Original Article

Tibiofemoral Contact Forces during Walking, Running and Sidestepping

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Introduction

Instrumented prosthetic implants can directly measure knee contact forces *in vivo* [1, 2], but are costly and invasive. Consequently, surrogates of knee contact loading, such as the external knee adduction moment (KAM) [3], have received considerable research focus. The shape of the KAM has been shown to correlate with implant-measured medial tibiofemoral (MTF) contact force across the stance phase of walking [4, 5]. However, when the KAM was altered by a targeted intervention, concomitant changes to the MTF contact force did not necessarily occur [6]. Thus, the KAM may not be a robust surrogate of tibiofemoral contact loading during different gaits or control tasks.

Despite the limitations of the KAM, surrogates remain potentially useful if they can well estimate the tibiofemoral contact forces during different gaits or control tasks. Moreover, while single external measures (*i.e.* the KAM or vertical shank resultant force), have shown highly variable relationships with walking tibiofemoral contact forces [6, 7], combining several external measures in multiple regression models has been shown to improve the strength of the relationships [8, 9]. However, previous studies [8, 9] have examined only small numbers of individuals performing low-intensity activities, leaving unexplored the relationships between external measures and tibiofemoral contact forces during more vigorous gait tasks.

Healthy individuals engage in many different gait tasks, including sporting movements such as running and rapid changes of direction. To date, only one study [1] has reported knee contact forces during jogging from three elderly total knee arthroplasty patients who had received an instrumented prosthetic implant. Due to the slow speed of the jogging (~1.6 m's⁻¹), age of the patients (>65) and the prosthetic knee, the knee contact forces were likely not representative of those experienced by younger adults performing similar or more vigorous

tasks. Moreover, as prosthetic, and now tissue engineered implants, are increasingly used in younger populations [10], there is a clear need to study the joint contact loading that arises during vigorous gait tasks in which younger populations commonly engage.

Neuromusculoskeletal computational models provide an alternative to both direct measurement and surrogates of the joint contact forces. However, a major challenge has been to account for muscle activation patterns that are known to vary between individuals [11] and control tasks [12], and are affected by joint pathology [13]. To incorporate subject- and task-specific muscle activation patterns, electromyography (EMG)-driven models [14, 15] combine an individual's experimentally measured muscle activation patterns and external joint biomechanics to estimate the tibiofemoral contact forces [16, 17].

The aims of this study were to estimate the tibiofemoral contact forces, as well as the relative muscle and external load contributions to those contact forces, in healthy individuals during walking, running and running with diagonal sidestepping (referred to as sidestepping). Furthermore, we aimed to assess whether traditional external measures would well predict the tibiofemoral contact forces during the different gait tasks. We hypothesised that 1) sidestepping would have larger maximum tibiofemoral contact forces compared to straight running, 2) the magnitude of the KAM and MTF contact force would have weak relationships during both the running and sidestepping gait tasks, and that these relationships would be gait task-specific, and 3) multiple external measures would well predict tibiofemoral contact forces for a particular gait task, but would perform poorly when applied to other gait tasks.

Methods

Sixty adults (35 male, 25 female) participated with mean±standard deviation age, height and mass of 27.3±5.4 years, 1.75±0.11 m, and 69.8±14.0 kg, respectively. Participants were free of disease and recreationally active with no history of severe lower-limb injury. Data were

equally acquired at Griffith University's Centre for Musculoskeletal Research (CMR) and University of Melbourne's Centre for Health, Exercise and Sports Medicine (CHESM). Human research ethics committees approved the study (CMR: PES/36/10/HREC, CHESM: 0932864.3) and participants provided written informed consent. Testing involved first walking at a self-selected pace, then running at 4-5 m's⁻¹ followed by sidestepping to 45°, all performed shod (Dunlop Volleys, http://www.volley.com.au/) similar to our previous protocols [16-19]. A 10- (CMR) or 12- (CHESM) camera motion capture system (Vicon, Oxford Metrics, UK) (200 and 120 Hz, respectively) was used to acquire three-dimensional motion of participants wearing a full-body marker set [18]. The lower-limb portion of the marker set was modified to include 10-marker clusters on the thighs and shanks that were positioned on regions of the limbs to minimize soft tissue artefact [20]. Ground reaction forces (GRFs) were acquired using two (CMR) (Kistler Instrumente, Switzerland) or three (CHESM) (Advanced Mechanical Technology, USA) force plates (1000 and 2400 Hz, respectively). EMGs were acquired from the 8 major knee muscles from a randomized limb using Wave Wireless (CMR) (Zero Wire, Aurion, Italy) or Telemyo 900 (CHESM) (Noraxon, Arizona, USA) systems sampling (1000 and 2400 Hz, respectively). Similar to our previous studies [16, 17, 19] that used SENIAM guidelines (http://www.seniam.org/) [21], circular pre-formed bipolar Ag/AgCl electrodes (Duo-Trode, Myotronics, USA) were placed over the medial and lateral gastrocnemii, hamstrings, vasti, as well as the rectus femoris and tensor fasciae latae.

