PAIN AND FUNCTION IN KNEE OSTEOARTHRITIS: ARE THEY RELATED TO LOCAL INTRINSIC FACTORS?

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by
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The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

PAIN AND FUNCTION IN KNEE OSTEOARTHRITIS:
ARE THEY RELATED TO LOCAL INTRINSIC FACTORS?

Presented by Kyle Gibson,

A candidate for the degree of Doctor of Philosophy

And hereby certify that, in their opinion, it is worthy of acceptance.

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Stephen Sayers

…..to Rita

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PAIN AND FUNCTION IN KNEE OSTEOARTHRITIS:
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ABSTRACT

OBJECTIVE: The study of knee osteoarthritis (OA) has been hampered by the inability to adequately characterize the subject pool with respect to local intrinsic factors and there is little evidence to guide the selection of factors for future study. This study characterized a subject pool by local intrinsic factors and makes an evidence-based recommendation for the inclusion of specific factors in future study of knee OA.

METHOD: Forty six subjects with knee osteoarthritis were examined. Observed function was measured by the Timed Chair Rise Task. Self-reported function was measured by the WOMAC Function Scale and pain was measured by the WOMAC Pain Scale. Local intrinsic factors measured included Varus/Valgus Alignment, A/P Laxity, Proprioception, Knee Extension Strength by Bodyweight, Knee Flexion Strength by Bodyweight, and Knee ROM.

RESULTS: Factors were recommended for inclusion in future research if they were significantly correlated with at least one measure of function or pain and if the factor made a significant unique contribution to a regression model when more than one local intrinsic factor was correlated with the same measure of function or pain. Extension Strength by Bodyweight was correlated with observed function ($r=0.32$, $p=0.03$). Varus/Valgus Alignment was correlated with pain ($r=0.48$, $p=0.001$) and self-reported function ($r=0.38$, $p= 0.009$). A/P Laxity was also correlated with pain ($r=0.30$, $p=0.04$) and self-reported function ($r=0.37$, $p= 0.01$). Knee ROM was correlated to self-reported function ($r=-0.35$, $p= 0.016$). Varus/Valgus Alignment made a significant contribution to prediction of pain ($p=0.003$), A/P Laxity to self-reported function ($p=0.004$), and Knee ROM to self-reported function ($p=0.008$).

CONCLUSION: It is recommended that future studies of knee OA characterize the subject pool by Varus/Valgus Alignment, A/P Laxity, Knee ROM, and Extension Strength by Bodyweight.

Pain and Function in Knee Osteoarthritis: Are They Related to Local Intrinsic Factors?

Osteoarthritis (OA) is one of the most common conditions affecting the quality of life of older adults. Twelve percent of the US population between the ages of 25-75 have clinical signs and symptoms of the disease (Lawrence et al., 1998) and 80% of adults 65 years and older have radiographic evidence of the disease (Burckhardt, 1990). The monetary costs of OA are staggering, with annual outpatient medical costs double that of individuals without the disease. Prescription drug costs were also 102% higher for patients with OA (Mapel, Shainline, Paez, & Gunter, 2004). The knee (tibio-femoral) joint is a common site of osteoarthritis with 33% of individuals between the ages of 63-94 having some radiographic evidence of the disease (Felson et al., 1987). Eleven percent of individuals 65 years old and older report pain "on most days" due to knee OA (Felson et al., 1995).

Pain is not the only consequence of knee osteoarthritis. Knee OA is a leading contributor to disability in the elderly population. The risk of disability secondary to OA of the knee is as great as cardiovascular disease and greater than any other medical condition (Guccione et al., 1994). The effective management of this prevalent and disabling disease presents an important challenge that will improve the health of many individuals as well as reduce the financial burden to our healthcare system.

The American College of Rheumatology recommends exercise as a non-pharmacological tool for the management of osteoarthritis of the knee (Hochberg et al., 1995). However, effects of exercise on common outcome measures (typically pain and function) are inconclusive with positive effects of exercise on pain and function observed

in some (Deyle et al., 2000; Ettinger et al., 1997; Kovar et al., 1992; Maurer, Stern, Kinossian, Cook, & Schumacher, 1999; Minor, Hewett, Webel, Anderson, & Kay, 1989; O'Reilly, Muir, & Doherty, 1999; Schilke, Johnson, Housh, & O'Dell, 1996; van Baar, Assendelft, Dekker, Oostendorp, & Bijlsma, 1999) but not all studies (Fisher, Kame, Rouse, & Pendergast, 1994; Thorstensson, Roos, Petersson, & Ekdahl, 2005). Strength, a common correlate of knee function (Slemenda et al., 1997), might show a significant gain in some studies (O'Reilly et al., 1999), while showing surprisingly modest gains or even non-significant change in others (van Baar et al., 2001).

Some of the variability of outcomes may be due to difference in study design, exercise protocols and participants (Baker & McAlindon, 2000), but some investigators have hypothesized that individual differences within the study populations might diminish the effect of exercise on function and/or pain (Sharma, 2003). Exercise intervention studies have typically admitted participants using general inclusion criteria limited to type of arthritis (osteoarthritis) and site of joint effected (knee) with no attempt to describe any further individual differences within the sample. Individual differences in and around the joint have been recently recognized as important factors to consider when interpreting outcomes of exercise.

Researchers have proposed that the effect of exercise in patients with knee OA may be moderated by individual differences in structural or physiological factors (Sharma, 2003). These factors influence how load is distributed across the articular surface of the knee as well as the neuromuscular control of the joint. These structural/physiological features that directly affect the biomechanical properties of the joint have been termed “local intrinsic factors” (Sharma, 2001). The degree to which

these factors are present vary from person to person in individuals with knee OA. If local intrinsic factors do indeed alter an individual's response to exercise, it then becomes necessary to consider these factors when interpreting exercise outcome studies for knee OA.

Local intrinsic factors that have received recent attention in the literature are knee joint alignment, laxity, proprioception, range of motion (ROM), and strength. There are however, few studies that have measured these factors or been able to investigate whether these factors might mediate the effect of exercise on function/pain in individuals with knee OA. To begin to identify important local intrinsic factors and understand their mediating role, it is necessary to examine existing relationships between these factors and measures of pain and function.

Knee Joint Alignment

No studies to date have examined knee alignment as a modifier of the effect exercise has on function and pain in a population of individuals with knee OA. However, varus/valgus knee alignment (the degree of "knock-kneed" or "bowleggedness") has been demonstrated to be related to function in some circumstances. Individuals with knee OA and knee varus/valgus alignment deviating more than 5° from midline in both knees, have been shown to exhibit significantly decreased function (measured by a chair stand task) when compared to individuals with knee OA with 5° or less mal-alignment (Sharma et al., 2001). However, this difference did not hold true for individuals with mal-alignment in only one knee.

Laxity

Anterior/posterior (A/P) laxity is defined as non-physiological motion between the tibia and the femur in the saggital plane. Much information exists regarding A/P laxity's role in the development or worsening of OA in human and animal models (Lopez et al., 2003; Lundberg & Messner, 1997; Sherman, Warren, Marshall, & Savatsky, 1988; van Osch, van der Kraan, Blankevoort, Huiskes, & van den Berg, 1996), but no published studies have reported A/P laxity as a potential modifier of the effect of exercise on function/pain. Furthermore, no studies relate any findings regarding relationships between A/P laxity and function/pain in a population with knee OA.

Proprioception

Well coordinated muscular activity helps attenuate shock and distribute load during weight bearing activities. Muscular activity is also an important component in the protective response that occurs when a joint is being subjected to abnormal load or motion. Proprioception, the conscious and unconscious perception of limb position in space (Sharma, 1999), together with other sensory input (i.e. visual, vestibular) helps coordinate this muscular activity (Lephart, Pincivero, & Rozzi, 1998).

The relationship between the presence of OA of the knee and deficits in proprioception has been demonstrated (Hassan, Mockett, & Doherty, 2001; Marks, 1996; Pai, Rymer, Chang, & Sharma, 1997), although the severity of the disease has not been found to correlate with proprioception deficits (Birmingham et al., 2001; Sharma, Pai, Holtkamp, & Rymer, 1997). The relationship between proprioception and function has not clearly been shown. Although some investigators have found evidence of a relationship between deficits in proprioception and limitations in function (Pai et al.,

1997; Sharma, Cahue et al., 2003), others have found no relationship (Bennell et al., 2003; Hassan et al., 2001). The relationship between proprioception and pain is likewise equivocal, with some investigators reporting a relationship between pain and proprioception deficits (Pai et al., 1997) and others showing none (Bennell et al., 2003; Hassan, Doherty, Mockett, & Doherty, 2002; Sharma et al., 1997). There have been no studies reported to date that address proprioception as a possible mediator of the effect of exercise on function/pain.

Range of Motion

Decreased range of motion (ROM) of the knee secondary to stiff noncontractile structures (e.g. ligaments, joint capsule) or muscles exhibiting decreased flexibility (e.g. tight hamstrings), could potentially alter forces encountered at the joint. The inability to fully extend one's knee is an example of a common ROM impairment associated with knee OA (Hertling & Kessler, 2006). Lack of knee extension alters the weightbearing experienced at the knee during gait. With normal gait, peak weightbearing occurs near full knee extension, maximizing the tibiofemoral joint contact area. With a knee flexion contracture, weightbearing occurs over a smaller and less congruent joint surface leading to greater concentration of force over a smaller surface area (Hertling & Kessler, 2006). The long term effect of more pressure over a smaller joint surface area could lead to degeneration of the joint.

Although prospective studies investigating the predictive value of decreased ROM in the development of OA have not been reported, it is well documented that individuals with OA of the knee tend to have decreased flexion and extension at the joint (Ersoz & Ergun, 2003; Fishkin, Miller, Ritter, & Ziv, 2002; Messier, Loeser, Hoover,

Semble, & Wise, 1992). The severity of the OA has also been shown to be related to decreased ROM (Ersoz & Ergun, 2003). ROM has not been shown to be a mediator of exercise effectiveness, but decreased knee flexion has been shown to be related to decreased function (Lin, Davey, & Cochrane, 2001; Steultjens, Dekker, van Baar, Oostendorp, & Bijlsma, 2000).

Strength

Strength, especially strength of the quadriceps musculature, is another local intrinsic factor that has been shown to affect the biomechanical environment in which the knee joint functions. Although research is ongoing regarding the role strengthening plays in the treatment of OA of the knee, it is well known that lower extremity strength plays a major role in knee joint shock attenuation during weightbearing activities (Minor, 1999). Increased or uncontrolled loading places the joint at risk for development or progression of disease, making strength an important intrinsic factor that needs to be considered in the study of knee OA.

Decreased quadriceps strength has been shown to be related to the presence of OA in the knee (Hassan et al., 2001; Slemenda et al., 1997). The relationship between hamstring strength and the presence of OA however, is less clear. Some findings demonstrate that individuals with OA were more likely to have hamstring weakness (Fransen, Crosbie, & Edmonds, 2003; Tan, Balci, Sepici, & Gener, 1995) and other studies dispute this result (Slemenda et al., 1997). Researchers also have found that the presence of OA in the knee is related to a decreased ability to maximally contract the quadriceps (Hassan et al., 2001), however this finding has not been supported by others (Lewek, Rudolph, & Snyder-Mackler, 2004). The relationship between weakness and the

development of OA of the knee is likewise unclear with some data supporting this conclusion (Thorstensson, Petersson, Jacobsson, Boegard, & Roos, 2004) and other results showing no such relationship (Slemenda et al., 1998). Strength deficits have not been shown to be linked to the progression of the disease (Brandt et al., 1999). No studies have been reported that describe strength as a modifier in the response to an exercise program in individuals with OA of the knee, but strength has been shown to be positively correlated to function (Topp, Woolley, Khuder, Hornyak, & Bruss, 2000).

Researchers studying knee OA have identified a critical need to describe the subject pool beyond the basic characteristics of arthritis type and joint affected. Investigators are now calling for the inclusion of local intrinsic factors in the interpretation of results of exercise outcome studies in knee OA (Krebs, Herzog, McGibbon, & Sharma, 2003; Sharma, 2003). These factors affect the biomechanical environment of the joint and might influence outcomes associated with exercise in patients with knee OA. However, several barriers exist to the collection of these data in both research and clinical settings. First, data describing these factors can be time consuming to collect, a burden on both the patient and professional. Second, necessary equipment may be cost prohibitive or not commercially available. Finally, special training is needed for the collection and interpretation of certain measures.

When deciding what local intrinsic factors are important to measure, investigators cannot consult the literature for guidance, as there are no definitive data that demonstrate the mediating action of local intrinsic factors on the effect of exercise in patients with knee OA. Therefore, it would be beneficial to identify whether these factors are related to the common outcome measures (typically function and pain) utilized in knee OA

studies. The purpose of this study was to provide an evidence-based recommendation for the inclusion of important, specific local intrinsic factors in the future study of knee OA.

Method

Participants

Data for this study came from participants who are taking part in the Missouri Arthritis Rehabilitation Research and Training Center (MARRTC) Project II, "Exercise for People with Knee Osteoarthritis: Does One Size Fit All?" (a randomized controlled trial funded by the National Institute on Disability and Rehabilitation Research). Forty-six community dwelling adults (29 women, 17 men), 50 years old or older with physician diagnosed OA of the knee, were recruited by advertising in local media, physician offices, and internet sources. Mean age of the participants was 60.4 years of age (SD= 9.22, range 50-90). Mean body mass index (BMI) was 32.25 kg/m^2 (SD=5.47, range 19.54-46.87).

Necessary sample size was determined by the use of a sample size planning table (Cohen, 1988). Parameters necessary for the use of the table include strength of correlation, power and alpha level. For this study, a power of 0.8 and alpha level of 0.05 were selected.

Expected correlations between the specific local intrinsic factors of interest and the measures of function/pain utilized, were not available from the literature. In the absence of data describing the specific variables in question, general descriptors of strength of correlation can be utilized to assist in determination of necessary sample size. Cohen (Cohen, 1988) describes a small correlation as one that ranges from 0.1 to 0.29 and a moderate relationship between 0.3 and 0.49. However, healthcare researchers often use a more robust description of correlational strength, increasing the level defining a small correlation as one ranging from 0.26 and 0.49 and moderate as 0.50 to 0.69

(Munro, 1997). This elevation of the range describing the strength of correlation is in response to the tendency in healthcare research for relatively small correlation coefficients to be statistically significant while not describing a clinically meaningful relationship (Domholdt, 2000). To help assure clinically meaningful results, a correlation within the upper limits of "small" as described by Munro (Munro, 1997) and "medium" as defined by Cohen (Cohen, 1988) was selected. When consulting the sample size planning table, the column for strength of correlation that most closely approximated our selection of correlational size was .4. Utilizing this parameter, in addition to the power and alpha level described previously, generated a required sample size of 46.

Volunteers satisfied the American College of Rheumatology (ACR) Criteria for Classification of OA of the Knee (R. D. Altman, 1991a) summarized as follows:

Yes to one of the following:

- 1,2,3 & 4
- 1,2 & 5
- 1,4, & 5

1. Knee pain for most days of prior month
2. Crepitus on active joint motion
3. Morning stiffness ≤30 min in duration
4. Age ≥ 50 years
5. Bony Enlargement of the knee

Additional inclusion criteria included: a) willingness to exercise regularly and perform all testing sessions over a 6 month timeframe, b) ability to exercise safely and independently at a moderate level of intensity, c), knee pain within the last year, d) qualifying level of pain or functional deficit as noted on the WOMAC Pain or WOMAC Function Scales (Pain: 1 response of at least "moderate" or 2 responses of "minimal"; Function: 2 responses of at least moderate or 4 responses of mild).

Exclusion criteria consisted of: a) age younger than 50, b) inability to independently walk or exercise, c) physical limitations secondary to a condition that is not modifiable with exercise (e.g. active cancer), d) health problem that might be worsened with exercise, e) current participation in conditioning exercise, f) total joint replacement of the knee (past or scheduled) or total joint replacement of the hip within the last 6 months. Eligibility was established by phone interview conducted by the Coordinator of Protocol Services. Approval of this study was obtained from the University of Missouri-Columbia Health Sciences Institutional Review Board, number 1037838.

Materials

This study investigated clinically applicable tests and measures of pain, function, and local intrinsic factors. Pain and alteration of function are the main symptomatic complaints of people with knee OA (Klippel & Dieppe, 1998) and were therefore used as patient-centered measures of disease severity. Measures of function and pain were chosen in accordance with the consensus statement issued from the Outcome Measures in Arthritis Clinical Trials III (Bellamy et al., 1997). Two measures of function (self-reported and observed performance) were utilized, as it has been postulated that these

measures capture unique aspects of the construct function (Sharma, Cahue et al., 2003). Description of materials and methods for the collection of data regarding pain, function, and local intrinsic factors follow.

Western Ontario MacMasters Osteoarthritis Index (WOMAC). Self-Reported function and pain was assessed by the Western Ontario MacMasters Osteoarthritis Index (WOMAC). The WOMAC is a questionnaire (Likert-type scale) developed specifically for the study of OA. The WOMAC is separated into sections describing pain (5 items) and self reported function (17 items). The Likert scale is represented by five responses (0=none, 1=mild, 2=moderate, 3=severe, 4=extreme). Aggregate subscale scores for function (WOMAC Function Scale) and pain (WOMAC Pain Scale) were created by summation of the component item scores. The reliability and construct validity of the WOMAC Pain and Function subscales have been established via a random controlled trial regarding the efficacy of two pharmaceuticals developed for the treatment of OA (Bellamy, Buchanan, Goldsmith, Campbell, & Stitt, 1988).

The reliability of the WOMAC Pain Scale and Function Scale was established for both internal consistency and test–retest values. Internal consistency was tested using Cronbach's alpha and test-retest reliability was tested using Kendall's tau c. Internal consistency for pain was 0.86 and 0.89 (reflecting the two different medications studied). The test-retest reliability (one week interval) was found to be 0.68. The internal consistency for physical function tested 0.95 for each medication. Test-retest reliability was 0.68

Construct validity was established by comparing the results from the WOMAC to indices previously developed for describing OA of the knee. Convergent construct

validity was shown with statistically significant correlation ($p \leq 0.05$) to the (modified) Doyle Index (Doyle, Dieppe, Scott, & Huskisson, 1981) (compared to WOMAC Pain) and the Lequesne Pain and Physical Function Index (Faucher et al., 2003) (compared to WOMAC Pain and Physical Function). Divergent construct validity was also shown by showing differences between indices measuring other constructs (i.e. Bradburn Index of Wellbeing).

Timed Chair Rise Task. Observed functional level was measured via the Timed Chair Rise Task. This test has demonstrated a 2 week test-retest reliability of 0.73 in a group of high functioning individuals aged 70-79 (Seeman et al., 1994) and has been shown to be significantly related to future disability in older adults (Guralnik, Ferrucci, Simonsick, Salive, & Wallace, 1995). This test was performed using a published protocol (Guralnik et al., 1995) and the rate was calculated as per Sharma et al. (2003). Use of rate versus time elapsed allowed inclusion of individuals that could not complete the task (rate of 0). Volunteers placed their folded arms across their chests and stood up from a sitting position as an initial assessment. If subjects are able to accomplish this task, they were then be asked to complete a timed bout of five repetitions with the instructions to complete the activity as fast as they can. Subjects completed the activity from the same armless chair (height of seat 43.18 cm). The Timed Chair Rise Task was reported as the number of repetitions per minute calculated from the time required to complete five chair stands. If an individual was unable to complete the task, a rate of 0 was assigned.

Local intrinsic factors were measured with methods commonly represented in the literature. Clinically applicable measures were utilized when possible. Measurements were limited to devices that are commercially available.

Full leg radiograph. Varus/Valgus Alignment was measured radiographically in a manner similar to a previously reported study of knee OA (Sharma et al., 2001). Subjects stood without shoes with tibial tubercles pointing forward. X-ray beam was centered at knee. Knee alignment in the frontal plane (varus/valgus position) was measured as the angle formed from the intersecting femoral and tibial mechanical axes, reported in degrees to the nearest 10^{th}. The femoral axis was defined as a line drawn from the center of the femoral head to the center of the femoral intercondylar notch. The tibial axis was represented by a line from the center of the ankle talus to the center of the tibial spine. Reliability (one experienced reader) has been shown to be high for this method of measurement with an intraclass correlation coefficient of 0.99 for varus and 0.98 valgus alignment (Sharma et al., 2001).

Joint arthrometer. Total A/P Laxity was measured by a joint arthrometer (KT 1000®, MEDmetric Corporation, San Diego, CA). The KT 1000 ® is a shoebox sized device strapped to the lower leg that measures translation of the tibia on the femur in the sagittal plane (anterior/posterior direction). The reliability of this device has been established in a study on 43 healthy subjects with 2 examiners (Hanten & Pace, 1987). Intraclass correlation coefficients of 0.92 and 0.84 were found for inter-examiner and intra-examiner reliability respectively.

The validity of measurements of A/P laxity taken by the KT 1000® was established with in vitro and in vivo testing (Daniel et al., 1985). Results of in vitro

testing of A/P translation utilizing the KT 1000® were compared to direct measurement via a transducer in cadaveric knees with and without ligamentous disruption. The correlation coefficient between the KT 1000® and direct measurement was found to be 0.97. In vivo measurements of A/P translation were also analyzed in 338 normal controls and 89 individuals with unilaterally disrupted anterior cruciate ligaments. Results of this comparison revealed a significant difference between the translation of the control and the uninjured knees ($p<0.00005$).

The positioning of the arthrometer was completed as described by the manufacturer and the measurement protocol was consistent with a method described in the literature (Hanten & Pace, 1987) and manufacturer instructions. Participants were positioned supine with bolster under thigh such that knee is flexed 20-30° (confirmed with goniometer). Patella pad was aligned with the patella and contact was maintained by gentle constant pressure. The joint line indicator on the arthrometer was aligned with the knee joint line. Posterior pressure of 89 N (20 pounds) was applied to the force handle and released (2nd tone sounds when 89 N of force is applied). The scale measuring translation was then zeroed. This was completed until no zero adjustment was necessary after release of the posterior pressure. Next, an anterior force of 89 N (20 pounds) was applied to the tibia via the force handle (2nd tone) and a reading of anterior/posterior translation was taken (to the nearest 0.5 mm). The same procedure for posterior laxity was completed (zero with anterior force, test with posterior force). Three trials were completed in each direction and maximal translation (to the nearest 0.5 mm) in each direction was summed for total A/P translation.

Dynamometer. Proprioception and Isometric Strength were measured with a Biodex System III® Dynamometer (Biodex Medical Systems, Shirley, New York). The reliability and validity of this unit for assessment of isometric torque and static angular position has been established (Drouin, Valovich-mcLeod, Shultz, Gansneder, & Perrin, 2004). Intraclass correlation coefficients for trial-to-trial and day-to-day measurements were excellent, thus demonstrating excellent reliability (position: trial-to-trial=0.99, day-to-day=0.99; torque: trial-to-trial=1.00, day-to-day=0.99). Criterion validity was demonstrated by excellent correlations between criterion measures and tested values (0.99 for all trials, torque, and position). Number of testers was not reported.

The method of proprioception testing was similar to methods previously reported in research on OA of the knee (Birmingham et al., 2001). Individuals were seated and the knee joint was aligned with the dynamometer. Hips were positioned in neutral rotation and abduction. The trunk was slightly reclined (5° from vertical). Arms were crossed at chest. An air-cast was placed on foot-ankle and filled to 20 mm Hg (the air-cast distributes force of dynamometer pad as well as immobilizes the ankle). Subjects were blindfolded during data-collection, but allowed to view initial practice repetitions. Participants were asked to assume a 90° angle of knee flexion to start a trial (assessed by dynamometer after initial calibration with goniometer). Subjects were then asked to slowly extend the knee and the machine locked at 30°, 45°, or 65° (order randomly assigned). After the dynamometer locked, subjects were instructed to relax and concentrate on this "target" angle. The machine held the subject at the target angle for 15 seconds then released. Upon release, participant returned to 90° flexion. Subject then extended their knee to position they perceived matched the target angle and pressed a

button that locked the dynamometer. The angle and degree difference from target were recorded to the nearest degree. Subjects completed three practice repetitions, and three trials. Proprioception was reported as the average of the sum of degree difference from target angles during the three trials.

Isometric testing was similar to a previously reported study utilizing isometric testing in a knee OA population (Sharma, Hayes et al., 1999). The subject's trunk and lower extremity were positioned as previously described in proprioception section. The trunk was secured with waist and chest straps, and subject grasped handles next to chair. The pad on the tibia was placed 2 cm above the ankle joint line. Knee extension strength was measured at 60° flexion and knee flexion strength at 45°. One warm-up contraction was completed at approximately 50% (subject defined) effort for 5 seconds. The subject then completed four repetitions, each lasting 5 seconds, of maximal effort. One minute rest was given between all repetitions. Results for Extension and Flexion strength were reported as peak torque measured to the nearest 10^{th} in Nm divided by bodyweight in Kg. All instructions, including encouragement of maximal effort were read from a standardized script.

Goniometer. Range of Motion of the knee was measured with a standard plastic goniometer (25 cm movable arms). Knee ROM was reported as the result of subtracting measured extension from total flexion to the nearest degree. Landmarks were chosen consistent with a common ROM testing text (Norkin & White, 2003). The center of rotation of the goniometer was placed over the lateral condyle of the femur. The proximal arm of the goniometer was aligned with the greater trochanter, thus reflecting

the long axis of the femur. The proximal arm was aligned with the lateral malleolus, representing the axis of the tibia.

The reliability and validity of this technique has been established (Brosseau et al., 2001). In this study, two physical therapists completed knee flexion and extension ROM measurements on 60 subjects with various knee restrictions. The intra-tester reliability (ICC) of active knee flexion for both testers was 0.99. The intra-tester reliability of active knee extension was also shown to be high for each tester (ICC of 0.97 and 0.99). Inter-tester reliability was also shown to be high for active knee flexion and extension (flexion: ICC ranging from 0.98 to 0.98; extension: ICC ranging from 0.89 to 0.93).

The criterion validity of goniometric measurement of ROM of the knee was established by comparing values obtained with a standard goniometer with measurements taken from radiographs. Active knee flexion showed high correlations with radiographic measures with r values ranging from 0.98 to 0.99. Conversely, the criterion validity of active knee extension was shown to be moderate to low with correlations ranging from 0.39 to 0.44.

Procedure

Data was collected from individual participants in three test sessions within a 2 week period. Test session 1 consisted of informed consent, physical exam, completion of WOMAC Pain and Function Scales and the Timed Chair Rise Task. The physical exam was completed by a single, experienced physical therapist and consisted of measurements of ROM and A/P laxity. Time allotted for test session was approximately 2 hours.

Test session 2 consisted of proprioception and isometric strength testing. The order of right or left leg was randomized. After leg was chosen, variables of type of test

(isometric/proprioception), isometric strength of muscle group (hamstring/quadriceps contraction) and target angles for proprioception were randomized. Testing for the second leg was completed in the order determined from the first. All instructions to subjects were given from standardized script. Time allotted for test session 2 was approximately 1.5 hours.

Test session 3 occurred within 2 weeks of session 1 testing and consisted of a bilateral, full leg radiograph. Radiographs were viewed digitally. Measurement of varus/valgus at the knee was conducted with Centricity Pictures Archiving Communications System ^{TM} 2.0 software (General Electric Healthcare, Fairfield, CT). All measurements and grading of knee were completed by a radiologist.

Prior to the commencement of data collection for this study, 2-3 mock data collection trials were administered to improve the data collection process. Volunteers for the mock sessions also satisfied the inclusion/exclusion criteria for this study. One trial subject was naive to the experimental procedures. Upon completion of the mock data collection trial, oral feedback was gathered to refine the data collection process.

Design and Analysis

The purpose of this study was to provide an evidence based rationale for the inclusion of specific local intrinsic factors in the future study of knee OA. To accomplish this aim, the following statement was evaluated: if local intrinsic factors influence function/pain, then individuals with different levels of local intrinsic factors will have different levels of function/pain. This statement was evaluated by testing the following research hypothesis: there will be a significant relationship between function/pain and measures of local intrinsic factors. The null hypotheses were represented thusly:

H01: There will be no significant relationship between self-reported function as measured by the WOMAC Function Scale, and the following local intrinsic factors: Varus/Valgus Alignment, A/P Laxity, Proprioception, Knee Extension Strength by Bodyweight, Knee Flexion Strength by Bodyweight, and Knee ROM.

H02: There will be no significant relationship between observed function as measured by the Timed Chair Rise Task, and the following local intrinsic factors: Varus/Valgus Alignment, A/P Laxity, Proprioception, Knee Extension Strength by Bodyweight, Knee Flexion Strength by Bodyweight, and Knee ROM.

H03: There will be no significant relationship between pain as measured by the WOMAC Pain Scale, and the following local intrinsic factors: Varus/Valgus Alignment, A/P Laxity, Proprioception, Knee Extension Strength by Bodyweight, Knee Flexion Strength by Bodyweight, and Knee ROM.

Recommendations for inclusion of specific local intrinsic factors for future study were also based on the determination of whether significantly correlated factors made a unique contribution to a regression model.

This study contained three dependent variables: one measure of pain (WOMAC Pain Scale) and two measures of function (WOMAC Function Scale and Timed Chair Rise Task). The local intrinsic factors Varus/Valgus Alignment, A/P Laxity, Proprioception, Extension Strength by Bodyweight, Flexion Strength by Bodyweight and Knee ROM were considered independent variables. The local intrinsic factors were

measured on the knee that satisfied the American College of Rheumatology (ACR) Criteria for Classification of OA of the Knee described previously. If both knees satisfied the criteria, the measurements from the more affected knee (by local intrinsic factor) were utilized.

Prior to data analysis, all variables were inspected to ensure satisfaction of usual and customary parameters of normality, linearity and homoscedasticity (Appendix A). All variables were found to satisfy these customary assumptions. Because of this, parametric data analysis techniques were utilized. Further assumptions specific to regression (independence of errors, normality, linearity, and homoscedasticity between predicted DV scores and errors of prediction) were also satisfied (Appendix A).

Data analysis was performed in three steps. First, descriptive statistics were calculated for all variables. Next, bivariate analysis was completed between each local intrinsic factor and measure of function/pain using Pearson correlation procedures (r). Statistical significance was set at $p \leq 0.05$. Last, regression models were constructed for each measure of function and pain as the dependent variable. Models were constructed by entering all the independent variables that demonstrated significant bivariate correlation ($p \leq .05$) to the corresponding dependent variable. Squared semipartial correlations and significance levels for the unique contributions of each local intrinsic factor were reported.

Results

Three dependent variables (self-reported function, observed function, and pain) were utilized in this study. Self-reported function was measured by the WOMAC Function Scale (greater functional loss represented by higher scores). Observed function was measured by the Timed Chair Rise Task (higher scores indicative of better function). Pain was measured by the WOMAC Pain Scale (higher scores representing more pain). Correlations among the dependent variables were calculated. Pain was correlated with both measures of function (WOMAC Function Scale, r=0.73, p=0.000; Timed Chair Rise Task, r=-0.31, p=0.039). The two measures of function however were not significantly correlated (r=-0.24, p=0.105).

Descriptive statistics for all variables are included in Table 1.

Table 1.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
WOMAC Pain Scale (0-20)	46	2.00	15.00	6.67	2.76
WOMAC Function Scale (0-68)	46	.00	53.00	25.04	11.32
Timed Chair Rise Task (repetitions per minute)	46	7.07	39.22	24.06	7.06
Varus/Valgus Alignment (degrees)	46	.10	14.30	5.21	3.63
AP Laxity (mm)	46	4.00	19.00	9.32	3.10
Proprioception (degrees)	46	2.33	14.00	6.49	2.88
Extension Strength by BW (Nm/Kg)	46	.43	2.22	1.17	.46
Flexion Strength by BW (Nm/Kg)	46	.23	1.06	.57	.19
Knee ROM (degrees)	46	93.00	145.00	123.73	12.35

The correlations among local intrinsic factors are described in Table 2. The only local intrinsic factors that were highly correlated with one another were Extension Strength by Bodyweight and Flexion Strength by Bodyweight (r=0.73, p=0.000).

Table 2.

Correlations Among Local Intrinsic Factors

		Varus/Valgus Alignment	AP Laxity	Proprio-ception	Ext Strength by BW	Flex Strength by BW	Knee ROM
Varus/Valgus Alignment	Pearson r	1	.255	.049	-.094	-.271	-.317(*)
	Sig. (2-tailed)		.087	.746	.532	.069	.032
	N	46	46	46	46	46	46
AP Laxity	Pearson r	.255	1	.039	.065	.040	.199
	Sig. (2-tailed)	.087		.799	.667	.794	.184
	N	46	46	46	46	46	46
Proprio-ception	Pearson r	.049	.039	1	.019	-.089	-.129
	Sig. (2-tailed)	.746	.799		.898	.556	.392
	N	46	46	46	46	46	46
Ext Strength by BW	Pearson r	-.094	.065	.019	1	.731(**)	.314(*)
	Sig. (2-tailed)	.532	.667	.898		.000	.033
	N	46	46	46	46	46	46
Flex Strength by BW	Pearson r	-.271	.040	-.089	.731(**)	1	.371(*)
	Sig. (2-tailed)	.069	.794	.556	.000		.011
	N	46	46	46	46	46	46
Knee ROM	Pearson r	-.317(*)	.199	-.129	.314(*)	.371(*)	1
	Sig. (2-tailed)	.032	.184	.392	.033	.011	
	N	46	46	46	46	46	46

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

The correlations between each local intrinsic factor and measures of function and pain are included in Table 3. Four local intrinsic factors had a statistically significant correlation with measures of function/pain. Varus/Valgus Alignment was significantly correlated with the WOMAC Pain Scale (r=0.48, p=0.001) and the WOMAC Function Scale (r=0.38, p=0.009). A/P Laxity was also significantly correlated with WOMAC Pain Scale (r=0.30, p=0.043) and the WOMAC Function Scale (r=0.37, p=0.011). Knee ROM was significantly correlated to the WOMAC Function Scale (r=-0.35, p=0.016).

Knee Extension Strength by Bodyweight was correlated with the Timed Chair Rise Task (r=0.32, p=0.030).

Table 3.

Correlations of Local Intrinsic Factors with Measures of Function and Pain

		WOMAC Pain Scale	WOMAC Function Scale	Timed Chair Rise Task
Varus/Valgus Alignment	Pearson Correlation	.482(**)	.382(**)	-.044
	Sig. (2-tailed)	.001	.009	.770
	N	46	46	46
AP Laxity	Pearson Correlation	.300(*)	.372(*)	-.029
	Sig. (2-tailed)	.043	.011	.850
	N	46	46	46
Proprioception	Pearson Correlation	-.106	.004	.122
	Sig. (2-tailed)	.485	.980	.420
	N	46	46	46
Ext Strength by BW	Pearson Correlation	-.178	-.187	.320(*)
	Sig. (2-tailed)	.237	.214	.030
	N	46	46	46
Flex Strength by BW	Pearson Correlation	-.268	-.221	.218
	Sig. (2-tailed)	.072	.140	.146
	N	46	46	46
Knee ROM	Pearson Correlation	-.245	-.354(*)	.107
	Sig. (2-tailed)	.101	.016	.480
	N	46	46	46

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

The relationship between measures of function/pain and age was also investigated (see Table 4). No significant relationships were found.

Table 4.

Correlations of Measures of Function and Pain with Age

		Age today
WOMAC Pain Scale	Pearson Correlation	-.030
	Sig. (2-tailed)	.845
	N	46
WOMAC Function Scale	Pearson Correlation	.097
	Sig. (2-tailed)	.523
	N	46
Timed Chair Rise Task	Pearson Correlation	-.172
	Sig. (2-tailed)	.252
	N	46

Regression models were constructed with measures of function and pain serving as the dependent variable. Local instrinsic factors were selected as independent variables and entered into multiple regression models based on their statistically significant relationship with the dependent variable when analyzed singularly ($p \leq 0.05$). Data were examined for collinearity prior to analysis of regression models constructed utilizing more than one variable. For the model utilizing the WOMAC Pain Scale as the dependent variable (see Table 5) tolerances were high, with both at 0.94. Variance Inflation Factors (VIF) were low at 1.07. For the model using the WOMAC Function Scale (see Table 6), tolerances remained high ranging from 0.79 to 0.85. Variance Inflation Factors were low with a range of 1.18 to 1.26. Collinearity diagnostics demonstrated no redundancy in the independent variables.

Table 5.

Coefficients Summary- WOMAC Pain Scale as Dependent Variable

	Standardized Coefficients	t	Sig.	Squared Semipartial Correlation	Collinearity Statistics	
	Beta				Tolerance	VIF
(Constant)		2.882	.006			
Varus/Valgus Alignment	.434	3.211	.003	.176	.935	1.070
AP Laxity	.190	1.405	.167	.034	.935	1.070

a Dependent Variable: WOMAC Pain Scale

Table 6.

