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# Effect of lateral wedged insoles on the knee internal contact forces in medial knee osteoarthritis

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ABSTRACT

*Background:* Lateral wedge insoles (LWIs) are non-surgical interventions used in medial knee osteoarthritis (KOA) aiming at restoring correct joint biomechanics. However, the mechanical efficacy of LWIs, based on modulation of the external knee adduction moment, is partially proved and high variability in response to these devices was observed.

*Research question:* The principal aim of the study was to employ subject-specific musculoskeletal models to investigate the immediate effect of LWIs on the medial compressive force (MCF) in a population with medial KOA and varus alignment.

*Methods:* Fifteen adults (8 healthy controls age 56 ± 3.4, BMI 25.2 ± 2.2, hip-knee-ankle angle −1.3 ± 2.3; and 7 KOA participants age 62 ± 6.6, BMI 31.7 ± 3.9, hip-knee-ankle angle 6.3 ± 2) were recruited. Subject-specific LWIs were designed in CAD based on shape capture of the foot and manufactured via 3D printing. The required degree of heel post was added to the orthotic shell to create insoles with 0°, 5° and 10° of lateral wedge. Gait data were collected for each condition and a musculoskeletal model implemented in the Anybody Modeling System estimated the CFs normalised per bodyweight. The effect of the LWIs with respect to the baseline on the peak and the impulse of the MCF were tested with a Wilcoxon non-parametric test for paired samples.

*Results:* For the KOA group, LWIs did not reduce significantly the impulse and the peak of the MCF. No dose-response trend according to the degree of wedging was observed. A high inter-subject variability was found: the impulse of the MCF varied between −12%, +10%, the peak between −5%, +7%. Moreover, LWIs had no consistent effect on shifting the load from the medial to the lateral compartment.

*Significance:* Subject-specific response to LWIs in a cohort of medial KOA patients was observed. Further studies are necessary to maximise the mechanical effect of LWIs on restoring normal knee joint mechanics.

## 1. Introduction

Knee osteoarthritis (KOA) is a chronic degenerative joint disease and a leading cause of disability worldwide [1,2]. Laterally Wedged Insoles (LWI) are a non-surgical treatment that aims at re-establishing correct knee biomechanics in patients with medial KOA. The putative mechanism behind the effectiveness of LWIs is creating an external moment aiming at unloading the medial compartment [3]. However, there is limited evidence regarding the biomechanical effectiveness of this intervention [4]. Small reduction of first and second peaks and of impulse of the knee adduction moment (-0.19, 95% CI -0.23 -0.15; -0.25, 95% CI -0.32 -0.19; -0.14, 95% CI -0.32 -0.19, respectively) have been summarised in a meta-analysis [4]. The large variation in orthotic design (e.g. degree of lateral posting, material properties and presence of arch support) and disease severity contribute to the variability of treatment response [5,6].

In addition, in order to explain the large vairiability that characterize the KOA population, several clinical phenotypes have been hypothesized [7,8]. Targeting specific subgroup of patients (phenotypes) characterised by mechanical overload associated with structural changes such as varus alignment and medial KOA, may result in an increased treatment effectivness which can be missed when treatments are tested on heterogenous participants [7,9,10].

The Knee Adduction Moment (KAM) has been largely used as a surrogate of the medial compartment compressive force (CF) to measure treatment effectiveness [11]. However, the correlation between KAM and internal joint CF is extremely variable ranging between $R^2 = 0.09$ to $R^2 = 0.97$ [12]. In a recent work, Saxby et al. suggested

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that the KAM is a poor predictor of the internal CF and dependent on the task executed [13]. In another study, Walter and colleagues showed that reductions in the KAM do not always result in a reduction in the medial CF (MCF) and that knee flexion moment (KFM) plays a key role as a concurrent reduction of the KAM and an increase of KFM neutralise the correlation between KAM and MCF [14].

In the recent years, musculoskeletal models (MS) have been largely improved allowing relatively accurate estimations of the knee internal CFs [15,16]. However, the use of CF to investigate biomechanical effectivness of LWIs is scarce. Therefore, there is a need for new studies using this estimate of the internal joint load. The implementation of knee CFs in OA research could lead to a more advised understanding of the response to LWIs and therefore, it could lead to innovative insights on its effectiveness.

Therefore, the purposes of this study were: (1) to investigate the immediate effect of LWI on the impulse and on the peak of the CFs estimated via subject-specific musculoskeletal models in participants characterised by medial compartment KOA and varus alignment and in healthy volunteers; (2) to assess the effect of LWI on shifting the CF from the medial to the lateral compartment.

## 2. Methodology

### 2.1. Population

Adults with a clinical diagnosis of medial compartment KOA and varus alignment volunteered in the study. Participants were included if they were aged > 50 and had a KOA diagnosis confirmed by a physician following the American College of Rheumatology Criteria [17]. Potential participants were excluded if they had a current or past history of disease involving the neurological system, knee surgery or arthroplasty, or received intra-articular injection (e.g. corticosteroid) in the past 3 months. Healthy volunteers aged over 50 and with no history of knee pain or musculoskeletal pathologies were recruited within the staff members of Glasgow Caledonian University as a control population. A total of fifteen participants (7 KOA and 8 controls) volunteered for the study. Ethical approval was granted by the National Health System (NHS) of greater Glasgow and Clyde ethical committee (www.hra.nhs.uk 15-WS-0287 183203). Participants provided informed written consent and the study was undertaken in accordance to the Declaration of Helsinki.