All data were filtered using a 2nd order Butterworth filter design that was cascaded once to the remove phase shift [22]. Markers and GRFs were low-pass filtered using 10 and 15 Hz cutoff frequencies for walking and running/sidestepping, respectively. The raw EMGs were band-pass filtered (30-500 Hz pass–band), full-wave rectified and low-pass filtered (6 Hz cutoff) to yield linear envelopes. For each muscle, the EMG envelope amplitude was scaled to the maximum for that muscle from all acquired trials.

Gait biomechanics were determined using OpenSim v3.2 [23]. A generic anatomic model (Figure 1A), based on a previous study running of dynamics [24] was used. The model was customized by adding degrees of freedom (DOFs) and contact points to the knee. Specifically, the original 1 DOF knee [25-27], was provided 15°/5° internal/external rotation range of motion based on measurements from both *in vivo* bone pins [28] and cadavers [29]. Knee abduction/abduction rotations were locked, because these rotations cannot be accurately measured with skin-surface markers [28]. Moreover, allowing knee adduction/abduction rotations would have resulted in condylar lift-off, a feature not observed in instrumented prosthetic knee implants [2]. Overall, the customizations to the anatomic model enabled the calculation of three external knee moments, while preventing non-physiological knee rotations. To determine external moments and muscle tendon unit actuators (MTUA) moment arms about the medial and lateral tibiofemoral compartments, contact points were fixed to the tibia plateau (Figure 1B). Their positions were determined using a regression method based on the width of the femoral condyles [17] (Supplementary material).

For each participant, the customized generic anatomic model was scaled, registered and optimized to the participant's anthropometry and experimental marker configuration. Linear scaling does not necessarily preserve normal muscle and tendon operating ranges, therefore, we optimized the tendon slack and optimal fiber lengths of each MTUA to preserve the dimensionless operating ranges [30]. The final anatomic model was then used to calculate joint angles, moments and MTUA kinematics (lengths and moment arms) for walking, running and sidestepping trials using OpenSim inverse kinematics, inverse dynamics (ID) and muscle analysis tools, respectively.

Gait biomechanics and processed EMGs were then used to calibrate and execute an EMGdriven model [14, 15] that estimated muscle and tibiofemoral contact forces [16, 17]. For each participant, a walking, running, and sidestepping trial was used to calibrate the EMGdriven model by optimizing muscle activation dynamics and MTUAs parameters to best match the experimental knee flexion/extension moment from ID [15] and minimize the tibiofemoral contact forces [16].

For each participant, an average of three repeats of each gait task were used to create mean curves for all measurements. The traditional biomechanical measurements included gait spatiotemporal parameters (i.e. gait speed, stride length/time/cadence, etc.), GRFs, knee kinematics and moments, and muscle activation patterns. The EMG-driven model outputs were the total (TTF), medial (MTF) and lateral (LTF) tibiofemoral contact forces, as well as relative contributions of muscle and external loads. To calculate the relative contributions of muscle and external loads, we summed all loads that had a component in the frontal plane (*i.e.* external, muscle and contact moments) about both the MTF and LTF contact points. We then expressed the mechanical action of these muscle and external moments as a percentage of the total contact loading experienced by the relevant compartment. All variables were time-normalized to 100% of gait cycle and stance phase for walking and running/sidestepping, respectively. To address the first aim of the study, the maximum tibiofemoral contact forces were calculated for each participant during each of the gait modes, and a repeated measures ANOVA was used to test the main effect of gait task on the contact forces. If significant main effects were found, post-hoc paired t-tests with Bonferroni correction for multiple comparisons were used to test specific paired differences. Bonferroni corrections resulted in a significance level of 0.017.

