Moisture Management Liner At-Home Evaluation

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1. Background and Introduction

The comfort and fit of the residual limb within a prosthetic socket are of primary concern for many amputees. The residual limb is typically covered by non-breathable and non- thermally conductive materials that can create a warm and ultimately moist environment. Studies found increases in socket temperature after the prosthesis was donned (0.8°C) [1] and after 30 minutes of walking (2.5°C) [2]. Temperatures were found to remain elevated long after activity cessation and even a rest period of double the duration of the preceding activity period is insufficient to return the limb to its initial temperature [3]. Peery, et al. suggested that a modest temperature increase of only 2°C may be responsible for reports of thermal discomfort by amputees [1]. Therefore, a small amount of activity can cause the socket temperature to elevate and remain at an uncomfortable level for an extended period of time, which can lead to decreased wear times. In summary, an uncomfortable socket/residual limb interface decreases prosthesis use among amputees who want to remain active in their lives.

To address this, Vivonics, Inc. and Liberating Technologies, Inc. (LTI) have developed a silicone liner approach to passively conduct heat from the skin using thermally conductive elastomers. A technology that can provide thermal control while retaining adequate suspension, weight, and other prosthetic characteristics would benefit many prosthesis wearers.

2. Study Rationale

This study will focus on investigating the efficacy of this novel moisture and thermal management (experimental) liner.

The rationale for this study is to determine how well the new technology can regulate the residual limb temperature and reduce the moisture generation in a home environment where the device would ultimately be utilized.

3. Objectives

The primary objective of this study is to measure the effects of residual limb moisture and thermal management on quality of life (QoL) and functional outcomes. Reducing temperature increases of the residual limb inside the prosthetic socket would result in less sweating and greater comfort while wearing the prosthesis, and ultimately greater function and better quality of life as measured by standard functional and QoL outcome measures.

4. Study Design

A prospective design will be implemented for this study. Research participants will be consented by LTI over the phone. Residual limb measurements will be received from the participant to confirm liner sizing. One 'experimental' prototype liner will be created for each participant. Subjects with a similar liner size and profile to the available experimental liners will be targeted. If the experimental liner does not fit well with the subject's usual socket, a new socket will be fabricated for them to use throughout the study duration. Temperature and step-count sensors will be placed on the participant's prosthesis to log daily measurements. Testing will consist of 2 site visits, with the entire study lasting approximately 5 weeks.

5. Study Population

Lower limb prosthesis users will be recruited for the study and consented with an approved protocol. Research participants will represent a convenience sample and will reflect the local population of people with lower limb differences who use prosthetic sockets and could benefit from temperature control within the socket.

A convenience sample of 12 subjects will be used for this pilot study to gather data on the effects that this experimental liner may have on quality of life (QoL) due to skin issues. A pilot study is defined by Moore, et al. (2011) as a timely and cost-effective preparatory study intended to inform the successful design of future, often larger, clinical studies by testing study designs, measures, procedures, recruitment criteria, etc. While larger sample sizes can yield more precise estimates confidence intervals and variance estimates, there are diminishing returns with larger samples sizes. These diminishing benefits often become outweighed by practicalities such as time and funding. Therefore, we will follow the recommendation of Moore, et al. (2011) and include 12 participants to estimate average values and variances of the outcome variables in our target population.

While the recruitment of anything above a modest number of amputees can be challenging, we have mitigated this challenge by partnering with RISE Prosthetics & Orthotics (P&O). Testing will occur at LTI in Holliston, MA, and RISE P&O in Denver, CO to increase our pool of potential subjects from multiple geographic areas and to receive multiple prosthetists' input on the experimental liner. LTI will enlist the aid of its current in-house prosthetist, Jonathan Cook, CPO and its network of prosthetists including Next Step B&P, Cornell O&P, and several others, to assist in subject recruitment for their site. Additionally, prosthetists at RISE P&O will be recruiting from their own patient base to participate at their respective sites.

