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**TITLE: Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface**

**PRINCIPAL INVESTIGATOR:** Mark Pitkin

**RECIPIENT:** Poly-Orth International
26 Mallard Dr., Sharon MA 02067-1518

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**PREPARED FOR:** U.S. Army Medical Research and Materiel Command
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Sharon MA 02067-1518

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**14. ABSTRACT**
The investigators wish the American Veterans and civilians with amputations can use powered prostheses with direct skeletal attachment and direct bidirectional neural control. Since 2004, their work has been devoted improving a skin-device and bone-device interface. Current research is designed as a translational study to develop Skin and Bone Integrated Pylon with Peripheral Neural Interface (SBIP-PNI) directly attached to the residuum and the powered prosthetic hand with bidirectional control. .

**15. SUBJECT TERMS**- NONE LISTED

| **16. SECURITY CLASSIFICATION OF:** | | | **17. LIMITATION OF ABSTRACT** | **18. NUMBER OF PAGES** | **19a. NAME OF RESPONSIBLE PERSON** |
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**TABLE OF CONTENTS**

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The investigators wish the American Veterans and civilians with amputations can use powered prostheses with direct skeletal attachment and direct bidirectional neural control. Since 2004, their work has been devoted improving a skin-device and bone-device interface. Current research is designed as a translational study to develop Skin and Bone Integrated Pylon with Peripheral Neural Interface (SBIP-PNI) directly attached to the residuum and the powered prosthetic hand with bidirectional control.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Direct skeletal attachment; powered prosthesis; neural interface; bidirectional control system.

3. **ACCOMPLISHMENTS:**

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

*List the major goals of the project as stated in the approved SOW.*

Goals/Milestones

Year 1

 Manufacture the integrated pylons with peripheral neural interface (SBIP-PNI) for animal studies and fabricate the powered prostheses with sensory feedback

*Milestones #1: Meeting the Poly-Orth specification and passing the QC tests* – planned in Q2; current completion 100%

*Milestone #2: Ship the implants to the Pine Acre Rabbitry/Farm (PARF) and to Georgia Institute of Technology ( GIT* – – planned in Q2; current completion 100%.

Comment: the site #2 for animal studies with pigs has been changed from PARF to DaVinci Biomedical Research, Lancaster, MA, with corresponding approval.

 Implant SBIP-PNI into cats - planned in Q4; current completion 75%

 Supply cats with powered prostheses with sensory feedback and initiate gait study- planned in Q4: will be completed in Q1 of Year 3

Year 2

 Conclude cat gait study with and without sensory feedback. Will be completed in Q1 of Year 3.

 Implant SBIP-PNI into Yorkshire Swine and conduct gait study with and without sensory feedback: Gait study without sensory feedback completed.

Year 3

 Perform mechanical testing of device skin and device-bone attachment Perform histological analysis of the samples

 Conclude pig gait study with and without sensory feedback

 Demonstrate infection free sustainable device-body interface with the SBIP-PNI

 Demonstrate that adverse events rate (AER) in animal study is lower than the established threshold

 Submit application for IDE to the FDA Comments/Challenges/Issues/Concerns

Year 4

 A no-cost one-year extension has been approved to pursue the new approach being developed for amputation/implantation in the porcine sub-study at the DaVinci Biomedical, which has more translational value and for additional trials at GeorgiaTech with more functional powered prostheses.

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

*If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."*

Nothing to Report

**How were the results disseminated to communities of interest?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

**Abstracts and Publications**


Park H, Islam MS, Grover MA, Klishko AN, Prilutsky BI, DeWeerth SP. A prototype of a neural, powered transtibial prosthesis for the cat: Benchtop characterization. Frontiers in Human Neuroscience. *Frontiers in Neuroscience* **12**: 471, 2018.

Jarrell J, Farrell BJ, Kistenberg RS, Dalton JF, Pitkin M, Prilutsky BI. Kinetics of individual limbs during level and slope walking with a *unilateral transtibial bone-anchored prosthesis in the cat. Journal of Biomechanics, **76**: 74-83, 2018*.

*Park H, Klishko AN, Oh K, Dalton JF, DeWeerth SP, Pitkin M, Prilutsky BI. Cat locomotion with a powered prosthesi*s integrated with residua bone, skin, sensory nerves and muscles. In: Minisymposium of Society for Neuroscience Annual Meeting, San Diego, CA, 2018.

Pitkin, M., C. Cassidy, M. Shevtsov, J. Jarrell, H. Park, B. Farrell, J. Dalton, W. L. Childers, J. Temenoff, K. Oh, A. Klishko and B. Prilutsky (2019). Animal studies of the Skin and Bone Integrated Pylon with deep porosity for bone-anchored limb prosthetics with and without neural interface. Military Health System Research Symposium MHSRS-19-00758, Kissime, FL.

M.A. Shevtsov, N.M. Yudintceva, M.I. Blinova, I.V. Voronkina, D.N. Suslov, O.V. Galibin, D.V. Gavrilov, M. Akkaoui, G. Raykhtsaum, A.V. Albul, E. Pitkin, M. Pitkin, Evaluation of the temporary effect of physical vapor deposition silver coating on resistance to infection in transdermal skin and bone integrated pylon with deep porosity, J Biomed Mater Res B Appl Biomater 107(1) (2019) 169-177 (attached to this report).

Prilutsky, B., H. Park, K. Oh, J. P. Dalton IV, S. P. DeWeerth, M. Pitkin and A. Klishko (2019). Bidirectional Control of a Sensing Powered Transtibial Prosthesis during Walking in the Cat. Society for Neuroscience (to be presentation at the October Meeting).

