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Impaired Varus-Valgus Proprioception and Neuromuscular Stabilization in Medial Knee Osteoarthritis

Alison H. Chang, PT, DPT, MS¹, Song Joo Lee, MS², Heng Zhao, PhD³, Yupeng Ren, MS³, and Li-Qun Zhang, PhD^{2,3,4,5}

Alison H. Chang: hsinia@northwestern.edu; Song Joo Lee: song-lee@northwestern.edu; Heng Zhao: hengzhao@gmail.com; Yupeng Ren: y-ren@northwestern.edu; Li-Qun Zhang: l-zhang@northwestern.edu

¹Department of Physical Therapy and Human Movement Sciences, Northwestern University

²Department of Biomedical Engineering, Northwestern University

³Sensory Motor Performance Program, Rehabilitation Institute of Chicago

⁴Department of Orthopaedic Surgery, Northwestern University

⁵Department of Physical Medicine and Rehabilitation, Northwestern University

Abstract

Impaired proprioception and poor muscular stabilization in the frontal plane may lead to knee instability during functional activities, a common complaint in persons with knee osteoarthritis (KOA). Understanding these frontal plane neuromechanical properties in KOA will help elucidate the factors contributing to knee instability and aid in the development of targeted intervention strategies. The study objectives were to compare knee varus-valgus proprioception, isometric muscle strength, and active muscular contribution to stability between persons with medial KOA and healthy controls. We evaluated knee frontal plane neuromechanical parameters in 14 participants with medial KOA and 14 age- and gender-matched controls, using a joint driving device (JDD) with a customized motor and a 6-axis force sensor. Analysis of covariance with BMI as a covariate was used to test the differences in varus-valgus neuromechanical parameters between these two groups. The KOA group had impaired varus proprioception acuity ($1.08 \pm 0.59^\circ$ vs. $0.69 \pm 0.49^\circ$, $p < 0.05$), decreased normalized varus muscle strength ($1.31 \pm 0.75\%$ vs. $1.79 \pm 0.84\%$ body weight, $p < 0.05$), a trend toward decreased valgus strength ($1.29 \pm 0.67\%$ vs. $1.88 \pm 0.99\%$, $p = 0.054$), and impaired ability to actively stabilize the knee in the frontal plane during external perturbation (4.67 ± 2.86 vs. 8.26 ± 5.95 Nm/degree, $p < 0.05$). The knee frontal plane sensorimotor control system is compromised in persons with medial KOA. Our findings suggest varus-valgus control deficits in both the afferent input (proprioceptive acuity) and muscular effectors (muscle strength and capacity to stabilize the joint).

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Corresponding Author: Dr. Li-Qun Zhang, Professor and Senior Research Scientist, Northwestern University and Rehabilitation Institute of Chicago, Phone: (312) 238-4767, Fax: (312) 238-2208, l-zhang@northwestern.edu.

Conflict of interest statement

None.

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Keywords

Knee osteoarthritis; Proprioception; Instability; Varus-valgus motion

1. Introduction

Osteoarthritis (OA), a leading cause of chronic disability in the elderly, is believed to result from local mechanical factors acting in the presence of systemic susceptibility. There is a growing recognition of the role of knee varus-valgus laxity and instability in symptoms, physical function, and natural history of the disease. 44% of persons with knee OA reported knee instability affecting their physical function (Fitzgerald et al., 2004). Dynamic frontal plane instability, visualized as varus thrust during walking, was present in approximately 32% of persons at risk for or with knee OA and was associated with higher medial knee load and disease progression (Chang et al., 2004; Chang et al., 2010).

Instability is likely a multi-factorial problem, resulting from impaired sensory/proprioceptive input, altered neuromuscular stabilization, lax capsule-ligamentous structures, and structural damage to the knee cartilage and bone (Schipplein and Andriacchi, 1991). Among these possible causes, proprioceptive acuity and active muscular contribution to stability deserve attention and further investigation, because they are likely modifiable by exercise interventions (Fitzgerald et al., 2002; Hunt et al., 2011; Hurley and Scott, 1998; Jan et al., 2008; Thorstensson et al., 2007), which may prevent or lessen the deleterious effects of instability on knee OA disease course.

Persons with knee OA have impaired proprioceptive accuracy than age-matched persons without the disease (Felson et al., 2009; Hurley et al., 1997; Lund et al., 2008; Roos et al., 2011; Sharma et al., 1997). However, two longitudinal studies with a large cohort failed to demonstrate that proprioceptive deficit is a risk factor for the development or progression of knee OA (Felson et al., 2009; Segal et al., 2010a). Previous studies of proprioception relied on measurements in the direction of extension and flexion, although osteoarthritic knees are most vulnerable in the frontal plane, including varus mal-alignment, laxity, and dynamic instability (Brouwer et al., 2007; Chang et al., 2004; Hunt et al., 2011; Lewek et al., 2004a; Sharma et al., 2013; Sharma et al., 1999; Sharma et al., 2001; van der Esch et al., 2008a). Similarly, studies quantifying active neuromuscular control in knee OA often involve muscles primarily functioning in the sagittal plane (Amin et al., 2009; Lim et al., 2009; Mikesky et al., 2006; Roos et al., 2011; Segal et al., 2010b; Sharma et al., 2003). In a previous study of healthy participants, we found that using visual feedback display of torque magnitude, the participants could generate significant knee valgus and varus isometric torque measured by a 6-axis force sensor (Zhang et al., 2001). In addition, varus and valgus torques generated by differential knee muscle contractions (i.e. medial hamstrings and gastrocnemius for varus torque; lateral hamstrings and gastrocnemius for valgus torque) resulted in opening of lateral and medial tibiofemoral compartments respectively on fluoroscopic images, suggesting that active muscle contraction in the frontal plane may help to reduce knee compartment-specific load (Zhang et al., 2001).

