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The relationship between reductions in knee loading and immediate pain response whilst wearing lateral wedged insoles in Knee Osteoarthritis.

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Abstract

Studies of lateral wedge insoles (LWIs) in medial knee osteoarthritis (OA) have shown reductions in the average external knee adduction moment (EKAM) but no lessening of knee pain. Some treated patients actually experience increases in the EKAM which could explain the overall absence of pain response. We examined whether, in patients with painful medial OA, reductions in the EKAM were associated with lessening of knee pain. Each patient underwent gait analysis whilst walking in a control shoe and two LWI's. We evaluated the relationship between change in EKAM and change in knee pain using Spearman Rank Correlation coefficients and tested whether dichotomising patients into biomechanical responders (decreased EKAM) and non-responders (increased EKAM) would identify those with reductions in knee pain. In 70 patients studied, the EKAM was reduced in both LWIs vs. control shoe (**-5.21% and -6.29% for typical and supported wedges, respectively**). The change in EKAM using LWIs was not significantly associated with the direction of knee pain change. Further, 54% were biomechanical responders, but these persons did not have more knee pain reduction than non-responders. Whilst LWIs reduce EKAM, there is no clearcut relationship between change in medial load when wearing LWIs and corresponding change in knee pain.

Keywords: Osteoarthritis, knee; pain, adduction moment, lateral wedge

1 **Introduction**

2 Knee osteoarthritis (OA) is a chronic and highly prevalent disease that affects approximately
3 13% of individuals aged 60 years and older (1). Knee OA is most often present in the medial
4 compartment of the joint with estimates of disease prevalence 5-10 times higher than the
5 lateral compartment in Western populations (2, 3). This disproportionate increase between
6 compartments has been attributed to the greater biomechanical loading occurring in the
7 medial compartment, with approximately 60% of load going through the medial side of the
8 knee during walking (4).

9 A frequently used surrogate measure of medial joint loading is the external knee adduction
10 moment (EKAM). During walking the ground reaction force passes medial to the knee in the
11 frontal plane, creating a moment that adducts the tibia relative to the femur. During healthy
12 walking, the peak force on the medial compartment is almost 2.5 times more than that on the
13 lateral compartment (5). In persons with medial knee OA, the EKAM has been shown to
14 correlate with disease severity (6), with progression of disease (7) and with reduction in
15 cartilage thickness (8). Kito et al. (9) and Maly (10) further demonstrated that the EKAM and
16 knee adduction angular impulse (11) were correlated with higher levels of pain in individuals
17 with medial knee OA and suggested that reduction of medial loading may result in pain relief.

18 Many strategies exist that can lower medial load in those with medial OA. One widely used
19 strategy is the use of lateral wedge insoles (12). Lateral wedge insoles are placed inside
20 shoes and have been demonstrated to decrease the external knee adduction moment (EKAM)
21 during gait (13, 14) and stair ascent and descent (15) in individuals with medial knee OA.
22 Despite their favourable effects on medial loading, recent randomised trials have failed to
23 find a reduction in knee pain with the use of lateral wedge insoles (16, 17, 18), when
24 compared to a neutral insole. To be specific, previous studies have shown that despite an
25 average reduction in medial load in all treated patients, knee pain on average was not reduced

1 using wedge insoles compared with neutral insoles. There are at least three explanations for
2 this null effect. First, the average decreases in medial loading (5-6%) could have been
3 inadequate to reduce pain. If so those with greater reductions in medial knee load would have
4 had pain reduction and those without reductions would not. We note that 20-30% of
5 individuals, when treated with lateral wedge insoles actually experience a paradoxical
6 increase in their EKAM (19); if pain reduction relates to medial load reduction, these persons
7 should have little, if any, decrease in knee pain. Another explanation for findings of trials is
8 that the important reduction in medial load is not the percent reduction in load but rather the
9 absolute decrease in load and the third is that knees being studied do not need only medial
10 load reduction (e.g. they may have concurrent patellofemoral disease). We tested the first
11 two of these hypotheses in this paper.