Coefficients Summary- WOMAC Function Scale as Dependent Variable

	Standardized Coefficients	t	Sig.	Squared Semipartial Correlation	Collinearity Statistics	
	Beta				Tolerance	VIF
(Constant)		3.315	.002			
Varus/Valgus Alignment	.155	1.111	.273	.019	.794	1.259
AP Laxity	.410	3.027	.004	.142	.848	1.179
Knee ROM	-.386	-2.800	.008	.122	.816	1.226

a Dependent Variable: WOMAC Function Scale

Next, total variance explained by the model, unique contribution of each independent variable (squared semipartial correlation coefficients), and the significance of the unique contribution were obtained. As noted in Table 7, Extension Strength by Bodyweight was the only local intrinsic factor significantly related to the Timed Chair Rise Task. The R^2 value of the model was 0.10. Because this model contained only one variable, the squared semipartial correlation coefficient for Extension Strength by Bodyweight was also 0.10. and the contribution of the variable was significant at p=0.030.

Varus/Valgus Alignment and A/P Laxity combined had an R^2 value of 0.27 when predicting scores of the WOMAC Pain Scale (Table 8). The unique contribution of each independent variable (Table 5) was 18% and 3% respectively. Varus/Valgus Alignment contributed significantly to the model (p=0.003), while A/P Laxity did not (p=0.167) (Table 5).

Varus/Valgus Alignment, A/P Laxity, and Knee ROM combined had a R^2 value of 0.35 when predicting scores on the WOMAC Function Scale (Table 9). The unique contribution of each local intrinsic factor was 2%, 14% and 12% respectively (Table 6). A/P Laxity (p=0.004) and Knee ROM (p=0.008) both contributed significantly to the model, while Varus/Valgus Alignment (p=0.273) did not.

Table 7.

Model Summary-Timed Chair Rise Task as Dependent Variable

R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
				R Square Change	F Change	df1	df2	Sig. F Change
.320(a)	.103	.082	6.76359	.103	5.031	1	44	.030

a Predictors: (Constant), Ext Strength by BW

Table 8.

Model Summary-WOMAC Pain Scale as Dependent Variable

R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
				R Square Change	F Change	df1	df2	Sig. F Change
.516(a)	.266	.232	2.42338	.266	7.797	2	43	.001

a Predictors: (Constant), AP Laxity, Varus/Valgus Alignment

Table 9.

Model Summary-WOMAC Function Scale as Dependent Variable

R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
				R Square Change	F Change	df1	df2	Sig. F Change
.590(a)	.348	.302	9.46740	.348	7.480	3	42	.000

a Predictors: (Constant), Knee ROM, AP Laxity, Varus/Valgus Alignment

The null hypotheses for this study stated that there would be no significant relationship between the dependent variables (function and pain) and the independent variables (local intrinsic factors). Results of this study support the rejection of these hypotheses. The WOMAC Pain scale was significantly correlated to the local intrinsic factors of Varus/Valgus Alignment (r=0.48, p=0.001) and A/P Laxity (r=0.3, p=0.043). The WOMAC Function scale was related to Varus/Valgus Alignment (r=0.38, p=0.009), A/P Laxity (r=0.37, p=0.011) and Knee ROM (r=-0.35, p=0.016). Finally, the Timed Chair Rise Task was correlated to Extension Strength by Bodyweight (r=0.32, p=0.030).

Discussion

Knee osteoarthritis is one of the most common conditions affecting older adults, often leading to pain and decreased function. Exercise is a commonly prescribed treatment for this disease. Studies have investigated the effect of exercise on function and pain in individuals with knee OA, and although outcomes have been promising, consistently positive results have not been demonstrated. The ability of these studies to adequately describe the effect of exercise in a population of individuals with knee OA has been hampered by the heterogeneity of the subject pool in terms of the local intrinsic factors present in the knee. These factors are mechanical in nature, impacting the load distribution and neuromuscular control of the joint, and may influence the effect of a mechanical interventions, such as exercise.

Emerging research suggests that differences in local intrinsic factors may impact the effect of exercise in patients with knee OA, but few studies have adequately characterized the subject pool by these factors. Furthermore, the use of these factors in the interpretation of intervention outcomes is in its infancy. Researchers have acknowledged the need to more fully describe the subject pool in terms of local intrinsic factors, but several obstacles exist. Measurement of these factors are time consuming and costly, often requiring specialized equipment and training. In addition to the potential high cost of these measures, there is a paucity of evidence to guide the selection or interpretation of specific tests. This study provides valuable information that serves to characterize a subject pool in terms of six local intrinsic factors, as well as give recommendations on the selection of local intrinsic factors to include in future study.

Patient centered measures of knee OA severity were utilized in this study as dependent variables. As described previously, two measures of function (self-reported and observed performance) were utilized in this investigation. Researchers have theorized that different features of the construct "function" are described by self-reported vs. observed measures (Sharma, Cahue et al., 2003). The non-significant correlation between the WOMAC Function Scale (self report) and the Timed Chair Rise Task (observed) in this study supports this supposition ($r=-0.24$, $p=0.105$). Furthermore, regression models with each measure of function used as the dependent variable do not include any of the same local intrinsic factors as predictors (discussed later).

Although the WOMAC Function Scale and the Timed Chair Rise Task were not correlated with one another, pain was correlated with the two measures of function ($r=0.73$, $p=0.000$; $r=-0.31$, $p=0.039$, respectively). Functional deficits in individuals with knee OA are the consequence of many factors, one of which is the presence of pain (Klippel & Dieppe, 1998). The correlations among these measures support the role of pain contributing to functional deficits.

The descriptive statistics in Table 1 can be used to characterize the subject pool with respect to the local intrinsic factors examined. This characterization assists future investigators in making decisions regarding the ability to generalize the results of this study for use in future research. Comparisons between the factors in this study and factors reported in published research, demonstrate that the published means are within 1 standard deviation of the means contained in this study (Birmingham et al., 2001; Brage, Draganich, Pottenger, & Curran, 1994; Messier et al., 1992; Sharma, Hayes et al., 1999;

Sharma et al., 2001). This suggests that the volunteer pool studied in this investigation was similar to those reported in other knee OA research.

When attempting to adequately and efficiently describe a subject pool, it is beneficial to utilize variables that represent unique constructs. This can be demonstrated conceptually by the discussion of theory and also evaluated statistically by investigating the presence of correlations among the factors. Utilizing factors that are highly correlated and that describe similar theoretical constructs would unnecessarily duplicate testing-thus wasting valuable resources without providing additional information.

As can be seen in Table 2, the only local intrinsic factors that were highly correlated with one another were the strength of the knee flexors and extensors ($r=0.73$, $p=0.000$). From a conceptual standpoint, extension and flexion strength are related by the obvious construct of "strength". Contraction of the knee flexors and knee extensors both produce motion of the joint, but affect the knee differently with respect to other mechanical forces at the knee. Although co-contraction of the flexors and extensors are related to the stability of the knee (Hertling & Kessler, 2006), the knee extensors have been suggested to play a larger role in dampening the effect of weight bearing on the joint (Minor, 1999). The flexors and extensors also affect joint shear differently, with contraction of the flexors causing the tibia to move posterior on the femur and the extensors causing anterior translation. Because of the dissimilar effect on the mechanics of the joint, knee flexion and extension strength still warrant individual consideration, even in the presence of high correlation with one another.

Other statistically significant correlations were present among the variables but were generally small. Knee ROM was correlated with Varus/Valgus Alignment

(r=-0.32, p=0.032), Extensor Strength by Bodyweight (r=0.31, p=0.033) and Flexor Strength by Bodyweight (r=0.37, p= 0.011). Although statistically significant, correlations of this size do not pose issues with variable duplication (Tabachnick & Fidell, 2001).

In addition to statistical analysis, the conceptual and clinical background of the variables must also be considered. While strength relates primarily to muscular contraction, knee ROM and A/P laxity are associated with non-contractile elements such as the anterior cruciate ligament (ACL) and the joint capsule. Involvement of one of these structures might impact both A/P laxity and knee ROM, however the ACL has significantly more impact on A/P laxity, whereas the capsule is associated with joint ROM (Hertling & Kessler, 2006). Both structures have been shown to be negatively affected by knee OA, with stiffening of the joint capsule and degrading of the ACL occurring as OA progresses (Fishkin et al., 2002; Wada, Imura, Baba, & Shimada, 1996). Because of the mechanical dissimilarity between these structures, a correlation between Knee ROM and A/P Laxity would not be anticipated. Results from this study support this supposition (r=0.20, p=0.184, Table 2).

Varus/valgus alignment has been shown to be associated with joint laxity but in the frontal plane, not in an A/P direction. This increase in laxity may be due more to the tendency for individuals with high levels of varus/valgus alignment to develop decreased joint space (Sharma et al., 2001; Wada et al., 1996). In addition to laxity, varus/valgus alignment has also been shown to be related to significant alterations in the weight distribution at the knee. A varus position has been shown to place a greater load in the medial compartment while a valgus position increases weight bearing on the lateral side.

Because of the effect on weight bearing (unique to varus/valgus alignment with respect to A/P laxity) and the differing planes of instability associated with the variables, a correlation was not expected between the Varus/Valgus Alignment and A/P Laxity. This expectation was confirmed by our results ($r=0.26$, $p=0.087$, Table 2).

Joint proprioception is a multisystem mechanism by which the body consciously and unconsciously perceives limb position (Sharma, 1999). The body uses input from multiple different receptors originating from the muscle, joint capsule and ligamentous system to interpret joint position sense (Sharma, 1999). Because of the multifaceted nature of this function, a low correlation with other factors was anticipated. Our results supported this supposition with the highest correlation between proprioception and other local intrinsic factors equaling $r=-0.13$, $p=0.392$ (Knee ROM, Table 2).

In summary, the local intrinsic factors investigated in this study demonstrated a sound theoretical rationale for their inclusion. In addition, low correlations existed among the factors (with the exception of Knee Extensor and Flexor Strength by Bodyweight) Due to these low correlations, and the conceptual and clinical differences in the constructs represented by the local intrinsic factors, analysis of the relationship between these factors and measures of function/pain appear to be warranted at an individual level.

The second component of data analysis was to determine if any local intrinsic factors were significantly correlated to measures of function or pain. In this study, the relationship between six independent variables and three dependent variables were examined (a total of 18 correlations). An alpha level of 0.05 was chosen. To guard against the cumulative nature of type I error, some researchers complete a Bonferroni

correction to the alpha level required for statistical significance. Completing this correction for this study would adjust the significance level from p=0.05 to p=0.002. This would limit the significant correlations found in this study to the relationship between Varus/Valgus Alignment and the WOMAC Pain Scale (see Table 3). Because of the exploratory nature of this study the author felt that the potential negative consequence of incurring a type II error (and thus not collecting potentially important data) outweighed the potential negative effect of a type I error. Because of this, the Bonferroni correction will not be considered when making recommendations for inclusion of measures of local intrinsic factors in future research.

This study demonstrated that four of the six local intrinsic factors examined (Valgus/Varus Alignment, A/P Laxity, Knee ROM, and Extension Strength by Bodyweight) were significantly correlated with common measures of function/pain utilized in the study of knee OA (see Table 3). Valgus/Varus Alignment was significantly correlated with the WOMAC Pain Scale (r=0.48, p=0.001), and the WOMAC Function Scale (r=0.38, p=0.009). A/P Laxity was also significantly correlated with the WOMAC Pain and Function scales (r=0.30, p=0.043 and r=0.37, p=0.011 respectively). Knee ROM was correlated to the WOMAC Function Scale only (r=-0.35, p=0.016). Knee Extension Strength by Bodyweight was correlated with the Timed Chair Rise Task (r=0.32, p=0.030).

The final component of data analysis in this study was to determine if local intrinsic factors previously found to be related to a measure of function or pain, made a significant contribution to a model predicting the variance in that measure. Prior to performing this analysis, the possibility of age as a confounding variable was

investigated. As can be seen in Table 4, age was not significantly correlated with any of our pain and function measures. Because of this lack of correlation, it was not necessary to control for age in our models.

The presence of collinearity is also an important consideration when developing regression models. Tolerance values were considerably greater than 0, with the lowest value for any variable in any model being 0.79 (Tables 5, 6). Variance Inflation Factors for all models were also quite acceptable with the largest of any variable for any model being 1.26. Due to the absence of large bivariate correlations among the local intrinsic factors of interest, and the negative results of the collinearity diagnostics, no variable redundancy was found.

After confirming that age was not a confounding influence on the dependent variables, and finding no independent variable redundancy, regression models were constructed. Measures of function and pain served as the dependent variables. The local intrinsic factors that demonstrated significant bivariate correlations with the individual dependent variables ($p \leq 0.05$) were entered in the regression models as independent variables.

A regression model with the Timed Chair Rise Task as the dependent variable was constructed. Extension Strength by Bodyweight was the only local intrinsic factor significantly correlated to this measure of function and was used as the independent variable. This model was able to explain 10% of the variance in the Timed Chair Rise Task and was statistically significant ($p=0.03$, Table 7).

A regression model with the WOMAC Function Scale as the dependent variable. Varus/Valgus alignment, A/P Laxity, and Knee ROM were used as independent

variables. The model as a whole was able to explain 35% of the variance in the dependent variable and demonstrated a significant relationship between the independent and dependent variables (p=0.000, Table 9). Varus/Valgus Alignment's unique contribution to the model explained 2% variance of the dependent variable, while A/P Laxity and Knee ROM explained 14% and 12% of the variance respectively (Table 6). Individually, both A/P Laxity and Knee ROM contributed significantly to the model (p=0.004, p=0.008 respectively, Table 6). Although Varus/Valgus Alignment had the highest individual correlation with the WOMAC Function Score (r=0.38 compared to r=0.37 for A/P laxity and r=-0.35 for knee ROM, Table 3) it was not found to add significantly to the model (p=0.273, Table 6).

An explanation for why Varus/Valgus Alignment did not make a significant unique contribution to the model, even though it had the largest bivariate correlation to the dependent variable of all the factors, may lie with how the factors in question share variance. Varus/Valgus Alignment had a higher correlation with A/P Laxity (r=0.26; p=0.087) and Knee ROM (r=-0.317; p=0.03) than A/P Laxity had with Knee ROM (r=0.2; p=0.18; all Table 2). This suggests that the unique contribution of Varus/Valgus Alignment to the model was negatively affected to a greater degree by the relationship among the three local intrinsic factors.

The last dependent variable for which a model was constructed was the WOMAC Pain Scale. This model included A/P Laxity and Varus/Valgus Alignment as independent variables and was able to explain 27% of the variance in the dependent variable (Table 8). This model demonstrated a significant relationship between the independent and dependent variables (p=0.001, Table 8).

Analysis of the independent variables showed that Varus/Valgus Alignment and Knee Laxity had a unique contribution to the model of 18% and 3% respectively (Table 5). The unique contribution of Varus/Valgus Alignment was significant (p=0.003, Table 5). The unique contribution of A/P Laxity, however, was not found to be significant (p=0.167, Table 5).

Combinations of the local intrinsic factors Varus/Valgus Alignment, A/P Laxity, Knee Extension Strength by Bodyweight and Knee ROM have all been included (in some combination) in models that significantly predict measures of function or pain. When removing those variables that did not provide a significant, unique contribution, these four local intrinsic factors were still included in at least one model. This significant unique contribution to a model, coupled with the local intrinsic factor's initial bivariate correlation with at least one measure of function or pain, demonstrates a statistical rationale for considering these variables for future study. Further reflection on the neuromuscular and load distribution qualities of these local intrinsic factors, also demonstrates a conceptual and clinical reason to include them in future characterization of patients with knee OA.

The varus/valgus alignment of the knee has been demonstrated to influence the forces directed at the joint, specifically an adduction or abduction joint moment. A joint moment can be thought of as the turning or rotational effect caused by a force that is distant to the rotational axis. The alignment of the lower limb at the knee is a chief determinant of the length of the mechanical axis. During weight bearing, the location of the ground reaction force in relation to the mechanical axis of the joint, will determine the direction, either adduction or abduction, of the moment. The distance from the center of

rotation and the amount of force will determine the magnitude of the moment (moment = force x distance). In a position of malalignment (either varus or valgus), the ground reaction force will act at a distance from the joint line. Forces directed in this manner will cause a rotational effect at the knee, increasing the load on the joint (e.g. varus position increasing load on the medial aspect of the joint). As the malalignment increases, the ground reaction force is applied at a greater distance from the center of rotation, thus increasing the load on the affected joint surface. Likely due to this increase in load, varus/valgus malalignment has been shown to be associated with both the progression and severity of knee OA (Birmingham et al., 2001; Cerejo et al., 2002; Cicuttini, Wluka, Hankin, & Wang, 2004; Miyazaki et al., 2002; Sharma et al., 2001). This increased tendency for abnormal joint loading may influence the relationship between this factor and pain/function.

A/P laxity can be defined as the amount of intra-articular forward and backward sliding of the tibia with respect to the femur. Increased A/P laxity alters the force and shear distribution at the knee and has been associated future development of knee OA (Lundberg & Messner, 1997; McDaniel & Dameron, 1983; Sherman et al., 1988). It has also been demonstrated that A/P laxity has a tendency to increase as the disease progresses until the later stages of the disease (Brage et al., 1994; Wada et al., 2001). This lack of joint stability and alteration of force and shear distribution may impact the relationship between A/P Laxity and measures of pain/function.

As mentioned previously, decreased knee ROM could potentially alter the forces directed at the knee joint. Weight bearing on a partially flexed knee, due to the inability to fully extend the joint, decreases the joint contact surface area, thus concentrates the

force on a smaller articular surface (Hertling & Kessler, 2006). Although no prospective studies have been reported that relate decreased ROM to the incidence of knee OA, it is hypothesized that increase joint load could be related to the development of knee OA (Sharma, 2001). Change in the loading pattern of the knee with decreased ROM may not be the only deleterious effect of function. Many functional activities require a significant degree of knee ROM. Limitations in knee flexion or extension could directly interfere with activities such as walking, running or picking up something off the floor (Clarkson, 2000). This change in loading coupled with limitations in daily activites associated with decreased knee ROM may influence the scores on the WOMAC Function Scale.

Strength of the knee extensors assists in shock attenuation of the joint during weightbearing activities. Strength of the knee extensors also plays a crucial role in functional activities including sitting and rising from a chair. (Clarkson, 2000). This direct contribution to the action measured in the Timed Chair Rise Task is very likely to impact the score on this measure.

Researchers have recognized the need to measure local intrinsic factors of the knee and called for the inclusion of these data in future research (Sharma, 2003). The results from this study support the consideration of four specific variables: Varus/Valgus Alignment, A/P Laxity, Knee ROM and Extension Strength by Bodyweight. The local intrinsic factors associated with function and pain identified in this study can be assessed with measures commercially available to the clinician and researcher. Further research would be beneficial however to allow more widespread data collection of varus/valgus alignment and A/P laxity.

The gold standard for varus/valgus alignment requires a standing, long leg radiograph (Hinman, May, & Crossley, 2006) and was the method utilized in this current study. Although the gold standard, utilization of the long leg radiograph is somewhat problematic. This radiograph is expensive (typical cost over $200), exposes the patient to radiation, and often adds to the complexity of subject examination scheduling. Measures using an inclinometer, caliper, and plumb line are non-radiographic methods that have been shown to correlate with the gold standard for knee OA patients with primarily varus alignment (r=0.80, r=0.76, r=0.71 respectively) (Hinman et al., 2006). Further validation of these methods on a knee OA population not biased toward varus alignment is warranted before these methods can be routinely utilized by clinicians and researchers.

The gold standard for the measurement of A/P laxity is the use of an arthrometer. A commercially available arthrometer that is commonly utilized by clinicians and researchers seeking to quantify the amount of A/P laxity in the knee is the KT 1000® (MEDmetric Corporation, San Diego, CA). The cost of this arthrometer is approximately $4,000, making collection of this data cost prohibitive for some clinicians and researchers. Clinical methods of evaluation, such as the Lachman test, have not been show to be a reliable and valid method of quantification of A/P laxity (Benvenuti, Vallotton, Meystre, & Leyvraz, 1998). Further research is necessary to develop and validate a clinical measure for quantification of tibial translation that does not rely on a costly arthrometer.

The gold standard for measurement of knee extension strength is the use of a electric dynamometer (Martin et al., 2006). This method of data collections was used in this study. Although commercially available, this device is costly and requires a fixed

location for use. Portable, less costly methods do exist however, for strength assessment. One such method, the hand held dynamometer, has been shown be valid when compared to the gold standard (Martin et al., 2006). In this study, knee strength measured with a hand held dynamometer was highly correlated to measures taken by an electric dynamometer in an older population ($r=0.91$, $p<0.0001$). A hand held dynamometer is commercially available for under $1000 (AliMed ®, Dedham, MA). This method of measurement should allow more widespread data collection by future researchers and clinicians.

Unlike the assessment of knee alignment, laxity, and strength, measurement of the ROM of the knee requires minimal equipment and cost. Measurement of knee flexion and extension with a standard goniometer (cost under $25, AliMed ®, Dedham, MA) and has been shown to be a reliable and valid measure of knee ROM (Brosseau et al., 2001). Measurement of knee ROM is also not time consuming, adding only minutes to the physical exam.

Data from this study do not support the collection of proprioception measures. Although other methods exist for the collection of these data, the gold standard for this measure is the use of a dynamometer. One such dynamometer is the Biodex System III® Dynamometer (Biodex Medical Systems, Shirley, New York). Purchase of this equipment would be cost prohibitive for many clinicians and researchers with a cost of over $50,000. Collection of proprioception in this manner is also time consuming. In this study, one hour was set aside for this measurement.

Recommendations from this study may ultimately aid in the construction of more effective treatment programs for the person with knee OA. The pathogenesis of knee OA

is poorly understood. The information that is available suggests many factors may be involved (Sharma, 2001). The same can be said of the factors that influence progression of the disease. Although radiographic evidence of the disease (joint space narrowing, presence of osteophytes, sclerosis, etc.) tends not to improve over time, intervention via exercise can cause positive changes in function and pain. Studies reporting the effect of exercise have been conducted on groups poorly defined by characteristics that are mechanical in nature. Furthermore, outcomes have not been interpreted in light of these descriptors. Since the determinants of the development and course of the disease are mostly likely multifactorial, it is reasonable to consider that a "one size fits all" approach to exercise prescription would not be as effective as a more tailored method.

In this study, we have characterized a subject pool by six variables that impact the load distribution and neuromuscular control of the joint. Furthermore, we have identified four local intrinsic factors that are significantly related to measures of function or pain. We have also shown that these four factors play a significant, unique role in the prediction of measures of function and pain. Due to this statistical relationship, and supported by a strong clinical rationale, it is recommended that future researchers and clinicians include measures of Varus/Valgus Alignment, A/P Laxity, Knee ROM and Extension Strength by Bodyweight in the evaluation of knee OA. These data may assist in the formulation of hypotheses regarding how these individual differences in the mechanical environment of the joint might influence the effect of exercise as an intervention in knee OA. Noting the influence these local intrinsic factors have on the mechanical environment of the knee, and considering the relationship these factors have

with function and pain, researchers and clinicians may ultimately be able to improve the use of exercise as a treatment for knee osteoarthritis.

Appendix A

Data Screening and Satisfaction of Assumptions

The data in this analysis contains 9 variables.

Dependent:

1. WOMAC Pain Scale
2. WOMAC Function Scale
3. Timed Chair Rise Task

Independent:

1. Varus/Valgus Alignment
2. A/P Laxity
3. Proprioception
4. Extension Strength by Bodyweight
5. Flexion Strength by Bodyweight
6. Knee ROM

Prior to analysis, all variables were screened for accuracy of data entry, missing values and satisfaction of the usual and customary parameters of normality, linearity, and homoscedasticity. All data were examined for data entry errors and missing values by sorting each individual variable in ascending and descending order to visually inspect entries that were outside the scale of measurement. No missing or inaccurate entries were found with this inspection.

The data were next examined for univariate and multivariate outliers. Inspection of univariate outliers was accomplished both visually and statistically. Visual inspection included bivariate scatter plots (Figure A1), Histograms, and normal probability plots (Figures A3). Visual inspection revealed possible outliers for WOMAC Pain Scale, A/P Laxity, Proprioception, Flexion Strength by Bodyweight and ROM. Statistical

examination of outliers was then accomplished via frequency table of Z scores for all variables (Table A1). No z scores were noted above 3.29 (Tabachnick & Fidell, 2001). Multivariate outliers were examined by calculation of Mahalanobis Distances and subsequent inspection of its frequency table. No multivariate outliers were noted using $p<0.001$ (chi square value at 9 df). Because of the appropriate z scores and non-significant Mahalanobis Distances, no univariate or multivariate outliers were identified.

Data were next examined for normality both visually and statistically. Visual inspection of the histograms and QQ plots suggested a normal distribution (Figures A3). Skewness and kurtosis were examined for all variables. Skewness was found to be acceptable below ± 1 but Kurtosis was questionable at 1.628 for A/P Laxity (Tabachnick & Fidell, 2001). A Shapiro-Wilk test for normality ($p<0.001$) was then completed. No significant results were found with this testing (Table A4). Data were thus judged to satisfy the requirements of normality.

The linearity of the data were examined next. Between variable linearity was inspected using bivariate scatter plots (Figure A1). All scatter plots showed a generally ovid pattern. Linearity was thus judged to be satisfactory.

Homoscedasticity was demonstrate by visual inspection of the bivariate scatterplots (Figure A1) and residual scatterplots (Figure A2). A cone shaped pattern to the scatterplots indicates heteroscedasticity, and this was not found. A general ovid shape of the bivariate scatterplots was present and a rectangular shape of the residual scatterplots was found. Examination of scatterplots suggested homoscedasticity.

Further examination of the residual scatterplots demonstrated satisfaction of assumptions specific to regression (normality, linearity, and homoscedasticity between

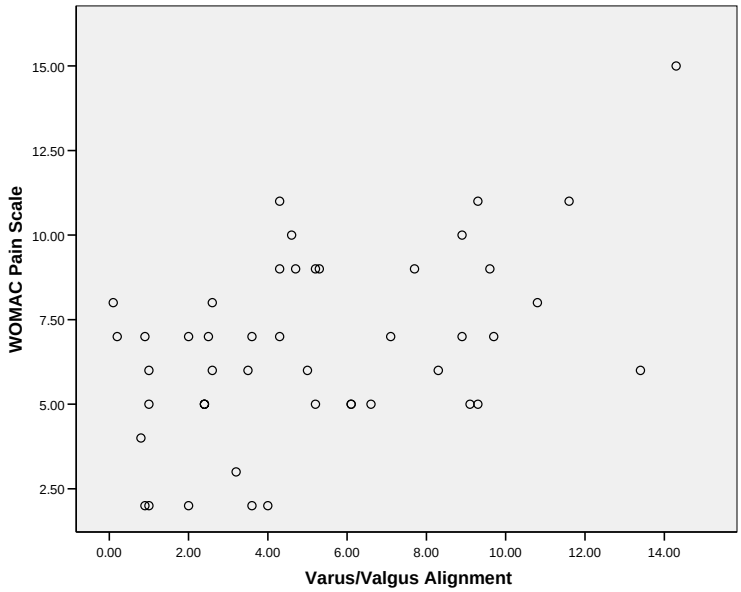
predicted DV scores and errors of prediction). Normality was demonstrated by a concentration of residuals in the center of plot and a generally trailing off symmetrically from the center. A rectangular shape of the residual scatterplot demonstrated both linearity and homoscedasticity.

Independence of errors is another important assumption. The effect of time was examined for all regression models. The Dubin-Watson statistic for all models was acceptably close to 2 (Pain as DV= 2.12, WOMAC Function=2.21, Timed Chair Rise Task=2.043). Results from this analysis demonstrated that variance was consistent as data collection progressed over time.

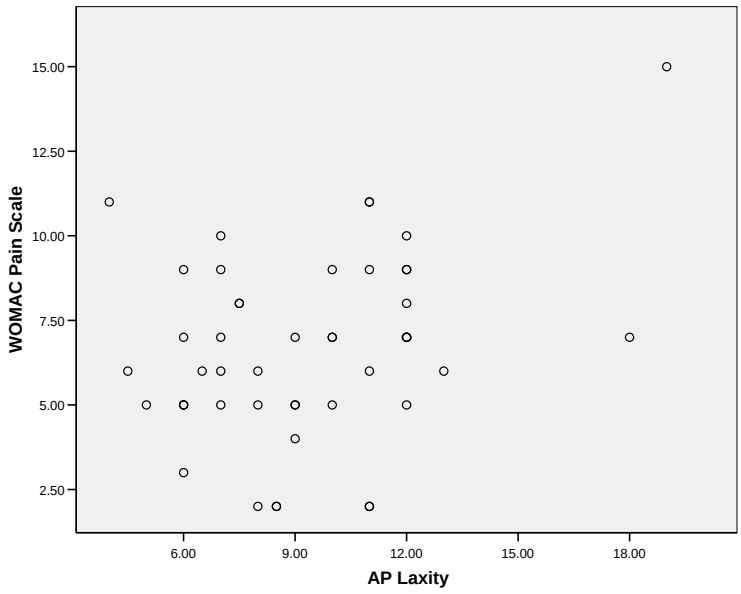
Figures A1

Bivariate Scatter Plots

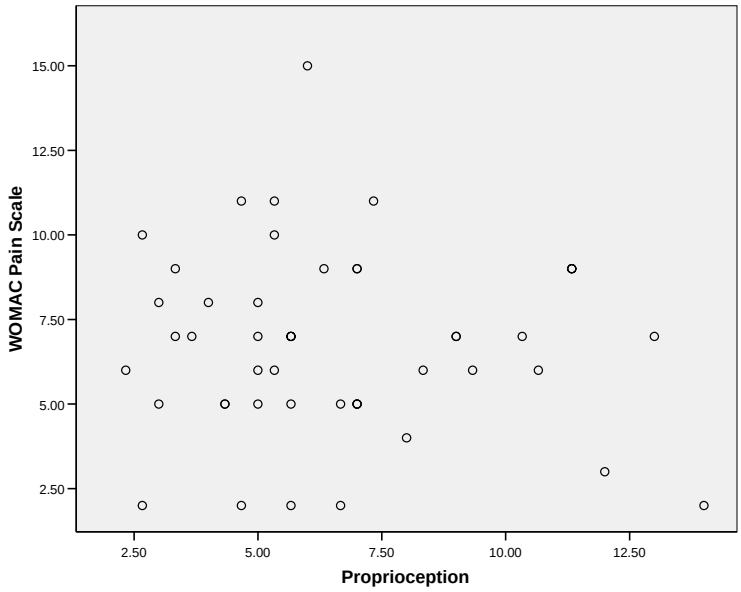
Dependent Variable: WOMAC Pain Scale
Independent Variable: Varus/Valgus Alignment



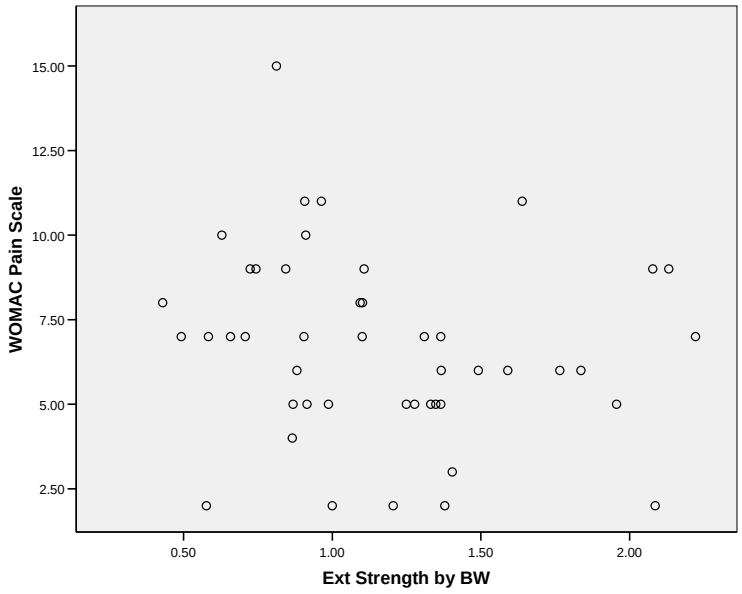
Dependent Variable: WOMAC Pain Scale
Independent Variable: A/P Laxity



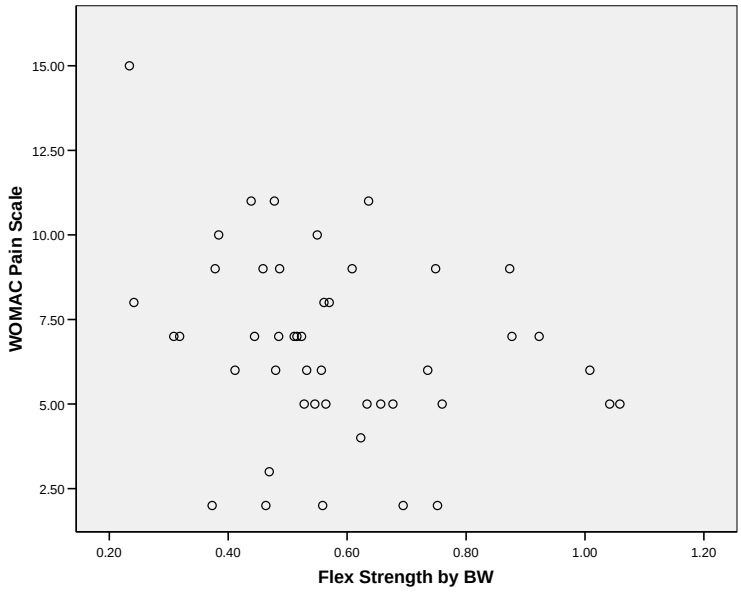
Dependent Variable: WOMAC Pain Scale
Independent Variable: Proprioception



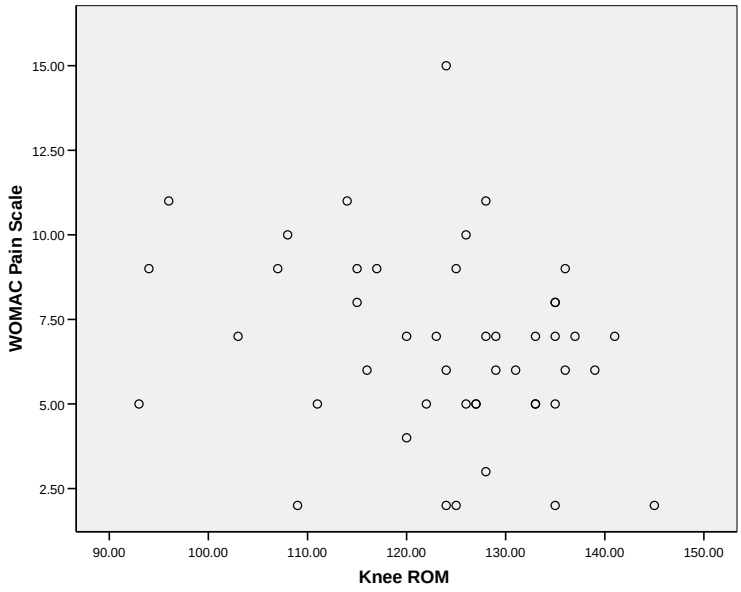
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee Extension Strength by Bodyweight



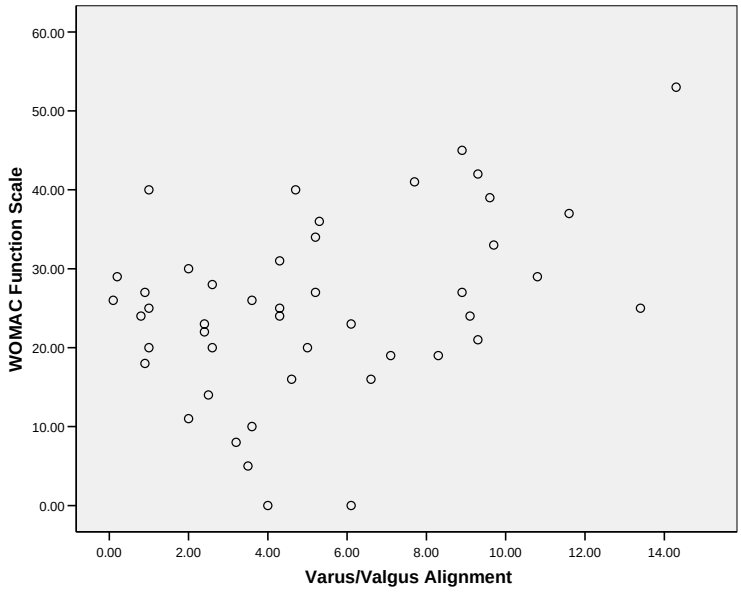
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee Flexion Strength by Bodyweight



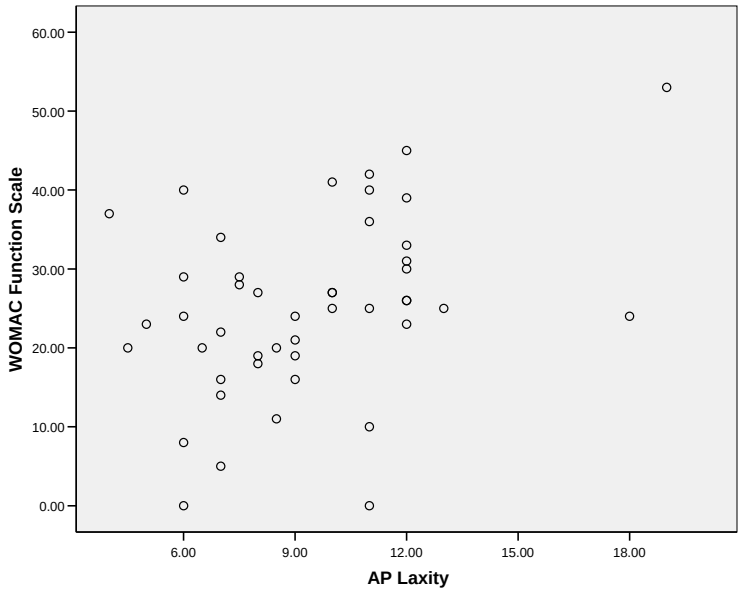
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee ROM