### 2.2. LWI manufacturing

In this study, an additive manufacturing process was adapted to produce 3D printed subject-specific LWI. The full manufacturing process is described elsewhere [18–20] Briefly, participants plantar foot shape was 3D surface scanned (SenseTM 3D Scanner, 3D System, Inc.) with the knee and ankle flexed at 90° in a non-weightbearing pose. A stereolithography (stl) file was created from the scan and manipulated with computer-aided design (CAD) software (Rhinoceros 3D V5, Robert McNeel & Associate, Barcelona, Spain) to create the orthotic shell shape. The final model was then altered to fit the rearfoot with three lateral wedging (0°, 5° and 10° of lateral wedge) in order to obtain the three pairs of insoles.

A fused deposition modelling (FDM) approach was used to manufacture the insoles with a desktop 3D printing system (Airwolf 3D HDx, Airwolf 3D printers, California, U.S.A.). A soft thermoplastic polylactic acid material (soft-PLA) was chosen for its material properties (www.orbi-tech.de; density: 1.35 g/cm3, tensile strength: 16 MPa, strain at yield: 290%, Young's modulus: 380 MPa, shore hardness: 92 A) and capability to produce semi-rigid devices. Previous successful studies have been conducted adopting the same material and a similar workflow [19,20].

### 2.3. Gait analysis

All data were collected at the Human Performance Laboratory at Glasgow Caledonian University. Fourty-two passive reflective markers (Supplementary file 1) were used to collect full lower limbs three-dimensional kinematic data using a 14 infrared camera system sampling at 120 Hz (Qualisys AB, Gothenburg, Sweden). Ground reaction forces were collected using two force platforms sampling at 2000 Hz (Kistler, Winterthur, Switzerland) embedded in the middle of the walking path. A static acquisition trial was collected to calibrate the gait model prior to the gait tasks. The knee alignment was measured manually by an operator (AD) with the participant standing in a neutral position. The knee alignment was considered as the angle between the line passing between the centre of the knee and the centre of the ankle and the line passing between the centre of the knee and the hip joint centre [21].

Each participant walked on a 10-meter pathway at self-selected normal walking speed for four different consecutive tasks as follow: standardised shoes only (SO), standardised shoes and LWI with a lateral wedge of 0°, 5° and 10°. Participants were blinded from allocation order. A convenient acclimatisation time was given to each participant to familiarise with the different LWI conditions. Five trials were recorded for each condition. To standardise the experimental setting of the study and to neutralise the effect related to different footwear, all participants wore the same shoes during the data collection. These shoes, used in previous studies [20], are designed with additional zips sewn into the medial and lateral aspects and with holes in correspondence of the foot landmarks to allow markers to be positioned directly on the skin. For the KOA population the symptomatic leg only or the most affected in case of bilateral KOA was included in the analysis. The dominant leg, defined as the leg used to kick a ball, was selected for the control population.

### 2.4. Musculoskeletal model

To estimate the knee internal CFs, a musculoskeletal model, adapted from previously validated models described in Lund et al and Marra et al., have been implemented using the Anybody Modeling System v.6.0.5 (AnyBody, Aalborg, Denmark) [15,16]. These studies reported a moderate to high correlation coefficient ($R^2 = 0.73$ and $R^2 = 0.85$, respectively) when internal forces were compared to a dataset acquired with an instrumented knee prosthesis [15,16]. Specifically, the Anatomically scaled Model of Lund et al. [16] was applied but with the muscle recruitment criterion updated to account for sub-divided muscles in the cadaver dataset applied as explained in Marra et al. [15]. The standing reference acquisition was used to generate a stick figure based on the anatomical landmarks. An inverse kinematics approach was used to estimate the joint kinematics during the dynamic trials [22]. A generic musculoskeletal model based on the Twente Lower Extremity (TLEM) dataset was morphed on the basis of the stick figure's morphology [23] as described in Lund et al. [16]. Finally, an inverse dynamic utilising a polynomial muscle recruitment criterion of third order was used to estimate muscles and joint reaction forces. The knee joint was modelled as spherical for the inverse kinematic approach to allow rotations. Two external moments, to account for varus/valgus and internal/external rotation, were added for the inverse dynamic analysis to account for resistance of ligaments. The tibial coordinate system, as in Grood and Suntay [24], was used to export the knee joint reaction forces. Finally, an equilibrium problem in the frontal between the total knee CF and the adduction/abduction moment was solved to estimate the medial and lateral component of the CFs; the moment arms used in this equilibrium problem has been described by Seedhom et al. [25]. More details are presented in the Supplementary material 2.