H. Park, E. Latash, Y. Morkov, A.N. Klishko, S.P. DeWeerth, A. Frigon, B. Prilutsky, Cutaneous Sensory Feedback from Paw Pads Affects Balance Control during Split-belt Treadmill Locomotion in the Cat, Journal of Experimental Biology 222(14, jeb198648) (2019).

**Describe the Regulatory Protocol and Activity Status (if applicable).**
Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state “Nothing to Report.

1. The Protocol MR150051.03 entitled, "Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface," IACUC protocol number GT27F, Protocol Principal Investigator Evan Goldberg, is approved by the USAMRMC Animal Care and Use Review Office (ACURO) as of 13-JUN-2019 for the use of cats and will remain so until its modification, expiration or cancellation. This protocol was approved by the T3 Labs IACUC on 25-MAR-2019.

2. The Protocol MR150051.02 entitled, "Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface," IACUC protocol number A16063, Protocol Principal Investigator Boris Prilutsky, is approved by the USAMRMC Animal Care and Use Review Office (ACURO) as of 29-AUG-2019 for the use of cats and will remain so until its modification, expiration or cancellation. This protocol was approved by the Georgia Institute of Technology IACUC on 28-MAY-2019.

**What do you plan to do during the next reporting period to accomplish the goals?**
*If this is the final report, state “Nothing to Report.”*

*Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

In Year 4, we plan

- to complete the study in cats with powered prostheses attached to the residuum via Skin and Bone Integrated Pylon with Peripheral Neural Interface (SBIP-PNI) to demonstrate effectiveness of the neural control in animal gait compared to passive prostheses.
- To complete the study in pigs with the silver coated pylons (SBIP-S) to demonstrate safe and sustainable bone-device and skin-device interface using modified pylons with oval, not-centered cross-sections.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

**What was the impact on the development of the principal discipline(s) of the project?**
*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

## 1. Cat study at the Georgia Institute of Technology

**1.1.** Recordings of walking with the powered sensitive transtibial prosthesis.

**1.1.1.** We have been recording mechanics of level and slope (±50% or $\pm 27^0$) overground locomotion in one cat implanted with the SBIP-PNI pylon and electrodes in the residual soleus (SO) and tibialis anterior (TA) muscles, as well as in the residual distal tibial nerve. This animal had the implants for over 20 months.

**1.1.2.** We have developed a sensing powered transtibial prosthesis for the cat (Park et al. 2018) to investigate effects of bidirectional prosthetic control on locomotor mechanics.

**1.1.3.** The prosthesis is attached to a percutaneous titanium pylon with deep porosity having central canal for wiring between the powered prosthesis and muscles and nerves in the stump (SBIP-PNI) (Pitkin, et al., 2012) implanted into the distal tibia marrow canal. The pylon has a channel inside through which leads of EMG electrodes in implanted residual SO and TA and of a cuff electrode on the residual distal tibial nerve are passed through. Nerve stimulation was triggered when a pressure sensor on the bottom of the prosthetic foot recorded contact with the ground.

**1.1.4.** Recorded EMG activity of the residual SO during level walking and the signal from the pressure transducer on the bottom of the foot, during which the stimulator stimulated the distal tibial nerve are demonstrated in Figure 1, of Exhibit A.

**1.1.5.** We have concluded that bidirectional control of the transtibial prosthesis can be used to modulate locomotor kinematics. In the next three months we plan to investigate the effects of intensity of stimulation of the distal tibial nerve on mechanics of prosthetic walking.

**1.2.** **A powered, sensing transtibial prosthesis for cats**.

The diagram (**Figure 1**) is illustrating exchange of information between the prosthesis and external devices is depicted in Fig. 1. An MCU CC2510F32 was used to control the wireless communications with the MCU on the prosthesis.

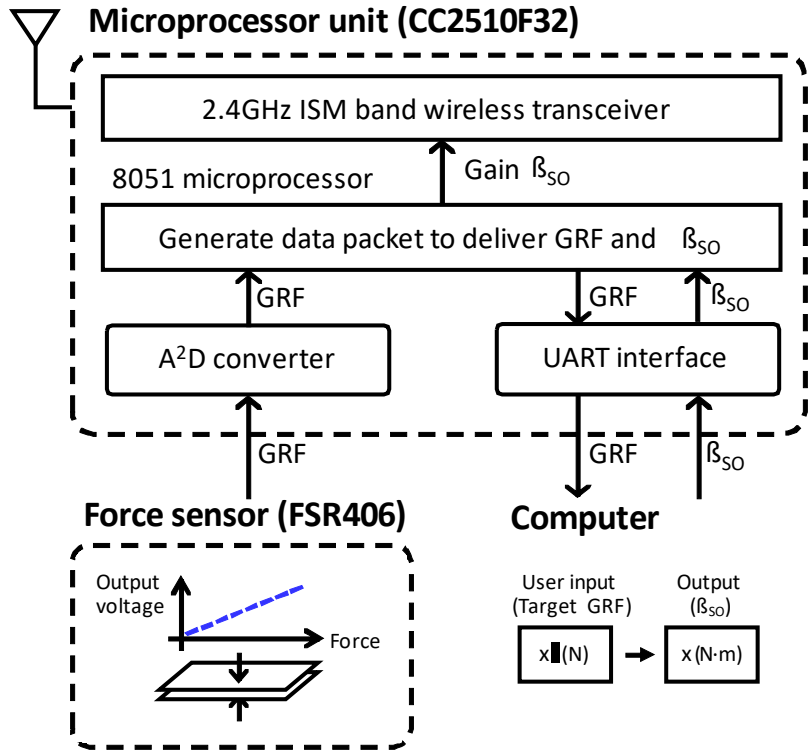



**Figure 1.** Detailed system block diagram of communications between the prosthesis and external devices (computer, force sensor and microprocessor unit.