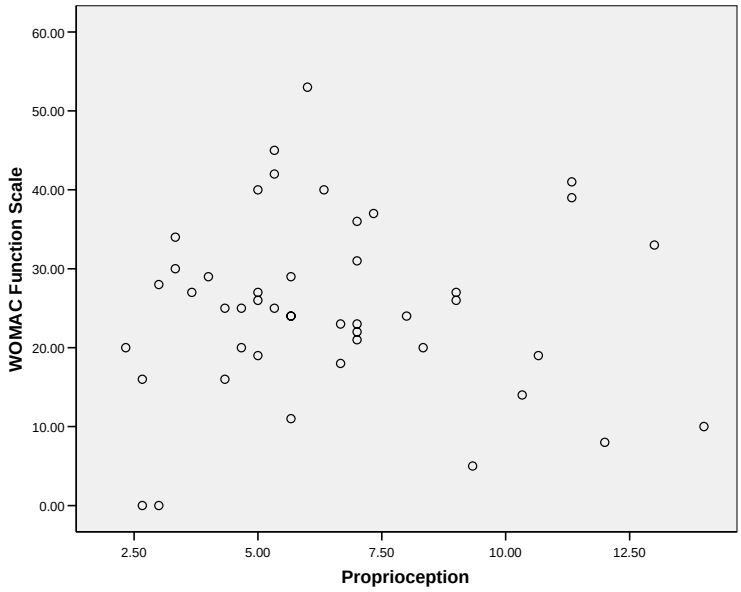
Dependent Variable: WOMAC Function Scale
Independent Variable: Varus/Valgus Alignment



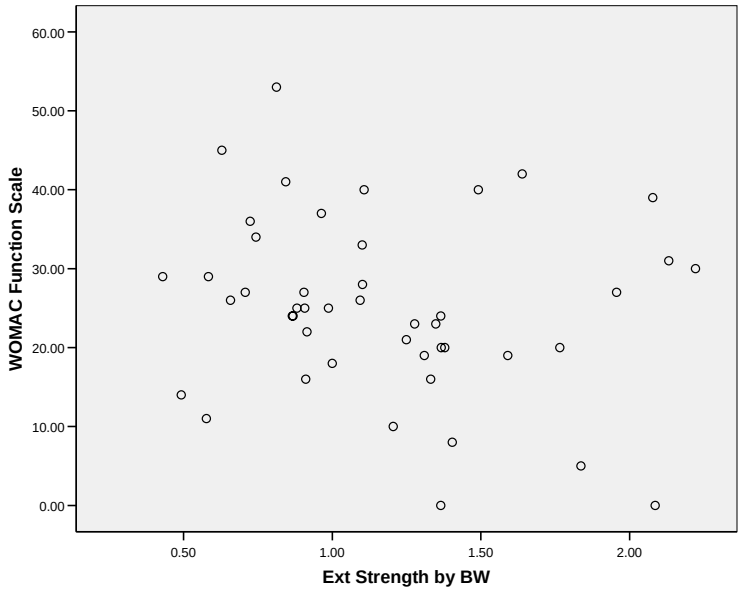
Dependent Variable: WOMAC Function Scale
Independent Variable: A/P Laxity



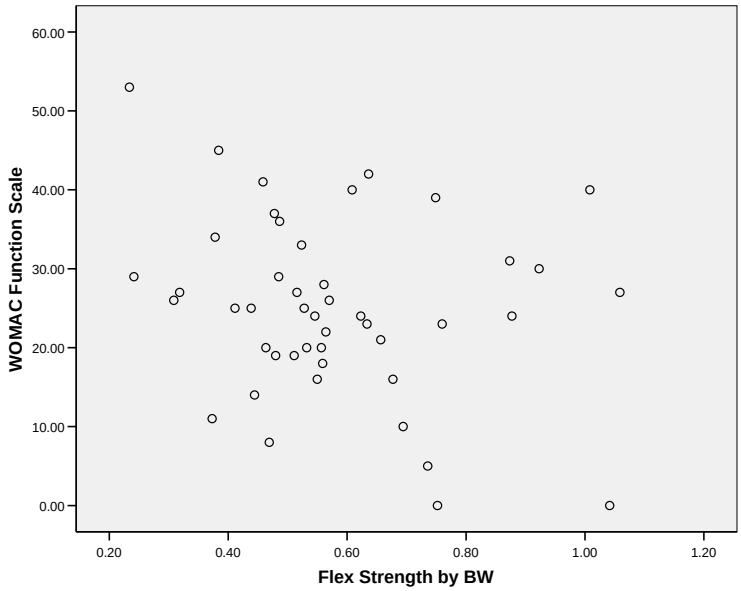
Dependent Variable: WOMAC Function Scale
Independent Variable: Proprioception



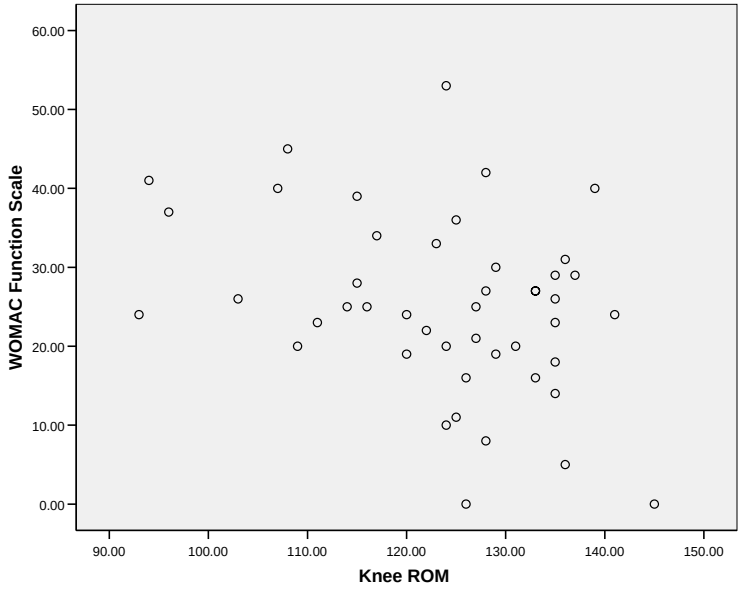
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee Extension Strength by Bodyweight



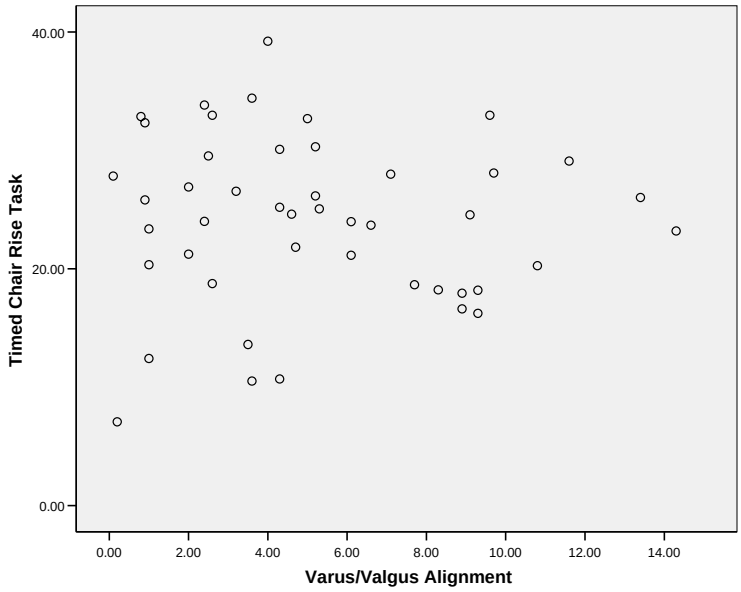
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee Flexion Strength by Bodyweight



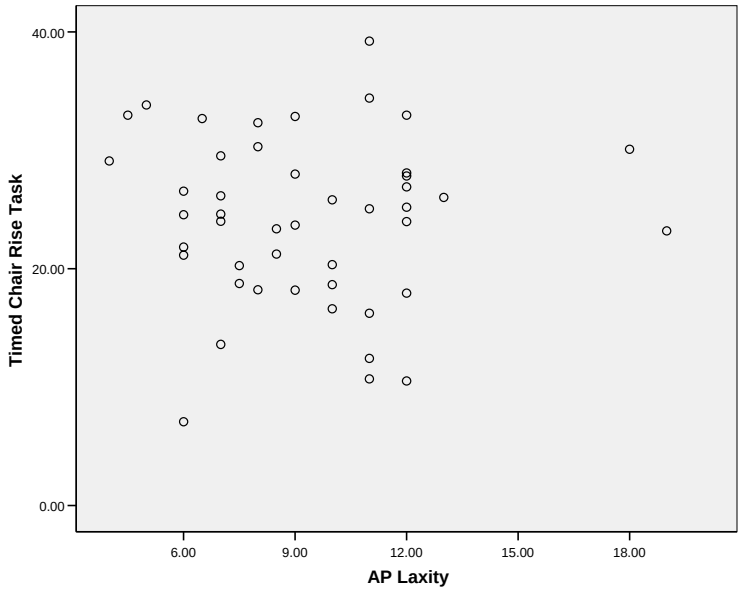
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee ROM



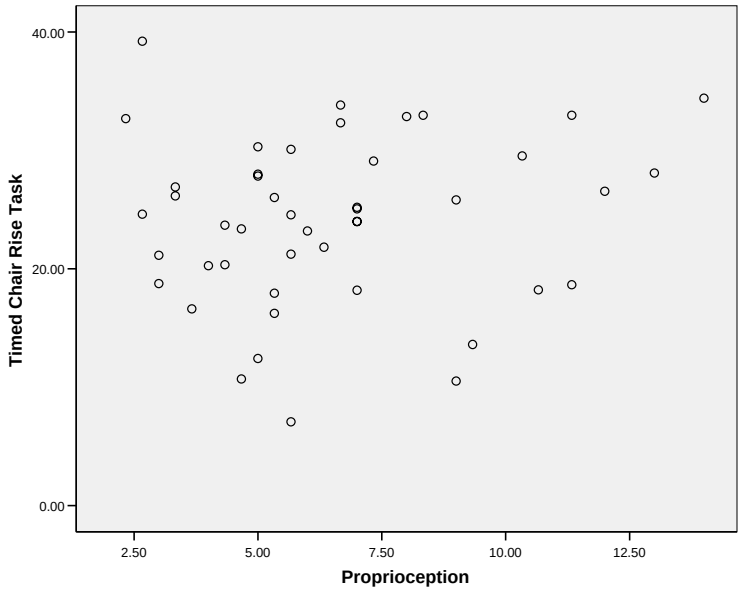
Dependent Variable: Timed Chair Rise
Independent Variable: Varus/Valgus Alignment



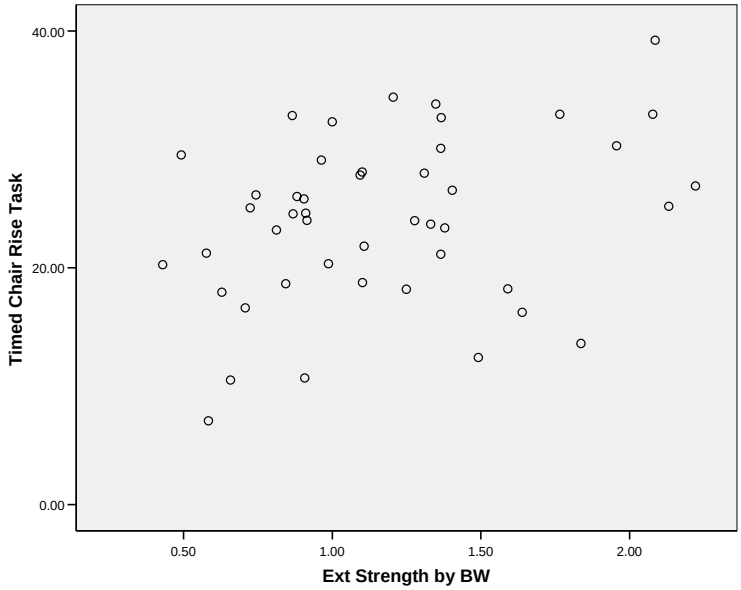
Dependent Variable: Timed Chair Rise
Independent Variable: A/P Laxity



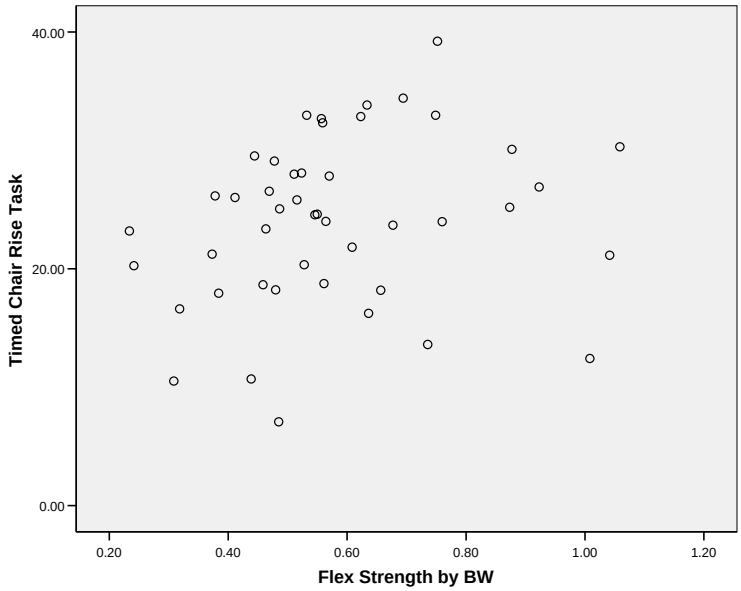
Dependent Variable: Timed Chair Rise
Independent Variable: Proprioception



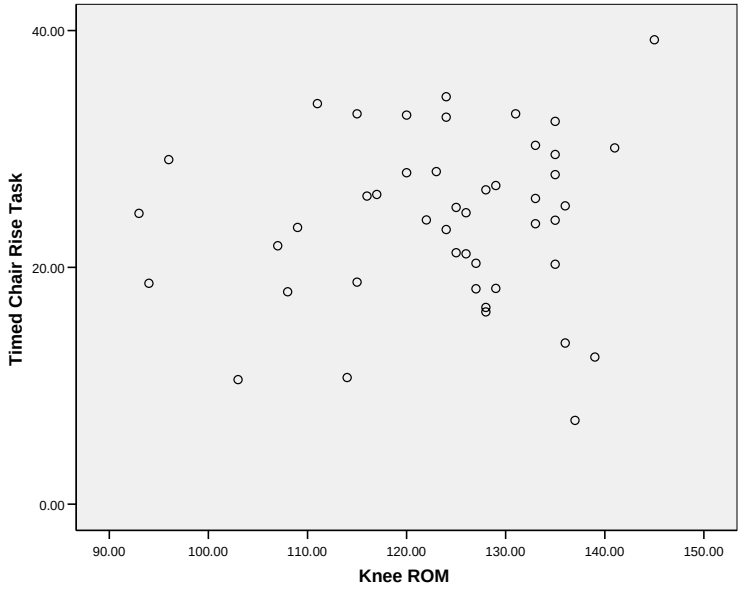
Dependent Variable: Timed Chair Rise
Independent Variable: Knee Extension Strength by Bodyweight



Dependent Variable: Timed Chair Rise
Independent Variable: Knee Flexion Strength by Bodyweight



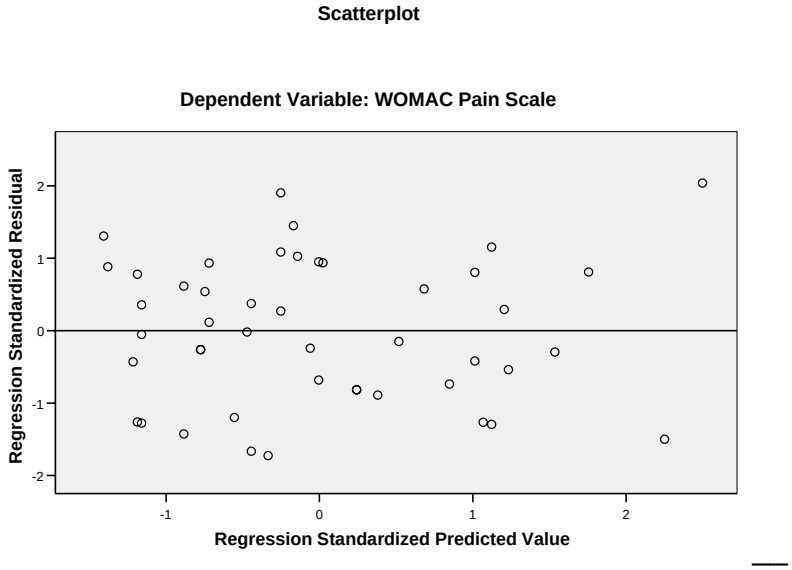
Dependent Variable: Timed Chair Rise
Independent Variable: Knee ROM



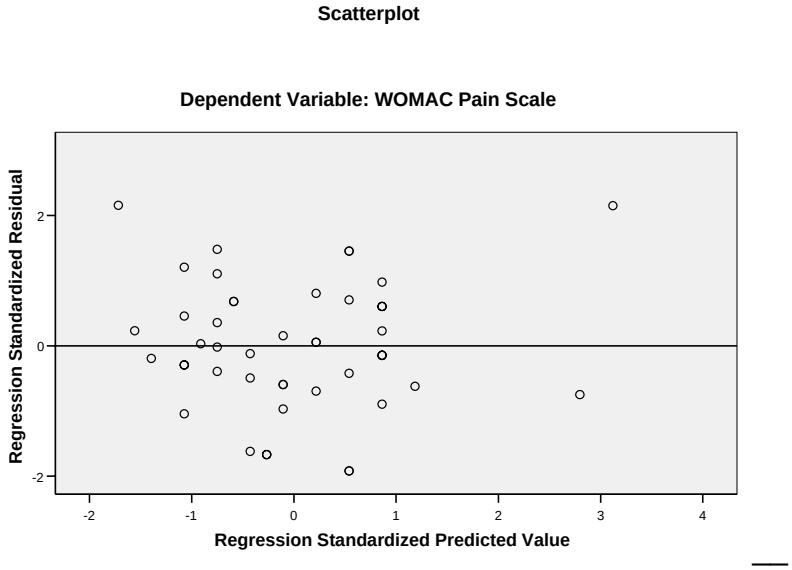
Figures A2

Residual Scatter Plots

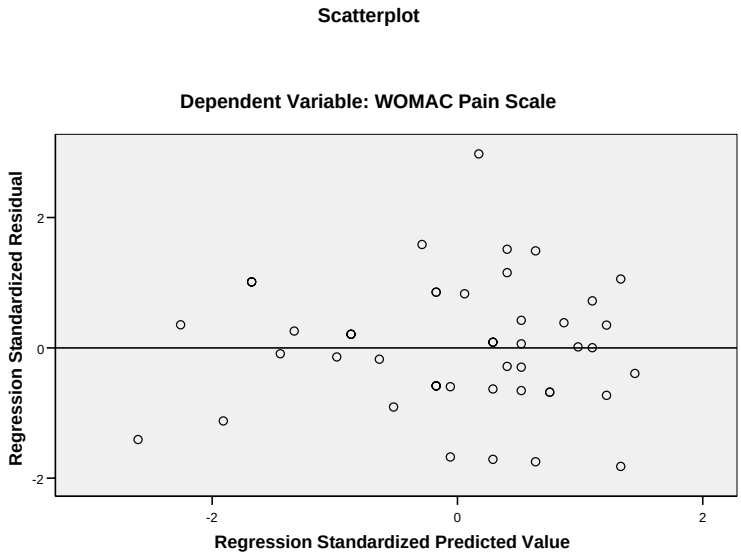
Dependent Variable: WOMAC Pain Scale
Independent Variable: Varus/Valgus Alignment



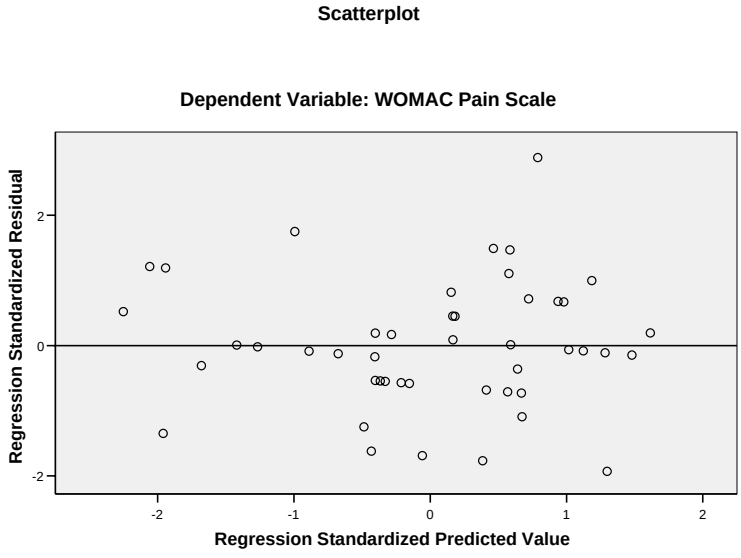
Dependent Variable: WOMAC Pain Scale
Independent Variable: A/P Laxity



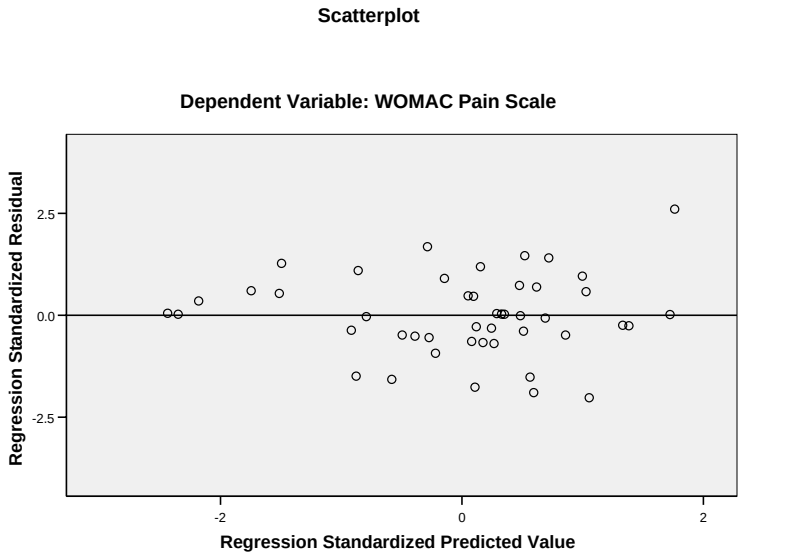
Dependent Variable: WOMAC Pain Scale
Independent Variable: Proprioception



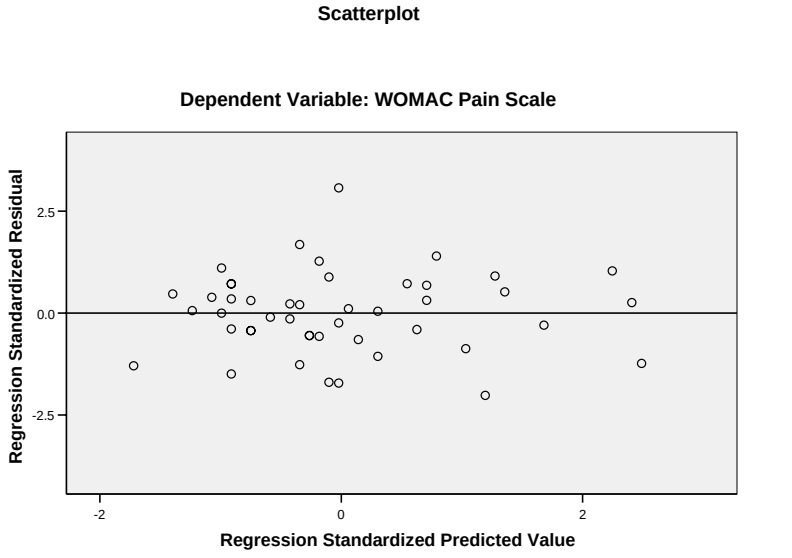
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee Extension Strength by Bodyweight



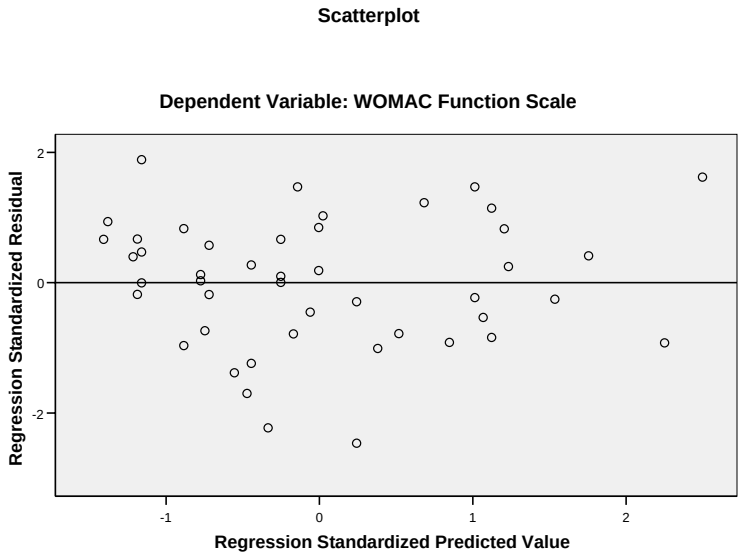
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee Flexion Strength by Bodyweight



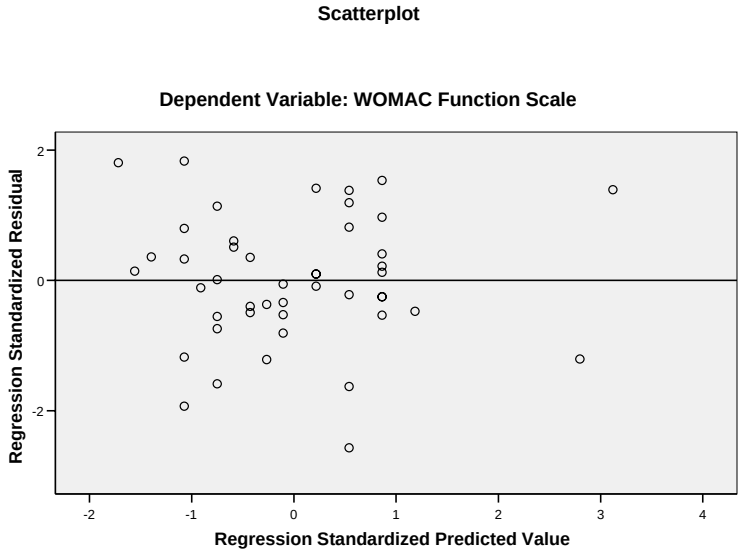
Dependent Variable: WOMAC Pain Scale
Independent Variable: Knee ROM



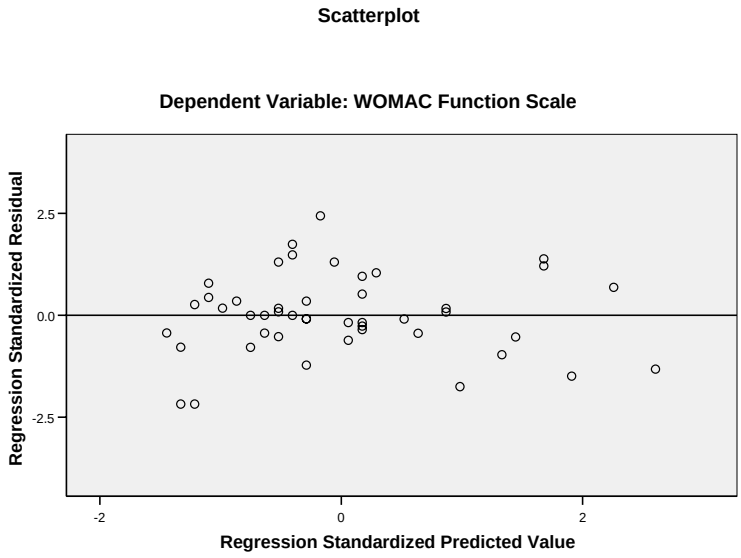
Dependent Variable: WOMAC Function Scale
Independent Variable: Varus/Valgus Alignment



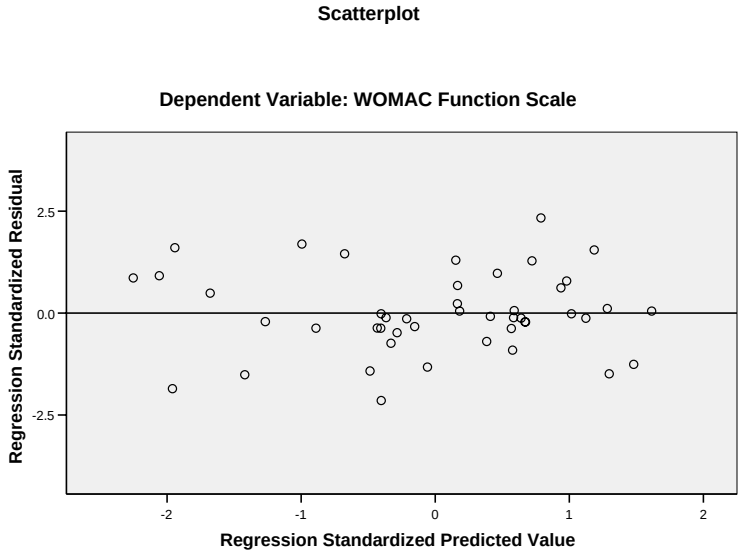
Dependent Variable: WOMAC Function Scale
Independent Variable: A/P Laxity



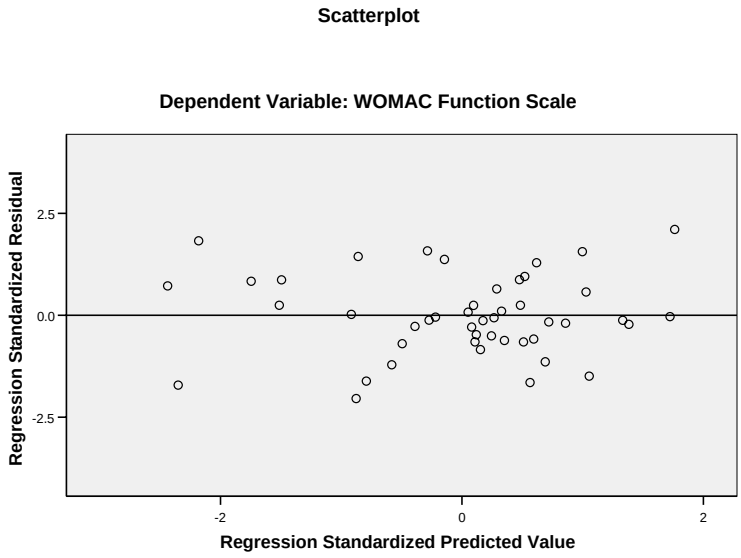
Dependent Variable: WOMAC Function Scale
Independent Variable: Proprioception



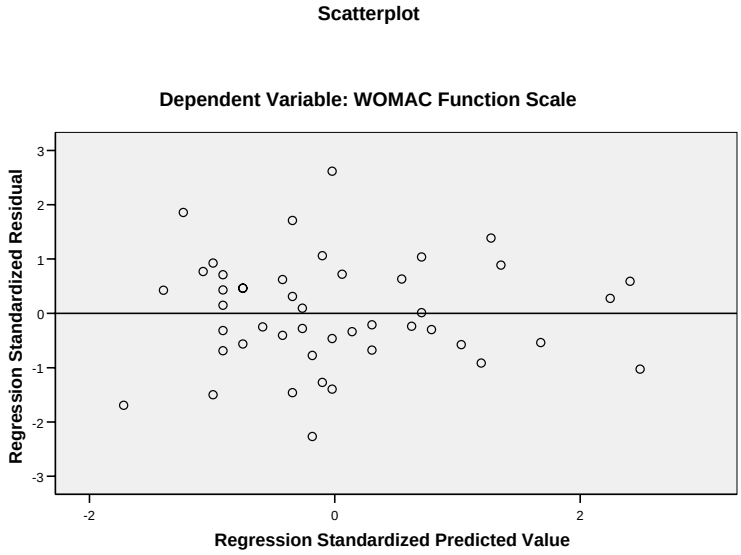
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee Extension Strength by Bodyweight



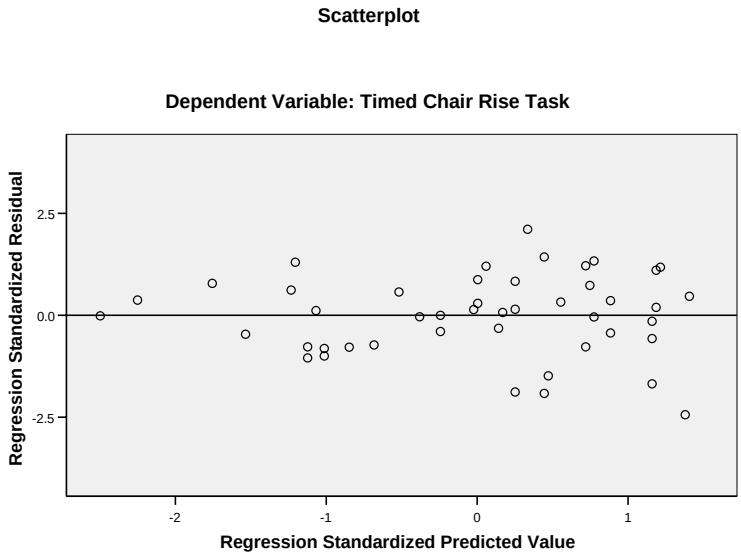
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee Flexion Strength by Bodyweight



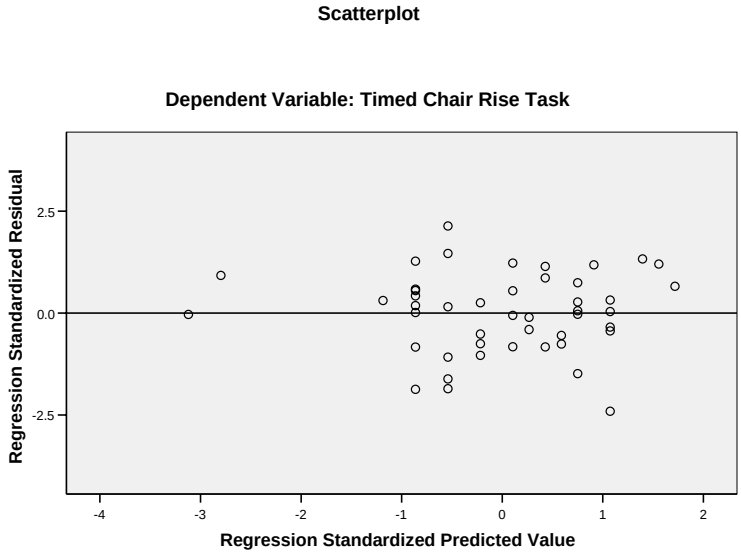
Dependent Variable: WOMAC Function Scale
Independent Variable: Knee ROM



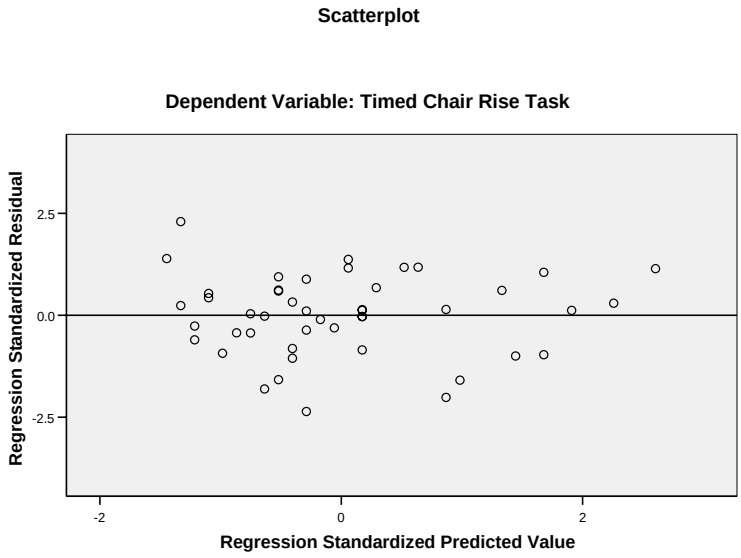
Dependent Variable: Timed Chair Rise
Independent Variable: Varus/Valgus Alignment



