Knee joint kinetics in response to multiple three-dimensional printed, customised foot orthoses for the treatment of medial compartment knee osteoarthritis

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Introduction

Osteoarthritis (OA) is one of the most prevalent musculoskeletal joint conditions throughout the world. In the UK alone, it is estimated that more than 4.7 million people over the age of 45 years have sought treatment from their general practitioner for knee osteoarthritis (1). As a weight-bearing joint the knee is highly susceptible to OA, with the medial compartment of the knee joint more commonly affected. An increased incidence of medial compartment knee OA (mKOA) has been attributed to the combination of greater varus alignment (2) and the higher percentage of overall joint load being transmitted across the medial compartment compared to the lateral compartment (approximately 70:30) (3).

Direct measurement of knee joint load is complex, with most in vivo contact loading studies restricted to case studies, conducted using instrumented prostheses following knee replacement surgery (4–8). For non-invasive studies, the knee adduction moment (KAM) is routinely adopted as a surrogate measure whereby it is used to infer the dynamic load placed on the compartments of the knee (3,9,10). This external moment is mainly determined by the ground reaction force vector and its lever arm to the centre of the knee joint. Using this measure, increased KAMs reflect greater medial compartment loading.

Foot orthoses (FOs) incorporating lateral wedges are routinely issued for individuals with mKOA. These are intended to assist in the control and management of the disease by redistributing the total knee joint load across the joint during weight bearing tasks, alleviating load on the affected medial compartment. They function by causing an increased valgus moment at the ankle which causes a lateral shift of the centre of pressure at the foot. This lateral shift causes the lever arm length of the ground reaction force vector relative to the knee joint origin to reduce, resulting in the theoretical reduction in the KAM.

The use of lateral wedged FOs has been shown to reduce the peak KAM by approximately 4-12 % in KOA cohorts (11,12). However, there is growing evidence that the biomechanical response to orthotic intervention is heterogeneous and can, in some individuals, in fact elevate the KAM. Indeed it has been

estimated that 13–33% of people with mKOA demonstrate a negative response to lateral wedged insoles, despite beneficial effects reported at group level (12–16).

The majority of RCTs that have applied FO interventions for mKOA have generally focused on the application of a single intervention device and compared it to a control condition, which varied between studies(14,15,17,18). It should however be considered that the requirements for a beneficial biomechanical response are likely to be more complex than a straightforward one-size-fits-all intervention. It may be that different design characteristics will be effective in some individuals and not others, especially when the heterogeneity of the OA population is taken into consideration.

Advances in 3D printing technologies have resulted in the expansion of these techniques into the orthotic environment (19–22) with numerous companies currently offering 3D printed FOs including Peacocks Medical Group© and SOLS Systems©. Studies which have adopted the combination of 3D surface scanning, computer-aided design and computer-aided manufacturing (CAD/CAM) have produced custom FOs of equivalent quality to traditional methods with improved reproducibility and design standardisation (23). The application of these methods serves as a useful alternative to standard methods as it allows the creation of multiple personalised FOs facilitating small scale orthotic production for research. The ability to optimise orthotic design is specifically relevant in the mKOA population given the high variability between responses previously reported. The aim of this study therefore was to evaluate the immediate biomechanical effect, at both group level and individual level when two key design features are altered in personalised FOs: orthotic length and degree of lateral wedging.

Materials and methods

Study design

This cross-sectional observational study was conducted in a human performance laboratory at Glasgow Caledonian University from November of 2013 to February 2015. Participants completed all orthotic conditions on the same day.

Participants

Approval was obtained from the Institutional Research Ethics Committee at Glasgow Caledonian University. The procedures followed were in accordance with the ethical standards of the aforementioned research committee and with the Helsinki Declaration of 1975, revised in 2000. 20 participants were enrolled in the study, 10 in the mKOA group and 10 in the control group. All participants provided informed, written consent upon enrolment.

A convenient sample of mKOA participants was recruited via email to staff members of departments within the university and their associated friends and family as well as a MSK rehabilitation research email address which targets the community. Inclusion criteria for the mKOA group were ≥50 years of age and physician-confirmed unilateral or bilateral mKOA. Inclusion criteria for the control group were: ≥50 years; no history of unilateral/bilateral KOA; and have no chronic/stable knee pain in the past 3 months. Exclusion criteria for both groups were: BMI ≥ 36 kg/m^2; history of lower limb, hip or spinal surgery within the past 6 months; any other joint pathology which causes knee pain; received corticosteroid or other injections to or around the knee in the past 6 months; current or past (within 4 week) use of oral corticosteroids; any medical condition that may affect walking; current use of wedge insole/custom-made orthotics; and an aggregate foot posture index score (FPI) < -9 or 9 > (24). This was assessed by a UK Health and Care Professions Council registered podiatrist (MA).

FO design and manufacturing

To design the FOs first weight-bearing 3D surface scans of both feet were taken with the foot in a relaxed standing position using an Easy-Foot-Scan 3D scanner (Baltic Orthoservice UAB, Kaunas, Lithuania. The application of 3D scanners to measure characteristics of foot shape have previously demonstrated reduced measurement variability compared to a traditional neutral suspension casting technique, irrespective of clinical experience (25) . The generated 3-D model was converted into stl format and then exported into OrthoModel Pro 2013 computer aided design (CAD) Software (Delcam Plc, Birmingham, UK) to undergo the FO design steps. One CAD user with low level prior experience to CAD software and of biomechanical background (RA) was responsible for all stages of the design and manufacturing process. The user however had received formal training in its use prior to study commencement from a CAD expert (ST), who was in regular user of the OrthoModel software, designing 2 or 3 pairs of FOs per week over the previous 2/3 years.

In the software, all FOs were designed using the "standard orthosis from scan" mode. This mode used the identification of specific anthropometric measurements of the foot model obtained from the foot scans to design the FO. These measurements included; forefoot width (mm), rearfoot width (mm), orthotic length (mm) and medial arch height (mm). Forefoot width was determined by the locations of the centre of the 1st and 5th metatarsal heads, rearfoot width based on the medial and lateral aspect of the heel at its widest point and the medial longitudinal arch height was determined by selecting the most proximal point of the arch relative to the plantar surface.

