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14. ABSTRACT The aims of this work are i) to establish an online platform to curate, distribute, and reuse data and models of multi-layer tissue structures of musculoskeletal extremities, ii) to collect and disseminate anatomical and mechanical data for building and validating reference models, iii) to build, validate, and disseminate mechanically advanced reference models representative of nonlinear material properties and realistic anatomy, and iv) to build and evaluate fast and mechanically simplified yet visually and haptically realistic surrogate models to be used for surgical simulation. At the time when this report was written, a web based data management system was fully operational; in vivo testing data were published; in vitro testing data dissemination has evolved; a multiplicity of models were built; and work on a variety of scholarly publications has progressed. The project continues to provide the foundations for development of authentic and individualized models for simulation of haptics of musculoskeletal extremities for training.

15. SUBJECT TERMS
musculoskeletal, muscle, skin, fat, tissue interface, extremity injury, extremity response, surface mechanics, ultrasound, surgical simulation, finite element analysis

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Table of Contents

Page

1. INTRODUCTION

High incident rates of combat injuries to the musculoskeletal extremities dictate the immediate need to understand and simulate contact mechanics and internal mechanical interactions of layered tissue organization of these body regions. The mechanical response of multi-layer tissue structures around the legs and arms is a function of the underlying muscle, skin, and fat tissues and the junctions in between. With the knowledge of individual tissue material properties, layered anatomy, and the mechanical capacity of tissue interfaces, it will be possible to develop computational models to conduct descriptive and predictive simulations. Such in silico analyses have utmost importance to develop and evaluate diagnostic strategies, surgical interventions, and protective equipment. The overall goal of this study is to establish the founding knowledge, data and models for the mechanics of multi-layer tissue structures of the limbs, particularly of the lower and upper legs and arms. By delivering this lacking information, the activity promotes scientific research in layered tissue structures and allow reliable virtual surgery simulations for clinical training and certification. All data and models have been provided in an open and freely available manner to maximize outreach of this information.

2. KEYWORDS

musculoskeletal, muscle, skin, fat, tissue interface, extremity injury, extremity response, surface mechanics

3. ACCOMPLISHMENTS

What were the major goals of the project?

Major milestones and relevant tasks of the project as stated in the Statement of Work are provided below.

YEAR 1	***Milestone.*** Web-based interfaces for data curation, queryable data and model databases. *Tasks.* Web design and programming to incorporate new features in online collaboration infrastructure. *Deliverables.* Prototype of web-based tools for data curation and analysis, model assembly, simulation, and post-processing.
YEAR 1	***Milestone.*** In vivo multi-layer tissue anatomy and indentation mechanics. *Tasks.* Recruitment of human subjects, acquisition of demographics, anthropometric measurements, ultrasound measurements of layered tissue thicknesses of legs and arms, indentation with ultrasound. *Deliverables.* Data on gross anatomy and indentation mechanics of lower and upper legs and arms of 100 human subjects.
YEARS 1-2	***Milestone.*** In vitro multi-layer tissue anatomy, mechanical properties, and indentation mechanics. *Tasks.* Acquisition of cadaver specimens, magnetic resonance imaging of cadaver legs and arms, indentation with ultrasound, sampling of skin, muscle, fat tissues and junctions, mechanical testing of tissues and junctions. *Deliverables.* Data on detailed anatomy, tissue and tissue-interface properties, and indentation mechanics of cadaver lower and upper legs and arms (10 specimens for each region).
YEAR 2	***Milestone.*** In vitro quantification of tool forces during surgery of multi-layer tissue structures. *Tasks.* Acquisition of cadaver upper leg specimens, mechanical manipulations using instrumented tools, magnetic resonance imaging, sampling and testing of skin, muscle, fat and their junctions. *Deliverables.* Data on mechanical and haptic responses of 10 cadaver upper leg specimens during surgical procedures.
YEAR 2	***Milestone.*** Physiologically realistic, fully specimen-specific, nonlinear reference models. *Tasks.* Finite element analysis of non-linear mechanics of cadaver specimens. *Deliverables.* Specimen- and region-specific reference models of upper and lower legs and arms confirmed against indentation data (8 models - 4 regions, 1 male and 1 female representative donors).
YEAR 2	***Milestone.*** Physiologically realistic, partially subject-specific, nonlinear reference models. *Tasks.* Finite element analysis of non-linear mechanics of multi-layer tissue regions of human subjects. *Deliverables.* Partially subject- and region-specific reference models of upper and lower legs and arms confirmed against indentation data (8 models - 4 regions, 1 male and 1 female representative subjects).
YEAR 3	***Milestone.*** Computationally efficient surrogate models for multi-layer tissue structures. *Tasks.* Model reduction and simplification to develop cost-effective models of surface manipulation of multi-layer tissues. *Deliverables.* Specimen- (or subject) and region-specific surrogate models of upper and lower legs and arms confirmed against indentation data and reference models (16 models - 4 regions, 2 male and 2 female representatives).
YEAR 3	***Milestone.*** Demonstration of efficient surrogate models of multi-layer tissue structures. *Tasks.* Model reduction and simplification to develop cost-effective models of surgical manipulation. *Deliverables.* Specimen-specific surrogate models of upper legs confirmed against data from lifelike manipulations of surgical procedures (2 models - 1 male and 1 female representative donors).
YEARS 1-3	***Milestone.*** Population and dissemination of data and models. *Tasks.* Routine utilization of web-based interfaces to curate data, populate databases, and disseminate models. *Deliverables.* Free and open access to all deliverables of the project.

What was accomplished under these goals?

Milestone. *Web-based interfaces for data curation, queryable data and model databases.*

Major Activities. Web-based data management and querying system is fully functional. It is in routine use for dissemination of data.

Specific Objectives. Specific goals of the annual reporting period in regard to this milestone were updates and maintenance of the data management and querying system and its branching to support dissemination of in vitro testing data.