To address the second aim of this study, three types of general linear models (GLMs) were used to explore the relationships between external measures and tibiofemoral contact forces. We first identified the timing of each participant's maximum tibiofemoral contact forces during stance, and then parameterized the external measures at that same time point. This ensured temporal alignment between predictor and response variables in the GLMs, and overall dynamic consistency in our analysis. For the first GLM, GLMSimple, we regressed the maximum tibiofemoral contact forces (scaled to bodyweight (BW)) onto the corresponding KAM (N^{·m·kg⁻¹}) for each gait task. As gait task may influence these relationships, we added a categorical variable to the simple regression (GLMCat) that, when specified for each gait task (one or zero), adjusted for different intercepts. We selected six external measures that have previously been shown to correlate with the tibiofemoral contact forces: KAM [4, 5, 7], external knee flexion moment (KFM) [8, 9], vertical ground reaction force (VGRF) [31], body mass (MASS) [1], gait velocity (VEL) [1] and gastrocnemii activation (GAST) [32]. As described above, the time varying external measures (KAM, KFM, VGRF and VEL) were evaluated at the same time as the maximum tibiofemoral contact forces. These six variables were then used in step-wise regression (GLMStep) with the maximum tibiofemoral contact forces. Finally, the GLMStep equations from a particular gait task (e.g. walking) were applied to the other two gait tasks (e.g. running and sidestepping) and assessed by R^2 and normalized root mean squared error (NRMSE).

Results

Participants walked with velocity 1.44 ± 0.22 m's⁻¹, stride length 1.51 ± 0.12 m and cadence 55.7 ± 4.45 strides min⁻¹, ran at 4.38 ± 0.42 m's⁻¹, and sidestepped at 3.58 ± 0.50 m's⁻¹. The gait velocities were all significantly different from each other (p<0.001).

Maximum tibiofemoral contact forces differed significantly across gait tasks (all p<0.0001). Maximum walking tibiofemoral contact forces (TTF 2.83±0.64 BW, MTF 1.82±0.47 BW and LTF 1.15±0.35 BW) were significantly lower than running (TTF 7.83±1.48 BW, MTF 5.10±0.95 BW and LTF 2.97±0.7 BW) (p<0.0001) and sidestepping (TTF 8.47±1.57 BW, MTF 4.62±0.83 BW and LTF 4.30±1.05 BW) (p<0.0001) (Figure 2). Running had significantly larger maximum MTF contact forces than walking and sidestepping (p<0.0001), while maximum TTF and LTF contact forces were significantly larger in sidestepping than walking and running (p<0.0001). During walking and running the MTF compartment bore the majority of the contact force, while during sidestepping maximum MTF and LTF contact forces were similar.

The mean relative contributions of muscle to MTF and LTF (Figure 3) contact forces differed significantly across gait tasks (all p<0.0001). Mean muscle contributions to MTF contact force increased significantly from walking ($48\pm10\%$) to running ($83\pm20\%$) (p<0.0001) and to sidestepping ($91\pm12\%$) (p<0.0001), while mean muscle contributions to LTF contact increased from walking ($63\pm19\%$) to running ($88\pm11\%$) (p<0.0001) and then decreased during sidestepping ($79\pm12\%$) (p<0.0001).

Overall, the GLMs revealed significant weak-to-moderate relationships between external measures and tibiofemoral contact forces (Table 1). Weak correlations existed between KAM and contact forces (GLMSimple) (all $R^2 < 0.36$) and varied depending on both the gait task and tibiofemoral compartment (TTF, MTF and LTF). GLMSimple showed incrementally larger y-intercepts from walking, to running, to sidestepping (Figure 4), with the categorical gait task variable (GLMCat) improving the strength of the relationships compared to GLMSimple. GLMStep revealed the most important external measures: VGRF (first predictor in 5 of 9 equations and present in 8 of 9 equations), KAM (first predictor in 4 of 9

equations), MASS (present in 6 of 9 equations) and KFM (present in 3 of 9 equations) (Table 1). GLMStep yielded stronger relationships $(0.20 < R_{adj}^2 < 0.78)$ compared to GLMSimple, however, the strength of the relationships varied substantially depending on both the gait task and tibiofemoral compartment. Furthermore, the specific external measures retained by the step-wise process were different depending on the gait task and tibiofemoral compartment. Consequently, when a GLMStep equation from a particular gait task (*e.g.* walking) was used to estimate contact forces for a different gait task (*e.g.* running or sidestepping) the NRMSE significantly increased (from 0.76 ± 0.11 to 4.76 ± 2.7 , p<0.0001).