Given the biomechanical and functional significance of knee frontal plane movement control in persons with knee OA, examining the varus-valgus neuromechanical characteristics will provide valuable insight into the pathogenesis or progression of knee OA. We tested the following hypotheses. Compared to age-, gender-matched healthy controls, persons with medial knee OA have (1) decreased proprioceptive acuity measured as threshold to detection angle in varus direction and in valgus direction, (2) diminished knee varus and valgus isometric muscle torques, and (3) impaired ability to actively stabilize the knee in response

to external perturbation in the varus-valgus direction. Understanding these modifiable knee frontal plane neuromuscular features will aid in the development and implementation of novel interventional approaches aiming at optimizing varus-valgus neuromuscular control in persons with knee OA.

2. Methods

2.1. Participants

Twenty-eight individuals (57% women), 14 with medial knee OA and 14 age- and gender-matched healthy controls, participated in this study. Participants with OA met the American College of Rheumatology clinical criteria for knee OA (Altman et al., 1986) and had medial radiographic knee OA, Kellgren/Lawrence grade 2, without evidence of lateral compartment OA, in the tested knee (Kellgren and Lawrence, 1957). Testing was performed on the worse knee. People with systemic inflammatory arthritis, secondary OA, intra-articular steroid or hyaluronic acid injection in the prior 12 months, or joint replacement were excluded. The control subjects reported no history of knee pain, stiffness, or injury in the past 5 years and never had past knee surgery. Neither groups had neuromuscular pathology or other serious medical conditions that would interfere with muscle strength testing. Informed consents approved by the Institutional Review Board were obtained.

2.2. Experimental Setup

To quantify the knee frontal plane neuromechanics, we used a custom-designed chair with a 6-axis force sensor (JR3 Inc., Woodland, CA) and a motor placed underneath the knee joint center (Fig. 1). This knee joint driving device (JDD) controls the angular velocity of knee varus-valgus motion and records joint angle and torque. The participant sat upright on the chair with the trunk supported by a backrest reclined at 20° from vertical. The knee was placed at full extension to minimize tibial/femoral rotation during testing. The knee varus-valgus axis was chosen at the midpoint between the femoral epicondyles, pointing anteriorly, and parallel to the tibial plateau (Grood and Suntay, 1983; Lin et al., 2003; Pennock and Clark, 1990). To ensure accurate knee joint axis of rotation approximation, a custom-built joint centering device was used to align the axis of the sensor/motor with the anatomical knee varus-valgus axis. To minimize limb rotation during testing, we employed multiple stabilization methods, which provided more satisfactory stabilization than Velcro belts (Figure 1). Knee mechanical neutral position in the frontal plane was established by “0” torque reading on the sensor. This setup showed good test-retest reliability in knee frontal plane angle and torque measures (Zhang and Wang, 2001; Zhang et al., 2001). Each participant’s knee varus-valgus (v-v) passive range of motion (ROM) was determined when 8 Nm passive torque resistance were reached. Similarly, v-v ROM was also measured with 12 Nm torque limit.

2.2.1. Varus-Valgus Proprioceptive Acuity—Knee varus-valgus proprioceptive acuity was measured by the threshold to detection of a passive movement in the respective varus and valgus directions. Placed at mechanical neutral position at the start of testing, the knee was randomly moved into either varus or valgus direction by the JDD at a constant slow speed of 0.1°/sec. The blind-folded participant was instructed to push a trigger and report the direction of motion when (s)he first sensed which direction the knee is moving into. The motor stopped the movement once the trigger is activated. Each participant completed 6 trials without complaints of pain or discomfort. Proprioceptive acuity was quantified by the varus or valgus joint angle where the participant sensed the motion, with greater angle indicating worse acuity.

2.2.2. Varus-Valgus Strength in Isometric Maximal Voluntary Contraction (MVC)

Participants performed isometric knee varus and valgus MVC at mechanical neutral in sitting (Zhang et al., 2001). The force sensor recorded and simultaneously displayed torque signals on a monitor. The visual feedback display helped the participants generate the desired varus and valgus muscle torques. To minimize hip adduction contributing to knee varus torque, subjects pressed the lateral femoral condyle against the lateral part of the knee clamp while performing knee varus MVC. Similarly, subjects pressed the medial femoral condyle against the medial part of knee clamp during the knee valgus MVC. Before data collection, each participant practiced to generate knee varus and valgus torques 3–5 times. Three trials of 5-sec isometric contraction with 30-sec rest in between each trial were recorded: first for knee varus torque, then for valgus torque.

