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TITLE: Assessing biomechanical function and hip stabilizing muscle quality associated with transfemoral osseointegration

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CONTRACTING ORGANIZATION: University of California, San Francisco, CA

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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

In order to assess the walking mechanics and effects on hip function that accommodate lower limb osseointegrated prosthetics, we propose a study comparing walking mechanics from motion analysis and hip muscle health from MRI between osseointegrated and socket transfemoral amputees who are at least two years following final surgery with no outstanding complications. Results from this work stand to 1) report the biomechanical outcomes of lower limb osseointegrated prosthetics in comparison to conventional socket prosthetics, 2) clarify the role of muscle function on biomechanical outcomes in lower limb amputees and explore the related risk for hip replacement on the affected side for transfemoral osseointegration, 3) inform targeted rehabilitation approaches for improving walking mechanics, and 4) motivate the development of regenerative therapeutics for muscle recovery.

**15. SUBJECT TERMS**
None listed.

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON<br>USAMRMC |
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## 1. Introduction

This work seeks to explore biomechanical function associated with osseointegrated prosthetics compared to conventional socket prosthetics. We aim to understand the biomechanical outcomes of lower limb osseointegrated prosthetics in comparison to conventional socket prosthetics and clarify the role of muscle degeneration and function on compensatory gait behaviors in lower extremity amputees. We intend use results from this study to guide safe rehabilitation and mitigate risk for hip replacement.

## 2. Keywords

Osseointegration, transfemoral amputation, muscle fat infiltration, hip stability, biomechanics, MRI

## 3. Accomplishments

**What were the major goals of the project?**

Aim 1: Establish whether there are differences in gait and biomechanical function between osseointegrated and conventional socket unilateral transfemoral amputees.

Aim 2: Examine asymmetry of hip stabilizing muscle quality using advanced MRI sequences and compare with outcomes for gait and biomechanical function.

**What was accomplished under these goals?**

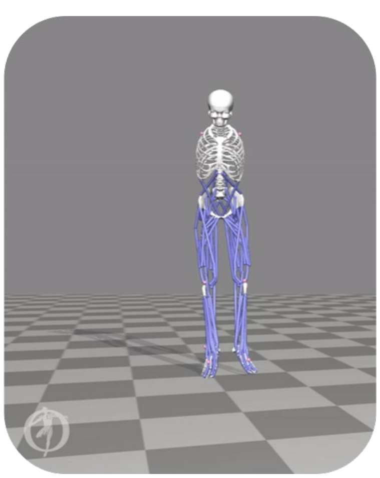
In Y1 of this project, we have completed the following:

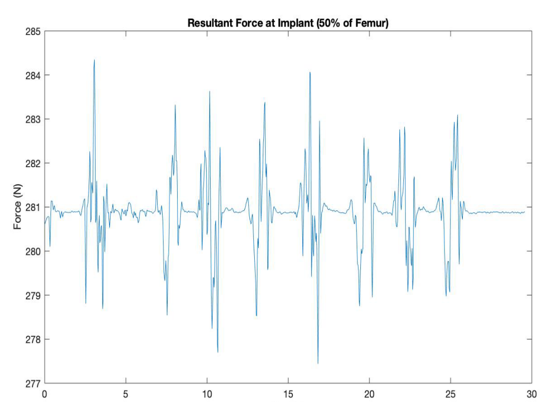
1) Subject enrollment: for osseointegration subjects, we have enrolled n=6 subjects. For non-osseointegrated subjects we have enrolled n=1 subject. We are approximately have way through our enrollment. We have several sources to recruit local TFA subjects without osseointegration for our non-osseointegration group, including our Orthotics & Prosthetics clinic and teaming up with local collaborators to recruit subjects from the community. We are on target to have subject enrollment complete before the end of the two-year study period.