A force sensing resistor FSR406 (Interlink electronics, CA, USA) measured ground reaction force exerted by the prosthesis, while a computer monitored the measured ground reaction force in real time and changed the ankle extension gain $\beta_{SO}$.

The cat transtibial prosthesis was designed based on the above information. The length of the aluminum rod was set at a half of the shank length, i.e. 55 mm. The linear motor PQ12-63-06-P, Li-polymer battery and other prosthetic components were selected to meet the requirements for the maximum prosthesis mass and moment generation ability. As a result, the prosthesis mass was 80 g and the maximum measured moment during the testing (see below) was 0.6 Nm, which is close to the maximum ankle moment during level walking in the cat.

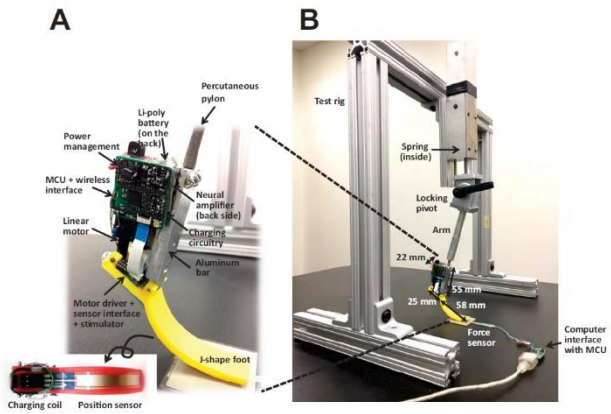



**Figure 2**. **A**: Prosthesis prototype. **B**: Test rig with the attached prosthesis.

We tested the developed prosthesis and control algorithms in a test rig that held the prosthesis slightly above the ground (Fig. 2B).

The prosthesis comprised (1) a microprocessor unit (CC2510F32 (Texas instruments, TX, USA), (2) EMG amplifier INA128 with gain of 1000 (V/V) (Texas Instruments, TX, USA), (3) current stimulator with a programmable resistor AD5162 (Analog Devices, MA, USA), (4) ThinPot linear force-position sensor (Spectra Symbol, UT, USA), (5) miniature linear actuator PQ12-63-06-P (Actuonix, BC, Canada), (6) Li-polymer rechargeable battery GM053040 with coil, (7) power management, and (8) prosthetic foot.

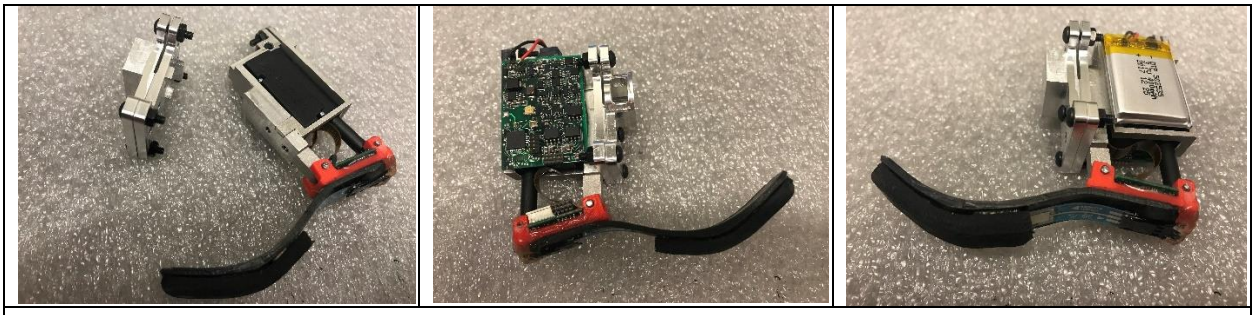


**Figure 3**. The powered prosthesis inside the holding frame. Left panel demonstrates the pylon holding plates (see Fig. 1) and the frame with a linear actuator and foot attached to the holding plates at the prosthetic joint. Middle panel shows a circuit board fixed to the right side of the linear actuator. The board includes a microprocessor unit, EMG amplifier, current stimulator and power management. Right panel shows the battery attached to the left side of the actuator. The battery supplies power for the actuator, circuit board with its components and force sensor on the plantar surface of the foot (see right panel).

### 1.3. Surgical implantation strategy

We implanted the pylon without electrodes and their leads in the first surgery. A small bone hole was drilled and suture inserted inside the pylon and the bone hole. Cast was placed on the residual limb to protect the implant, as was done in our previous studies. This procedure permitted good integration of the pylon with bone in the past. After integration is completed (in about 2 months), we conducted a second surgery, during which nerve cuff and EMG electrodes passed through the bone hole and pylon using the implanted suture. The wires are secured in the box of the pylon holder.

### 1.3. Recordings of walking with the powered sensitive transtibial prosthesis

During the period between April and June 2019, we have been recording mechanics of level and slope (±50% or $\pm 27^0$) overground locomotion in one cat implanted with the SBIP-PNI pylon and electrodes in the residual soleus (SO) and tibialis anterior (TA) muscles, as well as in the residual distal tibial nerve. This animal had the implants for over 20 months.