2.2.3. Active Muscular Contribution to Varus-Valgus Angular Stiffness

To examine if persons with medial knee OA had impaired ability to actively stabilize the knee against external perturbation in the varus-valgus direction, we analyzed how much the active muscular contraction contribute to increased knee frontal plane angular stiffness. Frontal plane knee angle (horizontal axis) vs. torque (vertical axis) were recorded and plotted to calculate knee stiffness (Fig. 2) in two conditions. First, the participant was completely relaxed while the motor moved the knee into varus and then valgus to a preset resistance torque limit of 8 Nm in each direction at a speed of 1°/sec. 6 cycles of continuous passive varus-valgus movements were recorded, which served as the marker for passive tissue stiffness in the frontal plane. Surface electromyography signals from key muscles were monitored to ensure no active muscle activity occurred during these movements. Second, not knowing the timing or direction of the external perturbations, the participant was instructed to resist the varus-valgus movements imposed by the motor and to “try not let the machine move your leg” while the motor moved the knee into varus-valgus to a preset resistance torque limit of 8 Nm in each direction at 1°/sec. Adding active muscle contraction to stiffen/stabilize the joint, 6 cycle of continuous varus-valgus movements were recorded. Active muscular contribution to v-v stiffness was computed as the difference in stiffness between these two conditions. Repeating the same protocol, joint stiffness was also recorded at a 12-Nm resistance torque limit.

2.3. Functional Measures

Participants reported their knee function using the Knee Outcome Survey-Activity of Daily Living Scale (Irrgang et al., 1998). Knee instability severity was evaluated on a 6-point numeric scale in response to the question: “To what degree does giving way, buckling or shifting of the knee affect your level of daily activity?” Instability was defined as a score of less than 5. This particular question has adequate test-retest reliability (ICC = 0.72) in individuals with knee pathologies, including knee OA (Fitzgerald et al., 2004).

Self-reported knee pain, stiffness, and difficulty with physical function were assessed with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The reliability, validity, and responsiveness of WOMAC scores have been well established in individuals with knee OA (Bellamy et al., 1988; McConnell et al., 2001).

2.4. Data Analysis

For proprioceptive acuity, the threshold to detection angles (°) in the varus or valgus direction were averaged over three trials. For muscle strength, the body-weight-normalized and the absolute peak varus or valgus muscle torque was averaged over three trials. Frontal plane angular stiffness is defined as the change of joint torque divided by the change of joint angle (Nm/degree). For v-v angular stiffness, the slope of angle (horizontal-axis) vs. torque (vertical-axis) curve within 2 degrees of varus-valgus motion, 1 degree in each direction,

was computed. Active muscular contribution to stability in the frontal plane was assessed by the stiffness increase after voluntary muscle contraction to stabilize the knee against external varus-valgus perturbation. Analysis of covariance (ANCOVA) with BMI as a covariate was used to test the differences in varus-valgus neuromechanical parameters between persons with medial knee OA and controls, with $p < 0.05$ as significant. Pearson correlation coefficients were calculated to assess the association of WOMAC pain and function with each frontal plane neuromechanical parameter.

3. Results

Table 1 summarized the participants' characteristics. Compared to controls, knees with medial tibiofemoral OA had a statistically significantly higher threshold to detection angle in the varus direction, but not in the valgus direction (Fig. 3). Knees with medial OA had a statistically significantly decreased body-weight normalized varus torque, mean $\pm$ SD: 1.31 ± 0.75 (OA) % body weight vs. 1.79 ± 0.84 (controls), $p < 0.05$. Similar trend approaching statistical significance was noted in the normalized valgus torque, mean $\pm$ SD: 1.29 ± 0.67 % body weight (OA) vs. 1.88 ± 0.99 (controls), $p = 0.054$. No between-group difference was found in the absolute peak varus or valgus torques. Fig. 4 demonstrated that a person with OA had more difficulty increasing the v-v joint stiffness via active muscular stabilization than the age-, gender-matched control did. In the OA knee, the torque-angle curves with active muscular contribution to v-v stiffness (shown in red lines) had not only smaller stiffness slopes, but also greater variability than the control knee's, suggesting failure in achieving consistent knee frontal-frontal stiffness against external perturbation. Quantitatively, the OA group showed impaired ability to actively stabilize the knee in the frontal plane indicated by significantly smaller change of varus-valgus stiffness with voluntary muscle contraction at each torque limit (Fig. 5).

Among persons with knee OA, we examined the relationship between subjective complaints of instability and objective measures of active muscular contribution to v-v stiffness against external perturbation in the varus-valgus direction. Persons with subjective complaints of instability (defined by a score of < 5) had a significantly lower stiffness change than those without instability complaints (2.75 ± 2.30 vs. 6.64 ± 3.07 Nm/degree at 12 Nm torque limit, $p < 0.05$; 2.19 ± 1.77 vs. 4.94 ± 2.14 Nm/degree at 8 Nm torque limit, $p < 0.05$).