2) For biomechanical assessments in Aim 1:

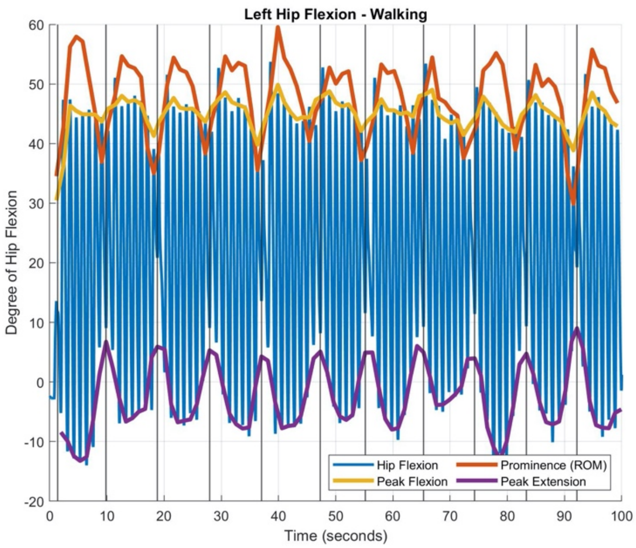
    a. Based on analysis of intial biomechanical data, we have finalized our biomechanical testing protocol to have repeated staggered sit to stand assessment (with Kinect and IMUs) and two minutes of walking (IMUs only) before and after up to 10 minutes of walking (or until they choose to stop due to discomfort). In addition sit to stand assessments will be completed on a force-plate.

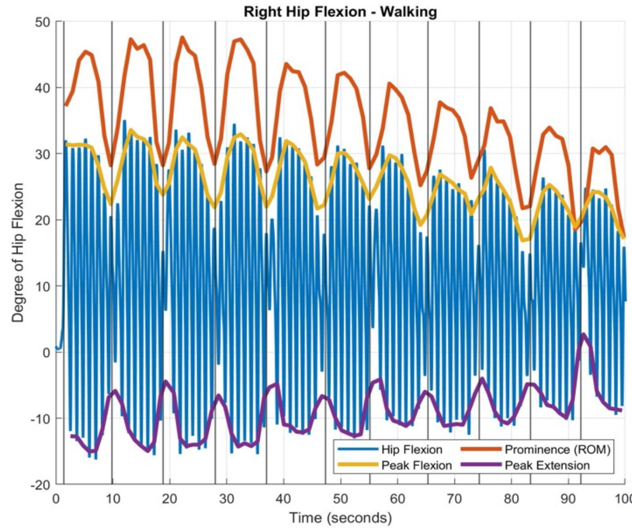
        i. Patient-specific hip muscle forces (using OpenSim) will be calculated for the staggered sit to stand assessments (reason for needing force plate with kinect). This modeling approach has been used by our group to estimate forces on the osseointegrated implant (see figures). Bilateral differences hip muscle force recruited from the staggered sit to stand assesments will be compared 1) between groups and 2) to bilateral differences in MRI hip muscle quality.



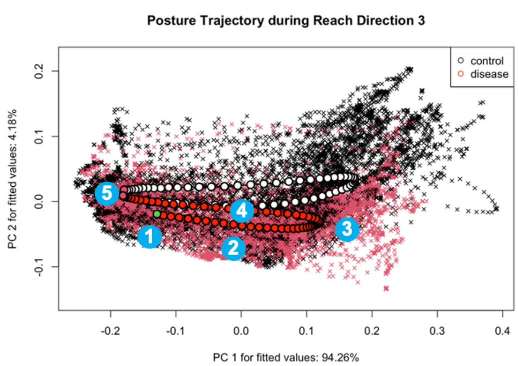


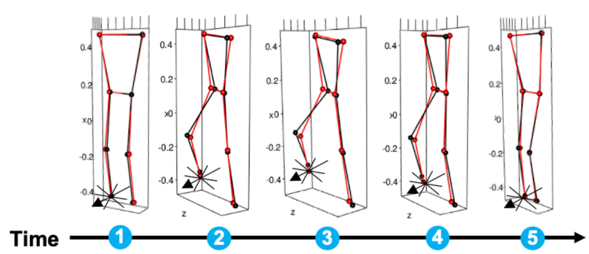
b. Trunk and hip kinematic behaviors will be extracted from the IMUs during 2-minute gait assessments and assessed for temporal changes potential due to fatigue. Temporal chages in trunk and hip kinematics will be compared 1) between groups and 2) to bilateral differences in MRI hip muscle quality.