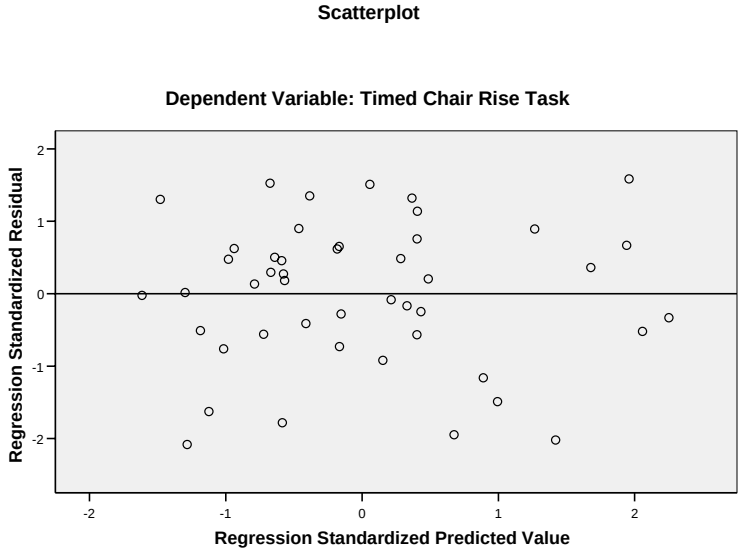
Dependent Variable: Timed Chair Rise
Independent Variable: A/P Laxity



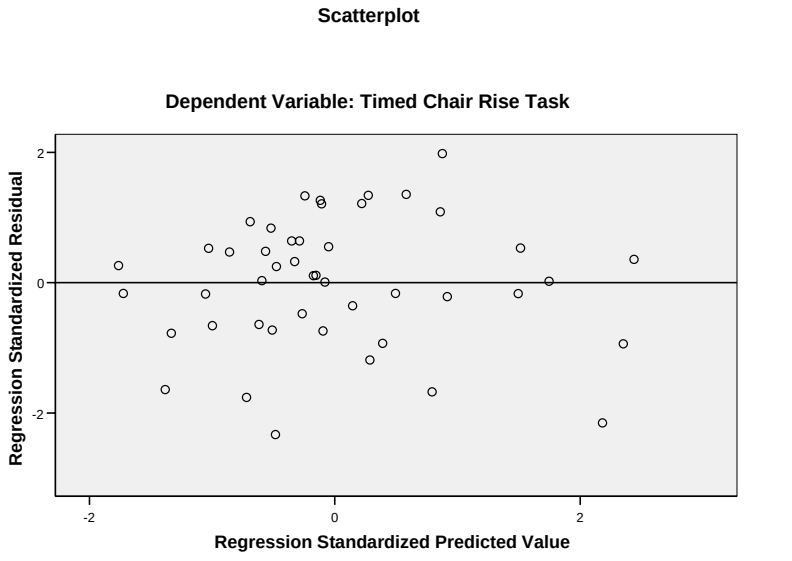
Dependent Variable: Timed Chair Rise
Independent Variable: Proprioception



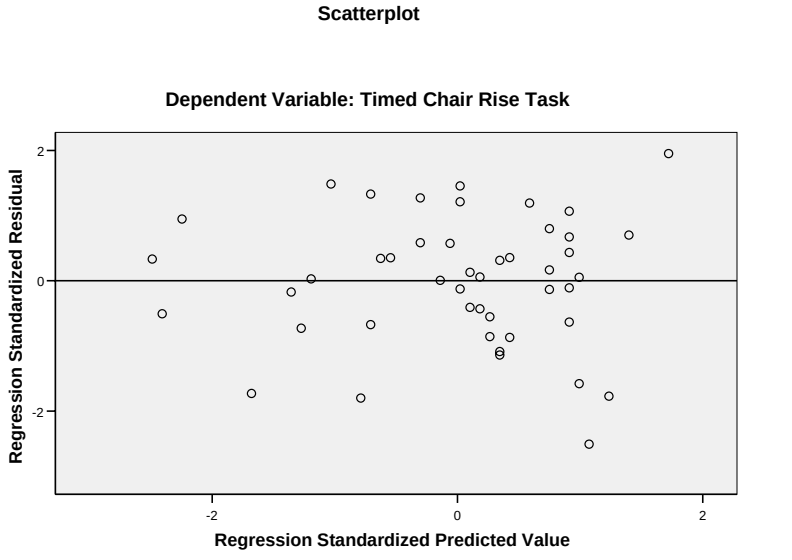
Dependent Variable: Timed Chair Rise
Independent Variable: Knee Extension Strength by Bodyweight



Dependent Variable: Timed Chair Rise
Independent Variable: Knee Flexion Strength by Bodyweight



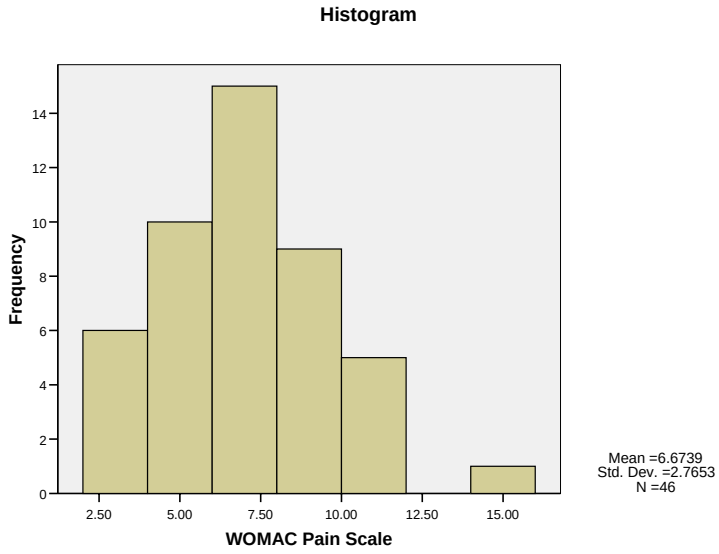
Dependent Variable: Timed Chair Rise
Independent Variable: Knee ROM

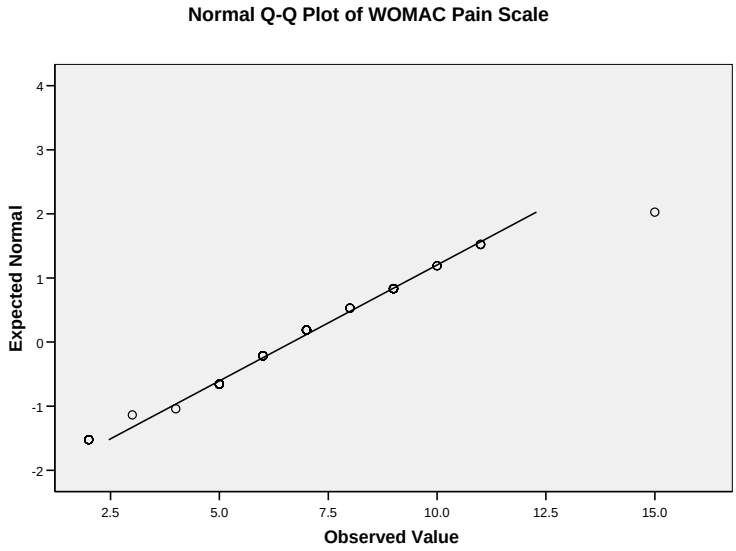


Figures A3

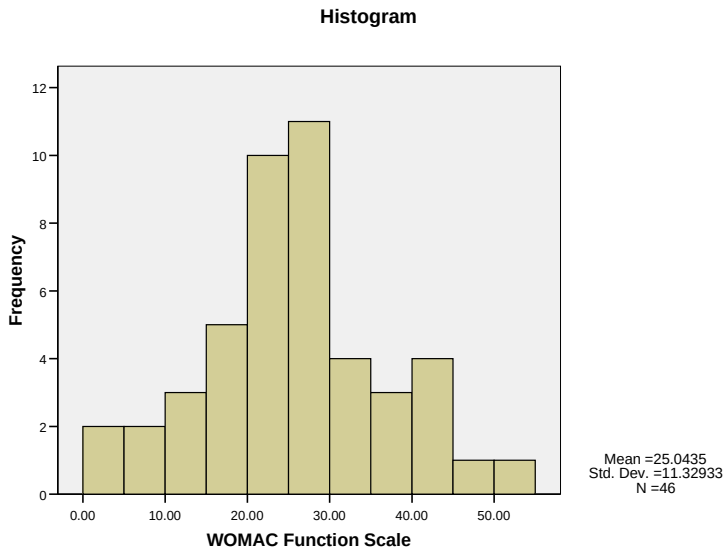
Histograms and Probability Plots

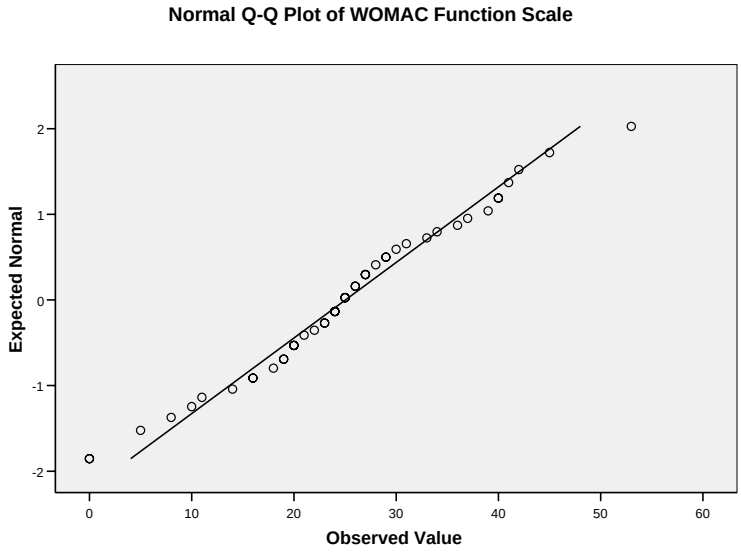
WOMAC Pain Scale



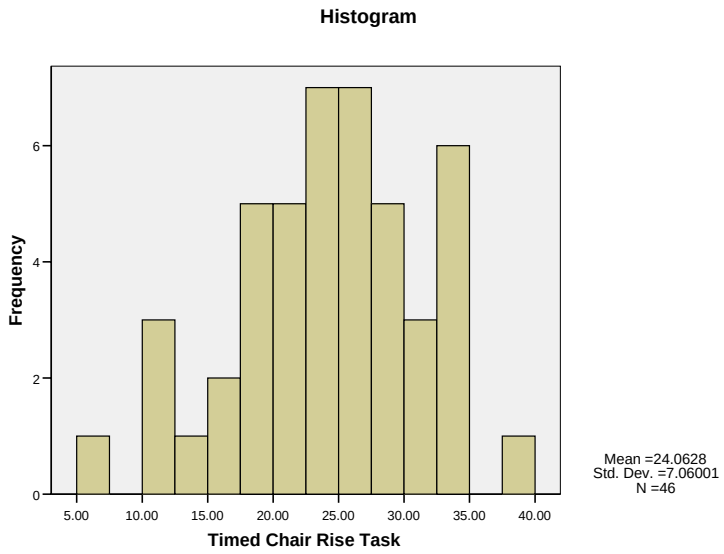


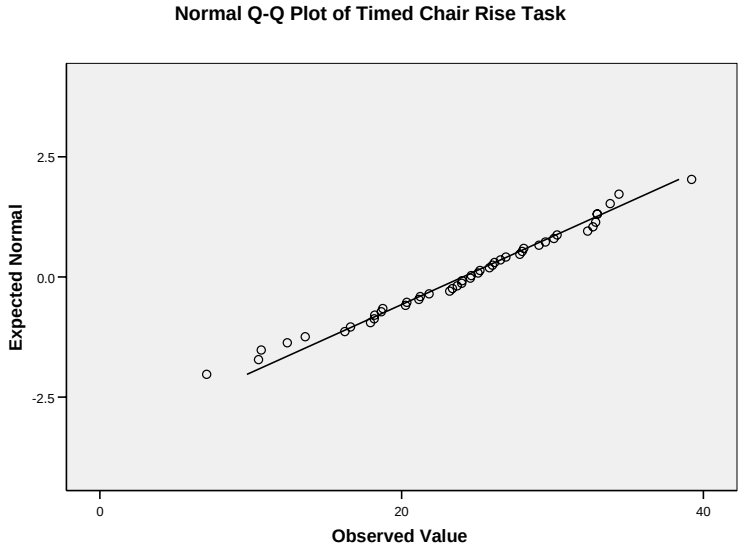
WOMAC Function Scale



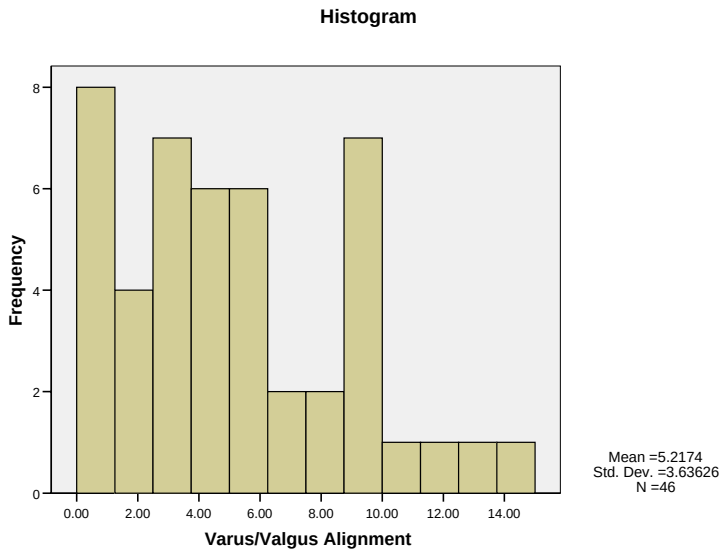


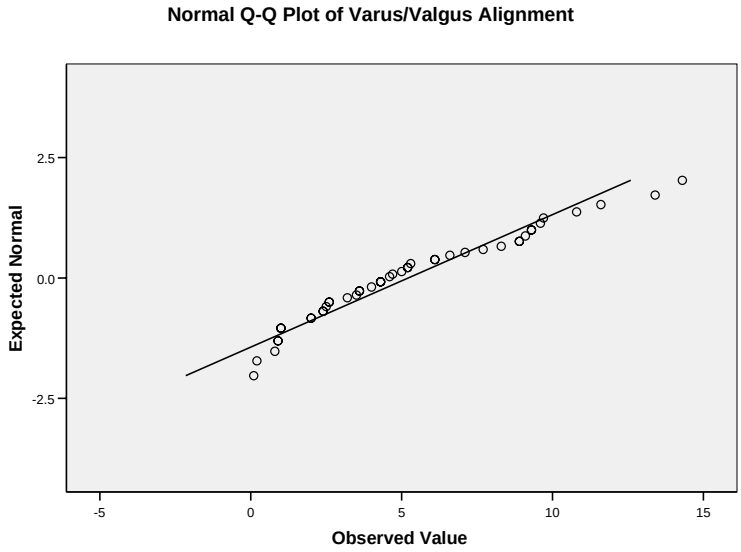
Timed Chair Rise Task



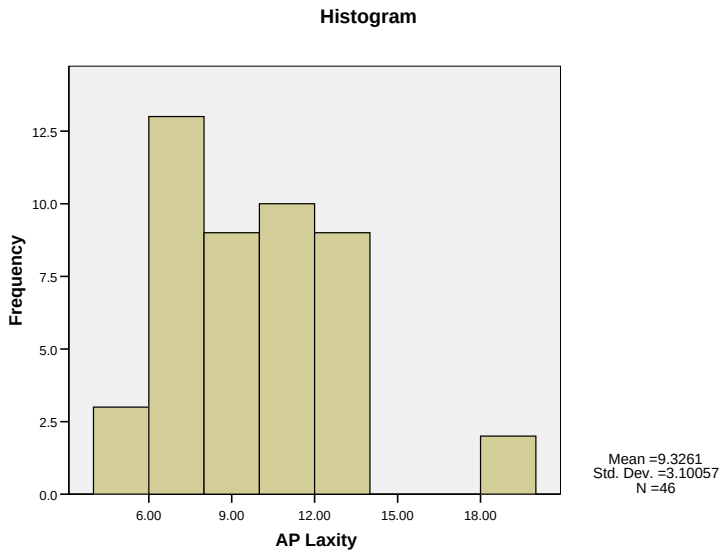


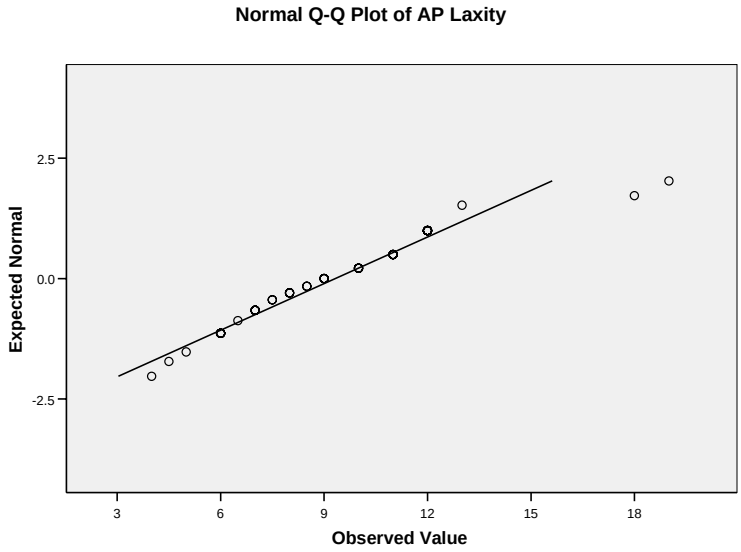
Varus/Valgus Alignment



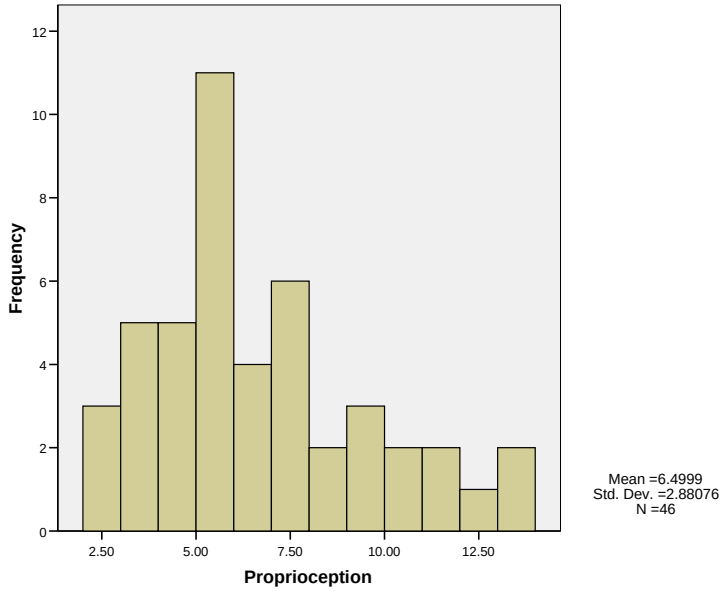


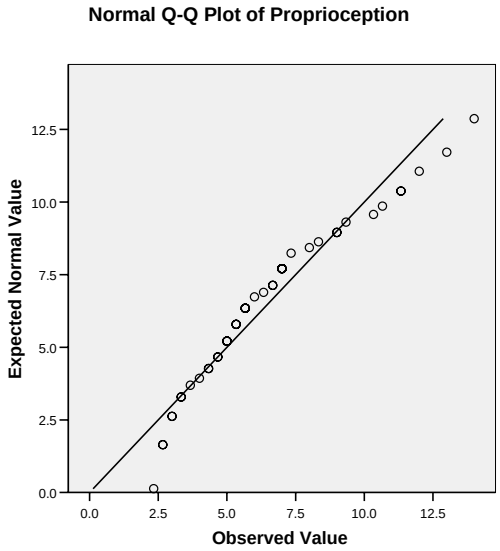
A/P Laxity


Histogram
Frequency
12.5
10.0
7.5
5.0
2.5
0.0
6.00
9.00
12.00
15.00
18.00
AP Laxity
Mean =9.3261
Std. Dev. =3.10057
N =46

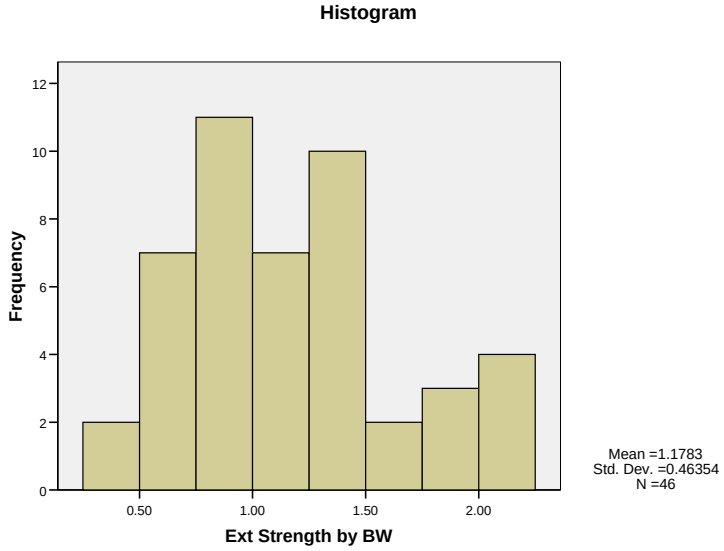

Normal Q-Q Plot of AP Laxity
Expected Normal
2.5
0.0
-2.5
3
6
9
12
15
18
Observed Value

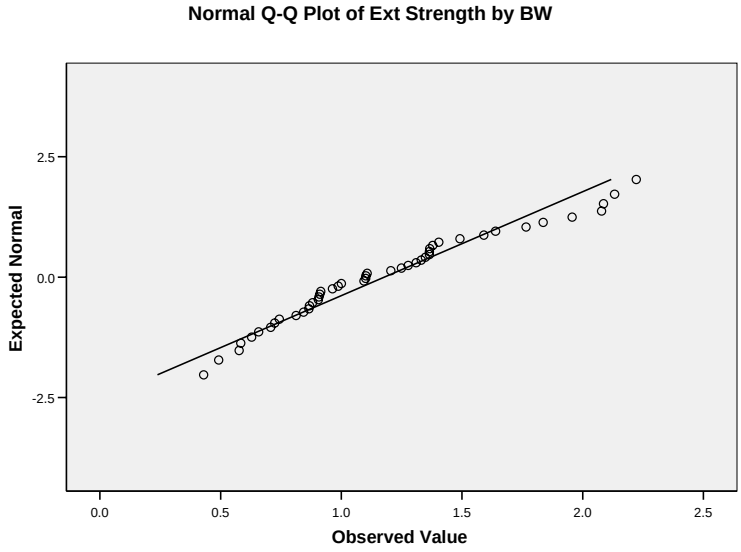
Proprioception



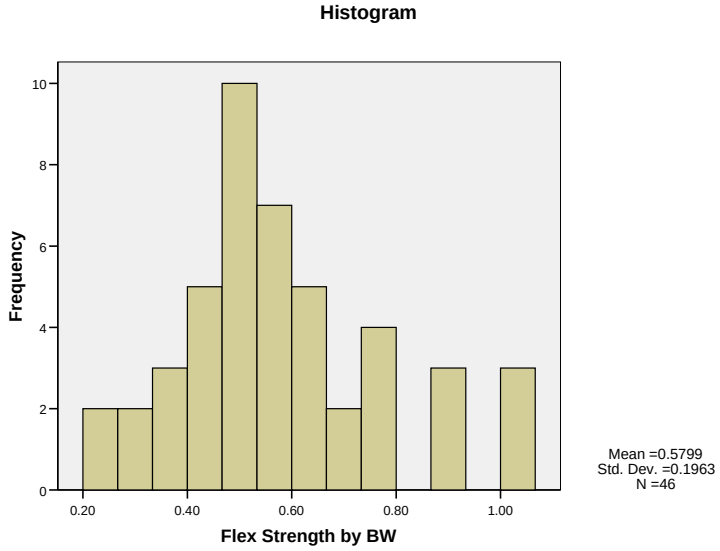


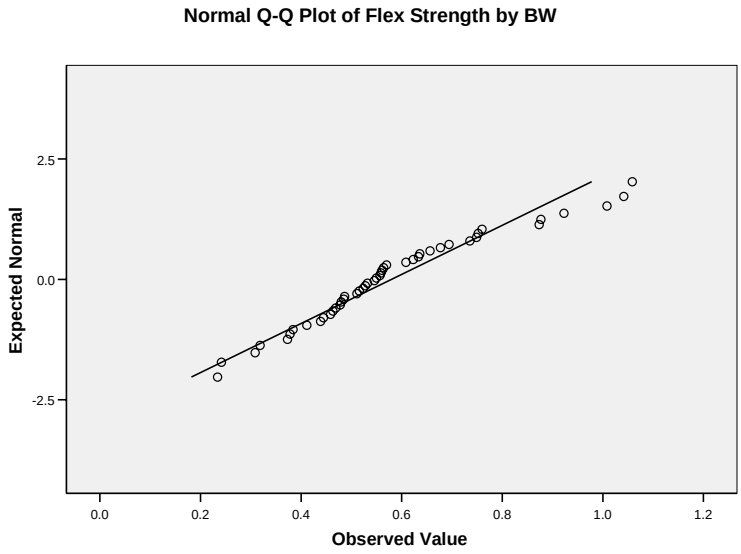
Knee Extensor Strength by Bodyweight



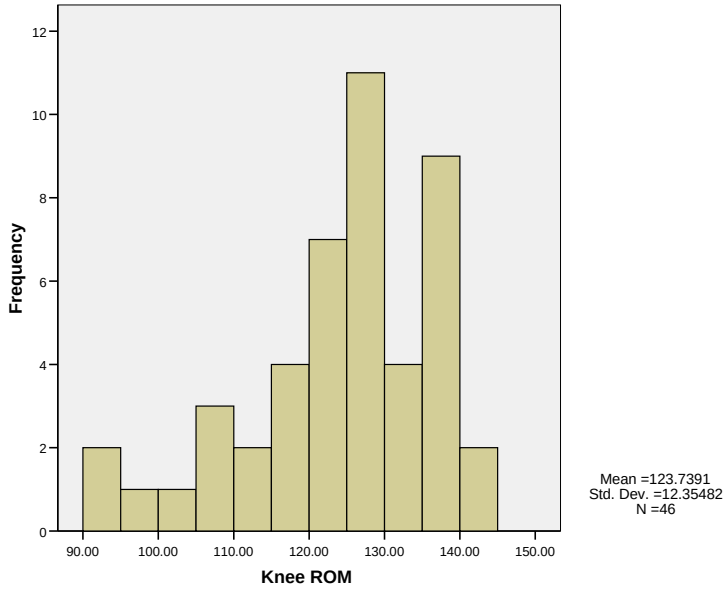


Flexor Strength by Bodyweight





Knee ROM


Frequency
Knee ROM
Mean =123.7391
Std. Dev. =12.35482
N =46

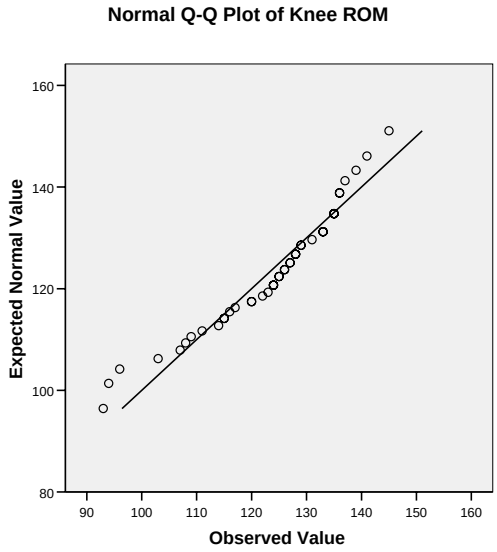

Normal Q-Q Plot of Knee ROM
Expected Normal Value
Observed Value

Table A1

Z Score Frequency Tables

Zscore: WOMAC Pain Scale

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.69020	5	10.9	10.9	10.9
	-1.32858	1	2.2	2.2	13.0
	-.96695	1	2.2	2.2	15.2
	-.60533	9	19.6	19.6	34.8
	-.24370	6	13.0	13.0	47.8
	.11792	9	19.6	19.6	67.4
	.47955	3	6.5	6.5	73.9
	.84117	6	13.0	13.0	87.0
	1.20280	2	4.3	4.3	91.3
	1.56442	3	6.5	6.5	97.8
	3.01092	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: WOMAC Function Scale

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-2.21050	2	4.3	4.3	4.3
	-1.76917	1	2.2	2.2	6.5
	-1.50437	1	2.2	2.2	8.7
	-1.32784	1	2.2	2.2	10.9
	-1.23957	1	2.2	2.2	13.0
	-.97477	1	2.2	2.2	15.2
	-.79824	2	4.3	4.3	19.6
	-.62170	1	2.2	2.2	21.7
	-.53344	2	4.3	4.3	26.1
	-.44517	3	6.5	6.5	32.6
	-.35690	1	2.2	2.2	34.8
	-.26864	1	2.2	2.2	37.0
	-.18037	2	4.3	4.3	41.3
	-.09210	3	6.5	6.5	47.8
	-.00384	3	6.5	6.5	54.3
	.08443	2	4.3	4.3	58.7
	.17270	3	6.5	6.5	65.2
	.26096	1	2.2	2.2	67.4
	.34923	2	4.3	4.3	71.7
	.43749	1	2.2	2.2	73.9
	.52576	1	2.2	2.2	76.1

	.70229	1	2.2	2.2	78.3
	.79056	1	2.2	2.2	80.4
	.96709	1	2.2	2.2	82.6
	1.05536	1	2.2	2.2	84.8
	1.23189	1	2.2	2.2	87.0
	1.32016	2	4.3	4.3	91.3
	1.40843	1	2.2	2.2	93.5
	1.49669	1	2.2	2.2	95.7
	1.76149	1	2.2	2.2	97.8
	2.46762	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Timed Chair Rise Task

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-2.40637	1	2.2	2.2	2.2
	-1.91891	1	2.2	2.2	4.3
	-1.89397	1	2.2	2.2	6.5
	-1.64951	1	2.2	2.2	8.7
	-1.48121	1	2.2	2.2	10.9
	-1.10893	1	2.2	2.2	13.0
	-1.05545	1	2.2	2.2	15.2
	-.86840	1	2.2	2.2	17.4
	-.83300	1	2.2	2.2	19.6
	-.82831	1	2.2	2.2	21.7
	-.76737	1	2.2	2.2	23.9
	-.75252	1	2.2	2.2	26.1
	-.53912	1	2.2	2.2	28.3
	-.52745	1	2.2	2.2	30.4
	-.41376	1	2.2	2.2	32.6
	-.40104	1	2.2	2.2	34.8
	-.31793	1	2.2	2.2	37.0
	-.12449	1	2.2	2.2	39.1
	-.09891	1	2.2	2.2	41.3
	-.05451	1	2.2	2.2	43.5
	-.01161	1	2.2	2.2	45.7
	-.00889	1	2.2	2.2	47.8
	.06900	1	2.2	2.2	50.0
	.07756	1	2.2	2.2	52.2
	.14162	1	2.2	2.2	54.3
	.15951	1	2.2	2.2	56.5
	.24855	1	2.2	2.2	58.7
	.27709	1	2.2	2.2	60.9
	.29637	1	2.2	2.2	63.0
	.35211	1	2.2	2.2	65.2

	.40270	1	2.2	2.2	67.4
	.53350	1	2.2	2.2	69.6
	.55556	1	2.2	2.2	71.7
	.57041	1	2.2	2.2	73.9
	.71320	1	2.2	2.2	76.1
	.77404	1	2.2	2.2	78.3
	.85375	1	2.2	2.2	80.4
	.88388	1	2.2	2.2	82.6
	1.17065	1	2.2	2.2	84.8
	1.22053	1	2.2	2.2	87.0
	1.24588	1	2.2	2.2	89.1
	1.26122	2	4.3	4.3	93.5
	1.38230	1	2.2	2.2	95.7
	1.46471	1	2.2	2.2	97.8
	2.14630	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Varus/Valgus Alignment

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.40732	1	2.2	2.2	2.2
	-1.37982	1	2.2	2.2	4.3
	-1.21482	1	2.2	2.2	6.5
	-1.18732	2	4.3	4.3	10.9
	-1.15982	3	6.5	6.5	17.4
	-.88481	2	4.3	4.3	21.7
	-.77481	2	4.3	4.3	26.1
	-.74730	1	2.2	2.2	28.3
	-.71980	2	4.3	4.3	32.6
	-.55480	1	2.2	2.2	34.8
	-.47230	1	2.2	2.2	37.0
	-.44480	2	4.3	4.3	41.3
	-.33479	1	2.2	2.2	43.5
	-.25229	3	6.5	6.5	50.0
	-.16979	1	2.2	2.2	52.2
	-.14229	1	2.2	2.2	54.3
	-.05978	1	2.2	2.2	56.5
	-.00478	2	4.3	4.3	60.9
	.02272	1	2.2	2.2	63.0
	.24272	2	4.3	4.3	67.4
	.38023	1	2.2	2.2	69.6
	.51773	1	2.2	2.2	71.7
	.68274	1	2.2	2.2	73.9
	.84774	1	2.2	2.2	76.1
	1.01275	2	4.3	4.3	80.4

	1.06775	1	2.2	2.2	82.6
	1.12275	2	4.3	4.3	87.0
	1.20525	1	2.2	2.2	89.1
	1.23275	1	2.2	2.2	91.3
	1.53526	1	2.2	2.2	93.5
	1.75527	1	2.2	2.2	95.7
	2.25028	1	2.2	2.2	97.8
	2.49779	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: AP Laxity

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.71778	1	2.2	2.2	2.2
	-1.55652	1	2.2	2.2	4.3
	-1.39526	1	2.2	2.2	6.5
	-1.07273	5	10.9	10.9	17.4
	-.91147	1	2.2	2.2	19.6
	-.75021	5	10.9	10.9	30.4
	-.58895	2	4.3	4.3	34.8
	-.42769	3	6.5	6.5	41.3
	-.26643	2	4.3	4.3	45.7
	-.10517	4	8.7	8.7	54.3
	.21735	4	8.7	8.7	63.0
	.53987	6	13.0	13.0	76.1
	.86239	8	17.4	17.4	93.5
	1.18492	1	2.2	2.2	95.7
	2.79752	1	2.2	2.2	97.8
	3.12004	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Proprioception

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.44633	1	2.2	2.2	2.2
	-1.33062	2	4.3	4.3	6.5
	-1.21491	2	4.3	4.3	10.9
	-1.09920	2	4.3	4.3	15.2
	-.98349	1	2.2	2.2	17.4
	-.86778	1	2.2	2.2	19.6
	-.75207	2	4.3	4.3	23.9
	-.63636	2	4.3	4.3	28.3
	-.52065	4	8.7	8.7	37.0

	-.40494	3	6.5	6.5	43.5
	-.28923	4	8.7	8.7	52.2
	-.17352	1	2.2	2.2	54.3
	-.05780	1	2.2	2.2	56.5
	.05791	2	4.3	4.3	60.9
	.17362	5	10.9	10.9	71.7
	.28933	1	2.2	2.2	73.9
	.52075	1	2.2	2.2	76.1
	.63646	1	2.2	2.2	78.3
	.86788	2	4.3	4.3	82.6
	.98359	1	2.2	2.2	84.8
	1.33072	1	2.2	2.2	87.0
	1.44411	1	2.2	2.2	89.1
	1.67785	2	4.3	4.3	93.5
	1.90927	1	2.2	2.2	95.7
	2.25640	1	2.2	2.2	97.8
	2.60353	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Ext Strength by BW

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.61459	1	2.2	2.2	2.2
	-1.48002	1	2.2	2.2	4.3
	-1.29778	1	2.2	2.2	6.5
	-1.28302	1	2.2	2.2	8.7
	-1.18602	1	2.2	2.2	10.9
	-1.12341	1	2.2	2.2	13.0
	-1.01604	1	2.2	2.2	15.2
	-.98033	1	2.2	2.2	17.4
	-.93820	1	2.2	2.2	19.6
	-.78893	1	2.2	2.2	21.7
	-.72202	1	2.2	2.2	23.9
	-.67438	1	2.2	2.2	26.1
	-.66949	1	2.2	2.2	28.3
	-.64090	1	2.2	2.2	30.4
	-.58983	1	2.2	2.2	32.6
	-.58487	1	2.2	2.2	34.8
	-.57685	1	2.2	2.2	37.0
	-.56837	1	2.2	2.2	39.1
	-.46373	1	2.2	2.2	41.3
	-.41179	1	2.2	2.2	43.5
	-.38463	1	2.2	2.2	45.7
	-.18238	1	2.2	2.2	47.8

	-.16717	1	2.2	2.2	50.0
	-.16540	1	2.2	2.2	52.2
	-.15342	1	2.2	2.2	54.3
	.05748	1	2.2	2.2	56.5
	.15282	1	2.2	2.2	58.7
	.21295	1	2.2	2.2	60.9
	.28367	1	2.2	2.2	63.0
	.32999	1	2.2	2.2	65.2
	.36626	1	2.2	2.2	67.4
	.40286	1	2.2	2.2	69.6
	.40309	1	2.2	2.2	71.7
	.40576	1	2.2	2.2	73.9
	.43199	1	2.2	2.2	76.1
	.48615	1	2.2	2.2	78.3
	.67523	1	2.2	2.2	80.4
	.88903	1	2.2	2.2	82.6
	.99361	1	2.2	2.2	84.8
	1.26645	1	2.2	2.2	87.0
	1.41968	1	2.2	2.2	89.1
	1.67821	1	2.2	2.2	91.3
	1.94108	1	2.2	2.2	93.5
	1.95868	1	2.2	2.2	95.7
	2.05741	1	2.2	2.2	97.8
	2.25116	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Flex Strength by BW