Significant Results. The data management website for curation and dissemination of in vivo data (multi-layer tissue anatomy and mechanics data collected on 100 human subjects) has been in operation throughout the whole year. Branch to support dissemination of in vitro testing data has been built and fully tested; it is awaiting for a separate web domain name for launch.

Other Achievements. None noted.

Milestone. *In vivo multi-layer tissue anatomy and indentation mechanics.*

Major Activities. Major activities included preparation and submission of journal articles and statistical analysis guided by an in-house biostatistician, which was recommended by the in-progress review panel.

Specific Objectives. Specific goals of the annual reporting period in regard to this milestone were related to work on relevant scholarly publications.

Significant Results. A data description article was published and a conference abstract on experimentation strategies was presented (see section 6. PRODUCTS). Statistical analysis was performed to understand the role of musculoskeletal extremity region on surface mechanical response (Figure 1) and a related manuscript is under development. Additional statistical analysis has been under consideration to delineate the influence of tissue layers on surface mechanical response and a manuscript on that topic is planned.

Other Achievements. None noted.

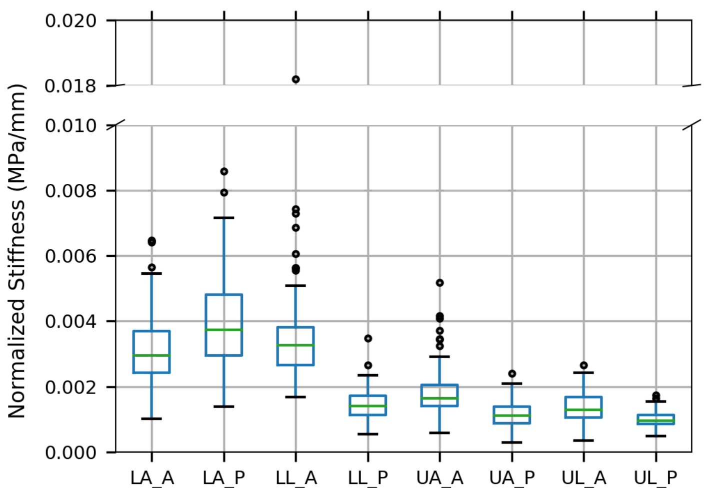

Figure 1. Normalized indentation stiffness for different regions of musculoskeletal extremities. A: anterior. P: posterior. LA: lower arm. LL: lower leg. UA: upper arm. UL: upper leg.

Milestone. *In vitro multi-layer tissue anatomy, mechanical properties, and indentation mechanics.*

Major Activities. Major activities included iterations of tissue testing protocols and evaluation of donor inclusion criteria to reach desired number of specimens for testing.

Specific Objectives. Specific goals in regard to this milestone were continuation of data collection on additional cadaver extremities, commencement of data collection for characterization of tissue mechanical properties, and work on relevant scholarly publications.

Significant Results. Access to extremity specimens from young donors was not possible during the annual reporting period. We decided to relax the inclusion criteria for donor age to allow acquisition of cadaver specimens from middle age donors in order to reach target number of specimens. Preliminary tissue testing has been ongoing to evaluate reproducible determination of tissue properties. Simplifications on tissue testing has been considered in relevance to their intended use in computational A conference abstract was presented as part of describing comprehensive experimentation strategies (see section 6. PRODUCTS). Goals of multiple publications have been decided: a data descriptor, one for comparison of tissue thickness measurement modalities, and another to understand in vivo and in vitro surface stiffness variations.

Other Achievements. None noted.

Milestone. In vitro quantification of tool forces during surgery of multi-layer tissue structures.

Major Activities. Major activities included preliminary testing to ensure the quality of experimental protocols. Data collection has also started.

Specific Objectives. Specific goals in regard to this milestone for the annual reporting period were completion of mock testing, commencement of data collection to characterize surgical tool forces, and work on relevant scholarly publications.

Significant Results. A conference manuscript on instrumentation of surgical tools was presented (see section 6. PRODUCTS). This article will be indexed in IEEE Xplore and PubMed. Experimentation on cadaver specimens has started. Another tool, an indenter, was added to characterize surface mechanics in more detail. Three-dimensional strain measurements have been collected successfully for different tools (indenter, forceps, scalpel) during various acts (Figure 2). Measurement of surgical tool forces in concert with strain measurements was possible and at the moment, collected on three specimens (Figure 3).

Other Achievements. None noted.

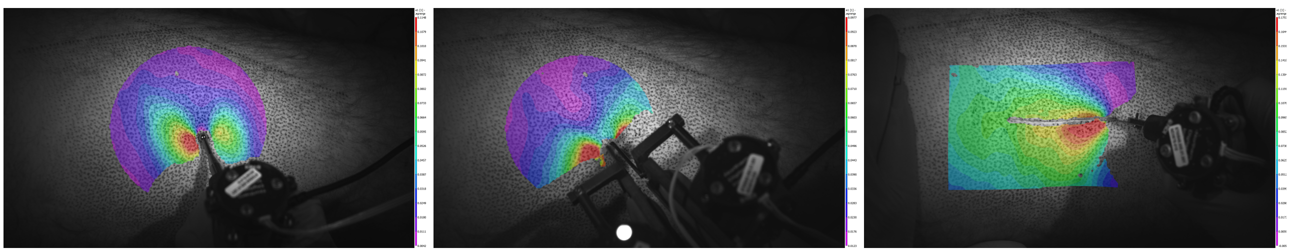

Figure 2. Strain measurements during various manipulations of skin surface on an upper leg specimen; indent, pinch, cut (from left to right).

