Personalization improves the biomechanical efficacy of foot progression angle modifications in individuals with medial knee osteoarthritis

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ABSTRACT

Modifying the foot progression angle during walking can reduce the knee adduction moment, a surrogate measure of medial knee loading. However, not all individuals reduce their knee adduction moment with the same modification. This study evaluates whether a personalized approach to prescribing foot progression angle modifications increases the proportion of individuals with medial knee osteoarthritis who reduce their knee adduction moment, compared to a non-personalized approach. Individuals with medial knee osteoarthritis (N=107) walked with biofeedback instructing them to toe-in and toe-out by 5° and 10° relative to their self-selected angle. We selected individuals' personalized foot progression angle as the modification that maximally reduced their larger knee adduction moment peak. Additionally, we used lasso regression to identify which secondary kinematic changes made a 10° toe-in gait modification more effective at reducing the first knee adduction moment peak. Seventy percent of individuals reduced their larger knee adduction moment peak by at least 5% with a personalized foot progression angle modification, which was more than (p≤0.002) the 23–57% of individuals who reduced it with a uniformly assigned 5° or 10° toe-in or toe-out modification. When toeing-in, greater reductions in the first knee adduction moment peak were related to an increased frontal-plane tibia angle (knee more medial than ankle), a more valgus knee abduction angle, reduced contralateral pelvic drop, and a more medialized center of pressure in the foot reference frame. In summary, personalization increases the proportion of individuals with medial knee osteoarthritis who may benefit from a foot progression angle modification.

1. Introduction

Knee osteoarthritis is a leading cause of disability worldwide (Zhang and Jordan, 2010) and is accelerated by excessive compressive loading in the joint (Brisson et al., 2021). The medial compartment of the knee is affected 3.5 times more frequently than the lateral compartment (Wise et al., 2012), likely because the majority of compressive knee contact force is transmitted through the medial compartment (Kutzner et al., 2017). Since medial compartment force cannot be directly measured in a native knee, surrogate measures, like the peak knee adduction moment (KAM), the area under the KAM curve (i.e., impulse), and peak knee flexion moment are commonly used to evaluate knee loading during

walking (Bennell et al., 2011; Sharma et al., 1998; Walter et al., 2010). The KAM is related to the medio-lateral distribution of loading in the knee (Kutzner et al., 2013), and the KAM peak is associated with the presence (Hurwitz et al., 2002), severity (Sharma et al., 1998), and progression (Miyazaki et al., 2002) of medial compartment knee osteoarthritis. Thus, reducing the KAM peak is a common target for non-surgical interventions for medial knee osteoarthritis (Simic et al., 2011). The early-stance KAM peak (i.e., the first peak) is larger than the late-stance KAM peak (i.e., the second peak) in ensemble-averaged curves (Simic et al., 2010), but some individuals walk with a larger late-stance KAM peak (Ogaya et al., 2014; Uhlrich et al., 2018). While the proportion of healthy individuals who walk with a larger second

KAM peak has been estimated to be between 15% and 35%, the proportion of individuals with medial knee osteoarthritis who walk with a larger first versus second KAM peak is unknown (Ogaya et al., 2014; Uhlrich et al., 2018).

Modifying the foot progression angle (FPA) during walking can reduce the KAM on average, but not all individuals experience a reduction from the same modification. On average, toe-in reduces the first KAM peak (Shull et al., 2013a) and toe-out reduces the second KAM peak (Guo et al., 2007; Lin et al., 2001). Six-week gait retraining programs that uniformly assigned individuals with medial knee osteoarthritis to toe-in (Shull et al., 2013b) or toe-out (Hunt and Takacs, 2014) have improved knee pain and reduced the first and second KAM peaks, respectively. However, not all participants in these studies reduced the targeted KAM peak, and the effects of the modification on each individual's larger KAM peak were not reported. Personalization may increase the achievable reduction in KAM for individual subjects (Favre et al., 2016; Gerbrands et al., 2014; Shull et al., 2015; van den Noort et al., 2015). For example, healthy subjects who were assigned a personalized FPA modification reduced their larger KAM peak by 19%, which was greater than the 8–11% reductions achieved when all subjects uniformly toed-in or toed-out (Uhlrich et al., 2018). The effect of personalization on the ability of FPA modifications to reduce the larger KAM peak in individuals with medial knee osteoarthritis is unclear.