The implementation of these dimensions provided the basis for the model which could then be altered as such based on key design characteristics of degree of wedging and FO length. In the software, degree of wedging was set at extrinsic, lateral (valgus) resulting in alterations to the wedging of the surface in contact with the foot. Position of wedging could be applied to the rearfoot, forefoot or a combination of

both to give the required design. FO length was adjusted in the software with finer adjustments being made based on individual foot shape. All FOs had a set default thickness of 3.5mm with a solid heel component section. This was selected in accordance with routinely applied and generally accepted insole thickness measurements.

In total eight variations to the neutral design FO were produced and manufactured for the most symptomatic side in the mKOA group, as measured by a VAS scale for pain; or randomly chosen for the healthy group. Variations under investigation included both a ¾ length and a full length FO with the following degrees of wedging; 0° 'neutral', 5° rearfoot lateral wedging, 10° rearfoot lateral wedging and combination of 5° forefoot and 10° rearfoot lateral wedging. The non-test leg received a 0° 'neutral' posted FO of equivalent length during each test condition to remove any chance of altered gait patterns from differences in FO length. The FO design process took approximately 1.5-2 hours for all eight variations per participant. The fabrication time for the eight variations (10 insoles per participant; one set of neutral full length, one set of three-quarter full length and the six variations of the assigned test leg) was approximately 70-120 hours, depending on participants shoe size.

Fused Deposition Modelling (FDM)

All FOs were manufactured via a Fused Deposition Modelling (FDM) approach using a desktop 3D printing system (3d Touch; Bits from Bytes, Clevedon, UK). FDM is a method of additive manufacturing (AM) first patented and trademarked by Stratasys Inc. which involves building a 3D object layer-by-layer. Also commonly referred to as plastic jet printing (PJP) and fused filament fabrication (FFF), recently the method has become open sourced resulting in a more consumer driven application and increased number of marketed products.

The 3D printing system used was a commercially available 3D printer and although its application is not specific to FO manufacturing, it had previously been used in similar published studies by the research group, allowing manufacturing to be performed in-house (23,26). FOs were manufactured in a soft polylactide (PLA) thermoplastic (www.orbi-tech.de: density- > 1.35 g/cm3, tensile strength- ~ 16 MPa, strain at yield- ~ 290%, e-modulus- ~ 380 MPa, shore hardness- 92A). This semi-rigid thermoplastic polymer was selected as the material of choice based on previously published studies by the research group (23,26).

Axon 2 software (Bits from Bytes, Clevedon, UK) was used to prepare the FOs for printing. The software functions by mathematically slicing the FO into layers and creating the toolpaths for each layer which the 3D printer follows. Build settings used to print the FOs involved; a layer height of 0.25mm, fill density of 52% and a printing temperature of 195°C with the inclusion of a printed raft and support material.

The FDM process of the 3D printing system functions by feeding the thermoplastic material at a set feed rate (16mm/s) through a temperature controlled nozzle head. Once in contact with the heating element inside the nozzle, the solid thermoplastic filament is heated towards its melting temperature, altering its structure into a molten, semi-liquid state. The nozzle travels in the X and Y directions and extrudes the molten thermoplastic material at a set flow rate (20 RPM) according to the toolpath for the layer, creating a cross sectional 2D layer on the build platform. Once complete, the build platform is lowered by a set height (0.25mm) and the next layer is printed based on the next cross sectional layer. During this process, the two layers are bonded together through thermal fusion and then solidify together as the layers cool down. This process is repeated for each of the toolpath layers until the FO is complete. Once printed, support structures and rafts were manually removed and each FO was hand finished using sandpaper to ensure a sufficient surface quality suitable for wear during biomechanical evaluation.

***INSERT FIG* 1**

132 ***Measurements***

133 Participants were tested in their own footwear to replicate their normal daily wear and comfort levels. A
134 four segment unilateral model was created for the test leg using a modified version of the Cleveland
135 Clinic marker set. This included markers placed bilaterally on the anterior and posterior superior iliac
136 spine and greater trochanters. Additionally, for the test leg, markers were placed on the lateral femoral
137 condyle, lateral malleolus, and on the shoe itself, over the posterior calcaneus, 1st metatarsal head and the
138 5th metatarsal head. To track the thigh and shank segments, shell-mounted clusters of four tracking
139 markers were placed on the lateral aspects of these segments. During the initial static standing trial
140 additional markers were placed on the medial femoral condyle and medial malleolus to determine relative
141 positioning of joint centres and were removed for dynamic trials.

142 For trials, a 14 camera motion capture system (Qualisys AB, Gothenburg, Sweden) operating at a
143 frequency of 120 Hz was used to capture the retroreflective markers. Simultaneously, a force plate
144 (9286B; Kistler Winterthur, Switzerland) embedded into the walkway was used to measure the ground
145 reaction forces at 2400 Hz. These data capturing methods are standard practice in research investigating
146 the biomechanics of human movement.

147 After an initial FO fitting session and accommodation period of approximately one week, participants
148 returned to the laboratory for the main evaluation. A static trial was recorded with the participant standing
149 in the shod condition, and then anatomical markers were removed prior to collection of dynamic trials.
150 Walking trials were measured for the shod condition followed by eight FO conditions. Testing order was
151 randomised for each participant to avoid order effects and participants were blinded to the condition
152 during testing.

153 Participants were given time to acclimatise to each FO until a consistent gait pattern was observed. They
154 were then asked to walk along the walkway until a total of 7 successful force plate strikes with the test leg

were recorded. Walking speed was standardised to within ±10% of their self-selected walking speed during the shod test using photoelectric timing gates (Brower timing system, Draper, Utah, USA). A rest period was included between FO conditions to reduce potential effects of fatigue.