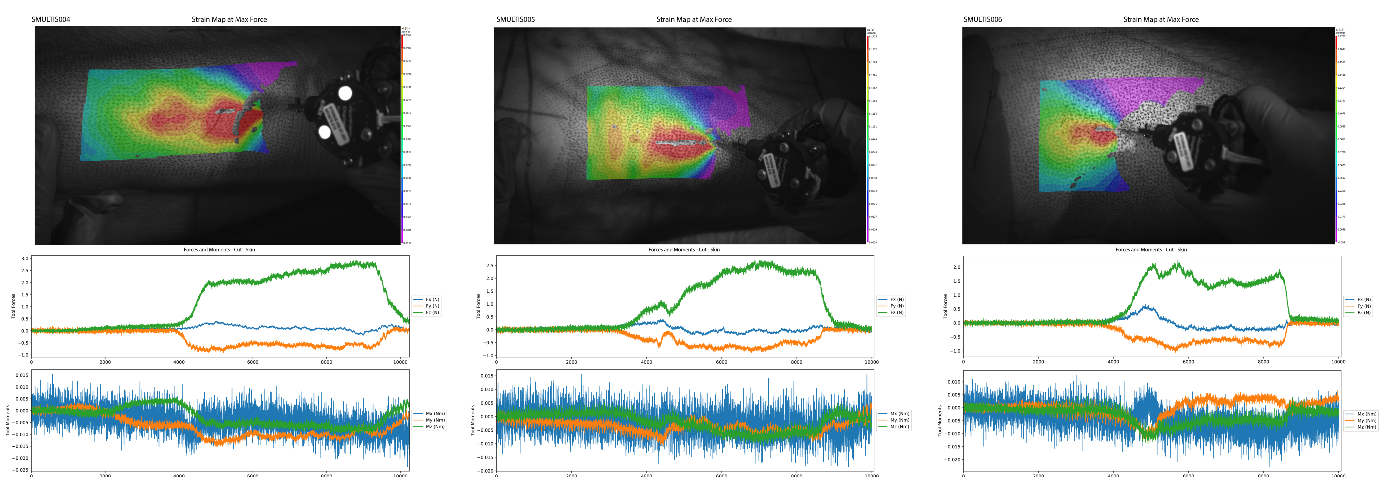

Figure 3. Strain map and cutting forces during the use of a scalpel on three upper leg specimens; strain distributions at peak force are shown.

Milestone(s). *Physiologically realistic reference models.*

Major Activities. Major activities focused on development and testing of models, this time including a variety of musculoskeletal extremity regions.

Specific Objectives. Specific goals for the annual reporting period were related to update and maintenance of scripts for streamlined execution of modeling and simulation workflows, continued development of models, and work on relevant scholarly publications.

Significant Results. Segmentation to reconstruct multi-layer tissue anatomy from images collected on cadaver extremities was completed. Lumped tissue models of musculoskeletal extremities of a male and a female donor were developed (Figure 4). Simulations were performed to demonstrate convergence characteristics of these models during indentation (Figure 5). Models including layered representations of the same regions are under development. A draft manuscript on automated model assembly is under development.

Other Achievements. None noted.