Table 2 showed the correlation between WOMAC pain/function and varus-valgus neuromechanical parameters. Valgus isometric muscle strength was inversely related to WOMAC pain and function ($p < 0.05$). Active muscular contribution to v-v stiffness against external perturbation was inversely related to WOMAC pain score ($p < 0.05$).

4. Discussion

Compared to age- and gender-matched controls, individuals with medial knee OA had impaired proprioceptive acuity in the varus direction, decreased body-weight-normalized varus and valgus muscle strength, and diminished ability to actively stabilize the knee in the frontal plane. Among persons with medial knee OA, those reported subjective complaint of knee instability during daily activities had more difficulty stabilizing the knee in the frontal plane than those without. These findings supported our hypothesis that the knee *frontal plane sensorimotor control system* is compromised in persons with medial knee OA.

The role of knee frontal plane biomechanics in the OA disease process has been a main research interest in the literature. Knee varus-valgus characteristics, such as varus mal-alignment, laxity, and dynamic instability, are common features observed in persons with medial knee OA and associated with disease development and progression (Brouwer et al., 2007; Chang et al., 2004; Hunt et al., 2011; Lewek et al., 2004a; Sharma et al., 2013;

Sharma et al., 1999; Sharma et al., 2001; van der Esch et al., 2008a). The maintenance of frontal plane joint functional stability requires both intact somatosensory afferents and responsive muscular effectors. To our knowledge, this is the first study reporting that osteoarthritic knees had varus-valgus control deficits in both the afferent input (proprioceptive acuity) and muscular effectors (muscle strength and capacity to stabilize the joint).

Persons with medial knee OA were less able to detect passive knee varus motion than were the controls. Specifically, there was a 57% increase (worsening) in the threshold to detection of passive varus motion. No difference in detecting passive valgus motion was observed between these two groups. Although a 0.4° between-group difference in varus proprioceptive acuity appeared small, it was approximately 10% of the total available varus-valgus ROM. Comparing to proprioceptive acuity testing in the sagittal plane between 0 and 120°, this 10% deficit in the varus direction could be equivalent to a 12-degree impairment in the knee flexion-extension direction. Proprioception is a complex sensation derived from multiple inputs that provide the conscious and subconscious perception of joint or limb position and movement in space and depends on afferent receptors in the muscles, ligaments, synovial capsule and skin (Sharma, 1999). A decline in varus motion sense in medial knee OA may be related to diminished sensation on the thickened medial bone plates, coupled with dysfunctional capsule-ligamentous mechanoreceptors and muscle spindles in the lateral aspect of the knee, resulting in diminished ability to perceive varus motion.

Knee motion sense deficits in the flexion-extension direction have been studied extensively in persons with knee OA. The sagittal plane threshold to detection in knee OA were on average 56% (range of 21–87%) worse than that in age-matched controls (Barrack et al., 1983; Hewitt et al., 2002; Koralewicz and Engh, 2000; Lund et al., 2008; Pai et al., 1997; Sharma et al., 1997). The 57% deficit in varus motion sense observed in our study was in close agreement with these investigations. Only one previous study examined knee frontal plane motion proprioceptive accuracy in knee OA and reported that varus and valgus threshold to detection in healthy controls were 0.77° and 0.71° respectively (Cammarata and Dhaher, 2012; Cammarata et al., 2011), which is similar to our recording of 0.69° and 0.70°. In contrast to our findings of motion sense detection deficit in varus direction only, they found that OA knees had impaired accuracy in both varus and valgus directions. This discrepancy was possibly attributed to the difference in knee OA participants' disease features. Only knees with medial tibiofemoral compartment disease were included in our sample, rendering a more homogenous group of potentially similar joint and peri-articular tissue neuromechanical properties. In addition, the knee was passively moved at a speed of 0.1°/sec in our protocol, a slower speed than 1°/sec employed in the other study.

The knee OA group had decreased body-weight normalized varus and valgus isometric muscle torque. This finding adds to the current established evidence of knee extensor weakness in knee OA (Hurley et al., 1997; Lewek et al., 2004b; Slemenda et al., 1997) and underscores the importance of addressing muscle strength in both the sagittal and frontal planes in this population.

Knee frontal plane muscle strength has been investigated in a very limited scope. Using similar experimental setup, a previous study (Zhang et al., 2001) involving 8 healthy young male participants (mean age = 36 years) reported an absolute knee isometric varus torque of 22.3 Nm and valgus torque of 23.6 Nm. Our healthy older participants (57% women, mean age = 58 years) generated smaller absolute torque at the range of 11.88 to 17.04 Nm, perhaps due to the age and gender disparity between these two groups.

Given that persons with OA were heavier, we further compared the absolute varus and valgus torque between OA and controls, and found no statistically significant between-group difference. Although muscle strength data is commonly normalized to body weight, absolute values could provide valuable insight, considering that heavier weight in OA group may be related to extra adipose tissue rather than muscle mass. It is important to point out that muscle torque output (strength) in maximal isometric contraction may not correspond with muscle activation patterns during movement control. It is well accepted that muscle strength does not equate to motor control.

