IRB Minimal Risk Protocol Template

Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at http://intranet.mayo.edu/charlie/irb/

First-time Use: Use this template to describe your study for a <u>new</u> IRB submission.
1. Complete the questions that apply to your study.
2. Save an electronic copy of this protocol for future revisions.
3. When completing your IRBe application, you will be asked to upload this template to the protocol section.

Modification: To modify this template <u>after</u> your study has been approved:
1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
2. Open the saved document and activate "Track Changes"..
3. Revise the protocol template to reflect the modification points , save the template to your files
4. Create an IRBe Modification for the study and upload the revised protocol template.

General Study Information

Principal Investigator: Kenton Kaufman, Ph.D., P.E.

Study Title: Comparative Effectiveness between Microprocessor Knees and Non-Microprocessor Knees

Protocol version number and date: Version 1.3, September 2014

Purpose

Hypothesis:
Hypothesis 1a: Differences exist between Microprocessor Knees and Non-Microprocessor Knees.
Hypothesis 1b: Differences exist between the prosthetic and non-prosthetic limb for each prosthetic knee.
Hypothesis 2: Differences exist in fall rates between amputees using Microprocessor Knees and Non-Microprocessor Knees.

Aims, purpose, or objectives:
This study will assess if the functional performance and musculoskeletal outcome of transfemoral amputees are improved after receiving a Microprocessor Knee (MPK) compared to a Non-Microprocessor Knees (NMPK).

Aim 1: Quantify the functional efficacy and satisfaction of transfemoral amputees wearing different prosthetic knee joints.
Aim 2: Assess the safety of transfemoral amputees wearing different prosthetic knee joints.
Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc.*):

MPKs are prosthetic knees that use a microprocessor to control the prosthetic knee mechanism and adjust knee stiffness. Comparative studies have documented improved gait symmetry (Kirker, *Clinical Rehabilitation*. 10:267-273, 1996; Schmalz, *Gait and Posture*. 16(3):255-263, 2002) and lower energy consumption (Schmalz, *Gait and Posture*. 16(3):255-263, 2002; Taylor, *Prosthetics and Orthotics International*. 20:116-121, 1996; Buckley, *Archives of Physical Medicine and Rehabilitation*. 78:330-330) when using a MPK. Multiple studies (Hafner, *Archives of Physical Medicine and Rehabilitation*. 88(2):207-217, 2007; Kahle, *Journal of Rehabilitation Research and Development*. 45(1):1-14, 2008; Highsmith, *Prosthetics and Orthotics International*. 34(4):362-377, 2010) have shown that MPKs are more effective at preventing falls than NMPKs. Blumentritt evaluated the safety of a MPK vs. NMPK in the gait laboratory and demonstrated that the MPK offered the highest degree of safety and was the most suitable prosthetic intervention for preventing falls (Blumentritt, *Journal of Prosthetics and Orthotics*. 21(1):2-15). Kaufman (Kaufman, *Gait and Posture*. 26:489-493, 2007) demonstrated significantly improved balance, a more normal gait, and significantly more reliance on the MPK prosthesis, and that amputees spontaneously increase their activity in the free-living environment when using MPKs. The users' subjective feedback was that the MPK improved their quality of life. This study seeks to gather additional experience of community-living, transfemoral amputees using MPKs.

Our previous and current research activities demonstrate our abilities to conduct this proposed research program and yield novel research findings. Of particular relevance to this study is our prior objective comparison of MPKs to NMPKs (Kaufman, *Gait and Posture*. 26:489-493, 2007; Kaufman, *Archives of Physical Medicine and Rehabilitation*. 87(7): 1382-1385, 2008). Additionally, we are currently able to quantify activity in the free-living environment using the Actigraph, a commercially available activity monitoring device. The monitor is able to measure 3D acceleration and record the data using on-board memory. The activity monitor has been used by this research team to record the activities-of-daily-living of a transfemoral amputee for four continuous days while using a MPK. These data revealed that a large portion of the day was spent performing low level activity. There was asymmetry between the prosthetic and sound limb with more activity on the sound side. Finally, we have the capability to measure variable cadence in the free-living environment and have used this capability to study patients before and after total hip replacement surgery. These data demonstrate our ability to measure activity level in the field over multiple continuous days and provide a meaningful interpretation, and are able to provide a unique perspective on the patient's prosthetic usage. Our laboratory has also been conducting multiple studies utilizing a biweekly fall tracking mailer to record number of falls and details surrounding these falls. We currently have more than 80 subject-years of fall tracking under these IRBs that demonstrate our ability to successfully monitor subject falls via biweekly mailings.

Subject Information – charts, records, images, or specimens are considered 'subjects'

Target accrual: *Proposed number of subjects to be included in your study at your site. "Subjects" may include Mayo Clinic charts, records, or specimens, **and/or** charts, records, or specimens received at Mayo Clinic from external sources for collaborating analysis by the investigator under this IRB application*:
Target accrual is 50 subjects. 75 subjects may be screened to reach this target accrual.