Prosthetists will be given flyers to distribute to their patients and if they are interested in participating, the patient can call the number on the flyer directly to discuss the study with the investigators. In addition, previous research participants who have given permission to be contacted for future studies may be contacted directly to assess interest in participating in this study. Additionally, flyers will be distributed online (e.g. LTI's website: LiberatingTech.com/research-studies) and in person to persons who may be within the target population. If subjects are interested in participating, they can call the number on the flyer and schedule a time to discuss the study with the investigators.

A maximum of 16 subjects will be recruited for this study. This sample size accounts for subject drop out and other losses (such as incomplete log data, etc.) to yield usable data from the target 12 subjects required by the power analysis.

6. Participant Eligibility

Lower limb amputees will be identified who meet the following inclusion criteria: must be 18-89 years old, be willing and able to complete the tasks outlined, are at least 6 months on a lower-limb prosthesis, fits within an experimental liner (cusion style liner and size 23.5-28 cm), and can understand English in order to be properly consented and provide their feedback to the study personnel. Subjects can be excluded at the discretion of the investigator for other unforeseen disqualifying criteria (such as specific cognitive issues, etc.).

Some subjects participating at the RISE Prosthetics & Orthotics research site may be employees of that research site. These employees cannot be directly involved in the execution, data collection, or analysis of this research study.

Subjects in this study will not be discriminated by sex or race.

The risks to pregnant women and fetuses are unknown and therefore pregnant women should not participate in the study and will be screened by self-disclosure.

7. Study Methodology

During all the test visits outlined below, we will follow all the guidelines set in place by RISE, LTI, the states of Massachusetts and Colorado, and the CDC to mitigate the risk of transferring or contracting Covid-19 between and amongst researchers and test subjects. This is described in more detail in the Covid-19 Procedures document.

Prior to the first visit, the subject will be screened and consented over the phone. After they fully understand the study they will send their signed consent form to LTI electronically and be enrolled in the study. Limb measurements will then

be provided by the subject or their prosthetist to allow an experimental prototype liner to be fabricated for them. Once the experimental liner is ready, the subject will come to the test site for their first visit.

Visit 1: During the first visit, the subject will be asked to fill out a questionnaire for quality of life (QoL) with respect to their current liner as a basis for comparison with the experimental liner. The assessment includes the following validated and verified measures: EuroQol-5D, the Dermatology Life Quality Index (DLQI), and the Modified Dermatology Life Quality Index (mDLQI) [4,5].

Residual limb measurements will either be already known by the sites or sent from the subject or their prosthetist before visit 1 so the proper liners can be ordered ahead of time. After completing the questionnaire, the subject will don the experimental liner to make sure the fit with their usual socket is comfortable and they are able to safely walk with the experimental liner.

At this time, the subject's socket would be fit with an activity monitor (such as the StepWatch™) to measure the use of the prosthesis and temperature sensors (such as the iButton) on the exterior of the socket to monitor the ambient temperature and on the interior of the socket/liner to monitor the intrasocket temperature. The Thermochron family of iButtons are tiny, durable data loggers that monitor time and temperature that have been used clinically and in take-home research studies in the O&P field. The StepWatch is an activity monitor/step counter that has been shown to have excellent accuracy at slower gait speeds typical of lower limb amputees. These measures would be used as reference measures to have a better understanding of the user's activity. The subject will wear their newly instrumented socket at home for 5 weeks.

The subject will be instructed to wear the new liner without the socket at home for roughly 1 hour a day for the first week (this can be accomplished during everyday tasks such as working at a desk or watching TV on the couch). This adjustment period will allow their limb to become accustomed to the experimental liner. After the one week period a research coordinator will contact the subject to check in and remind them to start wearing the experimental liner with their socket as they would with their standard everyday liner for the next 4 weeks.

During this time, the subject will be asked to give feedback on the thermal comfort and perspiration in the socket. The feedback will be obtained via a paper log on which the subject enters daily feedback on thermal comfort and perspiration over the course of the final 4 weeks. A research coordinator will be calling subjects periodically to remind them to fill out the log and answer any questions that they may have.

This visit will take up to 2 hours.