Persons with knee OA exhibited impaired ability to stiffen the knee when externally perturbed in the varus-valgus directions, signifying deficient knee frontal plane neuromuscular control. In theory, altered afferent somatosensory input coupled with inadequate efferent muscle force generation could influence neuromuscular control. Our findings that persons with knee OA had not only deficits in proprioceptive acuity (afferent) and muscle strength (efferent), but also diminished capacity to stabilize the knee in the frontal plane are consistent with this theoretical framework. The subjective report of difficulty in keeping the knee stiff and still when perturbed was reflected in the torque-angle curves during active muscle contraction to increase v-v stiffness (Fig. 4), where greater variability and lower stiffness slopes were noted in the individual with knee OA.

In persons with knee OA, 9 had subjective complaints of knee instability, but 5 did not. Interestingly, failure to significantly increase the joint angular stiffness during external perturbation successfully discriminated these two groups. In fact, there were an incremental worsening of joint stabilization when comparing control knees (8.26 Nm/degree), OA knees without instability complaint (6.64), and OA knees with instability (2.75). This may suggest that insufficient active muscular contribution to varus-valgus stiffness during external perturbation could potentially reflect joint instability experienced in daily functional activities.

Using a paradigm of laterally gliding platform to perturb the lower limb during walking, Schmitt and colleagues found that some persons with medial OA reported subjective sensation of knee instability during the perturbation despite greater medial muscle co-contraction, implying inadequate stabilization strategy (Schmitt and Rudolph, 2008). Interestingly, this subjective sensation of instability was not detected by frontal knee motion measured with 3-dimensional motion analysis system, probably due to the inherent error associated with skin-mounted markers on obese participants. In a study to characterize knee instability in persons with knee OA, no association was found between knee varus-valgus motion during gait, a marker for increased knee instability during weightbearing activity, and selective neuromechanical variables, including knee extensor strength, sagittal plane joint proprioception, frontal plane joint laxity, and goniometric knee alignment (van der Esch et al., 2008b). It is plausible that sagittal plane muscle strength and joint proprioception do not directly contribute to frontal plane joint stability and motion during gait.

Among persons with knee OA, lower WOMAC pain and better function scores were related to greater isometric knee valgus muscle torque. Greater knee valgus torque generated by differential activation of knee muscles (i.e. lateral hamstrings and gastrocnemius) could potentially unload the medial compartment (Zhang et al., 2001) and thus reduce pain and improve function. Greater WOMAC pain was associated with worse ability in active muscular stabilization against varus-valgus perturbation, supporting the clinical consequence of impaired ability to actively stabilize the knee in the frontal plane.

Taken together, our results have significant clinical implications. It appeared that persons with medial knee OA had both sensory afferent deficits and motor output insufficiency in

frontal plane control and that greater knee pain and poorer function were associated with diminished ability to stabilize the knee in the frontal plane. These findings suggest that intervention strategies aiming to address active muscular stabilization and sensory acuity in the frontal plane may be beneficial in improving knee stability, ultimately reducing pain and improving function in persons with knee OA. Future interventional studies and clinical trials are needed to test these hypotheses.

It is important to acknowledge that the cross-sectional nature of our study precludes us from determining whether these frontal plane neuromechanical impairments predates the onset of knee OA, are consequences of knee OA, or are by-products of physical inactivity secondary to pain. Future studies examining whether these frontal plane deficits are associated with disease onset or progression would shed light on the cause-effect relationship. The small sample in this investigation limits generalization to the population with medial knee OA. The current study was conducted in sitting. Non-weightbearing position, though not as functional, can isolate the knee by limiting the contributions from the hip and ankle and is the *best available* approach to specifically quantify the knee neuromechanical properties. Information gained from this study will inform future work examining the frontal plane lower limb integrated neuromechanics in a dynamic weightbearing position.

In summary, compared to age-, gender-matched healthy controls, persons with medial knee OA had decreased proprioceptive acuity in the varus direction, diminished body-weight normalized knee varus and valgus muscle strength, and impaired ability to actively stabilize the knee in the varus-valgus direction. Given that knee frontal plane stability is crucial for joint structure and function, the results underscore the importance of understanding knee frontal plane sensorimotor control in the patho-mechanics of knee OA.

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References

- Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis and Rheumatism*. 1986; 29:1039–1049. [PubMed: 3741515]
- Amin S, Baker K, Niu J, Clancy M, Goggins J, Guermazi A, Grigoryan M, Hunter DJ, Felson DT. Quadriceps strength and the risk of cartilage loss and symptom progression in knee osteoarthritis. *Arthritis and Rheumatism*. 2009; 60:189–198. [PubMed: 19116936]
- Barrack RL, Skinner HB, Cook SD, Haddad RJ Jr. Effect of articular disease and total knee arthroplasty on knee joint-position sense. *Journal of neurophysiology*. 1983; 50:684–687. [PubMed: 6619913]
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *The Journal of Rheumatology*. 1988; 15:1833–1840. [PubMed: 3068365]
- Brouwer GM, van Tol AW, Bergink AP, Belo JN, Bernsen RMD, Reijman M, Pols HAP, Bierma-Zeinstra SMA. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis and Rheumatism*. 2007; 56:1204–1211. [PubMed: 17393449]
- Cammarata ML, Dhaher YY. Associations between frontal plane joint stiffness and proprioceptive acuity in knee osteoarthritis. *Arthritis Care & Research*. 2012; 64:735–743. [PubMed: 22213576]

