In addition, physiological capacity to absorb or reduce the effects of saline may differ from subject to subject. However, the amount of saline should be standardized to produce pain and/or effusion stimuli. In our pilot study, the minimum amount of hypertonic saline was 1-ml to produce AKP for 10 minutes, which allows enough time for the measurements.

The neuromechanical alterations reported in our study are limited to immediate responses. Patients with chronic knee OA have likely been reprogramming their movement strategies for a relatively longer time period. In other words, it could take neuromechanical alterations greater than those observed immediately or 30 minutes post injury, to accelerate joint degeneration. Therefore, we assume that patients will maintain the neuromechanical alterations shown immediately post injection or further develop movement modifications as time progresses. During walking, we observed both an increase in the hip adduction angle and hip abduction moment on the contralateral side in the postcondition measurement. These compensatory adaptations were not observed in the condition measurements. Therefore, it is safe to assume that further compensatory movements will occur following knee joint injury.

Even though this artificial pain produced similar types of clinical pain such as aching and throbbing (14), the experimental pain model does not necessarily reproduce the clinical or

chronic AKP. Therefore, the movement adaptations due to the experimental injury models in the current study should not directly be considered as those in patients with clinical knee joint injuries. We only examined the isolated and combined effects of knee joint pain or effusion on altered neuromechanics in walking and drop landing. It should be noted that there are more complicated chemical and mechanical interactions following a knee joint injury. For example, a clinical knee joint injury typically involves the primary and secondary tissue damage with the resultant inflammatory response in addition to pain and joint effusion.

Conclusion

We were interested in examining how isolated joint effusion or joint pain, as well as combination of these two stimuli, would alter neuromechanics in functional movements. In quantifiable comparisons, a total number of 16, 7, and 3 dependent variables were altered during functional movements under the pain/effusion, effusion, and pain treatments, respectively. Based on our results, isolated joint effusion appears to play a wider role in neuromechanical alterations during functional movements. When pain stimulus is combined with effusion stimulus it appears to produce a summative effect that is greater than either isolated effusion or pain. Since joint effusion is typically accompanied by pain, both variables should be aggressively managed in all stages of knee joint injury and rehabilitation.

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Tables and figures

Figure 1-a. EMG during this isometric reference position was recorded to normalize the EMG amplitude. Subjects were asked to squat down until their butt slightly touches an edge of the desk.

Figure 1-b. A static standing trial was first measured and considered as each subjects' neutral body alignment. Twelve surface EMG electrodes and four clusters of four reflective markers were attached to the lower extremity. In addition to, twenty seven single reflective markers were attached to the lower extremity and trunk.

Figure 2. Mean and standard deviations for pain perception (VAS) for each treatment over time. † indicates a difference between the effusion and control treatment. § indicates a difference between the pain and control treatment. * indicates a difference between the pain/effusion and the control treatment. All differences indicate $p<0.0001$.

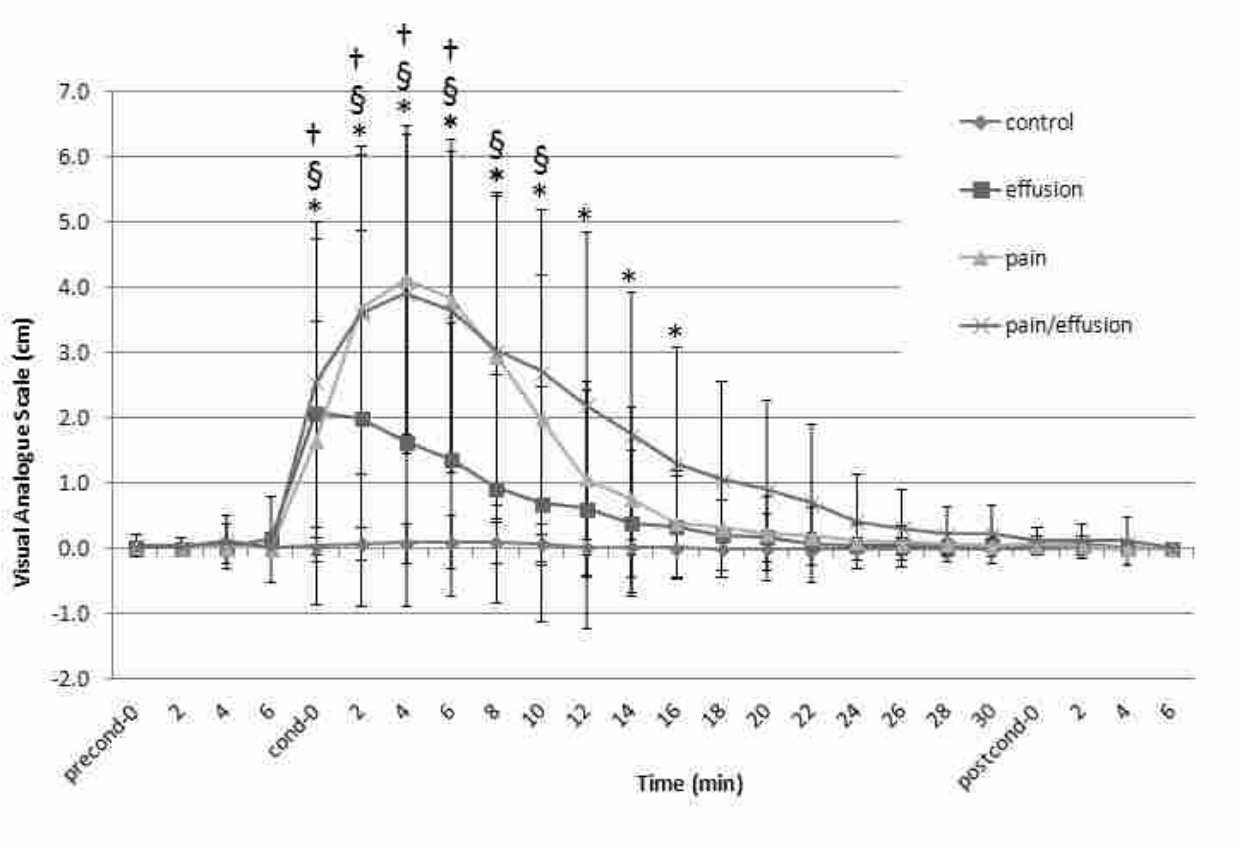


Figure 3. Plots are showing the results of the functional data analyses for VGRF during walking. The solid line within the shaded area indicates the mean difference in VGRF values between comparisons. The shaded area represents the 95% confidence interval bands.

Figure 3-a. 95% confidence interval for ipsilateral VGRF between the precondition and condition measurements under the control treatment.

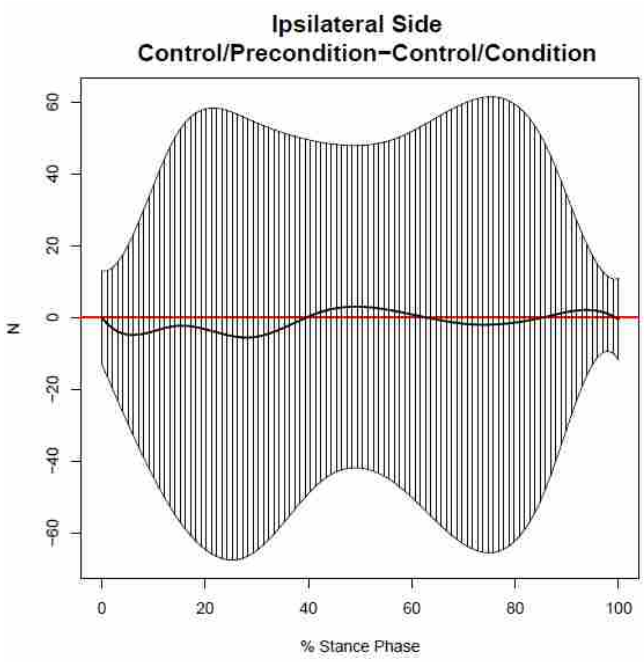


Figure 3-b. 95% confidence interval for ipsilateral VGRF between the condition and postcondition measurements under the control treatment.

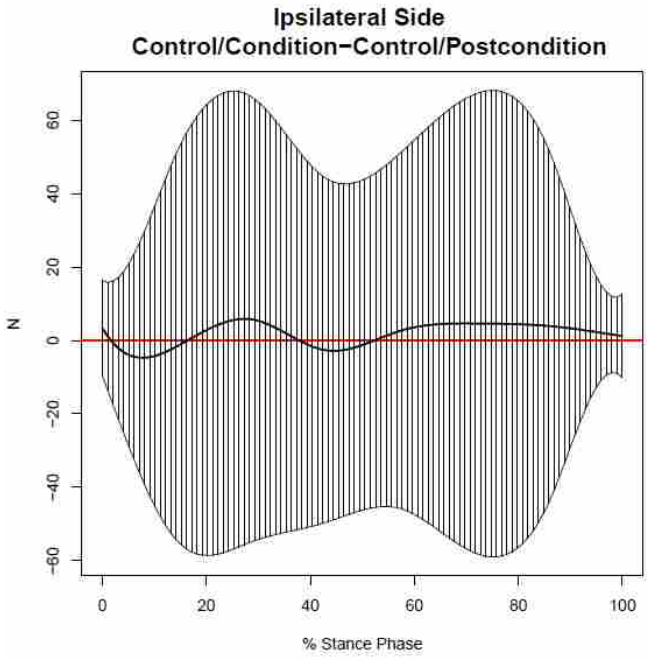


Figure 3-c. 95% confidence interval for ipsilateral VGRF between the precondition and postcondition measurements under the control treatment.

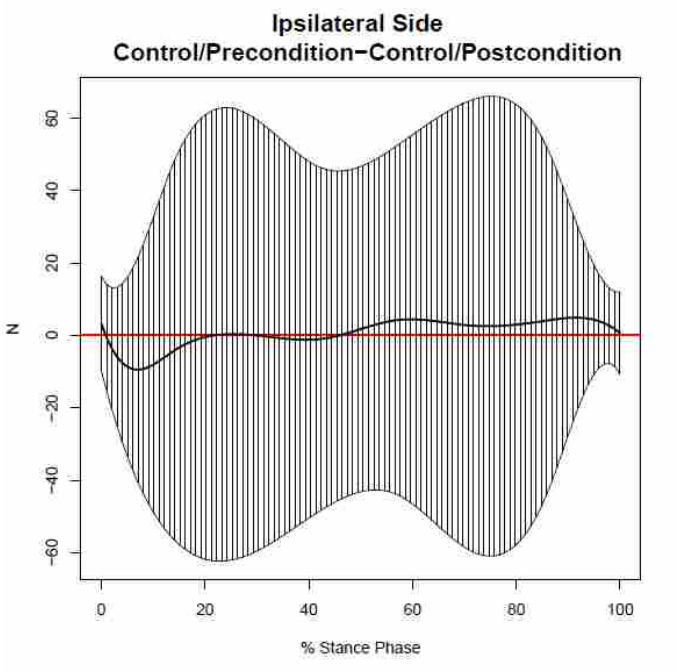


Figure 3-d. 95% confidence interval for ipsilateral VGRF between the precondition and condition measurements under the effusion treatment. Compared to precondition measurements, the mean VGRF recorded during condition measurements was approximately 25 N higher at 95% of stance.

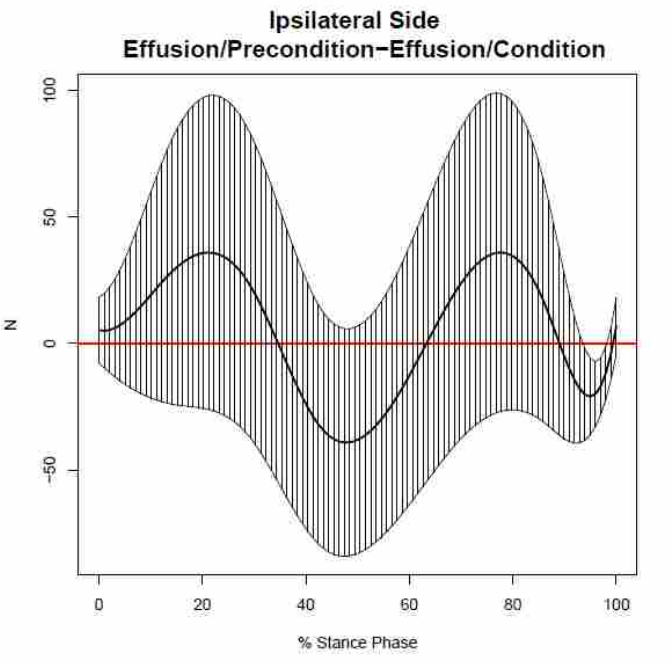


Figure 3-e. 95% confidence interval for ipsilateral VGRF between the condition and postcondition measurements under the effusion treatment. Compared to condition measurements, the mean VGRF recorded during postcondition measurements was approximately 20 N less at 95% of stance.

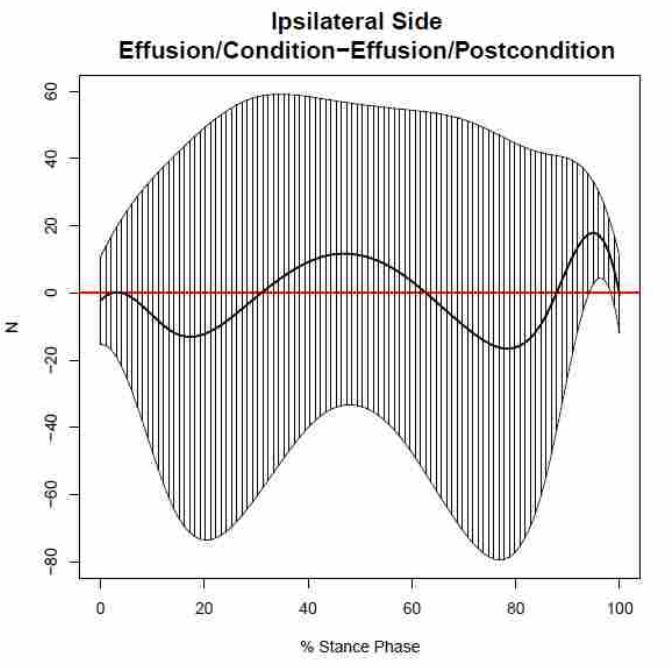


Figure 3-f. 95% confidence interval for ipsilateral VGRF between the precondition and postcondition measurements under the effusion treatment.

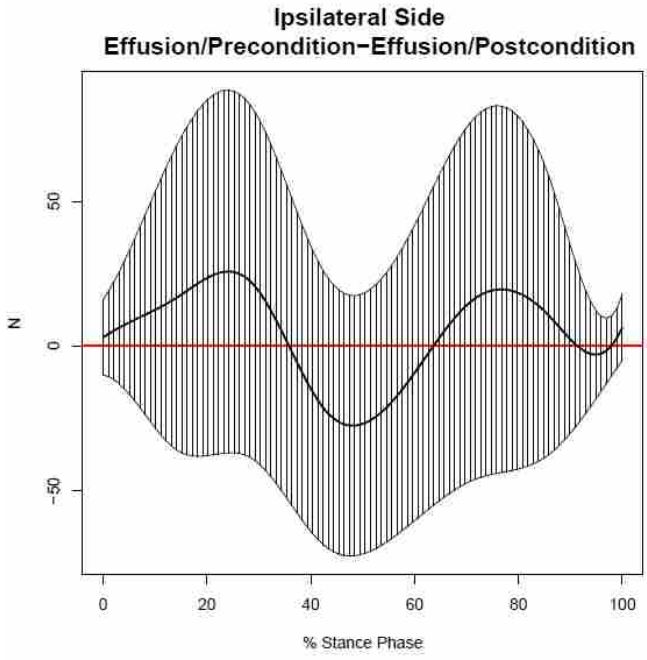


Figure 3-g. 95% confidence interval for ipsilateral VGRF between the precondition and condition measurements under the pain treatment.

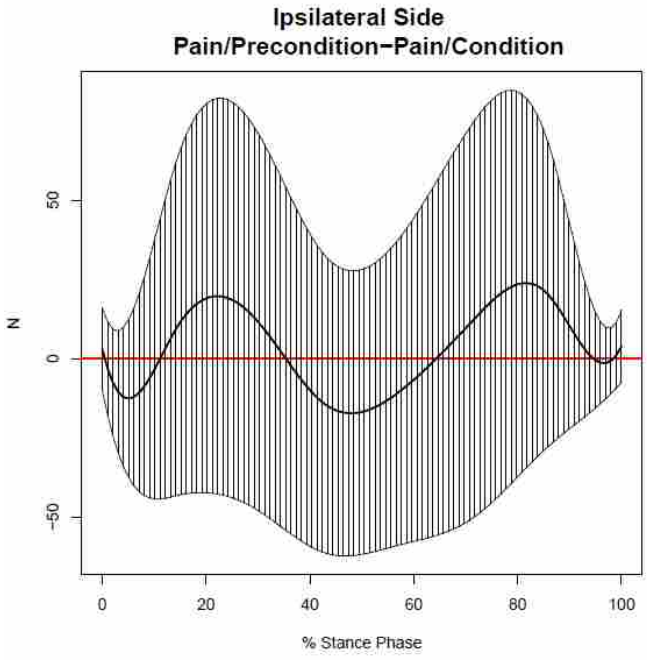


Figure 3-h. 95% confidence interval for ipsilateral VGRF between the condition and postcondition measurements under the pain treatment.

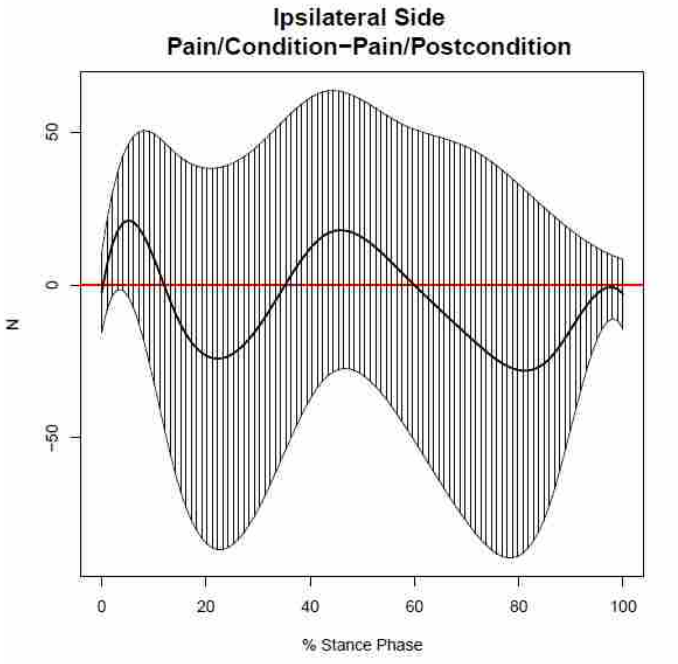


Figure 3-i. 95% confidence interval for ipsilateral VGRF between the precondition and postcondition measurements under the pain treatment.

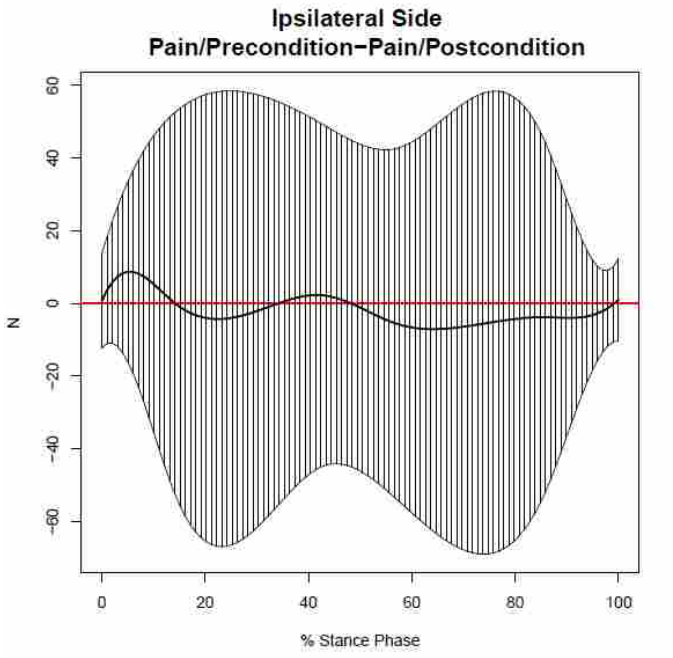


Figure 3-j. 95% confidence interval for ipsilateral VGRF between the precondition and condition measurements under the pain/effusion treatment. Compared to precondition measurements, the mean VGRF recorded during condition measurements was approximately 75 N less at approximately 20% and 80% of stance, but 75 N higher ranging between 40 and 55%, and 30 N higher at 95% of stance.

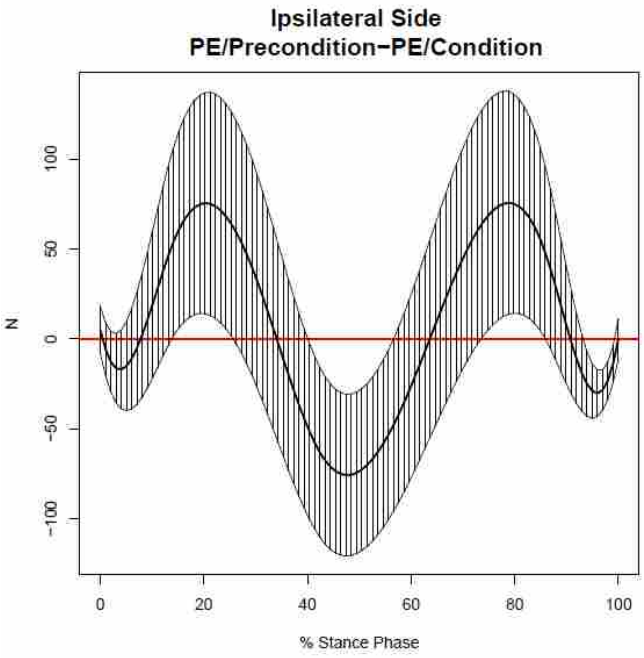


Figure 3-k. 95% confidence interval for ipsilateral VGRF between the condition and postcondition measurements under the pain/effusion treatment. Compared to condition measurements, the mean VGRF recorded during postcondition measurements was approximately 25 N higher ranging from approximately 90% until the end of stance.

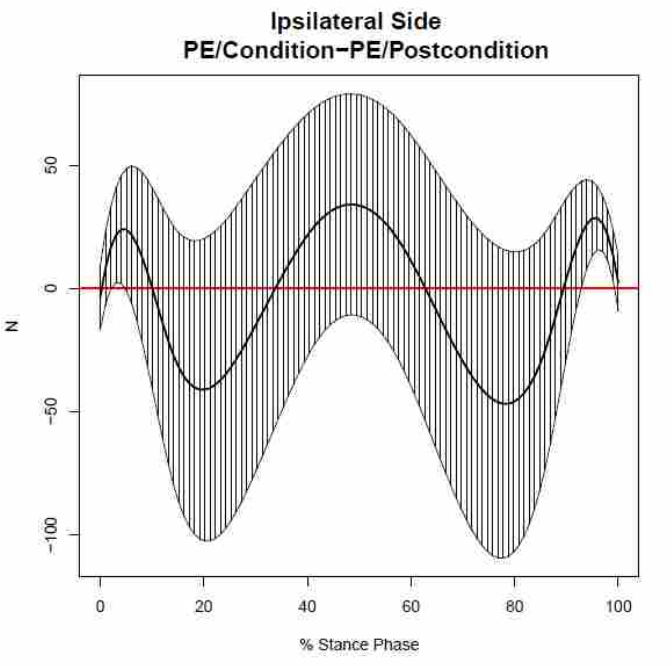


Figure 3-l. 95% confidence interval for ipsilateral VGRF between the precondition and postcondition measurements under the pain/effusion treatment.

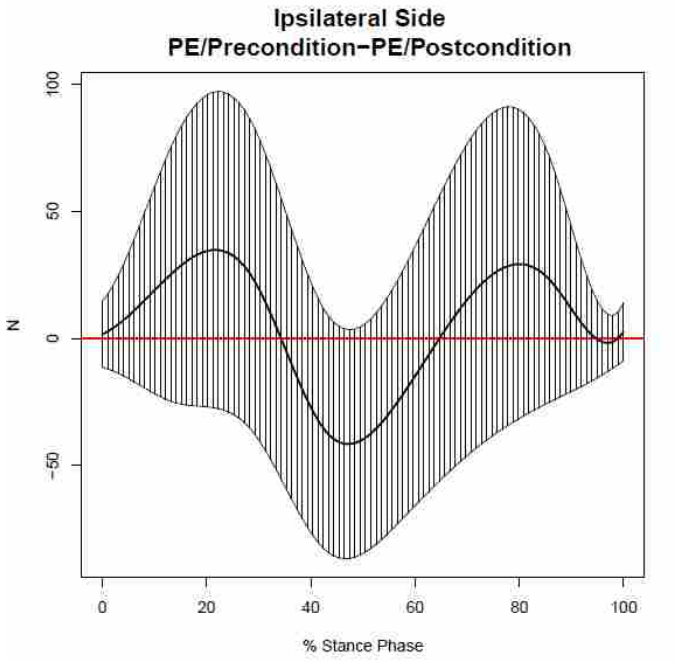


Figure 3-m. 95% confidence interval for contralateral VGRF between the precondition and condition measurements under the control treatment.

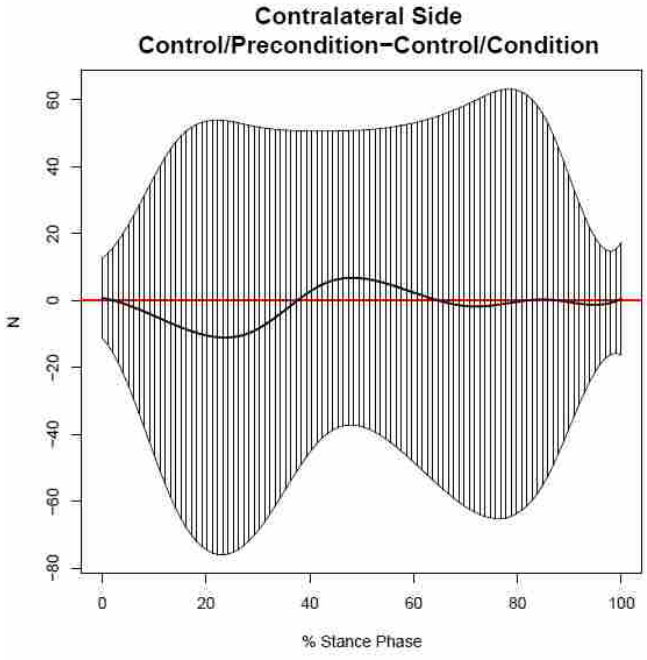


Figure 3-n. 95% confidence interval for contralateral VGRF between the condition and postcondition measurements under the control treatment.

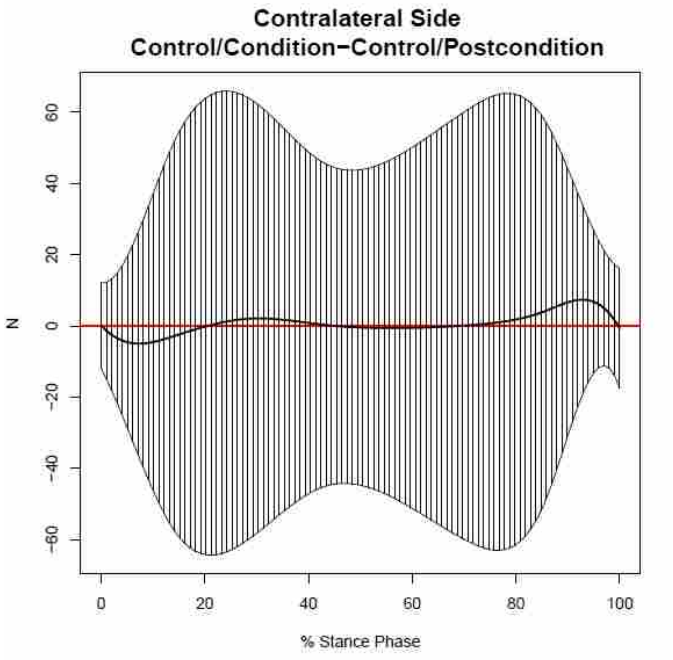


Figure 3-o. 95% confidence interval for contralateral VGRF between the precondition and postcondition measurements under the control treatment.

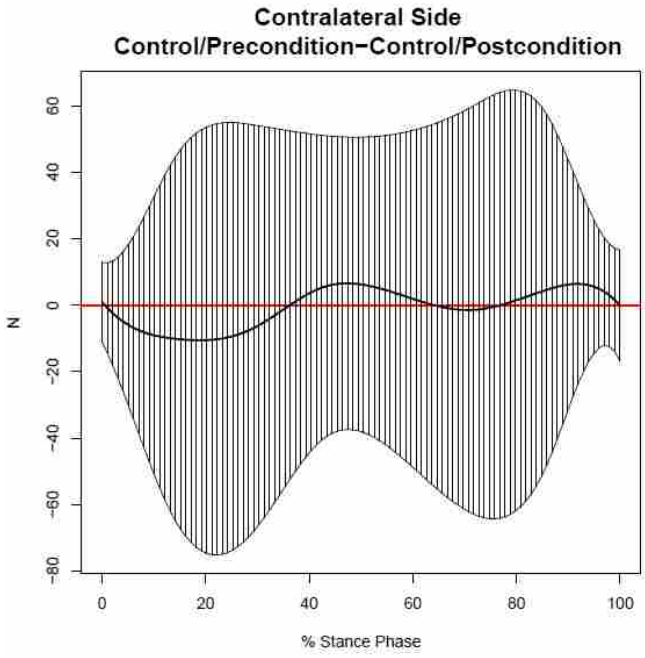


Figure 3-p. 95% confidence interval for contralateral VGRF between the precondition and condition measurements under the effusion treatment.

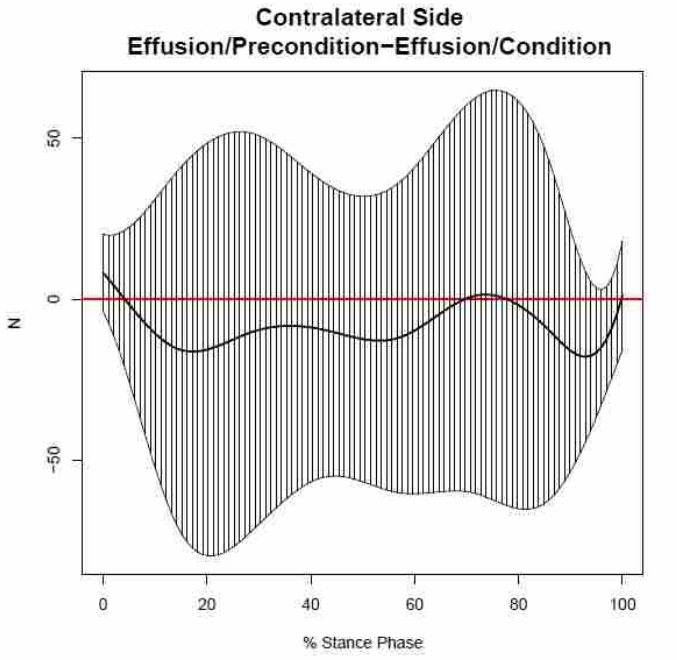


Figure 3-q. 95% confidence interval for contralateral VGRF between the condition and postcondition measurements under the effusion treatment.

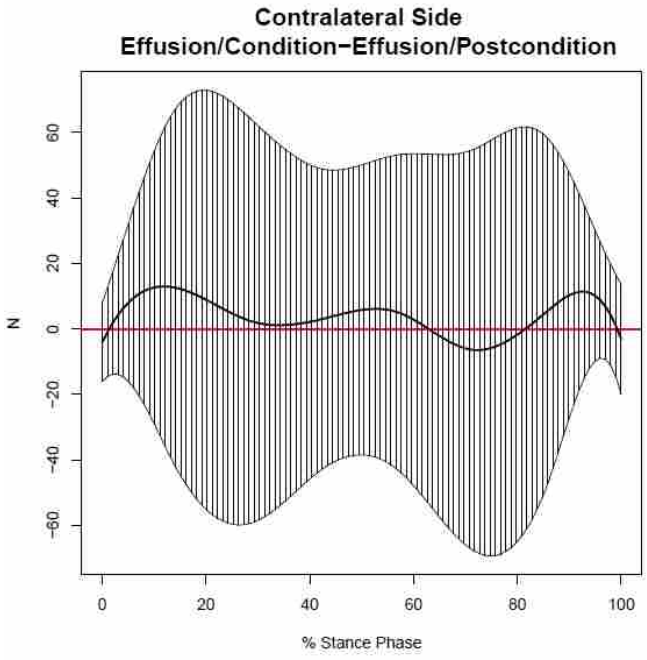


Figure 3-r. 95% confidence interval for contralateral VGRF between the precondition and postcondition measurements under the effusion treatment.

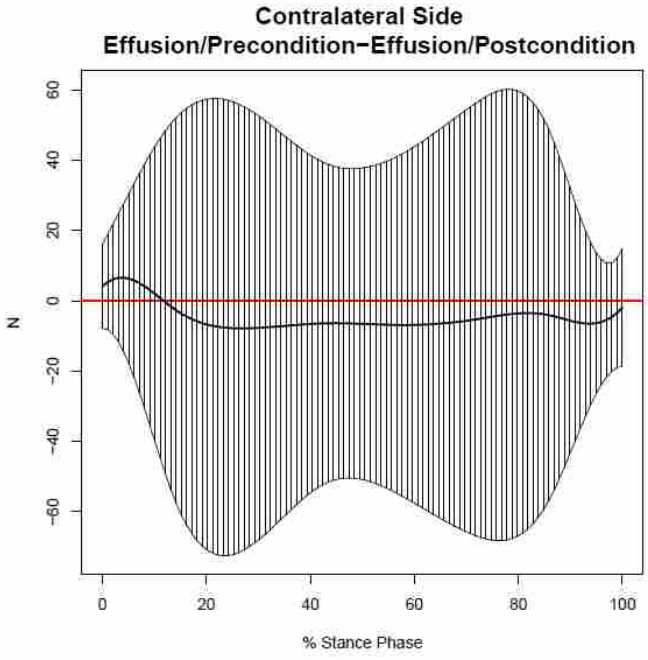


Figure 3-s. 95% confidence interval for contralateral VGRF between the precondition and condition measurements under the pain treatment.