Although the first KAM peak is the larger peak for most individuals, and toeing-in reduces this peak on average, one study found that 41% of healthy individuals with a larger first KAM peak did not reduce it by toeing-in (Uhlrich et al., 2018). The varied biomechanical efficacy of toe-in gait may be a result of the varied kinematic strategies that individuals adopt when changing their FPA. When instructed to toe-in, many individuals also change their hip internal rotation angle (van den Noort et al., 2015), ankle inversion angle (Charlton et al., 2018), tibia angle (Shull et al., 2010), knee abduction angle (Lindsey et al., 2021), and step width (Favre et al., 2016). Understanding which secondary kinematic changes are related to greater reductions in the first KAM peak could improve the efficacy of toe-in gait.

Our study examines the importance of personalizing FPA modifications in patients with medial knee osteoarthritis. We first investigated what proportion of individuals with medial knee osteoarthritis walk with a larger first versus second KAM peak. We next hypothesized that a greater proportion of individuals with medial knee osteoarthritis would reduce the KAM peak that was larger during natural walking (i.e., their larger KAM peak) by at least 5% with a personalized FPA modification compared to a uniformly assigned toe-in or toe-out modification. We also evaluated whether individuals who reduced their larger KAM peak with a personalized FPA modification also reduced other measures of medial knee loading related to disease progression. Finally, we identified which kinematic strategies for adopting a toe-in gait modification were associated with greater reductions in the first KAM peak.

2. Methods

2.1. Participants

One hundred seven individuals with medial knee osteoarthritis participated in this study after providing informed consent to a protocol approved by the Stanford University Institutional Review Board (Table 1). Individuals were included if they 1) had a medial compartment knee osteoarthritis grade between one and three on the Kellgren-Lawrence scale as determined by a radiologist (GEG) from anterior-posterior weightbearing radiographs in at least one knee, 2) had medial knee pain of three or greater on an 11-point numeric rating scale, 3) were able to walk safely on a treadmill without an ambulatory aid for 25 min, and 4) had a BMI less than 35. Individuals with a medial compartment Kellgren-Lawrence grade of four were excluded because KAM-reducing interventions are less effective for individuals with more severe radiographic osteoarthritis (Erhart-Hledik et al., 2012). Because

Table 1
Participant characteristics.

Characteristics	Mean (SD)
N	107
Age (yr)	59.2 (11.0)
Sex	F:64, M:43
Height (m)	1.70 (0.11)
Mass (kg)	78.6 (14.6)
BMI	27.2 (4.4)
Walking Speed (m/s)	1.20 (0.13)
Kellgren & Lawrence Grade	I:27, II:50, III:30

individuals were trained to adopt the FPA modification bilaterally, individuals with greater lateral pain, compared to medial pain, in either knee were also excluded.

2.2. Data collection

During two separate visits, participants walked on a force-instrumented treadmill (Bertec Corporation, Columbus, OH, USA) in an 11-camera motion capture volume (Motion Analysis Corporation, Santa Rosa, CA, USA). More details on the experimental setup can be found in *Supplementary Material: Motion capture procedure.* During the first lab visit, participants acclimated to walking on the treadmill and received feedback to modify their FPA. They first walked naturally for 10 minutes at a self-selected speed, then performed two 10-minute FPA modification trials where they received real-time vibrotactile feedback instructing them to toe-in and toe-out by 10° relative to their baseline FPA. Two vibrotactile motors (Model: *C*2; Engineering Acoustics, Inc., Casselberry, FL, USA) affixed to the medial and lateral aspects of the proximal tibia provided feedback at the end of stance phase following any step where the FPA was not within 2.5° of the trial's target angle (Uhlrich et al., 2018). Feedback was only given to the more symptomatic leg, but participants were encouraged to match the FPA modification with their contralateral limb to avoid introducing gait asymmetries that could have unintended effects on other joints. During the second lab visit, participants warmed up on the treadmill for five minutes, then performed a two-minute baseline walking trial. Participants next received feedback while they practiced walking with 5° and 10° of toe-in and toe-out for a minimum of one minute at each angle or until the participant reported being able to walk comfortably with the modification. FPA evaluation trials with feedback were then performed in random order for each of the four modifications for a minimum of two minutes or until the FPA of 30 steps fell within the target ±2.5° range.

