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Development and evaluation of a subject-specific lower limb model with an elevendegrees-of-freedom natural knee model using magnetic resonance and biplanar x-ray imaging during a quasi-static lunge

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Development and evaluation of a subjectspecific lower limb model with an 11 DOF natural knee model using MRI and EOS during a quasi-static lunge

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ABSTRACT

Musculoskeletal models can be used to study the muscle, ligament, and joint mechanics of natural knees. However, models that both capture subject-specific geometry and contain a detailed joint model do not currently exist. This study aims to first develop magnetic resonance image (MRI)-based subject-specific models with a detailed natural knee joint capable of simultaneously estimating in vivo ligament, muscle, tibiofemoral (TF), and patellofemoral (PF) joint contact forces and secondary joint kinematics. Then, to evaluate the models, predicted secondary joint kinematics were compared to in vivo joint kinematics extracted from biplanar X-ray images (acquired using slot scanning technology) during a quasi-static lunge. To construct the models, bone, ligament, and cartilage structures were segmented from MRI scans of four subjects. The models were then used to simulate lunges based on motion capture and force place data. Accurate estimates of TF secondary joint kinematics and PF translations were found: translations were predicted with a mean difference (MD) and standard error (SE) of 2.13±0.22 mm between all trials and measures while rotations had a MD±SE of 8.57±0.63°. Ligament and contact forces were also reported. The presented modeling workflow and resulting knee joint model have potential to aid in the understanding of subject-specific biomechanics and simulating the effects of surgical treatment and or external devices on functional knee mechanics on an individual level. Journal of Biomechanical Engineering. Received January 15, 2019; Accepted manuscript posted July 18, 2019. doi:10.1115/1.4044245 Copyright (c) 2019 Journal of Biomechanical Engineering

1 Introduction

2

Joint loads and movements in the musculoskeletal (MS) system are governed by complex 3 interactions between muscles, ligaments, bones, other soft tissues, and external loads. 4 5 These loads and movements are difficult to measure in vivo, therefore, MS models are applied to gain insight into internal kinematics and kinetics. However, many MS models 6 simplify joints [1], i.e. a revolute knee joint, and only recently have studies developed and 7 8 evaluated complex MS models that estimate knee joint contact forces and secondary joint kinematics [2–8]. An aim to investigate surgical outcomes or interventions for pathologies 9 such as osteoarthritis has driven the development of advanced MS joint models that go 10 beyond idealized joints. 11

The time-consuming and sometimes unethical processes of identifying 12 parameters required to build musculoskeletal models, steer researchers towards scaling 13 of cadaver-based templates [2,7]. Depending on the amount of subject-specific data 14 available to the user, different levels of personalization can be achieved. For instance, 15 16 geometric bone can be linearly scaled using anthropometric measurements of the subject [9], or based on bone geometry segmentations from medical images. The muscle origins 17 and insertions can be determined through manual identification [10] or using advanced 18 morphing techniques [2,7]. Although it is known that estimations of internal forces are 19 20 highly sensitive to musculoskeletal model geometry [11,12], most studies apply linearly 21 scaled models [4–6]. In rare cases, detailed joint models are used [2,7].

Strong headway has been made on the evaluation and validation of complex 1 2 subject-specific musculoskeletal models through projects like the "Grand Challenge Competition to Predict in vivo Knee Loads" [13]. This project provides an extensive 3 4 dataset, including knee contact force measurements obtained from an instrumented total 5 knee arthroplasty (TKA) prosthesis, for researchers to utilize in the development and evaluation of methodologies to estimate knee joint contact forces. Some relevant studies 6 7 under this framework include Hast and Piazza [4], who used a "dual-joint" paradigm that 8 alternatively predicts muscle forces by inverse dynamics in an idealized knee joint and thereafter analyzes a TKA model with 12 degrees of freedom (DOF) and an elastic 9 foundation contact model by forward dynamic integration in a linearly scaled model. A 10 coupled method, developed by Thelen et al. [6], allows for the concurrent estimation of 11 neuromuscular dynamics and joint mechanics, where a computed muscle control 12 13 algorithm drives a forward dynamics analysis with an elastic foundation model of a TKA implemented in a linearly scaled model. A similar method simulating muscle and 14 tibiofemoral (TF) contact forces, was developed by Guess et al. [5] using proportional 15 integral derivative (PID) feedback control schemes to track the joint angles during the 16 forward dynamic simulations and compute muscle forces. Their model used subject-17 specific partial femur, partial tibia, and patella geometries while the rest of the model was 18 19 linearly scaled. Marra et al. [2] proposed a methodology that simultaneously estimates muscle, ligament, and knee joint contact forces together with internal knee kinematics. 20 21 This was done by applying the force-dependent kinematics (FDK) method developed by 1 Andersen et al. [14] in a model that was morphed from subject-specific femur, tibia, and

2 patella geometries, while the remaining lower limb bones were linearly scaled.

The FDK method is an enhanced inverse dynamic analysis that assumes quasistatic equilibrium around the joints' secondary DOF. According to this method, secondary joint kinematics are computed based on contact models and interactions between ligaments, external loads, and muscle forces in the joint [14].

Although instrumented prostheses provide an extraordinary opportunity to validate models, patients with such devices are rare and the results obtained may not be transferable to natural knees of healthy subjects [5,15,16]. Methodologies developed through MS models of TKA have the potential to be applied in natural knees [7,8,15–18]. However, further validation efforts in subject-specific natural joint modeling must be conducted before generalizing their application.

13 A different validation approach comparing predicted muscle activation and measured electromyographic (EMG) data has also been taken previously to evaluate 14 models without internal load measurements available [1]. EMG amplitudes represent 15 muscle activation during isometric tasks and correlate well with muscle force [19,20]. 16 However, the EMG signal depends highly on electrode placement and cannot be linearly 17 related to muscle force during dynamic tasks due to complex interactions between 18 19 muscle forces and EMG signals, therefore allowing only for indirect validation [20,21]. Hence, the best approach to evaluate kinematic model predictions of healthy subjects is 20 21 with experimental measurements of joint kinematics. Dynamic magnetic resonance 22 imaging (MRI) provides a non-invasive option for measuring in vivo joint kinematics;

1	nonetheless, these measures must be carefully interpreted due to differences between
2	non-weight- and weight-bearing conditions [15,22–26]. On the other hand, fluoroscopy
3	allows for dynamic measurements of in vivo joint kinematics during weight-bearing
4	conditions [27]. Biplanar X-rays systems, such as EOS [™] Imaging, utilize slot-scanning
5	technology allowing to perform static measurements of in vivo joint kinematics during
6	weight-bearing conditions with a low radiation dose [28–31]. It is important to note that
7	kinematic measures obtained from quasi-static biplanar X-ray imaging do not necessarily
8	represent that of dynamic activities [30,31].
9	The specific goals of this study were to: (1) apply a subject-specific MS modeling
10	workflow based on MRI, motion capture, and force plate data to an enhanced inverse
11	dynamic analysis utilizing the FDK method [2], and (2) evaluate the accuracy of the
12	subject-specific MS models performing a lunge against in vivo kinematic data collected
13	during a quasi-static lunge [30].
14	
15 16	Materials and methods
17	Experimental data
18 19	Four healthy male subjects without pre-existing knee injuries (age 38 \pm 10 years,
20	body mass 74 \pm 7 kg, height 1.82 \pm 0.06 m) were recruited for this study. The following
21	procedures were approved by the Scientific Ethical Committee for the Region of
22	Nordjylland and informed consent was obtained prior to data collection.