### 2.5. Data analysis

The peak value and the impulse over the entire stance phase of the

CF were selected as the biomechanical variables of interest. A dedicated Matlab (The MathWorks, Inc., Natick, MA) script was implemented to extract and to process the data. Joint CFs were corrected per body weight. Joint moments were corrected per body weight and height. The stance phase was resampled at increments of 1%. The peak value and the impulse were calculated as the average of three trials for each gait condition. Medial to lateral ratio, defined as the ratio between the medial and the lateral CFs, was used to quantitatively assess the different distribution of load between the two-analysed groups. A value of one indicates an equal distribution of load while a number above one means that the load on the medial compartment is higher than the load on the lateral compartment.

Statistical analysis was performed with SPSS Statistics V24 (Norusis/SPSS, Chicago, IL) and statistical significance was set at $p < 0.05$. The relative differences of the CFs peak and impulse of the three LWI conditions with respect to the SO condition were used to estimate the immediate effect of the LWI during the stance phase and was tested using a Wilcoxon signed rank test for related sample. To test the differences between the two groups, a Wilcoxon non-parametric test for independent samples was used.

Walking speed was calculated as the average speed in the walking direction of the four markers attached to the pelvis.

## 3. Results

Demographic characteristics of the participants are summarised in Table 1. Normality of the samples with respect to the reported demographic variable was checked, and independent t-tests were used to assess the difference in patients demographic. The KOA group showed a significantly higher BMI, age and varus alignment when compared with the controls group ($p = 0.001$, $p = 0.43$, $p < 0.001$). Data on compartmental Kellgren-Lawrence (K-L) grades were available for KOA participants. The mean K-L grade was 3.86 (SD 0.38), 2 (0.58) and 2.43 (1.13) for the medial, lateral and patellofemoral compartment respectively.

As shown in Fig. 1, for the SO condition which was assumed as baseline reference, KOA patients showed a higher MCF and a lower lateral CF (LCF) when compared with controls. Moreover, the MCF remains higher during the entire single leg phase of the stance cycle.

On a group level, for the SO condition, the results indicated that the impulse of the MCF was significantly higher for the KOA group with respect to the control group (KOA: Mdn = 1.15, IQR = 0.26; Controls: Mdn = 0.86, IQR = 0.15; $p = 0.006$). For the peak, no difference was found (KOA: Mdn = 2.71, IQR = 0.44; Controls: Mdn = 2.32, IQR = 0.44; $p = 0.72$). Despite not significant, the impulse of the LCF for the KOA group was lower when compared with the control group (KOA: Mdn = 0.43, IQR = 0.12; Controls: Mdn = 0.57, IQR = 0.17; $p = 0.19$). The values for the peak of the LCF were comparable (KOA: Mdn = 1.34, IQR = 0.29; Controls: Mdn = 1.77, IQR = 0.46; $p = 0.54$).

On a group level, the effect of the three LWI on the peak and the impulse of the MCF was not statistically significant for each condition in the KOA population. In details, for the 0°, 4 participants reduced the impulse and 5 experienced a reduction in the peak value ($p = 1$, $p = 0.24$ respectively). Four participants had a reduction on both impulse and peak for the 5° ($p = 0.74$, $p = 1$ respectively). Three participants benefited from the 10° in terms of impulse and 5 in terms of peak ($p = 0.61$, $p = 0.49$ respectively). In addition, a high variability was found in the relative difference between the three LWI condition with respect to the SO condition (Tables 2 and 3).

The effect of the LWI on both impulse and peak of LCF is highly variable similarly to the MCF. The variation was non-statistically significant for each of the three conditions. No overall dose-response trend according to the degree of lateral wedging was observed. A high variability and no dose-response was observed in terms of peak and impulse of the KAM and peak of the KFM as reported in the Supplementary material 3. The medial to lateral ratio for the impulse of the CF (Table 4) was significantly higher in the KOA group when compared with the control group (KOA: Median [Mdn] = 2.44, Interquartile Range [IQR] = 0.86; Controls: Mdn = 1.61, IQR = 0.41; $p = 0.002$). None of the three conditions was effective in shifting the CF from the medial to the lateral compartment.

Walking speed did not differ significantly between controls and KOA participants for any of the conditions ($p = 0.152$, $p = 0.152$, $p = 0.336$ and $p = 0.232$ for the SO, LWI 0, LWI5 and LWI 10 condition respectively). The walking speed was not altered significantly in the KOA group and its variation was lower than ± 10% with respect to the SO task (Table 5).

**Table 1**
Demographic data.

| | Controls (n = 8) | KOA (n = 7) |
|---|---|---|
| Age (years) | 56 (3.4) | 62 (6.6)* |
| Gender (M:F) | 3:5 | 5:2 |
| BMI (Kg/m$^2$) | 25.22 (2.18) | 31.7 (3.89)* |
| Knee angle[¥] (°) | −1.3 (2.25) | 6.3 (1.97)* |
| Walking speed at baseline (m/s) | 1.32 (0.21) | 1.14 (0.19) |

*statistically significant ($p < 0.05$) [¥]varus angles are presented as positive value, valgus angles are presented as negative.