c. 3D motion patterns of whole body time-series motion patterns will be compared for the Kinect staggered STS testing using statistical parametric mapping and statistical shape modeling. Preliminary results from these methods show significant differences in trunk and hip trajectories when subjects are relying on the affected limb compared to the unaffected (figure on the right). We plan to develop this analytical approach to look at the "postural" movements encompassing the 3D trajectories of all the joints tracked and run a principal components analysis to compare motion profiles (example below from Kinect 3D skeletal tracking data for star excursion balance test on hip OA patients below).




d.

3) MRI Assessment: Currently, we have full bilateral hip MRI assessment for three osseointeration subjects and the one non-osseointegrated subject. I have currently an internal collaboration within UCSF with an investigator that has used the same advanced imaging sequence to assess hip muscle quality in pre-osteoarthritic adults and healthy controls. We will be comparing our amputee data with his existing data to gage the severity of muscle quality and hip OA. In addition, we have initiated a secondary collaboration to harmonize segmentation protocols for direct comparison of hip muscle quality data and this will include utilizing a novel automated segmentation approach. We have preliminary data of muscle fat infiltration from a 22yo male osseointegration patient from a single MRI slice (table below). Future analysis will have volumetric area and fat infiltration estimates for each muscle covering multiple MRI slices along the hip.

| | Left Side % fat | Right side % fat |
|---|---|---|
| Gluteus Maximus | 3.24 | 6.22 |
| Gluteus Medius | 8.07 | 3.85 |
| Gluteus Minimus | 1.33 | 1.78 |
| TFL | 0.104 | 3.53 |

4) There are no statistical results yet. Focusing on getting subjects in for data collection visits now that restrictions have lifted on subjects being able to visit for research purposes only. For the MRI imaging, we have tested the protocol and it works, however, for us to run the automated segmentation approach, we will have to wait until we have all the scans to run them as a batch. Therefore, results for MRI will not be ready until data collection is complete.

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

PhD Students: Development of biomechanical tasks for this study have been provided by Karim Khattab, a graduate student in the Joint Bioengineering PhD program between UCSF and UC Berkeley. This project has advanced his training through mentorship from myself and Dr. Matthew (study Co-Investigator) to further develop the sit-to-stand and staggered sit-to-stand biomechanical assessment for this study. He will also be helping develop the gait assessment.

Medical students: UCSF first-year medical student, Adrian Valderrama, attained a 2021 summer research fellowship to work on the MRI analysis component on this study.

Masters students: Dr. Matthew is working with a team of mechanical engineering masters students from UC Berkeley to develop relevant biomechanical modeling for the proposed study.

**How were the results disseminated to communities of interest?**

Nothing to report.

