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TITLE: Effects of Temperature Control Liner Materials on Long-Term Outcomes of Prosthesis Use

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14. ABSTRACT
The goal of this project is to investigate the clinical effectiveness of temperature-controlled prosthesis liners over the long-term. To that end, outcome data are being collected at two sites over a total period of 12 months, including two 6-month intervention periods with comparable climate conditions (i.e., equal amounts of cold and warm weather). In accordance with this project plan, no results are yet available. Preparations for the data collection, including ethics review and approval of the protocol, and participant recruitment have taken up the first months of the project period. The death of one site-PI in February of this year lead to unexpected delays in these efforts, as replacements needed to be identified and trained. Consequently, while the recruitment goals (25 enrollees per site) are being approached at the main site, recruiting has not yet started at the secondary site.

15. SUBJECT TERMS
Limb prosthetics; liner suspension; temperature control; phase-change material

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a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
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Table of contents:

- **INTRODUCTION:**

  The purpose of this research is to investigate the clinical effectiveness of temperature-control prosthesis liners. Such liners, which have recently become commercially available, promise to improve the micro-climate around the residual limb in users of limb prostheses. We investigate this claim in a multi-site double-blind randomized cross-over study design, intended to generate high-quality evidence.

- **KEYWORDS:**

  Artificial limbs, liner suspension, temperature control, phase change materials, clinical trial, outcome assessment, mobility, step count

- **ACCOMPLISHMENTS:**
  - **What were the major goals of the project?**
    - *Goals for the first year of the project were obtaining approval from the local IRBs and the USAMRMC ORP HRPO (Month 1), The recruitment of all 50 subjects (25 per site) by month 9, and the commencement of data collection (Month 6).*
  - **What was accomplished under these goals?**
    - *(1) Major activities, as related to the ethics approvals included the preparation and submission of the respective applications, followed by responding to change requests and homogenization of approved protocols across sites. Pitt IRB approval was obtained on 10/17/2017 and renewed for another year on 09/28/2018. The respective HRPO approval was issued 02/01/2018. A conditional approval from the Widener IRB was obtained on 02/23/2018. The passing of site-PI Dr. Akins on the same day and subsequent search for a replacement delayed the final approval until 09/11/2018.*
    - *Recruitment activities at the Pittsburgh site commenced in the spring of 2018, after it was clear that the recruitment materials were acceptable to all involved review boards. To date, a total of 27 potential participants were contacted and/or screened, of whom 8 were enrolled and 7 were found ineligible. While recruitment efforts are ongoing, formal enrollment of new participants was deferred to the fall when it became clear that the start of the data collection period would be delayed. (In order to cover warm and cold seasons of the year equally, the two consecutive 6-month intervention periods must start either in mid-July or in mid-January. For best comparability across the sample, all participants should start the protocol at the same time.) Recruitment at Widener started after the final IRB approval and the process of screening and enrolling candidates was ongoing by the reporting date.*
    - *In light of the unforeseen personnel changes, the start of the data collection period for the entire cohort was postponed from the initially planned July 2018 date, to January 2019. Meanwhile, the necessary personnel (graduate and research assistants) was hired and trained, the equipment (Stepwatch monitors and periphery)*

was purchased, and other preparations, such as those regarding the logistics of the randomization protocol and double blinded liner assignments were concluded.

- *(2) Specific objectives of this study were not yet met at this stage, owing to the nature of the long-term protocol and the associated unavailability of data for analysis*
- *(3) Results or key outcomes can likewise not yet be reported.*
- *(4) Other achievements: We have been working on publishing the protocol, which we believe may be adoptable for future randomized controlled trials in the field of prosthetics and orthotics. A respective conference abstract (submitted) is attached, and a journal manuscript is under preparation at this time. Several local news reports have mentioned the study and have been helpful in interesting potential subjects in participation.*
- *The methodology for recruitment and screening has been executed as proposed, using the Pitt+Me research registry, outreach through amputee support groups both offline and online, and disseminating information about the study at local P&O businesses and events. An IRB approved screening script is used to determine eligibility at intake of a potential participant. Recruitment and screening materials are essentially identical between the two sites.*