Single leg (right) dynamic lunges to roughly 20, 45, 60, and 90 degrees of knee 1 2 flexion (approximated with the help of a lab technician) were performed by the subjects. Simultaneously, motion from 15 retro-reflective markers was recorded using eight infra-3 4 red high-speed cameras (Oqus 300 series) sampling at 100 Hz operated with Qualisys 5 Track Manager v.2.9 (Qualisys, Gothenburg, Sweden). One force platform (AMTI Corp., Watertown, MA) placed under the right foot recorded ground reaction forces and 6 7 moments concurrently at a frame rate of 2000 Hz. Subjects underwent magnetic 8 resonance imaging (MRI) from pelvis to feet, recorded with a 1.5 T OptimaTM MR450W-70 cm scanner (General Electric Healthcare, Chicago, Illinois, USA) running a T1W-LAVA-9 XV-IDEAL, coronal plane acquisition. Before the full lower limb scans, 18 MRI-compatible 10 markers were placed on bony landmarks. Detailed right knee acquisitions were taken with 11 a 3T Hdxt upgrade scanner (General Electric Healthcare, Chicago, Illinois, USA) following 12 13 the Osteoarthritis Initiative (OAI) protocol and adjusted for use of a GE scanner [32,33]. A biplanar X-ray imaging system (EOS Imaging, Paris, France), with slot scanning technology 14 and micro-dose radiation exposure, was used to capture in vivo kinematics of the right 15 knee during quasi-static lunges at approximately 20, 45, 60 and 90 degrees of TF flexion 16 [30]. Biplanar X-ray imaging and motion capture experiments were performed non-17 simultaneously. 18

19

20 Musculoskeletal model

21 Template lower limb body model

1	The subject-specific MS models were developed using the AnyBody Modeling
2	System v.7.1 (AMS, Anybody Technology A/S, Aalborg, Denmark) [34]. The generic human
3	body model from the Anybody Model Repository (AMMR v.1.6) was the basis for the
4	subsequent modifications, consisting of a head, trunk, pelvis, two arms, and two legs. The
5	arms and the left leg were excluded from the model and the right leg was replaced with
6	the Twente Lower Extremity Model (TLEM) 2.0 dataset [10], which includes foot, talus,
7	shank, patella, thigh, and hip segments.

8 The TLEM 2.0 dataset includes coordinates of bony landmarks, muscle 9 attachments, bony wrapping surfaces, joint centers, and axes of rotation for the lower 10 limbs as well as mass, inertial, and mechanical properties for the muscles. The hip joint 11 was modeled as a spherical joint, while the TF, PF, ankle, and subtalar joints were modeled 12 as revolute joints. The revolute constraints in the TF and PF revolute joints were later 13 released, resulting in a 11 DOF knee joint (as patellar tendon was modeled as rigid). More 14 detail can be found in the FDK-based inverse dynamic analysis section.

15

16 Geometric morphing

Subject-specific bone geometries were used to morph the generic TLEM 2.0. dataset bone geometries and corresponding muscle attachments. To achieve this, the full pelvis, right: femur, tibia, talus, foot, and patella, and left femoral head were segmented from the lower limb stack of MRI images using Mimics Research v.19 (Materialise NV, Leuven, Belgium). Segmented 3D geometries were exported as stereolithography (STL) files. Post-processing of the segmented subject-specific bone meshes was performed in

1	Meshlab v.2016.12 (ISTI-CNR, Pisa, Italy) [35] to better facilitate the morphing process by
2	approximating the number of vertices in the subject-specific segmented bones (target
3	geometries) to the TLEM 2.0 generic bones (source geometries). The generic bones from
4	the TLEM 2.0 dataset were morphed following an advanced morphing technique,
5	developed by Materialise NV (Leuven, Belgium), to the topology of the subject-specific
6	bones based on the 3D reconstruction method of Reder et al. [36], and evaluated in detail
7	by Pellikaan et al. [37]. This method has been previously used in similar studies with good
8	results [2,7,30]. Geometry-based morphing was not possible for the foot due to an
9	incomplete MRI scan. Therefore, the foot was scaled using an affine transformation based
10	on 16 bony landmarks (see Appendix).

11 Bony landmarks, joint centers, and axes definition

Surfaces selections were made on the subject-specific bone STLs using 3-Matic Research v.11.0 (Materialise NV, Leuven, Belgium) to define bony landmarks, joint centers, and axes. The bony landmarks were computed with a custom MATLAB v.R2014B (The Mathworks Inc., Natick, MA, USA) script, averaging each selected cluster of triangles on the STL surface. Joint centers and axes were obtained in MATLAB through surface fitting techniques based on the various selections [2,38].

18 Kinematic analysis

19 The simulation workflow is divided into three steps: a Multibody Kinematics 20 Optimization (MKO) in a standing trial [39], a MKO in the dynamic trials, and an enhanced 21 inverse dynamic analysis with a FDK method [14].

In the first step, the position and orientation of each segment were found using 1 2 the segmented MRI markers and corresponding motion capture markers, during the standing reference trial. The local coordinates of the six cluster markers (superior, lateral, 3 and inferior on the thigh and shank segments) were computed and saved for later use. 4 5 Subsequently, in a second step, an optimization function that minimized the least-square differences between modeled and experimental markers developed by Andersen et al. 6 7 [40] was applied to determine the model kinematics during the dynamic motion capture 8 trials. Throughout the kinematic analysis, the pelvis segment had six DOF (three translations and three rotations) relative to the global coordinate system, and all joints 9 were assumed idealized with three DOF at the hip and one DOF at the TF, PF, talocrural, 10 and subtalar joints. The trunk was assumed rigidly attached to the pelvis. 11

12 FDK-based inverse dynamic analysis

The resulting optimized model kinematics and experimentally recorded ground 13 reaction forces and moments were used as input to the FDK-based inverse dynamic 14 analysis. In this third step, a second knee model was constructed for implementation into 15 16 the FDK solver [14]. This knee model removes the existing revolute joint and replaces it with an 11 DOF joint that is stabilized by articular contact forces and ligaments. The 11 17 DOF knee is made up of five DOF in the PF joint, as the patellar ligament was modeled 18 rigid, and six DOF in the TF joint. From these 11 DOF, only the knee flexion angle was 19 20 driven by the previous MKO results. The other 10 DOF were free to equilibrate between 21 the muscle, ligament, and contact forces, and the external loads in the FDK solver [14].

