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Effects of population variability on knee loading during simulated human gait

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Abstract

Cadaveric simulation models allow researchers to study native tissues *in situ*. However, as tests are conducted using donor specimens with unmatched kinematics, techniques that impose population average motions are subject to deviation from true physiologic conditions. This study aimed to identify factors which explain the kinetic variability observed during robotic simulations of a single human gait motion using a sample of human cadaver knees. Twelve human cadaver limbs (58 ± 16 years) were subjected to tibiofemoral geometrical analysis and cyclical stiffness testing in each anatomical degree of freedom (DOF). A simulated gait motion was then applied to each specimen. Resulting kinetics, specimen geometries, and various representations of tissue stiffness were reduced to functional attributes using principal component analysis and fit to a generalized linear prediction model. The capacity of knee topography to generate force was the largest contributor to kinetic variation in compression. Overall joint size, femoral notch height, translational laxity, and ad/abduction stiffness significantly contributed to kinetic variation in medial/lateral and anterior/posterior forces and associated torques. Future studies will investigate customizing kinematic paths to better simulate native conditions and reduce sampling variation, improving biomechanical test methods and evaluation strategies for future orthopedic techniques.

Key Terms

robotic manipulation; knee mechanics; cadaveric simulation; principal component analysis; variability

3. INTRODUCTION

Current methods of knee repair or reconstruction continue to result in long-term failure and/or premature onset of osteoarthritis.^{27, 42} This is likely related to the inability of current

repair methodologies to fully reproduce *in vivo* functionality across all six degrees of freedom at the knee during simulated clinical tests.⁵ These disparities may be further exacerbated by more dynamic loading tasks, for which functional requirements have not yet been adequately quantified following repair or reconstruction.^{5, 6, 8, 9} Measuring intra-articular function and mechanics *in vivo* is highly invasive and there is risk that sensing equipment will alter the native environment.^{11, 12} Therefore, the most efficacious method that researchers have employed to establish benchmarks and design criteria and evaluate repair functionality is *in vitro* investigation.^{6, 10, 20, 26}

Kinematic simulations of activities of daily living (ADLs) applied to tissues *in vitro* allows researchers to develop functional tissue engineering parameters (FTEPs) for knee structures in a physiologic context.^{3, 7-9, 15, 23, 24, 36} However, cadaver specimens are pooled from a wide variety of donors and encompass a vast population, even when specific criteria are disseminated. Furthermore, it has been demonstrated that variability and chaotic variation are pervasive and necessary to human movement.⁴¹ Therefore, a generalized test method using averaged kinematic data will likely not achieve precise physiological representation for every donor. Indeed, investigators have previously examined if individual anatomical measurements correlated with knee kinetics and kinematics in order to compensate for between-specimen variability during robotic simulations.⁴ It was concluded that these models failed to account for enough of the variance to serve as clinical predictors. Accordingly, more complex and potentially non-linear statistical methods may be required to model between specimen variability during motion tasks.⁴¹ Variability among the donor population can lead to statistically insignificant results and mask treatment effects.¹⁴ Multiple investigators have reported difficulty in managing variability between and within treatment groups when measuring joint kinematics and kinetics.¹³

While anthropometric models failed to clinically predict knee kinetics and kinematics, they did exhibit statistically-significant correlations with these outcomes.⁴ Similarly, anterior knee laxity has been correlated with the magnitude of anterior tibial translation during weight-bearing and ACL strain during astrometry exams.^{29, 40} Neither factor is enough to predict knee kinetic or kinematics individually, but they both have been shown to play definitive roles in the variability of these outcome between subjects. It was recently demonstrated that the combination of anterior tibial translation and axial rotation into a single biomechanical factor could improve the prediction of patient satisfaction following knee reconstruction.¹⁸ Therefore, the authors hypothesize that condensing and combining anatomical and laxity factors into principal component groups may be an effective strategy to account for variability and disseminate results of *in vitro* knee biomechanics. This strategy is similar to another recent study linking latent profile analyses clustered risk factors to athletes deemed most likely to preferentially benefit from core-stability-based interventions *in vivo*.²⁵