Despite the availability of the modern multi-degree of freedom powered limb prostheses, their users often are dissatisfied with them due to complex, non-intuitive control and lack of sensory feedback (Ostlie et al. 2012). Recent case studies of bidirectional control of powered prostheses in individuals with upper and lower limb loss have demonstrated drastic improvements in quality of movements (Ortiz-Catalan et al. 2014). We have developed a sensing powered transtibial prosthesis for the cat (Park et al. 2018) to investigate effects of bidirectional prosthetic control on locomotor mechanics.

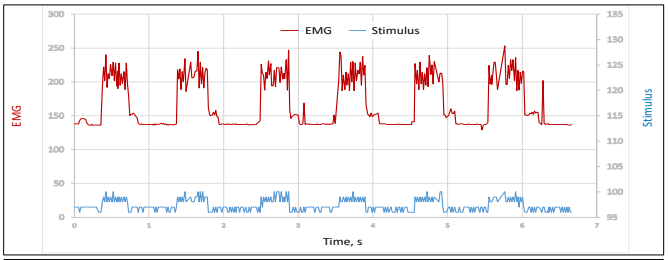



**Figure 4.** Recorded EMG activity (brown line, arbitrary units) and the signal indicating the period of contact of the prosthesis with the ground (blue line, arbitrary units) during prosthetic walking.

The prosthesis is attached to a percutaneous titanium pylon with deep porosity having central canal for wiring between the powered prosthesis and muscles and nerves in the stump (SBIP-PNI) (Pitkin, et al., 2012) implanted into the distal tibia marrow canal. The pylon has a channel inside through which leads of EMG electrodes in implanted residual SO and TA and of a cuff electrode on the residual distal tibial nerve are passed through to connect to a linear actuator and onboard nerve stimulator.

Nerve stimulation was triggered when a pressure sensor on the bottom of the prosthetic foot recorded contact with the ground. **Figure 4** demonstrates and example of recorded EMG activity of the residual SO during level walking (brown line). This figure also shows the signal from the pressure transducer on the bottom of the foot, during which the stimulator stimulated the distal tibial nerve.

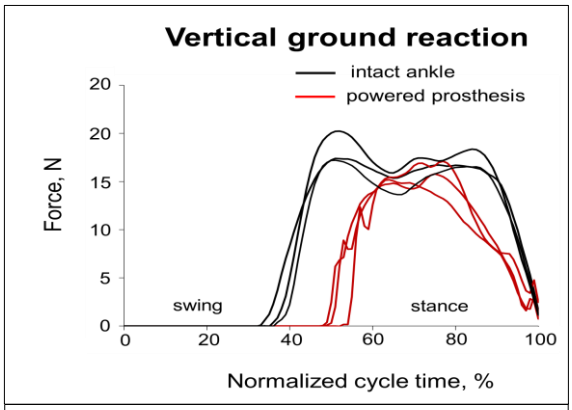



**Figure 5.** Vertical ground reaction during intact gait (black) and with powered prosthesis (red).

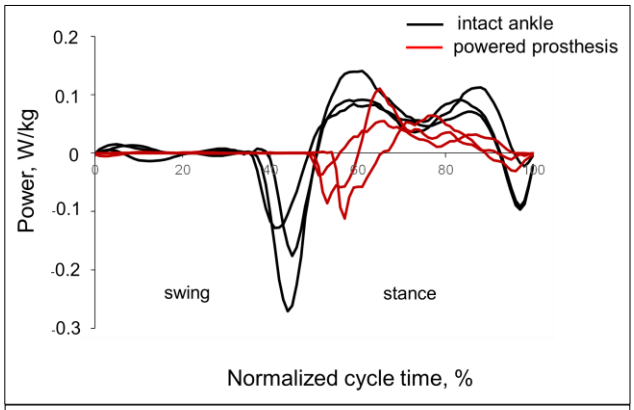



**Figure 6.** Ankle power during intact gait (black) and with powered prosthesis (red).

Three Modes of prosthetic operation were investigated: (1) pressure Mode, in which the linear actuator extended the prosthetic ankle during contact with the ground and flexed it during swing; (2) EMG Mode without stimulation, in which soleus EMG signal was used to control ankle extension during stance while ankle flexion was performed during swing; and (3) EMG Mode with nerve stimulation, in which in addition to Mode 2

the residual distal tibial nerve was stimulated during prosthesis contact with the ground. In total we recorded 346 cycles of overground prosthetic walking.

We found that the duty cycle of the prosthetic hindlimb was longer for Mode 2 than for Mode 1 or Mode 3 (p=0.004-0.050), **Fig. 5**. The relative duration of the double hindlimb support phase with the contralateral hindlimb being the trailing limb was shorter in Modes 1 and 3 than in Mode 2 (p=0.016-0.041).