- Cammarata ML, Schnitzer TJ, Dhaher YY. Does knee osteoarthritis differentially modulate proprioceptive acuity in the frontal and sagittal planes of the knee? *Arthritis and rheumatism*. 2011; 63:2681–2689. [PubMed: 21547895]
- Chang A, Hayes K, Dunlop D, Hurwitz D, Song J, Cahue S, Genge R, Sharma L. Thrust during ambulation and the progression of knee osteoarthritis. *Arthritis and Rheumatism*. 2004; 50:3897–3903. [PubMed: 15593195]
- Chang A, Hochberg M, Song J, Dunlop D, Chmiel JS, Nevitt M, Hayes K, Eaton C, Bathon J, Jackson R, Kwok CK, Sharma L. Frequency of varus and valgus thrust and factors associated with thrust presence in persons with or at higher risk of developing knee osteoarthritis. *Arthritis and Rheumatism*. 2010; 62:1403–1411. [PubMed: 20213800]
- Felson DT, Gross KD, Nevitt MC, Yang M, Lane NE, Torner JC, Lewis CE, Hurley MV. The effects of impaired joint position sense on the development and progression of pain and structural damage in knee osteoarthritis. *Arthritis and Rheumatism*. 2009; 61:1070–1076. [PubMed: 19644911]
- Fitzgerald GK, Childs JD, Ridge TM, Irrgang JJ. Agility and perturbation training for a physically active individual with knee osteoarthritis. *Physical Therapy*. 2002; 82:372–382. [PubMed: 11922853]
- Fitzgerald GK, Piva SR, Irrgang JJ. Reports of joint instability in knee osteoarthritis: its prevalence and relationship to physical function. *Arthritis and rheumatism*. 2004; 51:941–946. [PubMed: 15593258]
- Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. *Journal of biomechanical engineering*. 1983; 105:136–144. [PubMed: 6865355]
- Hewitt BA, Refshauge KM, Kilbreath SL. Kinesthesia at the knee: the effect of osteoarthritis and bandage application. *Arthritis and rheumatism*. 2002; 47:479–483. [PubMed: 12382295]
- Hunt MA, Schache AG, Hinman RS, Crossley KM. Varus thrust in medial knee osteoarthritis: Quantification and effects of different gait-related interventions using a single case study. *Arthritis Care & Research*. 2011; 63:293–297. [PubMed: 20824803]
- Hurley MV, Scott DL. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. *British Journal of Rheumatology*. 1998; 37:1181–1187. [PubMed: 9851266]
- Hurley MV, Scott DL, Rees J, Newham DJ. Sensorimotor changes and functional performance in patients with knee osteoarthritis. *Annals of the rheumatic diseases*. 1997; 56:641–648. [PubMed: 9462165]
- Irrgang JJ, Snyder-Mackler L, Wainner RS, Fu FH, Harner CD. Development of a patient-reported measure of function of the knee. *The Journal of Bone and Joint Surgery. American Volume*. 1998; 80:1132–1145.
- Jan MH, Tang PF, Lin JJ, Tseng SC, Lin YF, Lin DH. Efficacy of a target-matching foot-stepping exercise on proprioception and function in patients with knee osteoarthritis. *The Journal of Orthopaedic and Sports Physical Therapy*. 2008; 38:19–25. [PubMed: 18357655]
- Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthritis. *Annals of the Rheumatic Diseases*. 1957; 16:494–502. [PubMed: 13498604]
- Koralewicz LM, Engh GA. Comparison of proprioception in arthritic and age-matched normal knees. *The Journal of bone and joint surgery. American volume*. 2000; 82-A:1582–1588. [PubMed: 11097448]
- Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*. 2004a; 12:745–751.
- Lewek MD, Rudolph KS, Snyder-Mackler L. Quadriceps femoris muscle weakness and activation failure in patients with symptomatic knee osteoarthritis. *Journal of orthopaedic research: official publication of the Orthopaedic Research Society*. 2004b; 22:110–115. [PubMed: 14656668]
- Lim BW, Kemp G, Metcalf B, Wrigley TV, Bennell KL, Crossley KM, Hinman RS. The association of quadriceps strength with the knee adduction moment in medial knee osteoarthritis. *Arthritis and Rheumatism*. 2009; 61:451–458. [PubMed: 19333982]

