Subject-specific Computational Models of the ACL-deficient Knee Capture Inter-subject Variations in Tibiofemoral Instability

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INTRODUCTION: Anterior cruciate ligament (ACL) rupture is common in young, active individuals and often causes knee instability, which contributes to meniscal and cartilage damage and compromised function. Physical examination of the knee remains central to diagnosing ACL injury and planning treatment [1]. The pivot shift exam is especially important due to its high specificity and correlation with clinical outcomes [2]. A high-grade pivot shift has been associated with lower return-to-sport rates, worse patient-reported outcomes, and increased risk of graft failure [2]. Kinematics of the ACL-deficient knee, specifically internal tibial rotation (ITR) and anterior tibial translation (ATT), vary widely across subjects in response to the loads of the pivot shift exam [3]. This inter-subject variability suggests that knee anatomy, including articular geometry and soft tissue laxity, strongly influences knee stability after ACL injury. However, the anatomical factors responsible for inter-subject variability remain poorly understood. Computational modeling offers a novel means to isolate these mechanisms, but a model's ability to adequately capture ACL-deficient knee mechanics must be assessed. To this end, we performed a one-to-one, subject-specific comparison between model predictions and corresponding measurements from a cadaveric experiment in ten knee specimens. We hypothesized that the model estimates of tibiofemoral kinematics would be correlated with corresponding measures from the cadaveric experiment.

METHODS: *Cadaveric Experiment*: Ten cadaveric knees (5 males and 5 females; age: 33.5 ± 7.1 years) were procured for testing. First, computed tomography (CT) (0.625-mm slice thicknesses and 0.5 x 0.5-mm in-plane resolution) of each cadaveric knee were conducted including fiducial markers rigidly fixed to the tibia and femur for determination of bone-fixed anatomical coordinate systems. Then, each knee was mounted to a robotic manipulator (Kawasaki ZX165U) and tested using established protocols [4] (Fig. 1). We assessed kinematics of the ACL deficient knee in response to loads that are applied during the clinical pivot shift maneuver [5]. Loads were applied to the tibia in series and consisted of compression (100 N) followed by a valgus moment (8 Nm) while maintaining the compressive force. The knee was held at 15° of flexion, with the femur fixed in place and the tibia free to move in the remaining five degrees of freedom (DoF). Outcomes were tibiofemoral kinematics in all five DoF, including ITR, valgus angulation, and ATT.
Computational Model: Magnetic resonance imaging (MRI) of each specimen was also conducted (proton density weighted, 1.2 mm slice thickness, 0.3 x 0.3 mm in-plane resolution). We employed an established computational modeling workflow to these MRI and CT data [4]. This workflow consisted of first creating 3D renderings of the tibiofemoral bone, cartilage and meniscal geometries and then identifying ligament insertions and origins. Tissue stiffnesses were standardized via population means. Ligament slack lengths were also standardized using a published optimization algorithm [4]. Coordinate systems were registered between computational model and cadaveric experiment via the fiducial markers. The same loads and boundary conditions were applied to the tibia as described in the cadaveric experiment (ADAMS, Hexagon, Inc.). Outcomes were the same as for our cadaveric experiment. Differences in tibiofemoral kinematics between model and experiment were quantified via root mean square (RMS) error. To address our hypothesis, experimental measurements and model estimates were compared via Pearson's correlation coefficient (r) ($\alpha = 0.05$) (Fig. 1). Regression coefficients (β) were also reported to quantify the relationship between the change in model estimate for a one-unit change in experimental measurement.

RESULTS: RMS error between model estimates and experimental measurements for ITR, valgus, and ATT were 5.2°, 3.3°, and 4.9 mm, respectively. The correlations between model estimates and experimental measurements were r = 0.78 (p = 0.007) for ITR; r = 0.68 (p = 0.03) for valgus; and r = 0.76 (p = 0.01) for ATT (Fig. 2). Regression coefficients for ITR, valgus, and ATT were 1.04 °/°, 1.21 °/°, and 0.96 mm/mm, respectively.

DISCUSSION: Our most important finding was that the computational model estimates of ITR and ATT of the ACL-deficient knee were correlated with experimental measures (r = 0.78 and 0.76, respectively), and regression coefficients (β) were nearly 1-to-1 for ITR and ATT (β = 1.04 °/° and 0.96 mm/mm, respectively) with their corresponding experimental measurements on a specimen-specific basis (Fig. 2). Despite the prevalence of instability following ACL injury, no previous knee models have reported the ability to predict inter-specimen variations in these critical, defining kinematics of ACL-deficiency in response to key loads applied during the clinical pivot shift maneuver. These findings indicate that a model consisting of specimen-specific geometry and a standardized soft tissue envelope can capture much of the inter-specimen variability in ACL-deficient kinematics. Although the model predicted key features of an ACL-deficient knee, it has limitations. The sample size remains too small to conclude that the findings are generalizable. The applied loads reflect those of the pivot shift clinical exam, which are not the same as functional activities. However, these loads are known to induce wide inter-subject variations in kinematics, which was necessary to test our hypothesis, and the grade of the pivot shift exam is predictive of clinical outcomes including ACL graft failure and patient perceptions of function. Subject-specific calibration of ligament properties may further improve model estimates as needed based on use case.

SIGNIFICANCE/CLINICAL RELEVANCE: This computational model may be a useful tool for identifying those who are less prone to instability following ACL injury. Conversely, for those who are subject to instability following ACL injury, it may be useful in developing personalized rehabilitation strategies and for identifying those who may benefit from adjunctive surgical treatments to ACL reconstruction.

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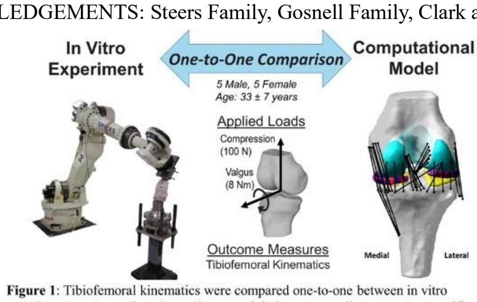

Figure 1: Tibiofemoral kinematics were compared one-to-one between in vitro experiments on ten cadaveric specimens and their corresponding geometry-specific computational models.

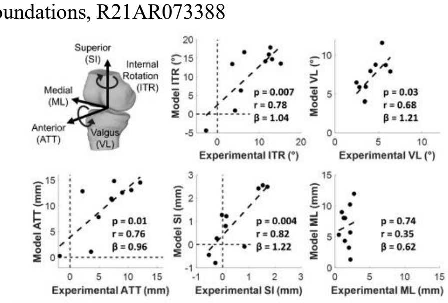

Figure 2. Model estimates plotted against experimental measures of internal tibial rotation (ITR), valgus angulation (VL), anterior tibial translation (ATT), superior translation (SI), and medial translation (ML).