Title: Validation of a Natural Knee Model for Muscle-Driven Single-Framework Simulation

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Computational modeling provides non-invasive estimation of muscle, ligament, and joint loading and enables investigation of joint biomechanics and treatments that cannot be achieved through experimental means alone. A key challenge of the computational approach is maintaining sufficiently complex joint-level tissue representations while avoiding computational burden that prohibits muscle force calculations at the whole-body scale. Our overall objective is to create multi-scale finite element (FE) models of the human lower extremity that combine sophisticated joint-level models with whole-body dynamic muscle modeling in a single FE framework and then apply this framework to study the mechanics of natural knees and those with total knee replacements (TKR). Achieving this goal requires first creating and validating a FE model of the natural knee. To do so, specimen-specific natural knee models of the normal knee were developed, calibrated with measurements of in vitro performance, and incorporated into a musculoskeletal model of the lower-extremity. The bones, cartilage, meniscus, and ligaments of cadaver knees were reconstructed from MR scans of normal healthy knee specimens. The bones of the femur, tibia, and patella were meshed with surface elements and represented as rigid bodies. The cartilage surfaces of the tibia, femur, and patella were meshed with hexahedral elements, enabling deformable or rigid-body analysis of joint contact. Efficient soft tissue representations of the ligaments and meniscus were developed by optimizing mechanical properties so that the behavior of the model knee matched kinematic profiles derived from in vitro experiments. Three experiments were used to provide knee kinematic profiles in response to known external and muscle loads: 1) instrumented anterior-posterior, internal-external, and varus-valgus forces applied manually to the tibia with varying knee flexion, 2) known loads placed on the quadriceps and hamstrings tendons with varying knee flexion, 3) simulated gait and deep flexion in a dynamic knee simulator (Fig. 2). The contribution of individual intra-joint structures was assessed by sequentially resecting the meniscus, and anterior and posterior cruciate ligaments. After resection of each structure, the three in vitro experiments were repeated. Simulations were developed in Abaqus/Explict (Simulia, Providence, RI) to reproduce the loading and constraint conditions used in the experiments. An optimization procedure (Isight, Simulia, Providence, RI) adjusted the properties of the modeled tissues until the simulations matched the experimental profiles. In addition, patellofemoral moment arm, patella position, and patellar tendon angles were calibrated with the experimental data. Each knee model was calibrated and validated in reverse order of structure removal in the in vitro experiments. The validated FE model of the knee has been incorporated into a multi-scale musculoskeletal model of the lower extremity and muscle and joint forces have been calculated for a squat-to-stand activity using a quasi-static inverse dynamics approach. Further calibration and validation of the lower extremity musculoskeletal model will be achieved using 3D dynamic imaging of knee mechanics. 3D fluoroscopy enables the precise measurement of bone and implant motion within the body with sub-millimeter accuracy. Analogous to the in vitro experiments, natural and TKR knee mechanics will be measured during dynamic activities and compared with model performance. The complete multi-scale musculoskeletal model will provide insight into pathology as well as conservative and surgical treatments of the natural knee to preserve the joint. These models can be used as vital tools to comparatively evaluate implant designs, understand the etiology of knee pathologies, and assess physical therapy strategies on joint mechanics.

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