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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 and the platform has been made available to general public; in vivo testing data were published; in vitro testing data publications were in review; a growing number of models were built and calibrated, and are under consideration for dissemination and publication. 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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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?

Major milestones as stated in the Statement of Work (see above) are provided below along with the outline of the work that was completed for each milestone. This information was also provided in the request for additional no cost extension (request was submitted on May 16, 2019, addendum was submitted on July 17, 2019 per funding agency's request, approval of modification to project performance period was received on October 10, 2019).

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

Three web-based interfaces and databases were developed, launched, and populated: https://multisbeta.stanford.edu/ (for in vivo anatomy and indentation mechanics); https://multisgamma.stanford.edu/ (for in vitro anatomy and indentation mechanics); and https://multisdelta.stanford.edu/ (for in vitro surgical tool movements and forces). The platform for data management and querying was generalized and now available as collaboration and dissemination technology for any project hosted at the publicly accessible SimTK site (https://simtk.org/), i.e., as a "Data Share" feature. Routine updates and maintenance will continue beyond project period.

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

All data were acquired and publicly disseminated. A journal article as a data descriptor was published. Routine activities for hardening of scientific knowledge and technology has been performed in relation to hypotheses, by extended data analysis and preparation of scholarly publications.

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

Data were acquired and publicly disseminated with the exception of leg and arm specimens from a final cadaver donor. Our requests with specimen providers are still active in case they become available. Testing of these specimens is not necessarily critical to wrap up the project appropriately. An in vitro data publication was prepared and submitted without these final specimens. When and if the specimens are received, the data set will be augmented. Specimen- and region-specific tissue material properties are now obtained through inverse finite element analysis relying on indentation data. In vitro tissue testing is still anticipated but now it is aimed for additional confirmation of the results of inverse finite element analysis. Routine activities for hardening of scientific knowledge and technology have been performed in relation to hypotheses, by extended data analysis and preparation of scholarly publications.

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

Data were acquired and publicly disseminated with the exception of a leg specimen from a final cadaver donor. Our requests with specimen providers are still active in case the specimen becomes available. Testing of this specimens is not necessarily critical to wrap up the project appropriately. An in vitro data publication was prepared and submitted without this final specimen. When and if the final specimen is received, the data set will be augmented. Routine activities for hardening of scientific knowledge and technology have been performed in relation to hypotheses, by extended data analysis and preparation of scholarly publications.

***Milestone.** Physiologically realistic, fully specimen-specific, nonlinear reference models.*

Lumped tissue models of upper and lower legs and arms of two donors were built and tissue properties were calibrated to capture specimen- and region-specific surface mechanical response (for authenticity of haptics simulations). Recalibration has been performed to more accurately capture specimen-specific response and activities are focused on hardening of technology through dissemination and scholarly publication. Layered tissue models of upper legs and arms of two donors were also built. Development of lower leg and arm models were hindered by complexity of geometry, e.g. thin layers, multiple bones embedded in soft tissue, required conformity of multiple tissue types at certain regions, etc. A modified modeling strategy was developed and now it is utilized to capture anatomical complexity of these regions. Calibration of tissue properties to capture specimen- and region-specific mechanics of tissue layers and hardening of technology through dissemination and scholarly publications are expected in near term.

Milestone. Physiologically realistic, partially subject-specific, nonlinear reference models.

Various morphed models of lumped and layered tissues of musculoskeletal extremities were built. The results were not satisfactory due to discrepancies in scaling for circumference and length measurements of the limbs and in morphing of tissue geometries to match recorded tissue thicknesses. The team decided to focus on capturing subject-specific tissue thicknesses with the anticipation that these geometric variables will likely dictate deformation characteristics of the tissue layers and emergent haptic response on limb surface. This morphing strategy is now frozen, models are being built and will be calibrated. In following, hardening of technology through dissemination and scholarly publications are expected.

Milestone. Computationally efficient surrogate models for multi-layer tissue structures.