Subject population: Subjects will include 50 unilateral transfemoral amputees, age 55 and over. No restrictions will be placed on gender or race. Efforts will be made to included equal numbers of subjects below and above 65 years of age.

Inclusion Criteria:
- Unilateral transfemoral amputee
- Medicare Functional Classification Level K2 or K3
- Currently using NMPK prosthesis
- Current NMPK prosthesis is well fitting at the socket
- No current stump problems, such as skin breakdown
- Able to ambulate without a gait aid

Exclusion Criteria:
- Previous neuromuscular complications currently affecting gait
- Currently undergoing dialysis treatments
- Amputation of the contralateral limb
- Poor fit of current NMPK prosthesis

Will a Certificate of Confidentiality be obtained? *If yes, provide an explanation.* No.

Study Design

Methods: *Describe, in detail, the research activities that will be conducted under this protocol*:

The study design is a reversal design whereby only the prosthetic knee joint will be changed. Each subject will be tested using their current NMPK, fit and tested with a MPK, and then tested again with their NMPK, e.g. A-B-A design. MPK prostheses from all manufacturers will be considered appropriate for testing. Each MPK to be used in this study is FDA approved. Each subject will be given an acclimation period (typically ~4 months) consistent with other similar studies (Hafner, *Archives of Physical Medicine and Rehabilitation*. 88(2):207-217, 2007; Kahle, *Journal of Rehabilitation Research and Development*. 45(1):1-14, 2008; Kaufman, *Archives of Physical Medicine and Rehabilitation*. 87(7): 1382-1385, 2008; Hafner, *Journal of Rehabilitation Research and Development*. 46(3): 417-433, 2009) before testing is commenced on the MPK. The foot will be in the L5981 class, e.g. flex foot or equivalent. The same socket, suspension, and foot will be used throughout the study in order to eliminate these confounding variables. All prosthesis fittings will be performed by the subject's own certified prosthetist according to manufacturers' fitting guidelines.

Patient Function (Efficacy): Field based measurements will be obtained using ActiGraph activity monitors attached to waist, and bilaterally to the ankle and thigh for a period of 4 consecutive days, including 2 weekdays and 2 weekend days. The subject will don the monitors in the morning after waking and remove them prior to sleeping.

Patient Satisfaction and Safety: The subject's self-assessed satisfaction and safety during the previous four weeks in their free-living environment will be measured at the end of each prosthetic rotation. The general health SF-36 questionnaire and condition-specific Prosthesis Evaluation Questionnaire (PEQ) will be used to quantify patient satisfaction. The PEQ addendum (PEQ-A), 14 additional questions used to quantify subject confidence, concentration, stumbles, and falls will also be administered to the subjects. To account for falls preceding the 4 weeks covered by the SF36 and PEQ surveys, bi-weekly fall tracking mailers will be filled out

by subjects. Subjects will also fill out the Patient-Specific Functional Scale at each of the 3 evaluation points. This scale asks the subject initially what activities that are important to them are impossible or difficult to do with their current (NMPK) prosthesis. These activities and difficulty levels are revisited when using the MPK and again when switched back to the NMPK.

All study materials will go to subjects via mail and will be returned to study staff by postage paid envelopes.

Resources: *Describe the available resources to conduct the research (personnel, time, facilities, mentor commitment, etc.)*:

All expenses (personnel, materials, postage) are covered by a research contract with the American Orthotic and Prosthetic Association (AOPA). Research activities will be carried out by the PI and Motion Analysis Laboratory staff listed on this IRB application. Costs associated with MPK prosthesis components and their fitting will be covered directly by AOPA.

Check all that apply. If none apply, leave blank:

☐ This is a multisite study involving Mayo Clinic and non-Mayo Clinic sites.
    When checked, describe the research procedures/activities being conducted **only** at Mayo Clinic:

☐ Mayo Clinic staff will be engaged in research activity at a non-Mayo Clinic site. *When checked, provide the location and a detailed description of the Mayo Clinic research staff involvement*.

☐ This study is to establish and/or maintain an ongoing database or registry for research purposes only.

☒ The research involves contact or interaction with subjects, for example, surveys, questionnaires, observation, blood draw.

☐ The study involves audiotaping or videotaping

Review of Chart, Images, Specimens

Provide the date range for collection of data and/or specimens that will be included in your research dataset. (*Example: 01/01/2000 to 12/31/2012*)

Date range: From ___/___/_____ to ___/___/_____

Check all that apply:

☐ This study involves only data and/or specimens that exist at the time this application is submitted to the IRB (IRB submission date). No data or specimens will be collected beyond this date.

☒ This study involves only data and/or specimens that will be collected after submission to the IRB.

☐ The study involves data and/or specimens that exist at the time of submission to the IRB **and** data and/or specimens that will be collected after submission to the IRB, for example a study that includes collection of existing data and prospective collection of specimens.