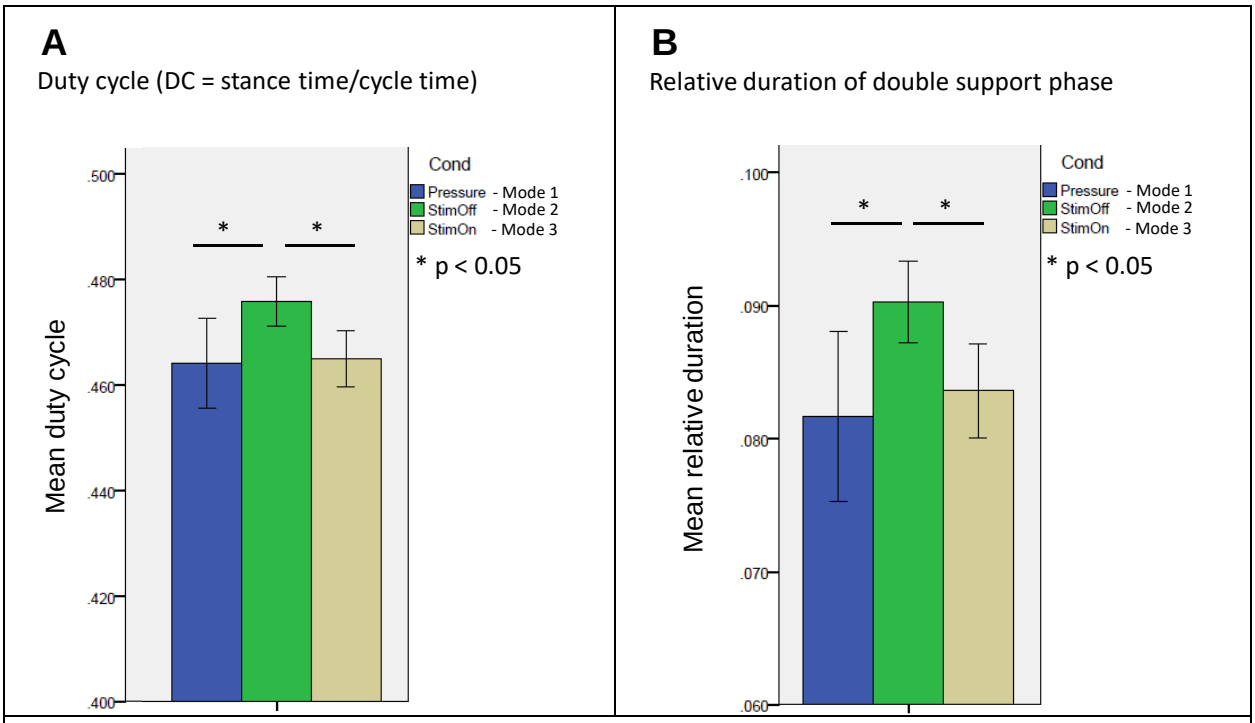



**Figure 7.** Effects of Mode of prosthetic operation on kinematic characteristics of prosthetic walking. In Pressure Mode 1, the prosthetic ankle extension was triggered by contact with the ground; In StimOff Mode 2, the ankle extension was controlled by EMG activity of residual soleus muscle during the stance phase; In StimON Mode 3, Mode 2 was supplemented with stimulation of the residual distal tibial nerve during the stance phase. **A**: Effects of Mode of prosthetic operation on the duty cycle. **B**: Effects of Mode of prosthetic operation on the relative duration of the double support phase of hindlimbs (the contralateral hindlimb being the trailing limb).

## 1.4. Results

The powered transtibial prosthesis, controlled by EMG signals from the residual muscles and providing electrical stimulation of the residual distal tibial nerve during contact with the ground (**Fig. 4**), generated ground reaction forces (**Fig. 5**), and ankle power (**Fig. 6**), comparable to those in the intact animal.

We have concluded that bidirectional control of the transtibial prosthesis can be used to modulate locomotor kinematics (**Fig. 7**).

## References

Pitkin, M, et al., Recording of Electric Signal Passing Through a Pylon in Direct Skeletal Attachment of Leg Prostheses with Neuromuscular Control. IEEE transactions on bio-medical engineering 59(5):1349-53, 2012.
Ortiz-Catalan M, Hakansson B, and Branemark R. An osseointegrated human-machine gateway for long-term sensory feedback and motor control of artificial limbs. Science Translational Medicine 6: 257re256, 2014.
Ostlie K, Lesjo IM, Franklin RJ, Garfelt B, Skjeldal OH, and Magnus P. Prosthesis rejection in acquired major upper-limb amputees: a population-based survey. Disabil Rehabil Assist Technol 7: 294-303, 2012.
Park H, Islam MS, Grover MA, Klishko AN, Prilutsky BI, and DeWeerth SP. A Prototype of a Neural, Powered, Transtibial Prosthesis for the Cat: Benchtop Characterization. Frontiers in Neuroscience 12: 471, 2018.

## 2. Pig study at DaVinci Biomedical

### 2.1. Development of instrumentation for implanting the SBIP pylons to the bone with oval shape of the marrow canal

The first study with implanting the SBIP pylon to a fore limb showed that the bond between the bone walls and the pylon showed that significant modifications in the pylon design are required. Our analysis revealed that the morphological differences between the hosted bones in hind and fore legs were of such significance that the pylon fabricate earlier and being used for procedures in hind limbs were not adequate to the fore limbs. This is demonstrated in the photograph (**Figure 1**) of the hind limb pylon positioned in the marrow canal of the cadaver fore radius bone.

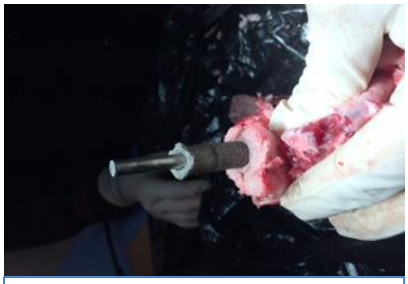


**Figure 1**. A pylon for the hind limb positioned in the marrow canal of the cadaver fore radius.

We conducted a cadaver study for detailed measurements of cross-sections in sagittal and frontal planes.