Discussion

We used an EMG-driven model to estimate the tibiofemoral contact forces in young healthy adults during walking, running and sidestepping. We found that the magnitude of the tibiofemoral contact forces increased from walking to the more vigorous gait tasks, with sidestepping having the largest tibiofemoral contact loading. Second, the relative contributions made by muscle to the tibiofemoral contact forces were larger than the contributions of the external loads and peaked during sidestepping. Third, the tested external measures were poor-to-moderate correlates of the tibiofemoral contact forces, gait task-specific, and not generalizable. To our knowledge, this study was the first to explore the tibiofemoral contact forces during these gait tasks in a young healthy population.

Consistent with our first hypothesis and instrumented prosthetic knee implant data [1], the magnitude of the tibiofemoral contact forces increased from walking to the more vigorous gait tasks of running and sidestepping were they were substantial (7.5-8.5BW). In previous studies, subject-specific measures of muscle activation patterns [33] and muscle strengths [34] were explicitly incorporated into the computational models, and the estimates of running [33] and sidestepping [34] tibiofemoral contact forces were similar to our results. In contrast,

traditional static optimization models [35] that did not incorporate these subject-specific measures, have estimated knee contact forces during running >12 BW. However, it has been acknowledged [35] that these traditional static optimization methods likely overestimated the lower-limb joint contact forces during vigorous gait tasks. Importantly, the inclusion of subject-specific measures into computational models in our study, and others [33, 34], has yielded more reasonable estimates of the tibiofemoral contact forces during running and sidestepping.

The large and continuous MTF and LTF contact forces across the different gait tasks demonstrated the knee was well stabilized. During sidestepping, Besier and colleagues [36] identified specific muscle activation patterns they suggested stabilized the knee against the large and complex external loads. However, their measures of stabilization were derived directly from surface EMG [36], and were thus indirect measures of muscle action that may not have reflected the actual mechanical stabilization of the knee. Our results indicated that muscle was the primary contributor to the tibiofemoral contact forces during running and sidestepping (>75% of compartmental contact loading), and were comparable to the relative contributions made by the external loads during walking (40-65%). During sidestepping in particular, the predominant external knee abduction moment would have concentrated contact loading to the LTF compartment and unloaded the MTF compartment [3], but, due to substantial muscle forces both compartments experienced large and approximately equivalent contact loads across stance (Figure 2). Our results showed that stabilization of the tibiofemoral joint was achieved primarily by muscle not only during walking (as has been previously suggested [3]), but during running and sidestepping as well.

Overall, we found that GLMSimple had weak correlations during the different gait tasks, particularly during running and sidestepping, thus partially confirming our second hypothesis. The KAM has previously been shown to correlate with the shape of the implant-measured MTF contact force during walking [4, 5]. However, when the KAM was altered by gait retraining or walking poles, changes to the KAM were not necessarily conferred to the MTF contact force [6]. Decoupling of the KAM and the MTF contact forces occurs because the KAM is just one of six generalized external knee loads and does not directly determine the load sharing amongst the many knee structures (*i.e.* articular surfaces, muscles, passive soft tissues). Understandably, the KAM was a worse predictor of maximum MTF contact forces during running and sidestepping compared to walking due to both the increased relative contributions of muscle, and decreased relative contributions of external loads to the tibiofemoral contact forces during the more vigorous gait tasks.

The gait task significantly affected the relationships between the KAM and maximum tibiofemoral contact forces, fully confirming our second hypothesis. In Figure 5, data were clustered along the x-axes due to different KAM values in each gait task, and the regression lines had significantly different y-intercepts due to different maximum tibiofemoral contact forces. If the relationships between the KAM and tibiofemoral contact forces were generalizable to different gait tasks, clustering along the x-axis would still occur reflecting the task-specific KAM, but the tibiofemoral contact forces would be on the same regression line with a common intercept. However, this was not the case, rather, the categorical variable for the gait task was significant for all tibiofemoral compartments, which indicated that the GLMSimple relationships were specific to the gait task. Therefore, other biomechanical and neuromuscular measures, rather than KAM alone, must have substantially influenced the tibiofemoral contact forces.

The strongest predictors of the maximum tibiofemoral contact forces were the VGRF, KAM, MASS and KFM. During gait, the VGRF has been shown to strongly influence the tibiofemoral contact forces [31], and Meyer et al [9] reported significant correlations between the vertical shank resultant force (a VGRF proxy) and the tibiofemoral contact forces at

discrete points throughout the gait cycle. As the GRFs during gait are generated by the combination of body, inertial and muscle loads, it is understandable their importance in determining the contact loading at the knee. Likewise, the heavier the individual the larger the body forces throughout the musculoskeletal system. As well, the KFM has been identified as an important contributor to walking tibiofemoral loading [8, 9]. The KFM during gait is generated primarily by knee flexion and extension muscles, and these muscles have substantial adduction or abduction moment arms [37] in addition to flexion and extension moment arms. Therefore, their activation loads both the MTF and LTF compartments [11, 17]. While GLMStep produced significant relationships to the tibiofemoral contact forces for specific gait tasks, it was unclear whether these relationships were generalizable to different gait tasks.