- Lin F, Makhsous M, Chang AH, Hendrix RW, Zhang LQ. In vivo and noninvasive six degrees of freedom patellar tracking during voluntary knee movement. *Clinical biomechanics*. 2003; 18:401–409. [PubMed: 12763436]
- Lund H, Juul-Kristensen B, Hansen K, Christensen R, Christensen H, Danneskiold-Samsøe B, Bliddal H. Movement detection impaired in patients with knee osteoarthritis compared to healthy controls: a cross-sectional case-control study. *Journal of Musculoskeletal & Neuronal Interactions*. 2008; 8:391–400. [PubMed: 19147977]
- McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis and Rheumatism*. 2001; 45:453–461. [PubMed: 11642645]
- Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA. Effects of strength training on the incidence and progression of knee osteoarthritis. *Arthritis and Rheumatism*. 2006; 55:690–699. [PubMed: 17013851]
- Pai YC, Rymer WZ, Chang RW, Sharma L. Effect of age and osteoarthritis on knee proprioception. *Arthritis and rheumatism*. 1997; 40:2260–2265. [PubMed: 9416866]
- Pennock GR, Clark KJ. An anatomy-based coordinate system for the description of the kinematic displacements in the human knee. *Journal of Biomechanics*. 1990; 23:1209–1218. [PubMed: 2292600]
- Roos EM, Herzog W, Block JA, Bennell KL. Muscle weakness, afferent sensory dysfunction and exercise in knee osteoarthritis. *Nature Reviews Rheumatology*. 2011; 7:57–63.
- Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society*. 1991; 9:113–119. [PubMed: 1984041]
- Schmitt LC, Rudolph KS. Muscle stabilization strategies in people with medial knee osteoarthritis: the effect of instability. *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society*. 2008; 26:1180–1185. [PubMed: 18404657]
- Segal NA, Glass NA, Felson DT, Hurley M, Yang M, Nevitt M, Lewis CE, Torner JC. Effect of quadriceps strength and proprioception on risk for knee osteoarthritis. *Medicine and Science in Sports and Exercise*. 2010a; 42:2081–2088. [PubMed: 20351594]
- Segal NA, Glass NA, Torner J, Yang M, Felson DT, Sharma L, Nevitt M, Lewis CE. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*. 2010b; 18:769–775.
- Sharma L. Proprioceptive impairment in knee osteoarthritis. *Rheumatic diseases clinics of North America*. 1999; 25:299–314. vi. [PubMed: 10356419]
- Sharma L, Chmiel JS, Almagor O, Felson D, Guermazi A, Roemer F, Lewis CE, Segal N, Torner J, Cooke TD, Hietpas J, Lynch J, Nevitt M. The role of varus and valgus alignment in the initial development of knee cartilage damage by MRI: the MOST study. *Annals of the rheumatic diseases*. 2013; 72:235–240. [PubMed: 22550314]
- Sharma L, Dunlop DD, Cahue S, Song J, Hayes KW. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. *Annals of Internal Medicine*. 2003; 138:613–619. [PubMed: 12693882]
- Sharma L, Lou C, Felson DT, Dunlop DD, Kirwan-Mellis G, Hayes KW, Weinrach D, Buchanan TS. Laxity in healthy and osteoarthritic knees. *Arthritis and Rheumatism*. 1999; 42:861–870. [PubMed: 10323441]
- Sharma L, Pai YC, Holtkamp K, Rymer WZ. Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? *Arthritis and Rheumatism*. 1997; 40:1518–1525. [PubMed: 9259434]
- Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA: The Journal of the American Medical Association*. 2001; 286:188–195. [PubMed: 11448282]
- Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, Wolinsky FD. Quadriceps weakness and osteoarthritis of the knee. *Annals of internal medicine*. 1997; 127:97–104. [PubMed: 9230035]

- Thorstensson CA, Henriksson M, von Porat A, Sjö Dahl C, Roos EM. The effect of eight weeks of exercise on knee adduction moment in early knee osteoarthritis--a pilot study. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*. 2007; 15:1163–1170.
- van der Esch M, Steultjens M, Harlaar J, Wolterbeek N, Knol D, Dekker J. Varus-valgus motion and functional ability in patients with knee osteoarthritis. *Annals of the Rheumatic Diseases*. 2008a; 67:471–477. [PubMed: 17604283]
- van der Esch M, Steultjens M, Harlaar J, Wolterbeek N, Knol DL, Dekker J. Knee varus-valgus motion during gait--a measure of joint stability in patients with osteoarthritis? *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*. 2008b; 16:522–525.
- Zhang LQ, Wang G. Dynamic and static control of the human knee joint in abduction-adduction. *Journal of Biomechanics*. 2001; 34:1107–1115. [PubMed: 11506781]
- Zhang LQ, Xu D, Wang G, Hendrix RW. Muscle strength in knee varus and valgus. *Medicine and Science in Sports and Exercise*. 2001; 33:1194–1199. [PubMed: 11445768]

Fig. 1.

Schematic representation of the experimental setup. Several stabilization methods were employed to minimize limb rotation during testing. First, the lower third of tibia, ankle joint, and the rear part of the foot were cast with fiberglass tape and placed within two aluminum half-rings with adjustable blunt screws to form a tight coupling between the cast and the rings. The cast-rings assembly was mounted onto one end of an aluminum beam located beneath the leg. Second, the femoral condyles of the tested knee were clamped from the medial and lateral sides and supported from below. Two threaded rods connecting the medial and lateral pieces of the knee clamp and wing nuts at both sides of the rods were tightened to press the femoral condyles from medial and lateral sides. Third, the left and right hips were blocked by a pair of hip clamps, which were moved medially through two screw mechanisms to press against the greater trochanters and prevented the hips from moving to the left or right side.