**I.** The radius bone of Yucatan mature pig was cut along the sagittal and frontal plane each of them (**Figure 2, A**). Two important distinctions from the hind limb canal were found.

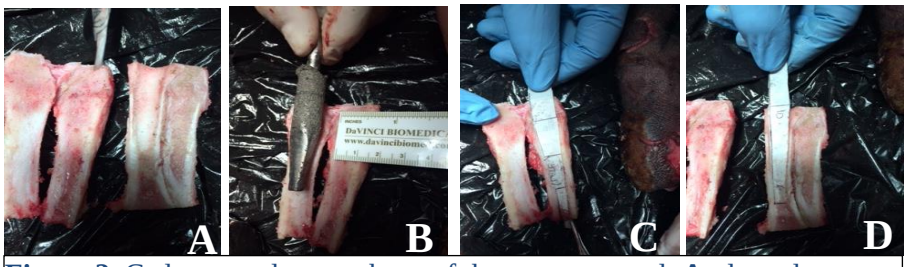



**Figure 2**. Cadaver study on a shape of the marrow canal. **A** - lateral cut (left) and frontal cut; **B** - adjustment of the implant's shape; **C** - lateral dimensions; **D** - approximation of the frontal dimensions.

1) A straight part of the canal is no longer than 30 mm (**Figure 2, B**);
2) Sagittal and frontal dimensions of the hosted canal compartment are within a ratio of 1.2:1 (**Figures 2, C, D**).

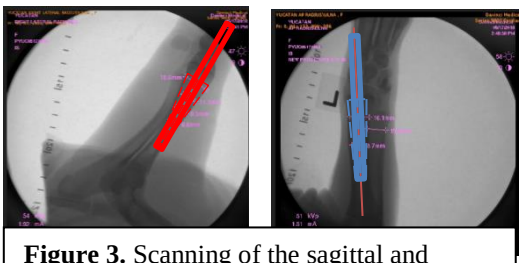
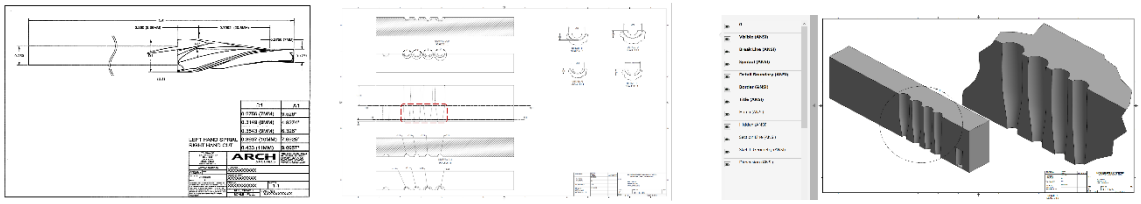


**Figure 3.** Scanning of the sagittal and frontal x-Ray images of the radius/ulna.

X-Ray images of the radius/ulna bone were scanned in the sagittal (red) and frontal (blue) planes. The shape of the pylons, which should be fitted to the canal's walls along their entire surface was established as conical with *oval* cross-sections with the ratio of the main and minor radii of the oval of 1.2:1.

**II.** Blueprints of the new reamers, broaches and molds for sintering new pylons are presented below.



**III.** The new molds are shown in **Figure 4**, where **A** - ovals of the upper cross-sections; **B** – inserts with tapered bottom tips for better fit the marrow canal; **C** – the mold with the inserts; **D** – side view of the mold with the inserts for sintering once the titanium particles of selected grade are poured in the spaces between the mold holes and the titanium inserts.

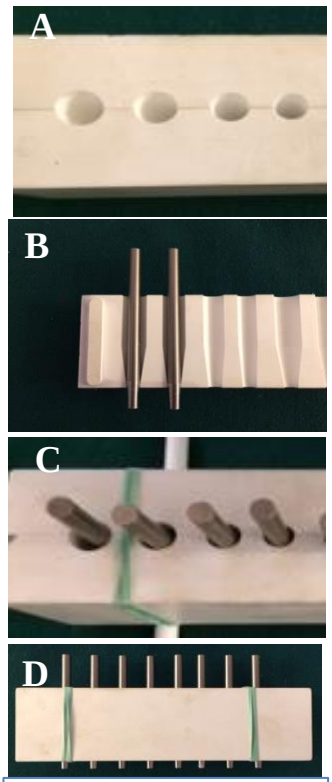



**Figure 4**. New mold for sintering the pylons with conical *oval* shape.

**IV.** The marrow canal in the hind limb had to be prepared for implantation of the conical circular pylons. In case of the conical oval cross-sectional new pylons, the rotating reamers corresponding the the minor axes of the ovals should be used only for the initial fitting. The final fitting will be achieved with the use of new broaches, which are not rotate, but protruded to the canal by the mallet.

**V.** The new broaches will be coupled with corresponding reamers and will be applied at the first time to the subject animal #64-152F on January 30, 2019 in ten weeks after the stage 1 procedure (amputation).

In the **Figure 5,** the postoperative photographs are depicted, where **A**, **B** – day of the step 1 surgery. Note a drainage for reducing postoperative swelling; **C** - day 6, showing a discharge via the drainage (**A, B**); **D** - residuum on Day 6; **E** - sagittal x-ray on Day 20.