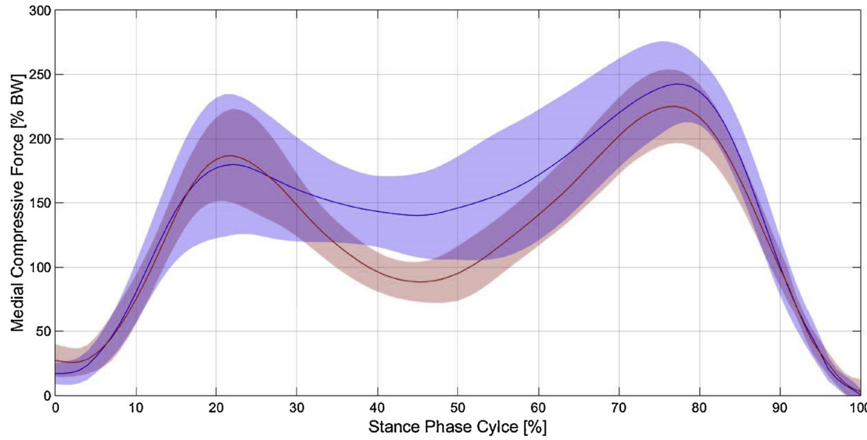
## 4. Discussion

In this study, the effect of 3D printed subject-specific LWI insoles on the MCF in a population characterised by varus alignment and medial compartment KOA was investigated and compared with a control group of healthy volunteers. Despite the KOA group showing a higher load on the medial compartment at baseline (SO), the use of LWI with different level of posting did not result in a consistent response in terms of MCF. Participants experienced a reduction of impulse and peak value of the MCF while others experienced an increase.

In the past decades, the use of foot orthotics has been largely advocated as a beneficial treatment for the management of KOA by reducing the medial compartment joint's load [26]. Despite few studies highlighted the mechanical efficacy of LWI on reducing KAM [27,28], there is still no consensus on the efficacy of LWI in reducing the biomechanical risk factor of KOA [4,5]. In line with these reviews, our results suggest that the response to these devices varies largely between subjects. Our finding on the immediate effect of LWI indicate that the efficacy of LWIs is highly subject-specific. Recent studies attempted to identify variables that may influence the response to biomechanical interventions [10,27,29]. However, more work is required to identify treatment responders and non-responders and to optimise the LWIs prescription for improved outcomes.

To the best of our knowledge, this study is the first using internal knee CFs to analyse the mechanical effect of LWI in a KOA population. The values of the CFs (both medial and lateral) of our sample are comparable with previous studies [10,30].

Our results showed a statistically significant difference between KOA and controls for the impulse only. Accordingly with the literature on the KAM, this result suggests that research evaluating the biomechanical effect of non-surgical interventions should take into consideration the impulse rather than focusing solely on the reduction of the peaks of the force [30]. Indeed, the impulse of the CF is a more sensitive measure than the peak and especially when analysing individual responses [30]. In our analysis, the change in peak values did not overcome the reported MDC of 8.7% for both the KOA and the control groups with the only exception of one participant from the control group who had a reduction of -10% for the 10° LWI. The relevance of considering the impulse has been also highlighted in a large scale long-term study by Bennell et al. where the authors concluded that the impulse of the KAM, but not the peak, is a good predictor of



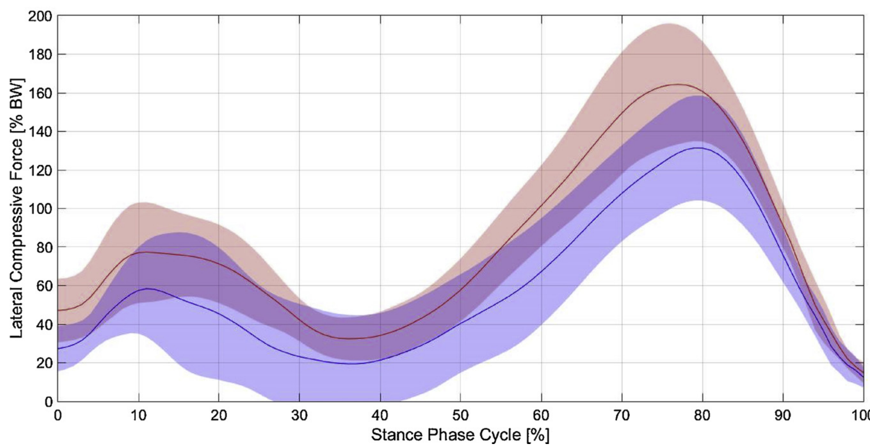




**Fig. 1.** Medial (top) and lateral (bottom) compressive force for the KOA (blue) and control (red) population at the baseline. Shaded area ± 1 std (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

**Table 2**
Individual relative difference [%] of the peak of the CF with respect to the SO condition for controls and KOA participants during the stairs ascending. Group results are presented as [median (25$^{th}$/75$^{th}$ interquartile)]. Negative values indicate a reduction with respect to the SO condition.