Robotic simulation of kinematics on cadaveric knee joints to assess the performance of ACL reconstruction grafts relative to the native knee has been performed in dozens of investigations in the past 20 years.⁵ These investigations have addressed many aspects of efficacy including graft type,^{16, 17} fixation method,^{30, 32, 33} tunnel placement location,^{28, 35, 43} bundle technique,^{21, 37, 44} and more. However, these investigations have not

explicitly considered how individual specimen variability in anatomical geometry, joint stiffness, and structural mechanical properties may confound outcomes. Identification of principal sources of variability in laboratory studies have the potential to eventually lead to the optimization of clinical treatments, by making patient-specific recommendations such as tweaking ACL reconstruction graft placement or implant total knee arthroplasty orientation relative to pre-defined, patient-specific variables.

To mitigate population variability effects, researchers must identify which donor attributes that lead to wide variations in the physiologic properties of interest and tailor *in vitro* tests towards meeting native circumstances and constraints for each specimen. Physical and material properties may impact studies such that test methods do not represent a physiologic condition for every specimen. Previous studies have attempted to leverage donor data by establishing linear correlations between anthropometric variables and knee kinematics, but have not proven robust enough to predict performance during *in vivo* athletic tasks.⁴ Therefore, this study takes a unique, model-driven approach to investigate an even broader range of factors in order to identify key factors of human knee joints which lead to the most kinetic variability for a standard simulated gait motion. Effects of human tibiofemoral geometry and 6-degree-of-freedom (6DOF) knee stiffness on 6DOF kinetic outputs were considered. It was hypothesized that both specimen size and stiffness would be predictive of resulting loads.

4. MATERIALS and METHODS

Anatomic Geometry

Twelve (12) fresh frozen human cadaver limbs (4 male, 8 female, 58 ± 16 years, 171 ± 49 lbs) were frozen at -20°C , thawed 24 hours before testing, and dissected free from all soft tissues, leaving the cruciate and collateral ligaments, menisci, and joint capsule intact. A coordinate measurement machine (CMM, Faro Digitizer F04L2, FARO Technologies Inc., Lake Mary, FL), probed anatomic landmarks to measure geometries and define the joint coordinate system.²² Landmarks were selected on both the tibial plateau and femoral condyles to encompass anatomic descriptors of the entire tibiofemoral interaction (Figure 1 & 2: Landmarks). From these landmarks, a custom MATLAB program calculated dimensions and surface areas suspected to most influence gait kinetics (Figure 1 & 2).

Recording 6DOF Stiffness

Specimens were placed on the end effector of a 6DOF robot (KR210; Kuka Robotics Corp., Clinton Township, MI) for testing. Using the CMM, the coordinate system of the tibia was aligned to a 6-axis load cell (Theta Model FT5498; ATI Industrial Automation, Apex, NC) attached to the end effector and the femur was rigidly fixed to a testing platform. This allowed the robot to manipulate the tibia about the femur. The limb was placed at 60 degrees of flexion, corresponding to the peak flexion during the swing phase of gait.³¹ This angle was chosen to minimize the risk of meniscal impingement and maximize the resolution of forces and torques measured. Once at 60 degrees, a custom force/torque controlled program explored the passive envelope of the knee between $\pm 100\text{N}$ and $\pm 10\text{Nm}$ until the center of laxity in each of the remaining DOFs was achieved. The program then cycled the knee

between positive and negative limits in each DOF, recording simultaneous 6DOF loads and displacements (Figure 3). This resulted in 6 sets of 6 hysteresis curves, one set for each DOF. Stiffness terms describing load changes in the same DOF of motion are referred to as main stiffnesses, and stiffness terms describing load changes in a DOF other than the direction of motion are referred to as cross-coupled stiffnesses.

Recording Gait Kinetics

All specimens underwent identical gait kinematics (Figure 4).¹⁴ Following stiffness testing, specimens were oriented relative to peak flexion during mid-stance and adjusted to produce a zero force condition before applying one cycle of gait motion. Initial compressive load was then increased until the peak compression achieved during a single gait cycle reached two times body weight, which was representative of the average load experienced by patients who underwent a total knee replacement.³⁴ In this manner, the application of compressive force was meant to mimic the pattern fluctuation observed on a single limb *in vivo*. Further details of the setup procedure can be found in literature.^{6, 9, 12, 17}

Each specimen was cycled through gait 20 times. Only the last 10 cycles were analyzed to minimize viscoelastic effects. During cycling, the load cell captured the forces and torques experienced by the knees about the defined joint center point. Testing was conducted on de-identified cadaveric subjects and did not meet federal standards to be classified as human subjects research; therefore, it did not require approval from the University of Cincinnati Institutional Review Board as stated in their policy.