When the GLMStep equations were applied to a different gait task (*e.g.* a walking equation used to predict running contact forces) they produced larger prediction errors for all of the tibiofemoral contact forces (1.04<NRMSE<10.3). This indicated that the GLMStep models were specific to the gait task, and should not be generalized to different gait tasks or external loading conditions, thus confirming our third hypothesis. To determine the tibiofemoral contact forces for different gait tasks or populations some form of neuromusculoskeletal modelling may be necessary. This is because muscle activation patterns have been shown to be dependent on the control task [12], and to vary with both joint health [13] and training [38]. Thus, it seems unlikely that external measures, when used in statistical models that are inherently linear and non-dynamic, can predict joint contact forces during dynamic locomotor tasks.

There were several limitations to this study. First, the estimation of the tibiofemoral contact forces was sensitive to the musculoskeletal [16] and knee contact geometries [39]. We linearly scaled a generic anatomic model to match each participant's dimensions, but linear

scaling is a crude method to personalize musculoskeletal anatomy. Moreover, the tibiofemoral contact points were estimated from a regression equation. Thus, our anatomic models, while personalized, were not fully subject-specific and this could have influenced the relationships we found between the external measures and the tibiofemoral contact forces. Second, we locked the knee adduction/abduction rotations in our anatomic model, enforcing neutral frontal plane alignment of the lower-limbs for all participants. The tibiofemoral contact forces are sensitive to the alignment of the lower-limb [39], thus, locking the knee adduction/adduction rotations for those participants with non-neutral alignment would result in inaccurate model predictions of knee contact forces. However, we did not have standing lower-limb radiographs, therefore, we cannot comment on the lower-limb alignment of the participants, but note that it is a limitation of this study. Third, we did not perform an exhaustive exploration of the possible external measures and their correlation with the tibiofemoral contact forces. Rather, we selected six external measures (KAM, KFM, VGRF, MASS, VEL, GAST) that had a potential biomechanical role in loading the tibiofemoral compartments and had been shown to correlate with the aspects of the tibiofemoral contact forces. However, the studies that reported these correlations were limited to walking gait and selected activities of daily living. Thus, it was possible that during more vigorous gait tasks of running and sidestepping other external measures (not included in our analyses) may have yielded stronger relationships. Finally, we used an EMG-driven neuromusculoskeletal model to solve the muscle redundancy problem required to determine the tibiofemoral contact forces. As such, our study presented the same limitations as other musculoskeletal modelling studies of human motion: a lack of direct validation of the model estimates of muscle force that are subsequently used to determine the tibiofemoral contact forces. The EMG-driven modelling methods have been verified against instrumented knee implants [16], but as vigorous gait tasks are not recommended to knee arthroplasty patients no implant-measure

contact forces are available to analyse the contact loading demanding gait tasks. Therefore, it should be noted that while our modelled tibiofemoral contact forces were similar to implantmeasurements from walking, and consistent with other subject-specific models for running and sidestepping, they were estimates.

In conclusion, the tibiofemoral contact forces increased from walking to the more vigorous gait tasks. Sidestepping was unique among the gait tasks, having similar peak MTF and LTF contact forces. In our young population, walking and running contact forces were considerably larger than those reported in elderly people with instrumented prostheses, indicating a need for implant design to be adapted for younger patients. During all the gait tasks, the tibiofemoral joint was well stabilized by muscles in the frontal plane. Both compartments experienced continuous contact forces, even in the presence of substantial external knee adduction and abduction moments. Overall, the KAM was a poor predictor of the maximum tibiofemoral contact forces during all the gait tasks, particularly during running and sidestepping as the relative contributions of muscle to contact loading increased. Multiple external measures yielded stronger relationships to the maximum tibiofemoral contact forces compared to KAM alone, with maximum VGRF, KAM, MASS and KFM as the strongest predictors. The relationships between multiple external measures and the maximum tibiofemoral contact forces were specific to the gait task and performed poorly when generalized. Therefore, neuromusculoskeletal modelling may be required to estimate tibiofemoral contact forces during different locomotion tasks and populations.