Knee joint moments were calculated from inverse dynamic analysis using Visual 3-D software (C-motion Inc., Germantown, MD). Variables associated with knee joint loading were identified and analysis was limited to these. These included; peak knee adduction moment during the 1st half of stance phase (1KAM); peak knee adduction moment during the 2nd half of stance phase (2KAM); knee flexion moment during the 1st half of stance phase (1KFM); and the knee adduction moment impulse (KAMI) i.e. integral of the total KAM. Kinetic variables were anatomically referenced to the proximal segment. All variables of interest were normalised by dividing by body weight multiplied by height and then expressed as a percentage (For 1KAM, 2KAM and 1KFM this was Nm/ % body weight x height; for KAMI this was Nms^{-1}/ % body weight x height. This normalisation approach allowed for the effects of height and bodyweight to be considered-factors which significantly influence joint kinetics (27). The mean of the final 5 successful walking trials from each test condition with complete marker tracking was used in the analysis. Marker trajectories and GRF data were low passed filtered with a 4th order Butterworth filter at 6 Hz and 25 Hz, respectively.

Statistical Analysis

Statistical analyses were performed with SPSS (Norusis/SPSS, Chicago, IL) using α level of 0.05. Data were checked for normality, through Shapiro-Wilks tests, prior to analysis. All kinetic variables used in the analysis indicated normally distributed results. For analysis, all variables were defined relative to the shod condition, considered the baseline for the study and evaluated using a 3-factor, repeated-measures ANOVA to determine the main effect for group, length, wedging type and any interaction effects.

Results

Demographic characteristics of study cohorts are presented in table 1. The mKOA group was significantly older and had a higher BMI than the healthy control group.

INSERT TABLE 1

Mean 1KAM, 2KAM, 1KFM and KAM Impulse values for each condition and group are presented in table 2.

INSERT TABLE 2

ANOVA results on all test variables are presented in table 3. Variable definitions include main effects of: orthotic length (three-quarter length/full length); group, (mKOA/control group); and wedging (0° 'neutral', 5° rearfoot wedging; 10° rearfoot wedging and a combination of 5° forefoot 10° rearfoot wedging). Interaction effects between these variables are also provided.

INSERT TABLE 3

1KAM

Significant main effects were found for orthotic length in 1KAM ($p= 0.038$). At the group level both FO lengths provided mean overall reductions in 1KAM compared to shod. This corresponded to a mean ± SD percentage reduction in peak knee adduction moment in the 1st half of stance of 1.1% ± 12.3 for the three-quarter length FOs and 2.8% ± 12.4 for the full lengths FOs.

Wedging condition was also found to be statistically significant for 1KAM ($p<0.001$). With the exception of the neutrally posted FOs (2% ± 11.3 increase) 1KAM was reduced for all wedging conditions. This

197 corresponded to a mean ± SD percentage reduction in 1KAM of 2.3% ± 9.2, 4% ± 8.3 and 3.5% ± 8.7 for
198 the 5° rearfoot; 10° rearfoot and combined 5° forefoot/ 10° rearfoot wedging conditions respectively.

199 No significant interaction effects were found between the length of orthotic or level of wedging.
200 Furthermore no significant difference existed between the mKOA and healthy group

201 ***2KAM***

202 Significant main effects were found for orthotic length in 2KAM ($p= 0.018$). At the group level both FO
203 lengths provided a mean overall increase in 2KAM compared to the shod condition. This increase
204 corresponded to a mean ± SD percentage increase in 2KAM of 6.5 % ± 16.9 for the three-quarter length
205 FOs and 4.1% ± 19.1 for full length FOs.

206 An interaction effect was also found between FO length and group ($p= 0.028$). For the mKOA group
207 these differences corresponded to mean ± SD percentage changes of 2.9% ± 16.9 and 2.7% ± 19.1 for the
208 three-quarter length and full length FOs respectively. The healthy group showed greater increases in
209 2KAM corresponding to mean ± SD percentage changes of 10.2% ± 16.9 and 5.5% ± 19.1 for the three-
210 quarter length and full length FOs respectively.

211 Significant main effects were found for wedging for 2KAM ($p< 0.0001$). Irrespective of the orthotic
212 length, FOs had a somewhat negative effect on 2KAM, corresponding to mean ± SD percentage
213 increases in peak 2KAM of 9.5% ± 12.9, 5.8% ± 12.5 and 6.1% ± 15.6 for the neutral, 5° rearfoot; 10°
214 rearfoot wedging conditions respectively. No significant differences were found between OA and the
215 healthy groups. Furthermore, significant differences existed between the combined 5° forefoot and 10°
216 rearfoot FO, considered the most biomechanically aggressive FO and all other wedging conditions. For
217 this condition when compared to other wedging conditions there was a reduction of 9.6%, 5.9% and 6.6%

218 when compared to the neutral, 5° rearfoot; 10° rearfoot wedging conditions respectively. However
219 compared to the shod condition it only produced a minimal 2KAM reduction of 0.1% (13.4).

220 Other significant interaction effects were found between orthotic length and wedging condition for
221 2KAM (p=0.002). For the three-quarter length FOs alterations to wedging corresponded to mean ± SD
222 percentage changes of 9.1% ± 10.1, 6.6 % ± 9.5, 5.9% ± 10.6 and 4.5 % ± 9.6 for the neutral, 5° rearfoot,
223 10° rearfoot and combined 5° forefoot/ 10° rearfoot wedging conditions respectively. Full length FOs
224 demonstrated a similar dose response with the exception of combined 5° forefoot/ 10° rearfoot wedging
225 condition, corresponding to mean ± SD percentage changes of 9.9% ± 9.2, 5% ± 10.3, 6.3% ± 12.6 and -
226 4.8% ± 12.3 for the neutral, 5° rearfoot, 10° rearfoot and combined 5° forefoot/ 10° rearfoot wedging
227 conditions respectively. No significant differences were found between mKOA and the healthy group in
228 relation to 2KAM.

229 ***1KFM***

230 For 1KFM, no significant main effects or any interaction effects were found. Although no statistically
231 significant findings were evident (p=0.109) between the groups the mKOA group demonstrated a mean
232 (±SD) 1KFM increase of 11.4% ± 26.6 compared to the healthy group, 4.3% ± 26.6.