2.3. Data analysis

Motion and force data were low-pass filtered at 15 Hz using a zero-lag, 4th order, Butterworth filter in MATLAB (R2015B, MathWorks Corporation, Natick, MA, USA). The KAM was defined as the frontal-plane component of the 3-dimensional knee moment, expressed in a proximal tibial reference frame as a percentage of bodyweight and height (%BW*ht). The knee moment was calculated as the cross product of the ground reaction force and the vector from the knee joint center to the center of pressure (Shull et al., 2013b; Uhlrich et al., 2018). The first and second KAM peaks were identified as the maximum value of the KAM timeseries during the first and second halves of the stance phase, respectively. To quantify the relative magnitude of the KAM peaks during the baseline trial, we computed the percent difference between KAM peaks by subtracting the first peak from the second peak, then dividing by the larger of the peaks. We analyzed the final 20 steps from the baseline trial and the final 20 steps from each modified FPA evaluation trial for which the FPA was within 2.5° of the trial's target angle. The 20 analyzed steps from the modified FPA trials were randomly divided into two sets of 10. The average KAM peak from one set of 10 steps of each trial was used to select the personalized FPA as the 5° or

10° FPA modification that maximally reduced the larger KAM peak as measured at baseline. The average KAM peak from the other set of 10 steps from each trial was used to compare reductions between personalized and uniformly assigned FPA modifications. A 5% reduction in the KAM peak was considered clinically meaningful based on previous cohorts who reduced pain with similar reductions in the KAM peak (Erhart-Hledik et al., 2019; Erhart et al., 2010). In addition to the KAM peak, we evaluated the effect of a personalized FPA modification on other measures of medial knee loading: the overall KAM peak (the peak value across the stance phase), the KAM impulse, the absolute value of the knee flexion moment peak corresponding with the larger KAM peak measured at baseline, and a regression-based estimate of medial contact force (Manal et al., 2015; Uhlrich et al., 2018; Walter et al., 2010). More details about these analyses are provided in *Supplementary Material: Effect of personalized gait modification on other knee loading metrics*.

We used a linear regression model with lasso (L1) regularization to identify the subset of kinematic changes that explained the most variance in first KAM peak reductions from a 10° toe-in modification. Inputs to the model were changes in kinematic features, with established relationships to the KAM, from the baseline trial to the 10° toe-in trial (Table 2). Unless otherwise noted, kinematic timeseries variables were reduced to scalar inputs by selecting the timeseries value at the time of the first KAM peak. Details on how these variables were computed can be found in *Supplementary Material: Calculation of kinematic variables*.

2.4. Statistics

The proportion of participants who reduced their larger KAM peak by at least 5% with a personalized FPA modification was compared to the proportion who reduced this peak when all participants were assigned a uniform 5° or 10° FPA modification using a mid-p-value McNemar's test of proportions. This test was performed in MATLAB. Changes in the larger KAM peak between modifications were compared using a Wilcoxon signed-rank test, and the median and 95% confidence interval (CI) of the differences are reported. These tests were performed in R (R Core Team, 2019) (v. 3.5.3, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set to 0.05 and p-values are reported with a Bonferroni correction for multiple comparisons.

A lasso regression model was used to select a reduced set of kinematic features that explained the most variance in first KAM peak reductions (Tibshirani, 1996). The lasso penalty coefficient, λ, was selected after performing 10 iterations of 10-fold cross-validation using the *glmnet* package (Friedman et al., 2010) in R (R Core Team, 2019). We used the one-standard-error rule for selecting λ: for each iteration, the λ value that yielded a prediction error that was one standard error greater than the minimum prediction error was selected, thereby removing

more features than the λ value that minimized prediction error. We used the average λ value from cross-validation for the final regression model with regularization. Post-selection p-values (α=0.05) and 95% confidence intervals for model coefficients conditional on the lasso selection were computed using the *selectiveInference* package in R (Lee et al., 2016; Taylor and Tibshirani, 2018; Tibshirani et al., 2017). We report coefficients (β) and r^2 (square of Pearson's r) values from an unregularized linear model with the lasso-selected features as covariates and a reduction in KAM considered positive. For this model, we report coefficients with both standardized (zero mean and unit standard deviation) and unstandardized inputs. To display the differences in the toe-in kinematic change variables that were selected by the lasso, the kinematic timeseries were averaged for the participants above the 90th percentile of first KAM peak reduction (i.e., KAM reducers) and below the 10th percentile (i.e., KAM non-reducers).