[1] Bergmann G, Bender A, Graichen F, Dymke J, Rohlmann A, Trepczynski A, et al. Standardized loads acting in knee implants. PLoS One. 2014;9:e86035.

[2] Fregly BJ, Besier TF, Lloyd DG, Delp SL, Banks SA, Pandy MG, et al. Grand challenge competition to predict in vivo knee loads. Journal of Orthopaedic Research. 2012;30:503-13.

[3] Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. Journal of Orthopaedic Research. 1991;9:113-9.

[4] Trepczynski A, Kutzner I, Bergmann G, Taylor WR, Heller MO. Modulation of the relationship between external knee adduction moments and medial joint contact forces across subjects and activities. Arthritis & Rheumatology. 2014;66:1218-27.

[5] Zhao D, Banks SA, Mitchell KH, D'Lima DD, Colwell CW, Jr., Fregly BJ. Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. Journal of Orthopaedic Research. 2007;25:789-97.

[6] Walter JP, D'Lima DD, Colwell CW, Jr., Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. Journal of Orthopaedic Research. 2010;28:1348-54.

[7] Erhart JC, Dyrby CO, D'Lima DD, Colwell CW, Andriacchi TP. Changes in in vivo knee loading with a variable-stiffness intervention shoe correlate with changes in the knee adduction moment. Journal of Orthopaedic Science. 2010;28:1548-53.

[8] Manal K, Gardinier E, Buchanan TS, Snyder-Mackler L. A more informed evaluation of medial compartment loading: the combined use of the knee adduction and flexor moments. Osteoarthritis and Cartilage. 2015;23:1107-11.

[9] Meyer AJ, D'Lima DD, Besier TF, Lloyd DG, Colwell CW, Jr., Fregly BJ. Are external knee load and EMG measures accurate indicators of internal knee contact forces during gait? Journal of Orthopaedic Research. 2013;31:921-9.

[10] Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. Journal of Bone & Joint Surgery - American Volume. 2005;87:1487-97.

[11] Lloyd DG, Buchanan TS. Strategies of muscular support of varus and valgus isometric loads at the human knee. Journal of Biomechanics. 2001;34:1257-67.

[12] Buchanan TS, Lloyd DG. Muscle activity is different for humans performing static tasks which require force control and position control. Neuroscience Letters. 1995;194:61-4.

[13] Hopkins JT, Ingersoll CD, Edwards JE, Cordova ML. Changes in soleus motoneuron pool excitability after artificial knee joint effusion. Archives of Physical Medicine and Rehabilitation. 2000;81:1199-203.

[14] Buchanan TS, Lloyd DG, Manal K, Besier TF. Neuromusculoskeletal modeling: estimation of muscle forces and joint moments and movements from measurements of neural command. Journal of Applied Biomechanics. 2004;20:367-95.

[15] Lloyd DG, Besier TF. An EMG-driven musculoskeletal model to estimate muscle forces and knee joint moments in vivo. Journal of Biomechanics. 2003;36:765-76.

[16] Gerus P, Sartori M, Besier TF, Fregly BJ, Delp SL, Banks SA, et al. Subject-specific knee joint geometry improves predictions of medial tibiofemoral contact forces. Journal of Biomechanics. 2013;46:2778-86.

[17] Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. Journal of Biomechanics. 2009;42:2294-300.

[18] Dempsey AR, Lloyd DG, Elliott BC, Steele JR, Munro BJ, Russo KA. The effect of technique change on knee loads during sidestep cutting. Medicine & Science in Sports & Exercise. 2007;39:1765-73.

[19] Winby CR, Gerus P, Kirk TB, Lloyd DG. Correlation between EMG-based co-activation measures and medial and lateral compartment loads of the knee during gait. Clinical Biomechanics. 2013;28:1014-9.

[20] Stagni R, Fantozzi S, Cappello A, Leardini A. Quantification of soft tissue artefact in motion analysis by combining 3D fluoroscopy and stereophotogrammetry: a study on two subjects. Clinical Biomechanics. 2005;20:320-9.

[21] Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. Journal of Electromyography and Kinesiology. 2000;10:361-74.

[22] Robertson DG, Dowling JJ. Design and responses of Butterworth and critically damped digital filters. Journal of Electromyography and Kinesiology. 2003;13:569-73.

[23] Delp SL, Anderson FC, Arnold AS, Loan P, Habib A, John CT, et al. OpenSim: opensource software to create and analyze dynamic simulations of movement. IEEE Transactions on Bio-medical Engineering. 2007;54:1940-50.