- **What opportunities for training and professional development has the project provided?**
  - *A number of graduate assistants are supported through this grant and are gathering hands-on research experience by taking on duties in the context of executing the protocol. Those students receive individual guidance and mentoring from the investigators, as well as standardized training in human subjects' protection and research ethics.*
  - *Also, the unanticipated necessity to replace part of the study team led to some activities in that domain. PI Fiedler met repeatedly with colleagues and students at Widener University, in order to convey knowledge specific to this research area, including the state of the science, typical barriers and limitations, and the importance of the goals of this project in this context.*
  - **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?**
  - *The next reporting period will be dedicated to completing the recruitment phase of this project and to starting the data collection. While, due to the previous delays, the one-year-data collection will not be completed by the end of the next period, this effort will help us adhere to the updated timeline to eventually accomplish the goals and objectives.*
- **IMPACT***:*
  - **What was the impact on the development of the principal discipline(s) of the project?**

- *Nothing to Report.*

- **What was the impact on other disciplines?**
  - *Nothing to Report.*
- **What was the impact on technology transfer?**
  - *Nothing to Report.*
- **What was the impact on society beyond science and technology?**
  - *Nothing to Report.*

- **CHANGES/PROBLEMS:**
  - **Changes in approach and reasons for change**
    - *One slight change in our approach to recruitment has become necessary when it became apparent that our preferred pathway of attracting participants through referrals by local practitioners is ineffective. Due to the nature of the protocol, which entails that participants receive study liners for the entire 1-year period, practitioners, who ordinarily bill their patients for such liners, have a conflict of interest. Upon realizing this issue, we have shifted our focus on advertising the study to prosthesis users directly, through support groups, online groups, and word-of-mouth.*
  - **Actual or anticipated problems or delays and actions or plans to resolve them**
    - *The main problem that affected the timeline of this project was the unexpected passing of Dr. Akins. We eventually managed to recruit a replacement at the same institution, after a long search and having to replace the initial, ineffective replacement after four months. There were associated delays in hiring the graduate assistants, though these had no adverse effects but were concomitant with the status of the study activities at the time.*
  - **Changes that had a significant impact on expenditures**
    - *Expenditures have been lower than anticipated, reflecting the delays in staffing for this study. If an extension of the study period becomes necessary, it is expected that these funds will be sufficient to cover the costs.*
  - **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
    - *No changes to report.*
  - **Significant changes in use or care of human subjects**
    - *No changes to report.*
  - **Significant changes in use or care of vertebrate animals.**
    - *Not applicable*
  - **Significant changes in use of biohazards and/or select agents**
    - *Not applicable*

- **PRODUCTS:**
  - **Publications, conference papers, and presentations**
    - **Journal publications.** *Nothing to report.*
    - **Books or other non-periodical, one-time publications.** *Nothing to report.*
    - **Other publications, conference papers, and presentations.** *Fiedler, G., Singh, A., Zigler, C. (2019). "Applicability of Double-Blinded Randomized Controlled Trials in Prosthetics & Orthotics Research", 45th Annual AAOP Meeting and Scientific Symposium, Orlando, FL, Mar 6-9, under review*
    - **Website(s) or other Internet site(s)**

      Pitt+Me study page: https://pittplusme.org/studyarms/publicdetails?guid=321eea6d-40c0-4cae-87f2-2e6a7e4ae34b

      Clinicaltrials.gov page: https://clinicaltrials.gov/ct2/show/NCT03428815
    - **Technologies or techniques**

      Nothing to report.
    - **Inventions, patent applications, and/or licenses**

      Nothing to report.
    - **Other Products**

      Nothing to report.
- **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**
  - **What individuals have worked on the project?**

Name:	*Goeran Fiedler*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	*Gfiedler*
Nearest person month worked:	*2*
Contribution to Project:	*IRB protocol modifications, equipment sourcing, recruitment (started Pitt+Me registry entry, started clinicaltrials.gov entry), enrollment of subjects, hiring of research assistant, visit/training of new personnel at Chester site*
Funding Support:	

Name:	*Jonathan Akins*
Project Role:	*Co-PI (through Feb 2018)*
Researcher Identifier (e.g. ORCID ID):	*jsakins*

Nearest person month worked:	*1*
Contribution to Project:	*IRB application and protocol modifications, preparation for recruitment, GSR hiring*
Funding Support:	

Name:	*Zhongping Huang*
Project Role:	*Co-PI (Mar-Jul 2018)*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*0*
Contribution to Project:	*n/a*
Funding Support:	