During the development of reference models, a variety of model reduction strategies were already implemented: lumped tissue modeling to capture haptic response at a lower cost than layered models; coarse meshes to decrease computational cost while accommodating visually acceptable simulations; and defining a deformable region of interest based on tool positioning to decrease memory footprint and simulation cost. Calibration approaches will ensure mechanical equivalence of these models to their detailed counterparts. Hardening of technology through dissemination and scholarly publications will likely follow.

Milestone. Demonstration of efficient surrogate models of multi-layer tissue structures.

Sample models were already pushed to SOFA, surgical simulation software, to test the modeling pipeline. Haptics device was configured to work with SOFA. Surrogate models will be used for demonstration. Hardening of technology is anticipated for usability and through dissemination, and scholarly publishing.

Milestone. Population and dissemination of data and models.

Public dissemination is routinely performed at data management and querying sites, supported by data manuscripts. All raw data are available for any interested party to utilize and conduct scientific studies and/or reproduce our investigations, see https://multisbeta.stanford.edu/ (for in vivo anatomy and indentation mechanics); https://multisgamma.stanford.edu/ (for in vitro anatomy and indentation mechanics); and https://multisdelta.stanford.edu/ (for in vitro surgical tool movements and forces). All derivative data (aggregated data to support hypotheses testing, anatomical reconstructions, computational models, simulation results, etc.) are routinely pushed to these sites to enrich content and increase usability and technology readiness of the deliverables.

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

The core Cleveland Clinic team includes a diverse array of research scientists and 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. Many journal articles were published and 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?

Milestones of the remaining work to be done during the extension are outlined below as an updated Statement of Work. The activities are within the scope of the original Statement of Work. This information was also provided in the request for additional no cost extension (request was submitted on May 16, 2019, addendum was submitted on July 17, 2019 per funding agency's request, approval of modification to project performance period was received on October 10, 2019).

Milestone. *In vitro tissue mechanical properties.*
(within the scope of ***Milestone.*** *In vitro multi-layer tissue anatomy, mechanical properties, and indentation mechanics.*)

Mechanical properties of skin, fat, and muscle tissue will be acquired and disseminated. These will be used to confirm calibration results, e.g. tissue properties obtained by inverse finite element analysis of indentation data. Hardening through a data publication is anticipated.

Milestone. *Models calibrated to in vitro specimen data.*
(within the scope of ***Milestone.*** *Physiologically realistic, fully specimen-specific, nonlinear reference models.*)

Lumped models of upper and lower extremity regions from two cadaver donors will be hardened through dissemination and scholarly publications. Layered models from upper and lower extremities will be rebuilt and calibrated with specimen- and region-specific data. Hardening of models (technology content) through dissemination and scholarly publishing is anticipated.

Milestone. *Models calibrated to in vivo subject data.*
(within the scope of ***Milestone.*** *Physiologically realistic, partially subject-specific, nonlinear reference models.*)

Lumped and layered models of upper and lower extremity regions from two subjects will be built and calibrated with subject- and region-specific data. Morphing based on capturing subject-specific tissue thicknesses will be used. Hardening of models (technology content) through dissemination and scholarly publishing is anticipated.

Milestone. Computationally efficient surrogate models.
(within the scope of *Milestone. Computationally efficient surrogate models for multi-layer tissue structures.*)
(within the scope of *Milestone. Demonstration of efficient surrogate models of multi-layer tissue structures.*)

Lumped, coarsened, and reduced region models will be ported to surgical simulation software, calibrated to capture mechanical equivalence to their detailed counterparts. Demonstration simulations will be performed. Hardening of models (technology content) through dissemination and scholarly publishing is anticipated.

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) using instrumented ultrasound. This data set essentially is the foundation for any scientific or clinical investigation focusing on multi-layer tissue response, its realism, and its diversity.

The project collected and disseminated anatomical and mechanical information on musculoskeletal extremities of cadaver donors (n = 9, upper and lower legs and arms for each). This data set augments the data collected on live subjects (see above) by providing more detailed anatomical information (through the acquisition of computed tomography and magnetic resonance imaging) and mechanical information (through measurements of ultrasound probe motion). This data set provides additional foundational information for any scientific or clinical investigation focusing on multi-layer tissue response, its realism, and its diversity.