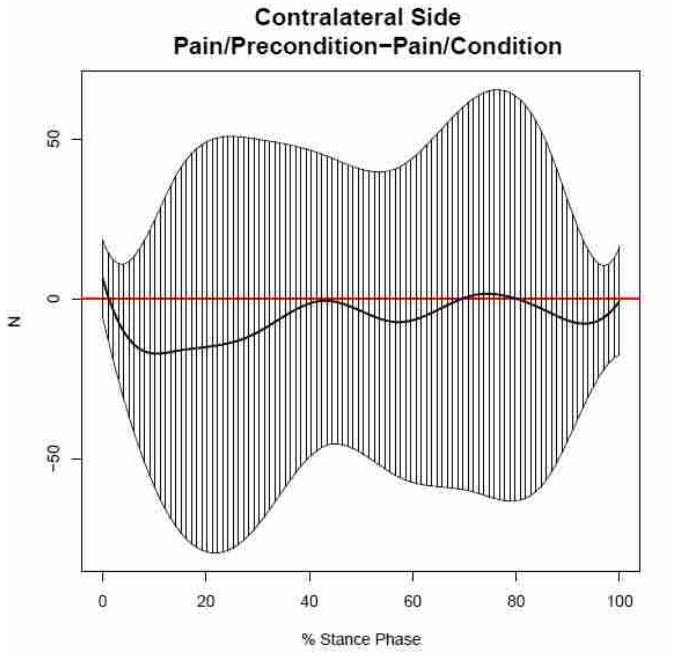


Figure 3-t. 95% confidence interval for contralateral VGRF between the condition and postcondition measurements under the pain treatment.

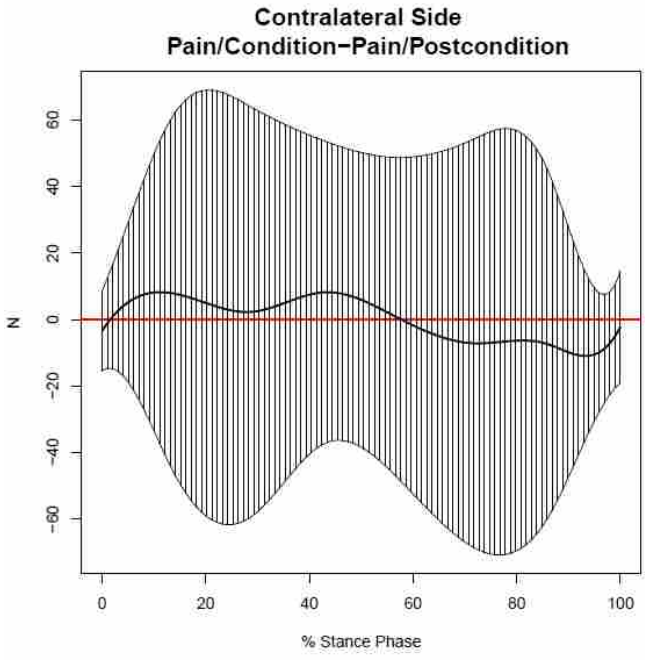


Figure 3-u. 95% confidence interval for contralateral VGRF between the precondition and postcondition measurements under the pain treatment.

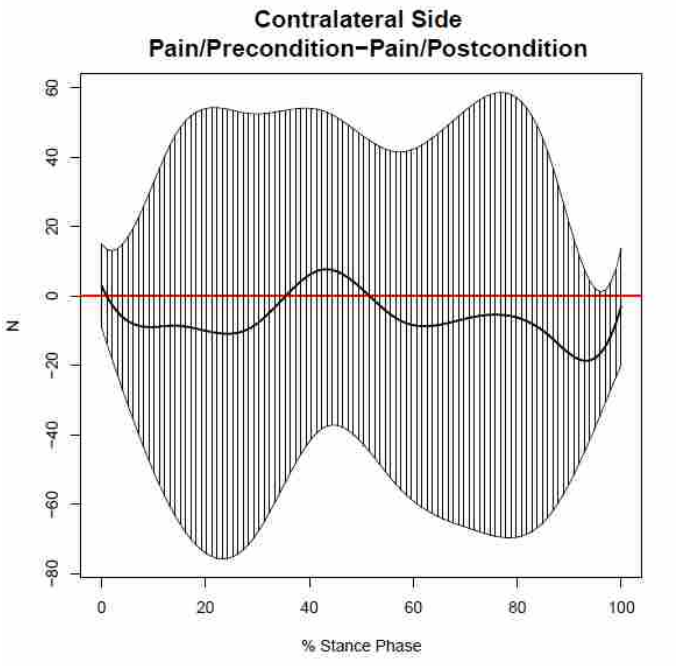


Figure 3-v. 95% confidence interval for contralateral VGRF between the precondition and condition measurements under the pain/effusion treatment. Compared to precondition measurements, mean VGRF during condition measurements was approximately 50 N higher ranging from approximately 90% until the end of stance.

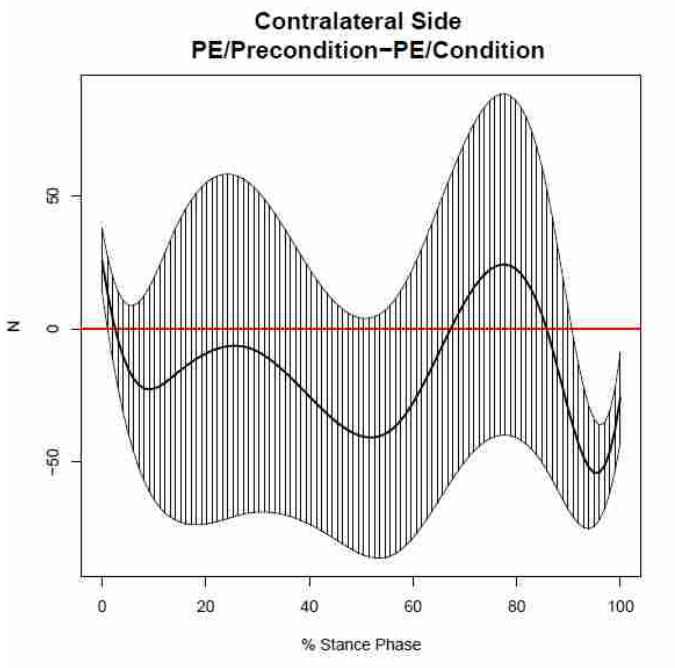


Figure 3-w. 95% confidence interval for contralateral VGRF between the condition and postcondition measurements under the pain/effusion treatment. Compared to condition measurements, the mean VGRF recorded during postcondition measurements was approximately 50 N less ranging from approximately 90% until the end of stance.

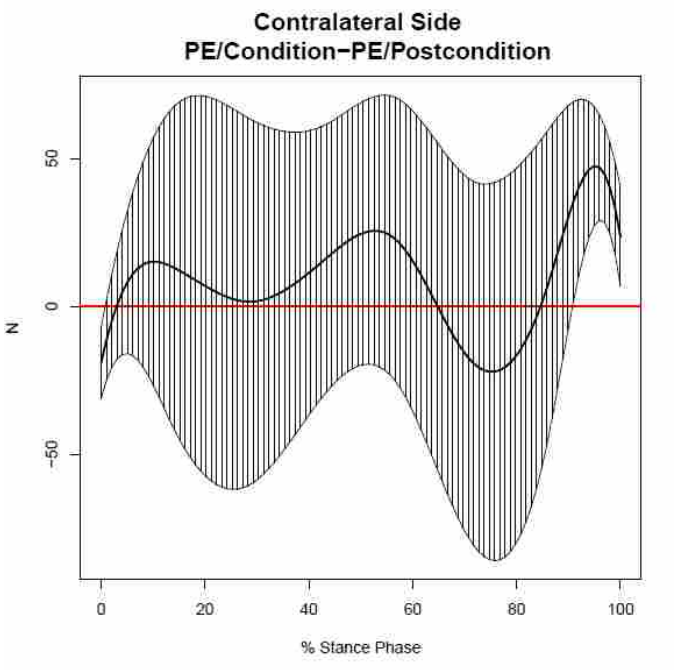


Figure 3-x. 95% confidence interval for contralateral VGRF between the precondition and postcondition measurements under the pain/effusion treatment.

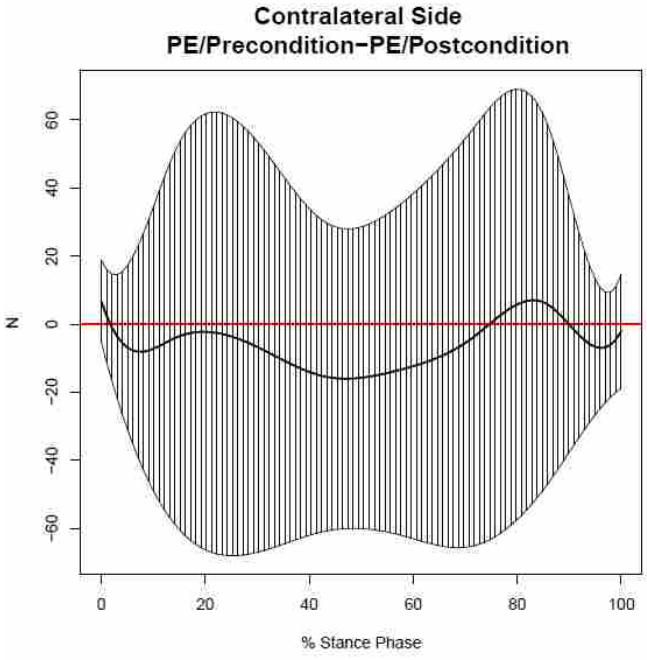


Figure 4-a. Means and standard deviations for walking speed during walking. ***** compared to the precondition (p=0.0001) and the postcondition measurement (p=0.0005) under the pain/effusion treatment. * the pain/effusion treatment compared to the control (p=0.0003) and the pain treatment (p=0.0005) during the condition measurement. † compared to the precondition measurement (p=0.002) under the effusion treatment.

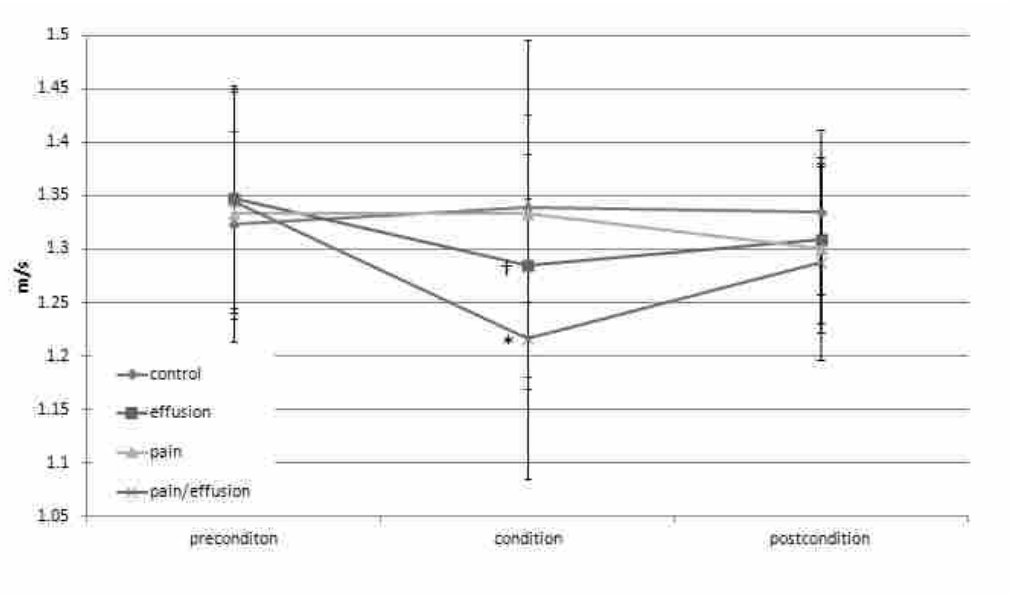


Figure 4-b. Means and standard deviations for stride length during walking. * compared to the precondition (p=0.0001) and the postcondition measurement (p=0.0005) under the pain/effusion treatment.

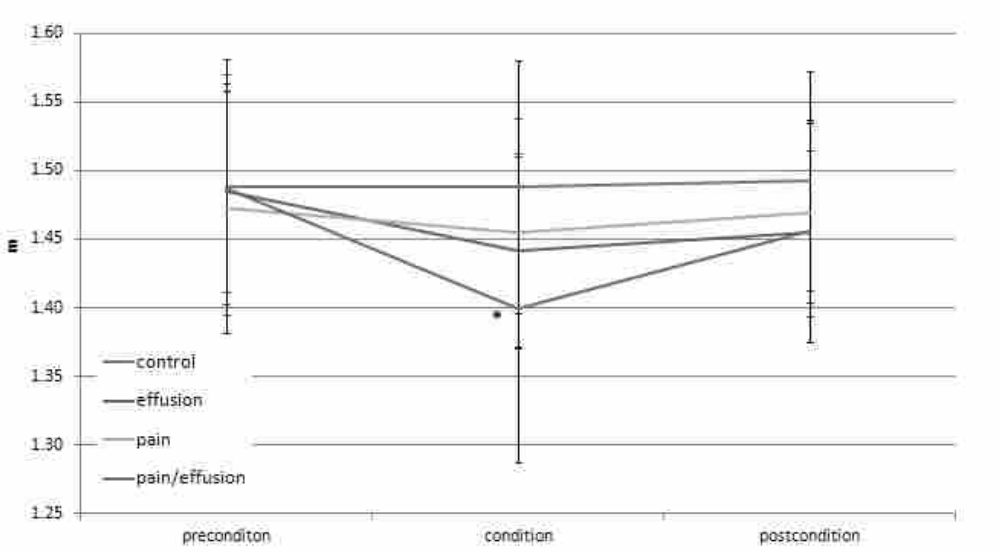


Figure 4-c. Means and standard deviations for the peak hip adduction angles during walking. * compared to the precondition measurement (p=0.002) under the pain/effusion treatment in the ipsilateral side. † compared to the condition measurement (p=0.004) under the pain/effusion treatment in the contralateral side.

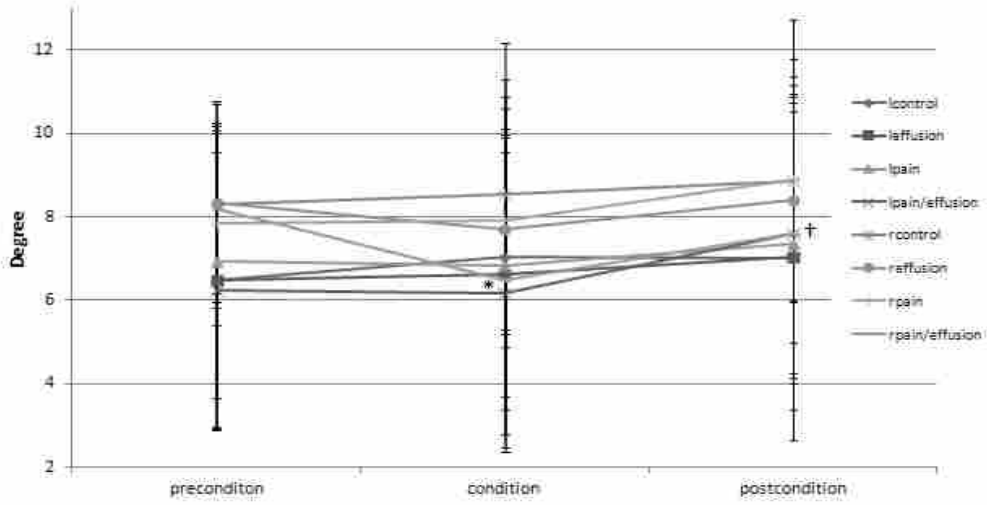


Figure 4-d. Means and standard deviations for the peak ankle dorsi-flexion moments during walking. * compared to the precondition (p=0.002) under the pain/effusion treatment in the ipsilateral side. † compared to the condition (p=0.004) measurement under the pain/effusion treatment in the contralateral side.

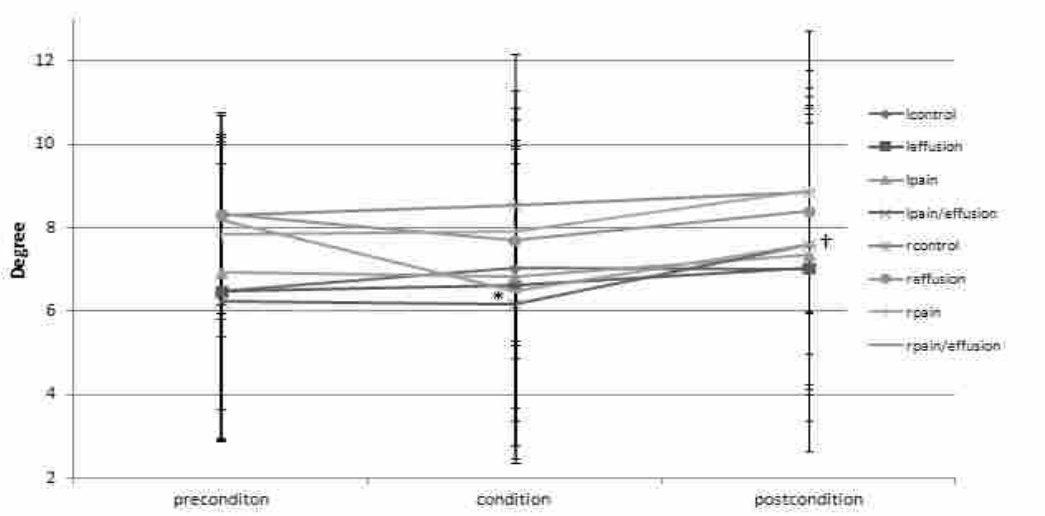


Figure 4-e. Means and standard deviations for the peak knee extension moments during walking. * compared to the condition (p=0.0008) and the postcondition measurement (p=0.004) under the pain/effusion treatment in the ipsilateral side. § compared to the precondition measurement (p=0.002) under the pain/effusion treatment in the contralateral side. ‡ compared to the precondition (p<0.0001) and the postcondition (p=0.002) measurement under the pain/effusion treatment in the contralateral side.

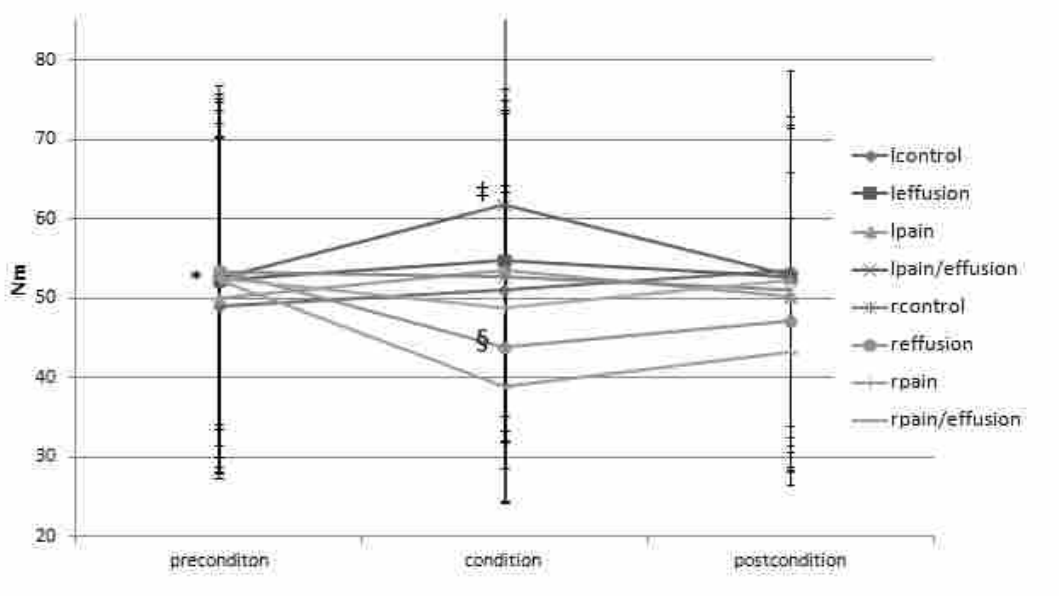


Figure 4-f. Means and standard deviations for the peak knee abduction moments during walking. * compared to the precondition (p<0.0001) and the postcondition measurement (p<0.0001) under the pain/effusion treatment in the ipsilateral side. † compared to the condition measurement (p=0.0002) under the pain treatment in the ipsilateral side.

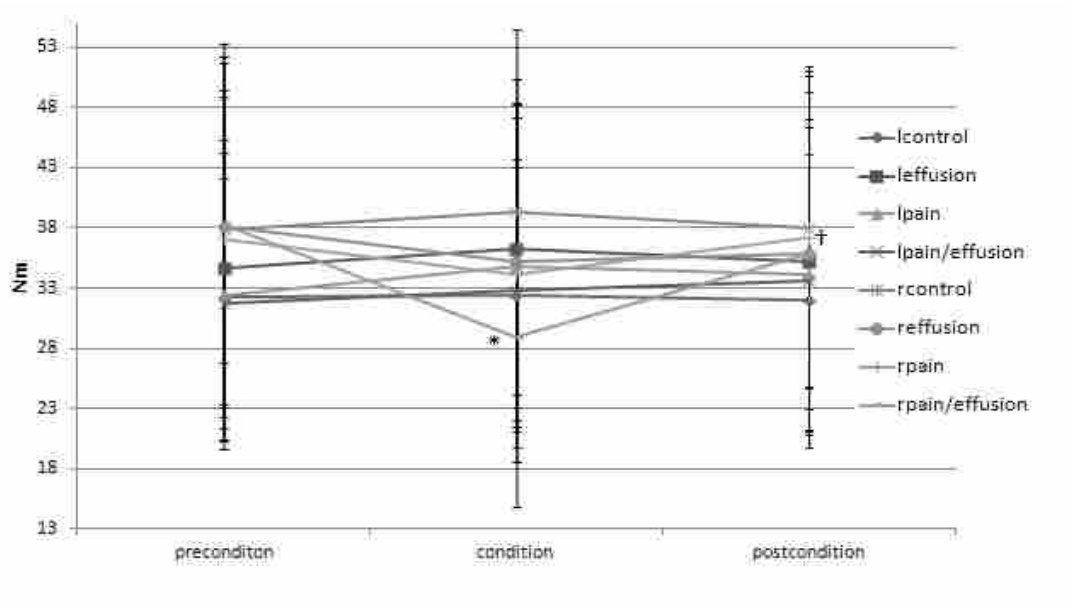


Figure 4-g. Means and standard deviations for the peak hip abduction moments during walking. * compared to the precondition and the postcondition measurement (p<0.0001) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition measurement (p=0.0007) under the pain treatment in the contralateral side.

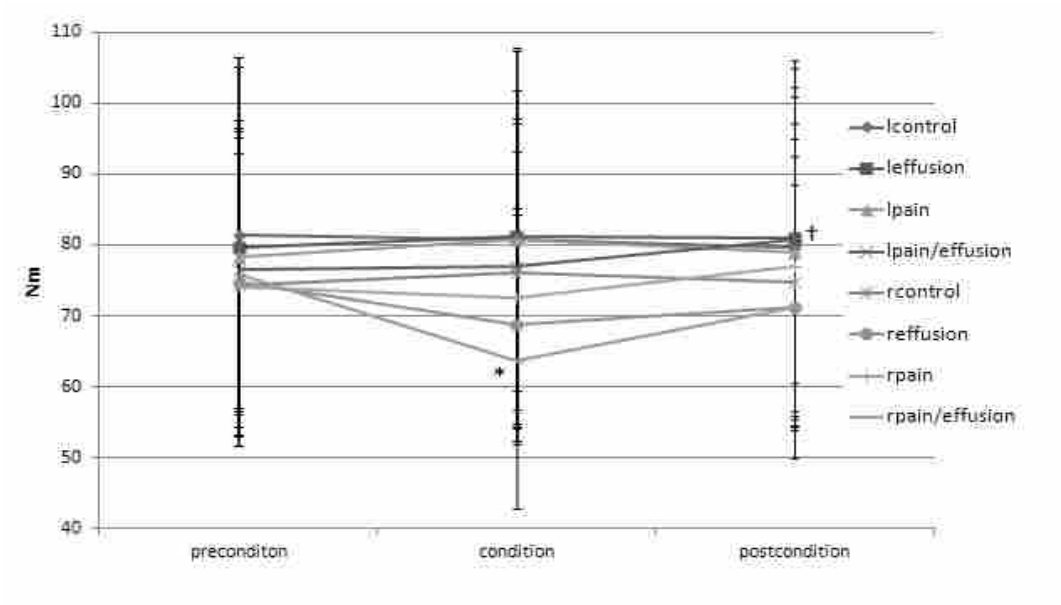


Figure 5-a. Means and standard deviations for the peak ankle dorsi-flexion angles during drop landing. * compared to the precondition (p<0.0001) and the postcondition measurement (p=0.001) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition (p<0.0001) and the postcondition measurement (p=0.003) under the pain treatment in the ipsilateral side. ‡ compared to the condition and the postcondition measurement (p<0.0001) under the effusion treatment in the ipsilateral side.

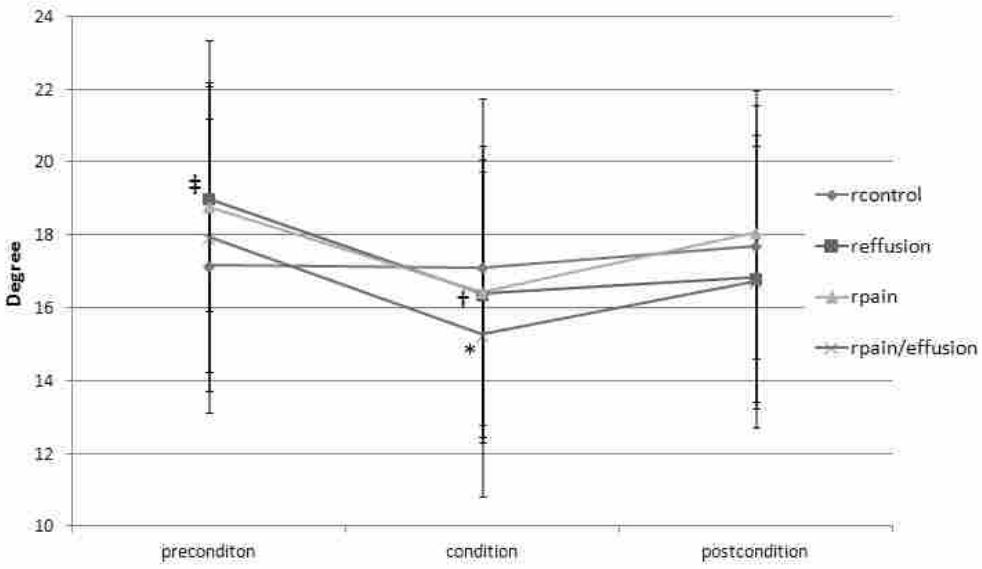


Figure 5-b. Means and standard deviations for the peak knee flexion angles during drop landing. * compared to the precondition and the postcondition measurement (p<0.0001) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition and the postcondition measurement (p<0.0001) under the pain treatment in the ipsilateral side. ‡ compared to the condition and the postcondition measurement (p<0.0001) under the effusion treatment in the ipsilateral side.

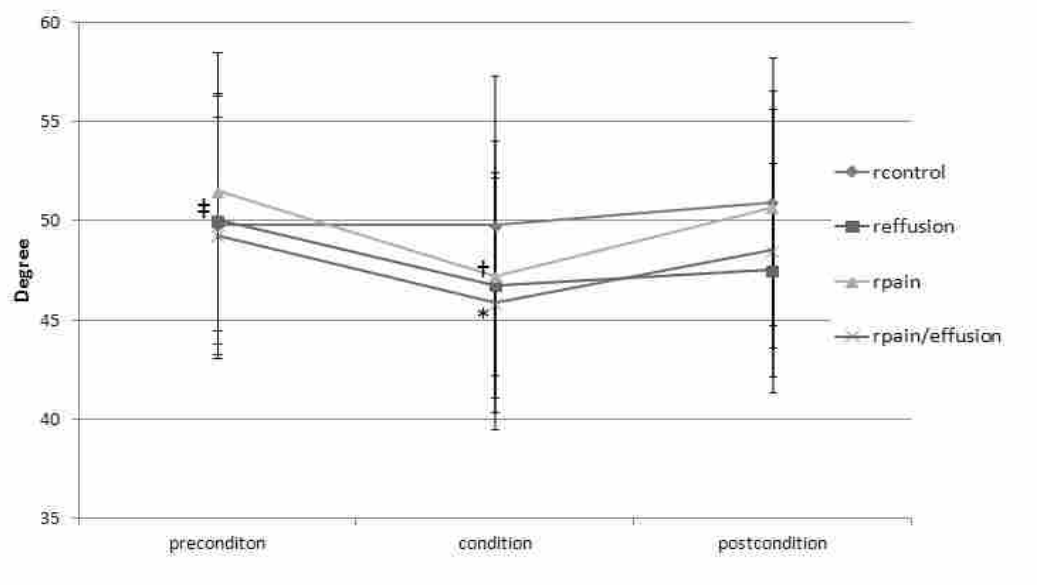


Figure 5-c. Means and standard deviations for the peak hip angles at initial contact during drop landing. * compared to the precondition (p<0.0001) and the postcondition measurement (p=0.05) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition (p=0.0005) and the postcondition measurement (p=0.02) under the effusion treatment in the ipsilateral side. ‡ compared to the condition measurement (p=0.002) under the pain treatment in the ipsilateral side.

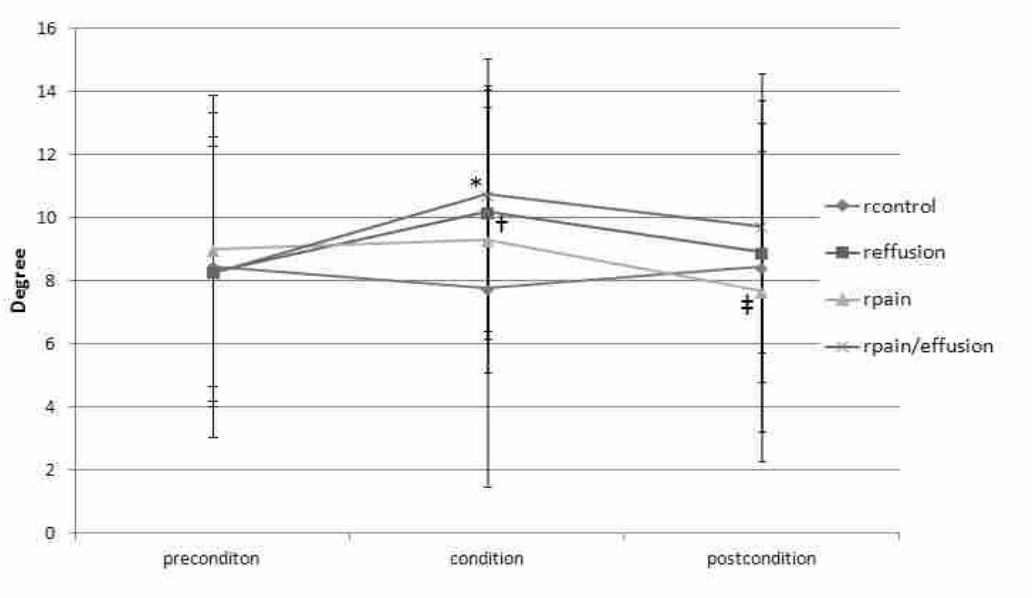


Figure 5-d. Means and standard deviations for the peak hip adduction angles during drop landing. * compared to the precondition measurement (p=0.002) under the pain/effusion treatment in the ipsilateral side.

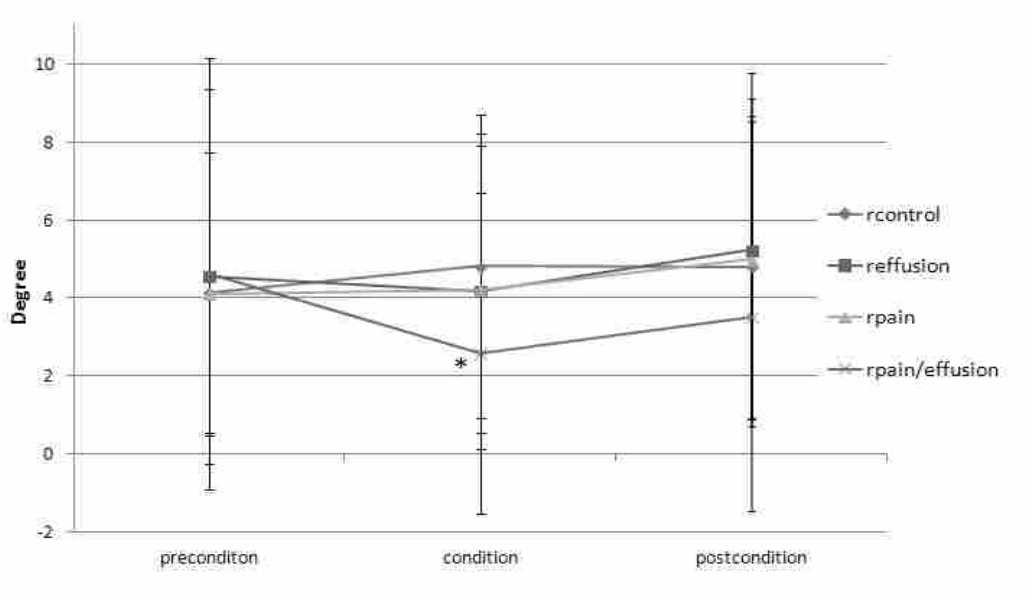


Figure 5-e. Means and standard deviations for PVGRF during drop landing. * compared to the precondition measurement and the postcondition (p<0.0001) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition measurement (p<0.0002) under the effusion treatment in the ipsilateral side.