Geometrical Analysis

Calculated dimensions of both the tibia and femur were combined to compose a data set of 21 geometries for each specimen. To reduce DOFs and identify the driving source of geometric variation, principal component analysis (PCA) was performed using the “prcomp” function within R 3.0.2 (The R Foundation, Vienna, Austria).^{1, 2} The first two principal components (g1, g2), accounting for 80% of the geometric specimen variability, were chosen to be representative of geometric differences for predictive modeling.

Stiffness Analysis

Stiffness hysteresis curves were recorded as load (N or Nm) over distance (mm or degrees of rotation; Figure 5). Due to highly non-linear response during cyclic stiffness testing, 5 different methods were used to analyze the resulting hysteresis curves. All 5 analytic methods are presented and discussed as part of a holistic approach to data interpretation. Each method is considered experimental for this application and further studies are needed to determine which is(are) most repeatable and reliable for describing knee joint kinetics.

1. Symmetric Linearized—Discrete quantification of stiffness in spinal segments has previously been described.¹⁰ This method utilizes matrix algebra and least squares to identify linear stiffness coefficients from hysteresis data. It results in a 6×6 stiffness matrix representing the relationship between load and displacement in each anatomical DOF. However, the solution requires that the resulting stiffness matrix be symmetric. Therefore, data points from each cross-coupled curve were combined with inverse cross-coupled values

(e.g. A/P force during M/L motion with M/L force during A/P motion) to calculate the linear stiffness estimates describing the overall loading interactions of 2 DOFs. A total of 21 terms were generated, which could be arranged into a symmetric stiffness matrix, describing the relationship of force and displacement for each specimen. These terms were subjected to PCA, as described above. The first three principal components, (s1, s2, s3), accounting for 82% of the variability in stiffness, were chosen to be representative of specimen stiffness differences for predictive modeling.

2. Linearized—This method utilized the “polyfit” function of MATLAB R2012a (The MathWorks, Inc., Natick, MA) to estimate a linear fit to each hysteresis curve. This allowed cross-coupled terms to remain separate from their inverses so that linearized stiffness values were estimated for each main and cross-coupled hysteresis curve. The result generated 36 terms which were subjected to PCA. The first three principal components, (s1, s2, s3), accounting for 74% of the variability, were chosen to be representative of stiffness differences for predictive modeling.

3. Split Linearized—This method is the same as above except that both main and cross-coupled terms were split into their positive and negative components of cyclic motion (e.g. anterior movement was considered separately from posterior movement). This broke the hysteresis curves apart at the center of laxity, and estimates of linearized stiffness coefficients were calculated for each segment using the polyfit function. 72 terms were generated and subjected to PCA. The first three principal components, (s1, s2, s3), accounting for 63% of the variability, were chosen to be representative of stiffness differences for predictive modeling.

4. Averaged Split Linearized—After split linearized terms were generated, both positive and negative halves of the hysteresis curves were brought together again by averaging the absolute values of each side. While this technique allowed stiffness data to be represented in fewer terms, it resulted in missing sign data. 36 terms were generated and subjected to PCA. The first three principal components, (s1, s2, s3), accounting for 68% of the variability, were chosen to be representative of stiffness differences for predictive modeling.