Name:	*Anita Singh (from Aug 2018)*
Project Role:	*Co-PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*0*
Contribution to Project:	*IRB protocol rectifications, recruitment, GSR hiring and training*
Funding Support:	

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
  - *No.*
- **What other organizations were involved as partners?**
  - **Organization Name:** *Widener University*
  - **Location of Organization:** *Chester, PA*
  - **Partner's contribution to the projec**t *(identify one or more)*
    - **Collaboration** *(external site for this multi-site study)*
- **SPECIAL REPORTING REQUIREMENTS**
  - **QUAD CHARTS:** *An updated Quad Chart is inluded with attachments.*
- **APPENDIX:** *Conference abstract submitted to AAOP 2019*

Applicability of Double-Blinded Randomized Controlled Trials in Prosthetics & Orthotics Research

Goeran Fiedler[1], Anita Singh[2], Christina Zigler[1,3]
University of Pittsburgh[1], Widener University[2], Duke University[3]

INTRODUCTION

A Randomized Controlled Trial (RCT) is generally considered to provide one of the highest levels of scientific evidence [1]. Key element of a RCT is that a large number of participants receive either the intervention in question or a comparison treatment, (i.e., the current standard of care or a placebo). Ideally, participants' random group assignment is also concealed from both themselves and the involved research personnel. This eliminates many potential biases that can affect responses to interventions, which increases the chances that the study findings are representative of real effects of the intervention.

Unfortunately, RCTs are uncommon in Prosthetics & Orthotics (P&O) research. While this is excusable with the logistical challenges of recruiting large enough samples [2] from a very heterogeneous target population, and of randomly assigning them custom-fitted devices while concealing the nature of those devices [3], the lack of RCTs remains a detriment to Evidence Based Practice (EBP) in our field.

We describe the pilot testing of a protocol that addresses most of the mentioned challenges and that may be applicable to other areas of P&O research.

METHOD

Among the few standardized prosthesis components that are easily interchangeable (and can thus be randomly assigned) are the liners that are used for socket suspension. Further, such liners can be made to look identical, irrespective of the used material, allowing the concealment of group allocation. This allowed the design of am IRB approved RCT protocol to compare different liner types.

Subjects: Users of trans-tibial prostheses with liner suspension were recruited for this pilot data collection

Procedures: Participants used one of two identical looking liners each for four weeks in a randomized sequence. One of the liners was from conventional gel material, the other one from phase change material (PCM) to better control limb temperature.

Blinding Protocol: Study liners were custom ordered in an identical design, and groups were assigned by a study team member without direct patient contact.

Data Analysis: Feasibility of the protocol for outcome comparison between interventions was assessed.

RESULTS

Three participants were enrolled in this study. All were adults (age >40 years), at a healthy weight (<100kg), and more experienced prosthesis users (≥8 years).

The protocol allowed measuring daily step count, two-minute walk distance and days where the prosthesis was not used (Fig 1), as planned. The self-reported burden of participation was very low. Users and investigators were unsuccessful in guessing the liner type, suggesting the blinding protocol was effective.

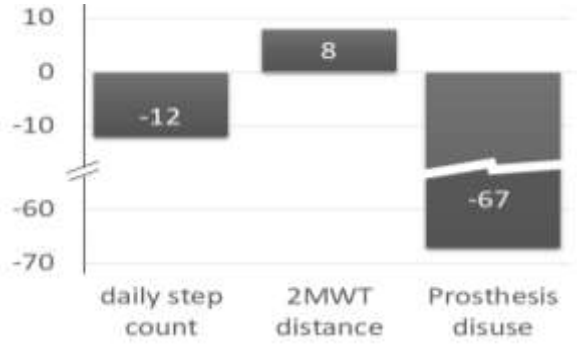

Figure 1: Percentage change with the PCM liner, sample data from one pilot subject.

DISCUSSION

Although small, the pilot data collection supported feasibility of this RCT protocol, and motivated a larger scale clinical study with 50 participants that is currently underway. Blinding and randomization was relatively uncomplicated. However, the logistics of long-term follow-up appeared to be most challenging.

CONCLUSION

The discussed approach may be considered for similar studies of P&O interventions.