12
13 Understanding the failure of lateral wedge insoles to reduce knee pain offers an opportunity
14 to develop treatments that are effective either by producing consistent reductions in medial
15 load, larger average reductions in medial load, absolute decreases in medial load or other
16 approaches. Few if any studies have examined whether load reduction is actually related to
17 diminished knee pain, and this would be a valuable first step in this inquiry. We approached
18 this question by asking individuals with medial knee OA their knee pain status at a time when
19 we were assessing their EKAM. This paper is the first paper, to our knowledge, to firstly
20 determine whether lateral wedge insoles produce an immediate pain reduction during walking
21 and, secondly, if the magnitude of change in the EKAM has any relationship with this change
22 in pain when wearing lateral wedge insoles.

1 **Methods**

2 **Participants.** Participants with knee pain were recruited for a trial testing shoe inserts and
3 wedges from the following sources: orthopaedic clinics, physiotherapy clinics and
4 advertisements in local media. The eligibility criteria for participation in the study were aged
5 45 years and above, medial tibiofemoral OA with radiographs demonstrating Kellgren and
6 Lawrence grade 2 or 3 in the affected painful knee with medial greater than lateral joint space
7 narrowing, and at least mild pain during walking on a flat surface during the last week
8 assessed by the KOOS pain subscale (P5) (20). Radiographs were generally acquired as part
9 of the patient's routine care and were read by an experienced academically-based
10 musculoskeletal radiologist according to the OARSI atlas (21). Patients were excluded if they
11 presented with pain more localised to the patellofemoral joint on examination than medial
12 joint (wedge inserts are not appropriate for disease in this compartment and lowering the
13 EKAM may make them worse), had tricompartmental knee OA or grade 1 or grade 4
14 tibiofemoral OA on the Kellgren and Lawrence scale. Other exclusions included a history of
15 high tibial osteotomy or other realignment surgery, total knee replacement on the affected
16 side, or any foot and ankle problems, such as hallux valgus; plantar fasciitis; peripheral
17 neuropathy or any foot and ankle pain, that contraindicated the use of the load modifying
18 footwear interventions. In addition, participants were excluded if they had severe coexisting
19 medical morbidities or used orthoses prescribed by a podiatrist or orthotist. Eligible participants
20 were invited to attend the gait laboratory where informed consent was obtained.

21 **Interventions.** The analyses were conducted in the context of a single visit randomised trial
22 testing different wedges and shoes for their effect on the EKAM. Two of these interventions
23 were lateral wedges which have been shown in prior studies to reduce EKAM in patients with
24 medial knee OA and in the contralateral knee (22, 13) and acceptable to patients. We also
25 wanted to test two wedges that had somewhat different designs. Both lateral wedge insoles

consisted of a 5 degree lateral wedge which was posted just proximal to the fifth metatarsal head to ensure fitting in the toe-box of the shoe and were used on both the affected and contralateral limbs of all participants (i.e. they were applied bilaterally). The major difference between the lateral wedge insoles is that one has medial support (referred to hereafter as the ‘supported’ wedge (23) whereas the other has no medial support (the ‘typical’ wedge) (22) (Figure 1). During the trial, these lateral wedges were inserted into a flat-soled control shoe (Ecco Zen) with participants having a minimum of 5 minutes familiarisation period to the condition.