3. Results

At baseline, 100 of 107 participants (93%) walked with a larger first versus second KAM peak (Fig. 1). Seventy-five participants (70%) reduced their larger KAM peak by at least 5% with a personalized FPA modification (Fig. 2, Table S1 in *Supplementary Material*). This was greater than (p≤0.002) the number of participants who reduced their larger KAM peak when every-one toed-in by 10° (61 participants, 57%), toed-in by 5° (41 participants, 38%), toed-out by 5° (27 participants, 25%), and toed-out by 10° (25 participants, 23%). Conversely, 12 participants (11%) *increased* their larger KAM peak by more than 5% when every-one toed-in by 10°, 20 (19%) *increased* it when every-one toed-in by 5°, 37 (35%) *increased* it when every-one toed-out by 5°, and 49 (46%) *increased* it when every-one toed-out by 10°. With a uniformly assigned FPA modification, one individual *increased* their larger KAM peak by 34% (Fig. 2, Table S1–S2 in *Supplementary Material*). Of the 75 participants who reduced their larger KAM peak with a personalized FPA, 48 maximally reduced it with 10° toe-in, 8 with 5° toe-in, 7 with 5° toe-out, and 12 with 10° toe-out.

Of the 75 individuals who reduced their larger KAM peak with a personalized FPA modification, 99% also reduced their overall KAM peak and 85% reduced their KAM impulse (Figure S1, *Supplementary Material: Effect of personalized gait modification on other knee loading metrics*). Fifty-two percent of these individuals increased their peak knee flexion moment, but 93% reduced their regression-estimated peak medial contact force.

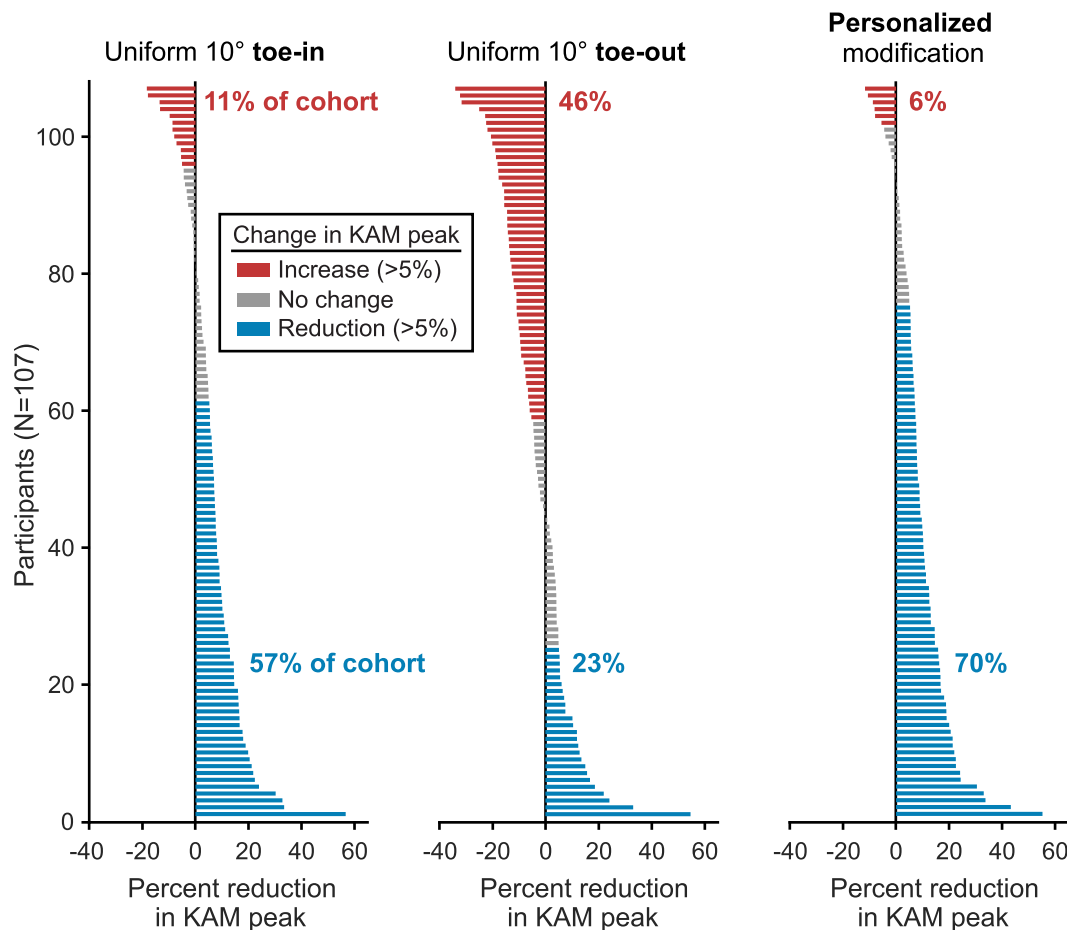Among all participants, a personalized FPA modification reduced

Table 2

Kinematic features related to the knee adduction moment (KAM) were used as covariates in a linear regression model with lasso regularization to predict changes in the first KAM peak (P1KAM) when participants toed-in by 10°. All covariates were the change (Δ) in scalar value from the baseline to the 10° toe-in trial. The time when the timeseries was evaluated is noted in parentheses.