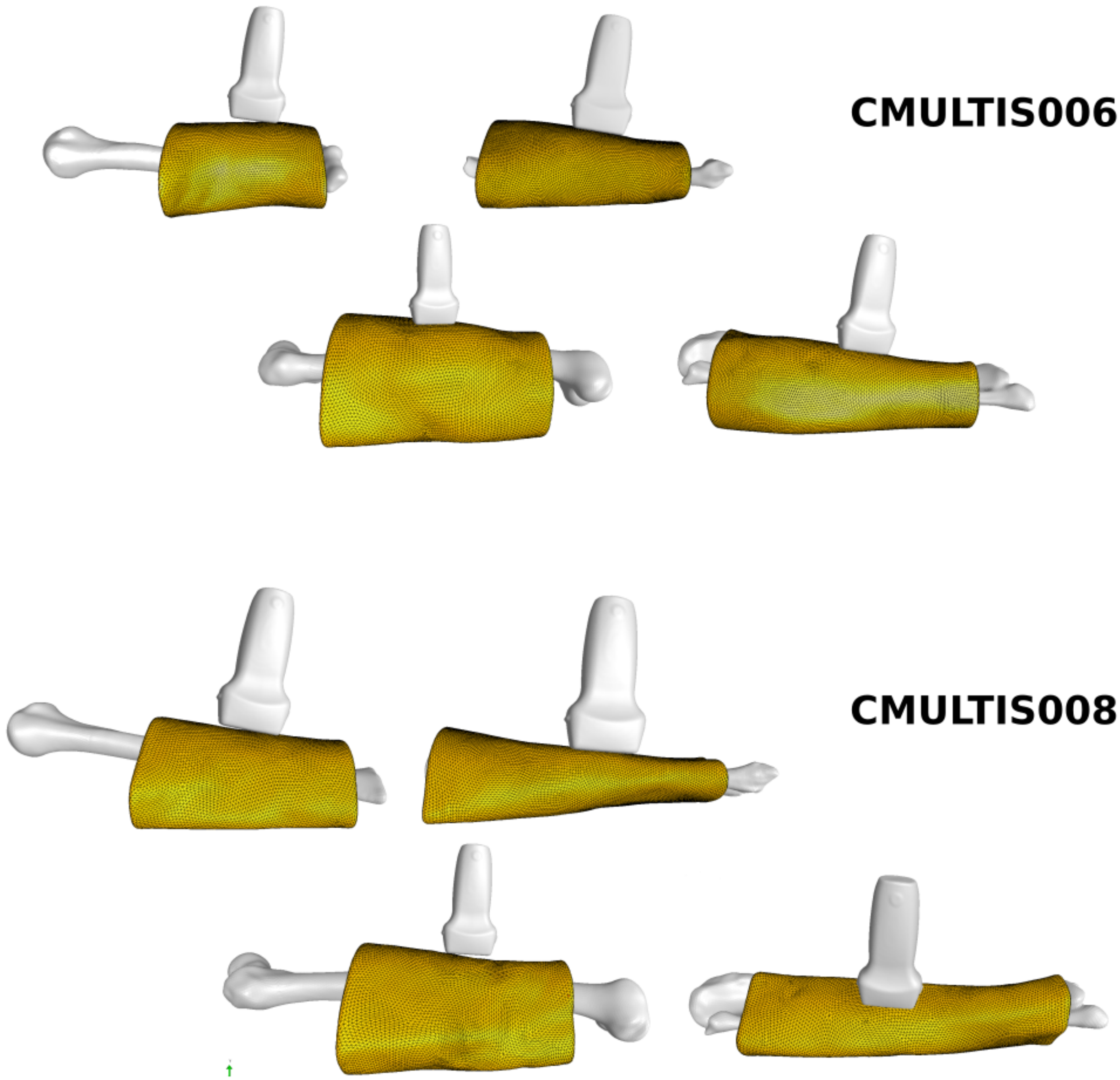

Figure 4. Computational models of upper and lower leg and arm regions of two donors; one male (CMULTIS006), one female (CMULTIS008).

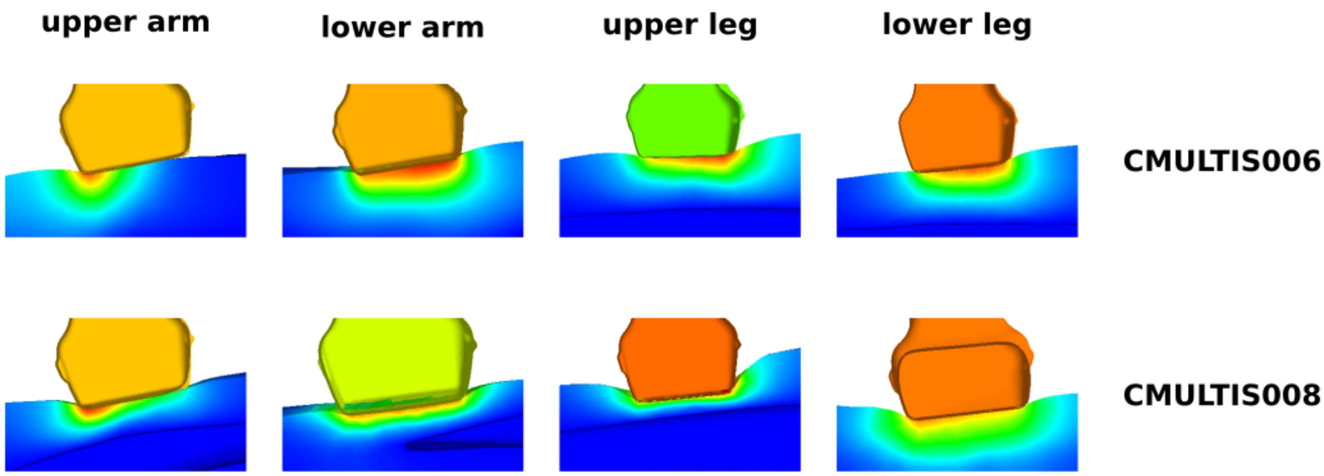

Figure 5. Indentation simulation using models of upper and lower leg and regions; finite element analysis results (displacement field) using FEBio are shown.

Milestone(s). *Surrogate models.*

Major Activities. Major activities for these milestones are related to work conducted for development of reference models (see above).

Specific Objectives. Specific goals were to document, develop, and update scripts for streamlined execution of modeling & simulation workflows.

Significant Results. Scripts used for reference modeling also provide models in formats that can be used in surgical simulation software, specifically SOFA. Model development also incorporates generating meshes at varying densities (Figure 6). During simulations, mechanics can be calculated on coarse meshes whereas visualization can be delivered using a higher surface mesh to capture authenticity at a decreased simulation cost.

Other Achievements. None noted.

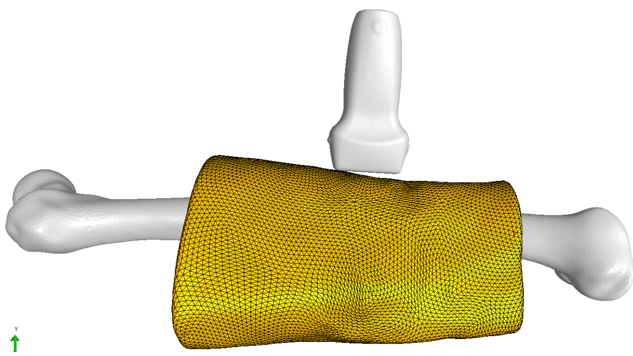

Figure 6. Model simplification or enhancement by generation of different mesh densities. Upper leg model is shown.

What opportunities for training and professional development has the project provided?

The core Cleveland Clinic team includes 2 research scientists and 6 engineers (full- or part-time) under the supervision of the principal investigator. The project provides apprenticeship and self-guided learning opportunities for the personnel as part of required activities in engineering design, biomechanics experimentation, computational modeling, programming, and data science. An added training and professional development opportunity is in scholarly communication. Employees are expected to write conference abstracts and journal articles, and prepare podium and poster presentations. Scholarly mentorship is routinely provided by the principal investigator. One journal article was published and four conference abstracts were prepared and presented by team members under Dr. Erdemir's guidance.

How were the results disseminated to communities of interest?

The project implements an open development approach supported by public dissemination. All information relevant to experimentation and modeling procedures, and infrastructure development (data, designs, models, code, documentation) are publicly accessible at the project website, https://simtk.org/projects/multis. Project members also reach out to relevant scientific communities through scholarly communication, e.g. conference participation, journal articles, etc.

What do you plan to do during the next reporting period to accomplish the goals?