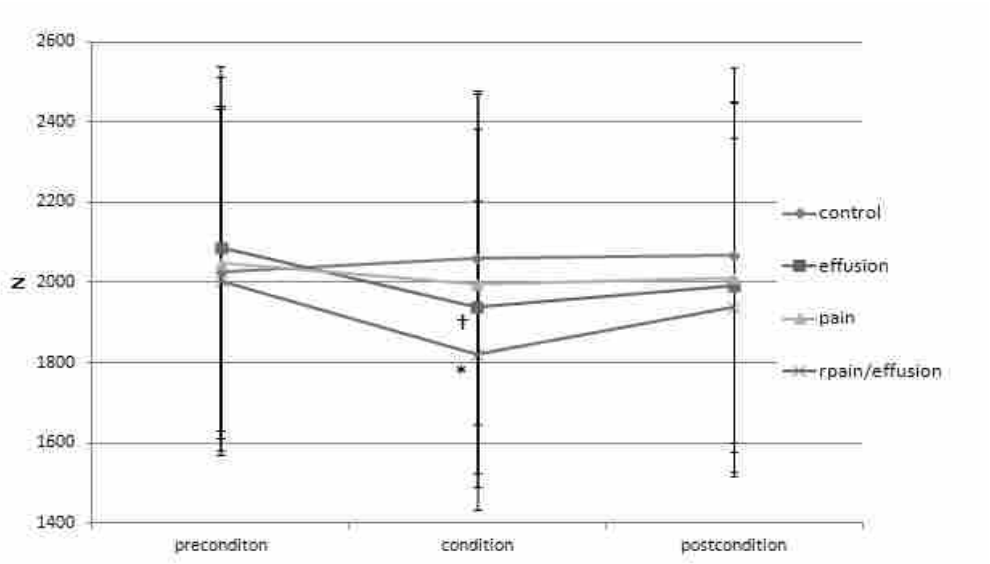


Figure 5-f. Means and standard deviations for time to PVGRF during drop landing. * compared to the control treatment (p=0.001) under the pain/effusion treatment in the ipsilateral side. † compared to the condition measurement (p=0.001) under the effusion treatment in the ipsilateral side.

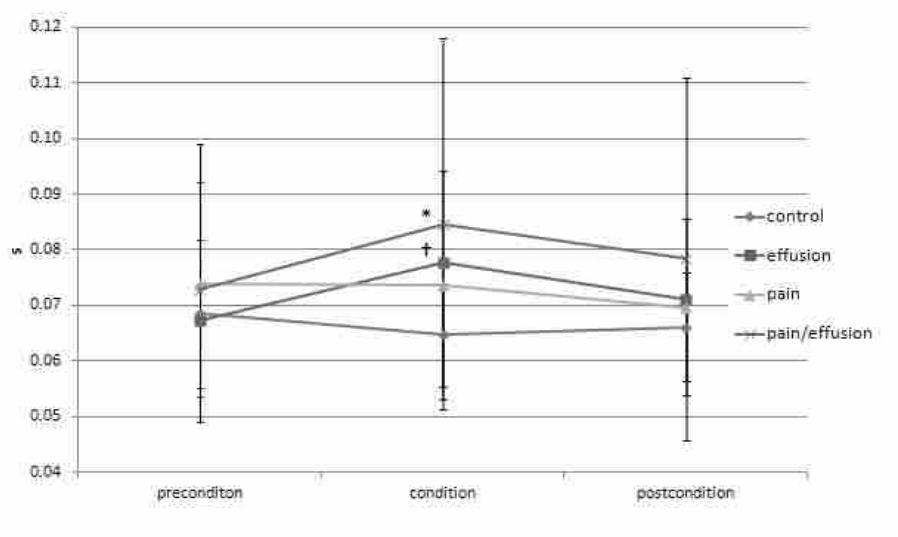


Figure 5-g. Means and standard deviations for the peak knee extension moments during drop landing. * compared to the precondition measurement (p=0.0001) under the pain/effusion treatment in the ipsilateral side. † compared to the precondition measurement (p<0.02) under the effusion treatment in the ipsilateral side. ‡ compared to the effusion (p=0.009) and the pain/effusion (p=0.005) treatment during the postcondition measurements.

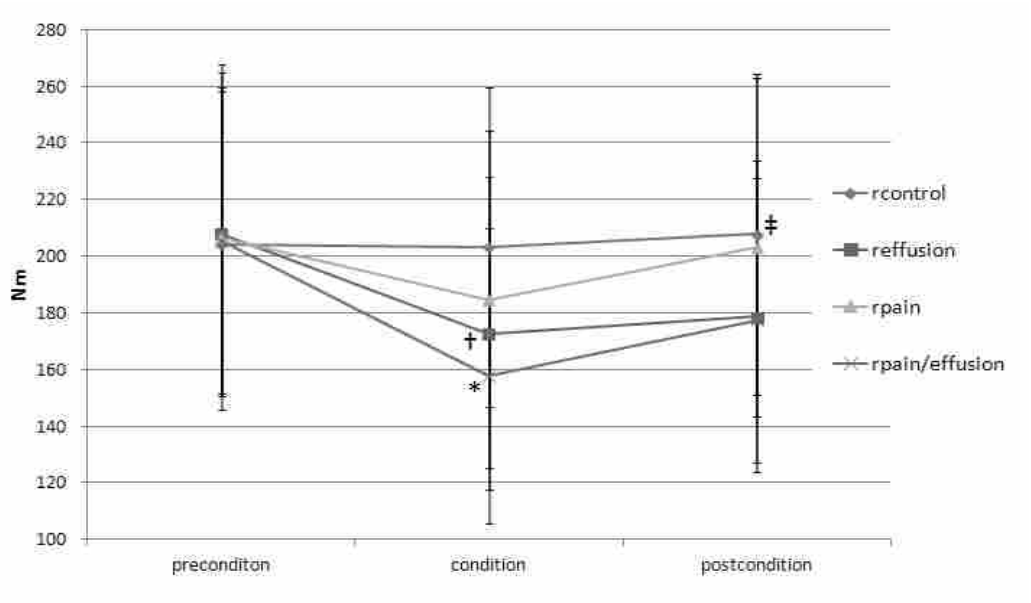


Figure 5-h. Means and standard deviations for the peak knee abduction moments during drop landing. * compared to the condition (p<0.0001) and the postcondition measurement (p=0.0004) under the pain/effusion treatment in the ipsilateral side. † compared to the condition (p=0.001) and the postcondition measurement (p=0.02) under the effusion treatment in the ipsilateral side.

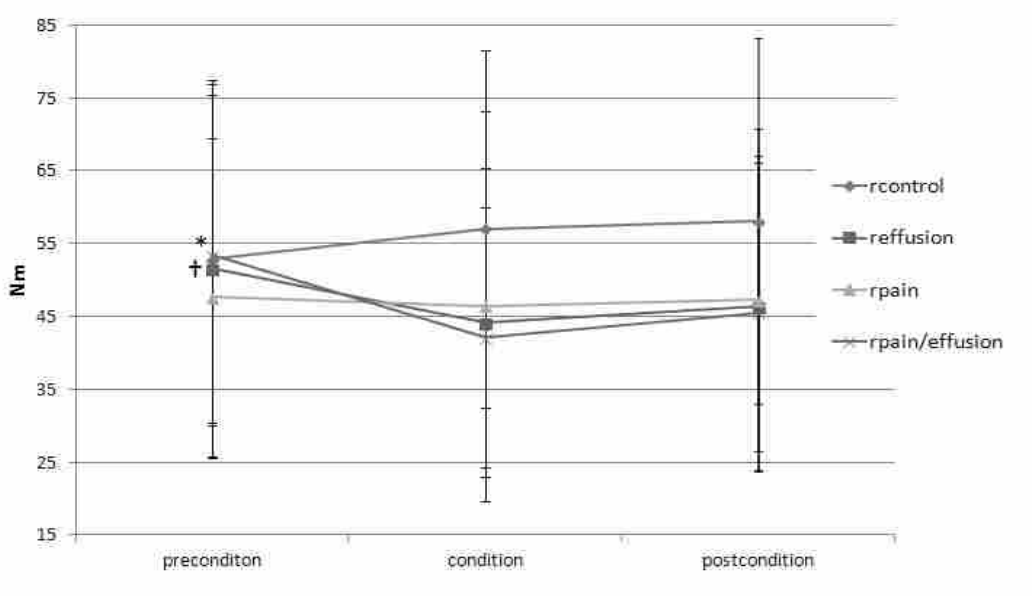


Figure 5-i. Means and standard deviations for the peak hip abduction moments during drop landing. * compared to the effusion (p=0.002) and the pain/effusion treatment (p=0.001) during the condition measurement. † compared to the effusion (p=0.04) and the pain/effusion treatment (p=0.007) during the postcondition measurement.

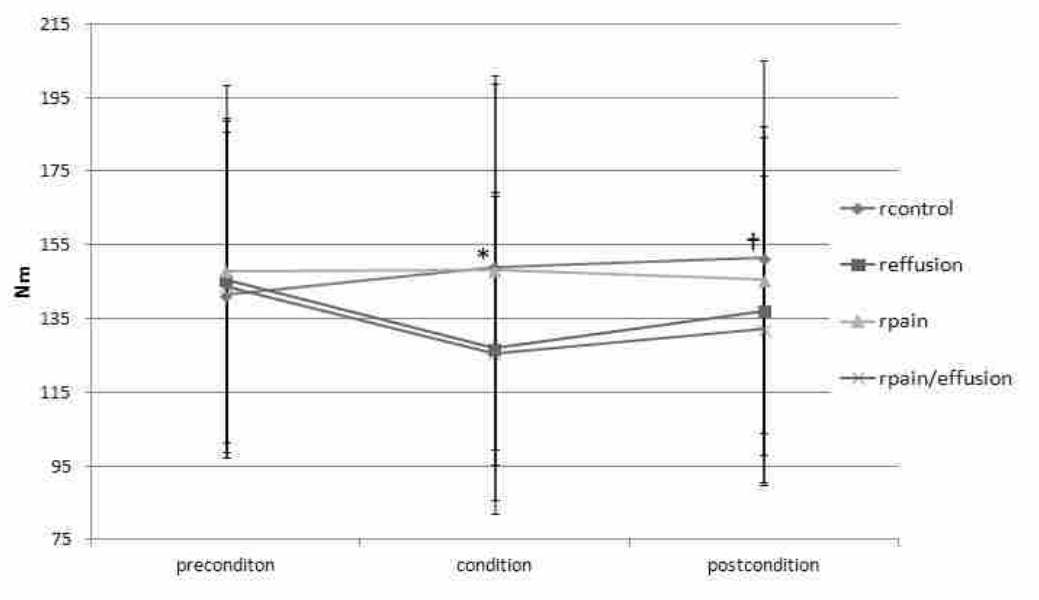


Table 1-a. Means and standard deviations for peak EMG for each muscle, side, and treatment during the first quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	7.33 (7.91)	5.88 (3.74)	8.7357 (6.12)	6.69 (4.49)
		condition	10.05 (12.79)	7.47 (5.87)	8.6813 (6.39)	7.36 (3.12)
		postcondition	9.82 (14.15)	6.39 (5.50)	8.2172 (6.86)	8.39 (8.65)
	Right	precondition	7.32 (3.60)	9.31 (11.69)	18.71 (44.91)	7.56 (4.70)
		condition	8.41 (5.73)	8.33 (7.23)	17.77 (44.15)	6.84 (4.06)
		postcondition	9.85 (8.63)	8.23 (7.34)	17.22 (45.11)	6.69 (4.72)
Vastus Medialis	Left	precondition	1.38 (0.73)	1.09 (0.50)	1.20 (0.78)	1.24 (0.64)
		condition	3.18 (4.66)	1.27 (0.44)	1.43 (1.09)	1.36 (0.64)
		postcondition	2.12 (2.22)	1.08 (0.42)	1.39 (1.36)	1.23 (0.63)
	Right	precondition	2.17 (3.63)	1.35 (0.8)	1.71 (2.06)	1.52 (1.24)
		condition	3.05 (6.40)	1.26 (1.18)	1.29 (0.98)	1.16 (1.01)
		postcondition	2.66 (4.52)	1.04 (0.97)	1.28 (0.93)	0.89 (0.56)
Vastus Lateralis	Left	precondition	1.76 (1.73)	1.92 (2.26)	2.05 (2.60)	1.42 (0.84)
		condition	3.03 (4.98)	1.93 (1.55)	1.81 (2.16)	1.51 (0.88)
		postcondition	4.55 (9.98)	1.39 (1.07)	1.56 (1.30)	1.16 (0.52)
	Right	precondition	1.45 (0.78)	1.42 (0.59)	2.85 (4.34)	1.47 (0.59)
		condition	1.94 (2.08)	1.34 (1.53)	1.72 (1.26)	1.08 (0.55)
		postcondition	2.03 (1.76)	1.12 (0.97)	1.96 (2.13)	0.92 (0.59)
Medial Hamstring	Left	precondition	8.06 (4.97)	8.76 (7.54)	10.69 (19.38)	6.29 (4.47)
		condition	12.95 (12.33)	6.24 (3.51)	11.27 (20.06)	6.88 (6.95)
		postcondition	12.35 (10.00)	10.06 (24.11)	9.72 (18.82)	5.30 (3.18)
	Right	precondition	5.73 (2.66)	6.10 (4.75)	10.00 (21.49)	5.94 (4.51)
		condition	6.98 (4.53)	8.86 (15.09)	9.18 (19.75)	5.86 (4.49)
		postcondition	7.20 (4.16)	7.97 (13.78)	9.65 (20.89)	5.10 (4.89)
Gluteus Medius	Left	precondition	6.02 (4.09)	8.21 (4.13)	7.81 (4.94)	6.50 (4.58)
		condition	6.04 (3.71)	9.21 (3.99)	8.13 (4.69)	6.77 (4.01)
		postcondition	5.99 (4.03)	8.58 (3.98)	8.19 (5.44)	6.78 (4.60)
	Right	precondition	5.70 (3.46)	7.47 (5.15)	8.79 (5.77)	6.19 (3.29)
		condition	6.15 (4.31)	8.16 (5.86)	8.09 (5.49)	6.08 (5.17)
		postcondition	5.88 (4.16)	7.98 (4.78)	8.67 (6.13)	5.98 (3.79)
Gluteus Maximus	Left	precondition	3.29 (1.25)	3.57 (1.56)	7.19 (14.66)	2.87 (1.52)
		condition	3.25 (1.23)	3.48 (1.30)	7.19 (14.63)	2.87 (1.36)
		postcondition	3.18 (1.12)	3.60 (1.74)	7.30 (14.95)	2.55 (1.15)
	Right	precondition	4.10 (2.61)	3.91 (3.02)	4.88 (5.27)	3.11 (1.96)
		condition	4.16 (2.92)	4.27 (2.95)	5.03 (5.62)	5.13 (8.14)
		postcondition	4.20 (2.36)	5.14 (4.83)	4.61 (5.32)	3.27 (2.29)

Table 1-b. Means and standard deviations for peak EMG for each muscle, side, and treatment during the second quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	13.31 (10.26)	13.82 (9.19)	12.64 (7.08)	12.50 (7.07)
		condition	13.70 (10.56)	14.65 (11.24)	12.93 (6.12)	14.83 (9.01)
		postcondition	13.77 (11.38)	13.97 (9.50)	14.67 (9.40)	13.99 (10.55)
	Right	precondition	13.21 (7.83)	14.20 (10.3)	22.32 (44.34)	11.68 (8.03)
		condition	12.52 (8.67)	12.27 (7.95)	21.96 (43.49)	10.70 (7.24)
		postcondition	13.51 (8.74)	13.24 (8.86)	22.51 (44.17)	11.34 (8.61)
Vastus Medialis	Left	precondition	0.50 (0.47)	0.49 (0.40)	0.55 (0.71)	0.39 (0.23)
		condition	1.03 (1.62)	0.50 (0.38)	0.54 (0.66)	0.40 (0.22)
		postcondition	0.78 (1.19)	0.34 (0.28)	0.50 (0.71)	0.41 (0.34)
	Right	precondition	1.07 (2.57)	0.55 (0.57)	0.92 (1.43)	0.55 (0.53)
		condition	1.06 (1.79)	0.68 (0.9)	0.67 (0.89)	0.56 (0.92)
		postcondition	0.90 (1.42)	0.46 (0.84)	0.59 (0.84)	0.30 (0.24)
Vastus Lateralis	Left	precondition	0.63 (0.36)	0.47 (0.21)	0.81 (0.97)	0.67 (0.54)
		condition	1.02 (1.40)	0.64 (0.28)	0.71 (0.57)	0.63 (0.43)
		postcondition	3.34 (11.01)	0.39 (0.20)	0.55 (0.52)	0.47 (0.20)
	Right	precondition	0.50 (0.35)	0.52 (0.33)	1.02 (1.62)	0.53 (0.45)
		condition	0.69 (0.68)	0.46 (0.32)	0.91 (0.98)	0.55 (0.34)
		postcondition	0.87 (0.95)	0.34 (0.18)	0.70 (0.65)	0.31 (0.17)
Medial Hamstring	Left	precondition	2.37 (1.29)	3.42 (3.43)	10.07 (34.57)	1.76 (1.08)
		condition	3.36 (2.46)	2.27 (1.35)	10.59 (35.72)	2.43 (1.72)
		postcondition	3.26 (1.93)	3.99 (9.23)	9.68 (34.24)	2.08 (1.68)
	Right	precondition	2.50 (1.98)	2.99 (3.06)	13.67 (50.17)	2.29 (1.55)
		condition	3.34 (2.92)	8.73 (26.87)	13.62 (48.93)	4.49 (7.05)
		postcondition	3.08 (2.26)	7.91 (24.78)	13.36 (49.69)	2.48 (2.07)
Gluteus Medius	Left	precondition	2.48 (1.30)	3.25 (2.12)	3.63 (3.5)	2.49 (1.57)
		condition	2.62 (1.88)	3.49 (2.36)	3.88 (3.49)	3.00 (1.94)
		postcondition	2.63 (2.02)	3.08 (2.05)	3.56 (3.12)	2.43 (1.59)
	Right	precondition	2.39 (1.28)	3.03 (3.12)	4.12 (3.96)	2.79 (2.66)
		condition	2.19 (1.10)	3.73 (3.74)	4.12 (3.78)	3.80 (4.65)
		postcondition	2.44 (1.13)	3.88 (3.99)	3.81 (3.86)	3.09 (2.46)
Gluteus Maximus	Left	precondition	1.09 (0.37)	1.12 (0.49)	2.79 (7.10)	1.07 (0.35)
		condition	1.09 (0.40)	1.19 (0.52)	2.77 (6.36)	1.25 (0.63)
		postcondition	1.06 (0.32)	1.01 (0.49)	2.98 (8.10)	0.95 (0.41)
	Right	precondition	1.14 (0.29)	1.12 (0.36)	4.52 (14.16)	1.12 (0.42)
		condition	1.14 (0.33)	2.90 (7.06)	4.56 (13.43)	2.42 (4.58)
		postcondition	1.31 (0.46)	1.52 (2.36)	4.79 (15.46)	1.09 (0.49)

Table 1-c. Means and standard deviations for peak EMG for each muscle, side, and treatment during the third quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	22.38 (14.63)	23.20 (16.80)	20.27 (11.66)	23.14 (15.79)
		condition	21.92 (14.65)	25.22 (19.55)	22.51 (14.10)	23.84 (14.64)
		postcondition	21.82 (13.45)	24.03 (17.79)	21.30 (12.88)	22.84 (14.13)
	Right	precondition	18.78 (13.18)	17.59 (9.27)	26.76 (44.19)	17.59 (11.06)
		condition	18.12 (11.87)	16.54 (9.14)	25.61 (43.38)	14.06 (10.67)
		postcondition	18.37 (11.78)	16.82 (10.43)	25.99 (44.09)	16.43 (13.62)
Vastus Medialis	Left	precondition	0.32 (0.29)	0.21 (0.13)	0.33 (0.71)	0.33 (0.38)
		condition	0.50 (0.70)	0.29 (0.23)	0.41 (0.70)	0.34 (0.30)
		postcondition	0.38 (0.46)	0.20 (0.19)	0.35 (0.69)	0.28 (0.32)
	Right	precondition	0.48 (0.91)	0.42 (0.71)	0.63 (1.14)	0.34 (0.34)
		condition	0.59 (1.28)	0.56 (1.04)	0.60 (0.99)	0.48 (0.99)
		postcondition	0.59 (1.25)	0.50 (1.07)	0.59 (1.05)	0.21 (0.17)
Vastus Lateralis	Left	precondition	0.26 (0.13)	0.23 (0.20)	0.47 (0.91)	0.27 (0.16)
		condition	0.29 (0.20)	0.26 (0.16)	0.43 (0.84)	0.34 (0.21)
		postcondition	1.11 (3.59)	0.21 (0.14)	0.50 (0.88)	0.24 (0.18)
	Right	precondition	0.23 (0.15)	0.25 (0.22)	0.36 (0.46)	0.22 (0.13)
		condition	0.26 (0.24)	0.27 (0.31)	0.36 (0.48)	0.32 (0.29)
		postcondition	0.25 (0.17)	0.24 (0.20)	0.27 (0.28)	0.13 (0.09)
Medial Hamstring	Left	precondition	1.66 (1.01)	1.40 (0.79)	9.58 (36.38)	1.46 (1.19)
		condition	1.66 (0.95)	1.80 (1.18)	1.40 (0.63)	1.49 (1.21)
		postcondition	1.65 (0.91)	2.62 (6.39)	6.79 (25.08)	1.16 (0.80)
	Right	precondition	2.08 (1.92)	1.72 (1.39)	14.62 (58.85)	1.30 (0.95)
		condition	2.12 (1.86)	1.42 (1.11)	14.50 (57.99)	3.43 (8.19)
		postcondition	1.82 (1.26)	1.27 (1.02)	14.32 (58.64)	1.09 (0.60)
Gluteus Medius	Left	precondition	1.99 (0.92)	2.42 (1.40)	2.57 (2.84)	1.84 (1.26)
		condition	2.30 (1.48)	2.25 (1.22)	2.20 (1.26)	2.03 (1.42)
		postcondition	2.52 (2.22)	2.23 (1.16)	2.46 (1.84)	1.65 (1.24)
	Right	precondition	2.09 (1.42)	2.45 (2.78)	3.47 (4.89)	2.30 (1.95)
		condition	1.84 (0.99)	2.59 (2.59)	3.29 (4.05)	2.84 (3.46)
		postcondition	1.94 (1.17)	2.26 (2.58)	3.31 (4.45)	2.28 (1.98)
Gluteus Maximus	Left	precondition	1.09 (0.70)	0.97 (0.37)	1.62 (2.63)	0.99 (0.30)
		condition	1.04 (0.56)	0.93 (0.38)	0.95 (0.34)	1.00 (0.40)
		postcondition	0.97 (0.40)	0.83 (0.37)	1.33 (1.82)	0.80 (0.33)
	Right	precondition	0.98 (0.34)	1.08 (0.46)	4.46 (14.31)	1.01 (0.38)
		condition	1.03 (0.35)	1.34 (2.29)	4.19 (13.85)	1.37 (1.56)
		postcondition	1.02 (0.33)	0.76 (0.35)	4.52 (15.55)	0.81 (0.32)

Table 1-d. Means and standard deviations for peak EMG for each muscle, side, and treatment during the fourth quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	10.24 (7.4)	10.26 (9.88)	12.34 (13.70)	8.97 (6.56)
		condition	8.64 (4.75)	11.22 (11.8)	12.92 (13.72)	12.34 (8.85)
		postcondition	9.46 (6.16)	9.45 (8.82)	12.41 (13.37)	9.52 (6.22)
	Right	precondition	8.38 (6.47)	9.04 (5.79)	19.99 (49.41)	7.86 (5.16)
		condition	7.79 (4.74)	9.34 (7.99)	18.43 (47.60)	8.25 (7.39)
		postcondition	9.76 (6.26)	10.72 (12.27)	18.51 (48.36)	7.14 (4.84)
Vastus Medialis	Left	precondition	0.50 (0.61)	0.38 (0.42)	0.73 (1.25)	0.57 (0.79)
		condition	0.74 (0.88)	0.50 (0.71)	0.49 (0.82)	0.56 (0.91)
		postcondition	0.81 (1.45)	0.54 (1.36)	0.51 (0.90)	0.47 (0.81)
	Right	precondition	0.65 (1.20)	0.63 (0.87)	0.82 (1.25)	0.56 (0.48)
		condition	0.88 (1.44)	0.83 (1.29)	0.70 (0.99)	0.88 (1.30)
		postcondition	1.05 (1.63)	0.61 (1.14)	0.79 (1.05)	0.39 (0.44)
Vastus Lateralis	Left	precondition	0.33 (0.26)	0.31 (0.35)	1.09 (2.89)	0.28 (0.16)
		condition	0.55 (0.80)	0.27 (0.25)	0.89 (2.79)	0.23 (0.15)
		postcondition	0.98 (2.00)	0.27 (0.38)	0.95 (2.78)	0.22 (0.17)
	Right	precondition	0.26 (0.14)	0.29 (0.23)	0.48 (0.78)	0.27 (0.19)
		condition	0.41 (0.63)	0.35 (0.64)	0.32 (0.36)	0.38 (0.79)
		postcondition	0.46 (0.61)	0.32 (0.64)	0.31 (0.27)	0.13 (0.08)
Medial Hamstring	Left	precondition	2.54 (2.35)	2.37 (2.57)	2.18 (2.03)	2.06 (1.72)
		condition	4.06 (7.18)	2.26 (2.07)	1.64 (0.87)	2.24 (2.13)
		postcondition	3.77 (5.75)	3.54 (9.47)	1.31 (0.65)	1.63 (1.51)
	Right	precondition	1.96 (1.28)	1.88 (1.93)	1.22 (0.62)	1.55 (0.99)
		condition	2.03 (1.42)	1.28 (0.71)	1.21 (0.55)	1.18 (0.58)
		postcondition	2.22 (1.89)	1.14 (0.59)	1.36 (1.57)	1.30 (1.34)
Gluteus Medius	Left	precondition	1.69 (2.70)	1.57 (1.36)	0.94 (0.46)	0.89 (0.40)
		condition	2.11 (2.89)	1.08 (0.53)	0.88 (0.40)	0.94 (0.78)
		postcondition	1.90 (2.31)	0.94 (0.39)	0.93 (0.49)	0.81 (0.88)
	Right	precondition	2.17 (4.67)	1.25 (1.33)	1.07 (0.83)	1.00 (0.42)
		condition	1.89 (2.96)	1.38 (1.80)	0.91 (0.62)	1.12 (0.57)
		postcondition	1.23 (0.77)	0.95 (1.07)	0.89 (0.54)	0.92 (0.45)
Gluteus Maximus	Left	precondition	1.09 (0.70)	0.98 (0.38)	1.05 (0.54)	1.00 (0.42)
		condition	1.08 (0.56)	0.89 (0.34)	0.95 (0.43)	0.94 (0.48)
		postcondition	1.03 (0.43)	0.75 (0.26)	1.01 (0.78)	0.75 (0.27)
	Right	precondition	1.04 (0.32)	1.08 (0.41)	1.13 (0.59)	1.05 (0.39)
		condition	1.11 (0.44)	1.13 (1.17)	1.01 (0.65)	1.00 (0.51)
		postcondition	1.08 (0.40)	0.75 (0.28)	0.86 (0.44)	0.83 (0.35)

Table 1-e. Means and standard deviations for mean EMG for each muscle, side, and treatment during the first quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	3.81 (4.48)	3.11 (2.11)	5.42 (4.88)	3.13 (2.33)
		condition	5.53 (8.14)	3.97 (3.65)	5.06 (4.55)	3.71 (1.70)
		postcondition	5.75 (10.16)	2.68 (2.00)	5.02 (5.01)	3.88 (5.14)
	Right	precondition	3.62 (2.030)	4.86 (7.16)	14.44 (45.2)	3.58 (1.71)
		condition	4.10 (2.92)	4.17 (3.81)	13.84 (44.51)	3.61 (1.92)
		postcondition	5.21 (4.78)	3.90 (3.28)	13.71 (45.26)	2.84 (1.59)
Vastus Medialis	Left	precondition	0.87 (0.45)	0.71 (0.39)	0.82 (0.70)	0.75 (0.34)
		condition	1.62 (2.01)	0.83 (0.28)	0.91 (0.65)	0.87 (0.39)
		postcondition	1.20 (0.96)	0.66 (0.27)	0.80 (0.68)	0.75 (0.41)
	Right	precondition	1.15 (1.41)	0.83 (0.53)	1.13 (1.26)	0.99 (0.70)
		condition	1.38 (1.95)	0.71 (0.68)	0.92 (0.86)	0.81 (0.93)
		postcondition	1.41 (1.93)	0.72 (0.88)	0.88 (0.84)	0.54 (0.34)
Vastus Lateralis	Left	precondition	1.07 (0.91)	0.92 (0.6)	1.19 (1.06)	0.94 (0.56)
		condition	1.71 (2.43)	1.07 (0.58)	1.03 (0.61)	1.00 (0.57)
		postcondition	2.54 (5.65)	0.78 (0.35)	0.90 (0.55)	0.75 (0.35)
	Right	precondition	0.92 (0.47)	0.91 (0.39)	1.54 (1.91)	0.97 (0.40)
		condition	1.11 (0.73)	0.76 (0.64)	1.05 (0.63)	0.72 (0.42)
		postcondition	1.24 (0.95)	0.66 (0.44)	1.18 (1.04)	0.57 (0.37)
Medial Hamstring	Left	precondition	4.32 (2.19)	4.71 (4.12)	6.59 (13.32)	0.93 (0.76)
		condition	7.10 (6.79)	3.45 (2.04)	6.86 (13.46)	3.69 (3.18)
		postcondition	6.88 (5.66)	5.55 (14.24)	6.04 (12.74)	2.82 (1.60)
	Right	precondition	3.18 (1.25)	3.35 (2.68)	3.94 (3.89)	3.24 (2.58)
		condition	4.10 (2.85)	3.09 (1.88)	3.53 (3.41)	3.45 (2.64)
		postcondition	4.08 (2.21)	4.81 (9.04)	3.40 (3.26)	3.09 (3.02)
Gluteus Medius	Left	precondition	3.64 (2.37)	5.06 (2.55)	4.93 (3.28)	3.84 (2.47)
		condition	3.70 (2.29)	5.41 (2.65)	5.09 (2.91)	3.99 (2.21)
		postcondition	3.69 (2.28)	5.10 (2.49)	5.17 (3.54)	3.95 (2.57)
	Right	precondition	3.45 (2.14)	4.43 (3.12)	5.30 (3.58)	3.76 (2.23)
		condition	3.64 (2.64)	4.55 (3.35)	4.87 (3.54)	4.21 (4.43)
		postcondition	3.56 (2.44)	4.87 (3.27)	5.05 (3.55)	3.82 (2.45)
Gluteus Maximus	Left	precondition	1.79 (0.54)	1.87 (0.70)	4.86 (12.43)	1.60 (0.71)
		condition	1.74 (0.50)	1.76 (0.57)	4.78 (12.07)	1.59 (0.76)
		postcondition	1.68 (0.48)	1.80 (0.83)	4.96 (13.15)	1.37 (0.55)
	Right	precondition	2.01 (0.72)	1.98 (0.92)	3.05 (4.73)	1.77 (0.93)
		condition	2.05 (0.82)	2.18 (0.97)	3.23 (4.98)	3.53 (6.99)
		postcondition	2.20 (0.91)	2.97 (3.97)	2.96 (4.62)	1.78 (0.90)

Table 1-f. Means and standard deviations for mean EMG for each muscle, side, and treatment during the second quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	7.81 (5.96)	8.19 (5.31)	8.59 (5.45)	7.72 (4.58)
		condition	8.15 (6.05)	7.44 (4.73)	8.35 (4.68)	9.07 (5.23)
		postcondition	8.34 (6.44)	8.29 (5.46)	9.10 (5.61)	8.77 (6.33)
	Right	precondition	8.71 (4.92)	8.82 (5.99)	18.47 (44.98)	7.84 (5.31)
		condition	8.63 (5.53)	8.03 (5.27)	18.38 (44.09)	7.31 (5.08)
		postcondition	8.82 (5.38)	8.47 (5.94)	18.49 (44.82)	7.85 (6.26)
Vastus Medialis	Left	precondition	0.28 (0.29)	0.19 (0.11)	0.33 (0.70)	0.22 (0.12)
		condition	0.47 (0.70)	0.24 (0.19)	0.36 (0.66)	0.22 (0.13)
		postcondition	0.42 (0.64)	0.17 (0.11)	0.34 (0.69)	0.21 (0.15)
	Right	precondition	0.35 (0.53)	0.29 (0.29)	0.56 (1.11)	0.27 (0.23)
		condition	0.48 (0.77)	0.27 (0.24)	0.43 (0.88)	0.41 (0.92)
		postcondition	0.42 (0.61)	0.35 (0.84)	0.37 (0.83)	0.16 (0.12)
Vastus Lateralis	Left	precondition	0.30 (0.22)	0.23 (0.10)	0.45 (0.64)	0.31 (0.19)
		condition	0.41 (0.39)	0.29 (0.13)	0.41 (0.52)	0.32 (0.22)
		postcondition	1.28 (4.01)	0.20 (0.09)	0.33 (0.51)	0.21 (0.11)
	Right	precondition	0.22 (0.08)	0.23 (0.14)	0.50 (0.83)	0.25 (0.20)
		condition	0.30 (0.34)	0.25 (0.18)	0.44 (0.52)	0.30 (0.20)
		postcondition	0.35 (0.32)	0.20 (0.14)	0.32 (0.35)	0.14 (0.07)
Medial Hamstring	Left	precondition	1.29 (0.53)	1.74 (1.54)	7.62 (27.94)	0.96 (0.48)
		condition	1.78 (1.30)	1.18 (0.61)	7.06 (25.70)	1.20 (0.70)
		postcondition	1.73 (1.06)	2.52 (6.59)	7.19 (27.08)	0.96 (0.61)
	Right	precondition	1.55 (1.10)	1.74 (1.73)	10.12 (38.81)	1.39 (0.87)
		condition	1.88 (1.26)	1.44 (1.07)	9.77 (37.05)	3.04 (5.77)
		postcondition	1.74 (1.12)	5.14 (17.18)	9.90 (38.25)	1.40 (1.02)
Gluteus Medius	Left	precondition	1.59 (0.76)	2.09 (1.45)	2.49 (2.81)	1.58 (0.92)
		condition	1.70 (1.07)	2.31 (1.48)	2.66 (2.60)	1.91 (1.20)
		postcondition	1.73 (1.18)	1.99 (1.39)	2.48 (2.47)	1.55 (1.00)
	Right	precondition	1.61 (0.77)	2.12 (2.43)	2.69 (2.56)	1.81 (1.67)
		condition	1.51 (0.73)	2.69 (3.07)	2.81 (2.59)	2.78 (3.87)
		postcondition	1.60 (0.75)	2.54 (3.17)	2.53 (2.52)	2.02 (1.74)
Gluteus Maximus	Left	precondition	0.82 (0.31)	0.84 (0.32)	1.75 (3.70)	0.80 (0.22)
		condition	0.81 (0.30)	0.82 (0.32)	1.65 (3.23)	0.85 (0.37)
		postcondition	0.80 (0.27)	0.73 (0.32)	1.74 (4.05)	0.70 (0.27)
	Right	precondition	0.85 (0.24)	0.84 (0.24)	3.04 (9.37)	0.82 (0.28)
		condition	0.85 (0.23)	1.69 (3.66)	2.92 (8.51)	1.49 (2.38)
		postcondition	0.90 (0.24)	0.93 (1.08)	3.17 (10.19)	0.79 (0.34)