- 1 Six residual forces and moments were implemented in the pelvis in substitution for the
- 2 upper body and excluded left leg.
- 3 Ligaments

To restrict and stabilize the TF and PF joints in the natural knee model used in the 4 FDK analysis, ligaments were introduced. Anterior cruciate ligament (ACL), posterior 5 6 cruciate ligament (PCL), lateral collateral ligament (LCL), medial collateral ligament (MCL), lateral epicondylo-patellar ligament (LEPL), medial PF ligament (MPFL), and lateral 7 transverse ligament (LTL) were segmented from the detailed MRI images in Mimics. 8 9 Ligament attachment sites were selected on the bone surfaces in 3-Matic and, 10 subsequently, averaged in MATLAB to determine the ligament attachment points. Ligaments were divided into bundles to account for wide origin insertion areas. The ACL 11 was represented by four bundles, PCL three bundles, LCL two bundles, MCL three bundles, 12 MPFL three bundles, LEPL one bundle, and LTL three bundles. The posterior capsule (PC, 13 four bundles) and the anterior lateral ligament (ALL, two bundles) could not be 14 15 determined from the medical images; therefore they were estimated according to 16 descriptions found in the literature [2,15,41]. Ligaments were characterized by three nonlinear force-displacement regions [42], with the linear strain limit set to 0.03 [43]. 17

The ligament parameters (stiffness and reference strain) of each bundle are shown in Table 3 in the Appendix. These ligament parameter values, originally adapted from Blankevoort et al. [42], were taken from comparable knee models in the literature [2,5,6]. Small adjustments to the ligament reference strains were made to the LCL, MCL and PCL for some subjects to increase the stability of the lateral TF compartment (Table 3).

1 Contact model

The articular cartilage from the PF and TF joints was segmented in Mimics and the 2 3 contact surfaces were selected in 3-Matic. Additionally, the contact surface between the 4 patella and femoral trochlear groove (bone) was also selected in 3-Matic. Four contact sites were then created based on an elastic foundation contact model, one at the PF joint, 5 two at the TF joint (dividing the medial and lateral compartments), and one between the 6 patella and the femoral bony surface. The STL surface meshes were used to compute the 7 contact forces based on an elastic foundation contact model with a pressure module of 8 9.26 GN/m³[2]. 9

10 Muscle modeling

11 Muscles were represented by 55 muscle-tendon units modeled using 166 Hill-type one-dimensional string elements running from origin to insertion points along via-points 12 13 and wrapping surfaces fit to the TLEM 2.0 bone geometries. Three-element Hill type models were used for defining muscle dynamics as proposed by Zajac [19]. Following Klein 14 Horsman et al. [44], the isometric strength of each muscle was determined from the 15 16 physiological cross-sectional area by multiplication with a factor of 27 N/cm². The isometric muscle strength of each muscle unit was further scaled using segment-specific 17 strength scaling factors based on the length and mass of the segment relative to the 18 generic TLEM 2.0 model [45]. Force-length and force-velocity relationships were included 19 in the definition of muscle strength to account for the length- and velocity-dependent 20 effects on the instantaneous muscle strength. 21

1 Muscle recruitment

To account for the fact that there are more muscles than DOF in the model, a muscle recruitment problem was set up to minimize a third order polynomial cost function. The objective function minimized cubed muscle activations while ensuring that the dynamic equilibrium equations are fulfilled and that muscles can only pull:

6

(4)

7

 $\min_{\mathbf{f}} G(\mathbf{f}^{(M)}) = \sum_{i=1}^{n^{(M)}} V_i \left(\frac{f_i^{(M)}}{N_i}\right)^3$ Cf=r $0 \le f_i^{(M)} \le N_i \qquad i = 1, 2, ..., n^{(M)}$

8 The objective function, *G*, is a function of unknown muscles forces $\mathbf{f}^{(M)}$. V_i is the 9 muscle volume [2] and is introduced to account for sub-divided muscles. The number of 10 muscle branches in the model is $n^{(M)}$, while $f_i^{(M)}$ is the *i*th muscle force. N_i is the 11 instantaneous muscle strength estimated from the Hill-type muscle model. **C** is the 12 coefficient matrix containing all unknown forces, **f** is a vector of all unknown forces and 13 **r** is a vector that represents the inertia, gyroscopic, and external forces [34].

14

16

15 Tibiofemoral and patellofemoral coordinate systems and measures

Anatomical coordinate systems for tibia and femur were defined following the ISB recommendations as described in Grood and Suntay [46]. The femoral local coordinate system (LCS) origin was situated between the medial and lateral epicondyles. The femoral LCS was orientated with the superior-inferior (SI) axis pointing from the origin to the hip joint center, the medial-lateral (ML) axis perpendicular to the SI-axis and pointing laterally, and the anterior-posterior (AP) axis orthogonal to both and oriented anteriorly

(Green coordinate system in Fig. 4). The tibial LCS had its origin midway between lateral 1 2 and medial tibial edges. The orientation of the tibial LCS was defined with the SI-axis running between the ankle joint center and the origin and pointing proximally, the ML-3 axis was perpendicular to SI-axis and oriented towards the lateral tibial edge, and the AP-4 5 axis was orthogonal to both and oriented anteriorly (Red coordinate system in Fig. 4). For the patella, the LCS was defined with its origin placed midway between nodes selected at 6 7 the most lateral and medial patellar protuberances. The ML-axis ran from the origin to 8 the lateral edge, the SI-axis was defined orthogonal to ML-axis and pointing towards the superior node (located at the middle of the patella's superior surface), and the AP-axis 9 was defined orthogonal to both and oriented anteriorly (Blue coordinate system in Fig. 10 11 4).

To compute the respective clinical measures, for the TF joint, non-orthogonal unit base vectors were defined (e_1 along femoral fixed ML-axis, e_3 along tibial fixed SI-axis, and e_2 as the cross product between e_3 and e_1 oriented anteriorly). The rotations followed the right-hand rule about these unit vectors and defined the flexion-extension (FE), abduction-adduction (AA), and internal-external (IE) rotations, respectively. To compute the translations, the vector from the femoral origin to the tibial origin was defined and projected onto each rotation axis.

19 The patellar kinematics were computed with respect to both femoral and tibial 20 (patellotibial: PT) coordinate systems. Translations were measured as the displacement 21 of the patellar LCS origin relative to both the femoral LCS and tibial LCS. Rotations were

- 1 measured with Cardan angles in the sequence FE, rotation about the floating axis (AA),
- 2 and rotation about its long axis (IE) relative to both femoral and tibial coordinate systems.