Kinematic Covariates in Lasso Regression Model
Δ trunk sway angle (max value during stance)
Δ pelvic list angle (P1KAM time)
Δ pelvic axial rotation angle (P1KAM time)
Δ knee flexion angle (P1KAM time)
Δ knee abduction angle (P1KAM time)
Δ frontal-plane tibia angle (P1KAM time)
Δ medio-lateral dist. between knee joint centers of consecutive steps (P1KAM time)
Δ medio-lateral dist. between centers of pressure of consecutive steps (P1KAM time)
Δ step width (50% stance)
Δ medio-lateral position of center of pressure in foot frame (P1KAM time)
Δ anterior-posterior position of center of pressure in foot frame (P1KAM time)
Δ foot progression angle
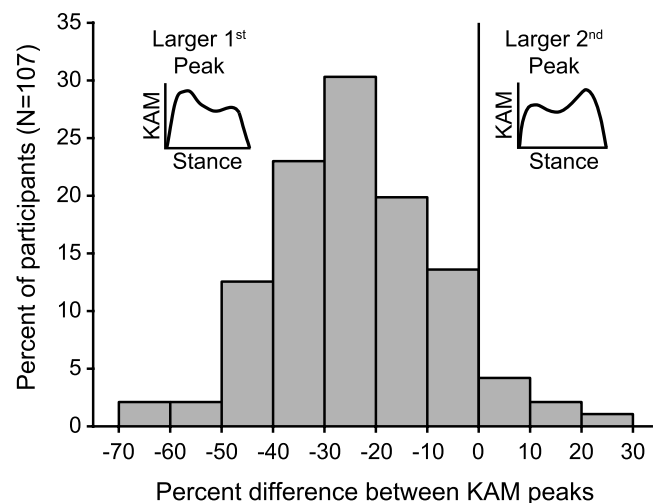
Fig. 1. One hundred of 107 individuals (93%) walked with a larger first knee adduction moment (KAM) peak at baseline, while the remaining seven walked with a larger second KAM peak.

Fig. 2. Changes in each individual's larger knee adduction moment (KAM) peak when all participants toed-in by 10°, toed-out by 10°, and walked with their personalized foot progression angle modification. A greater proportion (p≤0.002) of participants reduced (shown as positive) their larger KAM peak by at least 5% (blue) with a personalized modification (70%) compared to a uniformly assigned toe-in (57%) or toe-out (23%) modification. Importantly, 11–46% of individuals *increased* their larger KAM peak by more than 5% (red) when uniformly assigned a 10° foot progression angle modification, with one individual increasing their larger KAM peak by 34%.

Table 3

The reduction (mean±standard deviation) in the larger KAM peak for the personalized foot progression angle, compared to uniformly assigned foot progression angles. The median difference, 95% confidence interval, and p-values compare the reductions between the personalized and uniformly assigned foot progression angles.

	Reduction (%)	Reduction (%BW*ht)	Median difference (%BW*ht)	95% confidence interval (%BW*ht)	p-value
Personalized angle	9±10	0.28±0.28			
10° toe-in	7±11	0.20±0.30	0.08	0.07, 0.09	**<0.001**
5° toe-in	3±9	0.10±0.26	0.18	0.18, 0.19	**<0.001**
5° toe-out	−1±11	−0.04±0.28	0.31	0.31, 0.32	**<0.001**
10° toe-out	−3±14	−0.10±0.37	0.39	0.37, 0.41	**<0.001**

their larger KAM peak by an average of 9±10%, which was greater than (p<0.001) the average reductions achieved when all participants adopted 5° or 10° FPA modifications, which ranged from a 3±14% increase to a 7±11% reduction (Table 3). Additionally, a personalized approach allows for an intervention to only be prescribed to individuals for whom an FPA modification reduces their KAM. For example, among the 70% of individuals who reduced their larger KAM peak by at least 5% with a personalized FPA modification (Fig. 2), the average reduction was 14±9% (0.41±0.22 %BW*ht).