The project collected and disseminated detailed mechanical information on foundational surgical acts as they were performed on cadaver upper leg specimens (n = 9). This data set provides the full mechanical environment of surgical tool – tissue interaction (tool forces and movement, tissue surface deformations). This data set essentially is the foundation for authentic surgical simulations that aim to capture multi-layer tissue response.

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. It is already integrated as the "Data Share" feature at SimTK, a publicly accessible platform for biomedical computing.

What was the impact on society beyond science and technology?

The project adapted an open science approach. Experimentation and modeling workflows and infrastructure have been documented publicly as they matured. Know-how to conduct scientific work and to build resources has been part of the documentation effort. Data, models, and code have been publicly disseminated with F.A.I.R. data principles in mind. Overall, the project's open science philosophy 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 an additional year. An additional no cost extension request was submitted on May 16, 2019 and per funding agency's request, an addendum was submitted on July 17, 2019. Approval of modification to project performance period was received on October 10, 2019. Amendment No. P0002 indicates the new performance period as "01-Sep-2015 TO 31-Aug-2020". 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.
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: received amendment on 11/16/2016, approved through 12/22/2016 (Clinic Clinic Site IRB amendment to include additional personnel).
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: renewal application received on 11/22/2016, approved for the period 12/23/2016 through 12/22/2017 (Cleveland Clinic Site IRB for human subjects testing).
- 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.
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: renewal application received on 11/14/2018, approved for the period 12/23/2018 through 12/22/2019 (Cleveland Clinic Site IRB for human subjects testing).
- HRPO acknowledged receipt of the Cleveland Clinic Site IRB approval of the renewal application on 12/20/2018.
- IRB # 14-1597 – Reference Models for Multi-Layer Tissue Structures: received amendment on 11/21/2019, approved through 12/22/2019 (Clinic Clinic Site IRB amendment to remove personnel).

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:
- 22 extremities (11 legs, 11 arms) from 11 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. and Erdemir, A. (2019) Regional variations of in vivo surface stiffness of soft tissue layers of musculoskeletal extremities, Journal of Biomechanics, 95, 109307.
doi - 10.1016/j.jbiomech.2019.08.001
link - https://doi.org/10.1016/j.jbiomech.2019.08.001

Schimmoeller, T., Colbrunn, R., Nagle, T., Lobosky, M., Neumann, E. E., Owings, T. M., Landis, B., Jelovsek, J. E. and Erdemir, A. (2019) Instrumentation of off-the-shelf ultrasound system for measurement of probe forces during freehand imaging, Journal of Biomechanics, 83, 117-124.
doi - 10.1016/j.jbiomech.2018.11.032
link - https://doi.org/10.1016/j.jbiomech.2018.11.032

Schimmoeller, T., Cho, K. H., Colbrunn, R., Nagle, T., Neumann, E. and Erdemir, A. (2018) Instrumentation of surgical tools to measure load and position during incision, tissue retraction, and suturing, Conference Proceedings of IEEE Engineering in Medicine and Biology Society, 2018, 933-936.
doi - 10.1109/EMBC.2018.8512332
link - https://doi.org/10.1109/EMBC.2018.8512332

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

Mulugeta, L., Drach, A., Erdemir, A., Hunt, C. A., Horner, M., Ku, J. P., Myers, J. G. Jr., Vadigepalli, R. and Lytton, W. W. (2018) Credibility, replicability, and reproducibility in simulation for biomedicine and clinical applications in neuroscience, Frontiers in Neuroinformatics, 12, 18.
doi - 10.3389/fninf.2018.00018
link - https://doi.org/10.3389/fninf.2018.00018

Conference Abstracts and Presentations

Doherty, S. B., Landis, B., Owings. T. and Erdemir, A. Template models for surface manipulation of musculoskeletal extremity regions, Summer Biomechanics, Bioengineering and Biotransport Conference, June 25 -28, 2019, Seven Springs, PA.