| | LWI 0° | | | LWI 5° | | | LWI 10° | | |
|---|---|---|---|---|---|---|---|---|---|
| | Medial | Lateral | Total | Medial | Lateral | Total | Medial | Lateral | Total |
| CNTRL_1 | 1.41 | −5.14 | −1.46 | −1.88 | −9.69 | −5.18 | −1.28 | −7.2 | −3.82 |
| CNTRL_2 | −0.11 | −3.29 | −0.51 | 8.72 | −0.17 | 4.35 | 5.24 | −4.32 | 0.53 |
| CNTRL_3 | 1.13 | −2.01 | −2.17 | 0.82 | −0.17 | −1.08 | −1.55 | −6.52 | −3.52 |
| CNTRL_4 | −0.04 | −4.41 | −1.92 | −0.36 | −4.98 | −2.27 | 3.65 | 1.52 | 2.7 |
| CNTRL_5 | −5.03 | 0.2 | −3.07 | −6.78 | −3.36 | −5.74 | −9.45 | −8.93 | −9.5 |
| CNTRL_6 | −3.08 | −6.01 | −4.27 | −6.24 | −6.89 | −6.37 | 1.46 | −5.63 | −1.71 |
| CNTRL_7 | −6.07 | −8.3 | −7.14 | −2.8 | −5.17 | −3.96 | −7.34 | −9.63 | −8.59 |
| CNTRL_8 | 5.44 | −6.02 | −3.24 | 2.98 | −5.07 | −4.42 | 2.66 | −9.34 | −7.63 |
| Controls Mdn (IQR) | −0.07 (1.34/-4.54) | −4.77 (-2.33/-6.02) | −2.62 (-1.57/-4.01) | −1.12 (2.44/-5.38) | −5.02 (-0.97/-6.46) | −4.19 (-1.38/-5.60) | 0.09 (3.41/-5.89) | −6.86 (-4.65/-9.23) | −3.67 (-0.03/-8.35) |
| KOA_1 | 1.11 | −6.41 | 0.14 | −0.3 | −7.23 | −2.91 | −4.45 | −5.34 | −2.21 |
| KOA_2 | 3.63 | 8.69 | 5.29 | 5.24 | 9.79 | 6.99 | 7.57 | 10.32 | 8.85 |
| KOA_3 | −2.94 | −1.37 | −2.74 | 1.57 | 2.11 | 1.59 | −0.01 | −2.19 | −1.31 |
| KOA_4 | −1.31 | 3.24 | 0.39 | 0.87 | −10.8 | −3.05 | 1.6 | −5.67 | −0.79 |
| KOA_5 | −3.22 | −5.75 | −4.12 | −5.38 | −5.32 | −5.43 | −4.12 | −3.25 | −3.79 |
| KOA_6 | −2.48 | −5.04 | −3.25 | −1.75 | −9.03 | −3.54 | −0.69 | 4.06 | 0.33 |
| KOA_7 | −4.81 | −2.52 | −3.96 | −0.27 | −2.41 | −0.99 | −3.1 | −5.52 | −3.96 |
| KOA Mdn (IQR) | −2.48 (1.11/-3.22) | −2.52 (3.24/-5.75) | −2.74 (0.39/-3.96) | −0.27 (1.57/-1.75) | −5.32 (2.11/-9.03) | −2.91 (1.59/-3.54) | −0.69 (1.60/-4.12) | −3.25 (4.06/-5.52) | −1.31 (0.33/-3.79) |
| Total Mdn (IQR) | −1.31 (1.13/-3.22) | −4.41 (-1.37/-6.01) | −2.74 (-0.51/-3.40) | −0.30 (1.57/-2.80) | −5.07 (-0.17/-7.23) | −3.05 (-0.99/-5.18) | −0.70 (2.66/-4.12) | −5.52 (-2.20/-7.20) | −2.21 (0.33/-3.96) |

**Table 3**
Individual relative difference [%] of the impulse of the CF with respect to the SO condition for controls and KOA participants during the stairs ascending. Group results are presented as [median (25th/75th interquartile)]. Negative values indicate a reduction with respect to the SO condition.