Milestone. *Web-based interfaces for data curation, queryable data and model databases.*

- Updates and routine maintenance to support data management system.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

Milestone. *In vivo multi-layer tissue anatomy and indentation mechanics.*

- Completion of statistical data analysis to document the role of multi-layer tissue on indentation mechanics.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

Milestone. *In vitro multi-layer tissue anatomy, mechanical properties, and indentation mechanics.*

- Completion of ultrasound experimentation on additional cadaver extremities.
- Completion of data collection for characterization of tissue mechanical properties.
- Dissemination of data.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

Milestone. *In vitro quantification of tool forces during surgery of multi-layer tissue structures.*

- Completion of data collection for characterization of surgical tool forces.
- Dissemination of data.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

Milestone(s). *Physiologically realistic reference models.*

- Development and simulation of musculoskeletal extremity models with increasing fidelity.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

Milestone(s). *Surrogate models.*

- Development and demonstration of simplified but authentic musculoskeletal extremity models.
- Work on relevant scholarly publications, e.g., conference abstracts, journal articles.

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

An ultrasound system instrumented with a load transducer provides the capacity to measure internal deformations of organs as a function of external loading. In biomechanics, the principal discipline of the project, this tool helps quantify anatomical and mechanical variations of multi-layer tissues of musculoskeletal extremities, which are used for development of models for surgical simulations and can be leveraged to design protective gear for musculoskeletal extremities and for consumer product design (performance clothing). Such data also form the basis for scientific and clinical discoveries related to the function of multi-layer tissues, e.g., etiology and management of pressure ulcers.

Instrumented surgical tools provide the capacity to measure forces exerted on the tissue and on the tools during surgical acts. For biomechanics and for haptics research, such capacity and knowledge acquired from it can be used for design and development of new surgical tools and can also inform investigations in robotics assisted surgery and telemedicine.

The project collected and disseminated anatomical and mechanical information on musculoskeletal extremities of live subjects for a large sample population (n = 100). This data set essentially is the foundation for any scientific or clinical investigation focusing on multi-layer tissue response, its realism, and its diversity.

What was the impact on other disciplines?

As part of the project, a data management system has been developed and launched. This web-based system and the storage resources can be utilized by projects in any other discipline that requires management and dissemination of rich data.

What was the impact on technology transfer?

The project resulted in three primary technological advancements that may have an impact on public use. First, a robust engineering solution to integrate a load transducer to any ultrasound system for freehand measurement of ultrasound probe forces during imaging was developed. The know-how for this systems is currently documented in the publicly accessible wiki pages of the project. Similarly, a robust engineering solution to integrate load transducers to surgical tools, specifically surgical blade, retractor, and forceps, was developed. The design and know-how for surgical tool instrumentation can be accessed at the project site to assist prospective studies on quantification of forces of surgery. Last, a fully functional data management and query system was developed. This system can be adapted for data rich scientific and engineering projects for organization and orderly dissemination of information. Ongoing activities aim for the integration of the data management system as a feature at SimTK, a publicly accessible platform for biomedical computing.

What was the impact on society beyond science and technology?

The project adapts an open science approach. Experimentation and modeling workflows and infrastructure are documented publicly as they develop. Know-how to conduct scientific work and to build resources are part of these documentation. This will likely impact scientific practice and its perception in the society.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

The whole grant timeline has shifted by a year. A no cost extension request was submitted on August 2, 2018. Approval of modification to project performance period was received on August 21, 2018. Amendment No. P0001 indicates the new performance period as “01-Sep-2015 TO 31-Aug-2019”. This extension will be utilized to complete the work. The objectives, hypotheses, and milestones remain the same.

Changes that had a significant impact on expenditures

Delays in grant timeline has been reflected in delays in expenditures. Other than the time shift in expenditures outlined in the proposal, no additional expenses are anticipated.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report. Use and care of human subjects are ongoing in an orderly fashion. Current status is summarized below.

Human Use Regulatory Protocols

1 human subject research protocol will be required to complete the Statement of Work.

Protocol of total: 1

Human Research Protection Office (HRPO) assigned A-number:A-18650.a (Cleveland Clinic Site) & A-18650.b (Stanford University Site)

Title: Reference Models for Multi-Layer Tissue Structures

Target required for clinical significance:100 human subjects and 50 cadaver specimens

Target approved for clinical significance: 100 human subjects and 50 cadaver specimens

Submitted to and Approved by:

- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: received on 12/18/2014, approved for the period 12/23/2014 through 12/22/2015 (Cleveland Clinic Site IRB for human subjects testing)
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: received revised protocol version 2 on 01/16/2015, approved through 12/22/2015 (Clinic Clinic Site IRB amendment to the human testing application to include cadaveric testing section)
- IRB # 34361 – Reference Models for Multi-Layer Tissue Structures: notice of determination dated 05/26/2015 indicating that the project does not meet the federal regulatory definition of human subject research (Stanford University IRB in regard to dissemination of de-identified data)
- HRPO Log Number A-18650.a (Cleveland Clinic Site) and HRPO Log Number A-18650.b (Stanford University Site): approved on 06/22/2015.

- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: renewal application received on 12/01/2015, approved for the period 12/23/2015 through 12/22/2016 (Cleveland Clinic Site IRB for human subjects testing)
- HRPO acknowledged receipt of the Cleveland Clinic Site IRB approval of the renewal application on 12/17/2015.
- HRPO acknowledged receipt of the Cleveland Clinic Site IRB approval of the renewal application on 12/23/2016.
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: renewal application received on 11/13/2017, approved for the period 12/23/2017 through 12/22/2018 (Cleveland Clinic Site IRB for human subjects testing).
- HRPO acknowledged receipt of the Cleveland Clinic Site IRB approval of the renewal application on 12/21/2017.

Status:

- 100 subjects have been recruited.

Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

1 RDT&E, education or training activity involving human cadavers will be performed to complete the Statement of Work.

- Title: Reference Models for Multi-Layer Tissue Structures
- Relevant milestones: In vitro multi-layer tissue anatomy, mechanical properties, and indentation mechanics. In vitro quantification of tool forces during surgery of multi-layer tissue structures.
- Date of the activity: Experiments are ongoing.
- Responsible individual: Ahmet Erdemir (Principal Investigator)
- Brief description: Indentation of cadaver legs and arms using instrumented ultrasound probe; mechanical testing to identify properties of muscle, skin, and fat layers of extremities – a targeted total of 40 specimens (4 extremity regions from 10 donors). Characterization of surgical tools on cadaver upper legs – a targeted total of 10 specimens (upper legs from 10 donors).

Status:

- 18 extremities (9 legs, 9 arms) from 9 donors have been tested.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS

Publications, conference papers, and presentations

Journal Articles

Neumann, E. E., Owings, T. M., Schimmoeller, T., Nagle, T. F., Colbrunn, R. W., Landis, B., Jelovsek, J. E., Wong, M., Ku, J. P. and Erdemir A. (2018) Reference data on thickness and mechanics of tissue layers and anthropometry of musculoskeletal extremities, Scientific Data, 5:180193.
doi - 10.1038/sdata.2018.193
link - https://doi.org/10.1038/sdata.2018.193

Erdemir, A., Hunter, P. J., Holzapfel, G. A., Loew, L. M., Middleton, J., Jacobs, C. R., Nithiarasu, P., Lohner, R., Wei, G., Winkelstein, B. A., Barocas, V. H., Guilak, F., Ku, J., Hicks, J. L., Delp, S., Sacks, M., Weiss, J. A., Ateshian, D. G. A., Maas, S. A., McCulloch, A. D. and Peng, G. C. Y. (2018) Perspectives on sharing models and related resources in computational biomechanics research, Journal of Biomechanical Engineering, 140, 024701.
doi - 10.1115/1.4038768
link - https://doi.org/10.1115/1.4038768

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doi - 10.3389/fninf.2018.00018
link - https://doi.org/10.3389/fninf.2018.00018

Conference Abstracts and Presentations

Schimmoeller, T., Cho, K., Colbrunn, R., Nagle, T., Neumann, E., and Erdemir, A. Instrumentation of surgical tools to measure load and position during incision, tissue retraction, and suturing, IEEE Engineering in Biology and Medicine Conference, July 17-20, 2018, Honolulu, HI.
Proceeding - https://simtk.org/svn/multis/studies/SurgicalToolsIEEE_EMBS/doc/Schimmoeller_SurgicalTools_IEEE_EMBS_FINAL.pdf
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Erdemir, A. Perspectives on sharing models and related resources in computational biomechanics research, Interagency Modeling and Analysis Group, 2018 Futures Meeting - Moving Forward with the Multiscale Modeling Consortium, March 22-24, 2017, Bethesda, MD.
Abstract - https://www.imagwiki.nibib.nih.gov/sites/default/files/erdemir-abstract.pdf
Presentation - https://www.imagwiki.nibib.nih.gov/sites/default/files/erdemir-presentation.pdf

Erdemir, A., Owings, T. M., Schimmoeller, T., Neumann, E., Nagle, T. and Colbrunn, R. Comprehensive testing strategies for anatomical and mechanical characterization of layered tissue structures of musculoskeletal extremities, IMSH 2018 - International Meeting on Simulation in Healthcare, January 13-17, 2018, Los Angeles, CA.
Abstract - https://simtk.org/svn/multis/doc/imsh_2018.pdf
Presentation - https://simtk.org/svn/multis/doc/imsh_2018_presentation.pdf

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Abstract - https://simtk.org/svn/multis/doc/mhsrs_2017.pdf
Presentation - https://simtk.org/svn/multis/doc/mhsrs_2017.odp

Landis, B. and Erdemir, A. Automation of volumetric mesh generation, mesh assembly and model input from surface representations of tissue structures, 41st Annual Meeting of the American Society of Biomechanics, August 8-11, 2017, Boulder, CO.
Abstract - https://simtk.org/svn/multis/studies/Assembly/doc/MeshAssembly_ABS_2017.pdf
Poster - https://simtk.org/svn/multis/studies/Assembly/doc/Auto%20Mesh%20Generation%20And%20Model%20Assembly%20Poster.pdf

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Poster - https://simtk.org/svn/multis/studies/Anthropometrics/doc/ASB2017_Owings.pdf

Morrill, E. E., Owings, T. M., Schimmoeller, T., Colbrunn, R., Bonner, T., Landis, B., Jelovsek, J. E. and Erdemir A. A database of soft tissue layer thicknesses in musculoskeletal extremities, 41st Annual Meeting of the American Society of Biomechanics, August 8-11, 2017, Boulder, CO.
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Poster - https://simtk.org/svn/multis/studies/TissueThickness/doc/2017ASBposter_morrill.png

Erdemir, A., Bonner, T., Chokhandre, S., Colbrunn, R., Landis, B., Morrill, E., Owings, T. and Schimmoeller, T. Logistics of building virtual specimens for in silico biomechanics, 2017 Biomedical Engineering Society / Food and Drug Administration Frontiers in Medical Devices Conference: Innovations in Modeling and Simulation, May 16-18, 2017, Washington, DC.
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Abstract - https://simtk.org/svn/openknee/doc/msm_2017.pdf
Poster - https://simtk.org/svn/openknee/doc/msm_2017.png

Website(s) or other Internet site(s)

https://simtk.org/projects/multis
This is the project website launched through the SimTK infrastructure. SimTK is maintained and upgraded by our collaborators at Stanford University to assist organization, collaboration, dissemination, and visibility. The project website includes various components: a list of team members, a downloads section to disseminate resources, a documents section to provide documents, a wiki for collaboration, a publications area for listing abstracts, articles, etc. generated as part of the project, a news list, forums for discussions, and a source code repository with a version control system to assist software development. Within the goals of this project, SimTK infrastructure will be improved by our collaborators at Stanford University to provide services for data management and databases. All materials in the project site are publicly available.