Abstract - https://simtk.org/svn/multis/studies/LumpedModels/doc/SB3C2019_Sean.pdf

Poster - https://simtk.org/svn/multis/studies/LumpedModels/doc/Doherty_SB3C2019_PosterDraft.pdf

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

Poster - https://simtk.org/svn/multis/studies/SurgicalToolsIEEE_EMBS/doc/EMBSposter-01.pdf

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

Erdemir, A., Bonner, T., Colbrunn, R., Jelovsek, J. E., Ku, J., Lobosky, M., Landis, B., Morrill, E. E., Owings, T. M., Schimmoeller, T. and Wong, M. Reference data for modeling and simulation of layered tissue structures of musculoskeletal extremities, 2017 MHSRS – Military Health System Research Symposium, August 27-30, 2017, Kissimmee, FL.

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

Schimmoeller, T., Colbrunn, R., Bonner, T., Lobosky, M., Morrill, E. E., Owings, T. M., Landis, B., Jelovsek, J. E. and Erdemir A. Instrumentation for measurement of probe forces and orientation during freehand ultrasound, 41st Annual Meeting of the American Society of Biomechanics, August 8-11, 2017, Boulder, CO.

Abstract - https://simtk.org/svn/multis/studies/InstrumentedUltrasound/doc/ASB2017_InstrumentedUltrasound.pdf

Poster - https://simtk.org/svn/multis/studies/InstrumentedUltrasound/doc/ASBposter_schimmoeller.pdf

Owings, T. M., Morrill, E. E., Schimmoeller, T., Bonner, T. F., Colbrunn, R. W., Landis, B., Jelovsek, J. E. and Erdemir A. A database for musculoskeletal segment length and circumferences for individualized

anthropometric representation, 41st Annual Meeting of the American Society of Biomechanics, August 8-11, 2017, Boulder, CO.
Abstract - https://simtk.org/svn/multis/studies/Anthropometrics/doc/Owings_ASB_Abstract_2017.pdf
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.
Abstract - https://simtk.org/svn/multis/studies/TissueThickness/doc/morrill_ASB2017.pdf
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.
Abstract - https://simtk.org/svn/multis/doc/fmd_2017.pdf
Poster - https://simtk.org/svn/multis/doc/fmd_2017.png

Erdemir, A. Democratization of modeling & simulation in biomechanics, 10th Anniversary Multiscale Modeling Consortium Meeting, March 22-24, 2017, Bethesda, MD.
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 has been 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 has been 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/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 specifications and infrastructure to accomplish the project goals, and minutes of group meetings.. All wiki pages are accessible publicly.

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

https://multisbeta.stanford.edu/
This site provides a data management and querying system and is used for dissemination of in vivo experimentation data (ultrasound imaging), which are publicly accessible. Anyone can register to get an account

to access data; browse through or search data that fit certain criteria. The team has read-write access to upload raw and derivative data and organize.

https://multisgamma.stanford.edu/

This site provides a data management and querying system for curation and dissemination of in vitro experimentation data (CT/MRI, ultrasound imaging), which are publicly accessible. Anyone can register to get an account to access data; browse through or search data that fit certain criteria. The team has read-write access to upload raw and derivative data and organize.

https://multisdelta.stanford.edu/

This site provides a data management and querying system for curation and dissemination of in vitro data (surgical tool forces and deformations during surgical acts), 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.
Project specific prototypes are available at https://multisbeta.stanford.edu/, https://multisgamma.stanford.edu/, and https://multisdelta.stanford.edu/. A user's manual for querying data can be found at https://simtk.org/plugins/moinmoin/multis/Specifications/DataManagement/GettingStarted.
System is fully functional, publicly available and integrated into SimTK architecture (https://simtk.org) as "Data Share" feature that can be activated for projects hosted at SimTK.