Protocol. All participants underwent gait analysis whilst wearing both types of lateral wedge insoles after a reference trial collected for each condition. The order of presentation of the different conditions was randomised prior to participants’ enrolment using computer-generated permutations (using <http://www.randomization.com/>). As they completed each treatment, participants were asked to compare the knee pain experienced while walking to pain when wearing their own shoes and were asked to score this pain on a 5-point Likert scale scored from much worse to much better than their own shoes. In terms of assessing knee pain, the more affected side was assessed. As pain response may be affected by the comfort of the insole, we also asked individuals to rank the comfort of the insole on a 10cm visual analog scale (VAS) where 0 was extremely uncomfortable and 10 was extremely comfortable, in comparison to the control shoe. A 16 camera Qualisys Oqus3 motion analysis system operating at 100 Hz and four AMTI BP400600 force plates operating at 200 Hz were used to measure kinematics and kinetics during the trials. Each participant completed a minimum of three successful trials at a self-selected walking speed. A trial was defined as successful when the whole of the foot of the affected limb made contact within the boundaries of the force platform. The CAST marker set technique (24) was employed whereby rigid clusters of four non-orthogonal markers were positioned over the lateral shank,

lateral thigh and sacrum to track the movements of the limbs. Retroreflective markers were glued securely to the control shoes with the foot modelled as a rigid segment. A reference trial was collected in which retroreflective markers were placed on bony landmarks to specify the location of these in relation to the clusters and to approximate joint centre. Ankle and knee joint centres were calculated as midpoints between the malleoli and femoral epicondyles respectively. The hip joint centre was calculated using the regression model of Bell et al. (25) based on the anterior and posterior superior iliac spine markers. Using an inverse dynamic approach Visual 3D (C-Motion, Rockville, Maryland) we calculated the EKAM and external knee flexion moment (KFM) during stance phase for all of the individual trials per condition to create a cumulative average. A custom Matlab (Matlab, USA) programme was used to extract the maximum EKAM during early stance (up to 50% of stance phase) and to calculate the knee adduction angular impulse (KAAI) (11), which is the area under the adduction moment curve during the entire stance phase of gait. As individuals with knee OA have an increased duration of stance, the knee adduction angular impulse (KAAI) was seen as an appropriate addition to the EKAM, as KAAI gives a measure of average loading over the stance phase and not at one particular point. Additionally, the maximum KFM was extracted during early stance. EKAMs and KFM's were normalised to participant's mass (Nm/kg) with the KAAI normalised to participant's mass and stance time (Nm/kg*s).

Data analysis. Changes in EKAM, KAAI, and KFM between treatment conditions were examined independently in the analysis, as we did not want to assume that they would show the same effect. For each participant, we calculated the changes in the variables of interest in terms of both absolute, and percentage change. We calculated these changes independently for each of the two wedge conditions.

As an example, for EKAM, we calculated the absolute change as the difference between each participant's EKAM when using a wedge and their EKAM in the control condition. Additionally, the percentage change was calculated as follows:

$$\frac{(EKAM \text{ when wearing a wedge} - EKAM \text{ in control condition})}{EKAM \text{ in control condition}} \times 100$$

This expresses change in EKAM as a percentage of the value in the control condition. Absolute and percentage changes in KAAI and KFM were calculated using the same methodology.

We classified participants as biomechanical responders if participants had a decreased EKAM wearing both lateral wedge conditions (compared to the control shoe); biomechanical non-responders were classified if their EKAM increased when wearing both lateral wedges compared to the control shoe. Absolute change in EKAM was assessed using normal distribution 95% CIs constructed around the mean EKAM change. Due to the distribution of percentage changes being skewed, nonparametric 95% confidence intervals were calculated (using bootstrapped, bias-corrected accelerated [BCa] confidence intervals) around the median percentage changes, to assess the significance of the change. Patient perceived change in pain was tested for statistical significance using a Wilcoxon signed-rank test. Spearman's rank correlation was used to assess if the perceived change in pain rating was related to the change in EKAM, or change in KFM, and additionally to describe the correlation between the pain ratings and the comfort scores. Finally, given that KFM and EKAM could be seen to confound each other, we ran a fixed-effects panel multiple linear regression model which tested for the change in EKAM between wedge types, whilst controlling for change in KFM. All statistical analysis was performed using Stata Version 11.2 (StataCorp, College Station, Texas, US) with the significance level set at $p < 0.05$ (where significance tests were used).