233 ***KAM Impulse***

234 Significant main effects were found for orthotic length in KAM Impulse (p=0.022). Irrespective of the
235 group, the FO length provided different responses in terms of the KAM Impulse compared to the shod
236 condition. This corresponded to a mean ± SD KAMI percentage change of 2.1% ± 16.8 for three-quarter
237 length FOs and 0.4% ± 16.1 for full length FOs.

Significant interaction effects were found between orthotic length and group (p=0.036). For the mKOA group this corresponded to a mean ± SD KAMI percentage change of -0.5% ± 16.3 and -0.7% ± 16.1 for the ¾ length and full length FOs respectively compared to the healthy group who demonstrated an increase in KAMI of 4.6% ± 16.3 and 1.5% ± 16.1 for the ¾ length and full length FOs respectively.

Significant main effects were found for wedging for KAM Impulse (p<0.0001). Irrespective of group the effect of wedging condition corresponded to mean ± SD percentage changes of 5.9% ± , 0.9% ± 11, 0.9% ± 9 and -2.6% ± 10 for the neutral, 5° rearfoot; 10° rearfoot and combined 5° forefoot/ 10° rearfoot posted conditions respectively.

Although borderline the interaction between wedging and orthotic length was not significant (p=0.055). For the ¾ length FOs alterations to wedging corresponded to mean ± SD percentage changes of 3 % ±13, 1% ± 9 and 0% ± 9 for the 5° rearfoot; 10° rearfoot and combined 5° forefoot/ 10° rearfoot wedging conditions respectively. The full length FO demonstrated a slightly different pattern corresponding to mean ± SD percentage changes of 2% ± 9, 10% ± 2 and -6% ± 10 for the 5° rearfoot; 10° rearfoot and combined 5° forefoot/ 10° rearfoot wedging conditions respectively.

Individual Response

The variable magnitude of response to orthotic changes across the biomechanical outcome measures is evident when the high standard deviations and confidence intervals are considered. The variability in biomechanical response was present in both groups.

INSERT FIGURE 2

INSERT FIGURE 3

INSERT FIGURE 4

259 ***INSERT FIGURE 5***

260 Negative and positive responses to FOs were assessed in relation whether the percentage
261 increase/decrease was greater/less than the reported standard error of the mean (SEM) for each variable.
262 For 1KAM, 22/80 (27.5%) of the assessments, incorporating the various wedging conditions for the
263 mKOA group, resulted in a negative biomechanical response over the SEM. The healthy group had an
264 incidence of 22/80 (27.5%) negative responses. A positive 1KAM response above SEM was found in
265 44/80 (55%) for both mKOA and healthy groups. For the 2KAM, 41/80 (51.3%) of assessments for the
266 mKOA group caused an inverse biomechanical response over the SEM. This compared to 58/80 (72.3%)
267 negative responses for healthy group. A positive 2KAM response above SEM was found in 25/80
268 (31.3%) and 15/80 (18.8%) for mKOA and healthy groups respectively. For KAMI, 29/80 (36.3%) of the
269 assessments for the mKOA group demonstrated an inverse biomechanical effect over the SEM. This
270 compared to 42/80 (52.3%) for the healthy group. In relation to a positive KAMI response, a reduction
271 below the SEM was found in 34/80 (42.5%) and 25/80 (31.3%) for mKOA and healthy groups
272 respectively. For 1KFM, overall 50/80 (62.5%) of the assessments demonstrated an increase in 1KFM in
273 response for the mKOA group over the SEM. The healthy group demonstrated increased 1KFM in 43/80
274 (53.8%). Whereas a reduction in 1KFM was reported in 13/80 (16.3%) and 20/80 (25%) for mKOA and
275 healthy groups respectively

276

Discussion

The aim of this study was to investigate alterations in knee joint kinetics as a result of modifications in design features of personalised FOs. Our findings suggest that when two key design features are altered there is a significant heterogeneous mechanical response observed at the knee joint in both the OA and healthy groups during walking. These results enhance our knowledge and understanding as to the potential benefits of personalising FO interventions in order to provide a more positive immediate biomechanical effect even when a heterogeneous biomechanical response exists between conditions for individuals.

At the group level, the full length FOs caused a significant reduction in 1KAM compared to the ¾ length FOs indicating a better response to full length FOs by both study groups. These findings are similar to those previously reported that wedging applied to the entire lateral border is more effective at reducing 1KAM than just at the heel (15).

Although significant effects of wedging were found for 2KAM, the majority of conditions resulted in elevated values, indicative of greater medial compartment loading. Overall the reduction in 1KAM did not correspond to a reduction in 2KAM for most conditions. However there was a reduction in 2KAM for the ¾ length and the full length FOs which incorporated 5° forefoot/ 10° rearfoot wedging. For these conditions mean 2KAM reduced by 0.5% and 4.7% respectively relative to shod in the mKOA and healthy group respectively. These reductions in 2KAM are similar to previously reported results(15,28). During the majority of the 2nd period of stance the forefoot is the only component in contact with the ground. Biomechanically, it is hypothesised that wedging the entire forefoot section will further increase the rearfoot eversion moment, through an increase in its lever arm length across a longer period of the stance phase. Significant correlations have been reported between increased rearfoot eversion moments and reduced KAM moments (29). As such, increasing the overall period at which the FO is ‘

300 biomechanically effective' for therefore makes sense and has been reported to be a key design feature to
301 reduce KAM variables(15).

302 No significant main or interaction effects were found for 1KFM however it was evident that the lateral
303 wedged orthotics provided a concomitant elevation of 1KFM across all FO conditions compared to the
304 shod. The fact that no significant effects were found between FO conditions suggests that these increases
305 may be attributable to the orthotic design itself. Walter and colleagues (6) suggested that a corresponding
306 increase in KFM may attenuate any load reducing benefit of KAM reductions. In this study, our FOs
307 caused a general elevation in 1KFM of 11.4% in the mKOA group, compared to 4.3% the healthy group
308 (overall in ~77.5% of all participant responses) therefore it remains unclear as to whether a reduction in
309 medial contact force would have occurred even with the reported reductions in 1KAM and KAMI
310 variables.