CLINICAL APPLICATIONS

High level evidence is important for effective device prescription and EBP. We showed that RCTs in P&O are difficult to design, but not impossible.

ACKNOWLEDGEMENT

This work was supported by the Office of Assistant Secretary of Defense for Health Affairs, through the Orthotics and Prosthetics Outcomes Research Program, Prosthetics Outcomes Research Award under Award No. W81XWH-17-1-0700. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

REFERENCES

1. *The Oxford 2011 Levels of Evidence.* http://www. cebm. net/index. aspx? o= 5653, 2011.
2. Beaudette, Fiedler, JPO, 2018. **30**(2): p. 60-68.
3. Clark, Fiedler, *43rd Annual AAOP Meeting and Scientific Symposium*. 2017: Chicago, IL.

American Academy of Orthotists & Prosthetists
45th Academy Annual Meeting & Scientific Symposium
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Effect of temperature control liner materials on long term outcomes of prosthesis use

W81XWH-16-OPORP-PORA

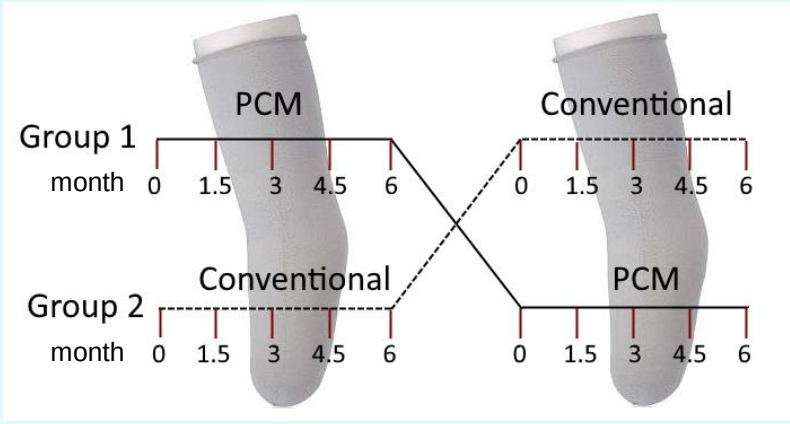
PI: Goeran Fiedler, PhD **Org:** University of Pittsburgh **Award Amount:** $498,685

Study/Product Aim(s)

- To compare PCM liners to conventional liners with regard to activity and participation
- To quantify the effect of PCM liners on activity, health related quality of life, and performance over time
- To investigate the relationship between perceived benefits of PCM liners and patient-centered outcomes

Approach

Trans-tibial prosthesis users will be recruited and randomly assigned to PCM or conventional liner groups. Prostheses will be equipped with activity monitors and participants will be asked to maintain a log of any perceived issues. Assessments will be at 6 week intervals and include daily step counts, residual limb volume, 2-minute walk test, and self-reported levels of discomfort and quality of life. After 6 months, participants will wear the other liner and be assessed at 6-week intervals.



Prosthesis liners containing phase-change materials (PCM) have been shown to have immediate effects on residual limb temperature. The proposed protocol will allow the investigation of long-term effects on residual limb health and prosthesis utilization.

Timeline and Cost

Activities CY	17	18	19
Finalize protocol and IRB approvals			
Participant recruitment and data collection			
Follow-up, Analysis			
Present results and progress at national meetings			
Estimated Budget ($K)	**100**	**250**	**150**

Updated: 12 Oct 2018

Goals/Milestones

CY17 Goal – Preparation and initiation

☐ Finalize protocol based on reviewers' feedback **- done**

☐ Update IRB approved protocol from pilot testing **- done**

☐ Begin recruitment for timely start of first cohort data collection in January 2018 – postponed for intervention period start Jan 2019

CY18 Goals – Data collection

☐ Complete recruitment for data collection start – **partly done**

☐ Prepare completion of data collection of 1st cycle, start 2nd cycle

☐ Preliminary results, abstracts, presentations – **partly done**

CY19 Goals – Data analysis, dissemination

☐ Complete data collection by July

☐ Analyze results, prepare manuscripts, presentations

Comments/Challenges/Issues/Concerns

- Necessary key personnel changes after the death of co-PI Akins caused delays in obtaining ethics approval and subjects' recruiting.

Budget Expenditure to Date

Projected Expenditure: $225,000

Actual Expenditure: $70,303.96