Title: Characterizing Intersubject Variability for Population-Based Evaluations of Joint Mechanics

Author: Peter Laz, Lowell Smoger, Clare Fitzpatrick, Lorin Maletsky*, Kevin Shelburne and Paul Rullkoetter

Center for Orthopaedic Biomechanics, University of Denver *Experimental Joint Biomechanics Research Laboratory, University of Kansas

Introduction: Intersubject variability presents a significant challenge in biomechanics, specifically in characterizing the anatomic variability in the population, understanding its impact and then in extending findings from a small set of experiments or models to the broad population scale. Many clinical studies have identified key geometric measurements that can be used to diagnosis pathologies and influence surgical treatment; examples include the patellar and trochlear geometry in patients with patellar maltracking and pain, and the process of sizing and aligning total knee replacement implants. Developed at scales ranging from individual structures and joints to whole-body musculoskeletal, mechanics-based computational models provide insight and quantitative data to support clinicians and are utilized in design-phase assessment of implants. The intensive processing and development time to create realistic, subject-specific models often results in studies consisting of a small number of subject models. Statistical shape models (SSM) have been previously developed to characterize bone morphology for a population of subjects. After establishing correspondence between the instances in the training set, the SSM approach applies principal component analysis (PCA) to describe the common modes of variation in the data. The objective of this study was to develop a statistical modeling framework to characterize the anatomic variability in multiple structures of a joint, to create a statistical model of the knee including bone, cartilage and ligaments, and to investigate relationships between anatomy and joint function. The statistical modeling approach provides a means to bridge scales from assessments of individuals to a population.

Methods: A statistical shape and alignment model was created for the structures of the knee: the femur, tibia and patella, associated articular cartilage, and cruciate and collateral ligaments for a training set of 40 subjects/specimens. The structures of the knee were segmented from magnetic resonance images and an iterative closest point algorithm established nodal correspondence between a fine mesh for each member of the training set and a template mesh. Each of the structures was described in their local coordinate system and a 4x4 transformation was used to describe relative alignment between the structures. The statistical model utilized the nodal coordinates for the knee structures and the transformation matrices in a principal component analysis to capture the shape and alignment variability. To describe relationships between shape and function, an additional PCA was performed on the shape and 6 degree-of-freedom tibiofemoral (TF) and patellofemoral (PF) kinematics from experimental testing in a cadaveric, whole-joint knee simulator for a subset of 20 specimens.

Results: The key results to date are the statistical model's description of intersubject anatomic variability in the shape and alignment of the knee structures and the ability to automatedly generate a joint-level finite element analysis for any member of the training set or virtual subjects derived from the statistical model. The statistical model captured scaling of the structures of the joint (Mode 1), relative alignments (e.g. patellar alta-baja and its relationship to tibial anterior-posterior alignment) and congruence of the articular surfaces (Mode 2, shape of the patella and trochlear groove). Similarly, the modes of variation for the statistical shape-function model characterized relationships between the shape of the knee and experimental TF and PF kinematics during a squat activity. For example, Mode 1 described changes in scaling and femoral condylar radius, which influenced anterior-posterior translation during the activity.

Discussion: The statistical finite element modeling approach will broaden the impact of current musculoskeletal modeling efforts by transforming them from the individual scale to the population scale. The statistical models are based on the nodes of a finite element mesh, which allows the automated generation of analysis-ready models of virtual subjects or members of the training set. The automated process enables evaluations of larger numbers of models and the population sample space can be fully explored with efficient sampling methods (e.g. Latin Hypercube). The link between the statistical and finite element models has been demonstrated at the joint-level scale and application to the whole-body scale is ongoing. This study has also demonstrated a novel approach to describe relationships between shape and function in a group of healthy normal natural knees; the approach can be extended to consider pathologic groups by considering outliers in a model of the whole population or parallel models for the two groups.

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