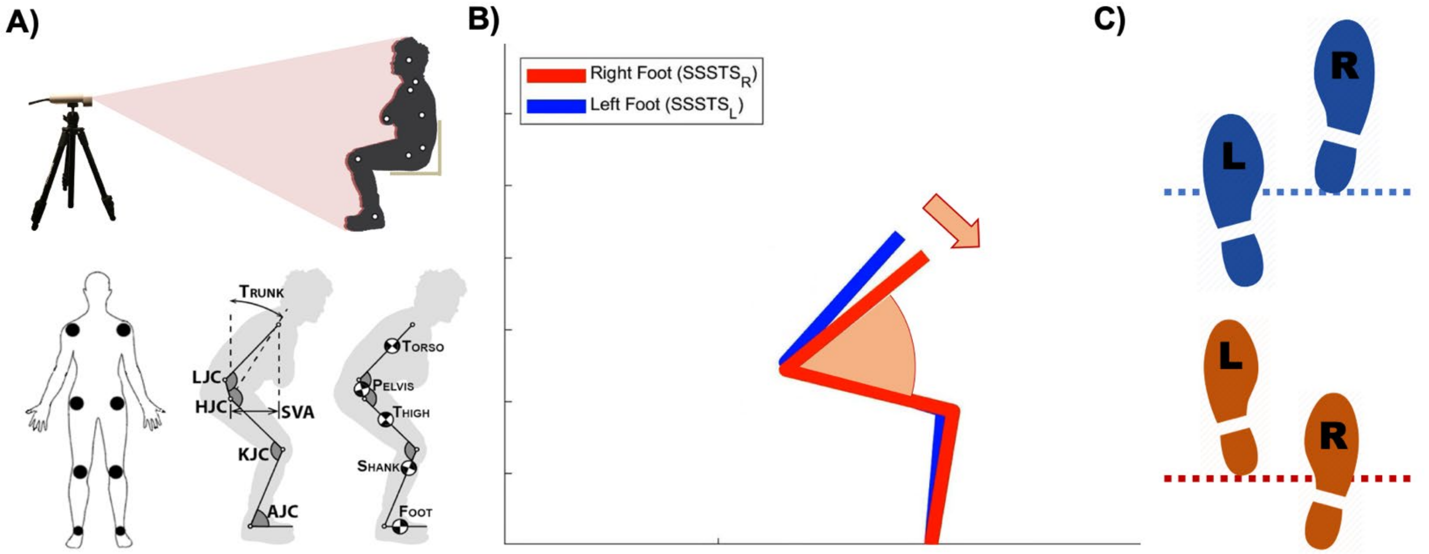
**What do you plan to do during the next reporting period to accomplish the goals?**

Our protocols are set and we will not be changing them. Over the next year we will complete data collecting and analysis. We plan for 2-3 publications. One on the kinematic motion patterns with fatigue and another on asymmetry in applied and resulting force at the hip and the location of center of pressure. The muscle quality data from MRI will be its own paper or be included with one of the motion/biomechanics papers listed above.

## 4. IMPACT:

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

Our growing work on developing the in-clinic biomechanical assessment for the staggered sit-to-stand has shown differential compensatory biomechanics that we are using to understand the effects of lower limb biomechanical dysfunction and pain on whole body biomechanical stability. We will be using this staggered sit-to-stand approach as a part of our biomechanical assessment within this grant, but we are also able to use it in the clinic with 3D depth mapping cameras to collect quick and non-invasive routine biomechanical data on our lower limb amputees. This will ultimately contribute more robust and quantitative outcomes for tracking patient function and recovery.




The figure above presents the staggered sit-to-stand biomechanical assessment. We use markerless 3D depth mapping to track joint positions of patients as they rise in and out of a seated position (Panel A, top). Then with limb length constraints and noise filtering algorithms we are able to estimate accurate patient-specific kinematics and dynamics during the maneuver (Panel A, bottom). For this test, we have the patients do separate trials with their feet staggered to require them to rely more on the posterior placed foot (Panel C). Doing this, we find distinct compensatory biomechanical strategies that correspond with loading on unaffected versus affected lower limbs (Panel B, Right side affected).

**What was the impact on other disciplines?**

Our study seeks to understand the effect of hip muscle health on biomechanical dysfunction in transfemoral amputees in order to understand risk if there is elevated risk for developing hip osteoarthritis or needing a future hip surgery. Therefore, there is a natural symbiosis between what we are developing as part of this study on hip health in transfemoral amputees and our non-amputee hip osteoarthritis and arthroplasty patients. This staggered sit-to-stand test is now also being used in the arthroplasty clinic at UCSF to amass a database of biomechanical data on subjects with advanced hip osteoarthritis in order for us to compare our transfemoral amputee data too in order to better understand how biomechanical behaviors in our amputees may be indicative of hip dysfunction. However, by integrating this tool into the hip clinic, we can use it to track changes pre- and post-op recovery of total hip replacement and ultimately use pre-operative biomechanical function to possibly predict risk for poor post-operative outcomes.