Results

We studied 70 participants (43 male and 27 female) with radiographically confirmed painful medial knee OA. Mean (SD) age was 60.3 years (9.6), mean height 1.69 (0.09) m, mean mass 87.3 (18.5) kg, and mean BMI 30.5 (4.9). Of the 42 participants with K-L data, 17 (40.5%) demonstrated Grade 2 disease on radiograph, with the remaining 25 (59.5%) demonstrating Grade 3 disease. Walking speed did not differ between treatment conditions.

Table 1 shows that both EKAM and KAAI were reduced when using a lateral wedge insole in comparison to the control shoe, in both of the lateral wedge insoles. Participants' biomechanical response to wearing both types of lateral wedge insole varied considerably with 54% (n=38) demonstrating a reduction in EKAM in both wedges. 20% (n=14) of participants demonstrated an increase in EKAM in both wedges. The remainder (25%, n=18) had inconsistent EKAM responses to the wedges, with an increase in EKAM using one wedge and a decrease using the other. Table 2 describes the magnitude of the changes in EKAM, KAAI, and KFM in the responder/non-responder groups.

Overall (N=70), pain ratings differed significantly (Figure 2) between wedges ($z = 3.00$, $p = 0.002$), with a significant reduction in pain only being observed when using the medial supported lateral wedge insole (Typical wedge $z = 0.51$; $p = 0.61$; Supported wedge $z = -3.67$; $p < 0.001$). Pain reduction did not differ between biomechanical responders (54% of participants) and biomechanical non-responders (20% of participants), for the typical wedge (N = 52, $z = -0.31$, $p = 0.76$), or the supported wedge (N = 52, $z = -0.62$, $p = 0.54$) (Figure 2). Those with a 'mixed response' to wedges were excluded from this analysis.

No relationship was seen between the perceived change in knee pain when wearing lateral wedges, and the absolute change in EKAM (Figure 3). For the typical wedge, absolute change in EKAM and perceived change in pain did not correlate ($r_s = -0.09$ 95% CI -0.32 to

0.15; $p = 0.45$), however an inverse relationship was found between pain and absolute change in EKAM in the supported wedge condition ($r_s = -0.25$; 95% CI -0.46 to -0.02; $p = 0.03$). Additionally, no relationship (also Figure 3) was seen between the perceived change in knee pain when wearing lateral wedges and the absolute change in KAAI, in either wedge (typical wedge $r_s = 0.00$; 95% CI: -0.23 to 0.24; $p = 0.98$; supported wedge $r_s = -0.11$; 95% CI -0.34 to 0.13; $p = 0.37$). Figure 4 shows similar trends when considering the percentage changes in EKAM/KAAI, rather than the absolute change.

The maximum KFM during early stance did not differ significantly between the control and the lateral wedge insoles (See table 1). Additionally, similar to the EKAM, there was no relationship with pain response in either the typical wedge ($r_s = 0.06$; 95% CI: -0.18 to 0.29; $p = 0.65$) or the supported wedge ($r_s = 0.02$; 95% CI -0.22 to 0.25; $p = 0.89$). Controlling for the maximum KFM, the EKAM was still reduced in both wedge conditions (mean absolute change in EKAM in the typical wedge, controlling for maximum KFM = -0.0234; 95% CI -0.0356 to -0.011; mean change in EKAM in the supported wedge, controlling for maximum KFM = -0.0205; 95% CI -0.033 to -0.008). No relationship was observed between the change in maximum KFM and change in EKAM, for either the typical ($r_s = -0.05$; 95% CI -0.28 to 0.18; $p = 0.66$) or the supported wedge ($r_s = -0.07$; 95% CI -0.30 to 0.17; $p = 0.56$).

Participants reported that, overall, they found both wedges to be more comfortable than their normal shoes (typical wedge mean comfort rating = +0.84cm; 95% CI +0.27cm to +1.42cm; supported wedge mean comfort rating = +1.35cm; 95% CI +0.84 to +1.86). The comfort ratings did not differ significantly between the two wedges. Comfort and pain ratings were strongly correlated (typical wedge $r_s = -0.56$; 95% CI -0.70 to -0.37; $p < 0.001$; supported wedge $r_s = -0.45$; 95% CI -0.62 to -0.24; $p < 0.001$).