☐ Data and/or specimens used in this study are collected under another IRB protocol. *When checked, provide the IRB number(s) from which the research material will be obtained and check the box below to attest that subjects have provided consent for future use of their data and/or specimens, as described in this protocol.*

    IRB Number(s):

    ☐ Subjects have provided consent for use of their data and/or specimens, as described in this protocol.

☐ Other data sources will be utilized in this study. When checked, provide all data sources:

Data Confidentiality, HIPAA Subject Identifiers

Review the list of subject identifiers below and, if applicable, check the box next to each subject identifier being recorded at the time you are collecting/abstracting data/specimens for use in this study.

Subject Identifiers: Individually identifiable information, including demographic data, that identifies the individual or for which there is reasonable basis to believe it can be used to identify the individual. NOTE: Identifiers apply to subjects enrolled in your study and to the subject's relatives, household members, employers, etc.

Internal refers to subject identifiers that will be included in the dataset maintained by the study team.
External refers to subject identifiers that will be shared with persons outside of the immediate study team, for example, sent to an external collaborator or shared with a national registry.

SUBJECT IDENTIFIERS Check all that apply	INTERNAL IDENTIFIER	EXTERNAL IDENTIFIER
Name	x	
Social Security number		
Medical record/patient registration number, lab accession, specimen or radiologic image number	x	
Study number, subject ID, or any other unique identifying number, characteristic or code that can be used to link the identity of the subject to the data	x	
Dates: All elements of dates [month, day, and year] directly related to an individual. Their birth date, date of death, date of diagnosis, etc. **Note:** Recording a year only is not a unique identifier.	x	
Medical device identifiers and serial numbers		
Biometric identifiers, including finger and voice prints, full face photographic		

images and any comparable images		
Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address		
Street address, city, county, precinct, zip code, and their equivalent geocodes	x	
Phone or fax numbers	x	
Account, member, certificate or professional license numbers, health beneficiary numbers		
Vehicle identifiers and serial numbers, including license plate numbers		
If None of the above identifiers will be recorded or maintained in the dataset and/or sent outside of the study team, please check "None".	☐ None	☐ None

Statistical Information

Note: Power analyses and study endpoints are not needed for a pilot or feasibility studies.

☐ No statistical information. *If checked, please explain*:

Statistical Considerations

Power Statement: The study power is based on an effect-size approach (Cohen, *Psychological Bulletin*. 112:155-159, 1992). Based on a paired design with 50 subjects enrolled, there will be 80% power to detect differences in means between the two devices (MPK vs. NMPK) of at least 0.56 standard deviations, which is considered to be a medium effect size. This sample size is larger than previous MPK studies (Hafner, *Archives of Physical Medicine and Rehabilitation*. 88(2):207-217, 2007; Kahle, *Journal of Rehabilitation Research and Development*. 45(1):1-14, 2008; Kaufman, *Archives of Physical Medicine and Rehabilitation*. 87(7): 1382-1385, 2008), where the number of subjects ranged from 15 to 21.

Data Analysis Plan:
The purpose of this study is to compare the functional efficacy, patient satisfaction, and safety of two prosthesis designs: MPK vs. NMPK. The effects of these two prosthesis designs on these outcome variables will be evaluated using a one-factor repeated measures ANOVA. If the data are not sufficiently Gaussian, a non-parametric procedure such as Friedman's test will be used. Comparisons of A1 versus B, and A2 versus B will be also conducted using multiple comparison procedures or contrasts following the global ANOVA or Friedman's test. All procedures and analysis methods proposed in this study have been used previously and have been thoroughly validated.

The tri-axial accelerometer signals will be processed to yield activity levels of none, low, medium and high. Statistical analysis will determine if there are differences in activity level between the two prosthetic designs. Post-hoc analyses will be performed to determine which activity subscales differ between the prosthetic designs. Asymmetry between the prosthetic and non-prosthetic limb will be quantified using the asymmetry index described by Kaufman et al (Kaufman, *Journal of Pediatric Orthopedics*. 16(2):144-150, 1996). Variations in cadence will be quantified, since the data suggests that K2 patients benefit from a MPK (Theeven, *Journal of Rehabilitation Medicine*. 43(10):906-915, 2011; Burnfield, *Prosthetics and Orthotics International*. 36(1):95-104, 2012). Age related changes in gait will also be quantified.

The SF-36 will be used to determine if quality of life improves with a MPK. A multivariate approach will be used to compare all PEQ subscales simultaneously. If the overall test is significant, post-hoc analyses will be performed to determine which subscales differ between prosthetic designs. The PEQ-A will be grouped according to subject matter content (concentration, confidence, stumbles, falls) and tested to determine if there are differences due to prosthetic design. The information about falls from the biweekly fall tracking mailers will be compiled and compared across prosthesis type (MPK vs. NMPK). The Patient-Specific Functional Scale scores will be compared across time points as well.

Endpoints

Primary: Complete data collection of all subjects and complete statistical analyses
Secondary: Manuscript publication