Table 1-g. Means and standard deviations for mean EMG for each muscle, side, and treatment during the third quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	15.08 (9.62)	15.61 (11.27)	14.10 (7.94)	15.21 (9.78)
		condition	14.55 (8.67)	16.57 (12.75)	15.52 (9.06)	16.07 (10.12)
		postcondition	14.88 (8.83)	16.13 (11.73)	14.70 (8.40)	15.16 (9.73)
	Right	precondition	12.95 (8.89)	12.15 (6.26)	22.07 (44.65)	12.17 (7.75)
		condition	12.37 (8.05)	11.65 (6.82)	21.09 (43.78)	9.79 (7.56)
		postcondition	12.59 (7.89)	12.05 (7.77)	21.21 (44.51)	11.10 (8.62)
Vastus Medialis	Left	precondition	0.21 (0.16)	0.15 (0.08)	0.32 (0.70)	0.20 (0.16)
		condition	0.32 (0.41)	0.16 (0.10)	0.31 (0.65)	0.21 (0.19)
		postcondition	0.26 (0.30)	0.13 (0.08)	0.29 (0.69)	0.16 (0.13)
	Right	precondition	0.26 (0.39)	0.24 (0.34)	0.45 (1.04)	0.21 (0.19)
		condition	0.31 (0.49)	0.21 (0.31)	0.42 (0.91)	0.37 (0.91)
		postcondition	0.30 (0.49)	0.35 (0.86)	0.38 (0.85)	0.13 (0.08)
Vastus Lateralis	Left	precondition	0.17 (0.08)	0.16 (0.08)	0.33 (0.65)	0.18 (0.09)
		condition	0.19 (0.13)	0.17 (0.10)	0.31 (0.62)	0.20 (0.12)
		postcondition	0.57 (1.69)	0.14 (0.08)	0.33 (0.63)	0.15 (0.10)
	Right	precondition	0.15 (0.07)	0.17 (0.11)	0.25 (0.36)	0.14 (0.08)
		condition	0.17 (0.14)	0.18 (0.22)	0.23 (0.30)	0.20 (0.19)
		postcondition	0.16 (0.11)	0.16 (0.15)	0.19 (0.25)	0.09 (0.05)
Medial Hamstring	Left	precondition	1.01 (0.42)	0.96 (0.48)	1.44 (2.67)	0.92 (0.61)
		condition	1.05 (0.49)	1.07 (0.61)	0.85 (0.39)	0.93 (0.66)
		postcondition	1.05 (0.50)	1.62 (3.71)	1.15 (1.94)	0.70 (0.40)
	Right	precondition	1.13 (0.98)	1.05 (0.76)	5.39 (20.24)	0.88 (0.68)
		condition	1.23 (1.00)	0.83 (0.50)	5.89 (22.46)	1.04 (0.89)
		postcondition	1.10 (0.68)	0.71 (0.33)	5.85 (22.85)	0.68 (0.31)
Gluteus Medius	Left	precondition	1.13 (0.50)	1.38 (0.66)	1.13 (0.53)	1.05 (0.62)
		condition	1.23 (0.70)	1.24 (0.60)	1.18 (0.64)	1.05 (0.58)
		postcondition	1.45 (1.21)	1.15 (0.51)	1.12 (0.53)	0.93 (0.63)
	Right	precondition	1.10 (0.59)	1.41 (1.33)	1.64 (1.64)	1.25 (0.92)
		condition	1.06 (0.51)	1.61 (1.41)	1.61 (1.59)	1.37 (0.98)
		postcondition	1.09 (0.61)	1.20 (1.26)	1.62 (1.73)	1.25 (0.98)
Gluteus Maximus	Left	precondition	0.83 (0.46)	0.77 (0.30)	0.81 (0.26)	0.77 (0.23)
		condition	0.78 (0.34)	0.72 (0.28)	0.76 (0.30)	0.75 (0.28)
		postcondition	0.75 (0.30)	0.65 (0.27)	0.74 (0.25)	0.65 (0.25)
	Right	precondition	0.76 (0.24)	0.83 (0.32)	2.06 (5.22)	0.80 (0.29)
		condition	0.80 (0.25)	0.96 (0.98)	2.10 (5.67)	0.77 (0.41)
		postcondition	0.78 (0.22)	0.61 (0.27)	2.18 (6.22)	0.64 (0.24)

Table 1-h. Means and standard deviations for mean EMG for each muscle, side, and treatment during the fourth quartile of stance during walking.

			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	2.94 (2.08)	3.09 (2.62)	4.74 (7.96)	2.60 (1.37)
		condition	2.70 (1.42)	2.71 (1.84)	4.78 (7.45)	3.62 (2.87)
		postcondition	2.95 (1.67)	2.63 (2.49)	4.85 (6.97)	2.93 (2.41)
	Right	precondition	2.60 (1.52)	2.83 (1.78)	13.48 (47.24)	2.34 (1.00)
		condition	2.53 (1.08)	2.46 (1.50)	12.89 (46.20)	2.68 (2.56)
		postcondition	3.05 (2.21)	3.60 (5.41)	13.08 (46.87)	2.08 (1.23)
Vastus Medialis	Left	precondition	0.29 (0.28)	0.22 (0.17)	0.43 (0.83)	0.28 (0.27)
		condition	0.44 (0.53)	0.24 (0.24)	0.34 (0.71)	0.25 (0.26)
		postcondition	0.40 (0.53)	0.22 (0.26)	0.33 (0.72)	0.24 (0.38)
	Right	precondition	0.34 (0.53)	0.32 (0.35)	0.55 (1.02)	0.30 (0.21)
		condition	0.45 (0.66)	0.54 (0.98)	0.48 (0.85)	0.49 (0.95)
		postcondition	0.53 (0.77)	0.40 (0.92)	0.48 (0.82)	0.20 (0.16)
Vastus Lateralis	Left	precondition	0.19 (0.11)	0.19 (0.14)	0.65 (1.79)	0.19 (0.11)
		condition	0.30 (0.43)	0.16 (0.10)	0.56 (1.73)	0.16 (0.09)
		postcondition	0.51 (1.03)	0.16 (0.14)	0.55 (1.69)	0.14 (0.10)
	Right	precondition	0.17 (0.09)	0.18 (0.14)	0.29 (0.42)	0.17 (0.11)
		condition	0.24 (0.33)	0.22 (0.40)	0.22 (0.25)	0.23 (0.49)
		postcondition	0.25 (0.30)	0.19 (0.37)	0.21 (0.23)	0.10 (0.04)
Medial Hamstring	Left	precondition	1.29 (0.72)	1.30 (1.19)	0.98 (0.49)	1.05 (0.68)
		condition	1.65 (1.43)	1.06 (0.50)	0.94 (0.40)	1.12 (0.78)
		postcondition	1.61 (1.18)	1.58 (3.28)	0.82 (0.34)	0.85 (0.54)
	Right	precondition	1.22 (0.75)	1.11 (0.82)	0.81 (0.35)	0.98 (0.49)
		condition	1.26 (0.87)	0.79 (0.37)	0.75 (0.27)	0.82 (0.37)
		postcondition	1.24 (0.82)	0.74 (0.34)	0.81 (0.67)	0.80 (0.69)
Gluteus Medius	Left	precondition	1.02 (1.41)	0.97 (0.49)	0.67 (0.29)	0.62 (0.28)
		condition	1.22 (1.42)	0.75 (0.29)	0.65 (0.31)	0.62 (0.42)
		postcondition	1.18 (1.26)	0.63 (0.20)	0.63 (0.31)	0.56 (0.48)
	Right	precondition	1.13 (1.61)	0.81 (0.62)	0.69 (0.35)	0.70 (0.26)
		condition	1.13 (1.48)	0.79 (0.79)	0.66 (0.35)	0.72 (0.30)
		postcondition	0.83 (0.43)	0.61 (0.44)	0.60 (0.28)	0.63 (0.28)
Gluteus Maximus	Left	precondition	0.81 (0.44)	0.76 (0.26)	0.80 (0.39)	0.72 (0.20)
		condition	0.79 (0.36)	0.69 (0.25)	0.74 (0.29)	0.71 (0.29)
		postcondition	0.77 (0.28)	0.61 (0.22)	0.75 (0.40)	0.69 (0.20)
	Right	precondition	0.78 (0.23)	0.81 (0.28)	0.79 (0.30)	0.77 (0.26)
		condition	0.81 (0.27)	0.70 (0.33)	0.79 (0.49)	0.74 (0.35)
		postcondition	0.81 (0.26)	0.59 (0.21)	0.69 (0.35)	0.65 (0.25)

Table 1-i. Summary data in peak joint angles during walking. For ankle angles, the neutral position (90 °) was referenced as zero °. Values are mean (SD).

Unit: °			Treatment			
Variable	Side	Time	control	effusion	pain	pain/effusion
Ankle dorsi-flexion	Left	precondition	15.19 (4.30)	14.70 (4.00)	14.27 (4.20)	14.18 (3.33)
		condition	14.11 (4.60)	14.61 (3.65)	14.38 (3.74)	13.85 (3.04)
		postcondition	14.46 (4.54)	15.08 (3.8)	14.30 (4.12)	14.30 (2.87)
	Right	precondition	12.51 (4.28)	13.14 (3.71)	12.80 (4.11)	12.51 (4.20)
		condition	12.59 (4.51)	12.97 (4.48)	12.78 (4.07)	12.59 (4.56)
		postcondition	13.11 (4.61)	13.21 (4.38)	13.09 (4.06)	13.11 (4.87)
Ankle plantar-flexion	Left	precondition	16.07 (4.20)	14.87 (4.44)	14.65 (4.20)	15.13 (3.75)
		condition	15.60 (4.10)	14.46 (4.01)	15.29 (4.37)	14.26 (3.71)
		postcondition	15.43 (4.26)	14.34 (4.01)	15.06 (4.37)	15.00 (3.32)
	Right	precondition	16.95 (5.80)	16.59 (5.00)	16.53 (5.24)	16.94 (5.80)
		condition	17.24 (5.70)	15.65 (5.31)	16.31 (5.20)	14.25 (5.63)
		postcondition	17.98 (5.40)	16.39 (4.75)	16.97 (4.69)	15.63 (5.30)
Knee flexion	Left	precondition	54.48 (3.22)	54.80 (4.26)	54.06 (3.00)	54.39 (3.06)
		condition	55.13 (3.05)	53.68 (4.27)	53.90 (3.11)	52.31 (4.47)
		postcondition	54.91 (3.11)	54.45 (3.77)	54.26 (2.82)	54.14 (4.19)
	Right	precondition	53.48 (2.55)	53.25 (3.45)	53.53 (3.50)	52.40 (4.44)
		condition	54.16 (3.01)	53.17 (4.0)	54.49 (3.73)	52.47 (4.80)
		postcondition	54.37 (3.06)	53.55 (4.0)	54.47 (3.84)	54.17 (4.41)
Knee abduction	Left	precondition	7.43 (4.42)	6.56 (3.04)	7.17 (3.85)	7.53 (4.32)
		condition	7.79 (5.16)	6.17 (3.07)	7.33 (3.97)	6.51 (4.34)
		postcondition	7.60 (5.10)	6.58 (4.32)	7.83 (3.79)	7.44 (4.52)
	Right	precondition	5.77 (3.67)	6.03 (3.58)	6.78 (4.58)	5.15 (4.32)
		condition	5.96 (3.77)	6.02 (3.64)	7.36 (4.90)	5.29 (4.25)
		postcondition	6.23 (3.87)	6.12 (3.66)	7.69 (5.29)	5.41 (4.44)
Knee adduction	Left	precondition	2.69 (2.05)	3.66 (2.30)	3.03 (2.09)	3.69 (3.07)
		condition	2.89 (2.05)	4.36 (2.54)	2.94 (2.24)	3.61 (2.40)
		postcondition	2.68 (2.26)	3.91 (2.75)	3.07 (2.17)	4.10 (3.13)
	Right	precondition	3.23 (3.16)	3.24 (2.46)	2.97 (2.78)	3.15 (2.14)
		condition	3.25 (3.21)	3.43 (2.14)	3.05 (2.75)	3.25 (2.22)
		postcondition	3.54 (3.18)	3.44 (2.28)	3.30 (2.51)	3.27 (2.13)
Hip flexion	Left	precondition	12.20 (6.64)	12.06 (6.43)	11.42 (5.25)	2.38 (5.92)
		condition	12.07 (6.88)	10.95 (6.29)	10.78 (5.40)	11.62 (5.07)
		postcondition	12.57 (6.76)	11.16 (7.10)	11.19 (5.57)	12.33 (5.41)
	Right	precondition	10.00 (5.41)	10.44 (6.92)	11.18 (5.84)	11.09 (5.04)
		condition	10.73 (6.13)	10.78 (7.63)	11.79 (6.63)	10.03 (5.50)
		postcondition	10.72 (7.01)	11.19 (7.39)	12.21 (6.19)	10.07 (5.14)
Hip extension	Left	precondition	25.01 (7.19)	25.03 (8.04)	25.41 (5.78)	25.21 (5.62)
		condition	25.26 (7.16)	26.02 (7.59)	26.32 (6.64)	24.91 (5.23)
		postcondition	25.03 (7.15)	25.36 (8.44)	25.99 (6.74)	24.81 (5.08)
	Right	precondition	23.97 (6.84)	24.46 (6.94)	24.93 (6.18)	24.61 (5.95)
		condition	23.97 (7.32)	24.24 (7.49)	24.38 (6.28)	22.11 (6.85)
		postcondition	23.87 (7.23)	24.67 (7.56)	24.54 (6.49)	22.78 (6.84)
Hip abduction	Left	precondition	6.95 (2.52)	6.24 (3.63)	5.98 (3.15)	6.94 (3.30)
		condition	7.11 (2.90)	5.76 (3.88)	5.78 (5.52)	5.28 (3.44)
		postcondition	6.87 (2.79)	5.64 (3.61)	5.95 (3.06)	6.14 (4.12)
	Right	precondition	6.25 (7.12)	5.16 (3.15)	5.81 (2.62)	5.58 (3.00)
		condition	5.70 (3.30)	4.74 (2.90)	5.94 (3.19)	5.45 (3.05)
		postcondition	5.71 (3.47)	4.21 (2.44)	5.43 (3.55)	6.50 (8.05)

Table 1-j. Means and standard deviations for the peak hip extension moments during walking.

Unit: N·m			Treatment			
Variable	Side	Time	Control	Effusion	Pain	pain/effusion
Hip extension	Left	precondition	67.18 (21.99)	66.32 (25.35)	66.91 (22.19)	63.36 (19.50)
		condition	69.76 (25.47)	62.90 (27.12)	63.32 (19.28)	58.40 (23.80)
		postcondition	68.73 (26.39)	66.31 (26.88)	63.73 (21.05)	62.94 (22.16)
	Right	precondition	47.21 (15.72)	46.61 (16.34)	48.62 (15.76)	46.56 (15.76)
		condition	48.74 (19.89)	44.05 (17.60)	43.10 (12.54)	38.18 (14.56)
		postcondition	49.21 (18.32)	46.76 (15.78)	45.94 (14.97)	44.10 (13.44)

Table 2-a. Means and standard deviations for peak EMG data of each muscle 200 ms prior to initial contact during drop landing.

			Treatment			
Variable	Side	Time	Control	Effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	13.85 (18.28)	12.80 (17.00)	15.67 (15.27)	17.14 (27.86)
		condition	16.39 (28.25)	10.89 (7.45)	13.70 (9.05)	18.29 (15.62)
		postcondition	11.52 (10.67)	13.48 (13.37)	13.23 (9.73)	12.70 (11.47)
	Right	precondition	41.96 (30.69)	37.45 (21.52)	39.05 (26.33)	34.96 (19.03)
		condition	38.14 (24.48)	28.06 (26.03)	32.79 (20.81)	31.98 (20.67)
		postcondition	38.91 (22.53)	36.45 (24.48)	34.89 (21.67)	35.04 (23.78)
Vastus Medialis	Left	precondition	7.18 (17.01)	1.35 (0.85)	2.14 (2.36)	3.22 (3.82)
		condition	2.79 (2.97)	4.01 (8.12)	2.29 (1.68)	3.59 (3.64)
		postcondition	4.31 (7.13)	2.02 (2.26)	1.99 (2.27)	2.76 (2.63)
	Right	precondition	6.41 (4.96)	5.32 (3.93)	4.25 (2.21)	4.58 (2.62)
		condition	5.27 (3.41)	5.38 (3.54)	3.57 (2.23)	4.16 (2.87)
		postcondition	5.25 (3.95)	4.94 (3.72)	3.88 (1.95)	4.47 (2.76)
Vastus Lateralis	Left	precondition	1.43 (1.21)	1.12 (0.73)	1.34 (0.89)	2.04 (2.16)
		condition	1.28 (0.77)	1.65 (1.25)	1.76 (1.38)	3.26 (3.91)
		postcondition	1.37 (0.90)	1.49 (1.44)	1.29 (1.07)	2.18 (2.14)
	Right	precondition	3.38 (1.42)	3.54 (1.72)	3.56 (1.65)	3.39 (1.47)
		condition	3.49 (1.30)	3.48 (1.51)	3.12 (1.63)	3.27 (1.88)
		postcondition	3.47 (1.50)	3.17 (1.54)	3.26 (1.29)	3.30 (1.88)
Medial Hamstring	Left	precondition	35.09 (23.80)	31.05 (15.57)	25.11 (13.93)	27.75 (18.96)
		condition	32.66 (28.03)	30.84 (15.09)	28.77 (17.47)	33.49 (23.93)
		postcondition	27.38 (18.55)	31.82 (15.34)	23.85 (16.43)	30.15 (30.22)
	Right	precondition	12.16 (6.62)	14.85 (13.59)	10.87 (7.23)	13.62 (11.49)
		condition	12.72 (7.58)	11.33 (7.78)	9.90 (6.50)	9.86 (7.54)
		postcondition	10.31 (5.25)	10.35 (7.90)	9.72 (7.03)	9.83 (8.49)
Gluteus Medius	Left	precondition	9.22 (7.03)	12.20 (9.68)	9.31 (7.71)	8.67 (8.20)
		condition	8.68 (5.43)	12.16 (10.10)	9.93 (5.87)	9.29 (8.35)
		postcondition	9.78 (6.72)	12.22 (9.82)	10.16 (8.01)	6.99 (6.25)
	Right	precondition	13.17 (16.36)	13.69 (7.45)	15.09 (10.98)	13.74 (16.96)
		condition	19.71 (29.51)	10.94 (6.78)	13.72 (12.06)	12.37 (16.03)
		postcondition	13.02 (16.50)	11.48 (6.69)	16.08 (12.22)	13.00 (15.33)
Gluteus Maximus	Left	precondition	2.37 (1.48)	2.68 (1.79)	3.43 (3.36)	2.33 (1.15)
		condition	2.45 (1.40)	2.68 (1.54)	2.93 (2.07)	2.39 (0.96)
		postcondition	2.66 (1.79)	2.45 (2.19)	2.99 (2.75)	2.00 (0.90)
	Right	precondition	10.51 (7.46)	9.36 (4.95)	8.88 (5.99)	7.14 (6.40)
		condition	8.65 (5.60)	8.56 (5.34)	9.28 (7.07)	7.57 (5.96)
		postcondition	9.85 (5.91)	8.39 (4.78)	7.88 (5.63)	7.94 (7.94)

Table 2-b. Means and standard deviations for peak EMG data of each muscle from initial contact to peak knee flexion during drop landing.

			Treatment			
Variable	Side	Time	Control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	64.96 (105.23)	35.83 (35.95)	77.14 (106.21)	38.35 (36.68)
		condition	63.34 (105.33)	38.15 (36.12)	38.50 (43.65)	51.44 (44.20)
		postcondition	67.43 (83.92)	30.29 (28.34)	51.30 (62.26)	36.12 (32.11)
	Right	precondition	11098 (133.87)	84.72 (119.34)	85.72 (84.90)	69.09 (59.48)
		condition	105.22 (12.077)	62.87 (66.07)	77.89 (88.99)	60.35 (57.07)
		postcondition	88.72 (119.34)	53.34 (38.32)	53.34 (107.34)	54.59 (42.66)
Vastus Medialis	Left	precondition	9.18 (17.45)	3.95 (6.21)	4.00 (4.79)	3.74 (4.82)
		condition	5.15 (7.43)	3.85 (5.95)	2.61 (3.07)	2.82 (2.76)
		postcondition	6.368 (7.09)	2.30 (1.81)	2.76 (2.77)	2.59 (1.75)
	Right	precondition	23.77 (13.18)	20.72 (9.01)	28.72 (23.54)	20.30 (14.39)
		condition	24.41 (14.18)	18.64 (10.11)	23.61 (16.83)	17.40 (15.53)
		postcondition	24.28 (13.39)	19.12 (9.61)	26.06 (16.06)	17.56 (14.99)
Vastus Lateralis	Left	precondition	3.87 (8.68)	3.36 (7.12)	3.56 (9.35)	2.23 (5.24)
		condition	1.87 (1.43)	1.40 (1.34)	2.95 (7.18)	1.38 (1.18)
		postcondition	2.18 (1.84)	3.26 (9.76)	2.76 (5.31)	1.15 (0.92)
	Right	precondition	19.30 (13.23)	19.18 (10.80)	24.41 (22.31)	18.24 (10.37)
		condition	20.79 (12.72)	14.39 (8.65)	21.93 (16.31)	11.94 (5.40)
		postcondition	20.03 (12.85)	15.03 (9.77)	20.97 (12.66)	12.98 (5.39)
Medial Hamstring	Left	precondition	37.88 (41.18)	25.94 (16.78)	25.88 (29.59)	27.55 (22.70)
		condition	34.08 (33.31)	22.79 (15.33)	23.42 (26.31)	23.37 (20.29)
		postcondition	28.93 (20.31)	21.52 (20.87)	16.16 (8.13)	19.49 (19.33)
	Right	precondition	25.76 (13.15)	29.32 (13.15)	26.61 (18.25)	25.01 (18.10)
		condition	37.01 (27.06)	22.00 (27.06)	22.30 (14.67)	20.39 (12.29)
		postcondition	41.02 (25.10)	18.83 (25.10)	20.93 (13.04)	18.74 (11.36)
Gluteus Medius	Left	precondition	15.11 (12.86)	23.50 (21.08)	15.71 (14.73)	13.29 (8.40)
		condition	15.76 (10.11)	22.93 (21.80)	16.87 (15.35)	13.75 (11.87)
		postcondition	16.27 (10.58)	18.53 (20.07)	20.10 (21.52)	12.75 (11.06)
	Right	precondition	36.39 (28.10)	36.32 (24.44)	36.85 (21.77)	31.79 (21.96)
		condition	42.40 (29.08)	31.87 (18.52)	36.34 (20.58)	28.50 (18.33)
		postcondition	35.17 (26.31)	33.32 (23.68)	35.77 (18.89)	35.35 (26.91)
Gluteus Maximus	Left	precondition	23.32 (30.40)	19.56 (20.68)	30.57 (56.99)	23.80 (33.32)
		condition	25.88 (34.05)	16.54 (19.17)	23.72 (44.21)	10.24 (9.47)
		postcondition	22.49 (26.75)	20.91 (33.91)	23.80 (57.64)	9.89 (9.41)
	Right	precondition	46.16 (30.05)	50.53 (36.51)	45.54 (34.90)	40.36 (41.75)
		condition	53.33 (51.35)	42.51 (28.58)	45.22 (34.17)	28.65 (18.43)
		postcondition	54.26 (63.64)	40.57 (23.95)	46.03 (39.06)	32.24 (21.67)

Table 2-c. Means and standard deviations for mean EMG data of each muscle 200 ms prior to initial contact during drop landing.

			Treatment			
Variable	Side	Time	Control	effusion	Pain	pain/effuseon
Medial Gastrocnemius	Left	precondition	4.74 (6.12)	3.75 (3.88)	11.49 (31.80)	4.51 (5.37)
		condition	4.34 (5.30)	3.22 (1.76)	4.39 (2.50)	4.74 (3.11)
		postcondition	3.82 (3.43)	3.09 (2.23)	4.06 (3.11)	3.76 (2.49)
	Right	precondition	15.59 (10.09)	14.70 (7.97)	14.51 (7.92)	13.29 (7.10)
		condition	15.09 (9.54)	14.40 (8.95)	12.90 (7.68)	12.06 (7.09)
		postcondition	15.10 (9.50)	13.99 (8.11)	13.70 (7.49)	13.17 (8.09)
Vastus Medialis	Left	precondition	4.05 (11.62)	0.51 (0.32)	0.68 (0.80)	0.96 (1.26)
		condition	0.89 (0.92)	1.10 (2.20)	0.65 (0.50)	1.08 (1.11)
		postcondition	1.19 (1.73)	0.61 (0.58)	0.60 (0.68)	0.78 (0.75)
	Right	precondition	2.43 (3.96)	1.51 (1.13)	1.26 (0.72)	1.36 (0.82)
		condition	1.47 (0.96)	1.51 (1.11)	1.17 (0.78)	1.30 (0.84)
		postcondition	1.43 (1.10)	1.55 (1.26)	1.24 (0.75)	1.36 (0.82)
Vastus Lateralis	Left	precondition	0.48 (0.42)	0.39 (0.25)	0.43 (0.32)	0.55 (0.51)
		condition	0.43 (0.29)	0.49 (0.33)	0.55 (0.45)	0.81 (0.69)
		postcondition	0.46 (0.30)	0.44 (0.40)	0.44 (0.38)	0.58 (0.57)
	Right	precondition	1.03 (0.51)	1.11 (0.55)	1.08 (0.47)	1.00 (0.43)
		condition	1.02 (0.52)	1.11 (0.57)	1.03 (0.55)	1.02 (0.58)
		postcondition	0.98 (0.48)	1.10 (0.590)	1.05 (0.56)	1.02 (0.49)
Medial Hamstring	Left	precondition	11.85 (7.98)	10.77 (4.98)	9.68 (5.53)	10.55 (7.46)
		condition	10.71 (8.59)	11.21 (4.79)	10.62 (5.59)	11.62 (7.93)
		postcondition	9.55 (6.89)	11.27 (5.20)	8.67 (5.05)	10.19 (6.80)
	Right	precondition	3.32 (1.48)	3.79 (2.53)	2.99 (1.64)	3.70 (2.52)
		condition	3.68 (2.05)	3.29 (1.94)	2.71 (1.45)	2.98 (1.94)
		postcondition	3.15 (1.36)	3.05 (1.87)	2.85 (1.81)	2.69 (1.85)
Gluteus Medius	Left	precondition	2.82 (2.09)	3.75 (3.53)	3.00 (2.91)	2.64 (2.21)
		condition	2.79 (1.59)	3.55 (3.28)	2.82 (1.96)	2.61 (2.09)
		postcondition	3.13 (1.91)	3.38 (3.14)	3.07 (2.83)	2.11 (1.65)
	Right	precondition	4.65 (5.41)	5.10 (2.81)	5.26 (3.49)	5.00 (6.39)
		condition	6.66 (9.07)	4.40 (2.60)	5.15 (3.68)	4.62 (4.96)
		postcondition	4.70 (5.77)	4.36 (2.33)	5.65 (4.38)	4.69 (4.79)
Gluteus Maximus	Left	precondition	1.11 (0.52)	1.24 (0.58)	1.40 (0.94)	1.11 (0.42)
		condition	1.17 (0.59)	1.19 (0.54)	1.26 (0.57)	1.14 (0.38)
		postcondition	1.32 (0.83)	1.09 (0.61)	1.26 (0.74)	0.97 (0.34)
	Right	precondition	3.39 (2.18)	3.16 (1.53)	2.82 (1.51)	2.22 (1.03)
		condition	3.10 (1.70)	3.11 (1.96)	3.04 (1.65)	2.62 (1.72)
		postcondition	3.18 (1.84)	2.95 (1.74)	2.70 (1.62)	2.71 (2.28)

Table 2-d. Means and standard deviations for mean EMG data of each muscle from initial contact to peak knee flexion during drop landing.

			Treatment			
Variable	Side	Time	Control	effusion	pain	pain/effusion
Medial Gastrocnemius	Left	precondition	28.56 (45.49)	15.07 (14.86)	26.87 (33.09)	14.56 (13.37)
		condition	22.19 (29.80)	15.01 (14.13)	15.78 (16.32)	18.94 (16.29)
		postcondition	25.67 (33.17)	11.83 (10.84)	19.68 (24.37)	13.37 (11.38)
	Right	precondition	43.76 (54.58)	33.40 (45.42)	32.65 (29.61)	26.63 (18.62)
		condition	38.65 (39.58)	21.74 (15.67)	27.62 (26.42)	23.02 (17.11)
		postcondition	30.70 (29.86)	20.43 (14.65)	27.63 (28.97)	20.77 (12.40)
Vastus Medialis	Left	precondition	4.75 (10.86)	1.57 (2.58)	1.53 (1.70)	1.59 (2.05)
		condition	2.06 (3.12)	1.51 (2.22)	1.04 (1.07)	1.23 (1.21)
		postcondition	2.33 (2.43)	0.88 (0.56)	0.98 (0.76)	1.01 (0.67)
	Right	precondition	10.59 (6.88)	9.39 (4.58)	12.26 (10.41)	8.65 (5.50)
		condition	9.85 (5.15)	8.00 (4.16)	9.26 (6.42)	7.40 (6.58)
		postcondition	10.24 (5.17)	8.13 (4.36)	9.93 (5.99)	7.09 (4.90)
Vastus Lateralis	Left	precondition	1.71 (4.20)	1.17 (1.90)	1.23 (2.75)	0.84 (1.52)
		condition	0.77 (0.51)	0.62 (0.59)	1.01 (2.06)	0.60 (0.49)
		postcondition	0.83 (0.63)	0.89 (1.88)	0.93 (1.60)	0.47 (0.31)
	Right	precondition	7.94 (4.55)	8.04 (4.19)	9.48 (7.49)	7.64 (4.13)
		condition	8.68 (4.89)	5.91 (3.28)	8.38 (6.16)	5.03 (2.03)
		postcondition	8.29 (4.65)	5.79 (2.98)	8.02 (4.73)	5.60 (2.07)
Medial Hamstring	Left	precondition	15.99 (14.20)	12.22 (7.51)	11.61 (10.33)	12.23 (8.49)
		condition	15.49 (11.82)	10.54 (5.74)	10.71 (8.93)	10.36 (6.71)
		postcondition	13.58 (7.85)	10.00 (7.12)	7.65 (3.43)	9.24 (7.13)
	Right	precondition	10.06 (4.70)	11.94 (11.61)	10.16 (5.89)	9.76 (5.82)
		condition	14.21 (9.34)	8.26 (5.00)	8.57 (4.71)	7.44 (3.31)
		postcondition	15.43 (9.44)	7.19 (3.71)	7.94 (4.21)	7.51 (3.73)
Gluteus Medius	Left	precondition	6.82 (5.27)	10.08 (8.91)	6.88 (5.67)	6.22 (4.03)
		condition	7.44 (5.50)	9.23 (8.06)	7.15 (5.82)	6.34 (5.99)
		postcondition	7.20 (4.46)	7.99 (8.47)	8.24 (7.00)	5.78 (4.75)
	Right	precondition	14.10 (8.20)	15.14 (8.65)	15.88 (8.19)	13.84 (8.13)
		condition	15.60 (8.36)	13.99 (8.13)	15.70 (8.37)	12.24 (8.10)
		postcondition	14.06 (7.48)	14.16 (9.16)	15.24 (8.12)	15.24 (10.77)
Gluteus Maximus	Left	precondition	6.66 (6.68)	7.02 (7.41)	9.42 (15.66)	7.66 (8.93)
		condition	7.35 (7.77)	6.17 (6.83)	7.88 (13.37)	3.49 (2.15)
		postcondition	6.86 (6.67)	7.17 (10.67)	8.94 (17.13)	3.57 (2.82)
	Right	precondition	18.68 (12.71)	19.28 (12.17)	16.08 (8.89)	14.74 (11.69)
		condition	19.57 (14.97)	16.36 (9.72)	17.20 (10.55)	12.09 (7.42)
		postcondition	19.60 (17.78)	16.31 (9.05)	16.71 (12.03)	12.68 (8.88)

Table 2-e. Means and standard deviations for vertical stiffness during drop landing. .

		Treatment			
Variables	Time	control	effusion	pain	pain/effusion
Stiffness (N/m)	precondition	26420.9 (11601.4)	26771.4 (10439.7)	27651.6 (15998.2)	27792.4 (15998.2)
	condition	27180.7 (12982.2)	25907.0 (14854.6)	27081.6 (11140.6)	27938.9 (19246.2)
	postcondition	24907.6 (11825.9)	27205.5 (13588.6)	25560.5 (10215.2)	26470.4 (14581.1)

Table 2-f. Summary data in peak joint angles during drop landing. For ankle angles, the neutral position (90 °) was referenced as zero °. Values are mean (SD).

