A. COVER PAGE

Project Title: Agonist-Antagonist Myoneural Interface for Functional Limb Restoration after Transtibial Amputation	
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Human Subjects: Yes **HS Exempt:** NA **Exemption Number:** **Phase III Clinical Trial:** NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

Statistical Design and Power

Toward demonstrating the efficacy of the AMI transtibial amputation paradigm, this clinical protocol uses the same prosthesis and primary outcome measures that were established in our first-in-human case study [T.R. Clites et al., 2018. Proprioception from a Neurally-Controlled Bionic Prosthesis. Sci Transl Med. 10:eaap8378]. The primary outcome measures are: 1. Stability of Joint Position Control in Free Space, 2. Economy of Motion for Free Space Movements, 3. Subtalar Eversion for an Obstacle, 4. Late Swing Ankle Plantar Flexion during Stair Descent, and 5. Late Swing Ankle Dorsiflexion during Stair Ascent. The investigators were aware that, due to the pioneering nature of the AMI intervention and functional testing involving a specially adapted prosthesis, these published pilot data were the only data that were available for determining the planned enrollment for this study protocol. Consequently, as a starting point, the number of test subjects for each of two equally sized groups was calculated using the MATLAB sampsizepwr function and the pilot study data obtained for each primary outcome measure. The power was set at 0.9, and the data obtained for the pilot study subjects and ratio of subjects in the two groups (4:1) were entered into a two-sample pooled t-test with a significance level set at a=0.05. The MATLAB function returned "n" as the number of participants needed in each group to obtain a power of 0.9. Based on the initial analyses of existing data, and assuming the worst ratio between the mean and standard deviation (which was obtained for outcome measure 1), the theoretically required number of test subjects was eight participants per group. However, to increase the chances of finding statistically significant differences between the intervention and control groups for all outcome measures, inclusion of eleven participants per group was proposed. Hence, the clinical study called for an experimental group of eleven participants who received AMI transtibial amputations, a control group of eleven matched participants who received standard transtibial amputations. We anticipated a total enrollment of thirty-two consented participants would allow for participant attrition over the five-year period of performance. Statistical comparisons of outcome data were conducted using standard statistical analytic software (e.g., SAS) with a significance level set at a=0.05.