| | LWI 0° | | | LWI 5° | | | LWI 10° | | |
|---|---|---|---|---|---|---|---|---|---|
| | Medial | Lateral | Total | Medial | Lateral | Total | Medial | Lateral | Total |
| CNTRL_1 | 8.59 | −1.81 | 4.63 | 6.53 | −1.58 | 3.44 | 1.57 | −4.58 | −0.78 |
| CNTRL_2 | 0.2 | −1.25 | −0.26 | −0.6 | −0.12 | −0.45 | 0.03 | 5.67 | 1.81 |
| CNTRL_3 | 0.93 | 0.54 | 0.79 | 0.55 | 2.84 | 1.36 | 2.41 | 1.57 | 2.11 |
| CNTRL_4 | 3.42 | −5.54 | −0.03 | 2.11 | −3.76 | −0.15 | 1.1 | −3.56 | −0.69 |
| CNTRL_5 | −0.35 | 0.52 | −0.02 | −3.55 | 2.43 | −1.28 | −1.4 | 1.23 | −0.4 |
| CNTRL_6 | 0.56 | −3.25 | −1.15 | −0.99 | −2.25 | −1.56 | 3.22 | 3.53 | 3.36 |
| CNTRL_7 | −0.59 | −8.89 | −4.16 | −4.55 | −7.77 | −5.94 | −7.67 | −10.58 | −8.92 |
| CNTRL_8 | −5.58 | −5.91 | −5.72 | −7 | −4.31 | −5.9 | −7.37 | −3.55 | −5.8 |
| Controls Mdn (IQR) | 0.38 (2.80/-0.53) | −2.53 (0.08/-5.82) | −0.14 (0.59/-3.41) | −0.80 (1.72/-4.30) | −1.9 (1.79/-4.17) | −0.86 (0.99/-4.81) | 0.57 (2.20/-5.88) | −1.16 (3.04/-4.33) | −0.55 (2.03/-4.54) |
| KOA_1 | −4.6 | −6.67 | −5.36 | −4.68 | −7.85 | −5.83 | −6.17 | −4.53 | −5.57 |
| KOA_2 | 4.8 | 9.46 | 6.01 | 4.16 | 4.69 | 4.3 | 4.42 | 6.29 | 4.9 |
| KOA_3 | −1.8 | −6.9 | −3.26 | −1.52 | −2 | −1.66 | 2.56 | −4.84 | 0.44 |
| KOA_4 | 3.35 | 3.91 | 3.51 | 0.6 | −1.81 | −0.1 | 2.6 | −0.57 | 1.68 |
| KOA_5 | −11.65 | −12.85 | −12.02 | −11.12 | −8.33 | −10.25 | −5.2 | 3.3 | −2.55 |
| KOA_6 | 10.22 | −17.23 | 5.67 | 5.36 | −8.51 | 3.06 | 5.93 | −2.01 | 4.61 |
| KOA_7 | −2.19 | −1.11 | −1.83 | −0.86 | −1.24 | −0.98 | −0.2 | −2.83 | −1.08 |
| KOA Mdn (IQR) | −1.80 (4.80/-4.60) | −6.67 (3.91/-12.85) | −1.83 (5.67/-5.36) | −0.86 (4.16/-4.68) | −1.20 (-1.24/-8.33) | −0.98 (3.06/-5.83) | 2.56 (4.42/-5.20) | −2.01 (3.30/-4.53) | 0.44 (4.61/-2.55) |
| Total Mdn (IQR) | 0.2 (3.42/-2.2) | −3.25 (0.52/-6.90) | −0.26 (3.51/-4.16) | 0.86(2.11/-4.55) | −1.20 (-0.12/-7.77) | −0.98 (1.36/-5.83) | 1.1(2.6/-5.2) | −2.01 (3.30/-4.53) | −0.40 (2.11/-2.55) |

**Table 4**
Medial to lateral ratio for KOA.

| | SO | LWI 0° | LWI 5° | LWI 10° |
|---|---|---|---|---|
| KOA_1 | 1.75 | 1.79 | 1.81 | 1.72 |
| KOA_2 | 2.85 | 2.73 | 2.84 | 2.8 |
| KOA_3 | 2.49 | 2.63 | 2.5 | 2.69 |
| KOA_4 | 2.44 | 2.43 | 2.5 | 2.52 |
| KOA_5 | 2.21 | 2.24 | 2.14 | 2.03 |
| KOA_6 | 5.03 | 6.7 | 5.79 | 5.44 |
| KOA_7 | 1.99 | 1.97 | 2 | 2.05 |

**Table 5**
Walking speed [m/s].

| | Shod | LWI 0° | LWI 5° | LWI 10° |
|---|---|---|---|---|
| CNTRL_1 | 1.66 | 1.50 | 1.54 | 1.58 |
| CNTRL_2 | 1.03 | 1.12 | 1.16 | 1.16 |
| CNTRL_3 | 1.33 | 1.37 | 1.35 | 1.33 |
| CNTRL_4 | 1.18 | 1.24 | 1.20 | 1.28 |
| CNTRL_5 | 1.44 | 1.41 | 1.37 | 1.41 |
| CNTRL_6 | 1.23 | 1.15 | 1.12 | 1.14 |
| CNTRL_7 | 1.15 | 1.09 | 1.13 | 1.16 |
| CNTRL_8 | 1.55 | 1.55 | 1.52 | 1.51 |
| Controls mean (SD) | 1.32 (0.21) | 1.30 (0.18) | 1.30 (0.17) | 1.32 (0.17) |
| KOA_1 | 1.32 | 1.38 | 1.40 | 1.38 |
| KOA_2 | 1.26 | 1.28 | 1.31 | 1.32 |
| KOA_3 | 0.99 | 0.97 | 1.01 | 0.95 |
| KOA_4 | 1.32 | 1.29 | 1.36 | 1.35 |
| KOA_5 | 0.82 | 0.90 | 0.87 | 0.85 |
| KOA_6 | 1.14 | 1.12 | 1.22 | 1.19 |
| KOA_7 | 1.17 | 1.12 | 1.12 | 1.13 |
| KOA mean (SD) | 1.15 (0.19) | 1.15 (0.18) | 1.18 (0.19) | 1.17 (0.2) |

cartilage degeneration which has been associated with KOA progression [26].

Despite this, KAM has been largely considered a good surrogate for the joint load but its correlation with the MCF is only partially proved [13,14,31]. Therefore, the estimated CFs could be a further variable for analyses on the mechanical effect of LWIs.

The analysis on the medial to lateral ratio confirmed our findings on the overall inefficacy of LWI of changing the compartmental load distribution in our population. In a previous study, LWIs were successful in moving the load-bearing line laterally, however, this result was generally assumed and not evidenced limiting the accuracy of the conclusion drawn. [26].