3 Experimental measures: biplanar X-ray imaging slot-scanning technology

To evaluate the model performance, previously collected [26] in vivo kinematic 4 5 measures of the TF and PF joints were used. The previously taken images were collected 6 using the EOS biplane X-ray system (Biospace med, France) utilizing slot-scanning technology. These biplanar X-rays were then used to estimate the pose of the femur, tibia, 7 8 and patella and subsequently compute the relative translations and rotations. First, the 9 bone contours of femur, tibia, and patella were manually marked from each pair of biplanar X-ray images in Mimics. Custom MATLAB code was then used to manually 10 11 transform the 3D MRI-based bone geometry until its projected contours roughly overlaid the biplane segmented contours. Then, the least-square difference between the biplanar 12 contours and the 3D MRI-based geometry contours was minimized using an iterative 13 closest point (ICP) optimization method [30]. Identical coordinate systems as explained in 14 15 the preceding section, were created for the 3D bone geometry reconstructions. The AMS was then used to compute the previously defined clinical rotations and translations for 16 17 3D bone geometry reconstructions for each of the quasi-static lunge positions (20°, 45°, 60°, and 90°). 18

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1 Model evaluation

2 Seventeen clinical measures (five TF, six PF, and six PT) were extracted from the models at each of the quasi-static lunge TF condition (20°, 45°, 60°, and 90°). The model 3 4 predictions were evaluated against the experimental measures by plotting the clinical 5 measures (subject mean and standard deviation) as a function of TF flexion. Range of 6 motion (ROM) means and standard deviations were also assessed for each clinical measure for both model predictions and experimental measures. Model predictions were 7 8 further evaluated against the experimental measurements in terms of mean difference (MD) and standard error (SE) for each clinical measure at each quasi-static lunge TF flexion 9 10 condition. The difference between the first and second halves of the movement were 11 negligible and, therefore, only the downwards portion of the lunge is shown in the graphs.

12

13 Results

14 Kinematics

15 TF (Fig. 5), PF (Fig. 6), and PT (Fig. 7) secondary joint kinematics were examined 16 for the experimental measures (circles) and the FDK model predictions (lines). Most FDK 17 model estimates were comparable to the biplane image reconstructions except in the TF 18 abduction-adduction (AA) and patellar rotation measures (Figs. 5-7). The mean kinematic 19 parameters for each quasi-static lunge condition were extracted for the experimental 20 measures (Table 1) and FDK model predictions (Table 2). ROM mean and standard 21 deviation values between the four lunge conditions were also calculated (Tables 1 & 2).

1	MD and SE between the experimental measures and model predictions are
2	reported in Table 3. Overall, a MD and SE of 2.13 \pm 0.22 mm for translations and 8.57 \pm 0.63 $^{\circ}$
3	for rotations were predicted for all subjects and measures (Table 3). TF translations
4	resulted in a MD of 0.7 \pm 0.23 mm and -0.15 \pm 0.48° for rotations. When investigating the
5	model predicted patellar kinematic rotations, only the PT-AA (MD \pm SE: -1.10 \pm 0.8°) was
6	comparable to the experimental measures. While, the other PT or PF rotational
7	predictions were not captured well by the FDK model (e.g. PF-FE MD±SE: 16.29±0.79° or
8	PF-IE MD±SE: -7.71±0.45°.Fig. 9 and table 3). In addition, PT-AP and PF-SI displacements
9	(MD±SE: 6.30±0.58 mm and 4.58±0.18 mm, respectively) also showed larger mean
10	differences than the other translational measurements.

11 Joint contact forces

Average femoral contact forces (normalized to body weight) at the medial 12 condyle, lateral condyle, and patellar groove were extracted from 0° to 90° TF flexion and 13 recorded in ISB tibial anatomical coordinate systems [46] (Fig. 8). A clear increase in SI-14 15 force (compressive force) was detected for all contact sites with increasing knee flexion. 16 In regards to AP-force, TF contact forces increased and shifted anteriorly, while the PF contact force increased and shifted posteriorly as TF flexion increased. There were no 17 significant changes in ML-force for the TF joint, however the PF ML-force increased and 18 shifted laterally with deeper TF flexion. 19

20 Ligament Forces

Ligament force estimates are presented for the major ligaments of the TF joint (ACL, PCL, LCL and MCL) and PF joint (LEPL, MPFL, and LTL) in Figures 9 and 10 respectively.

1	In the model simulations, the anterior lateral ligament did not contribute to the knee
2	stability and the posterior capsule produced only small forces near full extension, so are
3	not displayed. The ACL, LCL and all PF ligament forces decreased with increasing TF
4	flexion, and the opposite was true for the PCL and MCL. Moreover, despite these trends,
5	there were considerable differences between subjects. Especially for subject-2 (blue in
6	the figures), resulting in larger forces in the ACL, LEPL, LTL and LCL (Figs. 9-10). This may
7	have been due to the larger adduction and internal TF rotations at approximately 80° of
8	TF flexion compared to the other subjects (Fig. 5).
9	

Discussion 10

We have constructed four lower-limb MRI-based subject-specific musculoskeletal 11 models that can concurrently predict muscle forces, ligament forces, contact forces, and 12 secondary joint kinematics. The model estimations were evaluated against experimental 13 measures obtained through biplanar X-ray imaging using slot-scanning technology. The 14 specific goals of this study were to: (1) apply a subject-specific MS modeling workflow 15 based on MRI, motion capture, and force plate data to an enhanced inverse dynamic 16 analysis utilizing the FDK method [2], and (2) evaluate the accuracy of the subject-specific 17 MS models performing a lunge against in vivo kinematic data collected during a quasi-18 static lunge [30]. 19

The TF secondary joint kinematics model estimations were consistent with the in 20 21 vivo experimental measures and to the model predictions reported by Dzialo et al. [30]. 22 Compared to the moving-axis and revolute models developed by the same authors [30],

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1	our model performed slightly better in terms of mean difference and standard error for
2	the ML and AP translations of the TF joint. The FDK model showed displacement ROMs
3	(Table 2) of 1.6±0.92 mm (ML) and 12.35±2.82 mm (AP) which was in agreement with the
4	experimental measures and other biplanar fluoroscopic studies (ML 3.25±1.48 mm,
5	2.5±2.5 mm and 1.5±2 mm, and AP 14.4±5.09 mm, 11.5±4 mm and 16.5±4 mm)
6	[29,30,47], respectively. The same studies reported rotational AA (3.92±2.11°, 2.75±1.5°,
7	and $1.5\pm3^{\circ}$) and IE (11.84 $\pm5.23^{\circ}$, $6\pm6^{\circ}$, and $10\pm5^{\circ}$) ROMs which were consistent with our
8	TF rotational predictions (AA of 4.23±1.76° and IE of 7.34±4.85°, Table 2).
9	The accuracy of the patellar kinematic estimations varied when evaluated with
10	respect to the tibial and femoral coordinate systems. Better agreement was predicted in
11	the ML, SI, and AA (MD±SE: 0.88±0.64 mm, 1.71±0.2 mm and -1.1±0.86°, respectively)
12	when evaluating PT kinematics. While the PF kinematics only showed consistency with
13	the experimental measurements for ML and AP translations (MD±SE: -0.92±0.14 mm and
14	-0.42±0.09 mm, respectively) (Table 3). All PF rotational predictions disagreed with the
15	experimental measures (MD±SE: 16.79±0.79° FE, -7.71±0.45° IE and -10.43±0.33° AA), as
16	well as the PT-FE and IE (MD±SE: 14.73±0.84° and -14.43±0.6° respectively).