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-1.76260	1	2.2	2.2	2.2
	-1.72350	1	2.2	2.2	4.3
	-1.38253	1	2.2	2.2	6.5
	-1.33191	1	2.2	2.2	8.7
	-1.05383	1	2.2	2.2	10.9
	-1.02826	1	2.2	2.2	13.0
	-.99781	1	2.2	2.2	15.2
	-.85783	1	2.2	2.2	17.4
	-.71935	1	2.2	2.2	19.6
	-.68996	1	2.2	2.2	21.7
	-.61761	1	2.2	2.2	23.9
	-.59402	1	2.2	2.2	26.1
	-.56440	1	2.2	2.2	28.3
	-.52015	1	2.2	2.2	30.4
	-.50981	1	2.2	2.2	32.6
	-.48371	1	2.2	2.2	34.8

	-.47596	1	2.2	2.2	37.0
	-.35157	1	2.2	2.2	39.1
	-.32725	1	2.2	2.2	41.3
	-.28732	1	2.2	2.2	43.5
	-.26529	1	2.2	2.2	45.7
	-.24393	1	2.2	2.2	47.8
	-.17376	1	2.2	2.2	50.0
	-.15344	1	2.2	2.2	52.2
	-.11842	1	2.2	2.2	54.3
	-.10729	1	2.2	2.2	56.5
	-.09590	1	2.2	2.2	58.7
	-.08026	1	2.2	2.2	60.9
	-.05035	1	2.2	2.2	63.0
	.14547	1	2.2	2.2	65.2
	.21977	1	2.2	2.2	67.4
	.27322	1	2.2	2.2	69.6
	.28645	1	2.2	2.2	71.7
	.39014	1	2.2	2.2	73.9
	.49516	1	2.2	2.2	76.1
	.58238	1	2.2	2.2	78.3
	.79293	1	2.2	2.2	80.4
	.86040	1	2.2	2.2	82.6
	.87674	1	2.2	2.2	84.8
	.91677	1	2.2	2.2	87.0
	1.49519	1	2.2	2.2	89.1
	1.51390	1	2.2	2.2	91.3
	1.74675	1	2.2	2.2	93.5
	2.18196	1	2.2	2.2	95.7
	2.35172	1	2.2	2.2	97.8
	2.43908	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Zscore: Knee ROM

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	-2.48803	1	2.2	2.2	2.2
	-2.40709	1	2.2	2.2	4.3
	-2.24521	1	2.2	2.2	6.5
	-1.67863	1	2.2	2.2	8.7
	-1.35487	1	2.2	2.2	10.9
	-1.27393	1	2.2	2.2	13.0
	-1.19299	1	2.2	2.2	15.2
	-1.03111	1	2.2	2.2	17.4
	-.78829	1	2.2	2.2	19.6
	-.70735	2	4.3	4.3	23.9

	-.62641	1	2.2	2.2	26.1
	-.54547	1	2.2	2.2	28.3
	-.30265	2	4.3	4.3	32.6
	-.14077	1	2.2	2.2	34.8
	-.05983	1	2.2	2.2	37.0
	.02111	3	6.5	6.5	43.5
	.10205	2	4.3	4.3	47.8
	.18299	2	4.3	4.3	52.2
	.26394	2	4.3	4.3	56.5
	.34488	3	6.5	6.5	63.0
	.42582	2	4.3	4.3	67.4
	.58770	1	2.2	2.2	69.6
	.74958	3	6.5	6.5	76.1
	.91146	5	10.9	10.9	87.0
	.99240	2	4.3	4.3	91.3
	1.07334	1	2.2	2.2	93.5
	1.23522	1	2.2	2.2	95.7
	1.39710	1	2.2	2.2	97.8
	1.72086	1	2.2	2.2	100.0
	Total	46	100.0	100.0	

Table A2

Frequency Table for Probability of Significant D^2

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.0035	1	2.2	2.2	2.2
	.0198	1	2.2	2.2	4.3
	.0214	1	2.2	2.2	6.5
	.0378	1	2.2	2.2	8.7
	.0567	1	2.2	2.2	10.9
	.0617	1	2.2	2.2	13.0
	.0843	1	2.2	2.2	15.2
	.1357	1	2.2	2.2	17.4
	.1565	1	2.2	2.2	19.6
	.1573	1	2.2	2.2	21.7
	.2057	1	2.2	2.2	23.9
	.2172	1	2.2	2.2	26.1
	.2246	1	2.2	2.2	28.3
	.2247	1	2.2	2.2	30.4
	.2647	1	2.2	2.2	32.6
	.2729	1	2.2	2.2	34.8
	.3028	1	2.2	2.2	37.0
	.3057	1	2.2	2.2	39.1

.3388	1	2.2	2.2	41.3
.3470	1	2.2	2.2	43.5
.3569	1	2.2	2.2	45.7
.4346	1	2.2	2.2	47.8
.5037	1	2.2	2.2	50.0
.5666	1	2.2	2.2	52.2
.5712	1	2.2	2.2	54.3
.5746	1	2.2	2.2	56.5
.5995	1	2.2	2.2	58.7
.6389	1	2.2	2.2	60.9
.6646	1	2.2	2.2	63.0
.6710	1	2.2	2.2	65.2
.6770	1	2.2	2.2	67.4
.6963	1	2.2	2.2	69.6
.7597	1	2.2	2.2	71.7
.7965	1	2.2	2.2	73.9
.8115	1	2.2	2.2	76.1
.8196	1	2.2	2.2	78.3
.8234	1	2.2	2.2	80.4
.8336	1	2.2	2.2	82.6
.8384	1	2.2	2.2	84.8
.8502	1	2.2	2.2	87.0
.8518	1	2.2	2.2	89.1
.8738	1	2.2	2.2	91.3
.9029	1	2.2	2.2	93.5
.9456	1	2.2	2.2	95.7
.9627	1	2.2	2.2	97.8
.9861	1	2.2	2.2	100.0
Total	46	100.0	100.0	

$p<0.001$

Table A3

Skew and Kurtosis

	N	Skewness		Kurtosis	
	Statistic	Statistic	Std. Error	Statistic	Std. Error
WOMAC Pain Scale	46	.388	.350	.688	.688
WOMAC Function Scale	46	-.029	.350	.274	.688
Timed Chair Rise Task	46	-.310	.350	-.151	.688
Varus/Valgus Alignment	46	.642	.350	-.326	.688
AP Laxity	46	.901	.350	1.628	.688
Proprioception	46	.832	.350	.131	.688
Ext Strength by BW	46	.619	.350	-.307	.688

Flex Strength by BW	46	.734	.350	.369	.688
Knee ROM	46	-.835	.350	.303	.688
Valid N (listwise)	46				

Table A4

Significance Testing of Normality

	Shapiro-Wilk		
	Statistic	df	Sig.
WOMAC Pain Scale	.955	46	.073
WOMAC Function Scale	.983	46	.749
Timed Chair Rise Task	.984	46	.786
Varus/Valgus Alignment	.943	46	.025
AP Laxity	.927	46	.007
Proprioception	.934	46	.012
Ext Strength by BW	.949	46	.043
Flex Strength by BW	.947	46	.036
participant id number	.952	46	.057

$p < 0.001$

Appendix B

Extended Literature Review

Studies of OA of the knee have generally attempted to obtain a homogeneous group to analyze by utilizing simple inclusion criteria basically narrowed to type of arthritis (OA v. RA for example) and joints effected. Recent studies suggest that heterogeneity may exist within a population selected by inclusion criteria limited to type of arthritis and joint affected. This possible heterogeneity exists when the subject pool's local intrinsic mechanical factors are considered. These local factors can be thought of as features that alter the mechanical environment in which the knee functions

This potential heterogeneity negatively affects statistical analysis as well as the practical application of findings to the group as a whole. These local factors, when used to stratify or separate subjects into more homogenous groups, will improve the study of the effectiveness of exercise in the treatment of OA by decreasing within group variance on potentially important factors. Information gained could potentially lead practitioners to better identify groups of individuals with OA that might or might not benefit from exercise (or might actually be harmed). A more appropriate understanding of the role of the intrinsic factors in knee OA might also allow a better tailoring of an intervention program to the specific patient instead of a "one size fits all" exercise program that is now the norm. The purpose of this study is to investigate the heterogeneity of individuals with knee osteoarthritis by conducting a comprehensive examination of a large subject pool with OA with respect to local intrinsic factors and to investigate the relationship between these factors and measures of function and pain.

As stated previously, there have been few intervention studies that have attempted to stratify the response to exercise by subgroups of local intrinsic factors. However, past studies have examined these intrinsic factors as variables in other settings. A review of what is know about these local intrinsic factors and how they relate to the individual with OA is necessary to give context to this proposed study.

Varus/Valgus Alignment of the Knee

The alignment of the knee has been demonstrated to influence the forces directed at the joint, specifically an adduction or abduction joint moment. A joint moment can be thought of as the turning or rotational effect caused by a force that is distant to the rotational axis. The alignment of the lower limb at the knee is a chief determinant of the length of the mechanical axis. During weight bearing, the location of the ground reaction force in relation to the mechanical axis of the joint, will determine the direction, either adduction or abduction, of the moment. The distance from the center of rotation and the amount of force (moment = force x distance) will determine the magnitude of the moment. In a varus position, the ground reaction force will act at a distance medial to the joint line. Forces directed in this manner will cause a rotational effect in an adduction manner. Increasing the varus position of the knee will increase the distance between the ground reaction force and the center of rotation, thus increasing the moment.

Researchers have investigated whether the peak external knee adduction moments during walking in subjects with knee OA were correlated with the mechanical axis (alignment) of the leg (Hurwitz, Ryals, Case, Block, & Andriacchi, 2002). In this study, gait analysis was performed on 62 subjects with knee OA and 49 asymptomatic controls. The researcher found that the mechanical axis was the best single predictor of the peak

adduction moment during the early and late stance phase of gait ($R = .74$, $p < 0.001$). This relationship between the mechanical axis (varus alignment) and adduction moment has been confirmed by other investigators (Miyazaki et al., 2002).

The relationship between alignment of the knee and its influence on the forces around the knee suggest a possible association between alignment and the development or progression of OA. Sharma (Sharma et al., 2001) examined the relationship between varus/valgus angulation of the knee and severity and progression of knee OA. OA progression was defined as a grade 1 or greater increase in the severity of joint space narrowing in the medial or lateral compartment. A 4 grade scale was used: 0 = none; 1 = possible; 2 = define; and 3 = severe. Joint space was measured at the narrowest point in each compartment. Results showed that varus alignment of the knee at initial examination was associated with a 4x increase in the odds of medial compartment OA progression (adjusted for age, sex, and body mass index). Valgus alignment of the knee at baseline was associated with a near 5x increase in the odds of progression of lateral compartment OA. Severity of the angulation of the knee also correlated with increased joint space loss over the 18 month investigation (varus correlated with medial loss, valgus with lateral).

Knee alignment has been shown to predict progression of OA, with severity of the disease a mediating factor. Cerejo (Cerejo et al., 2002) studied 230 participants (377 knees) with knee OA (presence of osteophytes and symptoms of OA). Individuals were categorized by Kellgren/Lawrence grading into groups of mild OA (Kellgren/Lawrence grade 2) and moderate OA (Kellgren/Lawrence grade 3). Progression of the disease was defined as an increase in the severity of joint space narrowing on radiograph occurring

from baseline to an 18 month reexamination. Odds of compartment specific progression were calculated for knees in the presence of malalignment vs. knees without malalignment (medial progression with varus, lateral progression with valgus). These odds were then compared between groups of knees with minimal OA and moderate OA, with the moderate OA group having a higher likelihood of progression. The odds of medial compartment progression in the presence of varus malalignment over an 18 month time period for the two groups were 4 times for the minimal OA knee and 10 times for the moderate OA knee comparatively. Lateral compartment progression in the presence of a valgus alignment was 2 times more likely in the minimal OA group compared to a 10 fold increase in the moderate OA group. These results show that the risk for progression was higher for knees with moderate OA compared to minimal OA.

Miyazaki (Miyazaki et al., 2002) examined the relationship between varus alignment of the knee and the progression of OA but also considered the relationship of the knee adduction moment In this study, data were collected at baseline regarding pain, radiography and gait analysis from 106 participants with medial compartment OA of the knee. At 6 year follow up, 74 subjects were reexamined. Findings showed that varus alignment (mechanical axis) and adduction moment were significantly correlated. Further analysis went on to illustrate that the risk of progression of knee OA (more than one grade narrowing of minimum joint space of the medial compartment) increases 6.46 times with a 1% increase in adduction moment. These results imply that baseline adduction moment, which is significantly correlated with varus alignment, can predict radiographic progression of medial compartment knee OA.

Cartilage volume of the knee can also be used as a marker of progression of OA. Cicuttini (Cicuttini et al., 2004) studied the longitudinal relationship between knee alignment and tibiofemoral cartilage volume in 117 participants with knee OA. Knee cartilage was measured radiographically at baseline and then at approximately 2 years. The researcher found that for every 1 degree increase in baseline varus angle at the knee, there was 17.7 micro l (10^{-6} liter) average annual loss of femoral cartilage volume (medial). For every 1 degree of increase in baseline valgus, there was an average annual lateral femoral cartilage loss of 8.0 micro l. In summary, this study showed that baseline knee angle was associated with the rate of cartilage loss in the knee (increasing knee angles associated with increased cartilage loss).

Researchers have also attempted to construct statistical models to predict the severity of OA. Birmingham (Birmingham et al., 2001) analyzed data from a sample of 20 volunteers. Degenerative change, alignment in varus, standing balance, and knee proprioception were examined. Degenerate change and knee alignment were assessed via weight bearing radiograph. Proprioception was assessed by angle replication testing (dynamometer) and balance was measured on force platform. A predictive model was then constructed via a forward-stepwise regression model, attempting to quantify the contribution of the independent variables, alignment, proprioception, and balance. Results of the model construction showed that 64% of the variability in degeneracy change was associated with alignment and standing balance (37% varus, 27% balance).

Another crucial area of interest is the relationship between alignment of the lower leg and function. This relationship between has been studied by Sharma (Sharma et al., 2001). In this study, 237 individuals with primary OA (OA not occurring from direct

injury) were studied. Physical function was measured using the chair-stand performance test. The result of this test is the rate of chair stands per minute based on the time required to complete five repetitions of rising from a chair and sitting down. This test, calculated in this manner, allows inclusion of individuals unable to complete any repetitions (rate of 0). Participants were separated into three groups at baseline: alignment of 5° or less in both knees, 1 knee with alignment of more than 5° or both knees with alignment of more than 5°. The chair–stand rate was analyzed as a continuous variable, i.e. the change in rate from baseline to 18 months. Results showed that the chair-stand deterioration rate was significantly worse in the group with alignment of more than 5° in both knees vs. those who had alignment of 5° or less in both knees. Significance continued after groups had been adjusted for sex, age, and body mass index.

Knee alignment and its effect on ability to contract the quadriceps was studied by Marks (Marks, Percy, Semple, & Kumar, 1994). In this investigation, the researchers examined the role knee varus alignment had on surface electromyography of the quadriceps during concentric, isometric and isokinetic contractions of the quadriceps femoris. The results showed that the percentage utilization of motor units fro the quadriceps was higher in subject with genu varum ($p < 0.01$). This suggests that the quadriceps of a varus knee might function less efficiently than the quadriceps around a normally aligned knee.

Another important area of research is the mediating role of one joint factor on another and its effect on measures of osteoarthritis. Sharma (Sharma, Lou, Cahue, & Dunlop, 2000) investigated the possible mediating role of malalignment of the knee in the relationship between osteoarthritis of the knee and obesity. Obesity has long been

viewed as a high contributing factor for the development and progression of OA at the knee. This study sought to document the effect of obesity on OA and investigate if the effect of obesity was mediated by the alignment of the knee. In this study, 292 individuals with knee OA were examined. Severity of knee OA was described radiographically. Standing, semi-flexed radiographs were obtained. Compartment specific severity was described as narrowest joint space width in each respective compartment. Alignment was measured from a standing, full leg radiograph and was defined as the angle formed by the intersection of the line from the center of the femoral head to the center of the femoral intercondylar notch, with the line extending from the center of the ankle talus to the center of the tips of the tibial spines. Body mass index (BMI) was described as the weight in kg divided by the height in meters squared of the individual. Statistical analysis was performed in data obtained from the dominant knee (leg subject reported they would use to "kick a ball").

Results in this study found that in varus knee, BMI was negatively correlated with medial joint space width and with narrowest tibiofemoral joint space width (-.27 and -.29 respectively, n 154). This correlation did not hold true for valgus knees (-.10, -.13, n 115). No correlation between medial joint space width and narrowest joint space width was present in the 23 subjects with neutral (neither varus or valgus) knees. Result also showed a correlation between BMI and severity of malalignment in the varus knees (.26) but not the valgus knees (.16). Next, the relationship between BMI and varus malalignment and their effect on radiographic disease was investigated. Results showed a partial correlation of .24 between BMI and disease severity after controlling for sex. This partial correlation was reduced from .24 to .04 when malalignment was added to the

model, indicating that almost all of the effect of BMI on disease severity was explained by varus malalignment after controlling for sex.

Summary of the local intrinsic factor "Alignment".

- Static alignment, particularly varus position correlates with adduction moment at the knee.
- Larger adduction moment is correlated with increased joint space narrowing and also with pain.
- Severity of malalignment is correlated with joint space loss (varus with medial, valgus with lateral).
- Varus and valgus alignment is predictive of cartilage loss, especially for moderate OA v. min OA.
- Alignment coupled with balance can be used in a regression model to predict the severity of OA.
- Individuals with 5° varus or valgus had more functional deterioration overs time than individuals without 5° of malalignment.
- Varus alignment has been shown to correlate with decrease efficiency of quadriceps contraction.
- BMI correlates with severity in varus knees, not in valgus knees.
- Much of the effect of BMI on severity of knee OA was explained by varus alignment not BMI itself in varus knees (when controlled for sex).

Knee Joint Laxity

Knee laxity can be defined generally as the amount of intra-articular sliding, rotation or gapping of the tibia with respect to the femur. As discussed previously, special attention is warranted in the study of factors that might alter the force and shear distribution at the knee. Sharma (Sharma, Lou et al., 1999) notes that knee stability is an important component of the mechanical environment of the knee. Alterations of force and shear via different levels of laxity might contribute to the expression of OA at the knee. Three types of laxity have been examined in the literature: anterior-posterior (AP), varus/valgus, and rotation of the tibia on the femur.

Anterior/Posterior Laxity

The relationship between A/P laxity and demographic characteristics such as age and sex was evaluated by Sharma (Sharma, Lou et al., 1999). In this study, 25 young controls, 24 older control subjects without OA and 164 volunteers with knee OA were examined. A/P translation was measured with a KT 1000 knee testing system. Results of this study showed no difference in the control groups between men and women (6.0 mm ± 3.0 vs. 6.2 mm ± 1.8 respectively). No correlation in the control groups between A/P laxity and age was shown ($r = -.08$). This would suggest that A/P laxity is not a function of age or sex in the normal aging process.

Much of the information describing the relationship between A/P laxity and OA comes from studies examining the effect of damage to the anterior cruciate ligament (ACL). This ligament is a primary restraint to tibial translation on the femur with loss of its function causing increased anterior tibial translation or laxity. McDaniel (McDaniel & Dameron, 1983) examined 52 knees and found that one third of the ACL deficient knees

had joint space narrowing or unequivocal evidence of OA at 14 years after injury. Sherman (Sherman et al., 1988) studied 127 knees and also found that ACL insufficiency naturally progresses toward degenerative osteoarthritis. Consistent with this previous research, Lundberg (Lundberg & Messner, 1997) reported a higher incidence of radiographic OA in a subject pool that also exhibited increased A/P laxity after injury. In this matched pair study of 40 subjects, measures were taken initially and at a 10 year follow up. The group with combined medial collateral ligament and ACL injuries showed increased A/P laxity and higher incidence of radiographic OA when compared to a group with isolated medial collateral ligament injury and less A/P laxity (combined group had 9 instances of grade 1 OA, 1 instances of grade 2 OA vs. 0 instances of any radiographic OA for isolated group).

Radiological evidence of possible precursors to the development of OA have been studied in ACL deficient volunteers (with clinically confirmed joint laxity) by Buckland-Wright (Buckland-Wright, Lynch, & Dave, 2000). In this investigation, 19 ACL deficient subjects were examined at a mean time from injury of 34.3 months. Joint space width, vertical and horizontal trabecular organization of the bone, osteophyte area, and subchondral cortical plate thickness in the medial and lateral compartments were measured. Results showed no statistical difference between affected and uninjured knees in either medial or lateral joint space width (a surrogate for articular cartilage thickness) and subchondral cortical plate thickness. However, horizontal trabeculae in the medial compartment of the ACL deficient knees were shown to be significantly decreased when compared to the uninjured side ($p < 0.01$). In addition, osteophytes were present in 9 out of the 19 of the ACL deficient knees.

One of the limitations in using knees that have experienced a traumatic ACL rupture for study of A/P laxity and its relationship to OA is the confounding effect of trauma on the knee. Buckland-Wright (Buckland-Wright et al., 2000) notes in the introduction to the study described above that the "pathogeneses of cartilage damage and OA after joint injury is uncertain". Factors other than laxity that have been theorized to have a role in the development of OA are chronic low grade synovitis and reticular subcortical fractures ("bone bruising"). Because of these confounding factors, A/P laxity secondary to traumatic tears of the ACL offer limited information in the discussion of OA in an otherwise healthy individual. Non-traumatic ACL disruptions in animal studies offer another avenue of potential information.

Van Osch (van Osch et al., 1996) studied OA development in the knee of mice after injecting collagenase into the joint to disrupt ligamentous function. Collagenase injected into the knee joint caused diffuse ligamentous damage affecting not only the cruciates, but also the collaterals as well. This led to a possibility of laxity occurring in multiple planes. Statistical correction for influences of laxity in a non-A/P direction was therefore completed. Results demonstrated a significant correlation between amount of cartilage loss at the medial tibial plateau and the amount of laxity in the A/P direction ($r = .80$, $p < 0.01$). There was also a significant correlation between osteophyte formation and the medial compartment ($r = .78$, $p < 0.01$). There were no significant relationships found in this study regarding the lateral tibial plateau or either tibial plateau when corrected for A/P laxity.

Lopez (Lopez et al., 2003) conducted a study using a canine model that attempted to mimic the progressive degenerative changes associated with OA of the knee. In this

study, the ACL of 10 skeletally mature female crossbreed dogs (right or left knee randomly assigned) was treated with monopolar radiofrequency energy (MRFE) applied arthroscopically. The opposite knee had the same arthroscopic procedure without MRFE applied. This attempted to remove the effect of the arthroscopic procedure from the investigation. The treatment of the ACL with MRFE resulted in a slow degeneration of the ACL with eventual rupture at approximately 8 weeks post treatment (mean 52.5 days, SEM ± 1.0, range 48-56 days). This gradual degeneration of the ACL and eventual rupture offered a unique chance to approximate the ACL degenerative process that will occasionally occur in the human knee.

Radiographic analysis was completed at 4, 8, 12, 16, and 24 weeks after surgery for all dogs and at 34 weeks after surgery for 5 dogs. All pre-operative and 4 week post-operative radiographs showed no signs of OA. At 12 weeks post-op, 7 of the joints had very small osteophytes on the proximal trochlear ridges of the femur. At 16 weeks post-op, knees showed varying degrees of osteoarthritic changes on the tibial intercondylar eminences and femoral trochlear ridges. At 24 weeks, osteophytosis (growth of osteophytes) of the tibial articular surface and trochlear ridges of the femur and slight subchondral bone sclerosis was present. Thirty-four weeks after MRFE, osteophytosis and subchondral bone sclerosis was more prominent. The severity of the radiographic progression of OA varied among the animals over the period tested, but all joints treated with MRFE developed some degree of all the changes described.

From the studies discussed previously, it appears that the A/P laxity is related to the incidence and progression of OA of the knee, especially ACL deficient knees. Conversely, the severity of OA may have an impact on the tendency for the knee to

become more of less lax in an A/P manner. Brage (Brage et al., 1994) studied 22 subjects (43 knees) to investigate the effect of OA on A/P laxity of the knee. Radiographs were used to separate the subjects into 3 groups: mild OA = osteophytes with preservation of at least ½ the joint space; moderate OA = less than one ½ joint space, but some joint space remaining; severe OA = no detectable joint space at least in the medial compartment. Laxity of the knee was measured with a Genucom Knee Analysis System at a position of 20° flexion. Results of this study suggested a tendency for A/P laxity to decrease as severity increased. Mean (SD)A/P translation for the groups were as follows: control = 12.2 mm (SD 5), mild OA = 15.2 mm (SD 7.9), moderate OA = 10.5 mm (SD 7.1), severe OA = 6.6 mm (SD 6.4). Total A/P translation in severe OA knees was significantly different from that of controls (6.6 mm vs. 12.2 mm, $p < 0.025$). Knees with mild OA were significantly different from severe OA ($p < 0.009$). Although the mean A/P laxity in mild OA knees was slightly higher than the controls, this difference was not found to be clinically significant.

Findings by Wada (Wada et al., 1996) support the findings of Brage (Brage et al., 1994) that A/P laxity gradually decreases as severity of OA increases. In the study by Wada, 68 knees (34 subjects) were classified by the Kellgren/Lawrence grading system for OA severity. A/P laxity was measured by the Genucom system as used in the Brage study. Results showed knees with Grade I OA had an increased mean A/P laxity measure when compared to the mean of the control group. Means from Grades II – IV OA gradually decreased as the severity increased: Control = 6.1 mm ± 1.8, Grade I = 10.0 ± 6.3, Grade II = 9.1 ± 4.1, Grade III = 6.8 ± 3.2, Grade IV = 6.2±3.4). Control knees

differed significantly from Grade I knees only (ANOVA, $p < 0.05$). In summary, both studies showed a mean tendency for A/P laxity to decrease with severity.

Results regarding the tendency for A/P laxity to decrease as severity increased are consistent; however, results concerning differences between individuals with knee OA and those without have been equivocal. In the study by Brage, knees with OA had lower A/P laxity than the control, whereas in the study by Wada knees with OA had elevated A/P laxity when compared to the control group. In the study by Sharma (Sharma, Lou et al., 1999) described previously, AP laxity did not differ between subjects with combined severity levels of OA or individuals with mild OA only when compared to older control subjects.

As noted previously, results have been reported on A/P laxity and its relationship to the development and progression OA knee OA, but little investigation has been completed on the outcome of reducing A/P translation in an individual that already has OA. One such study has been completed by Reeves (Reeves & Hassanein, 2000). In this randomized, prospective, double-blind, placebo-controlled study, the investigator used dextrose prolotherapy in subjects with OA of the knee, with or without ACL laxity. One hundred eleven knees in 68 subjects were studied. Criteria for knee OA included 6 months or more of knee pain with grade 2 or more joint narrowing or grade 2 or more osteophytic change. Grade 2 joint narrowing was defined as the presence or less than or equal to 3 mm or cartilage. A grade 2 osteophyte was defined as a bone spur that was short, fat and obvious or a moderately long (10 mm or more), thin bone spur. ACL laxity was measured by KT 1000 with laxity judged to be present when anterior displacement difference greater than 2 mm occurred. Knee pain was measured via a 100 mm visual

analogue scale. Subjects self scored the following variables: pain level walking on level surfaces and stairs, swelling and knee buckling episodes. Injections, both prolotherapy and placebo were completed initially and again at 2 and 4 months. Prolotherapy injections were continued at 6, 8, and 10 months for the treatment group. Subjective variables, ROM via goniometry, radiographs, and KT 100 measurements were taken initially and at the 1 year mark.

Results from Hotelling multivariate analysis of paired values at 0 and 12 months revealed a statistically significant improvement ($p = 0.021$) for pain, swelling, joint flexion and joint laxity in the ACL laxity group treated with dextrose prolotherapy. Eight of the 13 dextrose treated knees with ACL laxity no longer tested as lax via the KT 1000 at the 12 month mark. No variables were found to be significantly changed at the 6 month mark. Prolotherapy is theorized to both increase growth factor effectiveness to promote tissue repair and also to improve stability of the joint. This study showed, albeit with a small subject pool of OA knees that also had ACL laxity ($n = 13$), that prolotherapy significantly decreased laxity as well as improved subjective measures of pain and function. Causation can not of course be implied, but the findings are of interest in the discussion of A/P laxity and knee OA none the less.

Varus/Valgus Laxity

Laxity in a varus/valgus manner can be described as gapping of the tibia on the femur in the frontal or horizontal plane. Varus laxity is defined as non-physiological motion between the tibia and femur in the frontal plane such that the tibia is directed toward midline with gapping of the lateral aspect of the tibial-femoral joint. Valgus laxity therefore consists of joint gapping on the medial side of the knee, with the distal

aspect of the tibia rotating away from midline. Currently, varus/valgus laxity is emerging as a very important intrinsic factor in the study of OA of the knee.

In addition to A/P laxity, Brage (Brage et al., 1994) also examined the relationship between varus/valgus laxity and severity of OA of the knee (presence of osteophytes and decreasing joint space). In review, 43 knees (22 subjects) were separated into three groups based on severity of knee OA from radiographs. Varus/valgus laxity was assessed via a Genucom Knee analysis System. Results for varus/valgus laxity reported in mean and standard deviation (SD) were as follows: control = 11.3° (SD 3), mild OA = 15° (SD 4.8), moderate OA = 10.9 ° (SD 3.9), severe OA = 10.4° (SD 3.6). Total varus/valgus laxity was significantly higher in the mild OA group when compared to the moderate OA group ($p < 0.046$) and those with severe OA ($p < 0.016$). This finding that varus/valgus laxity generally decreases as OA progresses, however, has not been consistently demonstrated in other research.

Wada (Wada et al., 1996) also studied the relationship between severity of knee OA and laxity (see previous discussion of methodology in A/P laxity section). Results for varus/valgus laxity were as follows (total varus/valgus laxity in mean degrees): Control = 12±3.8, Grade I = 11.5 ± 5.4, Grade II = 11.9 ± 4.3, Grade III = 15.1± 5.1, Grade IV = 15.9±5.4). A general tendency for total varus/valgus laxity to increase as severity worsens can be seen, however no statistical difference was found between controls and any group or among the groups themselves. Other studies have been able to demonstrate this relationship between increase laxity and worsening OA with statistical significance however.

Sharma (Sharma, Lou et al., 1999) investigated the relationship between severity (Kelgren-Lawrence [K/L] grading) and total varus/valgus laxity in 164 subjects with knee OA. In this cross-sectional study, a measuring system was constructed to measure varus/valgus laxity (previous devices utilized by other researchers to measure varus/valgus laxity such as the Genucom were no longer commercially available). Results of this study showed that varus/valgus laxity increased as joint space decreased (slope -.34; 95% CI -.48, -.19; $p < 0.0001$) and was greater in knees with bony attrition when compared to those without (5.3° vs. 4.5°; 95% CI of difference of .32, 1.27; $p = 0.001$). These findings are inconsistent with the findings of Brage (Brage et al., 1994) and support the findings of Wada (Wada et al., 1996).

Results of the previously reported study by Sharma also address sex differences in laxity as well as findings that suggest that varus/valgus laxity may precede the development of knee OA. It was noted that women in the control group tended to be more lax than men (3.6° versus 2.7°; 95% CI of difference .38, 1.56; $p = 0.004$).

Additional results showed that varus/valgus laxity was greater in the unaffected knees of OA subjects (K/L grade 0 or 1) than in older control knees (4.9° compared to 3.4°; 95% CI of difference .60, 2.24; $p = 0.0006$). It was also found that varus/valgus laxity was greater in knees with mild OA (K/L grade 2) than compared knees of older controls (4.4° compared to 3.4; 95% CI of difference .43, 1.52; $p = 0.0005$). These results in addition to the finding that laxity correlated modestly with age in healthy controls ($r = .29$, $p = 0.04$) supports the conclusion that at least some portion of the laxity measured occurs prior to OA onset.

Sharma also drew conclusions regarding the possible role laxity plays in the pathogeneses of knee OA. Sharma noted that incidence and progression of laxity due to OA appears to be a later stage phenomenon (joint space decrease and bony attrition allows ends of supporting structures such as ligament and capsule to approximate somewhat, lessoning their ability to stabilize the joint). If varus/valgus laxity present in OA were only the result of these changes, then unaffected knees of individuals with OA, and joints in the early stages of the disease would tend not to differ in the amount of varus/valgus laxity compared to age matched controls. Taking into account that varus/valgus laxity tends to increase with age ($r = .29$, 95% CI 0.01, .53), it would make it even less likely that knees of early stage OA and unaffected knees of individuals with OA would be more lax than older control subjects. This was, however, found to be true. These findings, considered together, suggest that a certain degree of laxity pre-dates the development of OA. Due to the cross-sectional nature of this study, these results however, can not be definitively generalized to OA progression.

Although research has found (somewhat equivocally) that varus/valgus laxity increases with decreasing joint space, other radiographic signs of OA have been associated with decreased laxity. Pottenger (Pottenger, Phillips, & Draganich, 1990) investigated the effect osteophytes have on the stability of the knee. In this study, 20 knees with unicompartmental osteoarthritis were examined in vivo during a total knee replacement surgery. Varus/valgus laxity increased from 11° to 13.1° ($p < 0.05$) after osteophytes were removed. This finding suggests that osteophytes at the knee margin added to the varus/valgus stability of the knee.

The mediating role of varus/valgus laxity between strength and function has also been studied (Sharma, Hayes et al., 1999). In this investigation, 164 volunteers with knee OA were examined. Inclusion criteria for this study included definite osteophyte presence in either the medial or lateral compartment of the knee and patient self reporting at least "a little" difficulty with knee-requiring activities. Strength (maximum torque production) was measured via both isometric and isokinetic contractions. Quadriceps isometric testing was done at 60° knee flexion and hamstrings were tested at 45° flexion. Isokinetic testing for both knee extension and flexion was completed at 120°/sec, motion limited from 0-90° of flexion. Varus/valgus laxity was measured with the device previously noted (Sharma, Lou et al., 1999). Laxity was defined as the total varus/valgus rotation for each knee.

Functional status was assessed using the Likert version of the Western Ontario and McMaster Universities OA Index Physical Function subscale (WOMAC-PF) and the chair-stand performance test. The WOMAC-PF is a 17 question, self-report of function that is disease specific for knee or hip OA (higher scores equal worse function). Chair test consisted of time required for 5 repetitions of rising from a chair and sitting down. This time was used to calculate a number of total repetitions that would have been completed in 1 minute. At score of 0 was used to represent individuals that were unable to complete the test. Evaluators of strength, laxity, and functional status were blinded to results from other categories of testing.

The results of this study demonstrate a relationship between strength and function and also suggest that knee laxity mediates this relationship. Moderate correlations were found between chair-stand rate and isokinetic quadriceps strength (r = .52, 95% CI .39,

.62) and isometric quad strength (r = .5, 95% CI .37, .60). Correlations were also noted between scores on the WOMAC-PF and quad strength tested isokinetically (r = -.32, 95% CI -.45, -.18) as well as isometrically (r = .44, 95% CI .31, .56). Note that values of WOMAC-PF scores are negatively related to function (high score, low function) while chair-test results are positively related.

Measures of function also correlated with strength of the hamstrings. Chair-stand measures correlated moderately with hamstring strength measured isokinetically (r = .52, 95% CI .4, .63) and somewhat more weakly isometrically (r = .44, 95% CI .31, .56). WOMAC-PF scores also correlated weakly with isokinetic hamstring strength r = -.36, 95% CI -.49, -.23). WOMAC-PF scores showed little correlation with isometric hamstring strength.

Laxity was also shown to have a significant relationship to function (laxity correlated with poorer function). The median varus/valgus laxity was 9.25° and this value was used to define groups of high laxity (above the median) and low laxity (below median). The low laxity group had lower WOMAC-PF scores when compared to the high laxity group (mean ± SD 20.8 ± 13.8 vs. 26.5 ± 13.3; 95% CI for difference -9.9, -1.5). Chair-stand scores also reflected the relationship between laxity and function described above, although results were statistically insignificant.

Next, the mediating effect of laxity on the relationship between strength and measures of function was examined. Eight combinations of strength and function were examined (isometric, isotonic, quad, hamstring, WOMAC-PF, and chair-stand). In each case, the correlation between strength and function was lower in the high laxity group (n=80) when compared to the low laxity group (n = 84). This relationship remained

when the results were controlled for age, sex, body mass index, and pain. In summary, results suggest that varus/valgus laxity mediates, in this cases decreases, the magnitude of the relationship between measures of strength and function at the knee.