5. Spline Modeling—To better represent the knee’s frequently nonlinear response to uniaxial motion, each of the 36 hysteresis curves generated during stiffness testing were modeled with sequential 4th order beta splines using the functional data analysis, “fda”, package of R.^{1, 2} Hysteresis load data were converted to percent body weight (% BW) for normalization. Three nodes defined the models at the negative extremes, center of laxity, and positive extremes, allowing a total of 5 beta coefficients to fully describe and differentiate each hysteresis curve (Eq. 1, Figure 6). High beta coefficients translate to high load values surrounding its location on the displacement axis. Betas 1 and 2 describe loads during the negative direction of motion while betas 4 and 5 describe loads during the positive direction of motion. The third beta coefficient was discarded, as it corresponded to the load at the center of laxity, which was normalized to zero for each model. Betas 1, 2, 4, and 5 from each of the 36 hysteresis models comprised a data set of 144 terms describing non-linear stiffness behavior. However, because of normalization, variation in all of the main stiffness hysteresis

curves was driven by body weight and not factors of interest. Consequently, beta coefficients from main curves were excluded from this analysis. The remaining 120 terms were subjected to PCA. The first three principal components, (s1, s2, s3), accounting for 68% of the variability, were chosen to be representative of non-linear stiffness differences for predictive modeling.

Gait Simulation Analysis

Gait kinetics were averaged over each cycle and expressed as load (% BW) across a normalized gait cycle (% Gait) for each of the 6DOFs (Figure 7). Metrics chosen for analysis were 1. Overall range of load, 2. Average load, 3. Load at simulated heel strike, 4. Load at driving phase of stance, 5. Load at toe-off, and 6. Load at peak flexion. These metrics stored for each of the 6DOFs generated 36 total terms describing specimen gait kinetics. As with previous specimen factors, these response measures were subjected to PCA to reduce DOFs and to identify the driving source of dynamic loading variation. The first three principal components, (K1, K2, K3), accounting for 79% of the variability, were chosen to be representative of dynamic gait loading differences for predictive modeling.

Predictive Modeling

By relating donor characteristics (joint size and stiffness) to joint kinetics through generalized linear models (GLMs), we may identify potential predictors of dynamic gait variation. Several types of GLMs were explored using the “lm” function of the built-in stats package of R. These types included GLMs generated by size predictors only (g1, g2), stiffness predictors only (s1, s2, s3), and a combination of both size and stiffness predictors (g1, g2, s1, s2, s3). See Table 3 for the full matrix of PC factors included in each GLM of the 3 gait kinetic PCs. GLMs were then optimized to include the most predictive subset of both the geometric and stiffness factor PCs by using the “leaps” package in R. 2, 3 14, 17 This function performs an exhaustive search for the best subsets of potential regressors using a branch-and-bound algorithm. This approach both simplified the models and allowed us to explore usage of each of the stiffness analysis techniques to identify the most appropriate for predicting dynamic loading response during physiologic motion.

Each model was evaluated by its adjusted R^2 term, calculating from it the Pearson's correlation coefficient (R), and P -value. As this study is exploratory in nature, significant factors were identified with an alpha value of 0.10.

5. RESULTS

Principal Components

PCA of the selected metrics of recorded gait kinetics revealed that the largest contributor to kinetic variation was a factor representing compression forces at simulated heel strike and stance-phase along with the associated A/P force and Ad/Ab torque ranges. This factor (K1) accounted for 31% of the variation within the analysis. The second highest contributor (K2, 25%) represents the average medial/lateral (M/L) force and associated internal/external (I/E) torques across gait, and the third (K3, 23%) represents the average anterior/posterior (A/P) force and associated flexion/extension (F/E) torques.

PCA of geometric properties of the tibiofemoral interaction revealed that the largest contributors to geometric variation were properties describing the overall joint size along with femoral notch height. The first principal component (g1) could be considered a scale factor, accounting for 64% of the total variation and containing properties such as total area of the tibial plateau, condyle depth, and condyle width. PC2 (g2) is clearly identifiable as a notch height factor, accounting for 16% of the variation and containing only lateral, medial, and average notch heights. Summaries and interpretations of principal components for specimen gait kinetics and joint geometries/stiffness can be found in Table 2.

Results of the 4 linear stiffness estimation techniques showed consistent PCA results across each technique. Each identified main and cross-coupled translational stiffness as the primary principal component (s1), cross-coupled stiffness (especially between transverse and sagittal plane DOFs) as the secondary principal component (s2), and cross-coupled terms of adduction/abduction stiffness as the tertiary principal component (s3). Together, these three PC's were found to consistently contribute to ~70% of the sample stiffness variation observed across linear stiffness estimation techniques. Table 1 details the results of specimen stiffness PCA according to each linearized modeling technique.