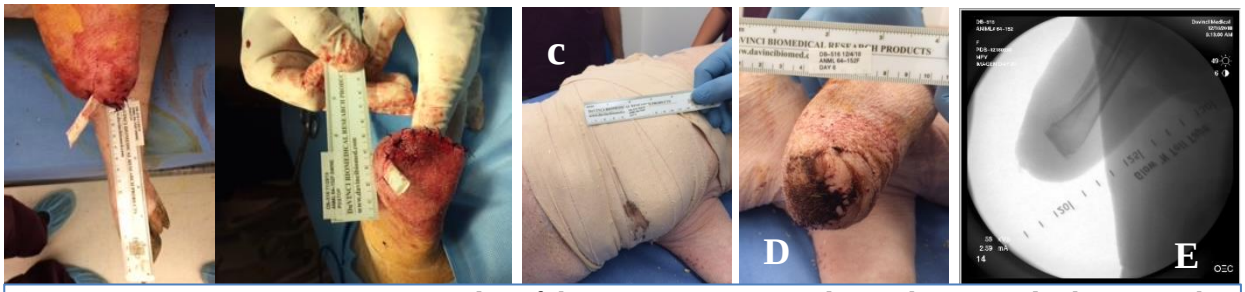



**Figure 5**. Postoperative images. **A**, **B** - day of the step 1 surgery; **C** - day 6, showing a discharge via the drainage (A, B); **D** - residuum on Day 6; **E** - sagittal x-ray on Day 20 showing minimal swelling.

## 2.2. Addition of silver coating to increase resistance to infection before the skin seal is fully developed

Implants with deep porosity fabricated with skin and bone integrated pylons (SBIP) technology allow for skin ingrowth through the implant's structure creating natural barrier against infection. However, until the skin cells remodel in all pores of the implant, additional care is required to prevent from entering bacteria to the still non-occupied pores.

Temporary silver coating was evaluated in the previous study lead by the PI [1] as a means to provide protection from infection immediately after implantation followed by dissolution of silver layer in few weeks.

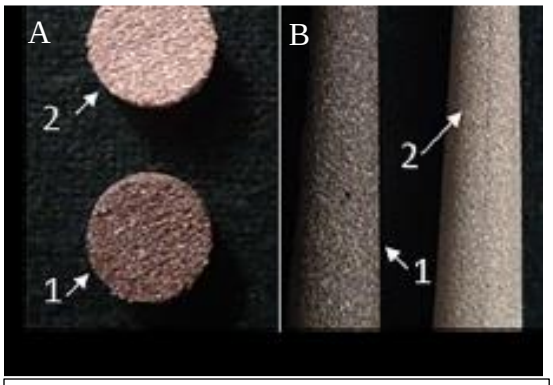



**Figure 6.** (A) – Tablets (10 mm diameter and 3 mm thickness) for in vitro study: 1 – without silver coating; 2 – silver-coated. (B) - SBIP samples for in vivo study: 1 – without silver coating; 2 – silver coated [1].

*In vitro* study showed less bacterial (Staphylococcus aureus, Staphylococcus epidermidis, and Pseudomonas aeruginosa) growth on silver coated tablets (**Figure 6, A-2**) compared to the control group. Analysis of cellular density of MG-63 cells, fibroblasts, and mesenchymal stem cells (MSCs) showed that silver coating did not inhibit the cell growth on the implants and did not affect cellular functional activity.

The *in vivo* study did not show any postoperative complications during the 6-month observation period in the model of above-knee amputation in rabbits when SBIP implants, either silver-coated or untreated (**Fig. 6, B**) were inserted into the bone residuum. Three-phase scintigraphy demonstrated angiogenesis in the pores of the pylons. The findings suggest that a silver coating with well-chosen specifications can increase the safety of porous implants for direct skeletal attachment.

## 2.3. The *In-vivo* feasibility study in pig with the silver-coated percutaneous implant SBIP-S.

The implant of the reverted mushroom design (**Fig. 7, a**) was inserted in the midscapular region (**Fig. 7, b**) for 6 months (**Fig. 7, c**) [2]. We investigated the role of a patented thin coat of silver in protecting the pig from infection and the dynamics of silver dissolution [3].

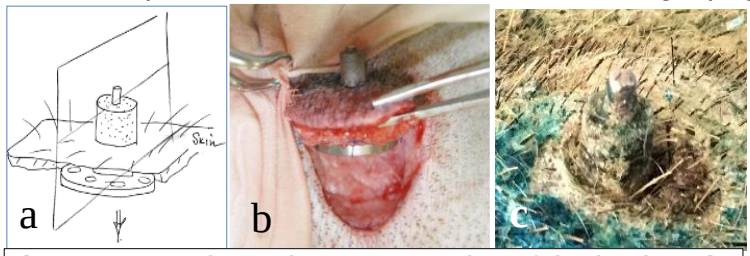



**Figure 7**. **a** - schematic representation of the implant; **b** - insertion of the implant; **c** – appearance of the implant in 6 months [2].

Both devices exhibited incorporation of the base into the subcutaneous tissue by minimal (control) to mild (silver-coated) mature fibrous connective tissue. Compared to non-coated control, there was no evidence of adverse device-related inflammation or other adverse tissue responses (infection, hemorrhage, necrosis, exuberant fibrosis/scarification) (**Figure 8**).