311 KAM impulse has been suggested as a more suitable measure to infer the loading of the medial
312 compartment (30,31) as it takes into consideration both the amplitude of the moment and the total period
313 of stance. For the mKOA group, KAMI was reduced by all FOs which incorporated lateral wedging. The
314 full length FO which incorporated 5° forefoot/ 10° rearfoot wedging was found to be the most
315 biomechanically effective FO. For this condition mean KAMI reduced by 4.9% relative to shod. Given
316 the slightly longer walking time, it could be argued that the elevated 2KAM values reported could have
317 translated into the KAMI however rearfoot wedged conditions, which reported increased 2KAM,
318 demonstrated reductions in KAMI indicating that overall loading still reduced.

319 The reductions in KAMI in response to lateral wedged FOs are in line with those previously reported in
320 the literature (32,33). These findings reinforce the suggestion that FOs incorporating increased wedging
321 across the full length of the lateral side will result in a greater reduction in cumulative load on the knee
322 joint throughout the stance phase. However, these findings were found at the group level which

demonstrated a high level of variability. It is important to note that other aspects such as individual response to pain and tolerance to FO condition have to be taken into consideration when the severity of lateral wedging is targeted.

In the present study, the variability between subjects in the knee joint loading characteristics of 1KAM, 2KAM and KAMI in response to the FO conditions appears greater to that reported in previous research. Hinman et al (32) reported a negative response in 23% of participants with a 5° lateral wedge. In the mKOA group alone, across the variables linked to medial compartment loading a negative response was evident and to a greater extent when FO conditions were grouped together, corresponding to an incidence of 27.5%, 51.3% and 36.3% negative responses over the SEM for 1KAM, 2KAM and KAMI respectively. Furthermore , for the 5° lateral forefoot/10° lateral rearfoot wedged FO, considered the most biomechanically aggressive for reducing medial tibiofemoral compartment loading, participants in both the mKOA group (2/10) and healthy group (3/10) experienced an increase in 1KAM compared to shod that was above the conditions SEM. One possible explanation to this variability is that the immediate assessment of the multiple variations in FO design may have exaggerated these negative effects compared to other studies which have tended to examine only one FO variation.

The capabilities of AM and FO design methods and their potential application in the orthotic sector have received increased awareness in recent years. The FO design and manufacturing methods adopted in this study offer a fast and effective alternative to the traditional orthotic manufacturing methods used in standard care. For our study, the average time between participant's fitting sessions to final assessment was approximately 25 days. Manufacturing time of the 8 remaining insoles only took approximately 56-96 hours print time (2 per day, approximately 4-5 days). Furthermore, the period between initial scan and printing of the neutral FOs for the acclimatisation session was as short as 2 days, but was dependent on total manufacturing volume. Traditional methods including plaster casting on the other hand often involve

more cumbersome processes which require additional time, particularly during the manufacturing stage (34). Future difficulties lie in the practical feasibility of integrating 3D design and manufacturing technologies into the clinical environment in a way which will optimise patient care, drive down overhead costs for health organisations and reduce the turnaround period between initial assessment and FO issue. Furthermore the feasibility of a truly personalised device for each individual using this approach still requires further assessment. The creation of a more streamlined approach to the process is required in order to effectively tailor the personalised intervention to the point that it can be confidently predicted that the intervention will provide a beneficial effect.

Limitations & Conclusion

There are a number of limitations which warrant further discussion. Firstly, participants were instructed to wear their own current trainer rather than a standardised shoe during testing. This may have contributed to the variability in biomechanical response, based on the differences in mechanical characteristics of the footwear, which could influence individual gait patterns. However, this approach was taken to reflect what participants would wear on a daily basis and was assumed not to disrupt their normal biomechanical gait pattern based on their routine use. Furthermore, as results are expressed relative to a shod test condition, this confounding factor is theoretically minimised in the results. We believe the methods applied in this study provide valid results whilst maintaining a pragmatic approach to an intervention study.

The cross sectional nature of the study focused on the immediate biomechanical response, with testing of each FO performed in a random order with little acclimatization period. It is unclear whether each of the conditions evaluated would have had a different effect if they were worn over an extended period of time. Turpin and colleagues (35) reported that an extended period of wear would allow suitable acclimatization to an FO design to occur. However, the immediate biomechanical effect can provide a valuable indicator

for longer term clinical outcomes. Hinman et al., (36) demonstrated a significant correlation between immediate 1st peak KAM reductions with lateral wedged FOs and improvements in WOMAC function score at 3 month follow up, whereby individuals who demonstrated a greater reduction in the adduction moment reported less physical disability

The OA population is known to be heterogeneous in nature. These findings of variability in response to orthotic intervention in people with medial compartment knee OA further support the requirement to develop a better understanding of responders/non-responders, perhaps based on other biomechanical and physical characteristics such as altered ankle joint motions (13).

To our knowledge, this study is the first to examine the immediate biomechanical response to multiple designs of personalised FOs in an mKOA group. These findings suggest that a blanket approach to orthotic prescription may not be an effective treatment plan irrespective of the perceived benefit at the group level. This may go some way to explain the negative findings from recent RCTs of this type of intervention and is a crucial consideration for the KOA population where orthotic prescription is routine practice. In theory under these methods there could be individuals with knee OA who are being prescribed FOs which cause increased KAMs possibly exacerbating their OA progression. A greater understanding is required as to which individuals respond to an orthotic intervention i.e. responder characteristics, as well as improving the ability to optimise the biomechanical response for each of these individuals. Difficulties lie in how we identify these "responsive" individuals early so that interventions can be implemented for long term benefit. Chapman and colleagues (13) reported that the biomechanics of the ankle/ subtalar joint complex plays an central role in KAM reduction and could perhaps predict those who are more likely to have a positive response. Furthermore Paterson and colleagues (37) recently reported a strong relationship between foot and knee pain in people with KOA, resulting in adverse effects on health outcomes and functionality. Future research requires the integration of in depth

biomechanical analyses as well as additional clinical and risk factor assessments to identify and perhaps predict FO responders. Increased involvement of the individual into this process may also be an important consideration.