Results of the spline modeled stiffness data revealed similar proportions (33%, 20%, and 16% respectively) but with slight differences in the interpretation of the primary PC, s1. Spline modeled s1 was found to represent cross-coupled terms of A/P and Ad/Ab stiffness during M/L translation, while s2 and s3 still represented transverse and sagittal plane interactions and Ad/Ab stiffness in addition to I/E stiffness cross-coupled terms. Overall, s1 still may be interpreted to represent translational laxity, as is recorded in Table 2.

Predictive Modeling

Models generated using only the two geometric PC factors (g1 and g2) did not adequately predict variation in any of the gait kinetics PCs (K1, K2, or K3) and did not identify either geometric PC as significant (Table 3). Models generated using only stiffness factors (s1, s2, and s3) showed the best results using only factors from the spline modeling technique. This model accurately predicts PC1 of gait kinetics, K1, ($R=0.902$, $P<0.001$) with s1 of the spline technique as the significant factor ($P<0.001$). The next best model generated using only stiffness factors from the averaged split linearized technique identified s2 and s3 as significant ($P<0.05$) in predicting K1 ($R=0.716$, $P<0.05$). Models combining geometric and stiffness PCs as factors (g1, g2, s1, s2, and s3) produced the best results when only spline modeled stiffness PCs were used to predict K1 ($R=0.879$, $P<0.05$). However, neither geometric nor stiffness factors were statistically significant in this combined model.

Models generated using the “leaps” function again were most statistically significant when using spline modeled stiffness factors compared to other techniques. K1 was accurately modeled ($R=0.915$, $P<0.01$) by spline stiffness s1 ($P<0.01$), K2 was modeled ($R=0.648$, $P<0.05$) by spline stiffness s2 ($P<0.01$), and K3 was modeled ($R=-0.621$, $P=0.099$) by spline stiffness s3 ($P<0.01$). Models using split linearized stiffness factors showed K2 modeled by split stiffness s2 ($R=0.662$, $P<0.05$, term significance $P<0.01$), K2 modeled by split stiffness s2 and s3 and geometry g1 ($R=0.680$, $P=0.06$, term significance $P<0.05$), and K3 modeled by split stiffness s1 and geometry g1 ($R=0.636$, $P=0.05$, term significance

$P < 0.01$). All other stiffness techniques show s_2 as a predictor of K_1 , and linear and averaged split linearized techniques also identified s_1 and geometry g_1 as predictors of K_3 .

6. DISCUSSION

Results of geometric PCA on anatomic features align with previous research correlating anatomic and kinematic data. Cadaveric simulations of squatting have previously correlated tibiofemoral shape modes to resulting kinematics. The first shape mode described uniform scaling while the second described the J-curve of the condylar radius.¹⁸ This is analogous to geometric PC1 (g_1 , scale factor) and PC2 (g_2 , notch height). Mode 1 accounted for the majority of variation in initial kinematic alignments, ad/abduction rotations, and joined with mode 2 to explain variability in sagittal translations. Similarly, this study found g_1 is a predictor of average A/P forces in the sagittal plane and associated torques.

PCA has effectively analyzed population variability within orthopedic research as systematic review has shown consistent findings among studies of anatomic variability.⁷ This study adds to the literature by investigating the impacts of anatomic variation and joint integrity on resulting dynamic loading patterns. Previous literature only investigated anatomic impacts on kinematics. This kinematic simulation in a repeatable *in vitro* environment showed that kinematic deviations alone do not fully translate to deviations in functional requirements for knee structures. For prediction purposes, joint stiffness metrics were much more powerful.

GLM discrepancies between stiffness modeling methods are driven by the assumptions made in manipulating the hysteresis curves (see Stiffness Analysis). However, without further testing and method validation, it is impossible to determine which assumptions are the most accurate for characterizing joint stiffness. For this reason, all 5 methods are presented to the reader. By analyzing Table 3 holistically across each method, and considering that the spline technique does not include main stiffness effects, results suggest the following relationships persist between gait kinetics and human donor knee joint properties:

- A. $K_1 \sim s_2$, *Compression at loading phases of gait are governed by C/D joint stiffness during transverse planar motions.*
- B. $K_2 \sim s_2 + s_3 + g_1$, *M/L forces during gait are governed by the above plus Ad/Ab joint stiffness and overall joint size.*
- C. $K_3 \sim s_1 + g_1$, *A/P forces during gait are governed by translational joint laxity and overall joint size.*

Interpretation of the generalized linear models concluded that topography of the joint articulation (PC2 of linearized stiffness terms) is related to compression during load bearing segments of activity (PC1 of gait kinetics). This is intuitive as uneven surfaces generate more variable normal loading profiles when articulated and moved with respect to another surface. While the spline-modeled non-linear stiffness terms showed a slightly different result, this technique was difficult to interpret as none of the main stiffness effects were considered in the data. Although joint topography is more of a geometric attribute of the anatomy, none of the calculated geometries encompassed this phenomenon. Stiffness terms

cross-coupled with compressive/distractive stiffness were the most representative of uneven articulations.

The second interpretation was that Ad/Abduction stiffness (PC3 of linearized stiffness terms) is predictive of medial/lateral joint kinetics with associated torques for simulated *in vivo* gait (PC2 of gait kinetics). Ad/Abduction stiffness can be considered the best approximation to overall joint stiffness as geometric features contributed least to load distribution. Variability can primarily be attributed to bone and ligament material properties. Therefore, it is fitting that this type of stiffness is related to medial/lateral force and associated ad/abduction and internal/external torques, as these values are primarily driven by material properties rather than geometric features.

The third interpretation was that translational laxity, including main stiffness contributors (PC1 of linearized stiffness terms), along with a joint size scale factor (PC1 of geometric stiffness) is loosely predictive of anterior/posterior kinetics with associated torques during gait. The larger and looser the joint, the less load will be observed in non-compressive DOFs during motion. Previous studies using this platform noted larger limbs generate less anterior force during simulated heel strike and drive phases of stance because they can accommodate larger ranges of motion as the knee extends.¹⁶ This is a consequence of using one standardized motion to test an entire sample cohort.

These findings have tangible implications for test method development using controlled kinematics to measure *in situ* loading. Smaller specimens likely require a scale factor to the anterior/posterior kinematic DOF to prevent excessively translating the joint past a physiologically-relevant position. This strategy has been employed to dampen skin marker errors in recorded athletic activities and enabled successful simulation of side step cutting and drop vertical jumps on 12 unique cadaveric donors.⁶ The models presented here may be used to develop tailored gait kinematics, according to the same recorded geometries and stiffness attributes, with the goal of recording more consistent and representative joint kinetics for *in vitro* simulations of *in vivo* motion. This will be critical for orthopedic research, where physiologically relevant test methodologies are in paramount.

Clinically, this study reaffirmed the value of joint laxity tests to assess functional deficits and characterize demands specific to individual patients. This value was affirmed in that stiffness tests across specific DOFs (typical of how clinical laxity is assessed) comprised at least a portion of the top three principal components for the linearized, split linearized, and average split linearized analysis methods (Table 1). Using the split linearized method, all three principal components of gait kinetics were best modeled entirely from laxity measurements across various axes (Table 3). Laxity tests such as anterior drawer and Lachman's test are widely used to assess ACL function. While these tests are typically done to diagnose injury, they may also be useful in establishing design criteria for reconstructions customized to the patient's individual joint biomechanics.

The current study has several limitations. PCA was only able to capture between 63% and 82% of the variability between specimens, with stiffness properties being the most difficult to summarize. Models predicting the 2nd and 3rd PCs of gait kinetics (K2 and K3) only