Tibial/Femoral Rotation Laxity

Tibial/femoral rotation was among the types of laxity studied by Wada (Wada et al., 1996) in a previously cited investigation. In review, 68 knees with medial compartment OA were studied. Knees were separated into groups based on Kellgren/Lawrence (K/L) grading. Tibial/femoral rotation was measured with a Genucom Knee Analysis system. The test consisted of an internal and external rotation stress test at 80° knee flexion. Results of this examination demonstrated that control knees had significantly greater rotation than knees with K/L grade IV OA (48.4 ± 5.9° vs. 38.3 ± 9.5°; ANOVA $p < 0.01$). Comparisons among the K/L groups showed a greater amount of rotation in grade I vs. grade IV (46.5 ± 16.5° vs. 38.3 ± 9.5°; ANOVA $p < 0.01$). In summary, tibial/femoral rotation laxity appeared to decrease as OA severity increased.

Summary of the local intrinsic factor "A/P Laxity".

- There is no correlation between sex and A/P laxity.
- A/P laxity does not appear to be function of the normal aging process; in individuals without OA of the knee, there is no clear tendency to become either more or less lax in a an A/P direction with age.
- Evidence suggests that individuals who have torn their anterior cruciate ligaments (a prime A/P stabilizer) are more likely to develop OA of the knee

later in life. Animal models that seek to lessen the possible confounding effect of trauma to the knee after ACL tear support this finding.

- A/P laxity tends to decrease as the severity of OA increases, but there is no consistent statistical evidence to support that individuals with OA of the knee are more or less lax in an A/P direction than those without OA.
- Prolotherapy has been shown in a small subject pool to decrease A/P laxity and improve measures of pain and function in knees with OA.

Summary of the local intrinsic factor "Varus/Valgus Laxity".

- Varus/valgus laxity tends to increase with age in a healthy population.
- Women tend to be more lax than men in a healthy population.
- Findings regarding the relationship between total varus/valgus laxity and level of knee OA severity are equivocal, with recent research showing increased laxity associated with worsening of the disease (decrease joint space, increased bony attrition).
- Marginal osteophytes tend to decrease varus/valgus laxity at the knee.
- Unaffected knees in individuals with OA tend to have more varus/valgus laxity than older control subjects.
- Knees with early stages of OA tend to have more varus/valgus laxity than older control subjects.
- Increase in varus/valgus laxity weakens the relationship between strength and measures of function.

Summary of the local intrinsic factor "Tibia/Femoral Rotation Laxity".

- Tibial/femoral rotation laxity appears to decrease as OA severity increases.

Proprioception of the Knee

Well coordinated muscular activity helps attenuate shock and distribute load during weight bearing activities. Muscular activity is also an important component in the protective response that occurs when a joint is being subjected to abnormal load or motion during trauma. Proprioception (the conscious and unconscious perception of limb position in space (Sharma, 1999)) together with other sensory input (i.e. visual, vestibular) helps coordinate this muscular activity (Lephart et al., 1998).

Proprioception as a construct includes different subcategories of afferent stimulation and consequently different anatomical structures and pathways. Proprioception includes the sensation of joint movement (known as kinesthesia) and joint position sense (Lephart, Pincivero, Giraldo, & Fu, 1997). Kinesthesia in the knee is commonly measured by a technique called "threshold to detection of motion". During this procedure, the joint is moved slowly (usually 0.5 to 2 deg/sec) while other afferent input is minimized (subject is blindfolded, pneumatic splints reduce ankle motion and reduce sensation from the moving portion of the apparatus). Because this activity is passive and very slow, threshold to detection of motion seeks to selectively measure joint mechanoreceptors. These mechanoreceptors include both rapidly adapting receptors (e.g. Pacinian corpuscles) and slow adapting receptors (e.g. Ruffini endings and Ruffini corpuscles) (Lephart et al., 1997).

Joint position sense at the knee can be measured by the reproduction of a target angle. The subject is asked to reproduce a target angle of knee flexion at which the knee had been previously positioned. This initial placement and reproduction can either be completed actively or passively. As with detection to threshold of motion, similar attempts are made eliminate or minimize visual or other stimulation not associated with the joint being tested. If completed actively, this form of testing measures both joint and muscle receptors and is believed to be a more functional method of assessing these afferent pathways (Lephart et al., 1997). Due to the role proprioception plays in both joint protection and load distribution at the knee, it warrants consideration as an important local intrinsic factor.

Many authors have investigated the relationship between proprioceptive acuity and the presence of OA of the knee. Marks (Marks, 1996) used a camera and reflective markers to study the angle reproduction capabilities of females with knee OA in a weightbearing position during a single leg squat. Ten healthy young women (ages 18-30), 11 older healthy women (ages 38-61), and 15 women with symptomatic knee OA (ages 37-74) were studied. Individuals with OA met at least 3 of six clinical criteria recommended by The American College of Rheumatology. Subjects were asked to stand on one leg and lower themselves to a target angle between 15-45°. After attaining this angle, the subjects were asked to hold the angle for 5 seconds and then returned to standing. After approximately 7 seconds rest in standing, the subjects then attempted to reproduce the target angle. Photographs were taken to document the target and reproduced angle. Two testing sessions were completed 3-5 days apart with 2 trials completed on each day (total of 4 trials per individual). The results showed that

individuals with OA performed the rematching tests with less accuracy than the controls ($p < 0.03$). When subjects with OA were compared to just the 11 older healthy controls, statistical difference remained ($p = 0.02$). It was also noted that subjects with OA tended to be more likely to make errors of overestimation of the angle, termed flexion errors by the author.

Other researchers have also found that individuals with OA have decreased proprioception when compared to control groups. Hassan (Hassan et al., 2001) studied proprioception, static postural control, and maximal voluntary contraction of the quadriceps in 108 subjects (59 with knee OA, 49 controls). OA was identified via both symptoms and radiographic evidence of the disease. The control group was matched for age and sex and OA was excluded by no symptoms, no history of knee trauma and normal clinical exam. Proprioception of the knee was assessed in a seated, non-weight bearing angle reproduction test. During this test, the knee was moved passively to the target angle, held for 5 seconds, and then passively returned to the start angle. The subject was then asked to actively reproduce the target angle. Target angles were randomly selected between 90° flexion and full extension. The results from this study demonstrated that subjects with knee OA had reduced proprioceptive acuity when compared to age and sex matched controls (controls: mean 7.9, 95% CI 6.9 to 8.9; subjects mean 12.0, 95% CI 10.5 to 13.6, $p < 0.001$). These findings, in addition to those reported by Marks (Marks, 1996), support the conclusion that individuals with knee OA have decreased knee joint position sense measured via angle reproduction.

Findings of decreased proprioception in a population with knee OA have also been found utilizing methods of assessment other than angle reproduction. Pai (Pai et al.,

1997) noted similar results using threshold to detection of motion. In this study, 30 subjects with bilateral knee OA (K/L grade of 2 or above in both knees) were compared to 29 elderly control subjects and 25 young controls. The elderly controls met clinical and radiographic criteria for exclusion for OA. This helped assure the elderly controls did not have sub-clinical OA of the knee. Starting angle for threshold to detection of motion was 45° knee flexion and speed of motion was 0.3°/sec. Visual, auditory, and tactile stimulation was controlled by use of blindfold, earphones, and foot/ankle air splint. Ten trials were analyzed with the mean angular displacement between initial and final position calculated. Results of the study demonstrated that proprioceptive accuracy is decreased in knees with OA when compared to elderly control subjects (Right Knee: $F[1,57] = 9.12$, $p = 0.0038$; Left Knee: $F[1,57] = 8.22$, $p = 0.0097$).

This investigation also found that proprioception accuracy declines with age (Right Knee: $r = 0.598$; $p < 0.001$); Left Knee: $r = 0.501$; $p < 0.001$). Previous studies with similar findings did not address the potential confounding effect of sub-clinical OA in their older control subjects. By selecting a control group with no radiographic or physical evidence of OA, Pai demonstrated more definitive evidence that proprioception decreases with age in a normal control population.

Differences in proprioception between affected and nonaffected knees in a population with OA were studied by Sharma (Sharma et al., 1997). Results provided information concerning the possible role proprioception plays in the pathogenesis of knee OA. Sharma studied 28 subjects with unilateral knee OA and 29 elderly controls. To be categorized as affected or unaffected, knees had to pass both radiographic (affected K/L grades ≥ 2; unaffected < 2) and clinical criteria. Proprioception was measured by

threshold to detection of motion in a manner identical to that described by Pai (Pai et al., 1997). Results of this study showed that there was no statistical difference in proprioception between the unaffected and the affected knees in individuals with unilateral knee OA (affected knee: mean 4.00° ± SD 2.68; unaffected knee 4.70° ± SD 3.99; p = .13). One of the stated objectives of this study was to explore the causal direction of the relationship between proprioception and the development of knee OA. The results of this study suggest that decreased proprioception is not solely the result of knee OA. Sharma reasons that if decreased proprioception were solely caused by OA, then "proprioception should be worse in the arthritic knee than in the unaffected knee in those with unilateral knee OA". Sharma was able to show in this study, that this was not the case. Sharma concludes in her discussion that this finding "adds support to the theory that the impairment (decreased proprioception) is a pathogenic factor in the age-related increase in knee OA".

The finding that proprioception was not different in the unaffected and affected knee in individuals with unilateral OA of the knee has also been shown utilizing angle reproduction measures. Garsden (Garsden & Bullock-Saxton, 1999) studied 20 subjects with unilateral OA of the knee and 20 age-matched controls using a partial weightbearing angle reproduction test. Subjects were included in the OA group if they satisfied the clinical criteria for knee OA as set forth by the American Rheumatism Association (R. D. Altman, 1991a). No radiographs were reported. Severity of disease was rated by an index of severity ranked mild, moderate, severe, very severe and extremely severe (Lequesne, 1991). Control group subjects consisted of individuals with no history of knee pathology. Unilateral knee angle reproduction testing was measured utilizing a 20°

reclining sliding platform and an electronic inclinometer. Target angles were chosen between 20° and 40°. Six trials were completed per subject with a new target angle being chosen for each trial. Results showed that there was no statistical difference between the affected and unaffected knees in the group with OA ($F[5,15] \leq 1.33$, non-significant). These results support the earlier findings by Sharma (Sharma et al., 1997) that deficits in proprioception are not solely caused by OA, but rather might serve a role in the development or progression of OA.

Further information regarding the role of proprioception in the development of knee OA can be obtained from studies utilizing animal models. O'Connor (O'Connor, Visco, Brandt, Myers, & Kalasinski, 1992) examined the effect of disrupting the peripheral, afferent nerve supply in combination with transaction of the anterior cruciate ligament (ACL) in dogs. In this study, the afferent nerve supply of the knee was partially interrupted by neurectomy of the primary articular nerves in the canine knee (medial, lateral, and posterior articular nerves). Four study groups were analyzed: Group A: 4 dogs with neurectomy only; Group B: 13 dogs had ACL transection only (7 sacrificed at 8 weeks [B/8], six sacrificed at 18 weeks [B/18]); Group C: 15 dogs with neurectomy, followed by 2 week later transection of the ACL (7 sacrificed at 8 weeks [C/8], 8 sacrificed at 18 weeks [C/18]); and Group D: 7 dogs with neurectomy and 2 week later sham ACL transection. The researchers found that OA developed in all dogs post transection of the ACL. Dogs with neurectomy alone did not develop OA in the time frame studied, but dogs that had neurectomy prior to transection of the ACL had OA lesions that were more frequent and severe than in those that had ACL transection alone ($p \leq 0.05$).

O'Connor also investigated the timing of the disruption of the peripheral, afferent stimulus in a unstable canine knee (O'Connor, Visco, Brandt, Albrecht, & O'Connor, 1993). A more complete disruption of afferent stimuli was also completed by dorsal root ganglionectomy (DRG) vs. the selected peripheral nerve transection completed in the study reported previously (O'Connor et al., 1992). Five study groups were analyzed: Group A: ACL transection only (n = 7); Group B: ACL transection, followed by DRG at 52 weeks (n = 8); Group C: DRG 2 weeks prior to ACL transection (n = 8) ; Group D: sham DRG 2 weeks prior to ACL transection (n = 7); and Group E: DRG 2 week prior to sham ACL transection (n = 8). The results of this study showed that the timing of the disruption of the peripheral afferent input was related to the development and severity of OA. All dogs with unstable knees (ACL transection) went on to develop OA. Dogs in group C (DRG 2 week prior to ACL transection) developed significantly worse OA lesions than the other 4 groups ($p \leq 0.05$) including group B (DRG 52 weeks post ACL transection). As with O'Connor's previous study (O'Connor et al., 1992), dogs with surgically decreased peripheral afferent sensation but intact anterior cruciate ligaments did not develop OA. This combination of results, supported by O'Connor's previously sited work, suggest that the presence of peripheral afferent sensation did not serve a role in the protection of a stable canine knee from developing OA, but rather assisted in protecting an acutely unstable knee from rapid and severe development of OA. The authors proposed that the presence of peripheral afferent sensation helped the central nervous system (CNS) "learn" to protect the unstable knee from damage. Peripheral afferent stimulation, the authors theorize, provides the CNS with feedback regarding pain and sensation of instability during trial and error usage of the limb. Once these new

patterns of motion are "learned" by the CNS, the role of peripheral afferent sensation becomes less important in protecting the knee from damage.

The relationship between radiographic severity of knee OA and proprioception has been investigated by Birmingham (Birmingham et al., 2001). In this study (reported earlier in this literature review emphasizing results related to alignment) proprioception, knee alignment, and standing balance were examined in 20 subjects with knee OA. The severity of OA was measured radiographically using a K/L grading system (grades I-IV, assessing joint space narrowing, osteophytes, sclerosis, and deformation of joint contour). Proprioception was measured utilizing an angle reproduction test. Subjects were seated and actively extended their knees to 1 or 5 randomly selected target angles between 30° and 60° of flexion. Subjects held this position for 3 seconds then returned to the start position. After a 5 second pause, they attempted to reproduce the target angle. Subjects completed 5 repetitions and the outcome score was the average absolute error between the target and reproduced angle for all trials. Pearson's r calculated for proprioception and the severity of degenerative change was very low and non-significant ($r = .04$, $p = 0.87$).

The finding that proprioception was not associated with degree of severity was also found in the study by Sharma reported previously in this literature review (Sharma et al., 1997). Sharma reported that the relationship between K/L grades and proprioception was not significant ($r = .33$, $p = 0.077$). The researcher noted however, that it was likely that there was insufficient power to test this hypothesis. The finding reported by Birmingham (Birmingham et al., 2001) that severity of OA and proprioception were not

related might have also been influenced by the low number of subjects. Due to this issue of power, it is unclear whether proprioception worsens as the severity of OA increases.

The relationship between proprioception and function is another important area of research. In the previously reported study by Pai (Pai et al., 1997), the relationship between proprioception (threshold to detection of motion) and a OA specific measure of function (WOMAC-PF) was examined in 30 subjects with bilateral knee OA. The results of this study showed a modest correlation between proprioception and function score ($r = .397$, $p = 0.030$). The direction of the correlation demonstrates that subjects who had worse proprioception tended to have more functional limitations.

The role of proprioception in determining physical functioning was also studied by Sharma (Sharma, Cahue et al., 2003). In this study the role of proprioception in the prediction of poor physical function outcome over a 3 year span in subjects with knee OA was investigated. Two hundred fifty seven individuals with knee OA were examined at baseline, 18 months, and 3 years. Proprioception was measured via threshold to detection of motion as described by previous authors (Pai et al., 1997; Sharma et al., 1997). Disease severity was assessed using K/L ranking assessing osteophytes, joint space narrowing, and presence of sclerosis. Physical function was assessed at baseline and 3 years by the WOMAC Physical Function Scale (WOMAC-PF) and the rate of chair-stand performance. Proprioception was analyzed as a continuous variable. WOMAC-PF scores were categorized into quintiles based on the cohort at baseline. The quintiles were defined as follows: first quintile (0-7), second quintile (8-14), third quintile (15-22) fourth quintile (23-33) and fifth quintile (>33). The chair-stand rate was also categorized

in quintiles: first quintile (≤ 15.0), second quintile (> 15.0 and ≤ 20.4), third quintile (> 20.4 and ≤ 23.8) fourth quintile (> 23.8 and ≤ 27.5) and fifth quintile (>27.5).

Functional outcomes were categorized in a manner that sought to address the limitation of ranking schemes that do not adequately describe a "good" result as one when a subject maintains a high level of function or conversely a "poor" outcome as one when a low level is sustained. In this study, WOMAC-PF scores were organized such that a "Good" outcome was noted over a 3 year span when a subject moved into a higher function quintile group or remained within the 2 highest function groups. A "Poor" outcome was noted when an individual moved into a lower functional group or remained in the lowest 3 functional groups. Functional outcome as measured by the chair-stand group was similarly categorized. Results of this study showed a statistically significant difference between the proprioception measures in the chair-stand rate "good" outcome and "poor" outcome groups (good outcome: $2.1° \pm 1.2°$; poor outcome: $2.5° \pm 2.0°$; $p < 0.05$). This outcome suggested that proprioception deficits placed individuals with knee OA at greater risk for a poor functional outcome during a 3 year interval. Proprioception did not show a similar relationship in the WOMAC-PF measured function group (non-significant difference between the groups).

Other authors have noted inconsistent findings regarding the relationship between proprioception and measures of function. Bennell (Bennell et al., 2003) studied this relationship in a cross-sectional analysis on 220 individuals with knee OA. The diagnosis of OA was confirmed by clinical and radiological classification criteria suggested by the American College of Rheumatology (R. Altman et al., 1986). Severity of OA was graded by the K/L system. The affected limb, or most affected limb in bilateral OA subjects was

studied. Proprioception was measured with a non-weight bearing angle recreation test. During this procedure the knee was passively moved to a target angle of either 20° or 40° where it was actively held by the subject for 3 seconds. The limb was then passively returned to the start position (approximately 80°). The participant was then asked to actively match the target angle. All measures were completed via a camera based assessment device.

Function was measured with several tasks and also by self report. A timed up and go test (TUG) was one of the tasks included. During this test, a the following activity was timed: subject rises from a standard arm chair, walks 3 meters, turns, returns to the chair and sits down. Pace was self-selected by the subject. Self-report of function was assessed by the WOMAC-PF.

The results of this study were mixed, but the authors concluded that there was little or no significant relationship between proprioception and function. Scores on the WOMAC-PF were not significantly related to proprioception at either angle. No functional tasks were found to be significantly related to proprioception (step test, or walking speed) except the timed up and go at 20°. This relationship was found to be significant at the 0.01 level, but the authors noted that the strength of the relationship was weak with a r value less .24. Further analysis reveled that function was also not significantly different between groups when separated into “best” and “worst” proprioception groups. This lack of relationship between function (WOMAC-PF) and proprioception was also noted in a secondary finding from a previous study discussed in this literature review. Hassan (Hassan et al., 2001) noted that proprioception (open chain,

angle reproduction) was not included in a model that predicted function (among variable such as postural control, maximal voluntary contraction of the quads, pain, age, weight).

As can be noted from the previously discussed literature, the relationship between function and proprioception is ill defined. The relationship between pain and proprioception however, has been somewhat more clearly illustrated. Hassan (Hassan et al., 2002) studied the effect of pain reduction on proprioception. In this study, a local anesthetic (5 ml 0.5% bupivacaine) or a placebo (5 ml 0.9% saline) was injected into a symptomatic knee with OA. Subjects had radiographic evidence of osteophytes with definite joint space narrowing in either (or both) the medial tibiofemoral or patellofemoral compartments. Each subject received intra-articular injection of either the anesthetic or the placebo spaced 2 weeks apart. Order of injection was randomized and the nature of injection (anesthetic vs. placebo) was blinded. The injection procedure included a small (5 ml or less) synovial fluid aspiration to confirm correct needle placement. Pain was measured via a 100 mm visual analog scale (VAS). Knee joint proprioception was measured with a seated, non-weight bearing angle reproduction test similar to that utilized in a previous study by the same author (Hassan et al., 2001). During this test, the knee was moved passively to the target angle (randomly selected between 90° flexion and full extension), held for 5 seconds, and then passively returned to the start angle. The subject was then asked to actively reproduce the target angle. One practice trial was completed. Proprioception acuity was defined as the mean error of the next 3 trials.

Results of this study demonstrated that proprioception did not improve with pain reduction. Rather, proprioception actually worsened with the injection of the anesthetic

(-28.15, IQR -83.47 to 19.74, p = 0.009). It is important to note that both the bupivacaine and placebo resulted in statistically significant reduction in reported pain ($p < 0.001$). Proprioception did not significantly change with the placebo (-10.26, IQR -35.91 to 24.82, p = 0.18). The authors proposed that the worsening of proprioception following the injection of the anesthetic was due to direct inhibition of intra-articular neuroreceptors that convey information regarding proprioception. They also concluded that the finding that proprioception did not improve with pain reduction suggests that proprioception deficits in individuals with knee OA are not the primary result of pain.

Sharma (Sharma et al., 1997) also examined the relationship between pain and proprioception in a study sited previously in this literature review. In this study, pain (average pain in the last week) was measured via a 100 mm VAS and proprioception was assessed with a device to measure threshold to detection of motion. Results of this demonstrated that proprioception had little correlation to pain in the knee with OA (r = .12).

Bennell's study (Bennell et al., 2003) examining the relationship between joint proprioception and disability reported previously, also investigated pain. Pain was measured with a 10 cm horizontal VAS (average pain on movement and activity restriction over the previous week and pain during proprioception testing). Pain was also measured as a component of the WOMAC. Proprioception was assessed with a non-weight bearing angle recreation test, measured via camera and reflective markers. Results between proprioception and all measures of pain showed little correlation between measures of pain and proprioception. The highest correlation coefficient (.23, between pain during proprioception testing and proprioception error) could explain only

approximately 5% of the variability in proprioception measures. When results were compared between groups separated into lowest and highest proprioception error tertiles, no significant differences were noted in relation to pain (significance level set at $p < 0.01$).

Only one study was found that demonstrated a statistically significant relationship between pain and proprioception. In the aforementioned study by Pai (Pai et al., 1997), pain was measured with a 10 cm VAS and proprioception was measured via threshold of detection of motion. Results of this study demonstrated a statistically significant relationship between pain and proprioception (right knee: $p = 0.046$; left knee: $p = 0.016$). Although the results were statistically significant, the correlation was weak (right knee: $r = .367$ left knee: $r = .436$).

Summary of the local intrinsic factor "Proprioception".

- Proprioceptive acuity decreases in the presence of OA.
- Proprioceptive acuity decreases with age.
- Individuals with unilateral OA of the knee show statistically non-significant differences in proprioception acuity between their affected and nonaffected knees.
- In canine studies, disruption of peripheral afferent sensation has been shown to accelerate and worsen the development in OA when the disruption occurs in the presence of an acutely unstable knee (ACL transection). This relationship has been documented not to occur if the ACL transection occurs 52 weeks prior to the disruption of peripheral afferent sensation.
- Proprioception acuity is not related to radiographic severity of knee OA.

- Proprioception has not been shown to consistently relate to function.
- Pain does not appear to be related to proprioception.

Balance

Balance, or the ability to maintain a stable position, is also an intrinsic joint factor that could impact the integrity and health of the joint. Gross damage to the joint can occur secondary to balance impairments due to falls and injury. More subtle damage may occur in the joint with less severe loss of balance episodes that cause sudden and unnatural loading of the joint in an attempt to maintain one's upright positioning. Because of the potential mechanical effect that this factor may have on the knee, balance warrants further discussion.

Balance is often assessed utilizing a force platform that can measure the location of the center of pressure while standing. Static postural sway is a common measurement completed by researchers studying balance. During this measurement, participants are instructed to stand still and the excursion of the center of pressure is measured. Vision, head motion, and stability of the surface are variables that are often modified. Researchers have also measured the location of the center of pressure during more dynamic activities such as reaching or leaning forward and back.

Some researchers have utilized functional activities in their measurement of balance. These activities often include standing on one leg or walking under differing conditions (e.g. eyes open or closed, with and without head motions). The test is terminated and a measure of time or distance is taken when performance parameters are violated (e.g. subjects moving from "balance" position or deviates from walking path).

Although variations of the aforementioned techniques are common, force platform center of pressure assessment and time/distance measures during functional activities constitute the bulk of the methodology used in the study of balance.

The relationship between balance and OA was examined by Wegener (Wegener, Kisner, & Nichols, 1997). In this study, the balance of 11 participants with OA of the knee was studied in addition to 10 age matched controls. Inclusion in the OA group required radiographic diagnosis of a physician. Balance was assessed via force platform measurement of the motion of the center of pressure (postural sway) during 2 trials of 6 different testing conditions. The 6 conditions tested consisted of 2 visual conditions and 3 platform conditions. Visual conditions consisted of eyes open and eyes closed. The platform conditions were stable (platform not moving), angular rotation (platform moving in a sinusoidal motion of 4° up and 4° down at a rate of 2° per sec) and linear translation (platform moving 0.75 inches forward and back at a rate of one inch per 0.8 seconds). Each test lasted 10 seconds and measurement reflected the standard deviation in centimeters of the center of force during that time frame. Results of this study found that members of the OA group had worse balance (increased postural sway or larger standard deviation of center of pressure) in all testing conditions ($p < 0.02$). Increased postural sway was also noted in individuals with OA when compared to the control group for each testing condition (visual deprivation, $p = 0.0006$; platform motion, both angular ration and linear translation, $p = 0.0001$). Results from this study support the conclusion that individuals with OA of the knee have decreased balance when compared to age matched controls.

The ability of functional balance measures to predict the presence or severity of knee OA has also been studied with equivocal results. Larsson (Larsson, Petersson, & Ekdahl, 1998) sought to determine if 3 commonly utilized functional measures of balance could discriminate between individuals with early OA of the knee and those with no radiographic evidence of the disease. Sixty-six individuals with Ahlbäck Grade I OA of the knee (showing joint narrowing) and 138 individuals without OA were included in the study. Exclusion criteria were presence of inflammatory joint diseases or history of knee joint trauma related to knee pain. Three functional balance tests were initially used to measure balance. Balance I consisted of standing on one leg with eyes open and both arms at side for 30 seconds. Test was stopped when subject moved from standardized position or after 30 seconds. Performance was assessed by the observer on a scale of 0 = no difficulties and 1 = decreased functional capacity. Balance II consisted of walking foot by boot on a 2 m line marked with tape on a flat, level surface. Test was stopped if side-steps or other movements from the standardized position were made or when 2 m were completed. The same 2 grade scale was utilized as Balance I. Balance III consisted of standing on one leg with simultaneous, rapid, repeated neck rotations, with eyes open and arms at side. Test was stopped when subject moved from standardized position or after 30 seconds and the same 2 grade scale was utilized.

Statistical analysis consisted of calculation of sensitivity, specificity, frequency of abnormal test results (%) and odds ratios. Sensitivity is the percentage of subjects with a positive finding of decreased functional capacity among those with OA. Specificity is the percentage of subjects with a negative finding among those who do not have OA. Odds ratios (OR) were calculate with a 95% confidence interval (CI). OR gives the ratio of

sensitivity (odds for a positive finding in subjects with OA) over the odds for a positive result in people without OA. An increased risk of OA is found with a positive test if the OR and CI are greater than 1.0.

Results of this study showed that the Balance II test (walking on line) was too easy to perform to provide valuable information in this study (all subjects were able to perform) and no further analysis was completed. Balance I test showed low sensitivity (0.15) and higher specificity (0.86). Balance III showed higher sensitivity (0.62) and lower specificity (0.39). Frequency of abnormal results (%) for Balance I and II were 15 and 59 respectively. Odds ratio between those with and without OA were 1.07 for Balance I and 1.14 for Balance III with 95% CI of -0.02;2.16 and 0.24; 2.04 respectively. The authors speculated that the balance tests showed a ceiling effect (were too easy) and concluded that they were of little value in predicting the presence of mild knee OA in the groups studied.

Birmingham (Birmingham et al., 2001) however did find that balance measures were useful in the prediction of the extent of degenerative changes in populations with OA of the knee. In a study previously reported in this literature review, 20 subjects with medial compartment OA of the knee were studied. Extent of degeneration was measured via radiograph using a 4 point K/L grading system. According to this rating system 2 subjects had grade II OA of the knee, 11 had grade III and 7 had grade IV levels of degeneration. Balance measures were taken via a computerized force platform. Individuals were instructed to stand on 1 leg, eyes open, looking straight ahead. Two testing conditions were utilized: 1. standing directly on the firm, level surface of the measurement platform and 2. standing on a 40 x 40 cm, 7 cm thick, medium density

foam. Condition 2 (standing on foam) was used to theoretically decrease proprioceptive feedback of the lower extremity. One practice trial was completed then 3 tests trials were measured. Ten seconds of data were collected per trial and the outcome measure was the average length of the excursion of the center of pressure during the trial. A linear regression analysis was then utilized to form a model that would predict the extent of degeneration. It was found that varus alignment (measured radiographically and discussed previously in this literature review) and standing balance on foam could predict the level of degeneration ($R = .80$, $F_{2,17} = 14.81$, $p = .0002$). Sixty-four percent of the variability of the degeneration could be predicted from a model that included varus alignment and the standing balance measure. Specifically, standing balance on foam could account for 27% of the variability in this model. Nothing was added by the addition of the other balance measure (standing on firm, level surface).

In review, the Larsson study (Larsson et al., 1998) found that functional balance measures were unable to adequately separate between individuals without knee OA and those with mild OA. The study by Birmingham (Birmingham et al., 2001) showed that force platform measures of static balance were useful in predicting the level of degeneration in a population with knee OA. It is important to note, when comparing these 2 articles, the different types of balance assessment utilized in the studies as well as the increased degenerative levels in the Birmingham study.

The relationship of balance to measures of function and disability in a population with knee OA is another important area of study. Marsh (Marsh, Rejeski, Lang, Miller, & Messier, 2003) studied 480 subjects with OA of the knee (245 women and 235 men). Subjects were included in the study if they were at least 65 years old, had knee pain on

most days and difficulty (due to pain) with one or more of the following: walking ¼ mile; climbing stairs, getting in and out of a car; rising from a chair; lifting and carrying groceries; getting out of bed; getting out of the bathtub; or performing shopping, cleaning, or self-care activities. Subjects were excluded if they were moving from the area win 3 years, under hospice care, were receiving active treatment for cancer (skin cancer excluded), experienced shortness o breath or chest pain at rest, scored less than 24 on the Mini-Mental State Examination, had a history of RA or psoriatic arthritis, or were currently participating in another study.

Balance was measured with electronic force plate. Subjects were instructed to lean as far forward and back (trying to limit motion to the ankle joint). "Balance" was defined as the A/P excursion of the center of pressure during these activities (normalized to foot length). In short, individuals that were able to maintain the test position (not step forward or back) while having a greater excursion of the center of pressure during the forward and backward lean, demonstrated better balance than those with smaller excursions of the center of pressure. One practice trial was conducted then four trials were recorded. The outcome measure of center of pressure excursion was the average excursion of the last 3 measured trials.

Functional measures consisted of ambulation activities (preferred walking speed and stair climbing) and a transfer task that sought to mimic getting into and out of a car. Preferred walking speed was measured with a digital timer and photocells 7.3 m apart. The stair climb task consisted of the time required to ascend and descend 5 steps "as quickly as you can". Self-reported disability was also obtained via The Functional Performance Inventory (a questionnaire consisting of items that assess the level of

difficulty with activities of daily living). These functional activities and self-reported disability were tested at baseline, 15 and 30 months. Balance data was collected at baseline and 30 months.

Results of this study showed that higher baseline scores on balance (better balance) were associated with less self-reported disability, less time needed to perform the stair climb task, car task and faster walking speed ($r = -.13, -.33, -.34$ and $.36$ respectively; all correlations above ± 0.1 were significant at $0 < .05$). It was also shown that higher baseline balance scores were associated with less decline in self reported disability, stair climb time and car time from baseline to month 30.

The relationship between balance and strength has also been investigated. Jadelis (Jadelis, Miller, Ettinger, & Messier, 2001) found that strength plays a significant role in the maintenance of balance in older individuals with OA of the knee. In this investigation data were taken from The Observational Arthritis Study in Seniors, otherwise known as the OASIS knee study. A regression model was used to study the relationship between balance and strength in 480 adults age 65 and older with knee pain while controlling for such factors as gender, BMI, radiographic severity of OA , knee pain and foot length. Balance was assessed with a force plate and the A/P excursion of the center of pressure during a forward and backward lean was calculated. Knee and ankle strength was measured isokinetically (concentric/eccentric knee flexion and extension; concentric/concentric ankle dorsiflexion and plantarflexion). The results of this study demonstrated that knee strength alone explained 18.4% of the variability in dynamic balance. Further statistical analysis showed that individuals with a combination of strong knees and ankles had the best dynamic balance scores. Individuals with lower

knee strength scores could still however, maintain high performance on balance measures if they high ankle strength.

Balance change over time was investigated by Messier (Messier, Glasser, Ettinger, Craven, & Miller, 2002). In this study, data were analyzed from the previously mentioned OASIS knee study. In this study 480 subjects with chronic knee pain (239 subjects had K/L grading of ≥ 2) underwent baseline testing. Balance was assessed as in the study by (Jadelis et al., 2001) previously reported in this literature review. Statistical methods were employed (maximum-likelihood regression analysis) that adjusted for possible dependencies between missing data due to the number of individuals completing baseline testing and follow up (for balance, 465 completed baseline and 311 completed follow up). Balance was therefore defined as the maximum-likelihood estimate of mean maximum excursion of the center of pressure changes during a voluntary forward and back lean (normalized to foot length). The results of this study showed that there was a significant decrease in balance over a 30 month period (baseline: 0.5751; 30 month follow-up: 0.5418; % change: 5.8; $p < 0.001$).

Loss of balance and falls among older individuals are a major public heath concern with one study finding that 32 % of individuals fell during a one year time frame (with 24% of those falling sustaining a serious injury) (Tinetti, Speechley, & Ginter, 1988). These results, coupled with findings that balance in individuals with knee OA worsens with age and the severity of the disease, suggest that interventions aimed at improving balance in an elderly population with knee OA could have important benefits. A noteworthy example of research investigating the effect of exercise on balance in this population has been completed by Messier (Messier et al., 2000).

In this study, 103 adults (78 women, 25 men), age 60 years or older were divided among 3 groups: aerobic exercise, n = 33; health education control, n = 36; weight training exercise, n = 34. The aerobic and weight training groups exercised 3 days a week for 18 months. This 18 month intervention was sub-divided into a 3 month facility based program, followed by 15 months of home exercise. The home exercise phase was divided into 2 phases: transition and maintenance. The transition phase lasted 3 months and included biweekly contact (4 home visits and 6 telephone contacts) to insure compliance with the exercise program. The maintenance phase consisted of the remaining 12 months and included tri-weekly telephone contact during the 1st 3 months and then phone contact monthly for the remainder of the program.

The aerobic program consisted of a 5 minutes warm-up, 40 minutes of walking (intensity 50%-80% of heart rate reserve) and 5 minute cool-down. The weight training program consisted of 9 strengthening exercises (both upper and lower body) utilizing dumbbell and cuff weights. Two sets of 10-12 repetitions were completed for each exercise. The health education group consisted of regularly scheduled contact (both face-to-face and phone) between subjects and investigators. The inclusion of this attention control group sought to minimize the effect of attention and socialization between the control and intervention subjects.

In this study, balance data were collected via a force platform under both single and double leg conditions. During the trials, displacement of the center of pressure (COP) was measured first with eyes open then with eyes closed. For single leg stance, subjects stood on the most affected leg. Each trial lasted 10 seconds (unless loss of balance occurred) and after one formal practice attempt, four trials of each testing

condition were recorded. The last 3 trials were analyzed with the 1st of the 4 trials serving as a 2nd practice trial (subject was not aware that the 1st of the 4 trials was an additional practice repetition).

The outcome of this study suggest that a long-term (18 month) program of either aerobic or strengthening exercise can have a positive effect on balance in individuals with OA of the knee when compared to a control group also with the disease. In the double leg stance group (eyes closed) both the aerobic and weight training groups had significantly better center of pressure values ($p = 0.02$ and $p < 0.001$ respectively) than the control group. In single leg stance (eyes open), the aerobic group was able to maintain the test position for a significantly longer time period than the control group ($p = .016$).

The authors noted that the relative difficulty (or ease) of the task influenced the lack of significant differences in some stance conditions. The authors reported that the relative difficulty of the eyes closed, single leg stance condition resulted in a large within and between subject variability that may have masked any potential discriminating results. Alternately, the relative ease of the eyes open, double leg stance condition allowed for very small variability, inhibiting the ability to distinguish difference between groups. These results suggest that care be taken in designing future research methods for the investigation of balance under similar conditions.

Summary of the intrinsic factor "Balance".

- Functional balance measures such as standing on one leg and walking on a line foot to foot were of little value in predicting the presence of early OA of the knee.

- Computerized force platform measures of balance were shown to be able to predict the presence of OA of the knee in a group of individuals with OA when compared to normal controls.
- Force platform measures of balance were a meaningful part of a statistical model that could predict the extent of degeneration in subjects with OA of the knee.
- Greater baseline balance was associated with better scores on functional activities (e.g. stair climbing, walking speed) as well as less self-reported disability in individuals with OA of the knee.
- Increased strength (especially a combination of strong knees and ankles) has been shown to play a significant role in the maintenance of balance in older individuals with OA of the knee.
- Balance tends to decrease over time in individuals with knee OA.
- Exercise, both aerobic and strengthening has been shown to improve balance in individuals with OA of the knee.

