Advancing the Quantification of Joint Mechanics and Computational Modeling For Improved Determination of *In Vivo* Tissue Stresses

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Too often, the activities of daily living produce loads that exceed the basic capabilities of the musculoskeletal system. This can lead to injury, profound impairment and ultimately physical disabilities. In order to improve the prevention, diagnosis, and treatment of physical disabilities, we must be able to quantify the demands placed on the musculoskeletal system by the activities of daily living, as well as the capabilities of this system to meet such demands. Ultimately, this requires an understanding of the loads placed on individual muscles, tendons, ligaments, cartilage surfaces and bones. Directly measuring these loads *in vivo* has been quite limited, due to the highly invasive nature of such experiments. Computational modeling can resolve the indeterminate nature of the muscle force-joint torque problem through optimization. However, this approach is hindered by an inability to accurately determine model parameters and to properly validate model calculations and assumptions.

Fortunately, recent advances in medical imaging have provided a wide ranging set of tools (MRI, fluoroscopy, motion analysis, ultrasound, and CT) for the 3D *in vivo* quantification of joint mechanics. Using these tools provides excellent insights in regards to joint kinematics, but using them in combination with each other or in combination with other tools (e.g., gait analysis and musculoskeletal modeling) will ultimately allow us to non-invasively quantify *in vivo* tissue stresses and forces and bridge the gap between joint mechanics and whole body function. In addition, focusing current studies on using these tools to correlate joint mechanics with clinical data will enable us to enhance the understanding of pathophysiology.

In order to bridge the gap between quantifying joint mechanics and quantifying tissue stresses and forces, along with explaining pathophysiology, there are key steps that need to be taken:

1. Our ability to accurately measure 3D in vivo joint mechanics is just coming into maturity. Further developments in this area will be catalyzed by establishing standards to permit easier collaboration and comparison. These developments include:
    a. Clear definitions of and standards for reporting accuracy, precision and subject repeatability; along with justifications for these requirements.
    b. A checklist of capabilities for easier comparison across techniques.
    c. Cross validation across modalities using standardized motion protocols.
    d. Reference databases of varied motions and joints for inter-laboratory comparisons of techniques/results.

2. We currently have the ability to provide valuable insights into human movement disorders, but 3D joint mechanics studies often do not effectively translate to the clinical domain. Thus, we need to:
    a. Develop associations and explanations for how altered joint mechanics create pathophysiology and how pathophysiology creates altered joint mechanics.
    b. Explain how alterations in joint mechanics result in functional limitations and disabilities.
    c. Find methods for fusing our results with whole body mechanics.
    d. Support large scale studies to evaluate trends across normal and pathological function.

3. Improved methodologies for developing and validating patient-specific models of the musculoskeletal system. The most important problems that need to be addressed are:
    a. Develop efficient non-invasive methods for accurately determining model parameters (e.g., muscle volumes, fiber lengths, tendon lengths, cartilage and bone properties, etc.) on a patient-specific basis.
    b. Develop new techniques for non-invasively validating model predictions.

4. A “holy grail” of musculoskeletal biomechanics remains the non-invasive measurement of *in vivo* forces:
    a. How do we optimally fuse various imaging techniques with each other and modeling to reach this goal?
    b. What advances are needed to do this with the current joint measurement techniques?
    c. How can the work in the tissue and whole-body-movement domains be used to help achieve this goal?