Author contributions

RA: collection and analysis of gait data, statistical analysis, and preparation of manuscript. JW: study design and preparation of manuscript. ST: study design and preparation of manuscript. MA: study design, data collection, and preparation of manuscript. MS: study design, preparation of manuscript and interpretation of results.

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Conflict of interest

The authors declare that they have no conflict of interest relating to the material presented in this article.

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521

522 **Table 1 Participant Demographics**

	mKOA Group (n=10)		Healthy Group (n=10)	
Subject characteristics	***Mean (SD)***		***Mean (SD)***	
Gender (F:M)	7:3		7:3	
Age (years)	63.3(8.0) ǂ		55.3 (4.0) ǂ	
BMI (kg/m^2)	27.1 (2.8) ǂ		23.6 (2.3) ǂ	
Foot Posture Index, TL/NTL*	2.6 (2.7)	2.2 (2.7)	2.4 (1.6)	2.7 (1.7)
Predicted Radiographic Alignment, TL/NTL*	1.36 (2.2)	2.3 (3.1)	1.4 (1.9)	0.7 (1.9)
Walking Speed (ms^{-1})	4.7 (0.6)		4.2 (0.9)	

*Test Leg (TL) and Non Test Leg (NTL)

ǂ Significant differences between groups ($p \leq 0.05$)

523 **Table 2 Percentage changes in biomechanical variables relative to the shod test condition (control).**

524

	3/4 length, 0° 'neutral'				3/4 length, 5° RF lateral wedging				¾ length, 10° RF lateral wedging				¾ length, 5° FF / 10° RF lateral wedging			
	mKOA		Control		mKOA		Control		mKOA		Control		mKOA		Control	
Parameter	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	mean ±SD	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
1KAM	0.1 (8.8)	-5.8,5.9	3.6 (8.9)	-2.2, 9.5	-1.7 (8.1)	-6.4, 3	-1.8 (5.8)	-6.5, 2.9	-4 (8.1)	-8.7, 0.7	-1.8 (5.7)	-6.4, 2.9	-2.6 (6.4)	-6.4, 1.3	-0.8 (5.2)	-4.6, 3.1
2KAM	6.9 (10.3)	2, 13.6	11.3 (9.9)	4.6, 18	1.5 (10.1)	-4.8, 7.8	11.7 (8.8	5.4, 18	3.7 (11.1)	-3.4, 10.7	8.2 (10.1)	1.2, 15.3	-0.5 (5.1)	-7, 6	9.4 (12.8)	2.9, 15.9
1KFM	7.9 (9)	8, 14.9	4.5 (12)	-2.5, 11.6	10.9 (21.6)	2, 21.6	1.7 (7.5)	-9, 12.4	17.3 (12.4)	9.7, 24.9	5.2 (10.5)	-2.4, 12.9	12.8 (15.5)	3.4, 22.3	6.2 (12.8)	-3.2, 15.7
KAMI	4.2 (9.4)	-1.7, 10..2	6.8 (8.5)	0.8, 12.7	-2 (10.9)	-8.9, 5	4.2 (9.9)	-2.7, 11.2	-1.4 (7.9)	-7.2, 4.3	4 (9.4)	-1.8, 9.7	-2.9 (5.8)	-8.3, 2.5	3.6 (9.9)	-1.8, 9

	Full length, 0° 'neutral'				Full length , 5° RF lateral wedging				Full length 10° RF lateral wedging				Full length , 5° FF / 10° RF lateral wedging			
	mKOA		Control		mKOA		Control		mKOA		Control		mKOA		Control	
Parameter	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI	mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
1KAM	-0.4 (5.9)	-5.8, 5	4.5 (9.8)	-0.8, 9.9	-3.6 (10)	-9.2, 2.1	-2 (6.7)	-7.6, 3.7	-6.8 (6.3)	-10.8, 5	-3.4 (5.6)	-7.4, 0.6	-5.4 (8.2)	-10.5, -2.3	-5.4 (7.2)	-10.6, -0.3
2KAM	8.6 (7.1)	2.6, 14.7	11.1 (10.8)	5, 17.2	3.2 (10.3)	-3.7, 10	6.8 (10.3)	0, 13.6	3.6 (11.4)	-4.7, 12	8.9 (13.7)	0.5, 17.3	-4.7 (10.2)	-12.9, 3.5	-4.8 (14.1)	-13, 3.4
1KFM	10.1 (11)	2.8, 17.4	1.5 (10.9)	-5.8, 8.8	12.9 (19.7)	1.2, 24.7	5.5 (15.4)	-6.3, 17.2	8.6 (15.2)	-0.1, 17.2	6.3 (10.3)	-2.3, 14.9	10.7 (20.6)	0.1, 21.4	3.1 (9.4)	-7.5, 13.8
KAMI	5.3 (7.5)	-0.5, 11.2	7.3 (9.9)	1.5, 13.2	-1.2 (8.7)	-7.1, 4.8	2.3 (9.2)	-3.6, 8.3	-2 (7.5)	-8.4, 1.5	2.4 (11.4)	-4, 8.8	-4.9 (7.6)	-11.4, 1.5	-4 (11.5)	-12.5, 0.4

525 **Table 3 Results of tests of within-subject effects from a two way mixed effects ANOVA (Significant values**

526 **are highlighted in bold)**

Parameter	Effect	F	p-value
1st Peak Knee Adduction Moment	**Length**	**4.986**	**0.038**
	Length x Group	0.161	0.693
	Wedging	**11.564**	**<0.0001**
	Wedging x Group	1.094	0.360
	Length x Wedging	1.391	0.255
	Length x Wedging x Group	0.318	0.812
2nd Peak Knee Adduction Moment	**Length**	**6.820**	**.018**
	Length x Group	**5.693**	**.028**
	Wedging	**14.865**	**<0.0001**
	Wedging x Group	0.467	0.706
	Length x Wedging	**5.466**	**0.002**
	Length x Wedging x Group	1.440	0.241
1st Peak Knee Flexion Moment	Length	0.571	0.460
	Length x Group	0.261	.616
	Wedging	0.800	.499
	Wedging x Group	0.097	0.961
	Length x Wedging	0.519	0.671
	Length x Wedging x Group	0.601	0.617
Knee Adduction Moment Impulse	**Length**	**6.280**	**0.022**
	Length x Group	**5.114**	**0.036**
	Wedging	**19.709**	**<0.0001**
	Wedging x Group	0.764	0.519
	Length x Wedging	**3.237**	**0.029**
	Length x Wedging x Group	1.008	0.396