Unit: °		Treatment			
Variables	Time	control	effusion	pain	pain/effusion
Knee abduction	precondition	4.92 (3.79)	5.29 (3.67)	6.85 (4.08)	4.71 (3.23)
	condition	5.02 (3.80)	5.32 (3.86)	7.84 (4.70)	5.19 (3.78)
	postcondition	5.14 (3.78)	5.81 (4.03)	7.77 (4.98)	5.40 (3.56)
Knee adduction	precondition	5.62 (4.51)	4.72 (3.49)	4.42 (3.32)	4.37 (3.54)
	condition	5.56 (4.55)	4.23 (3.25)	4.77 (4.05)	3.67 (2.96)
	postcondition	5.62 (4.63)	4.13 (3.32)	4.63 (3.78)	3.82 (3.37)
Hip flexion	precondition	20.39 (9.44)	20.41 (9.62)	20.08 (8.91)	20.12 (8.78)
	condition	18.97 (9.70)	19.37 (9.27)	21.16 (15.76)	21.19 (8.98)
	postcondition	19.51 (10.11)	18.90 (9.08)	19.37 (8.09)	20.56 (9.27)
Hip extension	precondition	6.87 (6.40)	8.16 (7.06)	8.52 (4.58)	8.50 (7.46)
	condition	8.29 (6.10)	7.97 (6.06)	11.64 (12.57)	8.24 (6.03)
	postcondition	8.01 (6.28)	8.82 (6.52)	7.43 (4.28)	7.36 (5.88)

Table 2-g. Summary data in peak joint moments during drop landing. Values are mean (SD).

Unit: N·m		Treatment			
Variables	Time	control	effusion	pain	pain/effusion
Ankle Plantar-flexion	precondition	160.62 (49.43)	162.37 (48.34)	164.82 (45.65)	161.31 (38.55)
	condition	156.03 (44.62)	157.81 (48.09)	163.01 (48.42)	153.73 (39.00)
	postcondition	158.76 (45.19)	157.04 (51.57)	157.33 (48.65)	158.94 (46.34)
Knee flexion	precondition	41.81 (17.41)	43.34 (16.41)	44.23 (20.09)	43.12 (13.25)
	condition	41.55 (15.69)	41.18 (17.51)	42.82 (18.68)	39.09 (14.85)
	postcondition	41.51 (17.76)	39.62 (19.65)	41.94 (16.67)	40.40 (16.53)
Knee adduction	precondition	24.90 (12.23)	31.78 (21.62)	32.48 (19.61)	26.06 (12.76)
	condition	23.80 (10.61)	27.60 (15.24)	34.39 (21.98)	25.51 (12.39)
	postcondition	26.04 (11.37)	27.86 (15.78)	32.43 (19.14)	26.15 (13.13)
Hip extension	precondition	217.54 (73.61)	230.34 (70.23)	205.76 (61.10)	210.00 (67.66)
	condition	229.95 (79.89)	215.31 (71.84)	202.91 (54.74)	195.97 (57.20)
	postcondition	228.51 (86.47)	214.13 (60.07)	207.04 (60.94)	198.23 (65.15)

Table 2-h. Means and standard deviations for the time between the toe off of the first landing and the initial contact of the second landing.

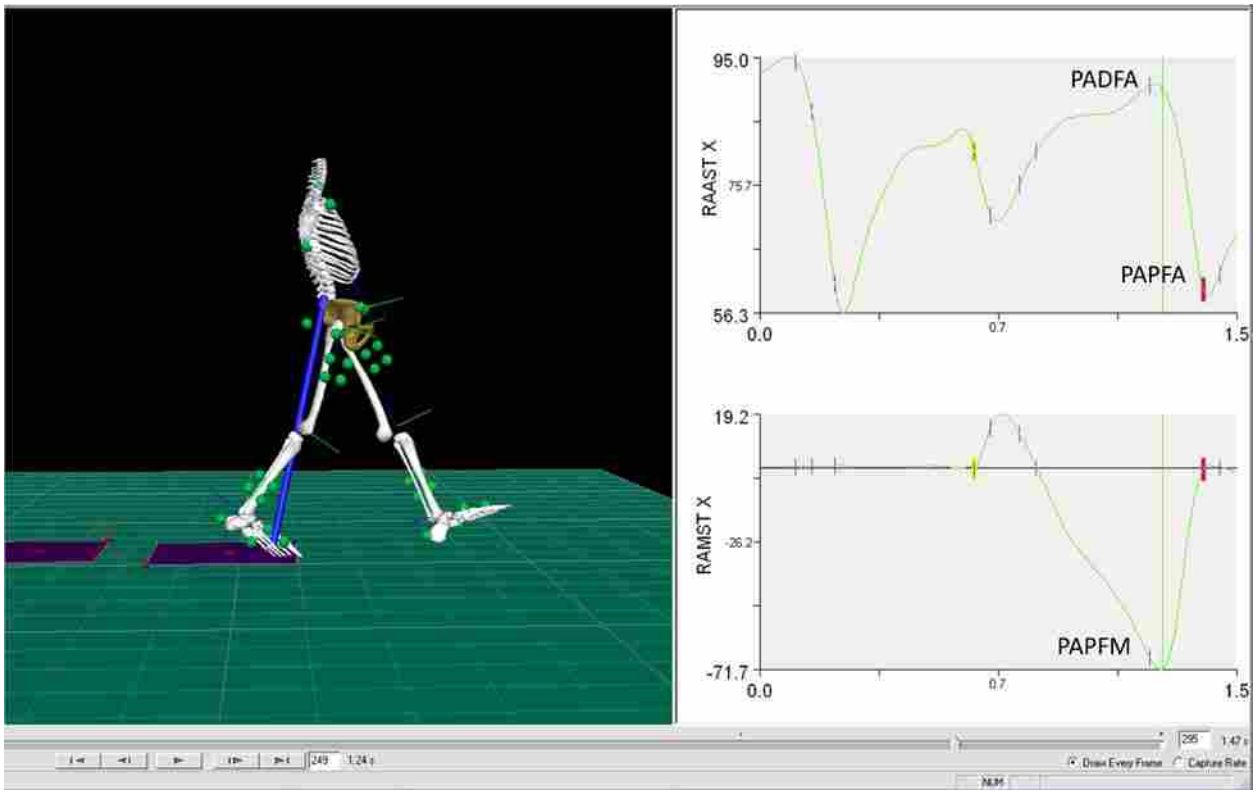
Unit: s	Treatment			
Time	control	effusion	pain	pain/effusion
precondition	0.19 (0.08)	0.19 (0.06)	0.20 (0.06)	0.19 (0.07)
condition	0.19 (0.06)	0.17 (0.06)	0.18 (0.06)	0.17 (0.07)
postcondition	0.19 (0.06)	0.18 (0.06)	0.18 (0.06)	0.17 (0.07)

Appendices

To provide a better understanding of when the peak joint angles and moments occur, pictures and graphs during walking and drop landing are presented in the appendices. All variables are in the ipsilateral side (the limb on the second force platform). Initial contact is highlighted in yellow and toe off is highlighted in red.

Walking

1. Ankle angles and moments in the sagittal plane.

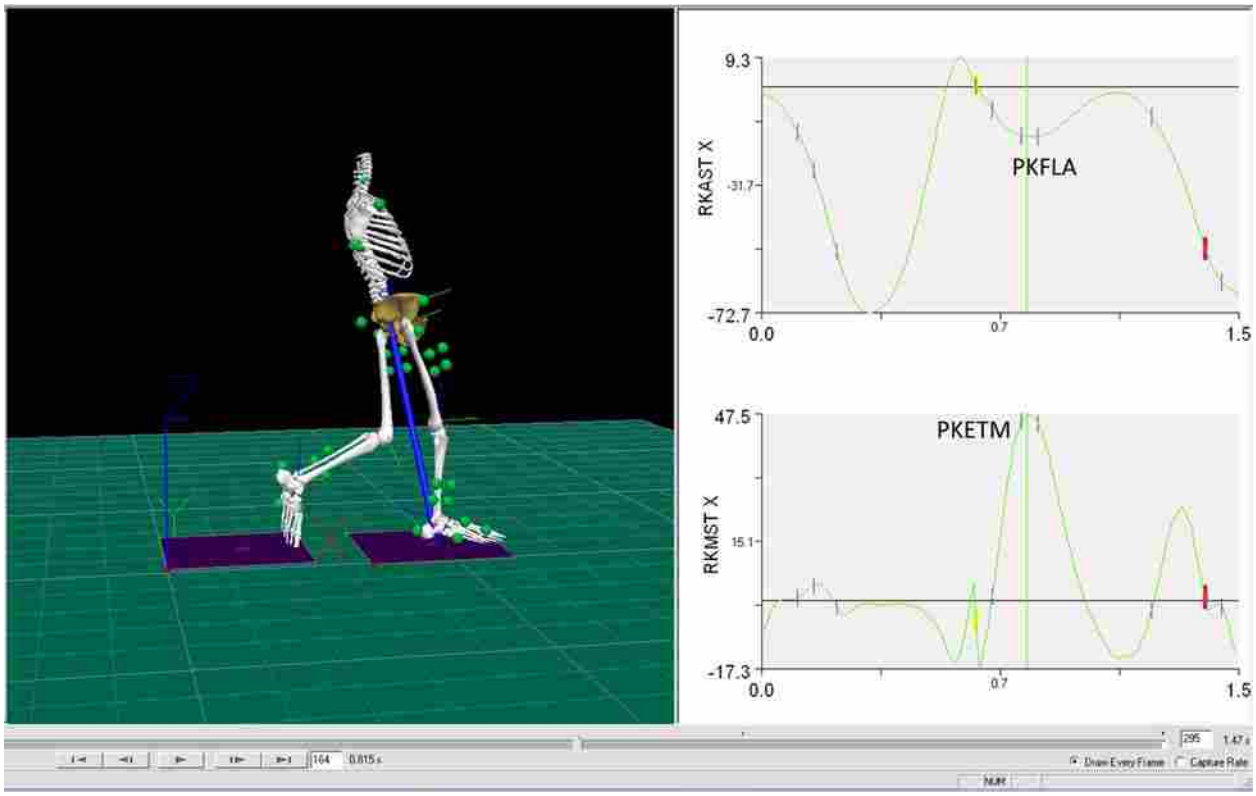


PADFA: peak ankle dorsi-flexion angle

PAPFA: peak ankle plantar-flexion angle

PAPFM: peak ankle dorsi-flexion moment

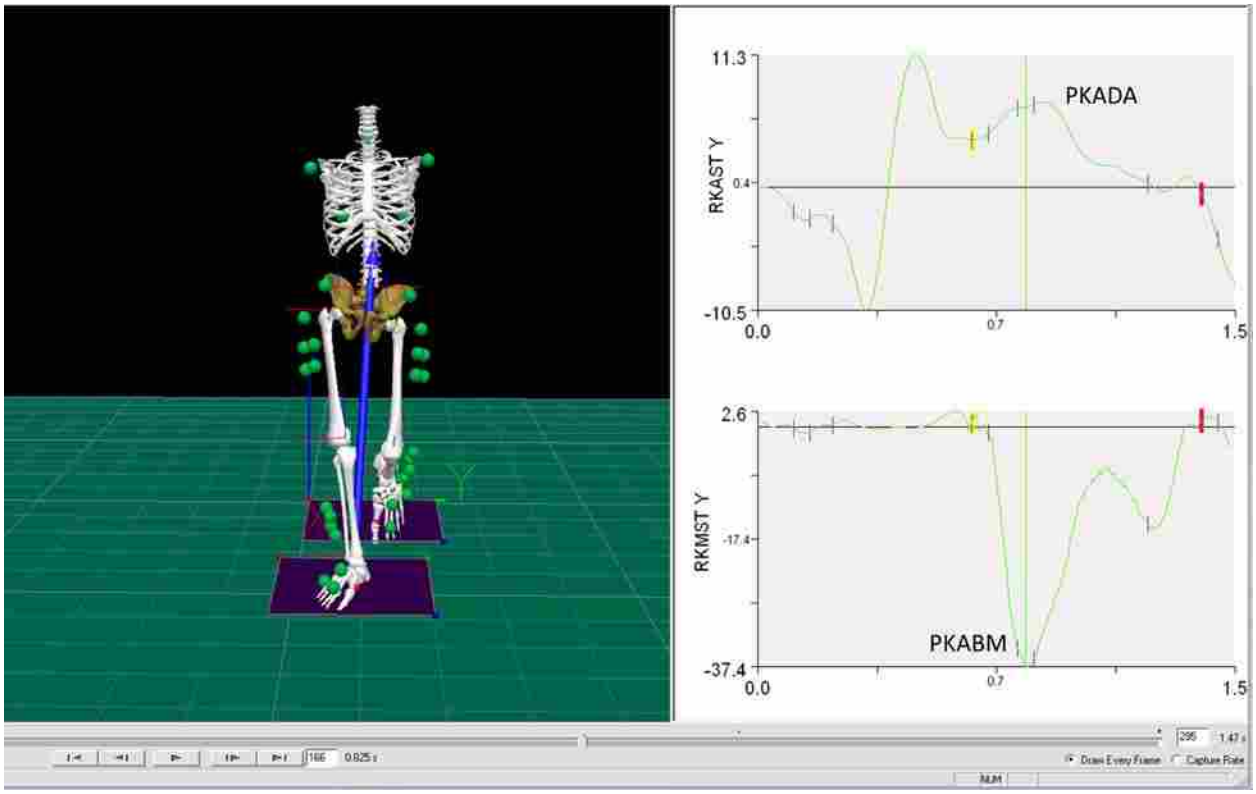
2. Knee angles and moments in the sagittal plane



PKFLA: peak knee flexion angle

PKETM: peak knee extension moment

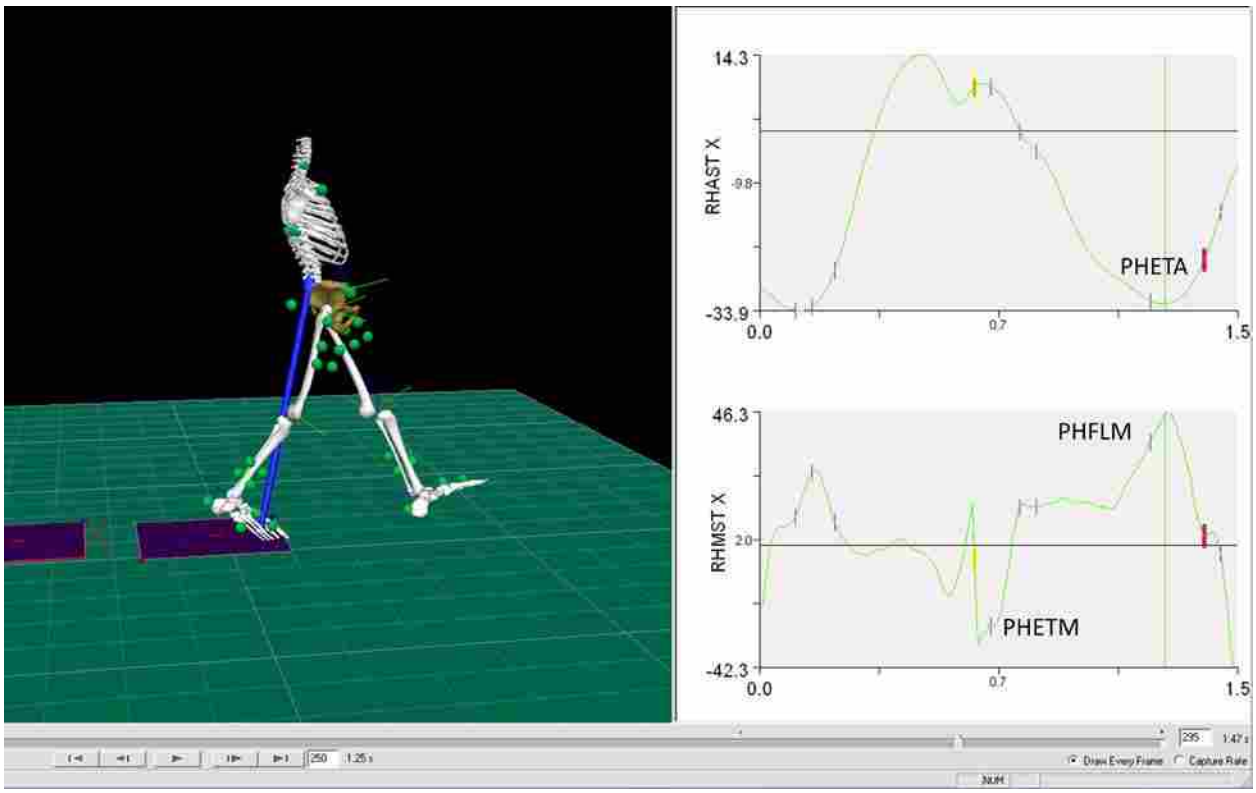
3. Knee angles and moments in the frontal plane



PKADA: peak knee adduction angle

PKABM: peak knee abduction moment

4. Hip angles and moments in the sagittal plane

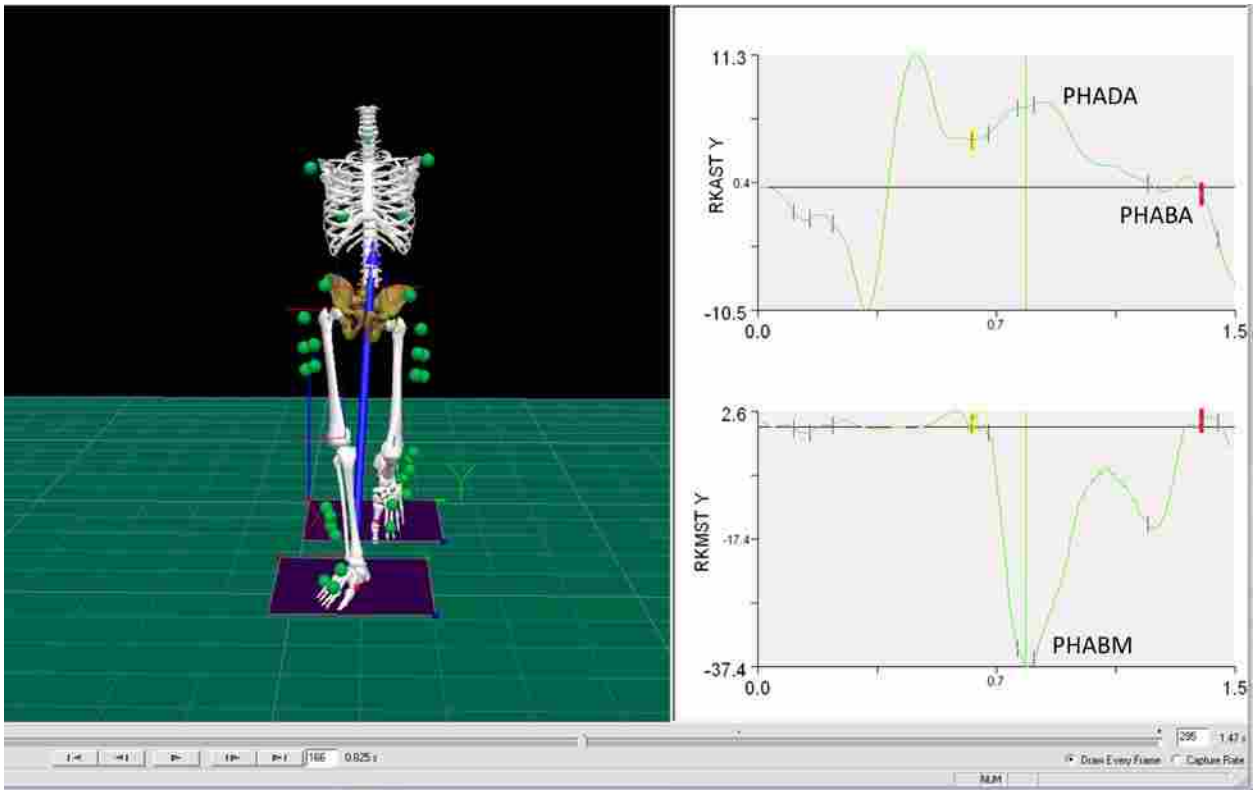


PHETA: peak hip extension angle

PHFLM: peak hip flexion moment

PHETM: peak hip extension moment

5. Hip angles and moments in the frontal plane



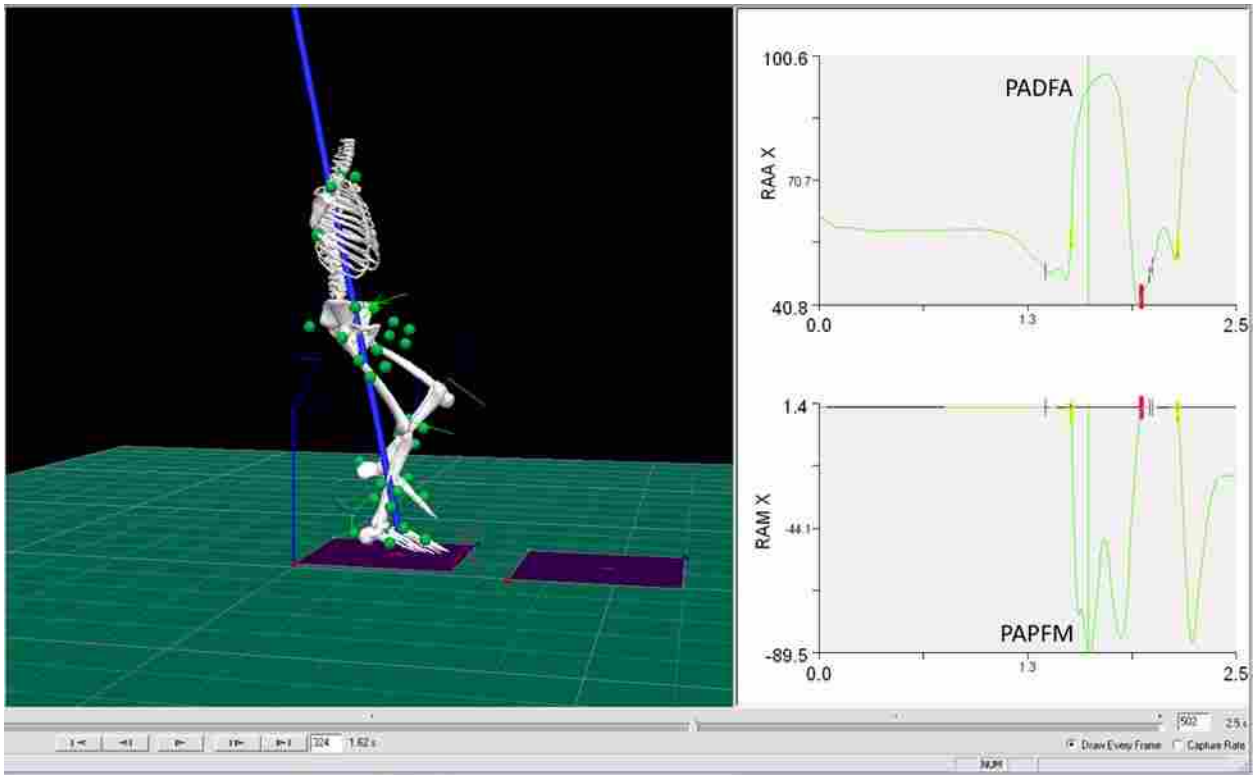
PHADA: peak hip adduction angle

PHABA: peak hip abduction angle

PHABM: peak hip abduction moment

Drop landing

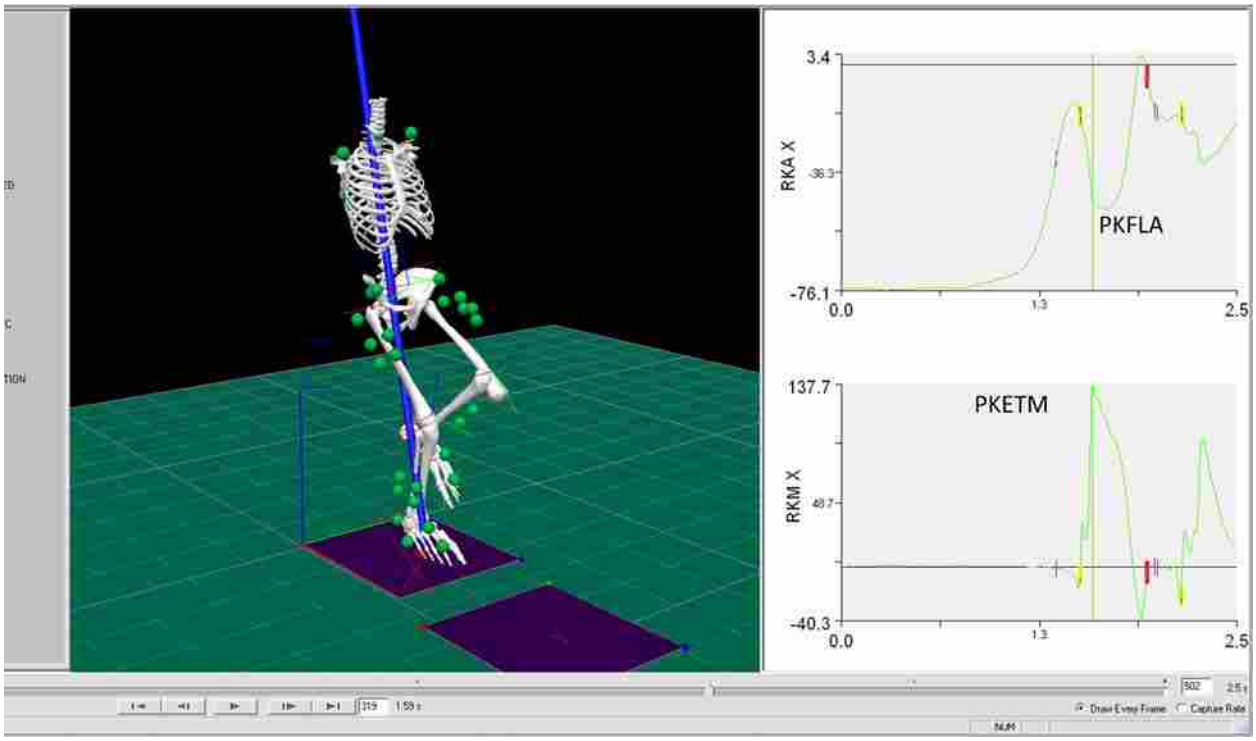
6. Ankle angles and moments in the sagittal plane



PADFA: peak ankle dorsi-flexion angle

PAPFM: peak ankle plantar-flexion moment

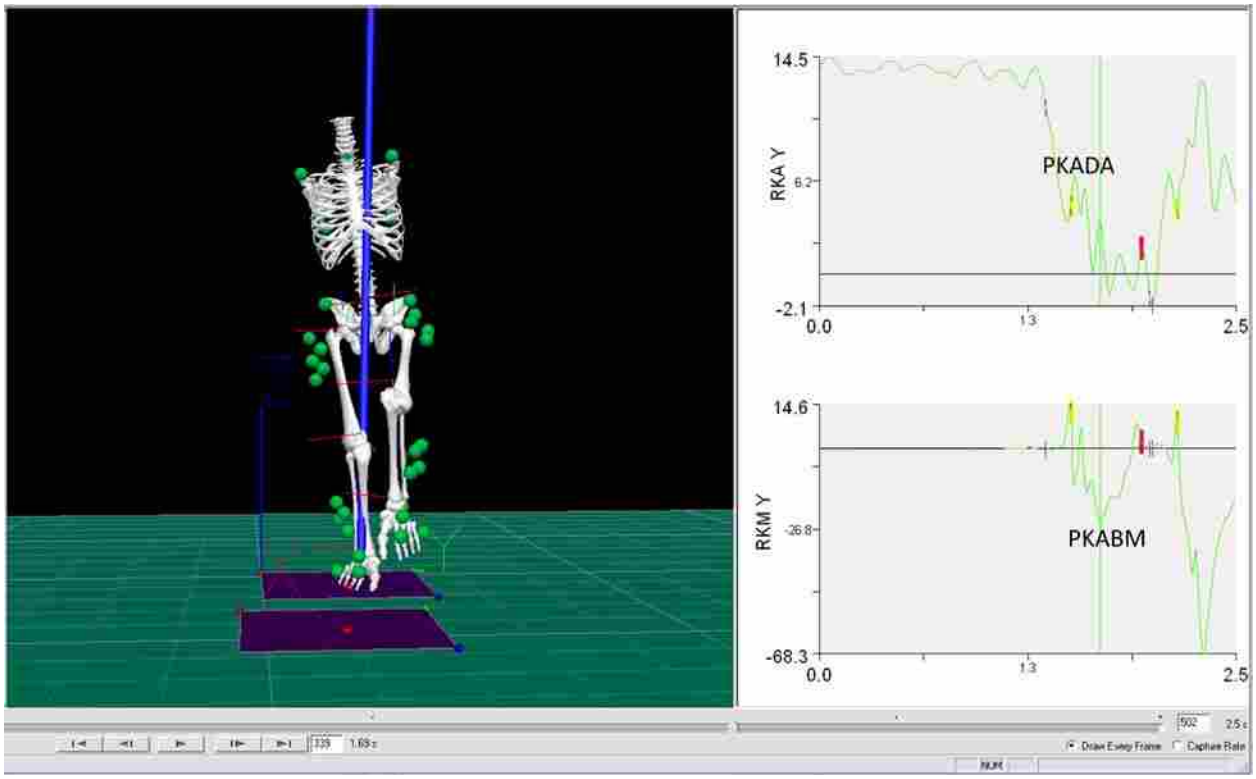
7. Knee angles and moments in the sagittal plane



PKFLA: peak knee flexion angle

PKETM: peak knee extension moment

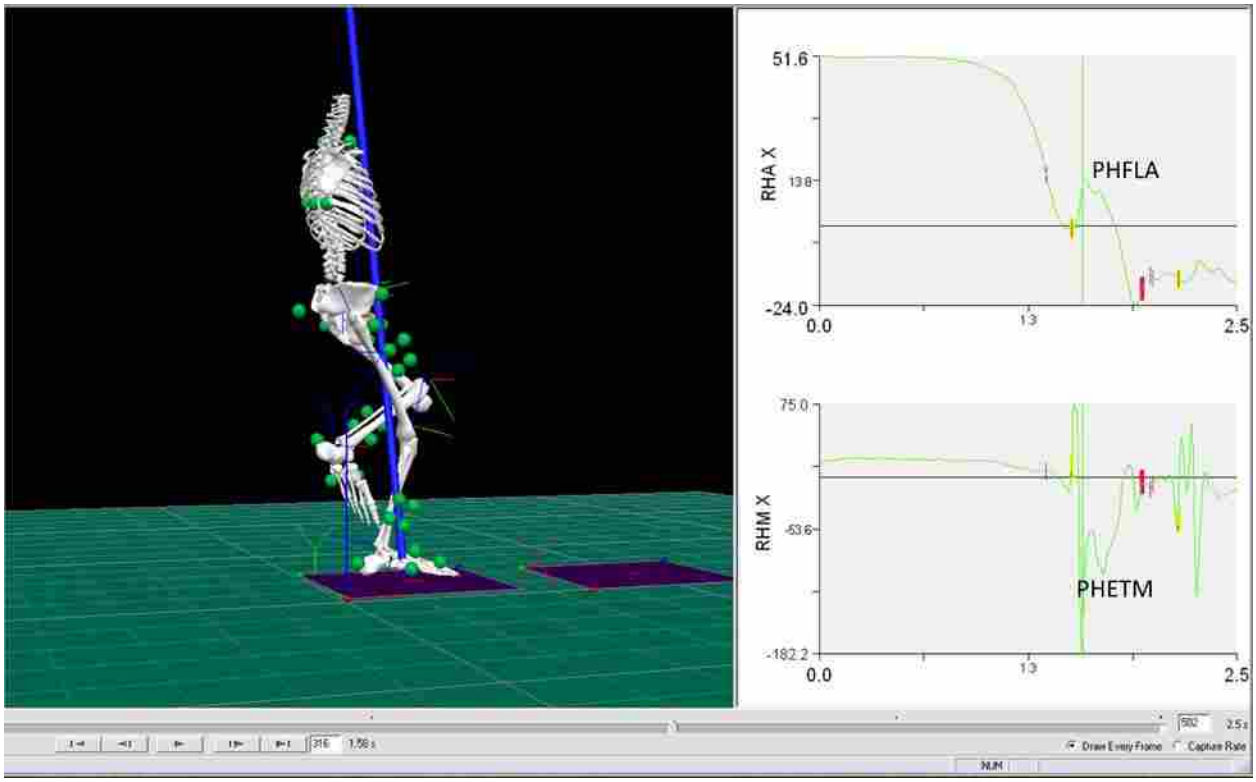
8. Knee angles and moments in the frontal plane



PKADA: peak knee adduction angle

PKABM: peak knee abduction moment

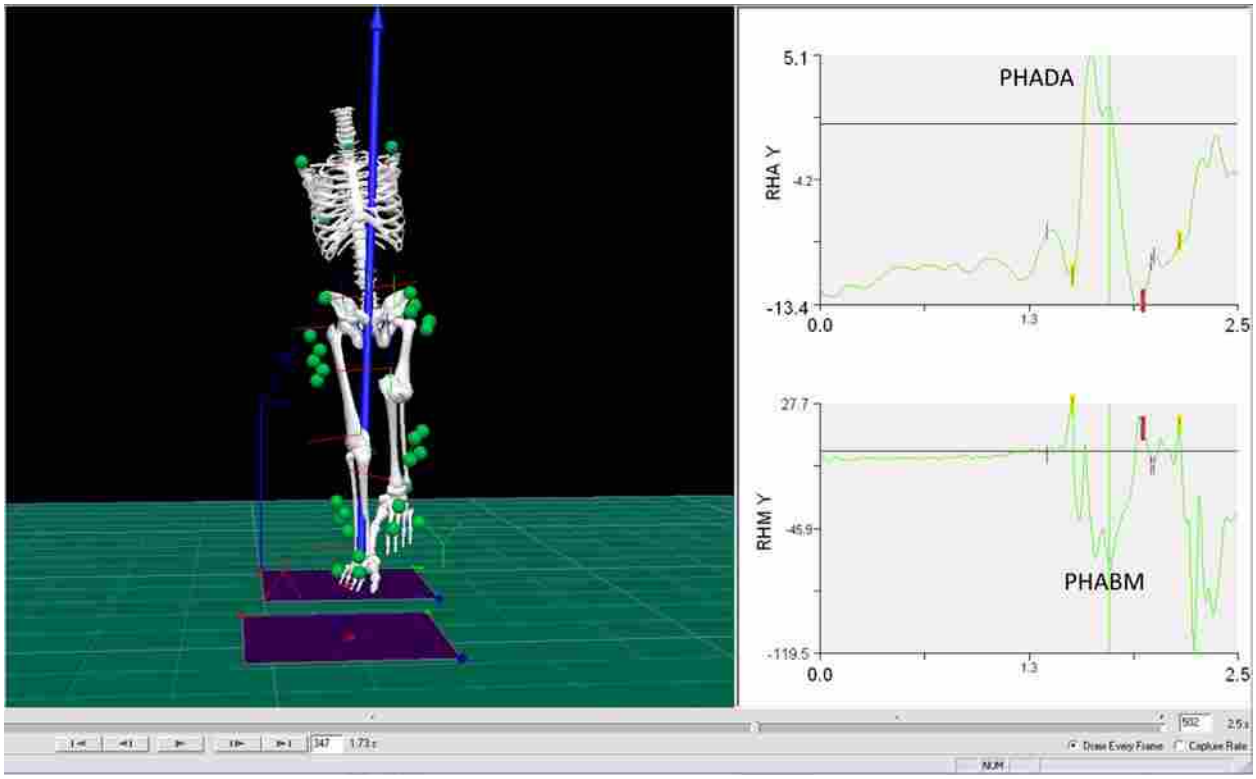
9. Hip angles and moments in the sagittal plane



PHFLA: peak hip flexion angle

PHETM: peak hip extension moment

10. Hip angles and moments in the frontal plane



PHADA: peak hip adduction angle

PHABM: peak hip abduction moment

Prospectus

Introduction

Knee joint injuries are common. For example, approximately 80,000 anterior cruciate ligament (ACL) ruptures are seen in the United States annually.[1] The estimated prevalence of knee osteoarthritis (OA) is 6.1 % in adults aged more than 30[2] and 12.5 % in those aged 45 and above.[3] Knee OA often requires total knee arthroplasty (TKA)[4] resulting in 443,008 TKAs from 1990 to 2000 in the United States alone.[5] Of all knee joint pathologies, anterior knee pain (AKP) is the most common[6] with prevalence rate as high as 25%.[7] Although diagnosis and etiologies vary, a reduction in quadriceps activation is a common consequence in individuals with knee joint pathologies.[8-12]

Quadriceps dysfunction resulting from a knee joint injury has been termed arthrogenous muscle inhibition (AMI).[13,14] AMI is a pre- and postsynaptic inhibition of periarticular musculature resulting from surgery, distension, pain, or structural damage of a joint.[15-17] AMI is the body's natural response following a traumatic injury.[15] AMI discourages the patient's ability to move the injured joint thus it helps prevent further structural damage[13] and provide time for tissue healing. The presence of AMI, however, may limit full recruitment of active motor units and reduce voluntary contraction.[18] Furthermore, AMI may mediate compensatory strategies in the functional kinetic chain of the lower extremity.[13,19,20] Long term consequences of these abnormalities could modify normal joint loading, eventually resulting in degenerative joint disease.[21-23]

Structural damage and the ensuing inflammatory response are believed to be initiating factors that alter normal afferent input, resulting in AMI.[11,24,25] Among these factors, pain and

joint effusion have been examined as independent contributing factors to AMI. In clinical and laboratory trials, quadriceps AMI has been associated with knee pain[8,26,27] and alterations in quadriceps muscle activity during stair ascending.[28] Joint effusion has also been shown as an independent cause of quadriceps inhibition.[13,19,20,29-31] Studies observing the effects of experimentally induced knee effusion on lower extremity muscles reported quadriceps inhibition with soleus[20] or hamstring[13,19] facilitation. These studies reported an increase in knee flexion during walking[19] and an increase in ground reaction forces during a drop landing task.[13]

Despite evidence of the consequences of each factor to AMI, the relative or additive contribution of pain and effusion to elicit AMI is still unclear. Since pain and effusion are from different sensory receptors (e.g. nociceptors[32] and Ruffini endings[20]), each stimulus may follow a different pathway. Although each injury model is effective in evaluating pain and effusion stimuli separately, we rarely see pain or effusion alone in knee joint injuries. Introduction of pain and effusion simultaneously in a controlled environment would simulate a condition in which both stimuli are present. The observation of neuromechanical alterations using this combined model may clarify if there is an additive effect with the two stimuli. Additionally, the combined model could potentially help us understand how this additive effect influences AMI and associated lower extremity compensatory strategies.