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Modeling the patellar ligament as a rigid link between two attachment points may be one of the reasons for the errors in the PF and PT kinematics, which may also affect PF contact forces and ligament strains [48]. In the future, modeling the patellar ligament with more bundles, better representing the thick patellar ligament, may help reduce patellar rotations. Another reason that may have influenced the PF kinematics was the segmented articular cartilage (AC), the border between the femoral and the patellar AC

1 in the MRI was not always obvious. Which may have introduced inaccuracies in our AC 2 segmentation, potentially affecting the PF contact area and thus how the patella tracks in the PF groove. Moreover, the stiffness, slack length, and reference strain of MPFL, LEPL, 3 and LTL ligaments used were defined based on the literature [2]. Marra et. al. introduced 4 5 the stiffness to be in the same range of other known ligaments, while defining the reference strain such that the patellar button always ran along the PF groove. Although 6 7 this choice proved accurate in their model, the geometry of their PF contact was directed 8 by the CAD of the Total Knee Arthroplasty (TKA) [2]. Furthermore, Lenhart et al. [15] used similar ligament parameters and evaluated patellar kinematics during gait against non-9 weight bearing conditions of similar TF flexion. They suggested that PF behavior was more 10 11 dependent on cartilage geometries than on ligament properties, supporting the theory that the AC may play a major role in the predicted PF kinematics and consequently in the 12 13 PF contact forces.

In FDK analysis, the secondary joint kinematics are estimated based on muscle, 14 joint loads, and all elastic forces [14]. Ideally, this would suggest that if the secondary joint 15 kinematics are overall well predicted, then the forces causing these movements should 16 consequently have sufficient accuracy. Marra et al. [2] previously provided evidence of 17 this; and Lenhart et al. [15] using a similar algorithm, achieved secondary joint kinematics 18 19 consistent with in vivo measurements. Although these previous studies have increased the confidence in MS modeling performance; the predicted kinetics using these methods 20 21 in natural knees have only been indirectly validated, not guaranteeing correct estimations 22 [49].

1	Despite differences in movement, the estimated TF and PF contact forces (Figure
2	8) are approximately double that of a squat trial modeled with a natural knee [50] of 1.95
3	BW and 3.78 BW respectively. In addition, Koh et al. (2017) reported the same increasing
4	trend of compressive contact forces relative to knee flexion with extremes occurring at
5	(>85°) flexion angles. Our results are consistent with findings in Trepczynski et al. [51];
6	although they modeled TKA, larger PF compressive forces at higher knee flexion angles
7	were also found. The FDK models estimated a peak PF compressive force of 7.47±1.91 BW
8	at 93.2±1.8° TF flexion, greater than forces reported in the literature [50,51].

PF ligaments were most active during 0 to 50° of TF flexion (Fig. 10). At higher TF 9 flexion angles, the radii of the femoral condyles in contact with the tibia plateaus are 10 smaller, causing the PF ligaments to shorten. This explains why low PF ligament forces 11 occur during higher TF flexion. Examining the TF ligaments, our results support previous 12 13 studies [48,50]; suggesting that the PCL helps stabilize AP translations at TF flexion angles greater than 45°. Interestingly, the mean ACL force from Subject 2 ranged between 100 14 and 212 N at TF flexion angles greater than 60°. For this same subject, an increased 15 internal rotation can be observed compared to the other subjects (Fig. 5), suggesting that 16 the ACL acts to prevent internal rotations at high flexion angles. 17

18 Nonetheless, this study includes some limitations. First, the biplanar X-ray imaging 19 and motion capture experiments were not conducted simultaneously. This was due to the 20 limited space in the EOS scanner. However, to ensure consistency between the two data 21 collections, the relative foot positions were recorded and ensured during each lunge 22 condition. Additionally, the motion capture lunges were performed dynamically in a slow and controlled form. This allowed us to safely assume quasi-static equilibrium and extract
the model kinematics at the same knee flexion angles form the model estimations and
biplane X-ray images. Secondly, the MKO used revolute TF and PF joints as input for the
FDK analysis which could have introduced inaccuracies in the model kinematics. Dzialo et
al. recently demonstrated that predicted secondary joint kinematics differ between
moving-axis and revolute joint models, especially with increasing TF flexion [30].

7 Next, subject-specific ligament parameters were not recorded, so generic 8 ligament parameters were used. In addition, ligament pre-strain had to be tuned for the LCL (+3%) and MCL (+2%) for subject 1 and the PCL (-1%) for subject 3. This was necessary 9 for the FDK residual forces of the model to approach zero and for the model itself to 10 replicate realistic secondary TF joint kinematics and forces when compared to other 11 studies [2,5,6,15]. In the future, we recommend that subject-specific ligament parameter 12 13 estimates from laxity tests be included in hopes of increasing model accuracy [52]. In addition, ligament wrapping surfaces were not included, which are normally used to 14 prevent the ligaments from penetrating the bone or cartilage surfaces. Without such 15 surfaces this could have affected the ligament moment arms and resulted in altered 16 ligament forces. Moreover, ligaments were represented as nonlinear springs, and unable 17 to simulate the 3D deformable characteristic of ligaments. 18

Additionally, the models in our study used generic muscle-tendon parameters, utilizing a length-mass scaling approach to scale the muscle strength from the original TLEM 2.0 to the subject-specific models [45]. Ideally this could have been personalized, for example adjusting the muscle model parameters in relation to experimental isometric

or isokinetic measurements. Such personalization was out of the scope for this project, 1 2 being such a time-consuming process and requiring maximal effort from the subjects that does not always yield realistic results [53]. Other limitations include the potential for 3 inaccuracies during manual segmentation of bones, articular cartilage, and ligaments; and 4 5 furthermore, the manual selection of bony landmarks. Therefore, an additional 6 segmentation review of the regions with high priority in terms of muscle attachment 7 sensitivity should be considered in future studies [12]. Additionally, our knee models did 8 not include the menisci, which are important structures to consider when simulating large-load TF kinematics [54]. It should be noted that the biplane image reconstructions 9 required manual operations, which could have increased the predicted error. The 10 accuracy of TF kinematics using these kind of ICP reconstructions has recently been 11 evaluated by Pedersen et al. [52]. They found a mean difference and limits of agreement 12 (LoA) of (0.08 mm and [-1.64 mm, 1.80 mm]) for translations measures and (0.10° and [-13 0.85°, 1.05°] for rotational measures when comparing reconstructions based on (1) bone 14 marker frames versus (2) the ICP optimization mention above. Furthermore, Pedersen et 15 al. found root mean square errors of 0.88 mm and 0.49° for translational and rotational 16 measures respectively [52]. 17

Extensive studies, requiring hundreds of repeated simulations, would be needed to assess the influence of parameters such as subject-specific geometries or soft tissue mechanical properties. Considering the model simulation time was on average 6 hours per trial, this left a sensitivity analysis out of the scope for this project. The bottleneck in FDK-based inverse dynamics occur when solving for contact, muscle recruitment, and

1 muscle wrapping. Fortunately, a recent study has introduced surrogate modeling to FDK-2 based inverse dynamics, reducing simulation times up to 4.5 min for a single gait cycle [55]. With surrogate modeling, extensive sensitivity studies are more feasible for future 3 researchers. 4 5 In conclusion, we have applied a subject-specific multibody musculoskeletal modeling workflow to the natural knee, capable of simultaneously simulating internal TF 6 7 and PF secondary joint kinematics and contact forces. We have evaluated our subject-8 specific model estimates against experimental data, extracted from biplane X-ray images, from the same subjects. Good agreement was achieved for all TF secondary joint 9 kinematics and PF translations; however, not for PF or PT rotations. The proposed 10 modeling framework provides a powerful tool to simulate individualized knee mechanics 11 and potentially optimize clinical treatments. 12