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.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Reference In Vivo Data for Anatomy and Mechanics of Multi-Layer Tissue Structures

Data to understand the mechanics of multi-layer tissue structures of the limbs, particularly of the lower and upper legs and arms. Anatomical and mechanical data were collected on extremities of 100 adult subjects (50 male, 50 female) from the general population. An ultrasound system was instrumented with a load transducer for in vivo characterization of skin, fat, and muscle thicknesses in the extremities at unloaded and loaded (indentation) states. The unloaded state provided anatomic measures of the tissue layers for 48 regions, while the loaded state provided the tissue mechanical response in 8 regions. Data package for 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 - 10.18735/S5R97F

link - https://doi.org/10.18735/S5R97F

Reference In Vitro Data for Anatomy and Mechanics of Multi-Layer Tissue Structures

Data to understand the mechanics of multi-layer tissue structures of the limbs, particularly of the lower and upper legs and arms. Anatomical and mechanical data were collected on extremities of 9 adult donors (5 male, 4 female). An ultrasound system was instrumented with a load transducer for in vitro characterization of skin, fat, and muscle thicknesses in the extremities at unloaded and loaded (indentation) states. The unloaded state provided anatomic measures of the tissue layers for 48 regions, while the loaded state provided the tissue mechanical response in 8 regions. Additionally, computed tomography (CT) and magnetic resonance (MR) imaging were performed on each. All imaging sets and relevant segmentations were included. Data package for Schimmoeller, T., Neumann, E., Owings, T., Nagle, T., Colbrunn, R., Landis, B., Jelovsek, J. E., Hing, T., Ku, J. and Erdemir, A. (in review) Reference data on in vitro anatomy and indentation response of tissue layers of musculoskeletal extremities, Scientific Data.

doi - 10.18735/JHE9-JH38

link - https://doi.org/10.18735/JHE9-JH38

Reference In Vitro Data for Mechanics of Fundamental Surgical Acts on Multi-Layer Tissue Structures

Data to capture tissue-tool interactions of basic surgical acts performed on upper leg extremities from 9 adult donors (5 male, 4 female). Tool positions and loads were measured while performing 16 different operations,

which included 8 different techniques: indenting, pinching, cutting, widening, closing, everting, suturing, and retracting. In addition, 3D surface strain measurement was captured during initial indentation, pinching, and cutting trials at the skin surface. Data package for Schimmoeller, T., Neumann, E., Nagle, T. and Erdemir, A. (in review) Reference tool kinematics-kinetics and tissue surface strain data during fundamental surgical acts, Scientific Data.

doi - 10.18735/n217-mb65

link - https://doi.org/10.18735/n217-mb65

Aggregated in vivo indentation data

Indentation stiffness and effective modulus of upper and lower musculoskeletal extremity regions for ~100 subjects. The data were supplementary to Neumann, E. E., Owings, T. M. and Erdemir, A. (2019) Regional variations of in vivo surface stiffness of soft tissue layers of musculoskeletal extremities, Journal of Biomechanics, 95, 109307.

access - Package "Study – In vivo indentation" in Downloads of project site at https://simtk.org/projects/multis

direct link - https://simtk.org/frs/download_confirm.php/file/5847/002_MasterList_indentation.csv?group_id=1032

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 publications and leads efforts to organize documentation, particularly in the project wiki.

Name: Snehal Chokhandre
Project Role: Principal Research Engineer
Research Identifier: N/A
Nearest person month worked: 3 months/year (current effort level)
Contribution to Project: Ms. Chokhandre is a tissue testing expert. She is mentoring engineers for implementation of mechanical tissue characterization protocols.

Name: Benjamin Landis
Project Role: Senior Research Engineer
Research Identifier: N/A
Nearest person month worked: 6 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 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:	0 months/year (current effort level, left on July 2, 2019)
Contribution to Project:	Mr. Schimmoeller. led in vitro experimentation efforts. He conducted in vitro experimentation to acquire anatomical and mechanical properties of multi-layer tissue structures. He also conducted in vitro testing procedures for measurement of surgical tool forces. He finalized drafting of data publications related to in vitro experimentation. Mr. Schimmoeller left the institution on July 2, 2019.
Name:	Erica Neumann (Morrill)
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. Neumann assists in publications and leads efforts for scripting for data analysis, and for data management and dissemination.
Name:	Ariel Schwartz
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	0 months/year (current effort level)
Contribution to Project:	On a need basis, Ms. Schwartz assists in testing and maintenance of modeling and simulation scripts and implements model reduction strategies.
Name:	Sean Doherty
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	9 months/year (current effort level)
Contribution to Project:	Mr. Doherty developed and calibrated lumped models of leg and arm regions. He has been developing, testing, and calibrating layered models and working on generation of models at varying levels of fidelity.
Name:	Ellen Klonowski
Project Role:	Research Engineer
Research Identifier:	N/A
Nearest person month worked:	12 months/year (current effort level, started on February 11, 2019)
Contribution to Project:	Ms. Klonowski is a recent recruit. She familiarized herself with tissue testing strategies. She has taken over the responsibility to perform mechanical characterization of tissues.
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. Nagle 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:	On a need basis, 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:	0 month/year (current effort level)
Contribution to Project:	On a need basis, Dr. Joy manages upgrades and maintenance of the web-based data management and data querying system and supports publications and data dissemination.