Fig. 2.

A typical torque-angle curve from 6 cycles of knee frontal plane angular motion. The horizontal axis represents knee varus-valgus angle, where (+) direction is valgus. The vertical axis represents knee varus-valgus torque, where (+) direction is valgus. The varus-valgus angular stiffness was calculated as the slope within 2 degrees of varus-valgus motion, 1 degree in each direction.

Fig. 3.

Proprioceptive acuity in varus and valgus directions. OA group had impaired proprioception acuity in the varus direction ($1.08 \pm 0.59^\circ$ vs. $0.69 \pm 0.49^\circ$, $p < 0.05$). There was no difference in valgus proprioceptive acuity between these two groups ($0.83 \pm 0.47^\circ$ vs. $0.70 \pm 0.49^\circ$, $p > 0.05$).

Fig. 4.

Change of knee varus-valgus torque-angle curves from without (in blue) to with (in red) active muscular contribution to v-v stiffness. Valgus direction is (+). Comparison was made between an osteoarthritic knee and an age-, gender-matched control knee in both 8 and 12 torque limit conditions. Both knees improved varus-valgus stiffness with active muscular contraction, but the OA knee had considerably smaller slope change.

Fig. 5.

Active neuromuscular contribution to v-v stiffness. The vertical axis is change of angular stiffness from without to with active muscular stabilization. At 12 Nm torque limit, OA participants increased their knee frontal plane stiffness by 4.67 ± 2.86 Nm/degree vs. by 8.26 ± 5.95 in controls, $p < 0.05$. At 8 Nm torque limit, OA participants had a change of 3.11 ± 2.26 Nm/degree vs. 7.26 ± 5.05 in the control group, $p < 0.05$.

Table 1

Summary of participants' characteristics. There were 28 participants consisting of 14 with symptomatic radiographic medial knee OA and 14 age- and gender-matched healthy controls. Among the persons with knee OA, 5 had no subjective complaints of instability, while the other 9 complained of instability.

	Control group (n=14)	Knee OA group (n=14)	Knee OA without instability (n=5)	Knee OA with instability (n=9)
Age (years), mean $\pm$ SD	58.4 $\pm$ 9.5	60.0 $\pm$ 8.7	60.8 $\pm$ 10.4	59.6 $\pm$ 8.2
Body mass index (kg/m ²)	23.9 $\pm$ 3.1	30.5 $\pm$ 8.0*	30.7 $\pm$ 10.2	30.4 $\pm$ 7.3
Body weight (kg)	70.5 $\pm$ 10.5	88.8 $\pm$ 25.5*	89.2 $\pm$ 27.6	88.6 $\pm$ 26.0
Gender	57% women	57% women	60% women	56% women
Kellgren/Lawrence (K/L) grade 2	NA	n = 8	n = 4	n = 4
K/L grade 3		n = 6	n = 1	n = 5
WOMAC pain score (0–20), <i>higher indicating worse status</i>	0.0 $\pm$ 0.0	5.6 $\pm$ 3.7*	4.4 $\pm$ 3.8	6.1 $\pm$ 3.9
WOMAC function score (0–68), <i>higher indicating worse status</i>	0.0 $\pm$ 0.0	21.5 $\pm$ 13.8*	18.4 $\pm$ 12.9	23.6 $\pm$ 14.6
Subjective report of instability (0–5), <i>lower indicating worse status</i>	5.0 $\pm$ 0.0	3.8 $\pm$ 1.2*	5.0 $\pm$ 0.0	3.1 $\pm$ 1.0 [#]
Varus-valgus passive range of motion at 8 Nm torque limit (°)	4.01 $\pm$ 1.52	4.13 $\pm$ 1.39	4.54 $\pm$ 1.75	3.8 $\pm$ 1.2
Varus-valgus passive range of motion at 12 Nm torque limit (°)	6.49 $\pm$ 1.92	6.83 $\pm$ 2.15	7.57 $\pm$ 2.44	6.2 $\pm$ 2.0

* Statistically significant difference between the OA and control groups.

[#] Statistically significant difference between OA without vs. with subjective complaints of instability.

Table 2

Correlation coefficients between WOMAC scores and varus-valgus neuromechanical parameters in persons with medial knee OA.

	WOMAC pain score (higher indicating worse status)	WOMAC function score (higher indicating worse status)
Varus proprioceptive acuity	-0.02	-0.11
Valgus proprioceptive acuity	0.12	0.08
Normalized varus strength	-0.46	-0.38
Normalized valgus strength	-0.64 [*]	-0.58 [*]
Absolute varus strength	-0.38	-0.34
Absolute valgus strength	-0.72 [*]	-0.67 [*]
Active muscular contribution to v-v stiffness at 8Nm torque limit	-0.50 [*]	-0.38
Active muscular contribution to v-v stiffness at 12Nm torque limit	-0.48 [*]	-0.27

* Statistical significance with $p < 0.05$.