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1 Figure Captions List

- Fig. 1 Illustration of MRI segmentation, morphing, and landmark identification.
 a) Bone segmentation and 3D reconstruction.
 b) Morphing of the TLEM
 bones (green) to the segmented bones (blue).
 c) Ligament segmentation and 3D reconstruction.
 d) Bony landmark and ligament attachment points selection.
- Fig. 2 Overview of the simulation process. Motion capture data from marker trajectories are input to the MKO that computes joint angles. Joint angles and ground reaction forces and moments are input to the FDK-based inverse dynamics model to compute quasi-static equilibrium in the secondary joint DOF to determine muscle forces, ligament and contact forces, and secondary joint kinematics.
- Fig. 3 The 11 DOF knee from one subject. The model consists of subject-specific bone, ligament, and cartilage structures.
- Fig4.Anatomical coordinate systems. Thigh (green) and shank (red) ISBanatomical coordinate systems. Patellar coordinate system (blue).
- Fig. 5 Estimates of TF secondary joint kinematics from FDK models, mean (line) ± deviation (shaded area), compared to experimental biplanar slot X-ray imaging data measures (circles). Subject 1 (red), subject 2 (blue), subject 3 (green), and subject 4 (cyan).

- Fig. 6 Estimates of PF secondary joint kinematics from FDK models, mean (line)
 ± deviation (shaded area), compared to experimental biplanar slot X-ray imaging data measures (circles). Subject 1 (red), subject 2 (blue), subject 3 (green), and subject 4 (cyan).
- Fig. 7 Estimates of PT secondary joint kinematics from FDK models, mean (line)
 ± deviation (shaded area), compared to experimental biplanar slot X-ray
 imaging data measures (circles). Subject 1 (red), subject 2 (blue), subject 3
 (green), and subject 4 (cyan).
- Fig. 8 Mean contact forces (lines) and deviations (shaded areas) for each contact site in the tibial ISB anatomical coordinate system. Forces normalized to body weight (BW) and related to knee flexion angle. Subject 1 (red), subject 2 (blue), subject 3 (green), and subject 4 (cyan).
- Fig. 9 TF ligaments forces. ACL = anterior cruciate ligament, PCL = posterior cruciate ligament, LCL = lateral collateral ligament and MCL = medial collateral ligament. Subject 1 (red), subject 2 (blue), subject 3 (green), and subject 4 (cyan).
- Fig. 10 PF ligaments forces. MPFL = medial PF ligament, LEPL = lateral epicondylopatellar ligament and LTL = lateral transverse ligament. Subject 1 (red), subject 2 (blue), subject 3 (green), and subject 4 (cyan).

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1 Figure 1.



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- 1 Figure 4.
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1 Figure 5.



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1 Figure 7.



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1 Figure 8.



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1 Figure 10.

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1 Table 1. Biplanar slot X-ray imaging experimental measures (mean ± standard deviation)

2 at each quasi-static lunge position and overall ROM for each clinical measure.

Tibiofemoral	Translations (mn	n)		Rotations (°)				
Condition	ML	AP	SI	AA	IE	_		
20° Flexion	2.29 ± 1.18	1.30 ± 2.57	38.00 ± 3.19	1.01 ± 2.16	7.11 ± 2.32	_		
45° Flexion	2.16 ± 0.58	6.86 ± 3.94	37.42 ± 1.86	-0.35 ± 1.16	9.63 ± 3.93			
60° Flexion	2.45 ± 1.24	9.43 ± 5.19	36.66 ± 2.44	-1.37 ± 1.13	8.47 ± 2.98			
90° Flexion	2.91 ± 2.58	14.05 ± 3.49	34.51 ± 2.42	-2.30 ± 1.69	9.84 ± 5.24			
Average (20°-90°)	2.45 ± 1.60	7.91 ± 6.04	36.65 ± 2.85	-0.75 ± 2.01	8.76 ± 3.94			
ROM	2.08 ± 1.05	12.75 ± 2.43	3.82 ± 1.79	3.72 ± 1.87	6.09 ± 3.10			
					.05	_		
Patellotibial	Translations (mn	n)		Rotations (°)		_		
Condition	ML	AP	SI	FE	IE	AA		
20° Flexion	5.16 ± 3.48	49.29 ± 3.30	48.96 ± 3.69	23.52 ± 9.86	4.83 ± 4.14	-12.53 ± 3.89		
45° Flexion	8.14 ± 1.95	40.85 ± 4.86	49.68 ± 3.17	30.85 ± 3.04	-2.21 ± 3.40	-12.51 ± 6.35		
60° Flexion	8.44 ± 0.92	36.18 ± 6.54	49.55 ± 3.19	34.65 ± 3.80	-1.24 ± 4.43	-12.83 ± 2.76		
90° Flexion	8.66 ± 1.16	27.27 ± 6.49	49.41 ± 3.32	38.67 ± 2.08	-2.22 ± 5.18	-12.21 ± 4.31		
Average (20°-90°)	7.60 ± 2.56	38.40 ± 9.66	49.40 ± 3.36	31.93 ± 7.90	-0.21 ± 5.24	-12.52 ± 4.52		
ROM	5.66 ± 1.84	22.20 ± 6.18	1.77 ± 0.39	17.09 ± 8.11	10.38 ± 3.87	9.67 ± 2.92		
			X					
Patellofemoral	Translations (mn	n)	.0	Rotations (°)				
Condition	ML	AP	SI	FE	IE	AA		
20° Flexion	2.24 ± 2.19	50.77 ± 1.28	-10.33 ± 8.78	-0.11 ± 10.36	5.79 ± 3.53	-3.38 ± 3.70		
45° Flexion	3.19 ± 1.47	41.27 ± 5.38	-27.38 ± 7.43	-16.75 ± 6.74	1.38 ± 1.90	-3.10 ± 6.14		
60° Flexion	4.30 ± 1.46	34.47 ± 3.18	-33.79 ± 4.98	-25.28 ± 2.57	3.49 ± 1.16	-2.01 ± 4.24		
90° Flexion	5.17 ± 1.54	21.16 ± 6.33	-39.62 ± 4.17	-43.01 ± 6.73	1.94 ± 0.62	-0.33 ± 4.09		
Average (20°-90°)	3.72 ± 2.02	36.92 ± 11.68	-27.78 ± 12.80	-21.29 ± 17.04	3.15 ± 2.71	-2.21 ± 4.79		
ROM	3.87 ± 1.53	29.60 ± 5.98	29.29 ± 5.12	42.90 ±10.53	5.38 ± 2.51	8.31 ± 3.29		

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1 Table 2. FDK model estimates (mean \pm standard deviation) at each quasi-static lunge

2 position and overall ROM for each clinical measure.