Discussion

We confirmed other reports that lateral wedges placed inside the shoe reduce the average EKAM in persons with medial knee OA. As others have suggested, this reduction was not consistent across patients. Further, we found that the change in EKAM was unrelated to the amount of decrease in knee pain whether examined as a population or dichotomising into biomechanical responders or non-responders.

For only one of the lateral wedge insoles, the one with medial support was there a significant change in pain. This is in agreement with Skou et al. (26). The major difference between the study by Skou et al and our study is that we used an off-the-shelf lateral wedge ‘typical’ insole which increases the generalizability to the medial knee OA population. We suggested earlier that paradoxical increases in EKAM using the lateral wedges might account for the failure of pain to improve in groups of patients treated with the lateral wedge. Assuming the immediate pain response reflects the pain treatment response, our results contradict this explanation. We found no direct relation between the degree of EKAM change and lessening of knee pain, and some with paradoxical increases in EKAM experienced knee pain reduction. Further, even among those with consistent and major reductions in EKAM, there was no consistent reduction in knee pain. These findings suggest that larger or consistent reductions in EKAM still might not influence knee pain. In fact, in one trial of lateral wedges, the mean reduction in EKAM was 8% (27) and this trial, like the others, still showed no effect of the treatment on knee pain. In this paper, we carried out secondary analyses in which we dichotomised individuals into biomechanical responders and non-responders based on loading response to lateral wedge insoles compared to the control condition. The median EKAM reduction in the biomechanical responder group was much greater than reported reductions in EKAM in studies of lateral wedge insoles when whole populations have been examined (13, 14, 19). Other strategies that effectively lower medial knee load, such as

1 realigning braces, produce larger reductions in EKAM (28) and have been shown to lessen
2 knee pain (29). If we ask why realigning braces reduce knee pain whereas lateral wedge
3 insoles do not, it may be that even larger reductions of medial load than have been produced
4 by wedge insoles are needed. Perhaps, dynamic laxity and proprioceptive deficits are a
5 critical element to causing knee pain in those with painful medial knee OA, and braces but
6 not shoe insoles, limit that laxity and enhance proprioception. Also, many persons with
7 apparently isolated medial knee OA may have coexistent patellofemoral OA and a brace
8 effectively treats the disease in both tibio- and patellofemoral compartments.

9 Importantly, immediate pain using the wedge insole may not reflect the pain experience of
10 longer term use and, for longer term use, there may be a stronger relation of medial unloading
11 and pain reduction. However, Hinman et al (14) reported that immediate pain response to a
12 lateral wedge predicted later pain response. We suggest that short term responses may speak
13 more directly to biomechanical effects on pain. The long term knee pain response may be
14 affected by factors other than the reduction in EKAM. First some subjects report discomfort
15 with the lateral wedge insoles and may not use them consistently (47% of individuals in a
16 recent trial (17)). Additionally, it must be recognised that the individual's pain response may
17 have been confounded by the comfort of the insoles and a longer adaptation period as in
18 longer term trials would be needed. With the strong relationship between comfort and knee
19 pain future studies should assess comfort in trials of lateral wedge insoles. To gauge pain
20 response to a biomechanical intervention, adherence to the device is needed. Second, if
21 analgesic use can be reduced or walking pain diminished, increased activity may
22 paradoxically cause more knee pain, minimizing the effect of the lateral wedge on knee pain.
23 An individual may have a reduction in medial loading which translates to a reduction in pain
24 which, in turn, leads to increased levels of physical activity, whereby the individual would
25 walk to their pain threshold. Our study took advantage of a controlled environment in which

ad libitum activity did not confound pain results. Another concern about our study is that EKAM and KAAI may not reflect in vivo medial load. Walter et al. (30) suggested that a reduction in these variables does not necessarily mean a reduction in medial contact load if there is a corresponding increase in knee flexor moment. In this trial, no difference was seen in sagittal knee flexor moment using wedge vs. the control condition, and therefore one could assume that a reduction in medial load would be seen (31). Additionally, we tested whether the knee flexor moment was correlated to the EKAM and no correlation existed nor did it have any relationship to pain response.