The lasso regression model selected four of the original 12 kinematic covariates to explain how effectively a 10° toe-in modification reduced the first KAM peak (Table 4, Fig. 3). An unregularized linear model using these four covariates explained the variance in the first KAM peak reduction with adjusted r^2=0.42. When adopting a toe-in gait

modification, greater reductions in the first KAM peak were related to an increased frontal-plane tibia angle (knee more medial than ankle, p<0.001, Fig. 3a), an increased knee abduction angle (more valgus, p<0.001, Fig. 3b), a smaller pelvic list angle (less contralateral pelvic drop, p=0.027, Fig. 3c), and a smaller lateral shift in center of pressure in the foot frame (p=0.004, Fig. 3d). Regression models that evaluate which kinematic covariates explain how effectively 10° toe-out gait reduces the first and second KAM peaks are provided in *Supplementary Material: LASSO regression analysis of toe-out walking* (Figures S2–S3 and Tables S3–S4).

4. Discussion

This study demonstrates the importance of personalizing foot

Table 4

The four covariates selected by the lasso regression model are used in an un-regularized multivariate linear model to explain changes in the first KAM peak when toeing-in by 10° compared to baseline. The Δ represents a change in a kinematic parameter between baseline and toe-in walking, and a reduction in the first KAM peak is considered positive. 95% confidence intervals are presented for the standardized coefficients.

| Covariate	β (standardized)	β (unstandardized)	corrected p-value	r^2 or Δr^2 when covariate removed from model
Multivariate model				$r^2=0.42$
Δ knee valgus angle (°)	0.113 (0.069, 0.156)	0.158	**<0.001**	$\Delta r^2=0.13$
Δ frontal-plane tibia angle (°)	0.092 (0.048, 0.134)	0.081	**<0.001**	$\Delta r^2=0.09$
Δ pelvic list (°)	−0.074 (-0.117, 0.002)	−0.057	**0.027**	$\Delta r^2=0.05$
Δ medio-lateral center of pressure location in foot (mm)	0.072 (0.022, 0.114)	0.022	**0.004**	$\Delta r^2=0.05$
intercept	0.199	0.069		

progression angle modifications in order to maximize the number of individuals with medial knee osteoarthritis who can reduce their knee adduction moment peak with a modification. Ninety-three percent of our participants walked with a larger first knee adduction moment peak. Although a toe-in gait modification reduces the first knee adduction moment peak on average (Shull et al., 2013a), only 57% of the participants in our study reduced their larger knee adduction moment peak when toeing-in by 10°. This was notably less than the 70% who reduced it with a personalized toe-in or toe-out modification.

Personalization not only enables a greater proportion of individuals to reduce their KAM peak, but perhaps more importantly, it also avoids *increasing* the KAM peak in a portion of the population. Previous studies that uniformly assigned KAM-reducing interventions to all participants reported that 18–33% of participants did not reduce the targeted KAM peak (Erhart et al., 2010; Hunt and Takacs, 2014), with some participants increasing it by as much as 10%. Eleven to forty-six percent of our participants increased their KAM peak by more than 5% with a uniformly assigned 5° or 10° FPA modification, with increases in KAM peak as large as 34%. Greater reductions in the KAM from an intervention are correlated with greater improvements in pain and function (Erhart-Hledik et al., 2019), suggesting that the clinical efficacy of load-reducing interventions may be improved by only prescribing them to the subset of

patients for whom the intervention reduces their KAM (Felson et al., 2019). Selecting patients who are most likely to benefit and selecting the intervention that maximizes their KAM reduction may reduce variance in clinical trial outcomes and improve our understanding of how these tools fit into the conservative management of knee osteoarthritis.

Forty-one percent of our cohort who walked with a larger first KAM peak did not reduce it by at least 5% when toeing-in by 10° (Table S1 in *Supplementary Material*); however, our lasso regression model identified kinematic strategies for adopting toe-in gait that could make it more effective in future studies. Instructing patients to toe-in with a medialized tibia angle, a more valgus knee angle, a more medialized center of pressure, and less contralateral pelvic drop may help them reduce their first KAM peak. Giving biofeedback on all four of these kinematic changes along with the FPA may result in larger KAM peak reductions than giving biofeedback on the FPA alone (Favre et al., 2016; Shull et al., 2011; Wheeler et al., 2011), but modifying a single parameter is preferable for patient learning and compliance (Shull et al., 2013b). To retain the simplicity of a single-parameter gait modification, these kinematic strategies for toeing-in could be verbally suggested alongside FPA biofeedback during gait retraining sessions to improve a patient's ability to reduce their first KAM peak.