The purpose of this study is to determine the contributions of AKP, knee joint effusion, and a combination of both stimuli on change in lower extremity neuromuscular activities, kinetics, and kinematics during walking and drop landings. These functional movements demand dynamic joint stability. Dynamic joint stability requires active muscle contraction along with proper sensory feedback and feed-forward controls. When AMI is present in the quadriceps, a decrease in knee extension moment and a reduction in knee flexion angle would be expected.

To compensate for these alterations, subjects may display a higher neuromuscular activation in the hip extensors and triceps surae.

Research questions

- Will induced pain, effusion, or a combination of pain and effusion cause neuromuscular, kinetic, and kinematic alterations in walking and drop landing?
- Will a combination of pain and effusion cause additive effects to elicit neuromuscular, kinetic, and kinematic changes?

Research hypotheses

- Compared to the control condition, all three injury models (pain, effusion, and a combination of pain and effusion) will cause neuromuscular, kinetic, and kinematic alterations during walking and drop landing.
    - Neuromuscular alterations during both walking and drop landing
        - Peak EMG activation in the quadriceps will be decreased in the involved leg
    - Kinetic alterations during walking
        - Internal knee extension moment will change in the involved leg
    - Kinematic alterations during walking
        - Knee flexion angle will change at initial contact and toe off.
    - Kinetic alterations during drop landing
        - Peak vertical GRF will change in the involved leg
        - Peak internal knee extension moment will change in the involved leg

    - Kinematic alterations during drop landing
        - Peak knee flexion angle will change in the involved leg

- A combination of pain and effusion stimulus will show a greater degree in alterations compared with pain and effusion individually. The pain condition and effusion condition will show a similar degree in alterations.

Operational definitions

- Anterior knee pain: this term is interchangeably used with patellofemoral pain syndrome in this literature review
- Arthrogenous (arthrogenic) muscle response: an ongoing reflex inhibition or facilitation of joint musculature after distension or damage to structures of the joint.[15]
- Drop landing: landing on the dominant leg from 30 cm height wooden box onto the force plate while the non-dominant leg is non-weight bearing
- External knee adduction moment: the torque that tends to adduct the knee during stance phase. Higher external knee adduction moment indicates a greater load on the medial compartment.
- External moment: equal and opposite to the net internal moment. (i.e. internal knee extension moment = external knee flexion moment)
- Feedback controls: process of motor responses within the corresponding system after an input of the sensory information[33]
- Feed-forward controls: a pre-programmed anticipated motor response before an input of the sensory information[33]

- Frontal plane lever arm: the perpendicular distance from the GRF to the knee joint centre of the rotation (tibial tuberosity)[34]
- Ground reaction force (GRF): a single equivalent force equal to the sum of a distribution of forces applied to a surface[35]
- Internal moment (the net joint moment): the net effect of the moments that are created about a single joint by muscle, bone, and soft tissue forces
- Kinematics: "the study of bodies in motion without regard to the causes of motion"[35]
- Kinesthesia: awareness of body segment or position during movement
- Kinetics: "study of the causes of motion"[35]
- Loading rate: the ratio between the peak vertical GRF and the amount of time from initial contact to the peak vertical GRF (VGRF/Δ time).
- Loading response: immediately after initial contact until double limb support ends[36]
- Nociception: ability to feel pain
- Peak joint angles: ankle, knee and hip joint angles relative to the joint position captured during static standing trial
    - Peak ankle angle: Ankle joint angle relative to the static standing trial position
        - A positive value: dorsiflexion and inversion
        - A negative value: plantarflexion and eversion
    - Peak knee angle: knee joint angle relative to a knee joint during the static standing trial position
        - A positive value: extension and adduction
        - A negative value: flexion and abduction
    - Peak hip angle: hip joint angle relative to the static standing trial position

  - A positive value: flexion and adduction
  - A negative value: extension and abduction

- Proprioception: "a specialized variation of the sensory modality of touch that encompasses the sensation of joint movement (kinesthesia), joint position sense, and force sense."[37]
- Quadriceps avoidance gait: a decrease in the internal knee extension moment at mid-stance
- Stiffness: the ratio between the peak GRF and the maximal vertical displacement of the whole body centre of mass during contact with the ground (VGRF/Δ y)[38]
- Stride length: the distance between the sequential points of initial contact by the same foot
- Total support moment: sum of the extensor moment of the ankle, knee, and hip joint[39]
- Weight acceptance phase of gait: initial contact (heel strike) to peak knee flexion[39]

Assumptions

- Subject will honestly answer the pre-participation health questionnaire and VAS.
- The reflective markers and EMG electrodes will be located at the same places over four condition sessions.
- A week will be sufficient time to wash-out any injection effects.
- Each subject's diet and regular exercising pattern will not be changed over the 4-week data collection period.
- Each subjects will not take any medication (over-the-counter and prescription) over the 4-week data collection period.

- Medial and lateral hamstrings have the same activation pattern.

Delimitations

- Subjects will be limited in age ranged between 18 and 35.
- All subjects will be free from neurological, vascular, or endocrine disorders.
- All subjects will be free from any lower extremity injury for the last six months and never had lower extremity surgery.

Limitations

- Induced AKP mimic but does not produce clinical AKP or knee joint pain.

Review of literature

This literature review discusses arthrogenous muscle inhibition and neuromechanical alterations in the lower extremity after knee joint injuries. These are organized by the following topics:

ARTHROGENOUS MUSCLE INHIBITION (AMI)
- What is AMI and why is it issue? Evidence of AMI
- Sensory receptors associated with AMI
- Afferent pathway: primary, secondary, and tertiary afferents
- Pain theories
- Mechanism of AMI: why is extension muscles inhibited?
- Types of inhibition
- Interneurons
- Does pain directly cause AMI?
- Pain model
- AMI with joint effusion
- Effusion model
- Limitations on the pain and effusion model
- Acceptable disinhibitory interventions
  - *Cryotherapy*
  - *Electrotherapy*
  - *Transcranial magnetic stimulation*
  - *Manual therapy*
  - *Thermotherapy*
  - *Voluntary exercise*

NEUROMECHANICAL ALTERATIONS RESULTING FROM KNEE JOINT INJURIES
- Ground reaction force
- Knee joint moments
- Joint range of motion and angles
- Walking speed and stride length
- Joint loading
- Gait adaptation and its long-term effects
- Drop landing task
- Stiffness

MEASUREMENTS
- Neuromuscular activity
- Kinetic
- Kinematic

Data base and key word searched

I searched Google Scholar, MEDLINE (EBSCO and PUBMED), SPORTDiscuss (EBSCO), and Web of Science (ISI). I also cross-referenced for identification of studies not found using original search terms. I used the following keywords:

Arthrogenous muscle inhibition OR arthrogenic muscle inhibition
Quadriceps inhibition OR quadriceps activation
Motoneuron pool excitability OR MNP excitability
Pre- AND post-synaptic inhibition
Knee injury OR knee joint injury
Anterior knee pain OR patellofemoral pain syndrome OR knee pain
ACL OR anterior cruciate ligament
Proprioception OR proprioceptors
Pain OR pain receptors
Pain theory OR pain theories
Gate control theory OR gate control
Beta endorphins
Opioid release
Central biasing
Nociception or nociceptors
Muscle receptors
Muscle spindles
Golgi tendon organs OR GTO
Thermoreceptors
Interneurons
Afferent pathway
Hypertonic saline OR experimental knee pain OR inducing pain OR pain model
Knee joint effusion OR effusion model
Transcutaneous magnatic stimulation OR TMS
Transcutaneous electrical nerve stimulation OR TENS or electrotherapy
Voluntary exercise OR volitional exercise
Cryotherapy OR cold application
Walking OR gait OR locomotion OR ambulation
Drop landing OR single leg landing OR single leg drop landing
Osteoarthritis OR knee osteoarthritis
Ground reaction force OR GRF
Kinetics
Kinematics
Knee adduction moment

Joint loading
Joint angle
Walking speed OR gait speed
Stride length
Stiffness

Arthrogenous muscle inhibition (AMI)

What is AMI and why is it an issue?

AMI is a pre- and post-synaptic ongoing reflex inhibition of periarticular musculature resulting from surgery, distension, pain, or structural damage of that joint.[15] AMI is the body's natural response following traumatic injury.[15] AMI discourages patients from moving the injured joint, therefore, preventing further structural damage[13] and providing time for tissue healing. The persistent presence of AMI, however, may limit full recruitment of active motor units thus reducing voluntary contraction.[18] Other negative effects of AMI include neuromuscular deficits and muscular atrophy. Therefore, patients may return to normal function with symptoms of AMI which place patients at a higher risk of recurrent injury.[14,40] Additionally, AMI may alter joint mechanics, resulting in long-term structural change such as degenerative joint disease.[21,22]

Evidence of AMI

Since the frequency of joint injury and measurable availability to the surrounding musculature, researchers have primarily focused on the quadriceps in knee joint injuries (Table 1).

Table 1. Knee joint injury and alterations of motor function in the lower extremity

Injury	Author (year)	Pathology or intervention	Main findings and significances
Patellar	Manal	Patellar contusion	Less knee extension force (MVIC) on the involved side

contusion	(2000)[41]	(<4 months)	compared to the uninvolved side.
AKP	O'Reilly (1998)[42]	Knee pain (aged 40-79)	Knee pain subjects had lower quadriceps strength (MVC) and activation (ITT) than those without pain.
	Suter (1998)[43]	Knee arthroscopy in AKP patients.	Surgery reduced pain but did not change quadriceps activation (ITT) and extension moment (N).
	Suter (1998)[8]	NSAIDs in AKP patients.	Direct relationship between pain and quadriceps inhibition (involved leg > contralateral limb > control). NSAIDs reduced pain but did not change quadriceps activation.
	Suter (1999)[27]	SI joint manipulation in AKP patients.	SI joint manipulation reduced quadriceps inhibition and increased knee extension torque and EMG activity.
	Suter (2000)[26]	SI joint manipulation in AKP patients. (RCT)	SI joint manipulation reduced quadriceps inhibition on the ipsilateral side but not on the contralateral side. No change in knee extension moments.
	Mellor (2005)[44]	anterior/retro patellar knee pain	Synchronized firing motor units in the VM are less than are these in the VL in the patients with knee pain, compared to normative.
Effusion	Fahrer (1988)[45]	Chronic effusion (aspiration)	Quad strength (MVIC) in the involved limb was weaker than the non-involved limb. Aspiration increased strength.
ACL	Suter (2001)[46]	ACL deficiency & reconstruction	Both ACL deficiency and ACL reconstruction groups had quadriceps inhibition (ITT) compared to the control. (quadriceps inhibition: ACL deficiency > ACL reconstruction > control)
	Urbach (2001)[10]	ACL deficiency & reconstruction	Quadriceps inhibition (ITT) presented before operation. After reconstruction quadriceps inhibition decreased but remained less than that of controls.
	Williams (2005)[47]	ACL deficiency	Quadriceps activation (SIB: involved/non-involved) was weaker on the ipsilateral side compared to the contralateral side.
	Drechsler (2006)[9]	ACL reconstruction	Post ACL reconstruction, quadriceps activation (EMG) was less compared to healthy control.
Meniscus	Shakespeare (1985)[48]	Medial meniscectomy	Injection of 0.5% bupivacaine decreased pain level but quadriceps inhibition (RF, IEMG) was still presented.
	Becker (2004)[22]	Partial menisectomy (48+/-9 months post surgery)	Patients with partial menisectomy had less quadriceps force output (MVIC) and activation (ITT) compared to healthy control.
	Thorlund (2010)[49]	Meniscectomy	Meniscectomised leg had reduced quadriceps muscle activity relative to the non-operated leg.
OA	Messier (1992)[50]	Knee OA	The OA group had less quadriceps strength (isokinetic).
	Hurley (1993)[11]	Typical rehabilitation in early onset knee OA (radiography)	The OA patients had quadriceps inhibition (ITT) on the involved leg compared to non-involved leg. Rehabilitation program decreased quadriceps inhibition but not when compared to the non-involved leg.
	Hassan (2001)[51]	Knee OA (radiography)	Patients with OA had less quadriceps strength (MVC) and activation relative to the control subjects.
	Lewek (2004)[52]	Knee OA (medial compartment)	The subjects with OA had less quadriceps strength (N/BMI) and activation (CAR) relative to BMI than the group of healthy control subjects.
	Petterson (2008)[53]	End stage of knee OA (K/L grade IV)	The OA side had weaker quadriceps strength (MVIC) and lower activation (CAR), and smaller lean muscle CSA compared to contralateral side.
TKA	Mizner (2003)[12]	TKA	TKA patients had lower knee extension force (N/BMI) and quadriceps activation (CAR) compared to the control.
	Stevens (2003)[54]	OA & TKA	OA patients had quadriceps inhibition and TKA decreased quadriceps inhibition.

VAS: Visual Analogue Scale
ITT: Interpolated Twitch Technique
RCT: Randomised Clinical Trial
JPS: Joint Position Sense
CSA: Cross Sectional Area
BMI: Body Mass Index

Sensory receptors associated with AMI

Characteristics of four different types of sensory receptors are presented in the Table 2. Quick adapted receptors respond by initial stimulus but stop responding if similar stimulation is maintained. Slow adapted receptors initially respond at a high impulse rate and then at a progressively slower rate until eventually they no longer respond.[55]

Table 2. Characteristics of sensory receptors[37,56-58]

Type	Receptor	Specific nature	Location	Adaption	Sensitive to
Mechanoreceptors	Meissner's corpuscle Pacinian corpuscle Merkel disks	Light pressure Vibration Touch	Skin (superficial) Capsule & ligaments Skin (superficial)	Quick Quick Slow	Joint motion and pressure
Nociceptors	Free nerve endings	Distension (stretch) & pain	Around hair roots and under surface of skin	Variable	Pain
Proprioceptors	Ruffini endings Muscle spindles GTOs Joint receptors	Distension Length changes Tension changes	Joint capsule and ligaments Intrafusal muscle fiber Musculotendinous junction Capsules & ligaments	Slow Slow Slow	Joint position
Thermoreceptors	Krause's end bulbs Corpuscels of Ruffini	Cold Heat	Skin Skin and capsules in joints and ligaments	Slow Slow	Temperature change

Meissner corpuscles and Pacinian corpuscles (type II) are quick adapting joint mechanoreceptors. Meissner and Merkel disks (type I) are located in the epidermis, underneath the skin surface. Pacinian corpuscels are the biggest (1-5 mm) cutaneous mechanoriceptors, located in the subcutaneous tissue.

Nociceptors (Type IV) are cutaneous receptors attached to a peripheral nerve.[59] They are located all over the body, both in the superficial and deep tissues. Two types are commonly

classified: mechanical and polymodal nociceptors (Table 4). Mechanical nociceptors (A δ, high-threshold) are activated by strong mechanical pressure or temperature. Polymodal nociceptors (C fibers) are activated by variety stimuli such as heat, mechanical pressure, and chemicals released by tissue damage.[60] Pain perception is affected by cognitive processes such as emotion, depression, past experience, cultural background, or motivation.

Ruffini endings (type II) are low-threshold and slow adapting articular mechanoreceptors located in skin, joint capsule and ligament.[33] These are sensitive to joint position and changes in position. An increased activity of Ruffini endings are believed to be the most responsible for AMI when artificial effusion is induced.[30,31] GTOs (type III) are slow adapting muscular mechanoreceptors located in musculotendinous junction. These are activated by tendon stretch (tension) resulting from muscle contraction. Increased stimulation from GTOs inhibits α-motor neurons, resulting in a relaxation of muscles that is being stretched—this is autogenic inhibition. Muscle spindles are muscle mechanoreceptors (slow adapting) located in the intrafusal fibers. Intrafusal muscles fibers are innervated by the gamma-motor neurons, while extrafusal muscle fibers are served by alpha-motor neurons (Table 3).[58] A decrease in muscle spindle activity from a reduction in γ MN activity following joint injury decreases proprioceptive acuity.[25]

Table 3. Classification of efferent fibers[59]

Type	Size (μm)	Conduction velocity (m/s)	Associated with
A α	12-20	70-120	Skeletal muscle efferent (extrafusal)
A γ	2-10	10-50	Muscle spindle efferent (intrafusal)
A β	8-12	30-50	Muscle and muscle spindle efferent

Afferent sensory fibers are classified in the Table 4. Numeric system from I (large) to IV (small) classified by their size.[61] Conduction velocity is based on the speed of each fiber transmit information. Both size and myelination influence conduction velocity.

Table 4. Classification of afferent fibers[37,56,57,59]

Type	Group	Subgroup	Size (μm)	Fiber characteristics	Conduction velocity (m/s)	Associated with
A α	I	Ia	12-20	Large, myelinated	70-120	Muscle velocity and length change, muscle shortening of rapid speed
		Ib	11-19		66-114	
	II	Muscle	6-12	Large, myelinated	36-70	Muscle length information from touch and pacinian corpuscles
A β	II	Skin	8-13	Large, myelinated	30-70	Mechanical stimuli (touch and vibration)
A δ	III	Muscle	1-5	Small, thinly myelinated	12-30	Temperature, fast pain (sharp & localized, quick stabbing), mechanical stimuli
	III	Skin			6-36	
C	IV	Muscle	0.3-1.0	Small, unmyelinated	0.5-2	Temperature, slow pain (duller & diffuse, dull throbbing), heat, cold, mechanical stimuli
	IV	Skin				

Afferent pathway: primary, secondary, and tertiary afferents

Location of sensory neuron synapses are presented in the Table 5. Primary, secondary, and tertiary afferents are also known as the first, second, and third order neuron, respectively. Primary afferent fibers from the peripheral sensory receptors go into the spinal cord through the dorsal side.[58] The sensory input at the spinal cord synapse with interneurons that give out as the secondary sensory neurons (afferents). Synaptic locations between primary and secondary afferents are dependent on the type of receptors.[56] Secondary afferents cross the midline of the body, so the afferent input is processed on the opposite side of the brain. Afferent input at the dorsal columns may trigger an automatic descending (ventral column) branch without input from the brain (e.g. withdrawal reflex or tendon reflex).

The secondary afferent neurons are in the dorsal column of the spinal cord and terminate in the thalamus.[56] The thalamus processes the sensory input and carries it to a higher brain

center.[58] The thalamus is an relay centre that receives sensory input from the spinal cord, eyes, ears and motor output from the cerebral cortex and cerebellum.[56]

Tertiary afferents from the synapse onto the thalamus project to the somatosensory region of the cerebral cortex, the integrating and decision-making center. The cortex interacts with the cerebellum and brain stem, and initiates motor commands. The cerebellum regulates voluntary motor action, balance, and coordination of movement. After the sensory information is integrated in the cortex, it is also passed to the limbic system. The cortex receives feedback from the limbic system and creates emotional attentiveness.[56]

Table 5. Location of the sensory neuron synapses[56]

Type of sensory neuron	Stimulus	
	Fine touch, 130otoneurons130on, vibration	irritants, temperature, coarse touch
Termination of the primary afferents	Medulla (path across midline of the body)	Dorsal horn of spinal cord (path crosses midline of body)
Termination of the secondary afferents	Thalamus	Thalamus
Termination of the tertiary afferents	Cerebral cortex	Cerebral cortex

Pain theories

The specificity theory (Muller, 1826) is the first pain theory. This theory postulates that specific pain receptors in the periphery are stimulated and the pain signal goes up to the pain centre in the brain via the spinothalamic tract, resulting in pain.[62] Specific receptors are a physiological fact, but this theory has an assumption that there is a direct-line for pain signals between skin and the brain. However, this assumption does not explain how patients missing their limb feel phantom limb pain or how animals can be trained to respond favorably to noxious stimuli.[60] Additionally, this theory cannot explain why patients differently respond to the same source of pain.

Pattern theory (Goldschneider, 1920) was proposed as a reaction aginst the specific theory; it assumes that there is no specific system for pain perception. Pattern theory suggests that patients feel pain when the magnitude and pattern of sensory input exceeds a threshold.[62] All receptors are alike and shared with other senses such as touch and pressure. When intense stimulation on certain patterns exceed threshold of the nonspecific receptors, action potential carrying pain signal goes up to the brain, causing pain sensation.[62] However, this theory ignored that the physiological evidence for the high degree nerve specialisation.[62]

Gate control theory (Melzack, 1965[62]) was developed by integration of specific and pattern theory.[60] When the pain receptors are activated, either large A δ (sharp and localized pain) and/or small C fibers (dull and diffused pain) takes the pain signal to the spinal cord (Table 3). At the spinal cord, A δ and/or C fibers synapses with transmission (T) cell which is the gate. The T cell determines which signal of sensation passes the gate and continues to travel up. The substantia gelatinosa in an interneuron located in the laminae II and III. Small fiber stimulation inhibits substantia gelatinosa which keeps the gates open. On the contrast, large fiber (A β) stimulation (i.e: rubbing the skin) excites the substantia gelatinosa which inhibits the T cell (closing the gate).

Central biasing theory, also known as Central control trigger theory or Lerant behavior, is a modification of the gate control theory.[62] It addresses how the brain affects afferent and efferent information.[63] Impulses from the thalamus and brain stem are delivered to the dorsal horn of the spinal cord. This impulse blocks transmission of pain signal at the dorsal horn synapse.[57] Through this blocking system, previous experience, emotional influences, sensory perception, and other factors could affect pain perception. Central biasing theory may be related to placebo effects.[64] Compared to no treatment condition, therapeutic ultrasound with intensity

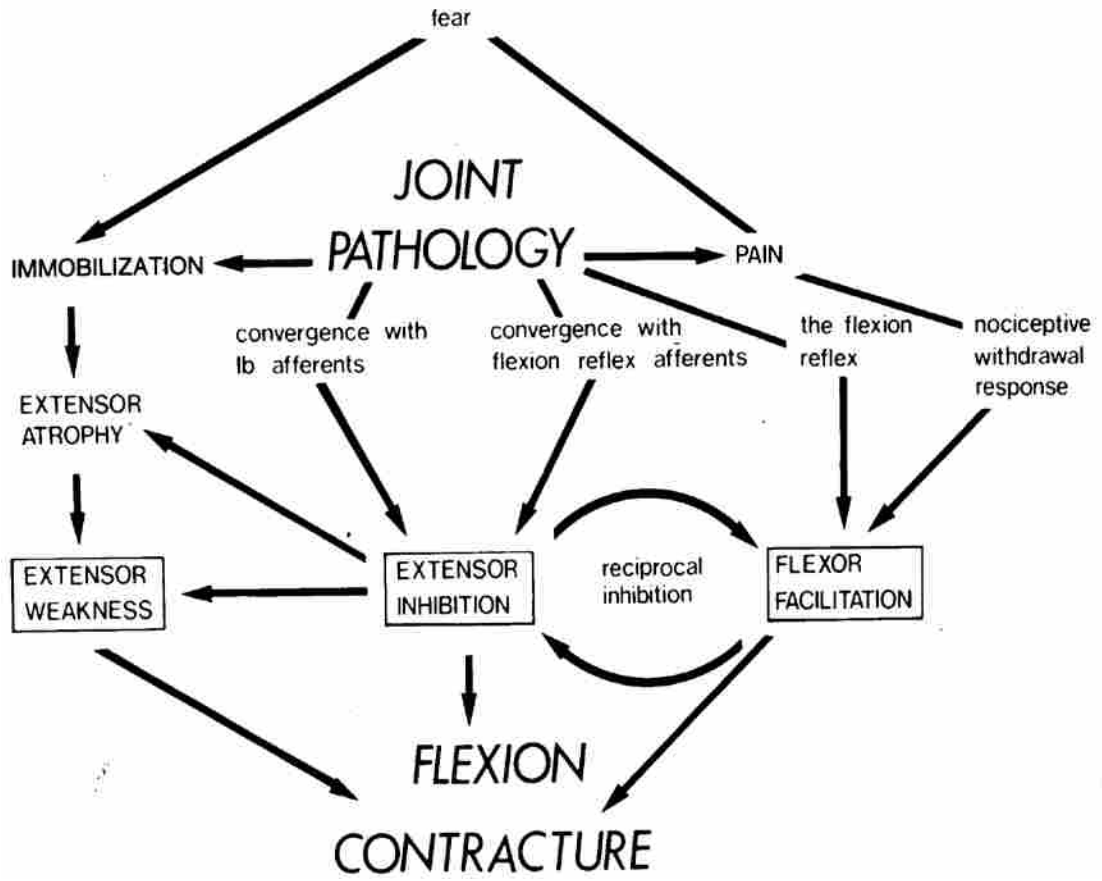
at zero resulted in a reduction in swelling and C-reactive protein in the patients with bilateral surgical extraction of the third molars.[64]

Body naturally produces endogenous painkillers such as β-endorphins, enkephalins, and dynorphins (Castel, 1979[65]). Descending endogenous opioid initiated from in the midbrain (periaqueductoal grey: PAG) and medulla (raphe nucleus) synapses with enkephalin interneurons. This results enkephalin into the dorsal horn, inhibiting the synaptic transmission of impulses to the secondary afferents neurons (Table 4).[57] Prolonged aerobic exercise results in β endorphin and enkephalin release.[66-68] β endorphin can produce a strong desire in the runner to keep running with pain until the "high" is achieved.[63]

Mechanism of AMI: why are extension muscles inhibited?

Abnormal afferent sensory input from the injured joint is thought to be a major cause of AMI.[11] Suggested sources of this abnormal afferent information include (1) deafferentation from structural damage caused by the primary and/or secondary injury, (2) an increased amount of certain sensory input (e.g. nociceptors), or (3) sensitization of the joint receptors.[69] When these abnormal afferent sensory input arrives at the CNS, several different pathways may result in a reduction of efferent drive to the extensor musculature (Figure 1).[24]

Figure 1. A network of extensor and flexor muscle response after joint injuries[24]



Due to injury, the knee joint is typically immobilized in the extended position. The atrophy is easily localized in the knee extensors (quadriceps) because knee joint is typically immobilized with an extended position. This atrophy results in quadriceps weakness, which may possibly lead to further atrophy. Additionally, it has been shown greater intra-articualr pressure is in the knee extended position[53,70] which is thought to cause more inhibition.[71] Convergence of Ib and joint afferents pathways may converge into the interneuron of spinal cord, resulting in extensor inhibition.[72] Painful stimuli may produce a withdrawal response,[73] resulting in flexor facilitation. Additionally, reciprocal inhibition from knee flexion facilitation may take a role to inhibit extensors.

Central mechanism may take part in AMI. Bilateral quadriceps inhibition has been reported in subjects with unilateral AKP[8] and partial menisectomy.[22] Afferent sensory input from the involved knee joint alters the γ-system in the spinal cord resulting in inhibition on both sides.[25] Reflex neurogenic inflammation—crossover effect of a unilateral inflammation to the contralateral limb—may also be responsible for AMI. Joint injury may cause mechanical alterations (e.g. joint moment & angle, and joint stiffness) in the involved limb. This changes a patient's neuromuscular control and gait pattern which may also affect muscle activation on the contralateral side.

Types of inhibition

Arrivals of excitatory stimuli always occur in the CNS. In order to avoid unnecessary motor effects, these excitatory stimuli need to be offset by inhibited stimuli. Presynaptic and postsynaptic inhibitions are responsible for controlling an inflow of excitation.[58] Both pre- and postsynaptic inhibition is likely to participate in AMI. Pathological conditions may affect balance between excitatory and inhibitory stimuli. Inhibitory stimuli become overwhelming, resulting in a reduction of motor output.

Presynaptic inhibition occurs when activity of inhibitory (or modulatory) neurons in the presynaptic axonal membrane decreases or blocks neurotransmitter release.[56] This inhibitory mechanism is selective on specific type of neurons while postsynaptic inhibition affects the whole membrane. GABA (γ-aminobutyric acid inhibitory interneurons) are located in the brain.[56] Glycine is considered a major inhibitory neurotransmitter in the spinal cord.[56] They are responsible for the presynaptic inhibition.[74]

Postsynaptic inhibition occurs when the net effect of action potentials are a negative (hyperpolarisation)[15] so action potential is not initiated.[56] When the excitatory stimuli reach the threshold, the postsynaptic membrane generates action potential. When the inhibitory potential is stimulated, a hyperpolarisation of the synaptic potential occurs. It moves the membrane potential farther away from the threshold. Thus, the generation of action potential from the membrane is less likely.[58]

Reciprocal inhibition is the relationships of the agonist (a muscle being contracted) and the antagonist (a muscle being stretched) activities. Proprioceptive neuromuscular facilitation (PNF) stretching technique, especially slow reversal-hold-relax, has been suggested to elicit reciprocal inhibition of the antagonist by contraction of the agonist.[57] Tendon reflex test results in a quick knee extension movement. A single stimulus of the tap to the patellar tendon activates muscle spindles (Ia interneurons). In the spinal cord, some afferent input synapses with motor neurons innervating the quadriceps while the other synapse on inhibitory interneurons innervating the hamstring.[56]

Interneurons

Interneurons are located in the brain and spinal cord containing α- and γ-motoneurons. An interneuron has many dendrites receiving information from afferent input through the dorsal horn, efferent input from supraspinal center, and other neurons in the CNS; many axon terminals project to other neurons in the CNS.[15,58] Interneurons may take an important role in inhibitory process.