Figure Legends

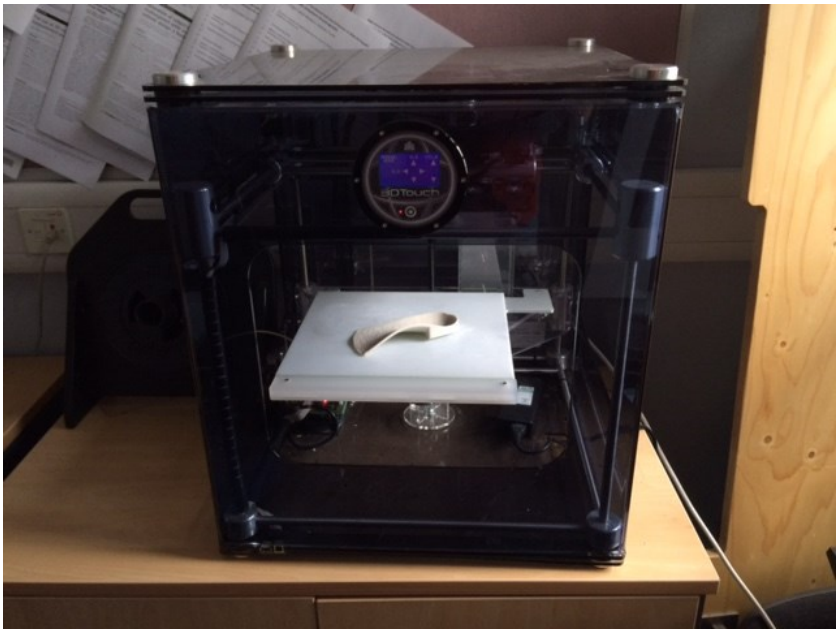
Figure 1. Picture of the 3D printing system used in the FDM process (3d Touch; Bits from Bytes, Clevedon, UK)

Figure 2. Group and individual changes in the first peak knee adduction moment (1KAM) for each FO condition, reported as the percentage change relative to shod condition.

Figure 3. Group and individual changes in the second peak knee adduction moment (2KAM) for each FO condition, reported as the percentage change relative to shod condition.

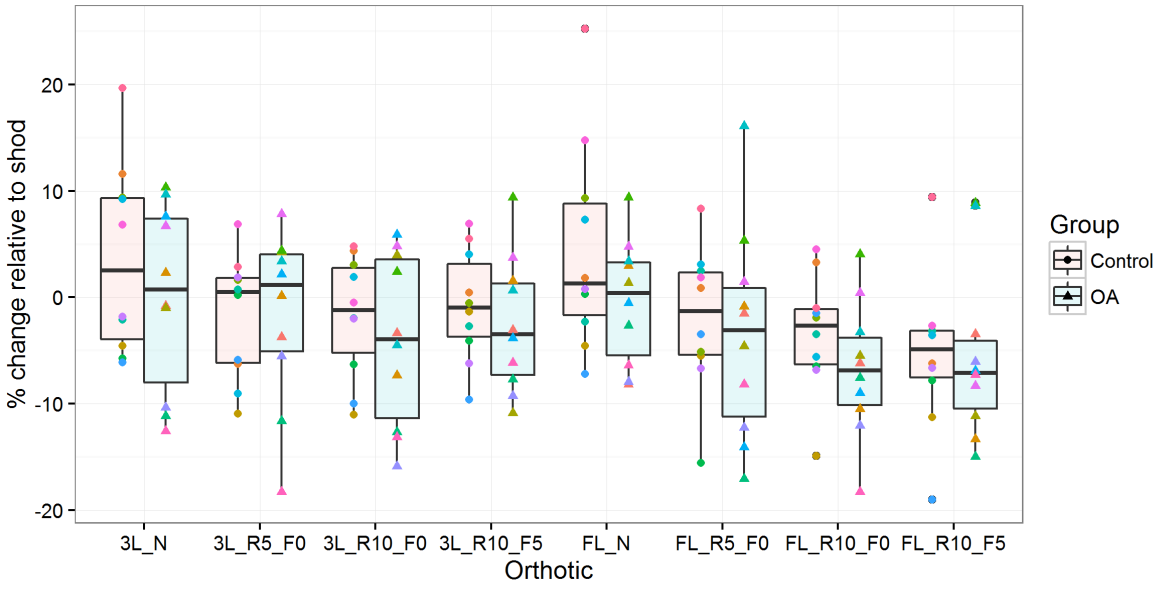
Figure 4. Group and individual changes in the first peak knee flexion moment (1KFM) for each FO condition, reported as the percentage change relative to shod condition.

Figure 5. Group and individual changes in the knee adduction moment impulse (KAMI) for each FO condition, reported as the percentage change relative to shod condition.