Joint Range of Motion

Decrease range of motion (ROM) of the knee secondary to stiff noncontractile structures (e.g. ligaments, joint capsule) or muscles exhibiting decreased flexibility (e.g. tight hamstrings), could potentially alter forces experienced at the joint. The inability to fully extend one's knee is an example of a common ROM impairment associated with OA of the knee. This lack of knee extension alters the weightbearing experienced at the knee during gait. With normal gait, peak weight bearing occurs near full knee extension,

maximizing the tibiofemoral joint contact area. With a knee flexion contracture, weightbearing occurs over a smaller and less congruent joint surface leading to greater concentration of force over a smaller surface area (Hertling & Kessler, 2006). The long term effect of more pressure over a smaller joint surface area could lead to degeneration of the joint.

Modulating pressure on the joint, in addition to improving comfort, function and safety are commonly cited as reasons for the inclusion of ROM exercises in the treatment of knee OA (Clyman, 2001; Minor, 1999; O'Grady, Fletcher, & Ortiz, 2000). The American College of Rheumatology lists ROM and stretching as one of the standards of care for the non-surgical treatment of OA of the knee (R. Altman, Hochberg, Moskowitz, & Schnitzer, 2000). Due to the frequent use of ROM exercises in the management of OA and the theorized effect stiffness might play in the forces experienced at the knee, the inclusion of ROM/flexibility as an important intrinsic factor in the study of OA of the knee appears to be warranted.

The relationship between OA of the knee and decreased ROM has been investigated by Messier (Messier et al., 1992). Passive range of motion (PROM) was among the variables examined in 15 subjects with OA of the knee. Diagnosis of OA was confirmed by radiographic evidence and symptoms of pain on motion or at rest plus at least one of the following: tenderness with pressure, mild swelling, crepitus on motion, or stiffness (either in the morning or after prolonged inactivity). Participants were excluded if there was evidence of rheumatoid or other types of arthritis or had symptomatic arthritis in joints other than the knee. PROM of the knee was measured with a standard goniometer. Knee flexion was recorded as the angle measured between the femur and

tibia (higher angle indicated decreased flexion). Extension (or conceptually, total available motion) was recorded as the difference from a starting position of full knee flexion and full available extension (with hip at 45° angle).

Results of this study demonstrated significant deficits of PROM in knees of subjects with OA compared to a control group matched on age, mass and gender (n = 15). A two-way ANOVA of knee extension data showed a significant difference between the ROM measured in knees of subjects with OA (affected and unaffected) when compared to the knees of those subjects without OA ($F[1,28] = 9.07$; $p = 0.005$). A between side difference in extension was also shown (OA group affected and matched control group side vs. OA group non affected and matched non-OA group side) ($F[1,28] = 4.43$; $p = 0.04$). An analysis of the interaction between group and side revealed a significant interaction ($[F1,28] = 5.48$; $p = 0.03$). Post hoc analysis demonstrated that extension values for both the affected and unaffected knees of individuals with OA had less PROM than the matched control side of the control group ($p = 0.03$). It was also shown that the affected knee had less extension ROM than the unaffected knee in a group with OA ($p = 0.03$).

A two-way ANOVA of knee flexion data revealed similar main effects, although no interaction effect was noted. Less flexion was noted in the group with OA (affected and unaffected) when compared to the control ($F[1,28] = 4.60$; $p = 0.04$). Less flexion was also demonstrated between sides ($F[1,28] = 5.93$; $p = 0.02$). No interaction effect (group by side) was found ($p = 0.10$).

Results from study of the stiffness of specific structures around the knee support the conclusion that decreased ROM is associated with OA. Stiffness (resistance to

deformation) of the medial and lateral collateral knee ligaments (MCL and LCL respectively) was studied by Fishkin (Fishkin et al., 2002). In this study, a group of individuals undergoing total knee arthroplasty (OAP, n = 10) due to OA of the knee, osteoarthritic cadaveric knees (OAC, n = 10) and cadaveric knees without OA (NOA, n = 10) were examined. A linear strain gauge and tissue spreader was used to measure force and deformation of the ligaments. A load-elongation curve was then calculated. Results of this study showed that both the groups with OA, that is patients receiving total knee arthroplasty and cadavers with OA (OAP and OAC respectively), had stiffer ligaments when compared to the cadaveric knees without OA ($p < 0.05$).

The relationship between the compartment specific severity of knee OA and ROM has been studied by Ersoz (Ersoz & Ergun, 2003). In this study, 20 subjects with bilateral OA of the knee were studied (40 knees). Subjects were included in the study if they fulfilled the criteria of the American College of Rheumatology for knee OA (R. D. Altman, 1991b). Kellgren/Lawrence grading of radiographic evidence of OA was used to describe the severity of the disease in the medial tibiofemoral, lateral tibiofemoral, and patellofemoral compartments. PROM was measured with a standard, plastic goniometer by one examiner. Measurements of knee flexion, extension, and tibial femoral internal and external rotation were taken. Results of this study demonstrated a significant compartment specific relationship between severity of knee OA and PROM (PROM decreased as severity increased). Internal rotation was correlated with degeneration of the lateral compartment of the knee ($r = -.439$, $p < 0.01$). External rotation and flexion were related to the medial compartment ($r = -.361$, $0 < 0.05$; $r = -.338$, $p < 0.05$; respectively). Extension measures were correlated with all compartments, with the

highest correlation associated with the patellofemoral joint ($r = -.533$, $p < 0.01$; $r = -.456$, $p < 0.01$; $r = -.327$, $p < 0.05$; patellofemoral, medial, and lateral respectively). This study helped demonstrate not only is ROM correlated with severity of OA, but direction of limitation might offer useful information to predict the compartment of the knee affected.

An additional area of interest in the study of the intrinsic factors of the knee related to OA is the relationship of that factor to function or disability. Steultjens (Steultjens et al., 2000) investigated the relationship between ROM and disability. In this study, the assisted, active ROM (AROM to end and then examiner holds the position) of 119 knees with OA were examined. Subjects qualified for diagnosis of OA of the knee if they satisfied the ACR criteria cited previously. ROM was measured with a goniometer by two experienced physical therapist. Disability was quantified via observation and by subject self-report. In the observational scoring of disability, trained observers graded videotaped performances of activities in a manner that had been previously shown to be internally consistent and valid (Steultjens, Dekker, van Baar, Oostendorp, & Bijlsma, 1999). These tasks included walking, sitting down in a chair, reclining onto a bed, and bending over to pick up a weight from the floor. The examiners measured the movement times of walking 5 m, sit to stand and stand to sit activities. The quality of the performances was also judged on level of guarding and level of rigidity. These five items were then used to formulate an overall score for observed disability. Results of this study demonstrated a negative correlation among knee flexion and observed and self-reported disability; that is as ROM increased reported disability decreased ($r = -.23$, $p < 0.01$; $r = -.29$ $p < 0.01$ respectively). Decreased knee extension was not found to be related to the measures of disability in this study.

Knee flexion ROM was also shown to be significantly correlated with physical performance measures and self-reported function in a study by Lin (Lin et al., 2001). In this study, knee flexion was measured with a goniometer and physical performance measures included walking, stair climbing and sit/stand activities. Self-report of function was measured via the WOMAC Osteoarthritis Index. Results of this study showed a significant relationship between knee flexion and the physical performance measures studied, although the authors did not report significance level. Knee flexion was also demonstrated to be significantly associated with the Physical Function dimension of the WOMAC ($r = -.39$, $p \leq 0.05$; $r = -.35$, $p \leq 0.05$, right and left knee respectively). These results support the previously discussed conclusions by Steultjens demonstrating the significant relationship between ROM and function.

Although intervention programs designed solely to address ROM restrictions in individuals with OA of the knee have not been described in the literature, changes in flexibility have been shown as outcomes of exercise based intervention studies for individuals with OA. In a study by Wyatt (Wyatt, Milam, Manske, & Deere, 2001), 46 subjects with OA of the knee were examined and then separated into an aquatic or land-based exercise group. Measurements at baseline and at 6 weeks were taken. Pre- and post-test measures consisted of knee passive ROM, thigh girth, subjective pain scale, and time for 1-mile walk. Land and water exercises consisted of manually resisted knee flexion and extension, 4 way straight leg lifts, mini-squats and walking 800 feet. Individuals exercised 3 times a week for 6 weeks. Results showed significant ($p < 0.05$) differences in all pre-post testing. No significant differences were found between exercise groups however.

Although common, not all individuals with OA have flexibility deficits. Instead, some even exhibit joint hypermobility. Are flexibility exercises a necessary component for all programs seeking to address function and pain in individuals with OA of the knee or can they be omitted for individuals without ROM deficits? Does the importance of this type of exercise increase with increasing deficits of ROM of the knee? Adequate characterization of the subjects is undoubtedly a key component in the investigation of these and other questions.

Summary of the intrinsic factor "ROM".

- PROM at the knee is decreased in knees with OA when compared to a control.
- PROM at the knee is decreased in the affected knee with OA when compared to the unaffected knee in a group with OA.
- In individuals with OA, total PROM at the knee in the unaffected knee is decreased when compared to a matched control group
- ROM decreases as severity increases; these changes have been shown to be compartment specific. Correlations have been shown between severity in specific compartments and direction of ROM deficit.
- Knees with OA have stiffer medial and lateral collateral ligaments than nonaffected knees.
- Deficits in knee flexion have been shown to be related to decrease in function; the same has not been shown for deficits in knee extension.
- Aquatic and land based exercise programs can positively affect ROM of the knee in the presence of OA over a 6 week time frame.

Strength

Strength, especially strength of the knee extensors, is another intrinsic factor that has been shown to affect the biomechanical environment in which the knee joint functions. Although research continues regarding the role strengthening plays in the treatment of OA of the knee, it has been accepted for many years that lower extremity strength plays a major role in knee joint shock attenuation during weightbearing activities (Minor, 1999). Increased or uncontrolled loading places the joint at risk for development or progression of disease, making strength an important intrinsic factor that needs to be considered in the study of knee OA.

Functional testing emphasizing strength of the LE has been shown to predict radiographic incidence (development) of OA of the knee over a 5 year span in individuals with chronic knee pain (Thorstensson et al., 2004). In this investigation, 94 individuals with chronic knee pain without radiographic evidence of OA were studied. Results demonstrated that decreased ability to perform one leg rises (rising and return from a stool using one leg only) predicted the development of radiographic OA of the knee in the span of 5 years (univariate odds ration at 95% confidence interval 2.55 [1.08 to 6.02]). It is interesting to note that other functional tests emphasizing constructs other than strength did not predict the development of radiological evident OA (i.e. time spent walking 300 m –emphasizing endurance and timed standing on one leg – emphasizing balance).

Lower extremity muscle strength measured by isokinetic dynamometry has also been shown to be somewhat related to development of OA in women (Slemenda et al., 1998). In this study, 141 women (mean age 70.4, community dwelling) with no baseline

radiographic evidence of OA in one or both knees were examined. Lower extremity muscle strength was measured via an isokinetic dynamometer. Subjects were seated with pad on dynamometer arm located 3 inches above ankle joint. Volunteers were allowed several trials to familiarize themselves with the machine. Peak torque was measured during a concentric contraction at 60 deg/sec. Three repetitions were completed with 20 seconds rest between repetitions. Subjects that developed OA of the knee (n = 13) were compared to a control group of individuals that did not develop the disease (mean interval 31.3 months). Findings approached significance for knee extensor strength (normalized to body weight) and development of OA of the knee ($p = 0.055$; 0.57 ± 0.02 for control, 0.47 ± 0.07 for incident OA).

Although the results of the study mentioned previously (Slemenda et al., 1998), were equivocal regarding the relationship between quadriceps strength and the development of OA of the knee in women, outcomes regarding quadriceps strength and incident OA in men were much clearer. Utilizing the same method, 14 men (18 knees) with incident OA of the knee were compared to a control group of 112 men (224 knees). No significant relationship was noted with quadriceps strength and incident OA (0.65 ± 0.02 control, vs. 0.61 ± 0.04 incident OA group). No significant relationship was also found between hamstring strength and development of OA in either sex.

The relationship between lower extremity strength and the progression of OA of the knee in a female population has been studied by Brandt (Brandt et al., 1999). In this study, 57 women with baseline OA of the knee were studied (graded by Kellgren/Lawrence classification). Because K/L grade of 4 can not by definition advance, these individuals were removed from the initial pool. For analysis, 14 women

(16 knees), mean age 70.1 had progressive OA and 43 women (66 knees), mean age 71.6 had static OA. Recruitment of subjects, and isokinetic strength testing was as described previously in this review (Slemenda et al., 1998). Results of this study showed no statistical relationship between quadriceps or hamstring strength (adjusted to either body weight or lower extremity muscle mass) and progression of OA of the knee. This result also remained after controlling for pain.

Sharma (Sharma, Dunlop, Cahue, Song, & Hayes, 2003) also studied the relationship between baseline lower extremity strength and progression of knee OA, this time in the presence of mal-alignment and knee joint laxity. In this study, 171 participants with OA of the knee were examined (328 knees). Inclusion criteria were definite osteophyte presence (K/L grading 2 or above in one or both knees and at least a "little difficulty" (on a Likert scale) on at least two functional items on a self report index (WOMAC). Subjects were excluded if hey had a steroid injection within last 3 months, avascular necroses, RA or other inflammatory arthritis, periarticular fracture, Paget disease, villonodular synovitis, joint infection, ochronosis, neuropathic arthropathy, acromegaly, hemochromatosis, Wilson disease, osteochondromatosis, gout, pseudogout, osteopetrosis, bilateral total knee replacement or plan for knee replacement with the next year.

Strength was operationalized as peak isokinetic torque at 120°/sec with motion limited from 0-90°. Alignment was measured from an A/P radiograph of the lower extremity. Laxity was measured with a device designed for this study. Further description of the protocols for strength, alignment and laxity measures were previously described in this review (Sharma, Hayes et al., 1999). Knees were described as

"malaligned" if the angle was 5° or greater from neutral. Knees were described as "high laxity" if they were in the highest laxity tertile ($\geq 5.75°$ combination of varus and valgus motion). Progression of the disease was measured radiographically over an 18 month period.

Results of this study demonstrated an interaction between baseline strength and alignment or laxity. Quadriceps strength alone did not have a significant relationship to progression of OA in the knee ($p = 0.09$). Comparisons were next made between the likelihood of progression of OA in neutral knees and malaligned knees in the presence of high and low baseline strength. Results showed that in neutral knees, there was no relationship between strength and progression of the disease ($p > 0.2$), but in malaligned knees, a significant positive relationship was present between strength and likelihood of progression of OA ($p = 0.03$). Restated, malaligned individuals that were stronger at baseline were more likely to have progressive OA of the knee vs. their weaker counterparts.

Similar results were demonstrated in the analysis of the relationship between laxity, strength, and progression. Strength was not significantly related to progressive OA of the knee in individuals with a low level of laxity ($p > 0.2$). In high laxity knees however, individuals with high baseline strength were more likely to have progressive OA at the knee when compared to high laxity individuals with low baseline strength ($p = 0.05$). In summary, greater strength at baseline appeared to have no protective effect on progression of OA; in fact, lax or malaligned knees tended to have more disease progression in the presence of increased baseline quadriceps strength.

Instead of the progression of OA in relationship to presence of strength deficits (or surplus), the progression of strength decline in the presence of chronic knee pain (many having knee OA) has been studied by Messier (Messier et al., 2002). In this study 480 subjects with chronic knee pain (239 subjects had K/L grading of ≥ 2) underwent baseline examination of numerous factors (for a more complete description of subjects and design, please see (Jadelis et al., 2001) and (Messier et al., 2002), two previously discussed studies contained in this literature review under the "Balance" section). Follow up testing was completed at 30 months. Maximum-likelihood regression analysis was used to adjust for possible dependencies between missing data and previously observed data due to concerns with number of individuals that did not return for followup testing (knee strength testing: 474 baseline, 267 followup; ankle strength: 468 baseline, 205 followup).

Strength was measured isokinetically at baseline and 30 months. Knee strength was tested both concentrically and eccentrically at 30°/sec. Ankle strength was measured concentrically at 30 °/sec. Results showed that knee strength significantly decreased over the 30 month time frame (concentric extension, concentric flexion, eccentric flexion $p < 0.001$; eccentric flexion $p = 0.003$). Results also demonstrated that ankle dorsiflexion also decreased over time ($p < 0.001$).

Several investigators have sought to describe differences between strength in individuals with OA of the knee and those without the disease. Slemenda (Slemenda et al., 1997) studied 462 individuals 65 years and older. One hundred forty-five volunteers had radiographic evidence of OA at the tibiofemoral or patellofemoral joint. Strength data was collected by isokinetic dynamometry at 60 and 120 °/sec, information regarding

function and pain were collected with the WOMAC and lean tissue mas was collected by dual-energy x-ray absorptiometry. Methods were same as reported earlier in this review (Slemenda et al., 1998). Results of this study showed that quadriceps weakness was significantly associated with the presence of OA (tibiofemoral and patellofemoral) of the knee ($p < 0.01$) but hamstring weakness was not ($p > 0.14$). This significant relationship between extensor strength and presence of OA remained after being normalized to body weight.

Further analysis demonstrated notable results concerning the relationship between strength and OA of the tibiofemoral joint in women without pain and with normal lower-extremity lean mass. Extensor strength was again found to be significantly decreased in women with OA even in the absence of pain and when those individuals with OA had normal lean body mass. The authors interpreted these finding to support the conclusion that in individuals with OA of the knee, weakness may not be solely caused by disuse atrophy (normal lean mass of the lower extremity) or by pain. Instead, the authors hypothesized that it is possible that quadriceps weakness might precede OA and may play an important role in the pathogeneses of the disease.

Similar results regarding the relationship between decreased extensor strength and the presence of OA of the knee have been reported by Hassan (Hassan et al., 2001). In this study, 59 subjects with symptomatic and radiographic knee OA and 49 controls with asymptomatic and clinically normal knees were compared. The control group was matched for age and sex and OA was excluded by no symptoms, or history of knee trauma and normal clinical exam. Isometric knee extensor strength was measured via a maximal voluntary contraction (MVC) at 90° of flexion. Peak torque was reported. The

degree of quadriceps activation was also estimated by superimposing an electrical stimulation during subsequent contractions. Results showed that individuals with OA of the knee had decreased extensor strength when compared to the controls ($p < 0.001$). It was also noted that participants with OA had significantly decreased ability to fully contract their quadriceps when compared to the control ($p < 0.001$).

This finding of decreased ability to maximally contract the quadriceps was contradicted by Lewek (Lewek et al., 2004). In this study, 12 subjects (7 male, 5 female) with symptomatic medial compartment knee OA were compared to a similarly aged control group (12 subjects, 6 male, 6 female). Inclusion criteria for OA group were clinical and radiographic evidence of OA. Controls had no symptom or radiographic evidence of knee OA. Isometric peak torque was measured during a four second maximum quadriceps contraction at 90°. Ability to maximally contract the quadriceps was assessed by applying a burst of electrical current to the quad approximately 2 seconds into the contraction. Results from this study confirmed past studies regarding decreased extensor strength relative to body mass index in a population with knee OA when compared to controls ($p = 0.010$). However, no difference in ability to maximally contract the quadriceps was observed ($p = 0.233$).

Contradictions in findings regarding the relationship between hamstring strength and knee OA also exist. As reported previously in this review, Slemenda (Slemenda et al., 1998) found no relationship between isokinetic (60 and 120°/sec) strength of the hamstrings and the presence of OA of the knee ($p > 0.14$). This finding is contradicted by Fransen (Fransen et al., 2003). In this study, 131 subjects with OA of the knee were compared with published normative data for 131 asymptomatic controls. Both hamstring

and quadriceps strength were assessed isometrically at 90° flexion. Results of this study supported previously reported findings that individuals with knee OA have weaker quadriceps (46-54% of control peak torque; $p < 0.01$) but also weaker hamstrings (35-46% of control peak torque; $p < 0.01$).

Results from a study Tan (Tan et al., 1995) also demonstrated a significant hamstring strength difference between individuals with OA and a control group (with both isometric and isokinetic contractions). In this study, 60 female volunteers that satisfied the criteria for diagnosis of OA put forth by Altman (R. D. Altman, 1991b) were compared to 30 female healthy controls. The OA group contained 30 subjects that had radiographic evidence of joint space narrowing, 30 did not. Results of this study found a significant difference in torque production at 60 °/sec for both knee flexors and extensors between individuals with OA and the control group ($p < 0.001$). This statistical difference also was demonstrated with isometric contraction of the knee flexors and extensors at 30° ($p < 0.0001$).

The relationship among quadriceps strength, pain, and function has also been investigated. In a study by O'Reilly (O'Reilly, Jones, Muir, & Doherty, 1998), 300 individuals, ages 40-79 with knee pain were compared to a similar control group with no pain. Function and pain were measured with the WOMAC OA index. Voluntary quadriceps strength was measured by a strain gauge during an isometric contraction at 90° of knee flexion (peak of 3 repetitions). Maximum quadriceps activation was calculated by twitch superimposition by electrical current. Radiographs were taken and scored by a standard atlas. Data on anxiety and depression was were also collected

(Hospital Anxiety and Depression Scale) due to the possibility of covariance with these factors.

Results of this study showed that individuals with knee pain had significantly decreased voluntary quadriceps strength measurements when compared to the control group ($p < 0.005$). Maximum quadriceps activation was also significantly lower in those subjects with pain ($p < 0.005$). Differences in voluntary quadriceps contractions between groups with and without pain remained when effect of maximum quadriceps activation was removed ($p < 0.005$). Voluntary quadriceps strength was also found to be inversely related to disability in the group with knee pain ($p < 0.05$). All relationships between pain, strength, and disability remained when adjusted to psychological factors of anxiety and depression.

Topp (Topp et al., 2000) also found that quadriceps strength combined with other factors such as pain, perception of functional ability and body weight can successfully predict time to perform functional tasks. In this study, 78 community dwelling volunteers, (22 male, 56 female, mean age of 62.75) with OA of the knee were studied. Subjects must have had a previous diagnosis of OA of the knee and be experiencing a moderate degree of pain due to the disease. Diagnosis of OA was validated by history and clinical criteria (R. Altman et al., 1986).

Concentric quadriceps and hamstring strength was measured isokinetically at 30° per second (peak torque of 3 maximal trials after warm up). Isometric quadriceps strength was also assessed at 30° flexion (peak torque of 3 maximal contractions after warm up). The WOMAC was utilized to measure perceived pain, stiffness, and perceived physical function. Four functional tests were completed: time for getting

down to and up from the floor (2 tests) and time to descend and ascend stairs (2 tests). One flight of stairs was defined as 27, 15.24 cm steps. Subjects could use handrails if needed. Subjects rated pain during activity on a 10 cm horizontal visual analog scale.

Results of this study demonstrated what strength can help predict measures of physical function. Initial analysis revealed that all measures of strength in uninvolved and involved legs were significantly associated with function ($p < 0.05$). Next, a regression model was constructed to calculate the ability of a predictor variable to account for the variance in the functional performance. Variables were include as in the regression model if they accounted for a significant amount of the dependent variables' variance at the .15 level. Involved knee strength was included in models associated with getting down onto the floor and time for stair ascent. Thirty-nine percent of the variance in getting down onto the floor was predicted from knee pain during the activity ($r^2 = .33$) and maximum isokinetic knee extension ($r^2 = .06$). Fifty-six percent of the variance for the time required for stair ascent was predicted by the following variables: maximum isometric strength in the affected leg ($r^2=.34$), WOMAC functional ability subscale ($r^2=.14$), maximum unaffected knee flexion torque ($r^2=.05$) and body weight ($r^2=.03$).

The role of strength as a protective factor against functional decline is somewhat equivocal. In a study by Sharma (Sharma, Cahue et al., 2003), 257 volunteers with knee OA were examined at baseline, 18 months and 3 years. Function was measured by the WOMAC scale and results were stratified into quintiles based on the cohort at baseline. Function was also measured by the rate of chair stand performance (results likewise stratified). Quadriceps and hamstring strength was measured isokinetically at 120 °/sec (reported as maximum peak torque observed in ft-lbs). Functional outcomes were

considered "Good" if over the 3 year span, a subjected moved into a higher functional group or remained within the 2 highest functional quintiles. A result was labeled "Poor" if an individual moved into a lower functional group or remained in the lower 3 functional quintiles.

As reported previously, 257 subjects completed the measures at baseline, 18 months and 3 years. Of the 257, 21 underwent a total knee replacement and were not considered in final data analysis. One hundred thirteen subjects had a good functional outcome over the 3 year study time as defined by the WOMAC scale (123 poor outcome). Eighty subjects had a good baseline to 3 year functional outcome as measured by the rate of chair stand performance (156 poor outcome). Results of this study revealed no protective relationship between self-report of function (WOMAC) and strength. Quadriceps and hamstring strength was significantly different at the $p < 0.05$ level between individuals with poor and good outcomes over time measured by the chair stand activity (good outcome = remained in top 2 quintile or improved, bad outcome = remained in bottom 3 quintile or worsened). Initial analysis revealed that greater baseline hamstring and quadriceps strength was protective of a poor functional outcome as measured by the chair stand activity. However, this relationship did not remain after adjusting results for subject self-efficacy. Quadriceps and hamstring strength did however appear to be statistically different ($p < 0.0001$) between individuals that sustained high function (top 2 quintiles) and sustained low function (bottom 3 quintiles).

The relationship among strength and other factors that can affect the mechanical environment in which the knee functions has also been investigated. The relationship between strength and balance has been studied by Hassan (Hassan et al., 2001). In this

study, data on maximal isometric voluntary contraction at 90°, degree of quadriceps activation and postural sway was collected from 59 subjects with symptomatic OA of the knee and 49 age/sex matched controls. Postural sway was collected via a standing platform with two foot plates connected to a feedback unit (Balance Performance Monitor). Postural sway is defined as the motion of the center of pressure (representing the center of gravity) during standing still. This postural sway can be described as wither anterior-posterior or lateral, with larger numbers representing poorer balance. Results of this study demonstrated that decreased maximum voluntary contraction normalized to body weight predicted increased lateral postural sway in a population with OA of the knee (controls: median 2.3 interquartile range 1.8 – 2.9; subjects: median 4.7; IQ range 1.9 – 4.7, $p < 0.001$). This relationship betweens strength (particularly quadriceps) and balance has also been shown in previously cited work by Jadelis (Jadelis et al., 2001) and Messier (Messier et al., 2002).

In addition to demonstrating the relationship between increased strength and better balance, Jadelis (Jadelis et al., 2001) also found that strength can mediate the effect pain has on balance. In this study, it was noted that individuals with weak quadriceps tended to have decreased balance in the presence of increased pain. Alternately, pain had no effect on balance if an individual's quadriceps were strong.

Miller (Miller, Rejeski, Messier, & Loeser, 2001) also found that strength has a mediating effect on individuals with OA; in this case, changing the relationship between radiological severity and function. In this study, the relationship between radiographic severity of knee OA and function were analyzed from data collected from The Observational Arthritis Study in Seniors (OASIS) knee study cited previously (Jadelis et

al., 2001). Preliminary results of this study showed that radiologic severity of OA at baseline was associated with decreased function measured by transfer and ambulatory tasks ($p = 0.06$ and $p = 0.04$ respectively). However, after controlling for baseline levels of strength (and pain), the relationship between severity and function became non-significant.

Strength as a mediating factor was also studied by (Steultjens, Dekker, & Bijlsma, 2002). In this study, the mediating role of muscle strength in relation to avoidance of activity and disability was investigated in 107 participants with knee OA. Avoidance of activity was assessed using the resting subscale of the Pain Coping Inventory. This subscale utilizes a 4 point scale with higher scores indicating increased use of rest as a coping mechanism for pain. Disability was measured observationally by scoring a videotaped performance of tasks such as walking, sitting, reclining into bed, and picking up a weight from the floor. A higher score indicated higher levels of disability. Quadriceps and hamstring strength was measured isometrically with a hand-held dynamometer. The authors defined a mediating role as one that decreases the established effect of one factor on another.

Avoidance of activity initially explained 21.5% of the variance in measures of disability. After controlling for muscle strength, avoidance of activity only explained 15.7% of the variance in disability. The authors interpreted these findings to support the conclusion that muscle strength has a mediating effect on the relationship between avoidance of activity and disability.

Comparisons of the strength of the unaffected knee in individuals with unilateral OA can offer some insight into the cause and effect nature of a factor. As reported

previously, proprioception was found to be decreased in the unaffected as well as the affected leg (Sharma et al., 1997) supporting the conclusion that the deficit was not solely caused by the disease, but was possibly a precursor to the development. This was not found to be the case however for strength (M. V. Hurley & Newham, 1993). In this investigation, 10 subjects (6 female, 4 male, mean age 56 years) were studied. Inclusion criteria consisted of unilateral knee joint OA, objective unilateral quadriceps weakness, pain-free quadriceps contraction, and no clinical signs of effusion. Isometric strength was measured during a contraction at 90°. Results of this study showed that the affected limb had significantly decreases quadriceps strength when compared to the unaffected side ($p < 0.02$).

Summary of the intrinsic factor "Strength".

- Functional measures of strength have been shown to predict future development of OA.
- Non-functional measures (i.e. isokinetic, isometric) measures have not shown the ability to predict development of OA.
- Deficits in strength have not been shown to relate to progression of knee OA.
- Increased strength at baseline, in the presence of mal-aligned or unstable knees, has been shown to be related to OA progression.
- Strength tends to decline over time in individuals with chronic knee pain.
- When compared to controls, individuals with OA have weaker quadriceps. This finding has not been consistently demonstrated for hamstring strength.
- Some studies suggest that significant muscular (quadriceps) inhibition also occurs in knees with OA. Other studies dispute this finding.

- Quadriceps strength has not been consistently shown to be protective in relation to functional decline.
- Increased knee strength has been shown to be related to better balance in individuals with of the knee. This also been shown (but with less consistency) of ankle strength in individuals with OA of the knee.
- Knee strength mediates the effect of pain on balance. If an individual is strong, increased pain does not appear to effect balance.
- Strength mediates the relationship of radiographic severity and function. If strength was taken into account, the relationship of radiographic severity and function become non-significant.
- Strength mediates the role of avoidance of activity and disability.
- In unilateral OA, the unaffected knee tends to be significantly stronger than the affected knee.

Summary

Individuals with knee OA are a heterogeneous group with respect to alignment, laxity, proprioception, balance, ROM, and strength. These local intrinsic factors effect the biomechanical environment in which the knee functions. Research has demonstrated significant relationships among these factors. Studies have also shown significant relationships between individual factors and measures of function and pain. This proposed study will identify factors or clusters of factors that are related to pain and function in individuals with knee OA. The identification of these factors will allow more appropriate study design and analysis, thus positively affecting the study of this disease.

Appendix C

Data Collection Forms

ID #: _____ Date: _____ Date Entered: _____ Initials: _____

MARRTC Knee OA-Project II **Physical Exam**

ACR Clinical Criteria:

Satisfies Criteria
1,2,3,4 or 1,2,5 or 1,4,5

Data Entry Use Only: Yes = 1 No = 0

Right:

1.	Knee pain for most days of prior month	**Y / N**	zRAC1Y
2.	Crepitus on active joint motion	**Y / N**	zRAC2Y
3.	Morning Stiffness ≤30 min in duration	**Y / N**	zRAC3Y
4.	Age ≥ 38 years	**Y / N**	zRAC4Y
5.	Bony Enlargement of knee	**Y / N**	zRAC5Y
6.	Satisfy Criteria	**Y / N**	zRACSY

Data Entry Use Only: Yes = 1 No = 0

Left:

1.	Knee pain for most days of prior month	**Y / N**	zLAC1Y
2.	Crepitus on active joint motion	**Y / N**	zLAC2Y
3.	Morning Stiffness ≤30 min in duration	**Y / N**	zLAC3Y
4..	Age ≥ 38 years	**Y / N**	zLAC4Y
5.	Bony Enlargement of knee	**Y / N**	zLAC5Y
6.	Satisfy Criteria	**Y / N**	zLACSY

Knee Pain and Stiffness:

Right:
On a scale of 0-10, with 0 being no pain and/or stiffness and 10 being the worst pain and/or stiffness imaginable, how would you rate your **right** knee:

_____
zGPSR

Left:
On a scale of 0-10, with 0 being no pain and/or stiffness and 10 being the worst pain and/or stiffness imaginable, how would you rate your **left** knee:

_____
zGPSL

Leg Dominance:

From a coordination standpoint, with which leg would you choose to kick a ball?

R **L**

Data Entry Use Only:
R = 1 L = 0

____
zzLD

Severity of Complaints of Self-Reported
Knee Instability in Individuals with Knee OA.

Some people say that their knee or knees are unstable. Examples of instability are the knee gives way, buckles, shifts, or feels like it is going to give way, buckle or shift. On the scale of 0-5 how unstable is your knee?

Knee Instability Ratings
0 = The symptom prevents me from all daily activity
1 = The symptom affects my activity severely
2 = The symptom affects my activity moderately
3 = The symptom affects my activity slightly
4 = I have the symptom but it does not affect my activity
5 = I do not have giving way, buckling, or shifting of the knee.

_____
zKIR

Med/Lat Cent of Knee-Ant	□	M/L Center Mall-Post	□
Med/Lat Cent of Patella	□	Fibular Head	□
l TuberosityTibia	□	Lat Malleoli	□
M/L Center Mall-Ant	□		

Knee Alignment-Varus/Valgus

Telescoping Goniometer
Patient position: Standing, feet together
Fulcrum: Center, M/L Knee
Stationary: M/L Mall-ant
Moving: ASIS

Data Entry Use Only:
Neutral = 0; Varus = 1; Valgus = 2

_____
zRKA

Umbilicus Right:

_____ Var Val

Right:
Knee Alignment (circle):

Neutral Varus Valgus

Umbilicus measurement is varus as long as proximal-medial part of angle is from the umbilicus

Measurement in Degrees: _____
zRKAD

.....