accounted for up to 40% of the variability between specimens. While these levels of cumulative proportion may be insufficient for numerically accurate predictive modeling, relationships between factors (geometries and stiffness) and responses (metrics of gait kinetics) are still directionally valid and aid in identifying key contributors. A second limitation is potential measurement error. While stiffness and gait kinetics were more repeatable with programmable robotics, variation can still arise from slight inconsistencies between limb set-up and orientation. However, initial orientation was controlled to $\pm 1^\circ$ and a previous methodological study demonstrated that small deviations between set-up positions do not induce significant differences in resulting kinetics.⁹ A third limitation of the present study is that the specimen was denuded of muscle tissue. *In vivo*, muscle activation would vary throughout the gait cycle and consequently produce fluctuations in the active stiffness across the knee joint. Accordingly, the current investigation is relative only to the passive stiffness of the joint. Another important limitation of this study is that while *in vivo* motion was simulated, the *in vitro* environment is not an exact replica of *in vivo* properties which may affect biomechanical response. A single gait pathway averaged from several *in vivo* subjects was utilized in this investigation.³¹ Variability in human motion is well established^{19, 41} and force minimization techniques have been used to adapt passive flexion articulations driven by robotic manipulators to the path of least resistance.^{38, 39} However, the precise effects of slight variation in anatomic geometry on kinematic response during an active task such as gait remains undocumented. Accordingly, adjustment of the *in vivo* recorded gait pathway to specimen-specific anatomy in the present study would have been based on speculation and conjecture and was therefore not incorporated in the present model.

Overall this study showed that condensing and combining anatomical and joint laxity factors into principal component groups can provide researchers with a set of donor-driven factors which may serve in interpreting the resulting kinetics of simulated ADLs. While additional studies are needed to more clearly define a preferred analytical method for characterizing joint stiffness, this study provides several proofs of concept with results pointing to specific elements of what we already suspected about the relationship between knee joint laxity and kinetics. With better models in place, researchers may even begin accounting for test specimen variability with tailored kinematics, leading to more powerful studies for knee biomechanics and orthopedics research.

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Figure 1.
Tibial landmarks and geometries.

Figure 2.
Femoral landmarks and geometries.

Figure 3.

Cyclic stiffness testing. The tibia cycles between $\pm 100\text{N}$ and $\pm 10\text{ Nm}$ in each DOF one at a time while corresponding 6DOF loads are recorded. In this test, the blue line represents the test direction. Note that the highest loads may not be observed in the direction of motion.

Figure 4.

Reproduction of gait kinematics as recorded by Lafortune et al. Translations correspond to anterior/posterior (A/P), medial/lateral (M/L), and compression/distraction (C/D). Rotations correspond to internal/external (I/E), flexion/extension (F/E), and adduction/abduction (Ad/Ab). Simulated heel strike occurs at 0 and 100% gait. Toe-off occurs at 64% gait.

Figure 5.

Representative set of hysteresis curves following stiffness testing. Zero displacement represents the center of laxity at 60 degrees of flexion. 6DOF forces resulting from pure motion in each of the 6DOFs make up a set of 36 curves. Note the nonlinearities present, particularly in compression/distraction forces, and large cross-coupled loading in the stationary DOFs.

A. Raw Hysteresis Data **B. Spline Model** **Figure 6.**

A. Recorded data and **B.** resulting spline models of a representative set of 6 hysteresis curves resulting from medial/lateral translation. Curves were normalized for the starting center of laxity to be located at 50% of the displacement and to be relative to any small residual forces recorded at the center of laxity due to viscoelastic effects. Beta coefficients of the model correspond to values at each of the 5 marked locations.

Figure 7.
Resulting kinetics of each of the 12 tested cadaver knees.

Table 1

Summary of PCA results for the four stiffness analysis techniques employing linear estimation of hysteresis curves. Main translational stiffness terms are present in each of the primary principal components. Interactions involving the M/L, C/D, and F/E DOFs are present in secondary PCs. Most of the Ad/Ab interactions are found in the tertiary PCs.

PCA Summary of Linear Estimation Techniques of Specimen Stiffness		
1. Symmetric Linearized	Proportion of Variance	Top 3 Contributors*
PC1 (s1)	53%	A/P main I/E and F/E cross-coupled A/P and C/D cross- coupled
PC2 (s2)	16%	M/L and C/D cross- coupled M/L and F/E cross- coupled A/P and M/L cross- coupled
PC3 (s3)	14%	A/P and Ad/Ab cross- coupled F/E and Ad/Ab cross- coupled
2. Linearized		
PC1 (s1)	35%	A/P main Ad/Ab stiffness during M/L translation C/D main
PC2 (s2)	26%	F/E main C/D stiffness during M/L translation C/D stiffness during F/E rotation
PC3 (s3)	12%	Ad/Ab stiffness during C/D translation Ad/Ab stiffness during F/E rotation M/L stiffness during Ad/Ab rotation
3. Split Linearized		
PC1 (s1)	28%	A/P stiffness during Anterior translation M/L stiffness during Medial translation Ad/Ab stiffness during Medial translation
PC2 (s2)	22%	F/E stiffness during Extension rotation C/D stiffness during Adduction rotation F/E stiffness during Adduction rotation
PC3 (s3)	13%	Ad/Ab stiffness during Extension rotation M/L stiffness during Extension rotation M/L stiffness during Adduction rotation
4. Averaged Split Linearized		
PC1 (s1)	31%	M/L main Ad/Ab stiffness during M/L translation A/P main
PC2 (s2)	21%	F/E stiffness during I/E rotation