In conclusion, lateral wedge insoles reduce the adduction moment across the knee in those with medial OA but they do not lessen knee pain. There was no relationship between the change in medial knee loading and the change in knee pain. Our data suggest that the failure of lateral wedges to reduce knee pain immediately in those with painful medial knee OA is probably not due to their failure to consistently reduce the adduction moment across the knee.

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Table and Figure Legends

Table 1: Change in EKAM and KAAI during the various lateral wedge insole conditions

Figure 1: The two lateral wedge insoles used in the study (Supported and Typical)

Figure 2: Distributions of Perceived pain reduction when using lateral wedge insoles, compared across the two study insoles

Figure 3: Correlation between perceived pain change, and absolute change in EKAM and KAAI, when using a lateral wedge.

Figure 4: Correlation between perceived pain change, and percentage change in EKAM and KAAI , when using a lateral wedge.

References

- ^{1.} Felson DT, Zhang Y. 1998. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. *Arthritis Rheum.* 41(8):1343-55.
- ^{2.} Ahlback S. 1968. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh): Suppl-72.*
- ^{3.} Felson DT, Nevitt MC, Zhang Y, Aliabadi P, Baumer B, Gale D, et al. 2002. High prevalence of lateral knee osteoarthritis in Beijing Chinese compared with Framingham Caucasian subjects. *Arthritis Rheum.* 46(5):1217-22.
- ^{4.} Prodromos CC, Andriacchi TP, Galante JO. 1985. A relationship between gait and clinical changes following high tibial osteotomy. *J Bone Joint Surg Am.* 67(8):1188-94.
- ^{5.} Schipplein OD, Andriacchi TP. 1991. Interaction between active and passive knee stabilizers during level walking. *J Orthop Res.* 9(1):113-9.
- ^{6.} Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD, Schnitzer TJ, Kirwan-Mellis G, Andriacchi TP. 1998. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis Rheum.* 41(7):1233-1240.

7. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. 2002. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann Rheum Dis*. 61(7):617-22.
8. Erhart J, Favre J, Andriacchi T. 2011. Walking loading at the knee predicts MRI-derived cartilage thickness changes in medial compartment knee osteoarthritis, Osteoarthritis Research Society International (OARSI), 2011, San Diego, CA September 15-18.
9. Kito N, Skinkoda K, Yamasaki T, Kanemura N, Anan M, Okanishi N, Ozawa J, Moriyama H. 2010. Contribution of knee adduction moment impulse to pain and disability in Japanese women with medial knee osteoarthritis. *Clin Biomech*. 25: 914-919.
10. Maly MR. 2008. Abnormal and cumulative loading in knee osteoarthritis. *Curr Opin Rheumatol*. 20(5): 547-52.
11. Thorp LE, Sumner DR, Block JA, Moision KC, Shott S, Wimmer MA. 2006. Knee joint loading differs in individuals with mild compared with moderate medial knee osteoarthritis. *Arthritis Rheum*. 54(12):3842-9.
12. Sasaki T, Yasuda K. 1987. Clinical evaluation of the treatment of osteoarthritic knees using a newly designed wedged insole. *Clin Orthop Relat Res*. 221):181-7.
13. Jones RK, Chapman GJ, Findlow AH, Forsythe L, Parkes MJ, Sultan J, Felson DT. 2013. A new approach to prevention of knee osteoarthritis: reducing medial load in the contralateral knee. *J Rheumatol*. 40(3):309-15
14. Hinman RS, Payne C, Metcalf BR, Wrigley TV, Bennell KL. 2008. Lateral wedges in knee osteoarthritis: what are their immediate clinical and biomechanical effects and can these predict a three month clinical outcome? *Arthritis Rheum*. 59(3):408-15.
15. Alshawabka A, Liu AM, Jones RK. 2013. The use of a lateral wedge insole to reduce knee loading when ascending and descending stairs in medial knee osteoarthritis patients. *Clin Biomech*. In Review.