Visit 2: At the end of the month-long testing period, the subject will return to the lab for a 2nd visit. During this visit, they will be asked to complete the same QoL questionnaire given previously, but this time with respect to the experimental liner. Then, all sensors will be removed from the subject's socket and the experimental liner will be returned to the site. The staff prosthetist at the site will inspect the limb to check for any skin issues and ensure their standard everyday liner is still comfortable within their socket.

This visit will take up to 2 hours.

At the end of this visit, the subject will have completed the study.

8. Study Conduct

Subjects will be consented and screened for eligibility criteria by LTI over the phone. According to each site's privacy standards and with the subject's permission, identifiable information such as name, phone number, and email address, will be shared from the involved prosthetists at RISE to LTI. After being consented the subject will share their own information (mailing address, etc.) to LTI for payment. If the subject decides to participate, their usual socket will be instrumented with an activity monitor and temperature sensors. The subject will wear the instrumented usual socket home with the experimental liner for 5 weeks, then return their experimental liner and sensors back to the lab. The study will consist of a 5 week period of participants wearing the experimental liner at home and logging their comfort, activity levels, temperatures, and feedback.

Subjects may withdraw at any time by simply telling the investigators they wish to stop their participation.

If a subject withdraws from the study, the data that were collected from them can still be used, and the withdrawn subjects may be replaced with a new subject. Deviations from the protocol that increase risks for subjects will be reported to Solutions IRB and HRPO for approval prior to being implemented.

Approved study staff from Vivonics, Inc. may also be present during testing visits at LTI to provide technical support or monitor testing activities. During these visits approved study staff from Vivonics, Inc. may be in contact with the subjects.

Subjects will be compensated $40 per hour for the in-lab visits for an estimated total of $160 per subject. For the take-home testing, each subject will receive $250 for the 5 weeks of wearing the experimental liner. The anticipated total to complete the study would be $410.

9. Study Treatment

This study is not a means of providing any sort of medical treatment to its participants. The purpose of the study is to evaluate the effectiveness of the experimental liner. No drugs will be administered to the participants.

10. Evaluation of Adverse Events

Based on past testing and data collection, no adverse events are expected. Adverse events could include discomfort or dermatological reaction due to either the experimental liner materials or socket/liner fit. These risks have been mitigated by using biocompatible materials as well as having a certified prosthetist present while the subject tests the fit of the experimental liner with their usual socket.

All unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study and subject deaths related to participation in the study will be promptly reported to Solutions IRB and HRPO. A written description of the adverse event will be stored in the study file maintained by the Principal Investigators. Also, the protocol will be reviewed in light of the adverse event to determine if modifications need to be made to prevent the event from occurring again. Major modifications to the research protocol and any modifications that could potentially increase risk to human subjects must be submitted to Solutions IRB and HRPO for approval prior to implementation.

11. Ethical Considerations

There is no direct benefit to the user. Participating in this study may potentially advance the scientific community's understanding of the effect of reducing intra-socket moisture and temperatures on the activity, comfort and quality of life of lower limb amputees.

The protocol, consent form, and recruitment flyer will require IRB review and approval. The principal investigator will be in continuous communication with the IRBs and HRPO and will forward information to the co-investigators. Subjects' participation is voluntary, and they may withdraw from participation in the study at any time by simply telling any one of the investigators that they wish to stop. The investigators may choose to terminate a subject's participation if he or she experiences discomfort or injury. In addition, participants will be given any new information which is discovered during the course of the study which may influence participants' willingness to continue the study. If they desire to do so, subjects will also have the option to discuss any concerns regarding the study activities or the investigators with an impartial staff member of the site IRB, whose duty it is to hear and review such concerns and provide advice or take any other appropriate actions.

