Development of a Computational "Worst Case" Device Performance Tool for Use in Evaluating Orthopaedic Implant Device Design Envelopes: ACL Graft Pilot

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Need and Industrial Relevance:
Today's orthopaedic devices can be subjected to variations of worst-case configurations under different use conditions, especially as more patients are receiving particular implant types (i.e., total hip, spinal cage) at younger, more active ages. Presently, the FDA regulatory review (i.e., 510k) process relies on evaluation of worst-case scenarios to evaluate device safety, but many new device types have few established standards, thus requiring sponsors to design tests that they think best represent physiologic use. Even with standards in place, devices may need to be tested in larger configuration envelopes because the standards may not fully represent be true worst-case scenarios.

Project Aims (including Hypotheses):
Fusion of in-vivo mechanics capture approaches and in-silico finite element (FE) modeling can drive surrogate models that improve device efficacy and efficiency by enhancing evaluation of orthopaedic implants. A similar approach has successfully identified key parameters and use conditions that led to increased wear of hip implants. Discussions with FDA, academia, and industry led to two primary aims: 1) to extend the aforementioned approach to a desktop tool (i.e.. a lookup table) that can be used by both industry and FDA reviewers to determine the worst-case testing configuration of implant systems and 2) initially apply and validate the proposed framework begun with hip implants to artificial ACL (knee) grafts.

Methods:

Probabilistic modeling techniques, such as those proposed herein, enable examination of the effects of uncertainty in a defined system. For example, in previous work on modular hip implants there was uncertainty about the effect of head diameter, neck length, and patient weight on wear. While normative values for these parameters were general known, their precise values were considerably variable through the effects of manufacturing tolerances and in the context of patient-specific parameter variability.

Motion capture (MOCAP) based musculoskeletal modeling enables accurate identification of in-vivo kinematics (motion) and kinetics (forces) generated by live human subjects while performing simulated

activities of daily living (ADLs). High resolution acquisition of these objective metrics is facilitated by the use of an advanced motion capture camera array and in-ground force measuring platform instrumentation. In-vivo derived data is then applied to in-silico musculoskeletal models where muscle forces are optimized and accurate estimation of total forces and joint moments (torques) are derived for relevant joints during selected patient activities. The resultant data is then available as a primary input for finite element-based surrogate modeling evaluation of implant performance.

Surrogate models and response surfaces are used as fast versions of more complex models, such as probabilistic models. In this case a predictive statistical model is calibrated to closely interpolate the results of a prior probabilistic model and enable fast prediction of new results that were not solved with the original model. Surrogate models from this project would be intuitively useable to reviewers, requiring input of the design parameters of the device under review and receive a worst case prediction in several seconds.

Modeling and simulation approaches will be extended from previous hip-based approaches (extension of work by PI while at FDA) to the knee (for ACL) as well. FDA-shared human in-vivo MOCAP data will be coupled with a parametric framework to simulate expected use conditions from a variety of patient, surgical, and device parameter ranges. Resultant simulated worst-case scenarios will inform industry and regulatory reviewers of potential red-flag combinations. We aim to make this tool directly and intuitively usable by reviewers, and industry alike, to aid them in determination of worst-case configuration outcomes, thus improving safety and efficacy while decreasing medical device clearance time.

Milestones (must include):

Fall 2015

1. Compile and review FDA and ASTM (publically available documentation) with respect to artificial ACL (knee) grafts for common mechanical worst-case determinations (e.g. component stress, component strain, contact pressures) as well as common physiological, anthropomorphic, and kinematic (functional ADL-pertinent) variables.

2. Identify a subset set of worst-case functional performance and mechanical device factors that could be determined through simulation and offer the greatest impact to reviewers and industry.

Winter/Spring 2016

1. Develop musculoskeletal (MSK) model

    a. Map representative patient (male and female, each at 10^{th}, 50^{th}, and 90^{th} percentiles for anthropomorhpics) boney geometry and muscle attachment sites to validated MSK model.

    b. Synthesize muscle-optimized kinematics and kinetics of pertinent simulated ADLs (separated into relevant categories) into input for FE modeling.

2. Develop FE Model

    a. Develop base joint and implant geometries and simulation templates.

    b. Solve simulations across a representative spectrum of pertinent parameters.

    c. Fit a response surface surrogate model to emulate the results of each worst-case simulation.

3. Develop, compile, and test software application (graphical user interface) that incorporates model data from 1 and 2.

Deliverables (must include):

Quarterly presentation updates:

- December 2015 – conference call
- Spring 2015 – Spring Symposium @ UT (conference call option for UCSF teams)
- June 2015 – conference call
- September 2015 – Fall Symposium @ UCSF (conference call option for UT teams)

Final written report including results - October 31, 2016

Other Deliverables:

- Delivery of a consistent mechanistic rationale for determining 'worst case' conditions for orthopaedic device testing (in this case, ACL surgical grafts).
- Increased device safety through testing of true 'worst cases' where these might otherwise have been missed.
- Reduced burden on the reviewers to make these determinations.
- Quicker review times in cases where a 'worst case' is unclear.
- More consistency and transparency in handoff from industry to FDA.

Impact:

Orthopaedic research literature reports increased use of hip, knee, and spine devices in ever more demanding applications as well as use of new material combinations. Pre-market testing must address safety for new, high-demand indications. Patient safety rests heavily on pre-market testing based on performance in worst-case conditions. Recall that metal-on-metal hip implants, for instance, performed very well in bench tests but failed at very high rates in patients in part because such tests did not successfully create worst-case in-vivo conditions. This project will facilitate more accurate prediction of critical-to-quality, worst-case testing scenarios, beginning with ACL (knee) grafts. Probabilistic simulations will create a repository of potential worst-case configurations that can be matched to device specifications and physically tested. Its availability to reviewers will promote consistency in review of novel devices and encourage manufacturers to bring devices to fruition.

General Budget Outline:

Example:

Personnel	$	24,000
Supplies	$	10,000
Imaging/Specimens	$	2,000
Total Direct	$	36,000
Indirects (10%)	$	3,600
Total	$	39,600

Start Date: October 2, 2015	**End Date**: September 2, 2016

Please limit this document to 2-3 pages and email it to PuiYee.Law2@ucsf.edu by August 14th.