Renshaw cells are closely located to α-motoneurons in the ventral horns. An excitation of α-motoneurons activate Renshaw cells which inhibit α-motoneurons (negative feedback).[58] This is called recurrent inhibition. Descending information from supraspinal centre controls excitation or inhibition of Renshaw cells which affects the activity of α-motoneurons. Renshaw cells may inhibit γ-motoneurons which affects muscle spindle activity.[58]

When the agonist muscle is stretched, muscle spindles excite the Ia-interneurons. Then, the Ia-interneurons inhibit α-motoneurons of the antagonist muscles (reciprocal inhibition).[15] Renshaw cells, excited by α-motoneurons from the agonist muscle, may inhibit the Ia-interneurons. This results in a reduction of inhibitory effects on antagonist (disinhibition).[58] The Ia-interneurons also receive information from descending inputs such as corticospinal, rubrospinal, and vestibulospinal tracts.[75]

Excitation of the Ib-interneurons, activated by Golgi tendon organs of the agonist muscles, inhibit agonist and excite antagonist.[15] Ib-interneurons receive information from afferents (joint receptors, mechanoreceptors, Golgi tendon organs) and descending signals originated from supraspinal center (other neurons in the CNS). Change in the net effect of the Ib interneurons has been thought to cause quadriceps inhibition and soleus facilitation under condition of artificial knee joint effusion.[20,29]

γ-motoneurons innervate intrafusal fibers within the muscle spindle.[56] They govern the stretch sensitivity of the muscle spindle so they are active when muscle is relaxed. When muscle contract, α-γ co-activation maintains spindle function.[56] A reduction of γ-motoneuron activity may affect muscle spindle sensitivity, consequently resulting in a decrease in proprioceptive function[76,77] and motor output.[25]

Does pain directly cause AMI?

Pain has been reported as a cause of quadriceps inhibition in the patients with experimentally induced AKP[28,78,79], clinical AKP[8,27,43], or post-operative knee pain[80] (Table 1). Experimentally induced knee pain caused a decrease in both voluntary[79] (isometric and isokinetic contractions) and involuntary[78] (H:M ratio) quadriceps activation. Pain relief by injecting 0.5% bupivicaine in the patients with knee OA resulted in an increase of quadriceps activation.[81] Additionally, a decrease in post-operative pain level by injection of epidural analgesia with local anesthetics resulted in an immediate increase in quadriceps activation.[80] Contrarily, NSAIDs[8] or knee arthroscopy[43] reduced AKP but did not change quadriceps activation. Patients in clinical pain may be involved in other pathological conditions (e.g. structural damage, effusion, or inflammation). Thus, factors other than pain may be accounting for quadriceps inhibition. The results from these studies suggest that AKP may have an association with quadriceps inhibition but other factors, alone or combined with pain, may be likely to contribute.

Patients with unilateral clinical AKP have shown that the contralateral limb had quadriceps inhibition.[8,43] Neuromechanical alterations from the involved limb may change the functional kinetic chain, which could affect the muscle activation on the non-involved limb.[8] An alteration in neural activity of the involved limb may cause a transfer of inhibitory mechanism to the non-involved limb. This neural cross-over effect has been called reflex neurogenic inflammation.[82] Since unilateral AKP affects both ipsilateral and contralateral quadriceps activation, the values of the quadriceps activation on the non-involved side cannot be a normal control.[8,43]

The neurophysiological mechanisms of how the sensory input (joint pain) affect the motor response (muscle activation) is not fully understood. The nociceptive-motor interaction may occur anywhere throughout the CNS and PNS.[79] When the abnormal sensory input resulting from a joint injury reaches the dorsal horn of the spinal cord, the motor unit recruitment pattern may be altered. The interactions may occur in the supraspinal level. The thalamus is a relay center receiving and sending the sensory and motor information.[56] Since the limbic system is associated with the thalamus, hypothalamus, and cortex, pain information coming up to this level affects emotional and affective behavior resulting in motor response alterations. The cerebral cortex regulates pain perception and voluntary movement[56] thus the pain fibers may change the efferent outcomes.

Do alterations in motor response (AMI) due to stimulation of nociceptors occur under patients' voluntary intention? Depending on the severity of nociception, patients may decide to avoid bearing their weight or contracting the surrounding muscles at the injured joint. This intentional avoidance in joint movement would remain as long as the nociceptor stimulation is present. This voluntary inhibition may accelerate AMI progression along with other factors such as swelling, structural damages, or inflammation. Despites patients' willingness, however, the CNS (spinal and/or supraspinal) may automatically reset the motor output in the adjacent musculature of the injured joint. This includes adjustments on the capacity of recruitment on the active motor units or excitation of inhibitory interneurons (i.e. increasing recruitment threshold). It is speculated that both mechanisms may be responsible for AMI. Quadriceps inhibition estimated by the H:M ratio was observed both during at voluntary and involuntary contraction.[30] This suggests that during voluntary and involuntary contraction may take the same inhibitory pathways.[30] Voluntary inhibition may have a larger role to contribute AMI in the acute stage of a

traumatic joint injury. Involuntary inhibition may be more difficult to reverse if the AMI remains throughout the rehabilitation process.

Pain models

Since subjectivity, magnitude, onset, and duration of pain confound the results, researchers experimentally induced pain by injection of hypertonic saline into the muscle[83-85] or infrapatellar fat pad[28,32,78,79,86-89] (Table 6). This pain model allows us to examine the neuromechanical changes under the condition of isolated pain. Subjects described pain induced by 5% hypertonic saline as aching (50%), annoying (44%), throbbing (38%), and nagging (38%), and dull (32%).[32] The infrapatellar fad pad is a sensitive structure and a potential nociceptor source for AKP.[87,90] Perceived pain level was average of 4.9 on the 11 point numerical rating scale. Injection of hypertonic saline is thought to cause chemical irritation on nociceptors within the fat pad. Mechanical pain was less likely because injection of isotonic saline (0.9%) caused minimal to no pain lasting up to 90s.[32] This pain model does not closely mimic clinical pain but it allows examination of the isolated effects and consequences on motor function parameters.[87]

Table 6. Summary of studies using pain model

Author (year)	Injection type (rate)	Injection site (saline concentration)	Main findings and significances
Bennell (2004)[32]	Single injection (0.2–0.25 ml)	Medial infrapatellar fat pad (5%)	Subjects felt pain 3 min after injection and pain free by 15 min. Average pain level: 5.8 in 11 point NRS
Bennell (2005)[87]			Pain did not change JPS. Average pain level: 4.9 in 11 point NRS.
Bennell (2005)[86]			Pain did not change balance. Average pain level: 6.2 in 1 point NRS.
Farina (2004)[83]	0.2, 0.5, and 0.9 ml separated by 140 s.	Tibialis anterior (5.8%)	Pain decreased motor unit firing rate (EMG). Motor unit firing rate was negatively correlated with the pain intensity (VAS).
Farina (2005)[84]	Infused (0.5 ml in 40 s.		Induced pain decreased motor unit discharge rate (EMG) during contractions.
Farina (2005)[85]	Infused (0.2, 0.5, and 0.9 ml)		Induced pain decreased voluntary EMG activity during contractions.
Hodges (2009)[28]	Single injection (0.25 ml)	Medial infrapatellar fat pad (5%)	The onset activation of VM was delayed relative to that of the VL during ascending. VL EMG amplitude was

			decreased from the no pain condition.
Long (2009)[78]	Intermittent (0.54 ml / min)	Lateral infrapatellar fat pad (5%)	Induced pain caused a decrease in the VM H:M ratio and cryotherapy reverse VM inhibition.
Tucker (2009)[89]	Single injection (0.25 ml)	Medial infrapatellar fat pad (5%)	Quadriceps 140otoneurons discharge rate was decreased while the force was maintained with experimental knee pain.
Henriksen (2010)[88]	Single injection (0.75 ml)	Medial infrapatellar fat pad (5.8%)	Experimental knee pain reduced the peak knee moments in the frontal and sagittal plane.
Henriksen (2010)[79]	Single injection (1.0 ml)		Pain decreased knee extension/flexion strength (isokinetic) than control condition.

NRS: Numeric Rating Scale

AMI with joint effusion

Effusion is a common symptom of patients with knee joint injuries. Although the relationship between AMI and joint effusion, relative to pain, has been well established, there are not many studies objectively conducted. Clinically, AMI associated with knee joint effusion has been presented in patients with traumatic injury[91], meniscectomy,[31] and degenerative joint damage[92] as well as both acute[31,48] and chronic[45] pain-free joint effusions.

Aspiration of chronic knee joint effusion resulted in an increase in quadriceps strength.[45] This may partly explain why voluntary contraction alone may not be beneficial. In the same study, EMG activity also increased. This supports the idea that AMI is mediated by neurogenic rather than mechanical effects. Another study examined the effects of aspiration of the chronic joint effusion did not find changes in quadriceps activation.[93] This study also suggested that amount of the effusion was not related to the inhibition.

Effusion models

Numerous studies used artificial effusion in the knee joint capsule (Table 7). This inhibition occurred in the absence of pain[13,19,94] thus this is an effective model to examine the isolated effects of joint pressure. Isotonic saline (0.9 %) is injected into the area superomedial[20]

or superolateral[13,19,29,95] to the patellar (Table 7). Small (<55ml)[13,19,20,31,94] or large volume (>55ml)[13,19,29,71,95,96] of saline infusion have been used. Both small and large volumes have been shown to produce mechanical inhibition of the quadriceps (Table 7). Higher volume (< 80ml) may stimulate nociceptors.[19] The minimal amount of volume injected into the knee joint to induce quadriceps inhibition has been suggested as 20-30 ml for the VM and 50-60 ml for the VL.[30] Additionally, knee joint effusion produced a greater inhibition in the VM than the VL and RF. For these reasons, the VM seems to be most sensitive muscle in the quadriceps and a good candidate for AMI studies.

Intra-articular pressure within the knee joint increased as the knee joint is in extended or flexed position and decreased in the mid range during passive movement.[70] Another study[53] showed that intra-articular pressure peaked in the mid-range (90-110° flexion) during active contraction. The volume of effusion is positively related to the intra-articular pressure[30,31,53] and amount of inhibition.[13,31] Increased activity of slow adapting Ruffini endings, resulting in stimulating of the Ib inhibitory interneurons seems to contribute to muscular inhibition.[29-31,94,97] Even a small volume (30 ml) of effusion causes inhibition.[24] Small volumes of effusion are not considered as a big limitation to rehabilitation process, thus it is often untreated. However, disinhibition should be addressed with effusion even in small amounts.[24]

As a result of mechanical distension in the knee joint, quadriceps inhibition[20,30,31,97] and soleus facilitation[94] has been observed in many studies. Using this knee effusion model, researchers have further reported quadriceps inhibition with soleus facilitation[20] or hamstring facilitation.[20] Quadriceps inhibition with hamstring facilitation has also been observed in the functional movements such as walking[19] and drop landing.[13] These alterations may be a compensatory process to maintain proper lower extremity kinetic chain.[20] Similar compensatory

patterns have also been observed in animal studies.[98] The net effect of Ib interneurons may mask the quadriceps projection to the soleus and hamstring, resulting in soleus and hamstring facilitation. It would be interesting to see how pain, effusion, or a combination of these two stimuli would change the measurements of voluntary contractions (MVIC or CAR).

The soleus facilitation with the quadriceps inhibition was observed in the supine position.[20] During walking, however, a reduction in soleus activity in the involved leg has been reported in the patients with acute ACL rupture.[39] Additionally, peak internal plantar flexion moment was reduced in the early stance phase in subjects with artificial AKP.[99] Tricep suare activation is thought to be associated with the internal plantar flexion moment. Facilitation of triceps suare against quadriceps inhibition may present only in the static position.

A unilateral knee joint effusion (60ml) caused ipsilateral inhibition but not contralateral quadriceps (VM) inhibition.[95,100] This data suggest that bilateral quadriceps inhibition, resulting from unilateral joint injury, may not be from pain-free knee joint effusion or isolated stimulation of slow adapting Ruffini endings.[95] Stimulation of nociceptors[8,43] or deafferentation from tonic descending inhibition[69] from the inflammation in the injured joint may have be responsible to initiate the contralateral AMI.

Table 7. Summary of studies using effusion model

Author (year)	Injection site (volume)	Main findings and significances
de Andrade (1965)[101]	Superolateral (800mm pressure)	Gradual distension of the knee joint resulted in quadriceps weakness. Reflex inhibition may lead to the muscle weakness.
Jones (1987)[93]	Aspiration	Knee aspiration in the patients with chronic effusion did not change quadriceps activation (ITT).
Kennedy (1982)	Lateral joint space (60 ml)	Effusion caused quadriceps inhibition (H-reflex). Lidocaine (10 ml) injection prior to the saline (50 ml) injection did not change quadriceps activation.
Spencer (1984)[31]	Intra-articular space (60 ml)	Effusion reduced the H-reflex in the VM, VL, and RF. A positive relationship between the volume of effusion and (1) intra-articular pressure and (2) the H-

		reflex amplitude.
Wood (1988)[70]	Anterolateral (up to 20 ml)	Intra-articular joint pressure increased as the limb was extension and flexion position. Minimal pressure occurred in the mid-range. Effusion decreased voluntary contraction (isometric and isokinetic).
Iles (1990)[30]	Lateral knee joint (100 ml)	Increased pressure gradually decreased the RF (H:M ratio), both at rest and during contraction.
Jensen (1993)[53]	Superolateral (60 ml)	Quad strength (isokinetic) decreased as the amount of effusion increased (20 ml increments), and then increased after aspiration.
Hopkins (2000)[94]	Superolateral (25 ml)	After joint effusion, the soleus was facilitated (H-reflex) at post injection-3 and -4h compared to the baseline.
Torry (2000)[19]	Superolateral (up to 80ml)	Knee effusion resulted in quadriceps inhibition, and hamstring facilitation (EMG) during gait. It also resulted in an increase in hip and knee flexion, a decrease in knee extensor torque,
Hopkins (2001)[20]	Superolateral (30 ml)	After joint effusion, the soleus was facilitated while the quadriceps was inhibited at all measurement intervals (post-30, -90, -150, and -210 min).
Hopkins (2001)[29]	Superolateral (60 ml)	Induced knee joint effusion resulted in quadriceps (VM) inhibition (H-reflex). Cryotherapy and TENS had disinhibitory effects.
Palmieri (2003)[95]	Superolateral (60 ml)	Joint effusion resulted on the ipsilateral quadriceps (VM) inhibition (H:M ratio) but not on the contralateral side.
Hopkins (2006)[96]	Inferomedial (55 ml)	Effusion resulted in a decrease in peak torque, peak power, and peak VL activity (EMG) compared to the control or effusion/cryotherapy group. Cryotherapy after effusion increased in knee joint reaction force.
Palmieri-Smith (2007)[13]	Superolateral (30 & 60 ml)	Effusion resulted in the quadriceps inhibition with hamstring facilitation, an increase in GRF, and a decrease in peak knee flexion angle during a single leg drop landing
*Rice (2009)[102]	Superomedial (until 50 mm Hg)	Effusion decreased the quadriceps MVIC, muscle fiber conduction velocity, and EMG signals. Cryotherapy increased the quadriceps MVIC compared with controls.

* Dextrose saline (4% dextrose and 0.19 NaCl) was injected

Limitations on the pain and effusion model

The pain and effusion model nullifies other confounding factors and allows us to examine how the isolation of specific stimuli affects motor patterns. Although pain and effusion are known to trigger reflex inhibition leading to AMI, each model still has limitations to make inferences to a clinical population. Induced pain by 5% hypertonic injection may have different quality than clinical pain. Additionally, the body's natural circulatory system absorbs the saline solution during testing.[19] Therefore, intra-articular pressure may diminish at the time of measurements. Different capsule (body) size may have various pressure effect within the

capsule[96], resulting in various response levels. An injury model that combines pain and effusion stimuli would more closely reproduce an acute condition of joint injuries.

Acceptable disinhibitory interventions

Cryotherapy: The use of cryotherapy has been shown an effective disinhibitory intervention in the patients with tibiofemoral knee OA[103] and artificial knee joint effusion.[29,96,102] Cryotherapy has also been reported to increase quadriceps activation in healthy subjects.[104] This disinhibitory effect has been observed in both voluntary (MVIC[102]; CAR[103,104]; EMG[96]) and involuntary (H-reflex)[29] measurements. The effects of increased muscle activation by cryotherapy seem to last up to 45 minutes. Most studies[29,96,103,104] used two crushed ice bags (1.5L) placed on the anterior and posterior.[29,103,104] A study used three crushed ice bags.[102]

Joint cooling may reduce nerve conduction velocity and slow the discharge rate from the joint mechanoreceptors. This would result in less afferent input to the spinal cord causing disinhibition.[29] Joint cooling also stimulates the cutaneous mechanoreceptors which excites Ia interneurons, resulting in excitatory potential at the motoneuron pool.[29] Activation of thermoreceptors may produce a decrease in the recruitment threshold of the active motorneurons, thus the inhibited motorneuons may become recruitable. Increased number of active motor units has been suggested as the primary contributor with an increase in motor unit firing frequency as secondary to increases in CAR.[104]

Electrotherapy: The use of electrotherapy (TENS[29,103] and NMES[105-109]) has been reported to increase quadriceps activation in patients with tibiofemoral knee OA,[103,110] ACL reconstruction,[105,106] TKA,[107-109] and artificial knee joint effusion.[29] This disinhibitory effect has

been observed in both voluntary (CAR[103,105,107] and isometric contraction[106]) and involuntary (H-reflex)[29] measurements. A single session of TENS treatment immediately increased quadriceps activation.[29,103] Multiple sessions of NMES treatments alone have been shown as a superior intervention over voluntary contraction of the quadriceps alone.[105-107] On the contrast, NMES did not have any treatment effects in female patients with knee OA (mild to moderate).[110] However, the female patients in this study had more than 87% activation prior to receiving the intervention, thus NMES was unable to produce a treatment effect.[110] [29,103] Compared to electrotherapy, cryotherapy may have a similar effect[103] or be more beneficial.[29]

Possible explanations for the disinhibitory effects of electrotherapy include: TENS may inhibit the activity of the Ib inhibitory interneuron or excitate the Ia excitatory interneuron, or decrease the descending inhibitory fibers connecting to the Ib interneuron. Any of these would result in an increase of MNP excitability.[29] The order of motor unit recruitment and synchrony for NMES is opposite of voluntary exercise—initially activating type II muscle fiber, then type I. Patients with ACL reconstruction may have selective atrophy in type II muscle fibers, thus NMES may be effective in recruiting inhibited type II fibers and reverse AMI.[105,106] A positive relationship between NMES dosage and quadriceps strength has been suggested.[107]

Transcranial magnetic stimulation (TMS): Direct electrical stimulation of the motor cortex region results in excitation of descending corticospinal tracts.[111] This efferent projects into the corresponding motoneurons within the target muscles.[111] TMS has been manually delivered (60%[112] to 90%[74] of maximal stimulator output) to the motor cortex while the subjects produce voluntary contraction (50%[74] or 100%[112] of MVIC). TMS increased voluntary activation in healthy subjects[113,114] and patients with TKA.[112] TMS did not change quadriceps activation (CAR) compared to no treatment condition in patients with partial meniscectomy.[74] In

the same study, however, strong effect sizes were found at 10 and 60 minute post-treatment in the TMS group compared to the control group. Excitation of neural drive by TMS is thought to increase number of active motoneurons, reducing pre-synaptic inhibition.[115]

Manual therapy: Sacroiliac (SI) joint manipulation, high-velocity low-amplitude thrust, has been shown to increase quadriceps strength (MVIC[27,116]) and activation (CAR[116] and ITT[26,27]) in AKP patients[26,27] and healthy subjects.[116] Lumbar manipulation has also shown to reduce triceps surae (soleus[117] and gastrocnemius[118,119]) activation (H-reflex) in healthy subjects. Soleus facilitation has been reported in artificial knee joint effusion[94] and considered as a compensatory strategy following quadriceps inhibition.[20] Hence, spinal manipulation may be an effective treatment to reverse the compensatory motor pattern that has been employed following joint injury. However, this treatment effect does not last longer than a few minutes after spinal manipulation.[116,118]

SI joint manipulation increased quadriceps strength (MVIC) while tibiofemoral joint manipulation did not change in individuals with patellofemoral pain syndrome.[120] If this is the case, knee joint (tibiofemoral) manipulation may not be beneficial. Since cryotherapy causes changes in peripheral neural drive from the injured joint and have been shown to increase quadriceps activation,[29,103,104] future studies should attempt lumbopelvic cooling to see how excitation of the thermoreceptors at the spinal level (L2 through S2: femoral and tibial nerves) assists disinhibition.

Little is known regarding the physiological mechanisms of spinal manipulation on the motor system. A change in afferent input by high-velocity, low-amplitude thrust may stimulate efferent pathways to the target muscles.[26] Joint manipulation is considered to influence the CNS

at the segmental level by stimulating receptors (mechanoriceptos, proprioceotors and free nerve endings) in and around the manipulated joint.[117,121] The SI joint (L2-S3), quadriceps (L2-L4), and knee joint (L2-S2) share similar nerve roots. Changes in afferent input from these spinal segments may affect efferent signals of the same nerve root.[116]

Thermotherapy: A 30 minute application of moist heat pack around the ankle joint did not change the H:M ratio and peak plantar flexion torque of the soleus.[122] Superficially, there are less thermoreceptors responding to heat than cold. Thus, there may be less quantity of thermal receptors stimulated with heat, resulting in no change in spinal or supraspinal MNP. Another study[123] showed that there was a 19% decrease in MNP excitability with using a heat blanket. The different result may be from the size of the surface area covered by the heat modality. Applying heat modality to a bigger area would stimulate more thermoreceptors. This increase in the quantity of stimulated receptors may disinhibit or excite the motoneuon pool.

Voluntary exercise: Many studies[12,18,54,105,106] suggested that performance of voluntary exercises alone may not be beneficial to improve quadriceps strength in patients with knee joint injuries. Multiple sessions (3 times/week for 4 weeks) of isometric quadriceps contraction was not as effective as high intensity NMES in increasing quadriceps activation (CAR) in patients with ACL reconstructions.[105] NMES produced higher thigh strength (knee extension and flexion torque in MVIC) than did voluntary exercise.[106]

Any potential source that disrupts normal afferent input (such as joint pain, effusion, inflammatory response, or structural tissue damage) should be removed prior to performing voluntary muscle training.[45,124] Without addressing neural inhibition, inhibited muscles associated with AMI (e.g. quadriceps) may employ new motor recruitment patterns based on the

modified pool of active motoneurons.[124] This may cause other musculature (i.e. hamstring or quadriceps in the contralateral limb) to adjust their activity in order to compensate for quadriceps inhibition. Therefore, modified muscle activation patterns during traditional voluntary exercises may lead to future injuries or chronic joint degeneration.

However, voluntary exercises in conjunction with other disinhibitory modalities may be successful in reversing AMI.[107] Cryokinetics[125,126] is well known for enhancing the rehabilitation process by allowing early active movement with less pain and restoration of normal ROM.[60] Initially, the benefits of cryokinetics were discussed based on cold-induced vasodilation.[127,128] However, active movement caused an increase in blood flow to a greater degree than cold or heat application alone.[129] Facilitating pain-free, early active exercises by numbing the injured area has been considered as the primary benefit.[60] However, disinhibitory effect on the motoneurons pools,[29,104,130] that were inhibited by join injury, may play a larger role than does the analgesic effect.

Neuromechanical alterations resulting from knee joint injuries

Many studies have reported the kinetic and kinematic changes during walking in subjects with knee OA,[131-141] AKP,[142-144] meniscectomy, [49] ACL deficiency,[145,146] ACL rupture,[39] artificial knee pain,[88,147] muscle pain,[148] and knee effusion[13] (Table 8).

Table 8. Summary of studies assessing kinetic and kinematic changes during walking

Author (year)	Injury	Main findings and significances
Brinkmann (1985)[139]	Arthritic (TKA)	TKA improved knee flexion and extension ROM during walking in the patients with rheumatoid or osteoarthritis.
Berchuck (1990)[146]	ACL deficiency	ACL deficient patients had less external knee flexion moment in the involved and non-involved limb, when compared to the control subjects.
Messier (1992)[50]	Knee OA	Knee OA group had (1) less knee ROM, (2) increased loading rate in the non-involved leg, and (3) less stride length, and (4) less quad strength than control.
Nadeau	AKP	AKP patients had a reduction in knee flexion angle during stance phase. No

(1997)[142]		difference was found in joint moments relative to control subjects.
Powers (1999)[143]	AKP	AKP patients had a less knee flexion, stride length, and average peak loading rate than the control subjects.
Hurwitz (2000)[137]	Medial knee OA (K/L grade)	The change in pain level has been negatively related to the change in the knee adduction moment (external) during walking.
Torry (2000)[19]	Induced knee effusion	Knee effusion resulted in increase in hip and knee flexion. Knee extensor and impulse were decreased with increased knee effusion.
Kaufman (2001)[135]	Knee OA	Knee OA patients had a less internal knee extensor moment than normal subjects.
Baliunas (2002)[132]	Medial knee OA (K/L grade)	Subjects with OA had (1) less knee minimal flexion angle and (2) greater knee adduction moments (external).
Hurwitz (2002)[136]	Knee OA	Knee OA patients had greater knee adduction moment (external). Mechanical axis of the leg was the best single predictor of the knee adduction moment.
Lewek (2004)[134]	Genu varum & medial knee OA	OA group had a greater knee instability, medial joint laxity, and knee adduction moments than the control group.
Shrader (2004)[149]	Medial knee OA	Pain relieving resulted in a increase in gait velocity, cadence, external knee/hip adduction moment, and ankle abduction moment.
Mundermann (2005)[131]	Medial knee OA (K/L grade)	Patients with OA made (1) more extended initial contact, (2) a faster increase of loading rate, and (3) greater knee adduction moments (external) than matched control subjects.
Henriksen (2006)[138]	Knee OA (WOMAC)	OA group had lower joint loads than the control group. Lidocaine injection decreased pain and increased joint loads in the OA group.
Henriksen (2006)[150]	Medial Knee OA	OA patients and control subjects did not differ in impulse forces and joint angles at heel strike. Pain relief resulted in more extended hip & knee joint.
Hurd (2007)[39]	Acute ACL rupture	Compared to the uninjured leg, the involved leg had less peak knee angles, higher co-contraction in quad/hamstring, and knee flexion moment.
Henriksen (2008)[148]	Induced quadriceps pain	Induced muscle pain did not change impact loading in either gender.
Zeni Jr. (2009)[141]	Medial knee OA (K/L grade)	OA patients had less knee and ankle joint moments, GRF, and knee reaction force relative to the control subjects. These changes possibly from slower walking speed.
Hunt (2006)[34]	Knee OA (K/L grade)	Knees with OA had greater knee adduction moments, frontal plane lever arm, and less frontal plane GRF relative to control subjects.
Henriksen (2010)[88]	Induced knee pain	Experimental knee pain reduced the peak knee moments in the frontal and sagittal plane. Knee angle was decreased in the early and late stance phase.
Hunt (2010)[140]	Medial knee OA (radiograph)	The relationship between quadriceps strength and loading rate become insignificant when controlling for other variables.
Lindstrom (2010)[145]	Chronic ACL deficiency	Walking speed, stride length, GRFA did not differ between ACL deficient patients and control.
Thorlund (2010)[49]	Meniscectomy	Meniscectomised leg had less peak vertical GRF and quadriceps muscle activity relative to the non-operated leg.
Seeley (2011)[147]	Induced knee pain	Induced pain resulted in a reduction of peak braking and lateral force, peak vertical GRF, and peak push off vertical GRF.
Seeley (2011)[99]	Induced knee pain	Induced pain reduced (1) the peak support moment, peak PF angle, and moment during late stance and (2) peak knee extension moment and hip abduction moment during early stance phase.

* Subjects in all studies had tibiofemoral OA

Ground reaction force

Induced knee pain in healthy subjects resulted in decreased peak braking GRF, peak horizontal and vertical GRF, and peak push-off vertical GRF.[147] Reduced peak braking GRF may be associated with a decrease in net internal knee extension moment,[88] possibly resulting from quadriceps inhibition. Vertical unloading GRF has also been shown to increase.[147] Subjects in this study[147] may have intentionally attempted to avoid bearing weight on the involved leg, resulting in an increase in vertical unloading GRF.

Many studies[49,141,147] have reported a reduction in peak vertical GRF of the involved limb with knee OA. Patients with AKP had less loading rate in the involved limb relative to the control subjects.[143] Patients with knee OA walked with an increased loading rate in the non-involved limb than the involved limb.[50] This may be from weakened vertical push off with the involved leg causing the non-involved leg to exert higher vertical GRF.

Knee joint moments

It has been suggested that external knee adduction moment is related to medial compartment joint loading,[151] tibial mineral bone content,[152] knee pain,[149] and progression of joint degeneration.[153] Patients with medial knee OA have shown a greater knee joint loading (external knee adduction moment) in the involved leg than control subjects.[34,131,132,134,136] This leads to greater load in the medial compartment which would accelerate degenerative changes on the medial side of the articular cartilage.[153] Contrarily, less knee joint loading (less internal knee extensor moment in patients with knee OA[135,138] and more external knee flexion moment in the patients with ACL deficient[146]) than control subjects has been reported. A reduction in knee adduction joint moment in patients with knee OA may be a compensatory mechanism to avoid

excessive joint loading of the knee joint[141] and/or pain.[154] Others reported that there is no difference in knee joint loading in the frontal[135] or sagittal planes[142] between patients with knee OA or AKP and normal subjects.[142]

Total support moment has been reported in patients with acute ACL rupture (non-copers)[39] and artificial knee pain.[99] During the weight acceptance phase of walking (initial contact to peak knee flexion), the contribution of the knee joint to the total support moment was less while the hip joint increased the moment in the ACL ruptured leg when compared to the non-injured leg .[39] During the mid-stance, the contribution from the ankle joint moment increased to compensate less joint moment from the hip and knee joint.[39] This suggests that ankle joint may be the primary stabilizer for the total support moment in the patients with knee joint injuries.

A study using the artificial pain model reported a reduction in the total support moment in the involved leg.[99] The relative contribution of each joint did not change throughout the stance phase. Experimentally induced AKP Patients' intentional unloading strategy may explain this. It would be interesting to observe how the contralateral leg changes its total support moment when the artificial knee pain and/or knee joint effusion is present.

Joint range of motion and angles

Lower extremity static joint range of motion (ROM), measured using the goniometer, in patients with knee OA were compared to those in matched control subjects.[50] No differences were found in the ankle and hip joint range of motion. However, patients with knee OA had less knee flexion and extension range of motion for both involved and non-involved legs than those

in the control group. Involved limb had less flexion and extension range of motion than non-involved leg in the OA patients. Interestingly, the non-involved leg of knee OA patients had less ROM than the control subjects. The non-involved leg may have adapted to the limited activity level of the involved limb. This adaptation seems to highly affect ROM of the knee joint.

In addition, AKP patients walked with less knee angle relative to control subjects.[142,143] Observations of the joint angles in the OA patients have not been consistent.[88,132,150] One study[132] reported no difference in the knee flexion angle (mid-stance) or the terminal extension knee angles between groups. Another study also reported no difference in ankle, knee, and hip angles at heel strike between groups.[150] Others[88] found that knee OA patients demonstrated more knee flexion at heel strike and during late stance phase than the control subjects. This reduced knee joint angle during the stance phase is thought to produce greater compressive forces in the knee joint.[145] Studies that observed the effects of pain relieving in OA patients found a reduction in knee flexion,[138,150] no difference in any joint angle (hip, knee, and ankle)[149], or a slight increased knee angle.[137] Rheumatoid and osteoarthritis patients increased flwx iona and extension ROM after TKA.[139]

Artificial knee pain resulted in an increase in knee angle (more flexed knee) in early stance phase and an increase in knee angle during late stance.[88] An artificial knee effusion study[19] also observed more flexed knee at initial contact and an increased hip flexion throughout the stance phase in the effused group compared to the control group. Additionally, hip flexion angle was positively related to the amount of effusion.[19]

Walking speed and stride length

Faster walking speeds affect joint moment, vertical GRF and loading rate measurements.[140,143,155] Slower walking speed have been observed in patients with AKP[143] and knee OA.[141] Decreasing pain by intra-articular injection has shown to increase walking speed in patients with knee OA.[149] Reduced vertical GRF and loading rate are correlated with slower walking speeds.[143] Slower walking speed reduces the demand of knee extension moment during initial contact.[156] Limited knee extension moment is associated with quadriceps inhibition.

Knee OA[50,132] and AKP[143] patients exhibit less stride length than the control subjects. However, walking speed, stride length, and stance time did not differ between patients with chronic ACL deficiency and healthy subjects.[145]

Joint loading

The literature has not been consistent regarding knee joint loading tendencies in knee OA patients. Knee joint loading (knee adduction moment) is associated with severity of pain.[153] Increased knee joint loading (by pain) causes higher compressive forces within the joint, resulting in accelerating joint degeneration progression. On the other hand, patients with knee OA walked with less joint unloading.[135] Decreased knee joint loading does not provide normal joint stress[157] to maintain articular cartilage health. Less joint compressive forces may lead (or accelerate) to degeneration of articular cartilage over the long term effects.[158] Additionally, OA knee pain relief by intra-articualr injection[138,149] and NSAIDs[137] resulted in a increase in joint loading (internal extensor moment,[138] external adduction,[137,149] and external flexion moment[137,149]) during walking. Pain may exist as protective mechanism to maintain optimal

joint loading. This suggests that reducing osteoarthritic knee pain may cause a more rapid disease progression.[88]

Knee joint unloading strategies are consistent in artificial knee pain[88] and effusion studies.[19] These studies suggest that both nociceptive activity from the infrapatellar fad pad and mechanical pressure within the joint may influence gait adaptations. Sudden artificial stimulus (pain or effusion) that the subjects have never experienced may lead to a simple unloading strategy on the involved side. Thus, intentional avoidance on the ipsilateral weight bearing side due to acute artificial pain or effusion should be considered as another contributing factor in any injury model study. Comparisons of abnormal joint loading responses due to pain, effusion, or a combination of these two stimuli could answer which stimulus places patients at greatest risk for early joint degeneration.

Gait adaptation and its long-term effects

It is evident that quadriceps activation is diminished following knee joint injuries (Table 1). As a result of quadriceps AMI, internal knee extensor moment decreases[99,135] which lead to a more flexed knee angle at initial contact and throughout the early stance phase of gait.[19] By intentional unloading of the involved limb, or perhaps due to an increase in quadriceps-hamstring co-contraction,[39] knee angle becomes in a more extended position during and after the mid-stance.[19,39,142] Reduction in walking speed[143] result in a shortened stride length. Due to longer duration of activation of the tibialis anterior[145] or activity of the ticeps surae,[39,99] push off at the terminal stance on the ipsilateral side decreases.[50] These adaptations would result in a decreased swing phase and an increased vertical GRF and loading rate of the non-involved leg. In order to

avoid weight bearing in the involved side, trunk would shift towards to the side of non-involved limb.