[24] Hamner SR, Seth A, Delp SL. Muscle contributions to propulsion and support during running. Journal of Biomechanics. 2010;43:2709-16.

[25] Yamaguchi GT, Zajac FE. A planar model of the knee joint to characterize the knee extensor mechanism. Journal of Biomechanics. 1989;22:1-10.

[26] Delp SL, Loan JP, Hoy MG, Zajac FE, Topp EL, Rosen JM. An interactive graphicsbased model of the lower extremity to study orthopaedic surgical procedures. IEEE Transactions on Biomedical Engineering. 1990;37:757-67.

[27] Seth A, Sherman M, Eastman P, Delp S. Minimal formulation of joint motion for biomechanisms. Nonlinear Dynamics. 2010;62:291-303.

[28] Benoit DL, Ramsey DK, Lamontagne M, Xu L, Wretenberg P, Renstrom P. Effect of skin movement artifact on knee kinematics during gait and cutting motions measured in vivo. Gait & Posture. 2006;24:152-64.

[29] Kanamori A, et al. The effect of axial tibial torque on the function of the anterior cruciate ligament: A biomechanical study of a simulated pivot shift test. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2002;18:394-8.

[30] Modenese L, Ceseracciu E, Reggiani M, Lloyd DG. Estimation of musculotendon parameters for scaled and subject specific musculoskeletal models using an optimization technique. Journal of Biomechanics. 2016;49:141-8.

[31] Shelburne KB, Torry MR, Pandy MG. Contributions of muscles, ligaments, and the ground-reaction force to tibiofemoral joint loading during normal gait. Journal of Orthopaedic Research 2006;24:1983-90.

[32] Demers MS, Pal S, Delp SL. Changes in tibiofemoral forces due to variations in muscle activity during walking. Journal of Orthopaedic Science 2014;32:769-76.

[33] Sasaki K. Muscle contributions to the tibiofemoral joint contact force during running biomed 2010. Biomedical Sciences Instrumentation. 2010;46:305-10.

[34] Weinhandl JT, Earl-Boehm JE, Ebersole KT, Huddleston WE, Armstrong BS, O'Connor KM. Reduced hamstring strength increases anterior cruciate ligament loading during anticipated sidestep cutting. Clinical Biomechanics. 2014;29:752-9.

[35] Rooney BD, Derrick TR. Joint contact loading in forefoot and rearfoot strike patterns during running. Journal of Biomechanics. 2013;46:2201-6.

[36] Besier TF, Lloyd DG, Ackland TR. Muscle activation strategies at the knee during running and cutting maneuvers. Medicine & Science in Sports & Exercise. 2003;35:119-27.

[37] Buchanan TS, Kim AW, Lloyd DG. Selective muscle activation following rapid varus/valgus perturbations at the knee. Medicine & Science in Sports & Exercise. 1996;28:870-6.

[38] Hakkinen K, Komi PV. Changes in neuromuscular performance in voluntary and reflex contraction during strength training in man. International Journal of Sports Medicine. 1983;4:282-8.

[39] Lerner ZF, DeMers MS, Delp SL, Browning RC. How tibiofemoral alignment and contact locations affect predictions of medial and lateral tibiofemoral contact forces. Journal of Biomechanics. 2015;48:644-50.

Figure 1. (A) The OpenSim [23] generic anatomic model used as a template for each participant. The model was subsequently scaled, registered and optimized to each participant's anthropometry and experimental marker configuration. (B) The tibiofemoral mechanism [25-27] was customized to permit $15^{\circ}/5^{\circ}$ internal/external rotations, while locking adduction/abduction rotations. Two contact points were added to enable the determination of net moments and muscle tendon unit actuator moment arms about the medial and lateral tibial compartments. These contact points were modeled as hinges (with axes perpendicular to the shank's frontal plane) that linked bodies with negligible mass/inertial properties, separated by distance *d* based on femur condylar width (Supplementary material).

Figure 2. The mean±95% confidence interval of the EMG-driven (solid line) medial (A, B, C), lateral (D, E, F) and total (G, H, I) tibiofemoral contact forces during walking (~1.44 m's⁻¹) (left column), running (~4.4 m's⁻¹) (middle column) and running with diagonal sidestepping (~3.5 m's⁻¹) (right column). All tibiofemoral contact forces were scaled to bodyweight (BW) and time was normalized to 100% of gait cycle for walking or stance for running/sidestepping.