The investigators will ensure the anonymity of all participants in this study. After completing the consenting process, subjects will be assigned a random identification number. The number will be used on all test data associated with the subject. No personal identifiers will be associated with the data collected from the subjects during the various tests. The PI will have a master document linking the subject name with ID number, and it will be stored on a password protected computer, with only the PI and approved study staff having access to the master list. Test data will be kept at Liberating Technologies, Inc., RISE, and Vivonics and stored in a secure manner depending on the media: either a password protected computer with access limited to the co-investigator, or in a locked filing cabinet in the investigator's office. A copy of the test data will also be retained by the PI in the program folder, also stored in a secured manner.

12. Study Monitoring and Oversight

The oversight of the study falls on the co-investigators. They will be responsible for ensuring the study follows the approved protocol and for reporting any deviations or adverse events that occur during the study to Solutions IRB and HRPO. The PI will ensure that an IRB continuing review (CR) approval will be obtained if necessary and per applicable regulation(s). Additionally, the PI will ensure that a final study report is submitted, including any supporting documents, to the DoD when available.

De-identified data, photos, and videos will be kept indefinitely to show in scientific presentations and publications. Photos will not contain any identifying information about the subject. The photographs will not include the subject's face or any identifying marks such as tattoos. If identifying photographs happen to be received from a subject, they will be de-identified by either cropping or blurring using photo-editing software.

Representatives of the U.S. Army Medical Research and Development Command (USAMRDC), Office of Research Protections (ORP), and Solutions IRB are authorized to review research records as part of their responsibility to protect human research volunteers. These research records can contain protected health information (PHI) as defined by HIPAA. Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by Solutions IRB, the study institutions, the Sponsor, or regulatory agencies will be promptly reported to the DoD regulatory office.

The knowledge of any pending compliance inspection/visit by the FDA, DHHS Office of Human Research Protections (OHRP), or other government agency concerning this research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any regulatory agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements, will be promptly reported to the DoD.

13. Investigational Product Management

The experimental liners tested in this study are modified to increase the thermal conductivity to regulate intra-socket temperature and reduce moisture accumulation

EXPERIMENTAL LINER

The experimental liner is a product of mixing thermally conductive additive to a base silicone material. The base material is a medical grade room temperature curing silicone rubber (RTV-2) from Wacker Chemie AG with characteristics of biocompatibility, low surface tension, thermal and chemical stability. This silicone can be sterilized easily for single as well as repeated use. The nature of the silicone is hydrophobic which prevents microbial growth. Additives such as boron nitride, carbon and graphene nanoparticles are added to enhance the thermal conductivity of the liner. These nanomaterials are skin safe and are currently being used in other skin contacting applications such as cosmetics and wearable electronics [6, 7, 8, 9]. The prototype liner material also passed an in vitro cytotoxicity test (L929 MEM Elution Test completed by Toxikon [Bedford, MA]).

The experimental liner will be manufactured and packaged at a manufacturing facility that makes commercial off the shelf (COTS) liners using the standard procedures.

SOCKETS

If necessary, a temporary socket will be fabricated for the participant to use with the experimental liner. This temporary socket will be fabricated by a Board-Certified Prosthetist, following conventional standardized methods. The socket characteristics will be similar to the subject's usual socket, monitoring and maintaining acceptable mobility and comfort throughout the testing procedure.

ACTIVITY MONITORS

Commercial activity monitoring devices such as the StepWatch will be used to record how many steps the subject has taken and may also be used to help determine when the subject is wearing his/her prosthesis.

TEMPERATURE SENSORS

Commercially available temperature sensors, such as iButtons, may be used to monitor the temperature of the ambient air and/or residual limb inside the prosthetic socket. The iButtons have been used in the approved protocols for the previous and current studies (NEIRB # 120180039/ HRPO Log A-20010.2).

14. Data Analysis

The data collected in this study will include ambient temperature, activity (steps), a daily log, and standard outcomes measures for both the usual liner and experimental conditions. Outcomes measures include surveys such as the EuroQol-5D, the Dermatology Life Quality Index (DLQI), and the Modified Dermatology Life Quality Index (mDLQI).

The primary outcome of this study will assess the effect of the experimental liner on the intrasocket comfort and thermal comfort of the residual limb; however secondary measures include activity level and satisfaction with the prosthesis using the above measures.

15. References

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