Name:	Henry Kwong
Project Role:	Web Administrator on Subcontract
Research Identifier:	N/A
Nearest person month worked:	0 month/year (current effort level)
Contribution to Project:	On a need basis, Mr. Kwong 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. First, Dr. Erdemir's effort level in the following activity, in which he is the Principal Investigator, ENDED. 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 $265,131
     (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.

In addition, Dr. Erdemir has STARTED a new project as one of the Principal Investigators (see below). This changed does not impact the effort on the project that is the subject of the project report.

R01EB025212 (Erdemir, Enquobahrie)   07/02/2019 – 03/31/2023   2.0 calendar
National Institutes of Health / NIBIB $223,434
(annual direct cost allocated to Co-PI's laboratory for 07/02/2019 – 03/31/2020)
(total budget includes 1 subcontract)
Software for Practical Annotation and Exchange of Virtual Anatomy

The goal of this proposal is to develop a novel software suite for pragmatic annotation and exchange of virtual anatomy. To accomplish this goal, a multi-platform software library will be developed as a foundation for the whole software suite. In following, a high level application interface, a graphical user interface, and a plug-in infrastructure will be provided.

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
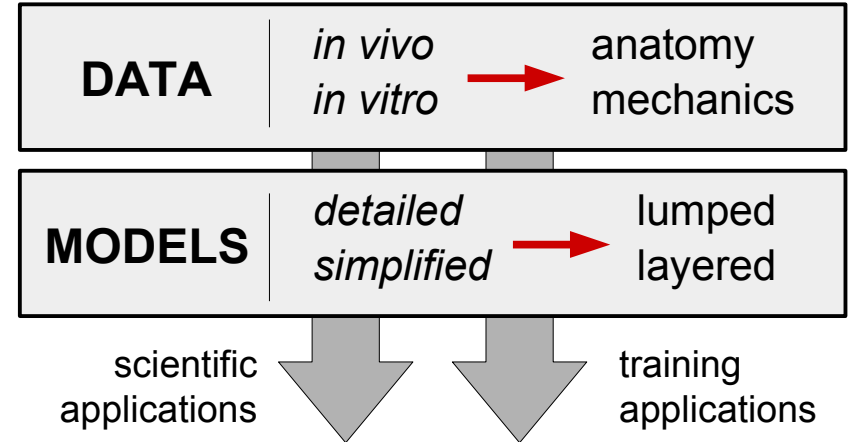
Study/Product Aim(s)

- 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

| DATA | *in vivo* *in vitro* → | anatomy mechanics |
| MODELS | *detailed* *simplified* → | lumped layered |

scientific applications   training applications

Publicly accessible reference data and growing number of models provide an ecosystem for scientific discovery and medical training related to multi-layer tissue structures of musculoskeletal limbs.

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: November 29, 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
☐ Reference models from in vivo & in vitro data – *In progress.*
CY18 Goal – Modeling & demonstration
☐ Surrogate modeling – *In progress.*
☐ Demonstration of surrogate models – *In progress.*

Comments/Challenges/Issues/Concerns

- The project is under no cost extension.
- Dissemination has been conducted in all years.

Budget Expenditure to Date
Projected Expenditure: $3,600k.
Actual Expenditure: ~$3,269k.