PCA Summary of Linear Estimation Techniques of Specimen Stiffness

1. Symmetric Linearized	Proportion of Variance	Top 3 Contributors*
PC3 (s3)	16%	M/L stiffness during A/P translation
		C/D stiffness during I/E rotation
		F/E main
		A/P stiffness during C/D translation
		A/P stiffness during Ad/Ab rotation

* Note: For example only, PC interpretations were made based on entire set of up to 22 significant ($p < 0.05$) terms.

Table 2

Combined summary of PCA interpretations. Stiffness PCs shown are most similar to linearized stiffness estimation techniques, as the spline technique did not incorporate main stiffness effects. Main stiffness effects had high contributions to the primary PC of each of the linearized stiffness PCA analyses.

Interpretations:	PC1	PC2	PC3
Gait Kinetics	K1: C/D stance assoc. A/P and Ad/Ab ranges	K2: M/L values and assoc. torques	K3: Avg A/P and assoc. torques
Geometries	g1: Joint Size Scale Factor	g2: Notch Height	N/A
Overall Stiffness	s1: Translational Laxity Factor	s2: Topography Effects on C/D	s3: Ad/Ab Stiffness

Table 3

Summary of linear modeling results, including results from spline modeled stiffness and each of the four stiffness analysis techniques employing linear estimation of hysteresis curves. The spline technique allowed more variability to be modeled but does not include main stiffness terms. This may explain why significant factors differed from the rest of the stiffness techniques.

General Linear Models of 3 Gait Kinetics PCs - K1, K2, K3									
K1: C/D stance assoc. A/P and Ad/Ab ranges			K2: M/L values and assoc. torques			K3: Avg A/P and assoc. torques			
GLM Types with Included Factors	R-squared	P-value	sig factors	R-squared	P-value	sig factors	R-squared	P-value	sig factors
<u>2 Geometry PCs - g1, g2</u>									
	0.072	0.541		0.147	0.778		0.145	0.704	
<u>3 Stiffness PCs - s1, s2, s3</u>									
Spline	0.814	0.001	s1	0.321	0.114	s2	0.186	0.219	s3
Symmetric	0.100	0.310	s2	0.068	0.544		0.000	0.441	
Linear	0.362	0.090	s2	0.026	0.479		0.065	0.353	
Split	0.300	0.127	s2	0.328	0.109	s3	0.073	0.342	
AvgSplit	0.513	0.033	s2,s3	0.034	0.492		0.033	0.489	
<u>Combination PCs - s1, s2, s3, g1, g2</u>									
Spline	0.772	0.021		0.223	0.316		0.423	0.172	
Symmetric	0.018	0.652		0.524	0.886		0.040	0.466	
Linear	0.223	0.315	s2	0.163	0.637		0.011	0.509	
Split	0.075	0.437	s2	0.270	0.279		0.196	0.337	s1
AvgSplit	0.433	0.166	s2,s3	0.369	0.792		0.130	0.390	s1
<u>Leaps - Optimized</u>									
Spline	0.837	0.000	s1	0.420	0.018	s2	0.386	0.099	s3
Symmetric	0.325	0.039	s2	0.023	0.295	s3	0.104	0.176	s3
Linear	0.533	0.006	s2	0.120	0.159	s1	0.269	0.117	s1,g1
Split	0.438	0.016	s2	0.462	0.064	s2,s3,g1	0.404	0.052	s1,g1
AvgSplit	0.528	0.020	s2,s3	0.069	0.220	s3	0.335	0.080	s1,g1