Tibiofemoral	Translations (mm)	I		
TF angle	ML	AP	SI	AA	IE
20° Flexion	1.01 ± 0.17	-0.82 ± 1.73	38.20 ± 0.21	3.82 ± 0.20	3.96 ± 2.19
45° Flexion	2.20 ± 0.28	3.89 ± 0.75	38.13 ± 0.09	1.36 ± 0.18	8.19 ± 1.33
60° Flexion	2.48 ± 0.27	7.49 ± 1.03	37.61 ± 0.13	0.53 ± 0.20	8.43 ± 1.35
90° Flexion	2.50 ± 0.19	11.53 ± 1.43	35.37 ± 0.14	-0.38 ± 0.32	7.39 ± 2.85
Average (20°-90°)	2.05 ± 0.23	5.52 ± 1.23	37.33 ± 0.14	1.33 ± 0.22	7.00 ± 1.93
ROM	1.60 ± 0.92	12.35 ± 2.82	3.19 ± 1.86	4.23 ± 1.76	7.34 ± 4.85
					0

Patellotibial	Translations (mm)		Rotations (°)		_
TF angle	ML	AP	SI	FE	IE	AA
20° Flexion	1.17 ± 2.17	55.25 ± 1.79	45.04 ± 1.18	9.21 ± 4.47	14.80 ± 1.66	-3.68 ± 2.80
45° Flexion	7.97 ± 1.24	47.88 ± 0.80	48.15 ± 0.27	15.36 ± 1.07	14.74 ± 1.27	-12.05 ± 1.18
60° Flexion	9.00 ± 1.01	42.21 ± 1.03	48.76 ± 0.18	19.36 ± 1.02	14.13 ± 0.97	-14.60 ± 1.22
90° Flexion	8.73 ± 1.32	33.42 ± 1.52	48.83 ± 0.12	24.87 ± 0.98	13.23 ± 1.49	-15.36 ± 2.48
Average (20°-90°)	6.72 ± 1.43	44.69 ± 1.29	47.69 ± 0.44	17.20 ± 1.88	14.22 ± 1.35	-11.42 ± 1.92
ROM	8.21 ± 4.82	21.82 ± 6.32	3.97 ± 2.33	15.65 ± 4.57	4.71 ± 1.82	11.85 ± 3.41

Patellofemoral	Translations (mm)	×	Rotations (°)		
TF angle	ML	AP	SI	FE	IE	AA
20° Flexion	1.47 ± 0.59	52.39 ± 0.33	-15.65 ± 1.19	-14.86 ± 4.36	9.84 ± 1.69	4.75 ± 0.77
45° Flexion	4.51 ± 0.13	42.12 ± 0.15	-32.00 ± 0.18	-33.85 ± 0.93	11.94 ± 1.18	7.28 ± 0.43
60° Flexion	5.67 ± 0.24	34.81 ± 0.18	-38.32 ± 0.16	-42.61 ± 0.88	11.91 ± 0.67	8.84 ± 0.59
90° Flexion	6.92 ± 0.29	20.03 ± 0.15	-43.49 ± 0.12	-59.00 ± 0.87	9.76 ± 0.46	12.02 ± 1.12
Average (20°-90°)	4.64 ± 0.31	37.34 ± 0.20	-32.36 ± 0.41	-37.58 ± 1.76	10.86 ± 1.00	8.22 ± 0.73
ROM	5.45 ± 1.87	32.36 ± 4.69	27.84 ± 4.58	44.14 ± 6.85	5.20 ± 2.33	7.77 ± 2.36

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- 2 Table 3. Mean differences ± standard error between model predictions and biplanar slot
- 3 X-ray imaging experimental measures.

Tibiofemoral	Translations (r	mm)		Rotations (°)		
TF angle	ML	AP	SI	AA	IE	
20° Flexion	1.28 ± 0.07	2.13 ± 0.77	-0.19 ± 0.10	-2.81 ± 0.09	3.15 ± 0.98	
45° Flexion	-0.05 ± 0.12	2.97 ± 0.34	-0.71 ± 0.04	-1.71 ± 0.08	1.44 ± 0.59	
60° Flexion	-0.02 ± 0.12	1.93 ± 0.46	-0.95 ± 0.06	-1.89 ± 0.09	0.03 ± 0.60	
90° Flexion	0.41 ± 0.08	2.52 ± 0.64	-0.86 ± 0.06	-1.92 ± 0.14	2.45 ± 1.27	
Average (20°- 90°)	0.41 ± 0.10	2.39 ± 0.55	-0.68 ± 0.06	-2.08 ± 0.10	1.77 ± 0.86	
					0	
Patellotibial	Translations (r	nm)		Rotations (°)	_	
TF angle	ML	AP	SI	FE	IE	AA
20° Flexion	3.98 ± 0.97	-5.96 ± 0.80	3.92 ± 0.53	14.31 ± 2.00	-9.96 ± 0.74	-8.84 ± 1.25
45° Flexion	0.17 ± 0.56	-7.03 ± 0.36	1.54 ± 0.12	15.49 ± 0.48	-16.94 ± 0.57	-0.46 ± 0.53
60° Flexion	-0.55 ± 0.45	-6.04 ± 0.46	0.80 ± 0.08	15.29 ± 0.45	-15.37 ± 0.43	1.77 ± 0.55
90° Flexion	-0.07 ± 0.59	-6.16 ± 0.68	0.58 ± 0.05	13.81 ± 0.44	-15.45 ± 0.67	3.15 ± 1.11
Average (20°- 90°)	0.88 ± 0.64	-6.30 ± 0.58	1.71 ± 0.20	14.73 ± 0.84	-14.43 ± 0.60	-1.10 ± 0.86

Patellofemoral	Translations (mm)		Rotations (°)		
Angle	ML	AP	SI	FE	IE	AA
20° Flexion	0.77 ± 0.26	-1.63 ± 0.15	5.31 ± 0.53	14.75 ± 1.95	-4.05 ± 0.76	-8.14 ± 0.35
45° Flexion	-1.32 ± 0.06	-0.85 ± 0.07	4.61 ± 0.08	17.10 ± 0.42	-10.56 ± 0.53	-10.38 ± 0.19
60° Flexion	-1.37 ± 0.11	-0.34 ± 0.08	4.52 ± 0.07	17.33 ± 0.39	-8.41 ± 0.3	-10.85 ± 0.26
90° Flexion	-1.75 ± 0.13	1.13 ± 0.07	3.87 ± 0.05	15.99 ± 0.39	-7.82 ± 0.20	-12.36 ± 0.50
Average (20°-90°)	-0.92 ± 0.14	-0.42 ± 0.09	4.58 ±0.18	16.29 ± 0.79	-7.71 ± 0.45	-10.43 ± 0.33

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APPENDIX

3 A) Motion Capture

The simulations used in the study were driven by motion capture data that was recorded 4 by an eight infrared high-speed cameras system (Oqus 300 series, Qualisys, Gothenburg, 5 Sweden) which captured 30 retroreflective markers that were placed on bony landmarks 6 (Fig. 1). Each subject performed one static standing trial and 3-4 slow dynamic lunges to 7 approximately 90 degrees of tibiofemoral flexion. In order to drive the model, 17 markers 8 were needed, the rest were excluded. Each of the Markers seen in figure 14 were 9 assigned a label accordingly to the anybody standard using Qualisys Track Manager 10 (QTM). Trials with marker drop outs below 10 percent were gap-filled with a polynomial 11 interpolation function by using the in-built gap-fill trajectory with preview tool in QTM. 12 In trials with marker gaps above 10 percent, the marker was excluded and noted in a 13 14 spread sheet to remove the marker in the specific trial in AMS.