https://simtk.org/svn/multis/
Source code repository includes data analysis code and models under development (public access).

https://simtk.org/plugins/moinmoin/multis/
The wiki is part of the project website. Nonetheless, it is worth mentioning in here as it provides dynamic documentation of project activities. At the wiki, one can find the narrative of the grant proposal (as submitted to the US Army), the roadmap of the project, an evolving set of experimentation and modeling specifications, descriptions of the infrastructure to accomplish the project goals, and minutes of group meetings. All wiki pages are accessible publicly.

https://multisbeta.stanford.edu/
This site provides the beta version of the data management and querying system and is used for data dissemination. The system is fully operational and currently hosts the in vivo experimentation data, which are publicly accessible. Anyone can register to get an account to access data; browse through it or search data that fit certain criteria. The team has read-write access to upload raw and derivative data and organize.

Technologies or techniques

Technologies developed as part of this project includes:

Load Transducer Instrumented Ultrasound (LINUS)
This is a customizable technology for physical integration of and signal communication between an ultrasound system and a spatial load transducer.
Know-how is described in https://simtk.org/plugins/moinmoin/multis/Infrastructure/InstrumentedUltrasound.
System is currently in use by the research team. Geometric modeling for physical assembly is available at the project site.

Load Transducer Instrumented Surgical Tools
This is a customizable technology for physical integration of surgical tool tips with a spatial load transducer for recording of forces during surgical acts.
Know-how is described in https://simtk.org/plugins/moinmoin/multis/Infrastructure/InstrumentedSurgicalTools.
System is currently in use by the research team. Geometric modeling for physical assembly is available at the project site.

Operation MULTIS Data Management System
This is a customizable data management system and data querying system, designed for the project.
Prototype is available at http://multisbeta.stanford.edu.

System is fully functional and publicly available. A user's manual for querying data can be found at https://simtk.org/plugins/moinmoin/multis/Specifications/DataManagement/GettingStarted.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Load Transducer Instrumented Ultrasound Data Analysis Software

This is a Python based software for association and time alignment of ultrasound images and load measurements and for assisted identification of skin, fat, and muscle thickness during anatomical imaging or indentation.

Know-how is described in https://simtk.org/plugins/moinmoin/multis/Specifications/DataAnalysis.

A working prototype is available in the source code repository at https://simtk.org/svn/multis/.

Software is currently in use by the research team.

Automation Software for Mesh Assembly and Model Input File

This is a Python based software for automation of model development; specifically to provide an unsupervised workflow for volumetric mesh generation, mesh assembly and model input file generation starting with surface representations of tissue structures.

Know-how is described in https://simtk.org/plugins/moinmoin/multis/Specifications/ModelAssembly.

A working prototype is available in the source code repository at https://simtk.org/svn/multis/.

Software is currently in use by the research team.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

The activity included effort from personnel in the Department of Biomedical Engineering at the Cleveland Clinic, those previously in the Multidisciplinary Simulation Center at the Cleveland Clinic, and at Simbios, NIH Center for Biomedical Computation at Stanford University. A list of these individuals are provided in following.

Name:	Ahmet Erdemir
Project Role:	Principal Investigator
Research Identifier:	N/A
Nearest person month worked:	4 months/year (current effort level)
Contribution to Project:	Dr. Erdemir leads the scientific and engineering direction of the proposed project. He provides supervision for all project members and gives insight to the collaborating team at Stanford University for the management and upgrade of web-based interfaces and online databases.

Name:	Tammy Owings
Project Role:	Project Scientist
Research Identifier:	N/A
Nearest person month worked:	0 months/year (current effort level)
Contribution to Project:	On a need basis, Dr. Owings assists in drafting of publications and development of computational models.

Name:	Benjamin Landis
Project Role:	Senior Research Engineer
Research Identifier:	N/A
Nearest person month worked:	11 months/year (current effort level)
Contribution to Project:	Mr. Landis is responsible for establishing the modeling and simulation workflows of the project. He has been developing and maintaining model generation scripts (to assist segmentation, model assembly, and simulation) and generating mesh morphing scripts. He develops sample lumped and multi-layered models of tissue for simulation. He also works on publications related to modeling and simulation.

Name:	Tyler Schimmoeller
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	11 months/year (current effort level)
Contribution to Project:	Mr. Schimmoeller. has been leading in vitro experimentation efforts. He conducts in vitro experimentation to acquire anatomical and mechanical properties of multi-layer tissue structures. He also conducts in vitro testing procedures for measurement of surgical tool forces. Mr. Schimmoeller works on publications related to instrumentation and in vitro experimentation.

Name:	Erica Neumann (Morrill)
Project Role:	Senior Research Engineer
Research Identifier:	N/A
Nearest person month worked:	3 months/year (current effort level)
Contribution to Project:	Ms. Neumann has been routinely analyzing in vivo and in vitro data to extract skin, fat, and muscle thicknesses and indentation response. She has been maintaining and utilizing scripts for data analysis. She regularly uploads data to the data management system for public dissemination. Ms. Neumann also works on publications related to data analysis.

Name:	Ariel Schwartz
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	2 months/year (current effort level, started on February 12, 2018)
Contribution to Project:	Ms. Schwartz is a recent recruit. She has been assisting in testing of modeling and simulation scripts and assisting development of models.

Name:	Sean Doherty
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	9 months/year (current effort level, started on June 25, 2018)
Contribution to Project:	Mr. Doherty is a new recruit. He has developed lumped models of leg and arm regions and has been working on generation of models at varying levels of fidelity.