Figure 3. The mean muscle (hollow dot (o)) and external load (horizontal line (-)) relative contributions (%) to the medial (A) and lateral (B) tibiofemoral compartment contact forces during walking, running and sidestepping. The boxes represent the 25-75 quartiles range, median value is marked by the notch and the whiskers approximate ± 2.7 standard deviations (~99% of the data).

Figure 4. The maximum medial (A), lateral (B) and total (C) tibiofemoral contact forces (BW) regressed against the external knee adduction moment (N[·]m[·]kg⁻¹) for walking (cross-hairs), running (squares) and sidestepping (diamonds). GLMSimple equations in Table 1 correspond to each gait task and tibiofemoral compartment in this figure.

| Tibiofemoral Contact Force | Gait Task | General Linear Model Equations | | | | | | | Prediction Errors using GLMStep Equations | | |
|-------------------------------|--------------|--|----------------|-------|---|-------------------------------|-------|------|--|--|--|
| | | GLMSimple | R ² | NRMSE | GLMStep | R ² _{adj} | NRMSE | | | | |
| | | & GLMCat | | | | | Walk | Run | Sidestep | | |
| Medial | Walk | $c_1 KAM + c_2$ | 0.36* | 0.79 | $c_1 KAM + c_2 VEL + c_3 MASS + c_4 GAST + c_5$ | 0.78* | 0.43 | 5.44 | 3.88 | | |
| | Run | | 0.13* | 0.92 | $c_1 V G R F + c_2 K F M + c_3$ | 0.45* | 6.11 | 0.72 | 4.79 | | |
| | Sidestep | | 0.03 | 0.98 | $c_1 V G R F + c_2$ | 0.34* | 5.05 | 7.61 | 0.80 | | |
| | All Tasks | $\sum_{i=1}^{3} c_1 KAM + c_{2i} c_{CAT_i} + c_3$ | 0.35* | 0.80 | NA | | | | | | |
| Lateral | Walk | $c_1 KAM + c_2$ | 0.01 | 0.99 | $c_1 VGRF + c_2$ | 0.35* | 0.76 | 6.16 | 10.3 | | |
| | Run | | 0.02 | 0.98 | $c_1KAM + c_2VGRF + c_3MASS + c_4$ | 0.20* | 2.54 | 0.86 | 9.61 | | |
| | Sidestep | | 0.29* | 0.83 | $c_{1}KAM + c_{2}VGRF + c_{3}VEL + c_{4}MASS + c_{5}GAST + c_{6}$ | 0.59* | 1.95 | 4.75 | 0.57 | | |
| | All Tasks | $\sum_{i=1}^{3} c_1 KAM + c_{2_i} c_{CAT_i} + c_3$ | 0.58* | 0.64 | N | ĬA | | | | | |

Table 1. The general linear models used to predict the maximum tibiofemoral contact forces.

| Total | Walk | $c_1 KAM + c_2$ | 0.15* | 0.91 | $c_1KAM + c_2VGRF + c_3KFM + c_4MASS + c_5GAST 0.63* + c_6$ | 0.56 | 2.62 | 1.33 |
|-------|-----------------|---|--------------|--------------|--|--------------|--------------|--------------|
| | Run Sidestep | | 0.05 0.01 | 0.99 0.99 | $c_1 VGRF + c_2 MASS + c_3$ 0.23* $c_1 VGRF + c_2 KFM + c_3 MASS + c_4$ 0.36* | 2.31 1.05 | 0.85 1.04 | 9.09 0.74 |
| | All Tasks | $\sum_{i=1}^{3} c_1 KAM + c_{2i} c_{CAT_i} + c_3$ | 0.43* | 0.76 | NA | <u> </u> | | |

*Significance p<0.05.

The external measures were the external knee adduction moment (KAM), external knee flexion/extension moment (KFM), vertical ground reaction force (VGRF), participant body mass (MASS), gait velocity (VEL), net gastrocnemii activation (GAST) evaluated at the time point of the maximum tibiofemoral contact forces.

GLMSimple was a simple regression of maximum tibiofemoral contact forces onto the corresponding KAM.

GLMCat added a categorical variable for the gait task to GLMSimple. c_{CAT_i} was the categorical variable for the i^{th} gait task in GLMCat, and was

specified as 1 for the particular gait task and zero for the other gait tasks.

GLMStep was a step-wise regression of the maximum tibiofemoral contact forces onto the corresponding external measures.

Figure 1. The generic anatomic model. Click here to download high resolution image



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