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Figure 1: Marker placement for the motion capture trials.

3 B) Imaging

4 The subject-specific multiscale model is based on MRI's. Subjects underwent two 5 different MRI protocols to gather the necessary data for creating detailed subject-6 specific models, and biplane X-Ray images to evaluate the simulations' performance.

7 B.1) Lowerlimb Magnetic Resonance Imaging

8	In the Lowerlimb MRI scans, the subjects were scanned from pelvis to feet using a 1.5 T
9	OptimaTM MR450W - 70 cm (General Electric Healthcare, Chicago, Illinois, USA) scanner
10	running a T1W-LAVA-XV IDEAL coronal plane scan. The subjects were scanned in three
11	overlapping sections, which were stitched together to make up the lower limb series.

1 B.2) Detailed knee Magnetic Resonance Imaging

- To create the detailed knee scans the subjects underwent MRI scans with a General
 Electric 3T (General Electric Healthcare, Chicago, Illinois, USA) scanner running five
 different protocols: COR PD, SAG 3D, SPGR IDEAL, COR 3D SPGR FS, SAG T1 and SAG PD
 FS (nomenclature in table 1).
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- 7

	Table 1: Table with MRI Acronyms						
MRI Acronyms	Meaning						
W	Weighted image						
LAVA-XV	Volume interpolated gradient echo						
IDEAL	Fat-Water separation						
PD	Proton density						
FS	Fat suppression						
TE	Echo Time						
TR	Repetition Time						
T1	Short TE and TR times						
Т2	Longer TE and TR times						
SPGR	Spoiled Gradient Echo (produces T1 images in 3D)						

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10 **B.3) Biplane X-ray images**

The biplane X-ray images were creates using EOS[™] biplanar X-ray system. The system
enables partial or full-body imaging creating continuous, distortion-free images in two
orthogonal planes. The subjects performed static lunges at tibiofemoral flexion angles of
0, 20, 45, 60 and 90 degrees. At each angle a pair of orthogonal X-ray images were taken.

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1 C) Segmentation and morphing





Figure 2: A) MRI Coronal view: Showing a mask of the left pelvis in one slice B) MRI Axial view: Showing a mask of the left pelvis in one slice C) Segmented lower limb 3D View.

In order to match the coordinate system of the Lowerlimb MRI bones to the detailed MRI bones segmented, the Lowerlimb MRI bones were aligned to the detailed bones using either the inertia axis alignment or the point registration tool. The Anybody source bones STLs were then imported into Mimics and morphed to the Lowerlimb's geometry using the 3D Mapping tool, with the parameters shown in table 2.

Table 2: Parameter settings in the morphing tool for the bones.

	Talus	Tibia	Fibula	Patella	Femur	Pelvis
Tolerance	0.005	0.005	0.05	0.005	0.005	0.05
Percentage	77	99	40	99	99	99
Gamma	0.56	0.90	0.50	0.05	0.05	0.5
Gamma	0.3	1.0	0.2	1.0	1.0	0.8
rate						6
Angle	90	90	20	90	90	60

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The incomplete right foot segmentation could not be morphed, and therefore the right foot STL was imported into Meshlab 2016.12 (ISTI-CNR, Italy) where the pick point selection tool was used to select 16 points on the bone surface (Fig. 3). The points where later used in the Anybody Modelling System (AMS, Anybody Technology, Denmark) to scale the foot model through an affine transformation.







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2 D) Surface Selections

3 All segmented objects except the foot were imported into 3-Matic Research v 11.00 (Materialise, Belgium). The lasso area mark tool was used to select bony landmarks, 4 5 contact surfaces and ligament attachment points on the segmented objects surfaces. The attachment points of the anterior cruciate ligament, medial collateral ligament, lateral 6 collateral ligament, posterior cruciate ligament, medial patellofemoral ligament, lateral 7 8 epicondylopatellar ligament and lateral transverse ligament were manually selected 9 based on the detailed knee MRIs ligament segmentations and used to select the ligament attachment points on the subjects-specific bone surfaces in 3-Matic. The posterior 10 11 capsule and anterior lateral ligament attachment sites were selected according to descriptions found in the literature. 12

- 13 E) Ligament parameters
- 14
- 15 Ligament stiffnesses and reference strains used in the simulations are shown in table 3.
- 16 17

Table 3: Ligament parameters used in the FDK natural knee model.

	Sub	ject 1	Subject 2		Subject 3		Subject 4	
Ligament	Stiffness	Reference	Stiffness	Reference	Stiffness	Reference	Stiffness	Reference
Bundle	(N)	strain (-)						
ACL _{lat}	2500	0.06	2500	0.06	2500	0.06	2500	0.06
ACLmed	2500	0.06	2500	0.06	2500	0.06	2500	0.06
ACL_{medP}	2500	0.10	2500	0.10	2500	0.10	2500	0.10
ACLIatP	2500	0.10	2500	0.10	2500	0.10	2500	0.10
PCLmed	6000	-0.02	6000	-0.02	6000	-0.03	6000	-0.02
PCLmid	6000	-0.02	6000	-0.02	6000	-0.03	6000	-0.02
PCL _{lat}	6000	-0.02	6000	-0.02	6000	-0.03	6000	-0.02
MCLant	2750	0.01	2750	-0.01	2750	-0.01	2750	-0.01

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MCL _{mid}	2750	0.01	2750	-0.01	2750	-0.01	2750	-0.01
MCLpos	2750	0.07	2750	0.05	2750	0.05	2750	0.05
LCLpos	3000	0.06	3000	0.03	2000	0.03	3000	0.03
LCLant	3000	0.20	3000	0.17	2000	0.17	3000	0.17
PT	∞	0	∞	0	∞	0	∞	0
ALLpos	2000	0.03	2000	0.03	2000	0.03	2000	0.03
ALLant	2000	0.03	2000	0.03	2000	0.03	2000	0.03
PCmed	1000	0.07	1000	0.07	1000	0.07	1000	0.07
PCmidM	1000	0.07	1000	0.07	1000	0.07	1000	0.07
PCmidL	1000	0.07	1000	0.07	1000	0.07	1000	0.07
PClat	1000	0.07	1000	0.07	1000	0.07	1000	0.07
	2000	0.12	2000	0.12	2000	0.12	2000	0.12
MPFLmid	2000	0.08	2000	0.08	2000	0.08	2000	0.08
MPFLinf	2000	0.08	2000	0.08	2000	0.08	2000	0.08
LEPL	1000	0.06	1000	0.06	1000	0.06	1000	0.06
LTL _{sup}	1000	0.06	1000	0.06	1000	0.06	1000	0.06
LTL _{mid}	1000	0.06	1000	0.06	1000	0.06	1000	0.06
LTLinf	1000	0.06	1000	0.06	1000	0.06	1000	0.06

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