**What was the impact on technology transfer?**

Nothing to Report.

**What was the impact on society beyond science and technology?**

Nothing to Report.

**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**

**COVID delays:** Currently, we do not anticipate any additional delays due to COVID and currently there are no more restrictions on non-essential human subjects research.

**MRI eligibility:** Our first three study subjects were all transfemoral osseointegration patients and two of which were not able to safely have hip MRIs due to unanticipated factors that can cause discomfort/heating, like 1) pre-existing shrapnel in the residual limb, and 2) existing hardware in the hip. These were the only two patients that we know of with factors that would impede their ability to have a hip MRI and fortunately, more osseointegration patients will become eligible for our study soon, enabling us to increase our sample size to have at least eight osseointegration patients with both MRI and biomechanical analysis.

**Changes that had a significant impact on expenditures**

Nothing to report.

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

Nothing to Report.

**Significant changes in use or care of human subjects**

Nothing to Report.

**Significant changes in use or care of vertebrate animals.**

N/A

**Significant changes in use of biohazards and/or select agents**

N/A

## 6. PRODUCTS:

**Publications, conference papers, and presentations**

i. **Journal publications.** Nothing to Report.

ii. **Books or other non-periodical, one-time publications.** Nothing to Report.

iii. **Other publications, conference papers, and presentations.** Nothing to Report.

**Website(s) or other Internet site(s)**

Nothing to Report.

**Technologies or techniques**

Nothing to Report.

**Inventions, patent applications, and/or licenses**

Nothing to Report.

**Other Products**

*Nothing to Report.*

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

**What individuals have worked on the project?**

| | |
|---|---|
| Name: | Jeannie Bailey |
| Project Role: | Principal Investigator |
| Researcher Identifier (e.g. ORCID ID): | https://orcid.org/0000-0003-4618-7512 |
| Nearest person month worked: | 2 |
| Contribution to Project: | Dr. Bailey has worked to initiate the study with IRB approval, establish MRI protocols and have them in place for human subjects, and mentored Graduate Student Karim Khattab on developing Biomechanical Assessment. |
| Funding Support: | This award. |

| | |
|---|---|
| Name: | Robert Matthew |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | https://orcid.org/0000-0002-8649-2506 |
| Nearest person month worked: | 2 |
| Contribution to Project: | Dr. Matthew has worked on developing analysis for the sit-to-stand testing and mentored Graduate Student Karim Khattab on developing Biomechanical Assessment. |
| Funding Support: | This award. |

| | |
|---|---|
| Name: | Richard O'Donnell |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. O'Donnell has helped with patient recruitment. |
| Funding Support: | This award. |

| | |
|---|---|
| Name: | Roland Krug |
| Project Role: | Co-Investigator |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Krug has worked advanced imaging MRI sequences for this study. |
| Funding Support: | This award. |

| | |
|---|---|
| Name: | Karim Khattab |
| Project Role: | Graduate student |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 1 |
| Contribution to Project: | Dr. Khattab has worked on developing Biomechanical Assessment. |
| Funding Support: | Graduate fellowship |

| | |
|---|---|
| Name: | Adrian Valderrama |
| Project Role: | Medical student |
| Researcher Identifier (e.g. ORCID ID): | |
| Nearest person month worked: | 1 |
| Contribution to Project: | Adrian is working on MRI analysis for this study. |
| Funding Support: | Research fellowship. |

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
Nothing to Report.

**What other organizations were involved as partners?**
Nothing to Report.

**8. SPECIAL REPORTING REQUIREMENTS**
**COLLABORATIVE AWARDS:** Nothing to Report.
**QUAD CHARTS:** Updated milestone timeline projections with Y1Q4 quad chart.

**9. APPENDICES:** N/A