Name:	Robb Colbrunn
Project Role:	Project Scientist
Research Identifier:	N/A
Nearest person month worked:	0 months/year (current effort level)
Contribution to Project:	On a need basis, Dr. Colbrunn maintains the data acquisition systems and contributes to publications.

Name:	Tara Nagle (Bonner)
Project Role:	Senior Research Engineer
Research Identifier:	N/A
Nearest person month worked:	0 months/year (current effort level)
Contribution to Project:	On a need basis, Ms. Bonner maintains the data acquisition systems and contributes to publications.

Name:	John-Eric Jelovsek
Project Role:	Co-Investigator
Research Identifier:	N/A
Nearest person month worked:	0 month/year (current effort level)
Contribution to Project:	On a need basis, Dr. Jelovsek contributes to publications.

Name:	Scott Delp

Project Role: Principal Investigator on Subcontract
Research Identifier: N/A
Nearest person month worked: 0 months/year (current effort level)
Contribution to Project: Dr. Delp continues to provide overall direction for upgrade and maintenance of the SimTK in relevance to this project.

Name: Joy Ku
Project Role: Project Manager on Subcontract
Research Identifier: N/A
Nearest person month worked: 1 month/year (current effort level)
Contribution to Project: Dr. Joy continues to lead the efforts to upgrade and maintain web-based data management and data querying system and its integration to SimTK infrastructure. She supports development of publications and data dissemination.

Name: Tod Hing
Project Role: Consultant on Subcontract
Research Identifier: N/A
Nearest person month worked: 1 month/year (current effort level)
Contribution to Project: Mr. Hing provides support for upgrades and maintenance of the web-based data management and data querying in SimTK infrastructure.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Since last reporting, other support for Ahmet Erdemir, PhD (Principal Investigator) has changed. Specifically, Dr. Erdemir's effort level in the following activity, in which he is the Principal Investigator, was decreased. This change does not impact the effort on the project that is the subject of the project report.

R01GM104139 (Erdemir) 09/15/2013 – 05/31/2019 1.0 calendar
National Institutes of Health / NIGMS
(direct cost allocated to PI's laboratory for 06/01/2016 – 05/31/2019)
(total budget includes 2 subcontracts)
Open Knee(s): Virtual Biomechanical Representations of the Knee Joint

The goal of this project is to establish experimentation, modeling, and simulation of musculoskeletal joints supported by community-driven science and cloud-based computing. Specifically, this project will develop a platform for exploring the biomechanics of health and diseased knees and generate knee joint models of different genders and ages, with and without osteoarthritis.

What other organizations were involved as partners?

The following organization contributes to the project.

Organization Name: Stanford University
Location of Organization: Stanford, CA

Partner's Contribution to the Project:

In-kind support – Partner provides the SimTK software infrastructure for collaboration and dissemination.

Facilities – Partner provides the SimTK hardware infrastructure for collaboration and dissemination.

Collaboration – Partner maintains web-based data management and data querying software for the project.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS

Nothing to report.

QUAD CHARTS

An updated Quad Chart can be found in the Appendix.

9. APPENDICES

An updated Quad Chart can be found as an attachment to the Annual Technical Report.

Reference Models for Multi-Layer Tissue Structures

14093001

W81XWH-15-1-0232

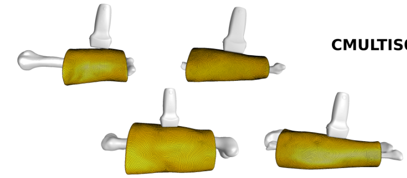
PI: Ahmet Erdemir **Org:** Cleveland Clinic **Award Amount:** ~$3,600,000

Study/Product Aim(s)

- To establish an online platform to curate, distribute, and reuse data and models of multi-layer tissue structures of musculoskeletal extremities.
- To collect and disseminate anatomical and mechanical data for building and validating reference models.
- To build, validate, and disseminate mechanically advanced reference models representative of nonlinear material properties and realistic anatomy.
- To build and evaluate fast and mechanically simplified yet visually and haptically realistic surrogate models to be used for surgical simulation.

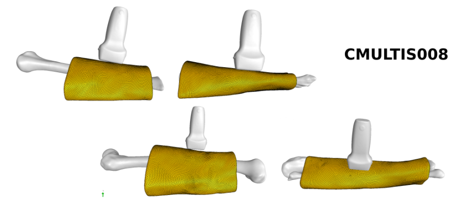
Approach

in vivo and in vitro experimentation - nonlinear finite element analysis – surrogate modeling in surgical simulation software - free and open source dissemination



CMULTIS006

55 years old male
Height: 1.78 m
Weight: 77.1 kg



CMULTIS008

62 years old female
Height: 1.80 m
Weight: 68.0 kg

An array of lumped tissue models were developed for simulations of surface mechanics at musculoskeletal extremities. Models are virtual representations of legs and arms of male and female donors.

Timeline and Cost

Activities CY	15	16	17	18
Project launch				
Web-based interfaces				
In vivo data collection				
In vitro data collection				
Reference models				
Surrogate models				
Estimated Budget ($K)	**$300**	**$1,200**	**$1,200**	**$900**

Updated: September 27, 2019

Goals/Milestones

CY15 Goal – **Project** launch
- ☑ Approval of human subjects testing and cadaver experimentation
- ☑ Project website

CY16 Goals – Data collection
- ☑ Web-based interfaces for dissemination
- ☑ In vivo anatomy & mechanics

CY17 Goal – Data collection & modeling
- ☐ In vitro anatomy & mechanics, mechanics of surgery – *In progress.*
- ☐ Reference models from in vivo & in vitro data – *In progress.*

CY18 Goal – Modeling & demonstration
- ☐ Surrogate modeling – *In progress.*
- ☐ Demonstration of surrogate models

Comments/Challenges/Issues/Concerns
- Dissemination will be conducted in all years.

Budget Expenditure to Date

Projected Expenditure: $3,600k.

Actual Expenditure: ~$2,430k.