Left
Knee Alignment (circle):

Neutral Varus Valgus

Umbilicus Left:

_____ Var Val

Data Entry Use Only:
Neutral = 0; Varus = 1; Valgus = 2

_____
zLKA

Measurement in Degrees: _____
zLKAD

Relaxed Calcaneal Stance:
Trimmed Goniometer
Patient position: Standing, feet natural apart
Fulcrum: Center, Post, M/L Malleoli
Stationary: Center, Post, M/L Knee
Moving: Center Calcaneus

Right/Left Caution

Right:
Calcaneal Alignment (circle):

Neutral Varus Valgus

Data Entry Use Only:
Neutral = 0; Varus = 1; Valgus = 2

_____
zRCA

Measurement in Degrees: _____
zRCAD

Left:
Calcaneal Alignment (circle):

Neutral Varus Valgus

Data Entry Use Only:
Neutral = 0; Varus = 1; Valgus = 2

_____
zLCA

Measurement in Degrees: _____
zLCAD

Q-Angle

Draw lines with yardstick
Patient position: Standing, feet natural apart
Center: Center of ***Patella***
Inferior: Tibial Tub
Superior: ASIS

Tib tub, Pat portion should be med part of angle on thigh

Right:
Q-Angle ° _____
zRKQD
Left:
Q-Angle° _____
zLKQD

A/P Laxity (Anterior: 20#, 2nd tone; Posterior: 20#, 2nd tone):

Right:
Anterior: Trial 1 _____ Trial 2 _____ Trial 3 _____ Max A: _____

Posterior: Trial 1 _____ Trial 2 _____ Trial 3 _____ Max P: _____

Total: Max A + Max P = Laxity _____ + _____ = _____ _____
zRAPM

Left:
Anterior: Trial 1 _____ Trial 2 _____ Trial 3 _____ Max A: _____

Posterior: Trial 1 _____ Trial 2 _____ Trial 3 _____ Max P: _____

Total: Max A + Max P = Laxity _____ + _____ = _____ _____
zLAPM

Knee Flexion/Extension-Passive (min resistance):

Patient position: Supine
Fulcrum: A/P Center of Knee
Stationary: Trochanter
Moving: Lateral Malleolus
Flex: Heel slide, *Ext:* Roll distal tibia

Full Extension = 0° Lacks 5 degrees = 5° Hyperextends 5° = -5° This method allows easier calculation of total ROM

Right:
Flexion ° _____
zRKFD
Extension° _____
zRKED

Left
Flexion ° _____
zLKFD
Extension° _____
zLKED

Hip Flexion-PROM(min resist)::
Patient position: Supine
Fulcrum: Grt Troch
Stationary: Mid Pelvis
Moving: A/P Knee

Right:
Flexion° _____ zRHFD

Left:
Flexion ° _____ zLHFD

Hamstring Length-Active:
Gravity goniometer
Patient position: Supine
Fulcrum: A/P knee
Stationary: Grt Troch
Moving: Lat Mall
Femur vertical with inclinometer
Active knee Extension

(Full Knee Ext = 180°)

Measures should be approximately 90 or more

Right:
Hams° _____ zRHLD

Left:
Hams° _____ zLHLD

Hip Abduction-Passive (min resistance)::
Patient position: Supine
Fulcrum: IP ASIS
Stationary: OP ASIS
Moving: M/L Knee
Note: No hip flex or rotation allowed

Right:
Abduction ° _____ zRHAD

Left:
Abduction ° _____ zLHAD

Ankle Plantar/Dorsi-Knee Bent > 30°: (min resistance):
Patient position: Supine, roll under knee
Fulcrum: Lateral malleolus
Stationary: Fibular head
Moving: parallel with 5th met

Neutral Plantar flexion = 90° angle, foot – lower leg (0° dorsi flexion). Normal P. Flex = 50°

Right:
Plantar Flexion ° _____ zRABPD

Dorsi Flexion° _____ zRABDD

Left
Plantar Flexion ° _____ zLABPD

Dorsi Flexion° _____ zLABDD

Ankle Dorsi-Knee Straight (min resistance):

Right:

Dorsi Flexion° _____
zRASDD

Left

Dorsi Flexion° _____
zLASDD

Bulge Sign for Effusion:

Patient position: supine, knee extended

Right:

Bulge Sign **Y / N** ☐
zRKBY

Left:

Bulge Sign **Y / N** ☐
zLKBY

Data Entry Use Only:
Yes = 1 No = 0

Valgus Knee Stability in Full Extension:

Right:
Valgus Stability (circle)

Normal Hypermobile

Data Entry Use Only:
Normal = 0; Hypermobile = 1

_____
zRVLS

Left:
Valgus Stability (circle)

Normal Hypermobile

Data Entry Use Only:
Normal = 0; Hypermobile = 1

_____
zLVLS

Varus Knee Stability in Full Extension:

Right:
Varus Stability (circle)

Normal Hypermobile

Data Entry Use Only:
Normal = 0; Hypermobile = 1

_____
zRVRS

Left:
Varus Stability (circle)

Normal Hypermobile

Data Entry Use Only:
Normal = 0; Hypermobile = 1

_____
zLVRS

Hip Extension (min resistance):

Patient position: prone, knee extended
Fulcrum: Grt Troch
Stationary: Mid Pelvis
Moving: A/P knee

Right/Left Caution

- 2 = 2 degrees from attaining neutral (flexion contracture)

****Right:*****
Hip Extension° _____
zRHED

Left:
Hip Extension ° _____
zLHED

Hip Rotation (min resistance):

Gravity Goniometer
Patient position: Seated, knees flexed
Fulcrum: Center knee
Stationary: vertical (leveled)
Moving: M/L malleolus

Right:

2 External Rot ° _____
zRHERD

1 Internal Rot° _____
zRHIRD

Left:

4 External Rot ° _____
zLHERD

3 Internal Rot° _____
zLHIRD

Proprioception-Randomization

30	45	60	30	45	60	30	60	45
60	45	30	45	60	30	60	30	45
30	60	45	45	30	60	30	45	60
60	45	30	30	45	60	60	30	45
45	60	30	60	45	30	45	60	30
45	30	60	60	45	30	45	30	60
45	30	60	60	30	45	45	30	60
60	45	30	30	60	45	30	45	60
60	30	45	45	60	30	60	45	30
30	60	45	60	30	45	30	60	45
45	60	30	30	45	60	30	60	45
60	30	45	45	60	30	60	45	30
30	45	60	30	60	45	30	60	45
45	60	30	60	30	45	60	30	45
30	60	45	30	45	60	45	60	30
60	30	45	60	30	45	45	60	30
30	45	60	45	60	30	30	60	45
60	30	45	30	45	60	60	30	45
45	60	30	60	45	30	30	45	60
45	30	60	30	60	45	45	30	60
45	30	60	60	45	30	60	30	45
30	45	60	45	60	30	60	30	45
60	45	30	45	30	60	30	60	45
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30	60	45	60	45	30	30	60	45
45	60	30	60	30	45	45	60	30
45	30	60	30	60	45	60	30	45
30	45	60	45	60	30	30	45	60
60	45	30	60	30	45	45	60	30
45	30	60	30	45	60	30	60	45
60	45	30	45	60	30	60	30	45

ID #: _____ Date: _____ Date Entered: _____ Initials: _____

MARRTC Knee OA-Project II **Isometric Strength**

- Isometric testing completed after proprioception
- Randomize flexion or extension
- Warm up: 2 reps, 5 sec, 1 min rest, all submax: 50%, 75% of subjective max
- Opposite leg tested in same order of flexion or extension as 1st limb

Circle side and direction completed 1st

Right Knee

Right Knee Extension:
Angle: 60° from full extension

Record Peak Torque, 5 sec contraction, 1 min rest between

_____ _____ _____ _____ _____ Peak Observed _____
Rep 1 Rep 2 Rep 3 Rep 4 Rep 5 RPET

Right Knee Flexion:
Angle: 45° from full extension

Record Peak Torque, 5 sec contraction, 1 min rest between

_____ _____ _____ _____ _____ Peak Observed _____
Rep 1 Rep 2 Rep 3 Rep 4 Rep 5 RPFT

Left Knee

Left Knee Extension:
Angle: 60° from full extension

Record Peak Torque, 5 sec contraction, 1 min rest between

_____ _____ _____ _____ _____ Peak Observed _____
Rep 1 Rep 2 Rep 3 Rep 4 Rep 5 LPET

Left Knee Flexion:
Angle: 45° from full extension

Record Peak Torque, 5 sec contraction, 1 min rest between

_____ _____ _____ _____ _____ Peak Observed _____
Rep 1 Rep 2 Rep 3 Rep 4 Rep 5 LPFT

MARRTC BIODEX SCRIPT

RANDOMIZE:

- We will test angle reproduction on one leg, then isometric flexion or extension on the same leg. We will then switch legs. We will randomize which leg starts first and whether we start with isometric flexion or extension.
- Flip coin to get leg order for testing (Heads=Right, Tails=Left), circle chosen leg on proprioception data collection sheet.
- Flip coin again for order of Isometric testing (Heads=Flex, Tails=Ext), circle either flexion or extension on isometric data collection sheet
    - For example by circling right leg and extension on data sheets we will know that the right leg was tested first and during isometrics, extension was completed first.
- Get order of target angles from randomization sheet and record on proprioception data collection sheet before subject arrives

COMPUTER AND MACHINE SET-UP

- **MAKE SURE NO ATTACHMENTS HAVE BEEN LEFT ON THE DYNAMOMETER**
- Turn on **power** switch at the bottom **rear** of the Biodex
- Wait for panel request to "press start" (LCD message box) and press "**Start"** on the **panel** to initialize the dynamometer
- Once initialization is complete, press **"Start"** on the panel
- **Turn on** the Dell **computer** and dynamometer operation screen will appear on computer screen
- Put on the appropriate knee attachment (R/L) – line up dots on dynamometer attachment. You may need to rotate the red dot on the dynamometer head to the 9 o'clock position using the "rotate" buttons on the dynamometer (press the hold button on dynamometer to keep dot in position and make putting attachment on easier)
- Make sure leg attachment is free to move or computer control won't kick on – If locked,
  press black hold button on dynamometer again.
- Press **"Computer Control"** button on panel
- Press "**Start"** on computer panel
- Using the computer software, click on **"patient selection**" icon (1st on top left of computer screen)

- Click **"Add Patient**" icon and complete the required fields indicated in red as directed
    - Name – **MARRTC**
    - Weight – actual participants weight (kg)
    - ID# - **M + *participant study number + A-C (A= 1st test, B= 2nd, etc)***
        - **For example: Participant number 3000, 2nd test**
            - **M3000B**
    - Involved - **NONE**

- Click **"Save"** icon
- Click "**Close"** icon

Angle Reproduction Setup

Return to the **"Patient Selection**" icon, and **click Open** then single click same patient ID# (MARRTC patient and ID highlighted) **click "New" icon**

- The exercise **"Protocol definition" menu screen** will appear
- Click **"Protocol" icon**
- Double-**click on "proprioception unilateral," "knee (extension/flexion)," "Active," and "MARRTCanglereproduction"** click **"select"**
- Click **"Edit"** icon on the protocol to change the randomized order of target angles
- **Protocol Warning** will come up on the screen. click **"Yes",** reset the target angles that we chose in randomization, click **"Save",** and click **"Close"**
- Select **R or L knee** (previously determined by randomization)

*******HAVE PARTICIPANT REMOVE SHOE AND SOCK BEFORE PUTTING BOOT ON**

Position the participant:

- Knee joint line aligned with the dynamometer,
- Hip in neutral rotation (tibias vertical)
- Hip in neutral abduction/adduction (femurs straight ahead)
- Hip in 85° of flexion (adjust seat back accordingly)
- Tibia pad above ankle joint line centered on boot.
- Arms crossed when testing starts, ankle straps secured. (NO OTHER STRAPS ON PARTICIPANT)
- Put on the stockinette and **pressure boot** as directed, 20 mm Hg

Now we are going to put a plastic boot on your lower leg. We are doing this because we want to concentrate our testing on your knee. This boot helps us do this by minimizing the movement of your foot. We will have to fill the boot up with air and you will feel some slight pressure on your leg, however, it will not be uncomfortable.

Setting the Goniometer:

***First, please straighten and bend your knee some to make sure everything feels OK. Did that feel* OK?**

- Position the participant's knee at 90º flexion by goniometer and press "**Hold button**" on the dynamometer
- Calibrate the **computer** software **goniometer** at **90º** by clicking the goniometer icon

Setting Motion Limits:

- Click **"Yes**" to set the ROM limits

Ok. Next we need to set some limits for the machine based on how far you can bend and straighten your knee.

*****Press "hold/release" button on dynamometer to release the leg*****

Away Limit:

Please straighten your knee out in front of you as far as you comfortably can and try to hold that position.

- Help them to get to their full extension and Click **"set away"** icon on computer

Ok. Now you can relax.

Toward Limit:

Now, bend your knee back as far as you comfortably can and hold that position. The machine might feel like it is bouncing a little when you get all the way back but that is normal.

- Click **the "SET TOWARD" icon**
- Click **"continue**"

Angle Reproduction

Explanation at start:

Ok. We want to see how well you can match a specific position with your knee.

There are two parts to this test.

- *First, you will **SLOWLY** move your knee to a certain position and the machine will lock and hold you in this position. You will rest at this position and concentrate on "feeling" how straight or bent your knee is. This is the **Target Angle.***
- ***In the 2nd part, after the machine lets you go, and I tell you to start, you will try to put your knee back in the same position. When you think it is in the same position, you will press this button (give the subject the button).***

Let's do an example. (NEW PART) Use black button on dynamometer and patient control button to run 1 or 2 "mock" reps

Complete one example with eyes open and then one or two with blindfold on.

Data Collection:

*****Important! Record each ending position after EACH REPETITION OF THE SET - This is your only chance to record this number. Record during the rest period prior to clicking "GO" icon for the next repetition**

1st Test Rep Person running computer needs to click "Go" then the interactor will position participant in start position, then computer person clicks "OK" and leg is released.

We are ready to start the real test. We will do the same thing as before. The real test consists of 3 different tries. (position them in the start position and then follow the complete directions on computer; make sure and free the limb).

- When ready to begin the test, click **"GO"** icon
- Follow the directions given by the computer screen
- **If dynamometer locks** after release from 1st target angle, press blinking "**isokinetic"** button on panel and press "**start"** button on panel.

As a reminder, you will ***SLOWLY*** straighten your knee and the machine will eventually lock. It might feel like a different position from the practice but that is OK.

Remember, when the machine locks, RELAX and try to concentrate on that position because this is the position you will try to match in just a moment. Do you have any questions?

(click appropriate icon "Go" to start test) Now slowly straighten out your knee and the machine will lock. Good. Now relax and concentrate on this position.

After time is up, machine will release leg, QUICKLY go through start position sequence. When they are ready to match angle say..

Good, now try to find that same position with your knee, when you think you are there press your button.

Good. End of first test rep. Record ending position after each repetition

2nd Test Rep

Now we are going to do try number 2. (position them in the start position and then follow the complete directions on computer; make sure and free the limb).

Remember, when the machine locks, relax and try to concentrate on that position because this is the position you will try to match in just a moment. Do you have any questions?

(click appropriate icon "Go" to start test) Now SLOWLY straighten out your knee and the machine will lock. Good. Now relax and concentrate on this position.

After time is up, machine will release leg, QUICKLY go through start position sequence. When they are ready to match angle say..

Good, now try to find that same position with your knee, when you think you are there press your button.

Good. End of 2nd test rep. Record ending position after each repetition

3rd Test Rep

We are ready to do the last try. (position them in the start position and then follow the complete directions on computer; make sure and free the limb).

Remember, when the machine locks, relax and try to concentrate on that position because this is the position you will try to match in just a moment. Do you have any questions?

(click appropriate icon "Go" to start test) Now SLOWLY straighten out your knee and the machine will lock. Good. Now relax and concentrate on this position.

After time is up, machine will release leg, QUICKLY go through start position sequence. When they are ready to match angle say..

Good, now try to find that same position with your knee, when you think you are there press your button.

Good. End of last test rep. Record ending position after each repetition

- **When the test is completed, select** the **"YES"** button
- **Have participant put shoe and sock back on. They may get up and walk around.**

Isometric Strength Test Data Collection

First Direction:

Computer Setup:

- Click the **"patient selection" icon**, click **"Open**" select the same subject, and **click "new" test**
- The exercise **"protocol definition" menu screen** will appear
- Click **"protocol"**
- Double-click on **"isometric unilateral," "knee (extension/flexion)," and Choose –** depending on randomization – Away:Test:**60** (**MARRTCextension) or Toward:Test:45(MARRTCflexion)**
  (select extension or flexion depending upon randomization)
- **Click "select"**
- **Click "close"**
- **Select R or L knee**

Position Subject for Isometric Strength Data Collection

Position the participant:

- Knee joint line aligned with the dynamometer,
- Hip in neutral rotation (tibias vertical)
- Hip in neutral abduction/adduction (femurs straight ahead)
- Hip in 85° of flexion (adjust seat back accordingly)
- Tibia pad 2 cm from ankle joint line and secured
- Subject secured at chest, pelvis, thigh straps
- Subjects place hands on handles at side of seat.

Setting the Goniometer

- Position the participant's knee and measure with goniometer placing subject Knee at 90º and **press "hold"** on the **dynamometer**
- **Calibrate** the **computer** software **goniometer at 90º** by **clicking** the **goniometer** icon on computer screen

- **You will see a Range of Motion Set error box.** It will ask "Do you want to set **ROM limits** now?" **(make sure you have selected the correct leg on computer screen)**

- You will click "**Yes"** – click "**Clear Limits**"
- Have subject extend knee as far as comfortable and click **"Set".**
- Have subject Flex Knee back (may hit chair) and click "**Set".**
- Click "**Continue"**

Calibration: Gravity Adjustment

Now I'm going to straighten your knee and the machine will lock. I need you to relax *COMPLETELY* after the machine locks (emphasize the need for them to relax)

- Position the participant's **knee at 20º** and press **"hold"** on the dynamometer (if subject unable to attain 20 degrees place in highest available extension). ***Ask them to relax***
- **Weigh the leg for gravity** correction by clicking the "**weight limb"** (looks like scale next to goniometer icon)
- **Release** limb by pressing "hold" button on the dynamometer
- **You can repeat the above to check if getting a consistent number.**

DO *NOT* JUST CLICK THE "GO BUTTON". There is NO count down to the start of the isometric contraction, so you and they need to be ready.

_____

Go to 1st Randomized Direction (Flexion or Extension)

Second Direction:

Computer Setup:

- Click the **"patient selection" icon**, click **"Open**" select the same subject, and **click "new" test**
- The exercise **"protocol definition" menu screen** will appear
- Click **"protocol"**
- Double-click on **"isometric unilateral," "knee (extension/flexion)," and Choose –** depending on randomization – Away:Test:**60** (**MARRTCextension) or Toward:Test:45(MARRTCflexion)**

(select extension or flexion depending upon randomization)

- **Click "select"**
- **Click "close"**
- **Select R or L knee**

Check repetitions to make sure it reads "5"

Setting the Goniometer

The goniometer still should still be set. Position the subjects knee at 90° and make sure the reading on computer still reads 90°. Click goniometer icon. Release leg by pressing "hold/release" button on dynamometer

- **You will see a Range of Motion Set error box.** It will ask "Do you want to set **ROM limits** now?" **(make sure you have selected the correct leg on computer screen)**
- You will click "**Yes"**
- Click "**Continue"**

Calibration: Gravity Adjustment

Now I'm going to straighten your knee and the machine will lock. I need you to relax *COMPLETELY* after the machine locks (emphasize the need for them to relax)

- Position the participant's **knee at 20º** and press **"hold"** on the dynamometer (if subject unable to attain 20 degrees place in highest available extension). ***Ask them to relax***
- **Weigh the leg for gravity** correction by clicking the "**weight limb"** (looks like scale next to goniometer icon)
- **Release** limb by pressing "hold" button on the dynamometer
- **You can repeat the above to check if getting a consistent number.**

DO *NOT* JUST CLICK THE "GO BUTTON". There is NO count down to the start of the isometric contraction, so you and they need to be ready.

Isometric Data Collection Extension:

When we start, this is what will happen:

- ***The machine will move you into a position***
- ***You will here a loud horn and I will tell you to kick out and try to straighten your knee.***
- ***The first try is a warm up. Please kick out for 5 seconds at about ½ your effort.***
- ***During the rest of the test, try to kick out as hard as you can for the full 5 seconds.***

Are you ready? Good.

Remember, the first try is just for warm up.

Do you have any questions?

The Test:

- ***THERE WILL BE NO COUNTDOWN.*** Be ready to say "GO" very soon after you click the "GO" icon

- Click "GO" icon.
- As the machine is moving the subject **QUICKLY** say **"OK, now the machine is moving you to position, in a moment you will start to kick out."**
- **HORN WILL BLARE!!!! Say "Go about ½ effort"**

Rep Ends

- ***Stop. Now you have 1 minute to rest.***
- ***For the next one, I will count down from 5 and then a horn will blast and I will say "GO".***
- ***At that time kick out again, THIS TIME AS HARD AS YOU CAN FOR THE FULL 5 SECONDS***

5,4,3,2,1, "GO".
"as hard as you can" at 2 and 4 seconds

Rep Ends-Continue the above for all 5 reps

- When the test is completed, click the **"YES"** button

- **Print out** the test results by clicking 4th icon on left **"Report"** and then under "Choose Report" click **"general evaluation**" then click "**Print".**

Isometric Data Collection Flexion:

When we start, this is what will happen:

- ***The machine will move you into a position***
- ***You will here a loud horn and I will tell you to pull back and try to bend your knee.***
- ***The first try is a warm up. Please pull back for 5 seconds at about ½ your effort.***
- ***During the rest of the test, try to pull back as hard as you can for the full 5 seconds.***

Are you ready? Good.

Remember, the first try is just for warm up.

Do you have any questions?

The Test:

- ***THERE WILL BE NO COUNTDOWN.*** Be ready to say "GO" very soon after you click the "GO" icon

- Click "GO" icon.
- As the machine is moving the subject **QUICKLY** say **"OK, now the machine is moving you to position, in a moment you will start to pull back."**
- **HORN WILL BLARE!!!! Say "Go about ½ effort"**

Rep Ends

- ***Stop.*** ***Now you have 1 minute to rest.***
- ***For the next one, I will count down from 5 and then a horn will blast and I will say "GO".***
- ***At that time pull back again, THIS TIME AS HARD AS YOU CAN FOR THE FULL 5 SECONDS***

5,4,3,2,1, "GO".
"as hard as you can" at 2 and 4 seconds

Rep Ends-Continue the above for all 5 reps

- When the test is completed, click the **"YES"** button

- **Print out** the test results by clicking 4th icon on left **"Report"** and then under "Choose Report" click **"general evaluation**" then click "**Print".**

MOVE CHAIR AND DYNAMOMETER TO OTHER SIDE AND REPEAT ALL PROTOCOLS AS RANDOMIZED

Switching Legs

- **Note the chair position settings**
- Slide the participant away from the dynamometer
- Get participant out of chair
- **Change the knee attachment** (R/L) as appropriate
- **Rotate** the chair **180º**
- **Position** the participant **with joint line aligned with the dynamometer and position as you did from other side**.

Session Completion

- Set all the seat **settings back to "0**", neatly fold the seat belts so that they do not touch the ground, and appropriately place the attachment back onto the attachment rack
- If deleting test records, select "patient selection", select a specific test, select "delete", and select "Yes." A subject will not stay in the database unless at least one test exists in the database. You may need to leave one test in the database, as directed.
- Using the **computer, select "start", and select "turn off"**
- Then **switch off the panel control unit using the bottom rear power switch**
- Replace all the necessary study materials to their proper locations and leave the area as you found it
- If you have encountered any problems (e.g., patient error codes or low ink on the printer), please report them to your supervisor immediately

WHAT TO DO IF……..

- If the "isokinetic" button on the panel control begins to blink after a repetition, select that button and then select "start" to continue the repetitions
- If the dynamometer locks in one position, select "setup" and select "start." Avoid re-setting ROM limits.
- If Dynamometer numbers go crazy and you are unable to do test protocol, click "file and then click "setup". Look at the Dynamometer Int. box and if simulation mode is checked, uncheck it and "close".
- If you get a "Patient Code error …," record the requested information in the error log book. Remove the attachment. (You will need to move the participant so remember the chair settings.) Select the red blinking "stop." The Biodex will reboot. When requested to do so, select "start" on the panel to initialize the dynamometer. Once initialization is complete, select "start" on the panel.
- If you cannot solve the problem on your own, you can call Biodex technical support for rehabilitation equipment using the 1-800… number on the Biodex manuals. If you have a cell phone, use it to call so that you can talk to them and use the Biodex at the same time.
- DO NOT make a request for an on-site service call without authorization from your supervisor as we will be billed for such service calls.

Answers to Common Questions

"I just forgot what position my knee was in, do I just guess?"

- Record on sheet as a X in slot and write a little note to that effect. We are using the average from the 3 in the data analysis, in this case, we will just use the average of the 2. Do not repeat the trial.

"Do I have to wear the blindfold? I'm claustrophobic (or whatever)".

- Explain that we try very hard to standardize the way we do things between subjects, but it they really, really don't want to wear it, they do not have to. Emphasize the need for them TO KEEP THEIR EYES CLOSED during the proprioception testing.

"I just got a cramp in my leg during the strength testing and I don't want to continue"

- They should stop. Note on sheet. If they were able to produce 1-2 max contractions, we might still be able to use the data.

"Why are you testing if I can reproduce an angle? What does that have to do with OA?"

- Keep it brief. You might say that the ability to know what position your legs are in without looking might offer some protection from injury. This is one of the things we are trying to figure out in the study.

ID #: _____ Date: _____ Date Entered: _____ Initials: _____

MARRTC Knee OA-Project II **Proprioception**

- Randomize right or left
- 2 practice reps at 15°
- Perform test; next isometric
- Opposite limb tested with same randomized order of angles.

Circle side of test done 1st.

Right Knee

Angle Reproduction

Start: 90° Target Angles: 30°, 45°, 60° (Pre-Randomized)

Target Angle Order From Randomization:

Target:	Actual:	Absolute Difference:
_____	_____	_____
_____	_____	_____
_____	_____	_____

Average Absolute Difference _____ Average Absolute Difference _____
RAR

Left Knee

Angle Reproduction

Start: 90° Target Angles: 30°, 45°, 60° (Pre-Randomized)

Target Angle Order From Randomization:

Target:	Actual:	Absolute Difference:
_____	_____	_____
_____	_____	_____
_____	_____	_____

Average Absolute Difference _____ Average Absolute Difference _____
LAR

Appendix D

Raw Data

idnumb	wop.1	woa.1	Chairrates	alignworst	laxworst
701.00	5.00	16.00	23.68	6.60	9.00
702.00	3.00	8.00	26.55	3.20	6.00
703.00	6.00	20.00	32.97	2.60	4.50
704.00	6.00	40.00	12.42	1.00	11.00
705.00	2.00	0.00	39.22	4.00	11.00
706.00	7.00	33.00	28.09	9.70	12.00
707.00	8.00	29.00	20.26	10.80	7.50
708.00	7.00	27.00	25.82	0.90	10.00
709.00	2.00	18.00	32.33	0.90	8.00
710.00	5.00	23.00	23.98	6.10	12.00
711.00	10.00	45.00	17.93	8.90	12.00
712.00	11.00	42.00	16.23	9.30	11.00
713.00	2.00	10.00	34.40	3.60	11.00
714.00	9.00	34.00	26.16	5.20	7.00
715.00	9.00	41.00	18.65	7.70	10.00
716.00	9.00	39.00	32.97	9.60	12.00
717.00	9.00	36.00	25.06	5.30	11.00
718.00	7.00	14.00	29.53	2.50	7.00
719.00	11.00	25.00	10.69	4.30	11.00
720.00	6.00	19.00	18.21	8.30	8.00
721.00	5.00	24.00	24.55	9.10	6.00
722.00	5.00	23.00	33.82	2.40	5.00
723.00	11.00	37.00	29.10	11.60	4.00
724.00	7.00	30.00	26.91	2.00	12.00
725.00	5.00	22.00	24.00	2.40	7.00
726.00	7.00	29.00	7.07	0.20	6.00
728.00	7.00	24.00	30.09	4.30	18.00
729.00	4.00	24.00	32.86	0.80	9.00
730.00	5.00	27.00	30.30	5.20	8.00
731.00	7.00	19.00	27.99	7.10	9.00
732.00	7.00	26.00	10.52	3.60	12.00
733.00	5.00	0.00	21.14	6.10	6.00
734.00	8.00	26.00	27.83	0.10	12.00
735.00	9.00	40.00	21.82	4.70	6.00
736.00	6.00	25.00	26.02	13.40	13.00
737.00	2.00	11.00	21.23	2.00	8.50
738.00	15.00	53.00	23.18	14.30	19.00
739.00	7.00	27.00	16.61	8.90	10.00
740.00	5.00	25.00	20.34	1.00	10.00
741.00	8.00	28.00	18.75	2.60	7.50
742.00	10.00	16.00	24.61	4.60	7.00
743.00	5.00	21.00	18.18	9.30	9.00
744.00	9.00	31.00	25.19	4.30	12.00
745.00	6.00	5.00	13.61	3.50	7.00
746.00	2.00	20.00	23.36	1.00	8.50
747.00	6.00	20.00	32.68	5.00	6.50

idnumb	Propave	ExtworstBW	FlxworstBW	ROMworst
701.00	4.33	1.33	0.68	133.00
702.00	12.00	1.40	0.47	128.00
703.00	8.33	1.77	0.53	131.00
704.00	5.00	1.49	1.01	139.00
705.00	2.67	2.09	0.75	145.00
706.00	13.00	1.10	0.52	123.00
707.00	4.00	0.43	0.24	135.00
708.00	9.00	0.90	0.52	133.00
709.00	6.67	1.00	0.56	135.00
710.00	7.00	1.28	0.76	135.00
711.00	5.33	0.63	0.38	108.00
712.00	5.33	1.64	0.64	128.00
713.00	14.00	1.20	0.69	124.00
714.00	3.33	0.74	0.38	117.00
715.00	11.33	0.84	0.46	94.00
716.00	11.33	2.08	0.75	115.00
717.00	7.00	0.72	0.49	125.00
718.00	10.33	0.49	0.44	135.00
719.00	4.67	0.91	0.44	114.00
720.00	10.66	1.59	0.48	129.00
721.00	5.67	0.87	0.55	93.00
722.00	6.67	1.35	0.63	111.00
723.00	7.33	0.96	0.48	96.00
724.00	3.33	2.22	0.92	129.00
725.00	7.00	0.91	0.56	122.00
726.00	5.67	0.58	0.48	137.00
728.00	5.67	1.37	0.88	141.00
729.00	8.00	0.87	0.62	120.00
730.00	5.00	1.96	1.06	133.00
731.00	5.00	1.31	0.51	120.00
732.00	9.00	0.66	0.31	103.00
733.00	3.00	1.37	1.04	126.00
734.00	5.00	1.09	0.57	135.00
735.00	6.33	1.11	0.61	107.00
736.00	5.33	0.88	0.41	116.00
737.00	5.67	0.58	0.37	125.00
738.00	6.00	0.81	0.23	124.00
739.00	3.67	0.71	0.32	128.00
740.00	4.33	0.99	0.53	127.00
741.00	3.00	1.10	0.56	115.00
742.00	2.67	0.91	0.55	126.00
743.00	7.00	1.25	0.66	127.00
744.00	7.00	2.13	0.87	136.00
745.00	9.33	1.84	0.74	136.00
746.00	4.67	1.38	0.46	109.00
747.00	2.33	1.37	0.56	124.00

idnumb	ZPropave	ZROMworst	Zwop.1	Zwoa.1	ZChairrates
701.00	-0.75207	0.74958	-0.60533	-0.79824	-0.05451
702.00	1.90927	0.34488	-1.32858	-1.50437	0.35211
703.00	0.63646	0.58770	-0.24370	-0.44517	1.26122
704.00	-0.52065	1.23522	-0.24370	1.32016	-1.64951
705.00	-1.33062	1.72086	-1.69020	-2.21050	2.14630
706.00	2.25640	-0.05983	0.11792	0.70229	0.57041
707.00	-0.86778	0.91146	0.47955	0.34923	-0.53912
708.00	0.86788	0.74958	0.11792	0.17270	0.24855
709.00	0.05791	0.91146	-1.69020	-0.62170	1.17065
710.00	0.17362	0.91146	-0.60533	-0.18037	-0.01161
711.00	-0.40494	-1.27393	1.20280	1.76149	-0.86840
712.00	-0.40494	0.34488	1.56442	1.49669	-1.10893
713.00	2.60353	0.02111	-1.69020	-1.32784	1.46471
714.00	-1.09920	-0.54547	0.84117	0.79056	0.29637
715.00	1.67785	-2.40709	0.84117	1.40843	-0.76737
716.00	1.67785	-0.70735	0.84117	1.23189	1.26122
717.00	0.17362	0.10205	0.84117	0.96709	0.14162
718.00	1.33072	0.91146	0.11792	-0.97477	0.77404
719.00	-0.63636	-0.78829	1.56442	-0.00384	-1.89397
720.00	1.44411	0.42582	-0.24370	-0.53344	-0.82831
721.00	-0.28923	-2.48803	-0.60533	-0.09210	0.06900
722.00	0.05791	-1.03111	-0.60533	-0.18037	1.38230
723.00	0.28933	-2.24521	1.56442	1.05536	0.71320
724.00	-1.09920	0.42582	0.11792	0.43749	0.40270
725.00	0.17362	-0.14077	-0.60533	-0.26864	-0.00889
726.00	-0.28923	1.07334	0.11792	0.34923	-2.40637
728.00	-0.28923	1.39710	0.11792	-0.09210	0.85375
729.00	0.52075	-0.30265	-0.96695	-0.09210	1.24588
730.00	-0.52065	0.74958	-0.60533	0.17270	0.88388
731.00	-0.52065	-0.30265	0.11792	-0.53344	0.55556
732.00	0.86788	-1.67863	0.11792	0.08443	-1.91891
733.00	-1.21491	0.18299	-0.60533	-2.21050	-0.41376
734.00	-0.52065	0.91146	0.47955	0.08443	0.53350
735.00	-0.05780	-1.35487	0.84117	1.32016	-0.31793
736.00	-0.40494	-0.62641	-0.24370	-0.00384	0.27709
737.00	-0.28923	0.10205	-1.69020	-1.23957	-0.40104
738.00	-0.17352	0.02111	3.01092	2.46762	-0.12449
739.00	-0.98349	0.34488	0.11792	0.17270	-1.05545
740.00	-0.75207	0.26394	-0.60533	-0.00384	-0.52745
741.00	-1.21491	-0.70735	0.47955	0.26096	-0.75252
742.00	-1.33062	0.18299	1.20280	-0.79824	0.07756
743.00	0.17362	0.26394	-0.60533	-0.35690	-0.83300
744.00	0.17362	0.99240	0.84117	0.52576	0.15951
745.00	0.98359	0.99240	-0.24370	-1.76917	-1.48121
746.00	-0.63636	-1.19299	-1.69020	-0.44517	-0.09891
747.00	-1.44633	0.02111	-0.24370	-0.44517	1.22053

idnumb	Zalignworst	Zlaxworst	ZExtworstBW
701.00	0.38023	-0.10517	0.32999
702.00	-0.55480	-1.07273	0.48615
703.00	-0.71980	-1.55652	1.26645
704.00	-1.15982	0.53987	0.67523
705.00	-0.33479	0.53987	1.95868
706.00	1.23275	0.86239	-0.16717
707.00	1.53526	-0.58895	-1.61459
708.00	-1.18732	0.21735	-0.58983
709.00	-1.18732	-0.42769	-0.38463
710.00	0.24272	0.86239	0.21295
711.00	1.01275	0.86239	-1.18602
712.00	1.12275	0.53987	0.99361
713.00	-0.44480	0.53987	0.05748
714.00	-0.00478	-0.75021	-0.93820
715.00	0.68274	0.21735	-0.72202
716.00	1.20525	0.86239	1.94108
717.00	0.02272	0.53987	-0.98033
718.00	-0.74730	-0.75021	-1.48002
719.00	-0.25229	0.53987	-0.58487
720.00	0.84774	-0.42769	0.88903
721.00	1.06775	-1.07273	-0.66949
722.00	-0.77481	-1.39526	0.36626
723.00	1.75527	-1.71778	-0.46373
724.00	-0.88481	0.86239	2.25116
725.00	-0.77481	-0.75021	-0.56837
726.00	-1.37982	-1.07273	-1.28302
728.00	-0.25229	2.79752	0.40309
729.00	-1.21482	-0.10517	-0.67438
730.00	-0.00478	-0.42769	1.67821
731.00	0.51773	-0.10517	0.28367
732.00	-0.44480	0.86239	-1.12341
733.00	0.24272	-1.07273	0.40286
734.00	-1.40732	0.86239	-0.18238
735.00	-0.14229	-1.07273	-0.15342
736.00	2.25028	1.18492	-0.64090
737.00	-0.88481	-0.26643	-1.29778
738.00	2.49779	3.12004	-0.78893
739.00	1.01275	0.21735	-1.01604
740.00	-1.15982	0.21735	-0.41179
741.00	-0.71980	-0.58895	-0.16540
742.00	-0.16979	-0.75021	-0.57685
743.00	1.12275	-0.10517	0.15282
744.00	-0.25229	0.86239	2.05741
745.00	-0.47230	-0.75021	1.41968
746.00	-1.15982	-0.26643	0.43199
747.00	-0.05978	-0.91147	0.40576

idnumb	ZFlxworstBW	MAH_1	p_mah_1
701.00	0.49516	2.58317	0.0214
702.00	-0.56440	8.38060	0.5037
703.00	-0.24393	10.27104	0.6710
704.00	2.18196	16.65433	0.9456
705.00	0.87674	14.78225	0.9029
706.00	-0.28732	7.69216	0.4346
707.00	-1.72350	12.70080	0.8234
708.00	-0.32725	4.64243	0.1357
709.00	-0.10729	6.44883	0.3057
710.00	0.91677	3.55285	0.0617
711.00	-0.99781	4.90250	0.1573
712.00	0.28645	6.94219	0.3569
713.00	0.58238	12.17702	0.7965
714.00	-1.02826	4.89319	0.1565
715.00	-0.61761	9.04257	0.5666
716.00	0.86040	10.60563	0.6963
717.00	-0.47596	3.05096	0.0378
718.00	-0.68996	12.46195	0.8115
719.00	-0.71935	11.54293	0.7597
720.00	-0.50981	9.40764	0.5995
721.00	-0.17376	10.34871	0.6770
722.00	0.27322	5.63904	0.2246
723.00	-0.52015	13.02146	0.8384
724.00	1.74675	9.09232	0.5712
725.00	-0.08026	1.58557	0.0035
726.00	-0.48371	12.62408	0.8196
728.00	1.51390	13.29360	0.8502
729.00	0.21977	6.12779	0.2729
730.00	2.43908	9.12999	0.5746
731.00	-0.35157	2.52628	0.0198
732.00	-1.38253	12.91689	0.8336
733.00	2.35172	20.73996	0.9861
734.00	-0.05035	6.42029	0.3028
735.00	0.14547	5.64036	0.2247
736.00	-0.85783	9.86961	0.6389
737.00	-1.05383	6.84780	0.3470
738.00	-1.76260	17.81986	0.9627
739.00	-1.33191	6.04595	0.2647
740.00	-0.26529	3.45843	0.0567
741.00	-0.09590	3.93370	0.0843
742.00	-0.15344	10.18884	0.6646
743.00	0.39014	5.56217	0.2172
744.00	1.49519	6.76829	0.3388
745.00	0.79293	13.89176	0.8738
746.00	-0.59402	13.33176	0.8518
747.00	-0.11842	5.44048	0.2057

Variable Name	Variable
Idnumb	ID Number
Wop.1	WOMAC Pain Scale
Woa.1	WOMAC Function
Chairrates	Timed Chair Rise Task
Alignworst	Varus/Valgus Alignment
Laxworst	A/P Laxity
Propave	Proprioception
ExtworstBw	Extension Strength by Bodyweight
FlxworstBW	Flexion Strength by Bodyweight
ROMworst	Knee ROM
Zpropave	Z score Proprioception
ROMworst	Z score Knee ROM
Wop.1	Z score WOMAC Pain Scale
Woa.1	Z score WOMAC Function
Chairrates	Z score Timed Chair Rise Task
Alignworst	Z score Varus/Valgus Alignment
Laxworst	Z score A/P Laxity
ExtworstBw	Z score Extension Strength by Bodyweight
FlxworstBW	Z score Flexion Strength by Bodyweight
MAH_1	Mah Distance
P_mah_1	Probability of Signficant D^2

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