The lasso regression results also provide insight into the mechanisms
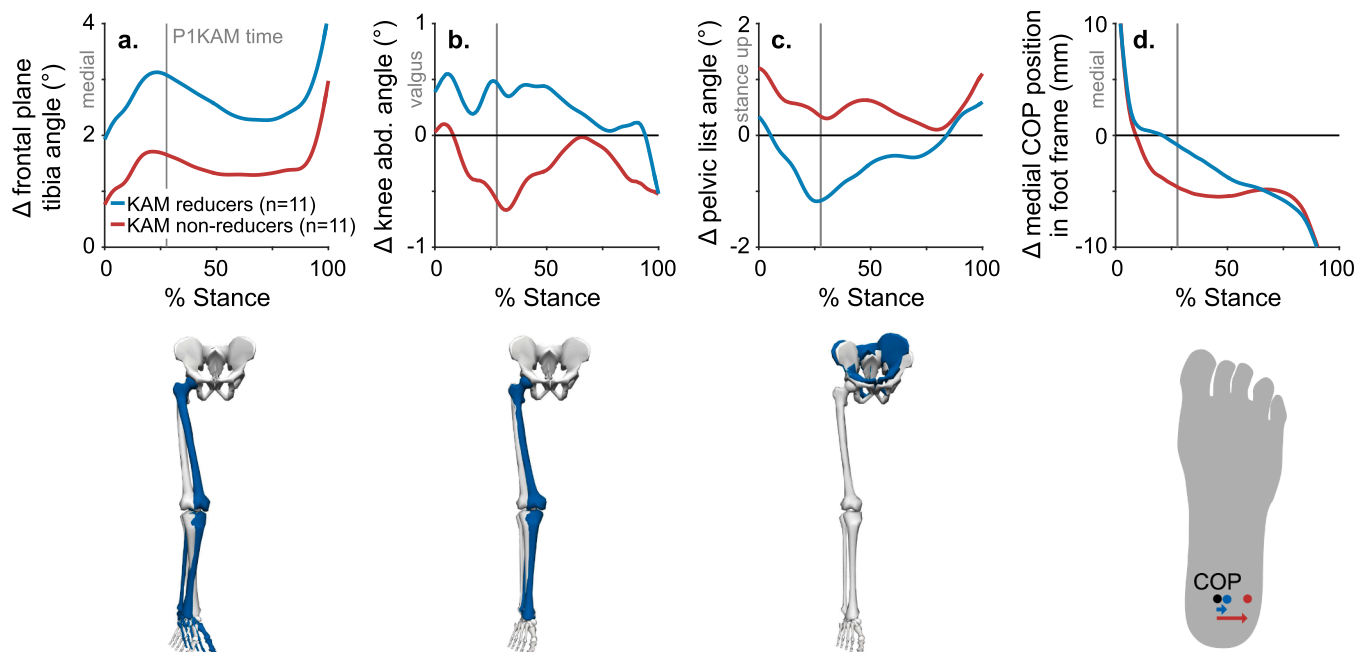
Fig. 3. Compared to baseline walking, toeing-in with a more medialized frontal-plane tibia angle (**a**), a more valgus knee abduction (abd.) angle (**b**), an elevated swing-side pelvis (i.e., more negative pelvic list angle), **c**), and a more medialized center of pressure (COP) in the foot frame (**d**) were associated with greater reductions in the first knee adduction moment peak (Table 3). Changes in kinematic timeseries from baseline to 10° toe-in are shown for individuals above the 90th percentile of KAM reduction (KAM reducers, blue) and for individuals below the 10th percentile of KAM reduction (KAM non-reducers, red). To generate scalar inputs for the linear model (Table 3), we selected the timeseries values at the time of the first KAM peak (P1KAM).

by which toe-in reduces the first KAM peak. Toe-in has been suggested to reduce the KAM lever arm during early stance by either increasing the tibia angle through hip internal rotation and knee flexion, lateralizing the center of pressure relative to the pelvis, or both (Shull et al., 2013a). In our study, the change in tibia angle explained the most variance of any covariate in the model, while the medio-lateral distance between the centers of pressure from consecutive steps was not selected by the lasso. Interestingly, the two variables that explained the most variance in the model, the change in tibia angle and the change in knee abduction angle, both relate to frontal-plane limb alignment. Although they are similar, the tibia angle is expressed in the laboratory frame, so it can be changed with a variety of multi-joint kinematic changes. The knee abduction angle, however, is expressed in the knee reference frame, making it specific to changes in the frontal-plane knee angle. Since both variables explained unique variance in the model, individuals likely altered their KAM lever arm with one or both of these strategies. Finally, all four covariates selected by the lasso relate to medial thrust gait, which involves medializing the knee and elevating the swing-side pelvis (Fregly et al., 2007) and has been observed to cause a medial shift in the center of pressure in the foot reference frame (Ferrigno et al., 2016). Together, these results suggest that when a toe-in gait modification is most effective, it may be reducing the first KAM peak with a similar mechanism as medial thrust gait.