Gait is the most common activity of daily living. Following knee joint injury, the lower extremities alter the normal gait pattern. This temporary adjustment not only helps to protect the injured joint (i.e. quadriceps avoidance gait and unloading strategy), but may also allows the lower body to maintain function. These adaptations, however, appear to have long-term negative effects. Adaptations of the normal gait program may include modifying neuromuscular activation patterns, changing the degree of contribution of each joint, and creating kinetic and kinematic asymmetry between limbs. These adaptations create a new motor program. This new gait program may lead to accelerate and/or early joint degeneration.

Quadriceps weakness has been considered as a strong predictor of joint degeneration.[42,159] Persistent quadriceps AMI may directly progress knee joint degeneration. As an active restraint, the quadriceps provides joint stability and aids in shock absorption within the joint.[22] Decrease knee extensor torque may directly cause alterations in knee joint loading. There have been many studies that examined alterations in the knee joint moment in the patients with knee OA. Although some reported[34,131] an increase in knee joint loading while others reported[135,138] reduced knee joint loading, it seems to be clear that knee joint injury shuts down the knee extensors and changes knee joint loading and mechanics. Quadriceps AMI from a acute injury may initiate gait adaptations which cause abnormal joint loading in each joint, eventually resulting in degenerative joint disease.

Drop landing task

The drop landing task is experimental movement to examine landing mechanics.[160] It has been used to describe active knee joint strain and mechanism of non-contact ACL injury.[13,161-164] ACL injury is two to eight times greater for females than males.[165] Studies examining sex differences during drop landings have reported that females landed with (1) less gluteus maximus activation[166] and greater quadriceps activation[161,162] compared to control (2) lower quadriceps to hamstring ratio,[161] (3) greater tibial internal rotation after immediate landing,[161] (4) greater vertical GRF,[163] (5) greater knee valgus position before and at landing,[164] and (6) less hip and knee flexion angle (more erect posture).[162,163]

Patients who have completed their rehabilitation post-injury may still exhibit quadriceps inhibition along with neuromuscular deficits.[167] These potential alterations would hinder active dynamic joint restraints, resulting in a reduction in knee joint stability. Due to alterations of the active restraints, passive joint restraints (i.e. ligaments or articular cartilage) compensate the energy absorption deficit from the quadriceps and exert more force during landing from a jump. Additionally, quadriceps inhibition may lead to alterations in other musculature (i.e. hamstring and gluteus medius) which could cause kinetic and kinematic changes.

Unfortunately, there is little data on adaptations in patients with clinical knee joint injuries during drop landing task. A controlled laboratory study examined how transient quadriceps inhibition, induced knee joint effusion (60 ml), causes kinetic and kinematic alterations in drop landing.[13] Knee joint effusion caused (1) less peak knee flexion angle (sagittal plane), (2) less peak knee extension moment, and (3) higher peak GRF compared to no effusion.[13] These findings are consistent with the observation of sex differences during drop landing. These alterations may be a consequence of clinical knee joint injuries and should be

addressed the rehabilitation. In the same study,[13] low amount of knee effusion (30ml) produced quadriceps inhibition but did not produce any kinetic or kinematical changes.[13] This study[13] also observed hamstring facilitation along with the quadriceps inhibition. The hamstring facilitation is thought to be a compensatory strategy.

Increasing peak GRF during drop landing is believed to increase joint stress from impact loading, resulting in lower extremity injury.[168] Improper landing technique could contribute to an even higher incidence of injury. Education in proper landing technique has been shown to decrease impact loading.[169]

Stiffness

Stiffness has been defined as a ratio between the force required to deform a material and the distance the material is deformed.[38] This can be simply calculated as the ratio between the maximal vertical GRF and the maximal vertical displacement of the centre of the body mass during a landing task. Stiffness is positively related to the demands[170] or velocity of the activity.[171]

Some level of stiffness is thought to be beneficial for preventing injury and improve performance. Stiffness is required to utilise the stretch-shortening cycle by storing elastic energy during eccentric loading phase.[172,173] Too much stiffness may increase risk of injury. Increasing peak vertical GRF, or reducing lower extremity excursion, would increase stiffness, resulting in an increase in loading rates.[174] Increased vertical GRF with an increased loading rate may put a patient at a greater risk for overuse bony injuries such as osteoarthritis or stress fracture.[175] Too

little stiffness may allow excessive joint motion, resulting in mechanical failure of the soft tissues.[170]

MEASUREMENTS

Neuromuscular activity

Walking

Author (year)	EMG locations; sampling rate	Normalization; data smoothing; cut off frequency	Dependent measurements
Torry (2000)[19]	VM, VL, MH, and LH;1200 Hz	MVIC (50 ms RMS moving window); 15 ms RMS moving window	-Stance phase (four equal time intervals of the norm base)
Burden (2003)[176]	LH, MH, VM, and VL; 1000 Hz	Mean dynamic, peak dynamic, MVIC, and isometric; 50 ms RMS moving window	-Inter- and intra-individual variability
Hurd (2007)[39]	VM, VL, TA, MG, LG, SL, MH, and LH; 1080 Hz	MVIC; 8th order Butterworth filter; 10 Hz	-Muscle co-contraction during mid-stance and weight acceptance (H:Q, Q:G)
Barr (2010)[177]	RF (fine wire and surface) and VM; 3000 Hz	MVIC; High-pass Butterworth filter with cutoff at 20 Hz then low-pass filter with cutoff at 9 Hz for linear envelope	-Peak EMG (5 gait cycles were averaged) during stance phase
Lindstrom (2010)[145]	TA, LG, VM, and LH;	Not specified.	-Onset/offset in each muscle, given as % of stance time

VM: vastus medialis, VL: vastus lateralis, GM: gluteus medius, BF: rectus femoris, BF: biceps femoris, TA: tibialis anterior, MH: medial hamstring, LH: lateral hamstring, MG: medial gastrocnemius, LG: lateral gastrocnemius

Drop landing

Author (year)	Height; distance for force plate	EMG locations; sampling rate	Normalization; data smoothing; cut off frequency	Dependent measurements
Russell (2006)[164]	60 cm; not specified	GM; 1080 Hz	IRP (single leg standing); Band-pass filter with 3 ms window RMS; 10-500 Hz	-100 ms before and after initial contact (used % IRP of averaged same interval)
Nagano (2007)	30 cm; 30 cm	RF, BF, and SM; 1000 Hz	% MVC; RMS	- H:Q ratio at 50 ms before and after foot contact
Palmieri (2007)[13]	30 cm; not specified	VM, RF, VL, MH, LH, MG, and LG;1080 Hz	% MVIC (50 ms RMS); 4th-order Butterworth high-pass; 20 Hz	- 250 ms after foot contact (used % MVIC of averaged 15 ms RMS window)
Kellis (2009)[178]	30 cm; not specified	VM, VL, LH, and LG; 2000 Hz	% MVIC; Zero phase shift digital high-pass; 10 Hz	-Preparatory: 100 ms before IC -Initial loading response: 100

				ms interval after IC -Main loading response: between 100-200ms after IC -H:Q ratio
§Smith (2009)[179]	50 cm; not specified	VM, VL, MH, LH, LG; 1000 Hz	Values in non-fatigue condition; Butterworth polynomial; 20-400 Hz	600 ms after IC
*Schmitz (2010)[180]	Drop-jump (45 cm;10 cm)	EMG data were not reported.		

IRP: isometric reference position,
GM: gluteus medius, BF: rectus femoris, BF: biceps femoris, SM: semimembranosis, MH: medial hamstring, LH: lateral hamstring, MG: medial gastrocnemius, LG: lateral gastrocnemius
IC: initial contact
RMS: root mean square
§ Bilateral drop landing
* Drop-jump task: double leg landing followed by an immediate vertical jump

Kinetics

Walking

Author (year)	Sampling rate	Normalization; Filter; cut off frequency	Dependent measurements
Torry (2000)[19]	1200 Hz	Moment: Nm / N (BW) * m (HT)	-Hip and knee sagittal plane joint moment and impulse
Mundermann (2005)[131]	120 Hz	-GRF: N / N(BW) -Moment: Nm / N (BW) * m (HT)	-External knee and hip moments -Hip and knee loading rates
Hurd (2007)[39]	1080 Hz	-Moments: Nm / kg (BW) * m (HT) -2nd order bidirectional low pass Butterworth; 50 Hz	-Internal knee moments -Total support moments
Henriksen (2010)[88]	1500 Hz	-Moment: Nm / kg (BW)	-Internal knee moments
Hunt (2010)[140]	1080 Hz	GRF: N / N (BW)	-Vertical GRF -Loading rate & time to max loading
Lindstrom (2010)[145]	Not specified.	GRF: N / N (BW)	-Vertical GRF -Peak posterior braking force -peak anterior propulsive force

BW: body weight, HT: height

Drop landing

Author (year)	Sampling rate	Normalization; Filter; cut off frequency	Dependent measurements
Ford (2003)[181]	1200 Hz	Not specified	-GRF data were used to determine initial contact and toe off
†Russell (2006)	1080 Hz	-Low-pass anti-aliasing filter; 1000 Hz	-Not reported
Nagano	1000 Hz	-Not normalized and filtered	-Vertical GRF

(2007)[161]			-Time to peak GRF
Palmieri (2007)[13]	1080 Hz	-Low- pass, anti-aliasing filter; 1000 Hz -Internal moment: Nm*kg (BW) -GRF: Nm/kg (BW)	-Peak vertical GRF -Peak net knee ext. moments
Lawrence III (2008)[182]	1200 Hz	-Moment: Nm/kg (BW) -Time series data sets were interpolated to 100 points during the impact phase	-Hip and knee extensor moment in the sagittal and frontal planes -Ankle plantar flexion moment
†Ford (2010)[183]	1200 Hz	Moment: unnormalized, Nm/Kg (BW), Nm/m (HT), Nm/kg/m (BW*HT)	-External moment
Smith (2009)[179]	1000 Hz	-GRF: N/N (body weight)	-Peak vertical GRF
†Schmitz (2010)[180]	1000 Hz	-4th-order Butterworth low-pass with zero lag; 60 Hz -Internal moment: Nm/N/m(body height) -GRF: N/N (body mass) -Energy absorption: J/N/m -Joint stiffness: Nm/N/m/degree (change in angular position)	-Hip, knee, and ankle extensor moments -Energy absorption -Hip, knee and ankle joint stiffness

BW: body weight, HT: height
§ Bilateral drop landing
† Drop landing task: double leg landing followed by an immediate vertical jump

Kinematics

Walking

Author (year)	Sampling rate	Marker set	Filter; cut off frequency; normalization	Dependent measurements
Torry (2000)[19]	120 Hz	13 on the leg	4th-order Butterworth: 5 Hz	-Hip and knee angles at hell contact -Average hip and knee angle during stance phase
Mundermann (2005)[131]	120 Hz	6 on the leg	Not specified.	-Hip and knee angles
Hurd (2007)[39]	120 Hz	Not specified.	Bidirectional 2nd order low pass Butterworth; 6 Hz	-Sagittal plane knee excursion
Henriksen (2010)[88]	100 Hz	8 on each leg	Not specified.	- Knee angle at heel strike, early stance, and late stance phase
Hunt (2010)[140]	120 Hz	8 on each leg	4th-order Butterworth with zero lag; 6 Hz	-Knee flexion angles (stance phase was normalized to 100 data points)
Lindstrom (2010)[145]	Not specified.	13 on the leg	-Not specified. -Stride length: % body height -Heel lift ht: % body height	-Knee and ankle angle in sagittal plane -Max heel lift-off height during swing -Stride length

Drop landing

Author (year)	Sampling rate	Marker set	Filter; cut off frequency	Dependent measurements
Russell (2006)[164]	120 Hz	16 on the each leg	Woltering filter (Vicon)	-Frontal plane knee angles -Sagittal plane knee angles

†Ford (2003)[181]	240 Hz	23 on the trunk and each leg	Low-pass Butterworth; 9 Hz	-Valgus knee angle (between IC-TO)
Nagano (2007)[161]	200 Hz	24 on the right leg	Not smoothed: due to the use of PCT (Point Cluster Technique)[184]	-Angular displacements -Anterior tibial translation
Palmieri (2007)[13]	120 Hz	18 on the dominant leg	4th-order Butterworth low-pass with zero lag; 6 Hz	-Sagittal plane knee angles
Lawrence III (2008)[182]	240 Hz	19 on the each leg	4th-order Butterworth filter; 10 Hz	-Knee flexion angle
§Smith (2009)[179]	1000 Hz	Electrogonio-meter	Frouth-order no phase shift Butterworth 2-pass; 6 Hz	- Knee angles in sagittal and frontal planes
†Ford (2010)[183]	240 Hz	37 on the trunk and each leg	Low-pass 4th-order Butterworth; 12 Hz	- Knee abduction angle
†Schmitz (2010)	100 Hz	7 on the leg and trunk	4th-order Butterworth low-pass with zero lag: 12 Hz	-Hip, knee, and ankle flexion angles

IC: Initial contact, TO: toe off from the jump
§ Landing task: double leg landing
† Landing task: double leg landing followed by an immediate maximal vertical jump

Methods

Experimental design

This study will be a crossover design. The independent variables will be condition (pain, effusion, pain/effusion, and control-no injection) and time (pre-condition, condition, and 30 min post-condition). The dependent variables will be neuromuscular activities, kinetic, and kinematic data on the lower extremity; and subjective pain perception. The specific dependent variables are as followed:

Neuromuscular activity

(1) Peak and mean EMG values of each muscle in four equal time intervals (0-25%, 26-50%, 51-75%, 76%-100%) during stance phase

(2) Peak and mean EMG values of each muscle 200 ms before and at peak knee flexion

Kinetic data

(1) Peak impact VGRF, unloading VGRF, peak push-off VGRF, and time to peak VGRF during stance phase

(2) Ankle, knee, and hip joint moment in the sagittal and frontal planes during stance phase of walking and at peak knee flexion angle during drop landing

(3) Vertical stiffness during walking drop landing

Kinematic data

(1) Peak joint angles (ankle, knee, and hip joint) in the sagittal and frontal planes during walking and drop landing

(2) Stride length and walking speed during walking

Participants

Sample size was calculated using an expected change in peak vertical GRF normalized by body mass (GRF: N/kg) of 10 and a standard deviation of 7.29 during drop landing.[13] Based on these estimations, 13 subjects in each group will be necessary in order to have an 80% chance of detecting a significant difference with P=0.01.

Twenty, (10 males and 10 females; aged between 18-35 years old) healthy subjects will volunteer to participate. Exclusion criteria will include current pregnancy, history of neuromuscular disorders, lumbar spine or lower extremity surgery, or lower extremity injury within the past 6 months. All subjects in this study will read and sign the informed consent form approved by Institutional Review Board.

Instrumentation

Measurements of the neuromuscular activities, kinetic, and kinematic data will be recorded and synchronized with Vicon Nexus 1.7 (VICON, Centennial, CO). EMG will be recorded using the Trigno system (Trigno, Delsys Inc., Boston, MA). All data will be exported into Visual3D (C Motion, Germantown, MD) for analysis.

Neuromuscular activity

Twelve wireless surface electromyography (EMG) electrodes (Trigno Wireless, Delsys Inc., Bostaon, MA) will be used to record neuromuscular activity of the lower extremity (sampling rate: 2,000 Hz). Electrode locations will be shaved, debrided with sandpaper, and

cleaned with isopropyl alcohol. The electrodes will be placed on the medial gastrocnemius (MG), vastus medialis (VM), vastus lateralis (VL), medial hamstring (MH), gluteus medius (GM), and gluteus maximus (GX) on both legs (Appendix 1; Figure 1). EMG during an isometric reference position will be recorded to normalize the EMG amplitude. Subjects will be asked to squat down until their butt barely touches a barrier (height of 0.74 m) and maintain the position for four seconds (Figure 2). EMG electrodes consist of band-pass filter of 20-450 Hz with a common mode rejection ratio greater than 80 dB and a gain of 1000. A 48 ms fixed delay, from sensor input to analog output, will be accounted for all EMG data to harmonize with kinetic and kinematic data.

EMG data will be smoothed using a root mean square (RMS) algorithm with a 50 ms moving window for walking trials and a 15 ms moving window for drop landing trials. The reference values of the EMG amplitude in each muscle with the same RMS moving window for each movement will be used to normalize neuromuscular activity changes in the same muscles.

Kinetic data

GRF data will be measured using two-floor-mounted force platforms (AMTI, Watertown, MA) at a sampling rate of 2,000 Hz. Prior to data collection, both force platforms will be calibrated to zero. GRF data will not be filtered using a 4^{th}-order low-pass Butterworth filter with cut off frequency of 20 Hz. Cut off frequency will be confirmed with residual analysis technique (Winter's method).[185] GRF data will not be normalized.

Kinematic data

The movements of the lower extremity and trunk will be measured using ten near-infrared cameras (Vicon MX, Oxford Metrics Ltd, Oxford, UK) at a sampling rate of 200 Hz (Appendix 2).

Twenty seven single reflective markers will be attached on the lower extremity and trunk. Four rigid clusters of four markers will be applied to the proximal-lateral thigh and distal-lateral shank on each leg. Single markers will be bilaterally placed over the acromion, inferior angle of the scapula, anterior superior iliac spine, greater trochanter, lateral and medial femoral condyle, medial and lateral maleoli, dorsal surface of the midfoot, toe (between the second and third metatarsal), lateral foot (fifth metatarsal), and heel. All subjects will wear athletic shoes and malioli-open socks. Foot markers will be attached onto the athletic shoes. Single markers will also be placed over the C7, T7, and medial sacral crest (Figure 1).

A static standing trial (subjects will stand with equal distribution of body weight on each foot) will be measured and considered as each subject's neutral body alignment (Figure 3); subsequent kinematic measurements will be referenced in relation of this position. Subjects will perform standing leg motions for each leg in order to estimate functional hip joint center (Figure 4-a & b).[186] These motions will consist of three hip flexions and extensions in the sagittal plane and three hip abductions and adductions in the frontal plane. Afterwards, ankle and knee joint markers on each leg will be detached for walking and drop landing trials.

After data collection, spatial coordinates corresponding to the reflective markers will be tracked using Vicon Nexus and then exported to Visual3D. A static model will be first built using the static standing trial. This model will be applied to each c3d file of walking and drop landing trials to calculate joint angles and moments. The model's coordinate system convention will be +X forward (posterior to anterior), +Y toward the subject's left (medial to lateral), and +Z up (distal to proximal). Kinematic data in walking and drop landing tasks will be smoothed using a 4^{th}-order low-pass Butterworth filter with cut off frequency of 6 Hz. Cut off frequency will be confirmed with residual analysis technique (Winter's method).[185]

Perceived pain

Subjective pain perception will be quantified using 10 cm VAS (Appendix 3).[187] Every two minutes throughout each time interval, subjects will be asked to mark where their pain level is at the time of measurement.

Conditions

Following the pre-condition trials (see the testing procedures below), subjects will sit on a chair and receive one of the four conditions (Figure 5). Saline injections will be used in each condition except for the control condition. A licensed, board certified physician will perform all injections on subject's dominant limb. Dominant limb will be defined as the leg use when kicking the ball. Prior to injection, area of the needle insertion will be cleaned with povidone-iodine. After removal of the needle, the puncture site will be cleaned with alcohol swab and covered with sterilised gauze.

Pain

The 25 gauge needle (Becton Dickinson Medical Systems Inc, Sandy, UT) will be inserted into the lateral infrapatellar fad pad. The needle will be inserted at an angle of 45 degrees, in an inferior-medial direction, with a depth of 1 cm (Figure 6).[87] Sterile hypertonic saline (5% sodium chloride, 1.0 ml, B. Braun medical, Inc., Irvine, CA) using 1 ml syringe (Becton Dickinson Medical Systems Inc, Sandy, UT) will be injected. In our pilot study, most subjects felt minimal pain (less than 2) in approximately eight minutes after a single injection of 1 ml 5% hypertonic saline.

Effusion

Sterile lidocaine (1%, 2.0 ml, Hospira, Inc., Lake Forest, IL) using the 25 gauge needle and 3 ml syringe will be injected subcutaneously for anesthetic purpose (Figure 7). The 18

gauge needle will be inserted into the superolateral knee joint (Figure 8). Sterile saline (0.9% sodium chloride, 50.0 ml, Hospira, Inc., Lake Forest, IL) using 50 ml syringe (Becton Dickinson Medical Systems Inc, Sandy, UT) will be used. An effusion wave and ballotable patella test will be performed to ensure that the effusion is within the knee joint capsule.[96]

Pain/Effusion

To induce a combination of pain and effusion, three injections will be used in the order of 1% lidocaine, 0.9% isotonic saline, and 5% hypertonic saline. The same volume of each saline solution will be injected as the volume used for pain and effusion conditions. Effusion will be induced first followed by pain due to limited amount of time for pain sensation.

Condition

The control condition will consist of no injection. For the control condition, subjects will simply sit on a chair for five minutes and perform the condition trials at the same time intervals.

Testing Procedures

In the orientation session, subjects will read and sign the informed consent form approved by the Intuitional Review Board. Subjects will also complete the demographic information. Subjects' height and mass will be measured. Subjects will perform several trials of drop landings for familiarization purpose. This will help ensure a consistent drop height between sessions. Qualified subjects will come back in a week for data collection.

Each subject will experience all four conditions (pain, effusion, pain/effusion, and control) in each session with a week wash-out period in between sessions. Each session will consist of three time intervals (pre-condition, condition, and 30 min post-condition). During each time interval, three trials of functional movements (walking trials first followed by drop landing trials)

will be recorded. Order of the conditions will be randomized using Latin Square designs (Appendix 4).[188]

Upon arrival in the laboratory, subjects will be asked to wear spandex shorts and shirts, socks, and athletic shoes during data collection. EMG electrodes and reflective markers will be attached. Subject's isometric reference position, static standing video, and standing leg motions will be recorded. Subjects will perform the pre-condition trials. Afterwards, subjects will sit on the table and receive one of the conditions (pain, effusion, pain/effusion, control). A minute after the injection, subjects will perform the condition trials. Data collection will be terminated if a subject complains of intolerable pain and/or fainting, or a subject does not begin condition trial in eight minutes following injection. Subjects will sit on the chair (same position as injection) and rest for 20-25 minutes before the post-condition trials. Resting time will be dependent on the length of time completing the condition trials.

Walking

Subjects will be walking over the force platforms at a self-selected walking speed. One gait cycle of each leg will be collected. A successful trial will be defined as subjects' each foot completely step on each force platform (Figure 9). Subjects will be asked to keep walking until three successful trials are recorded in each time interval.

Drop landing

Subjects will perform a drop landing task from a 30 cm height wooden box. The box will be placed 20 cm away from the rear edge of the force platform for all subjects. Three successful trials will be collected in each time interval. A successful trial will be defined as which the subjects will drop down (not step or jump down) on their dominant leg onto the force platform followed by an immediate vertical jump as determined visually by the assessor (Figure

10).[180,181,183] Subjects will be instructed not to touch the ground with the contralateral limb and to maintain balance after the second landing for two seconds.[164] The first landing will be used for analysis.

Statistical Analysis

Means will be computed from three trials at each time interval for each condition. To test condition effect over time, 3 X 4 mixed model analysis of covariances (covariate: pre-condition measurement) will be used for each dependent variable. To eliminate possible influence to joint kinetic and kinematics, self selected walking speed will be used as covariate for all walking trial analyses. In order to avoid the type I error, Bonferroni type adjustment for multiple comparisons with the significant level of 0.01 will be used for all tests.

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Appendix

Appendix 1. Location of the EMG Electrodes[189,190]

Muscle	Location
Medial gastrocnemius	50% of distance between medial knee joint space and the insertion of the gastrocnemius
Vastus medialis	20% of distance between the anterior superior iliac spine and the medial knee joint space
Vastus lateralis	Distal 33% of distance between the anterior superior iliac spine and the lateral knee joint space
Medial hamstring	50% of distance between the ischial tuberosity and the medial knee joint space
Gluteus medius	50% on the line from the iliac crest and the greater trochanter
Gluteus maximus	50% on the line between the sacral vertebrae and the greater trochanter

* No ground electrode will be attached since the Trigno System does not require it.

Appendix 2. Camera setup and calibration for the motion analysis system

Six cameras will be mounted on the wall (one camera at height of 2.6 m; two cameras at height of 2.5 m; three cameras at 2.4) and four cameras will be placed on tripods (height of 1.9 m). Prior to data collection, positions of the each camera will be confirmed to ensure all cameras capture the entire space required by functional movements. Calibration of the motion analysis system will be performed using dynamic wand data to calculate camera positions, lens distortion maps, and focal length.[191] Following the dynamic calibration, a 3D coordinate system will be originated.

Appendix 3. VAS

Appendix 4. Randomization of the condition using Latin Square design

subject	control	pain	effusion	P & E
1	2	3	4	1
2	4	2	1	3
3	1	4	3	2
4	3	1	2	4
5	2	4	3	1
6	4	1	2	3
7	1	3	4	2
8	3	2	1	4
9	2	4	3	1
10	4	1	2	3
11	1	3	4	2
12	3	2	1	4
13	4	1	3	2
14	3	4	2	1
15	1	2	4	3
16	2	3	1	4
17	3	4	2	1
18	4	1	3	2
19	2	3	1	4
20	1	2	4	3
21	4	3	2	1
22	2	4	1	3
23	1	2	3	4
24	3	1	4	2
25	3	1	2	4
26	4	2	1	3
27	2	3	4	1
28	1	4	3	2
29	1	3	4	2
30	3	2	1	4
31	4	1	2	3
32	2	4	3	1
33	2	1	4	3
34	4	2	3	1
35	1	3	2	4
36	3	4	1	2
37	2	3	1	4
38	1	2	4	3
39	4	1	3	2
40	3	4	2	1

Figure 1. Placements of the EMG electrodes and the reflective markers

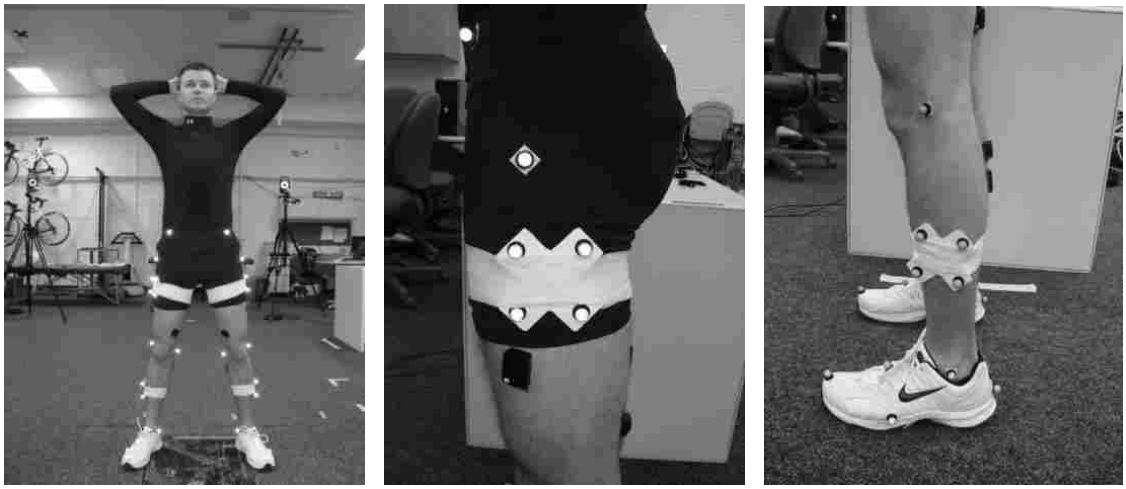


Figure 2. Isometric reference position for EMG normalisation

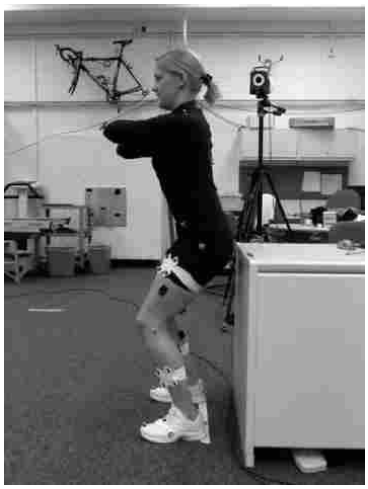
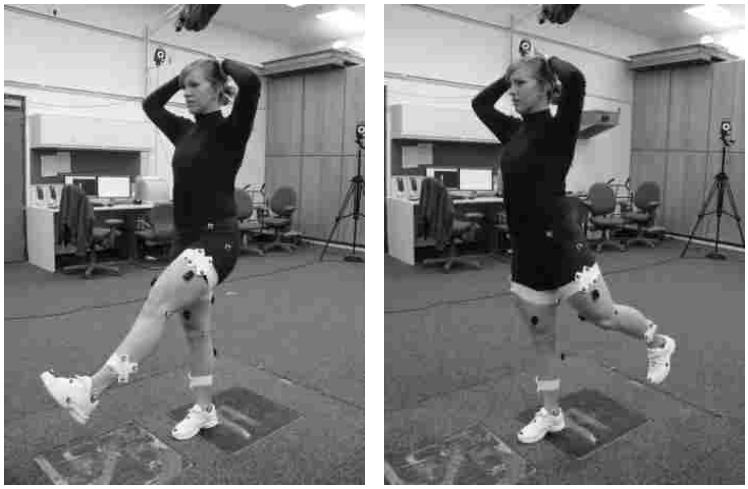


Figure 3. Static standing measurement for neutral body alignment

Figure 4. Single leg motions for functional hip joint centre

a. Sagittal plane



b. Frontal plane

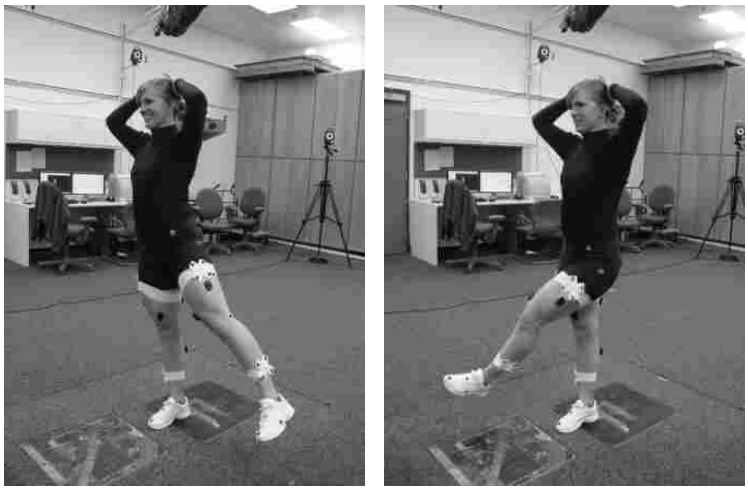


Figure 5. Subject position for injection

Figure 6. 5% hypertonic saline injection for pain model

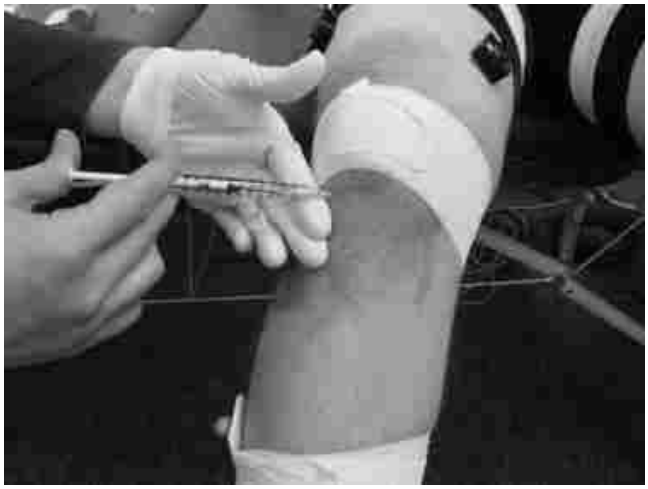


Figure 7. 1% lidocaine injection prior to effusion model

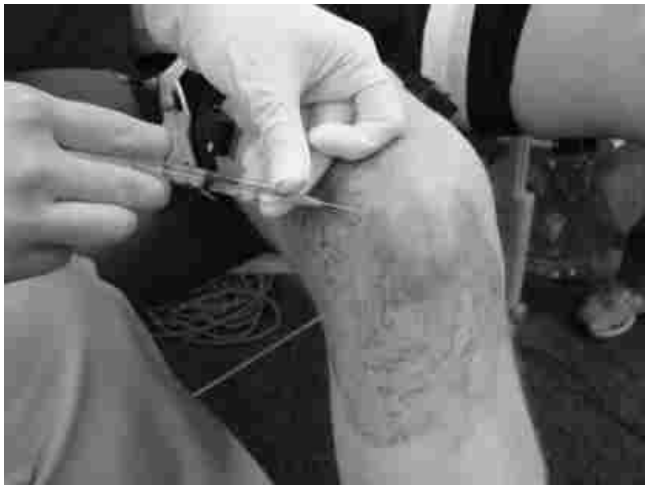


Figure 8. 0.9% isotonic saline injection for effusion model

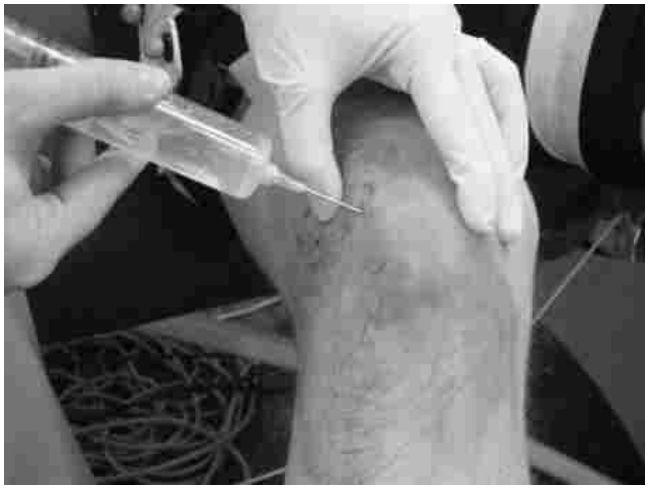


Figure 9. Walking task

Figure 10. Drop landing task