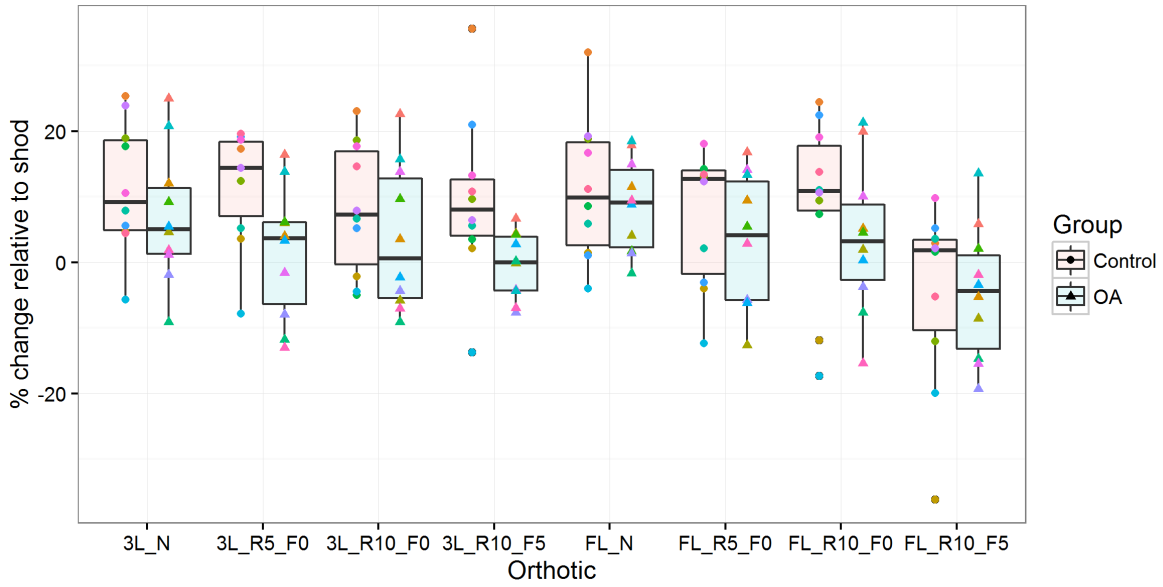
539

540 **Figure 1**



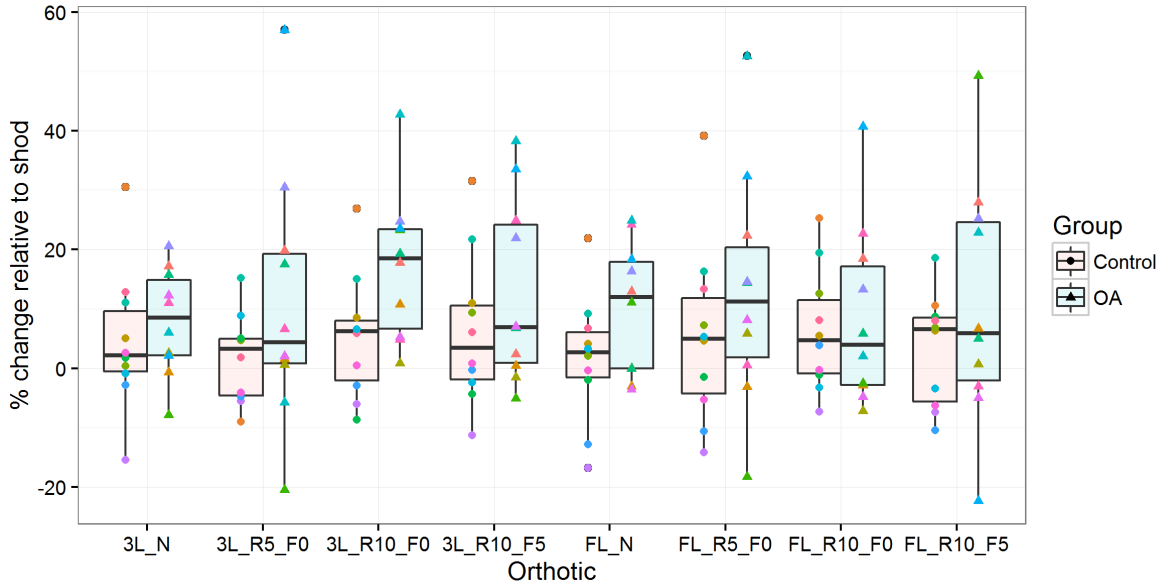
541

542 **Figure 2**



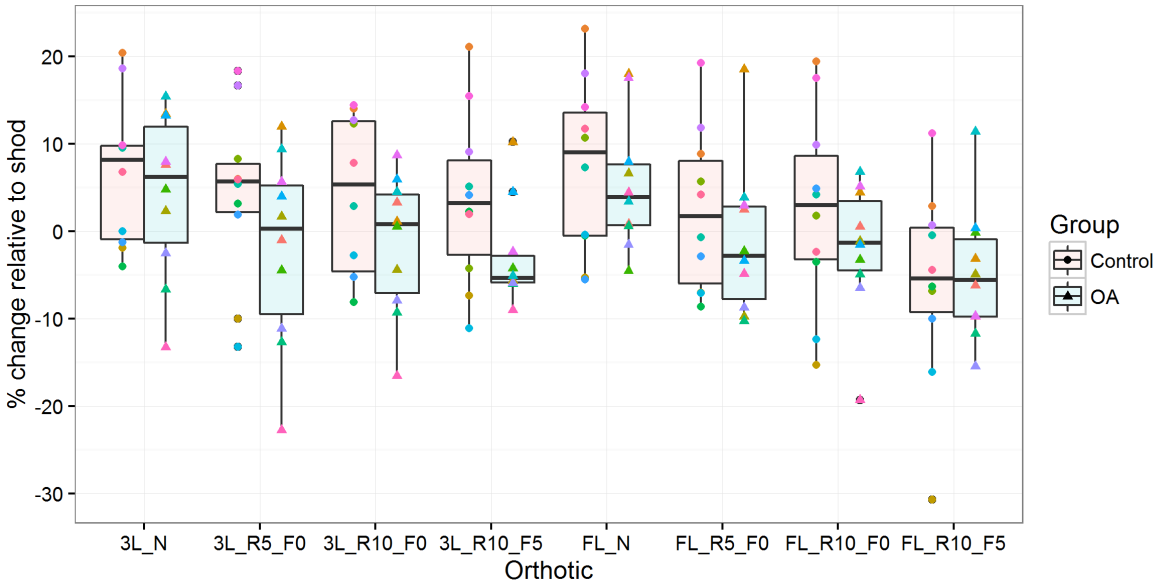
543

544 **Figure 3**



545

546 **Figure 4**



547

548 **Figure 5**

549