There is a strong body of literature linking the KAM peak to medial knee osteoarthritis outcomes, but the KAM peak may not be the optimal mechanical target for disease-modifying interventions. The KAM impulse provides information about cumulative loading, and some studies report that it is a better predictor of osteoarthritis severity and progression (Bennell et al., 2011; Kean et al., 2012) than the KAM peak. Additionally, the KAM does not capture changes in muscle force that occur from kinematic and coordination changes (Charlton et al., 2018; Richards et al., 2018; Uhlrich et al., 2018; Walter et al., 2010) that often accompany FPA modifications; increases in the force generated by knee-crossing muscles induced by gait modifications counteract the medial-compartment-offloading effect of reducing the KAM. The knee flexion moment is a surrogate measure of the muscle contribution to knee loading (Manal et al., 2015; Walter et al., 2010), and estimates of medial knee contact force from musculoskeletal simulations or statistical models incorporate changes in both the KAM and muscle forces. While we selected FPA modifications that maximally reduced larger KAM peak, these modifications also reduced other measures of medial knee loading in 85–99% of individuals. Further work comparing the relationships between medial knee osteoarthritis progression and the KAM peak, KAM impulse, and medial contact force would help clarify the optimal target for conservative interventions that alter joint mechanics. The gait modification that maximally reduces joint loading for an individual may change based on the mechanical measure targeted and the method used to compute it. Regardless of the loading measure targeted, *personalization* will likely remain an important step to maximize the efficacy of joint-offloading interventions.

It is important to identify the limitations of our study. First, we demonstrated the importance of personalizing FPA modifications for maximizing the number of individuals who can reduce their larger KAM peak, but we did not study the effects of personalization on clinical outcomes such as pain and function. Studies to assess these important clinical outcomes are underway. Second, the need to personalize gait modifications complicates clinical translation. Traditionally, measuring the KAM requires a force plate, motion capture, and a trained gait analyst. Mobile sensing techniques for estimating the KAM have been developed (Aljaaf et al., 2016; Boswell et al., 2021; Favre et al., 2012; Johnson et al., 2019; Karatsidis et al., 2018; van den Noort et al., 2012; Wang et al., 2020), but further work is necessary to validate their ability to accurately select personalized modifications. Additionally, we identified the FPA that maximally reduced the KAM peak after two visits of walking with biofeedback. The first acclimation visit aimed to attenuate the transient effects of learning on the KAM; however, an individual's gait pattern may continue to evolve over a longer-term gait retraining protocol, potentially changing the effect of the modification on the KAM (Hunt and Takacs, 2014; Shull et al., 2013b). Future studies could investigate whether the FPA that maximally reduces the KAM peak after two visits remains the optimal FPA after several weeks of gait retraining.

This study highlights the importance of a personalized approach for prescribing gait modifications to individuals with knee osteoarthritis. Gait modifications may become an important tool for improving symptoms and slowing disease progression, but not all individuals benefit from a uniformly assigned modification. Our study shows that personalization can improve the biomechanical efficacy of gait modifications, suggesting that load-modifying interventions for osteoarthritis should be personalized in future clinical trials and clinical practice. This approach both selects the patients who are most likely to benefit from the intervention and selects the intervention that maximally offloads each individual's joint. By leveraging rapid improvements in mobile sensing technology, clinicians may soon be able to prescribe personalized gait modifications in a clinical setting, potentially making them an effective tool for the treatment of knee osteoarthritis.

CRediT authorship contribution statement

Scott D. Uhlrich: Investigation, Formal analysis, Data curation, Conceptualization, Writing - original draft, Writing - review & editing. **Julie A. Kolesar:** Investigation, Conceptualization, Writing - original draft, Writing - review & editing. **Łukasz Kidziński:** Formal analysis, Writing - review & editing. **Melissa A. Boswell:** Formal analysis, Writing - review & editing. **Amy Silder:** Investigation, Conceptualization, Writing - review & editing. **Garry E. Gold:** Formal analysis, Conceptualization, Funding acquisition, Writing - review & editing. **Scott L. Delp:** Conceptualization, Funding acquisition, Writing - review & editing. **Gary S. Beaupre:** Funding acquisition, Conceptualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that influence the work reported in this paper.

Data availability

The dataset and lasso regression code are available at: https://github.com/suhlrich/ToeInKAMReduction.

Acknowledgements

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbiomech.2022.111312.

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