16. Baker K, Goggins J, Xie H, Szumowski K, LaValley M, Hunter DJ, et al. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis Rheum* 2007 Apr;56(4):1198-203.
17. Bennell KL, Bowles KA, Payne C, Cicuttini F, Williamson E, Forbes A, et al. 2011. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ*. 342:d2912.
18. Parkes MJ, Maricar N, Lunt M, LaValley MP, Jones RK, Segal NA, Takahashi-Narita K, Felson DT. 2013. Lateral wedge insoles as a conservative treatment for pain in patients with medial knee osteoarthritis: a meta-analysis. *JAMA*. 310(7):722-30.
19. Kakihana W, Akai M, Nakazawa K, Naito K, Torii S. 2007. Inconsistent knee varus moment reduction caused by a lateral wedge in knee osteoarthritis. *Am J Phys Med Rehabil*. 86(6):446-54.
20. Roos EM, Roos PH, Lohmander LS Ekdahl C, Beynnon BD. 1998. Knee injury and Osteoarthritis Outcome Score (KOOS): Development of a self-administered outcome measure. *Journal of Orthopaedic and Sports Physical Therapy*. 78(2):88-96.
21. Altman RD, Gold GE. 2007. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cartilage*. 15 Supple A: A1-56.
22. Kerrigan DC, Lelas JL, Goggins J, Merriman GJ, Kaplan RJ, Felson DT. 2002. Effectiveness of a lateral-wedge insole on knee varus torque in patients with knee osteoarthritis. *Arch Phys Med Rehabil*. 83(7):889-93.
23. Jones RK, Zhang M, Laxton P, Findlow AH, Liu A. 2013. The biomechanical effects of a new design of lateral wedge insole on the knee and ankle during walking. *Hum Mov Sci*. 32(4):596-604.

- ²⁴. Cappozzo A, Catani F, Croce UD, Leardini A. 1995. Position and orientation in space of bones during movement: anatomical frame definition and determination. Clin Biomech. 10(4):171-8.
- ²⁵. Bell AL, Brand RA, Pedersen DR. 1989. Prediction of hip joint centre location from external landmarks. Hum Mov Sci. 8(1):3-16.
- ²⁶. Skou ST, Hojgaard L, Simonsen OH. 2013. Customized foot insoles have a positive effect on pain, function, and quality of life in patients with medial knee osteoarthritis. J Am Podiatr Med Assoc. 103(1):50-5.
- ²⁷. Butler RJ, Marchesi S, Royer T, Davis IS. 2007. The effect of a subject-specific amount of lateral wedge on knee mechanics in patients with medial knee osteoarthritis. J Orthop Res. 25(9):1121-7.
- ²⁸. Schmalz T, Knopf E, Drewitz H, Blumentritt S. 2010. Analysis of biomechanical effectiveness of valgus-inducing knee brace for osteoarthritis of knee. J Rehabil Res Dev. 47(5):419-29.
- ²⁹. Kirkley A, Wedster-Bogaert S, Litchfield R, Amendola A, MacDonald S, McCalden R, Fowler P. 1999. The effect of bracing on varus gonarthrosis. J Bone Joint Surg Am. 81(4):539-48.
- ³⁰. Walter JP, D'Lima DD, Colwell CW Jr, Fregly BJ. 2010. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. J Orthop Res. 28(10):1348-54.
- ³¹. Zhao D, Banks SA, Mitchell KH, D'Lima DD, Colwell CW Jr, Fregly BJ. 2007. Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. J Orthop Res. 25(6):789-97.