Walking speed is a parameter that has been considered responsible for differences in the knee load [32]. In our study, in accordance with the finding of Kluge et al., the use of LWI did not vary the walking speed significantly [33].

This study has several key limitations. First, the complexity and length of the protocol required for such investigation led to a small sample size potentially leading to inconclusive or non-significant results. However, our results for both controls and KOAs were comparable with other studies from the literature. Additionally, aim of the study was to apply subject-specific models to emphasise the individual response to LWIs. A second limitation is the potential heterogeneity of our KOA population which was not stratified as suggested in previous studies. The small sample size did not allow to compare across disease severity. A larger sample with stratification by degree of varus alignment and disease severity is warranted to provide further insights. Third, because of the cross-sectional nature of the study, it was not possible to draw conclusion regarding the long-term effect of LWI. Long-term intervention studies are therefore recommended. Last but not least, our CF were estimated using a musculoskeletal model. Although the model was morphed to the geometry of the subjects, as represented in the standing reference trial, the MRI or CT were not used to personalize the model. An idealized knee model was also applied; a spherical joint was applied during the kinematic analysis to allow varus/valus and internal/external rotation, but two additional reaction moments were included in the inverse dynamic analysis to account for the passive structures of the knee. Additionally, the muscle recruitment criterion did not account for the neural alternations observed in OA patients [34].

## 5. Conclusion

In the present study, we investigated the immediate effect of different LWI on the MCF in a population characterised by medial KOA and varus malalignment. Our results showed an overall inconsistency with high variability across participants with reduction and increase of both the impulse and the peak of the MCF. Moreover, no overall dose-response trend, according to the degree of lateral wedging, was observed. The high variability observed suggests that the optimising LWI treatment to each participant remains challenging. Further work is required to understand more fully the mechanical efficacy of LWIs for personalised non-surgical management of KOA.

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## Competing interest statement

There are no competing interests to declare.

## Declarations of interest

None.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gaitpost.2018.12.030.

## References

[1] A.D. Woolf, B. Pfleger, Burden of major musculoskeletal conditions, Bull. World Health Organ. 81 (9) (2003) 646–656.
[2] J. Martel-pelletier, et al., Osteoarthritis, Nat. Rev. Dis. Prim. 2 (2016).
[3] K.B. Shelburne, M.R. Torry, J.R. Steadman, M.G. Pandy, Effects of foot orthoses and valgus bracing on the knee adduction moment and medial joint load during gait, Clin. Biomech (Bristol, Avon) 23 (2008) 814–821.
[4] J.B. Arnold, D.X. Wong, R.K. Jones, C.L. Hill, D. Thewlis, Lateral wedge insoles for reducing biomechanical risk factors for medial knee osteoarthritis progression: A systematic review and meta-analysis, Arthritis Care Res. (Hoboken) 68 (2016) 936–951.
[5] F. Xing, et al., A systematic review and meta-analysis into the effect of lateral wedge arch support insoles for reducing knee joint load in patients with medial knee osteoarthritis, Medicine (Baltimore). 96 (24) (2017) e7168.
[6] S. Shimada, et al., Effects of disease severity on response to lateral wedged shoe insole for medial compartment knee osteoarthritis, Arch. Phys. Med. Rehabil. 87 (November) (2006) 1436–1441.
[7] A. Dell'Isola, R. Allan, S.L. Smith, S.S.P. Marreiros, M. Steultjens, Identification of clinical phenotypes in knee osteoarthritis: a systematic review of the literature, BMC Musculoskelet. Disord. 17 (1) (2016) 425.
[8] L.A. Deveza, L. Melo, T.P. Yamato, K. Mills, V. Ravi, D.J. Hunter, Knee osteoarthritis phenotypes and their relevance for outcomes: a systematic review, Osteoarthr. Cartil. (2017).
[9] J.B. Arnold, D.X. Wong, R.K. Jones, C.L. Hill, D. Thewlis, Lateral wedge insoles for reducing biomechanical risk factors for medial knee osteoarthritis progression: A systematic review and meta-analysis, Arthritis Care Res. (Hoboken) 68 (2016) 936–951.
[10] A. Dell'Isola, S.L. Smith, M.S. Andersen, M. Steultjens, Knee internal contact force in a varus malaligned phenotype in knee osteoarthritis (KOA), Osteoarthr. Cartil. 25 (12) (2017) 2007–2013.
[11] O. Shinya, et al., Knee adduction moment and medial knee contact force during gait in older people, Gait Posture 40 (3) (2014) 341–345.
[12] I. Kutzner, A. Trepczynski, M.O. Heller, G. Bergmann, Knee adduction moment and medial contact force–facts about their correlation during gait, PLoS One 8 (2013) e81036.
[13] D.J. Saxby, et al., Tibiofemoral contact forces during walking, running and sidestepping, Gait Posture 49 (2016) 78–85.
[14] J.P. Walter, D.D. D'Lima, C.W. Colwell Jr, B.J. Fregly, Decreased knee adduction moment does not guarantee decreased medial contact force during gait, J. Orthop. Res. 28 (2010) 1348–1354.
[15] Ma. Marra, et al., A Subject-Specific Musculoskeletal Modeling Framework to Predict In Vivo Mechanics of Total Knee Arthroplasty, J. Biomech. Eng. 137 (2) (2015).
[16] M.E. Lund, M.S. Andersen, M. de Zee, J. Rasmussen, Scaling of musculoskeletal models from static and dynamic trials, Int. Biomech. 2 (1) (2015) 1–11.
[17] R.D. Altman, et al., The American College of Rheumatology criteria for the classification and reporting of ostoearthritis of the knee, Arthritis Rheum. 29 (1986) 1039–1049.
[18] R. Allan, J. Woodburn, S. Telfer, M. Abbott, M.P.M. Steultjens, Knee joint kinetics in response to multiple three-dimensional printed, customised foot orthoses for the treatment of medial compartment knee osteoarthritis, Proc. Inst. Mech. Eng. Part: H-J. Eng. Med. 231 (6) (2017) 487–498.
[19] S. Telfer, K.S. Gibson, K. Hennessy, M.P. Steultjens, J. Woodburn, Computer-aided design of customized foot orthoses: reproducibility and effect of method used to obtain foot shape, Arch. Phys. Med. Rehabil. 93 (5) (2012) 863–870.
[20] S. Telfer, M. Abbott, M. Steultjens, D. Rafferty, J. Woodburn, Dose-response effects of customised foot orthoses on lower limb muscle activity and plantar pressures in pronated foot type, Gait Posture 38 (3) (2013) 443–449.
[21] V.B. Kraus, T.P. Vail, T. Worrell, G. Mcdaniel, A comparative assessment of alignment angle of the knee by radiographic and physical examination methods, Arthritis Rheum. 52 (6) (2005) 1730–1735.
[22] M.S. Andersen, M. Damsgaard, J. Rasmussen, Kinematic analysis of over-determinate biomechanical systems, Comput. Methods Biomech. Biomed. Engin. 12 (4) (2009) 371–384.
[23] M.D. Klein Horsman, H.F.J.M. Koopman, F.C.T. van der Helm, L.P. Prosé, H.E.J. Veeger, Morphological muscle and joint parameters for musculoskeletal modelling of the lower extremity, Clin. Biomech. 22 (2) (2007) 239–247.
[24] E.S. Grood, W.J. Suntay, A joint coordinate system for the clinical description of Three-dimensional motions: application to the knee, J. Biomech. Eng. 105 (1983) 136–144.
[25] B.B. Seedhom, E.B. Longton, V. Wright, D. Dowson, Dimensions of the knee. Radiographic and autopsy study of sizes required by a knee prosthesis, Ann. Rheum. Dis. 31 (1) (1972) 54–58.
[26] B. Yilmaz, S. Kesikburun, O. Koroglu, E. Yasar, A.S. Goktepe, K. Yazicioglu, Effects of two different degrees of lateral-wedge insoles on unilateral lower extremity load-bearing line in patients with medial knee osteoarthritis, Acta Orthop. Traumatol. Turc. 50 (4) (2016) 405–408.
[27] G.J. Chapman, M.J. Parkes, L. Forsythe, D.T. Felson, R.K. Jones, Ankle motion influences the external knee adduction moment and may predict who will respond to lateral wedge insoles?: an ancillary analysis from the SILK trial, Osteoarthr. Cartil. 23 (2015) 1316–1322.
[28] R.S. Hinman, K.A. Bowles, B.B. Metcalf, T.V. Wrigley, K.L. Bennell, Lateral wedge insoles for medial knee osteoarthritis: effects on lower limb frontal plane biomechanics, Clin. Biomech. (Bristol, Avon) 27 (1) (2012) 27–33.
[29] K.L. Paterson, et al., Moderators and mediators of effects of unloading shoes on knee pain in people with knee osteoarthritis: an exploratory analysis of the SHARK randomised controlled trial, Osteoarthr. Cartil. 26 (2) (2017) 227–235.
[30] J. Barrios, J. Willson, Minimum detectable change in medial tibiofemoral contact force parameters: derivation and application to a load-altering intervention, J. Appl. Biomech. 33 (2) (2017) 171–175.
[31] R.E. Richards, M.S. Andersen, J. Harlaar, J.C. van den Noort, Relationship between knee joint contact forces and external knee joint moments in patients with medial knee osteoarthritis: effects of gait modifications, Osteoarthr. Cartil. (2018).
[32] J.A. Zeni Jr, J.S. Higginson, Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: a result of altered walking speed? [corrected] [published erratum appears in CLIN BIOMECH 2009 Jul;24(6):532], Clin. Biomech. 24 (2009) 372–378.
[33] F. Kluge, S. Krinner, M. Lochmann, B.M. Eskofier, Speed dependent effects of laterally wedged insoles on gait biomechanics in healthy subjects, Gait Posture 55 (April) (2017) 145–149.
[34] D.J. Rutherford, C.L. Hubley-Kozey, W.D. Stanish, M.J. Dunbar, Neuromuscular alterations exist with knee osteoarthritis presence and severity despite walking velocity similarities, Clin. Biomech. 26 (4) (2011) 377–383.