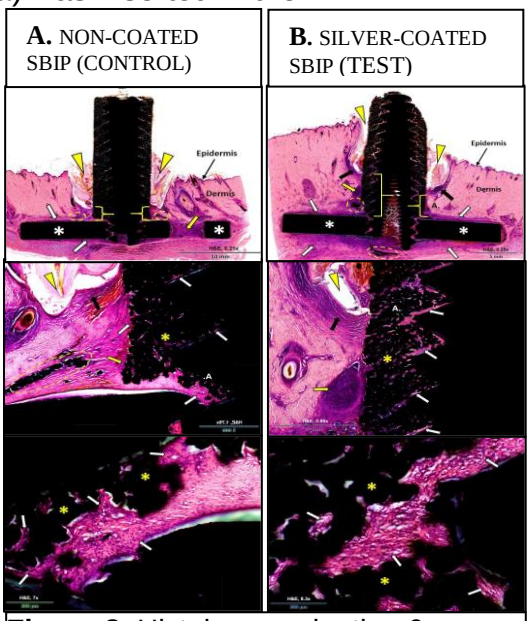



**Figure 8.** Histology evaluation 6 months after implantation of the skin-implant interface with non-coated SBIP as control - (**A**) and with silver-coated SBIP-S (Ag)- (**B**). Tissue integration into the surface pores of the device stem was encompassing approximately 30% (Control) to 30%-50% (Test) of the transcutaneous portion of the stem [3].

Histology evaluation in 6 months after implantation [3] showed better proliferation and creation of a viable skin seal within the porous structure of the SBIP-S and better tissue integration into the surface pores of the device stem. These antimicrobial and remodeling features of the silver-coated implant will be used in the proposed study in anticipation of its positive effect during initial post-implantation period.

## References

[1] M.A. Shevtsov, N.M. Yudintceva, M.I. Blinova, I.V. Voronkina, D.N. Suslov, O.V. Galibin, D.V. Gavrilov, M. Akkaoui, G. Raykhtsaum, A.V. Albul, E. Pitkin, M. Pitkin, Evaluation of the temporary effect of physical vapor deposition silver coating on resistance to infection in transdermal skin and bone integrated pylon with deep porosity, J Biomed Mater Res B Appl Biomater 107(1) (2019) 169-177.

[2] M. Pitkin, C. Cassidy, M. Shevtsov, J. Jarrell, H. Park, B. Farrell, J. Dalton, W.L. Childers, J. Temenoff, K. Oh, A. Klishko, B. Prilutsky, Animal studies of the Skin and Bone Integrated Pylon with deep porosity for bone-anchored limb prosthetics with and without neural interface, Military Health System Research Symposium MHSRS-19-00758, Kissime, FL, 2019, p. 44.

[3] S. Rousselle, Non-GLP Evaluation of Subcutaneous Titanium-Based Devices in Pig and Rabbit model, Alizée Pathology, LLC; FEE18-604, Institute of Cytology of the Russian Academy of Sciences Tikhoretsky Ave., 4 Saint-Petersburge, Russia 194064. Foreign Assurance Number: F18-00380, OLAW/NIH, 10/12/17I, Thurmont, MD, 2019.

**What was the impact on other disciplines?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

Nothing to report for Year 3.

**What was the impact on technology transfer?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*
*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Recommendations for implantation of the pylons with peripheral neural interface and on bidirectional control of powered prostheses are anticipated at the completion of the project.

**What was the impact on society beyond science and technology?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*
*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

The investigators wish the American Veterans and civilians with amputations can use powered prostheses with direct skeletal attachment and direct bidirectional neural control, which could improve the quality of life and social integration of the patients.

**5. CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Nothing to report

**Changes in approach and reasons for change**
*Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*

Nothing to report

**Actual or anticipated problems or delays and actions or plans to resolve them**
*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

1. **Cat study**

Despite delays in delivery and longer acclimation of the cats, last 2 cats will be taken for surgery in Q1 of Year 4.

2. **Pig study**

Main objective of the study in Year 4 is to develop the means for protecting the skin-implant interface against infection. We propose to objectively evaluate the antimicrobial and regenerative effects and demonstrate a translational value of coatings and treatments of the deeply porous SBIP implants during initial period following implantation until the protective skin seal is fully developed.

We anticipate that coating with Silver will protect the implant-skin interface from infection without inhibiting the skin remodeling process.

**Changes that had a significant impact on expenditures**
*Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

Nothing to Report

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
*Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also*

*specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

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

| |
|---|
| N/A |

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

| |
|---|
| All modifications in cat and pig studies have been approved by ACURO. |

**6. PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  **Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Park H, Islam MS, Grover MA, Klishko AN, Prilutsky BI, DeWeerth SP. A prototype of a neural, powered transtibial prosthesis for the cat: Benchtop characterization. Frontiers in Human Neuroscience. *Frontiers in Neuroscience* **12**: 471, 2018.

  Jarrell J, Farrell BJ, Kistenberg RS, Dalton JF, Pitkin M, Prilutsky BI. Kinetics of individual limbs during level and slope walking with a *unilateral transtibial bone-anchored prosthesis in the cat. Journal of Biomechanics, **76**: 74-83, 2018*.

  *Park H, Klishko AN, Oh K, Dalton JF, DeWeerth SP, Pitkin M, Prilutsky BI. Cat locomotion with a powered prosthesi*s integrated with residua bone, skin, sensory nerves and muscles. In: Minisymposium of Society for Neuroscience Annual Meeting, San Diego, CA, 2018.

  Pitkin, M., C. Cassidy, M. Shevtsov, J. Jarrell, H. Park, B. Farrell, J. Dalton, W. L. Childers, J. Temenoff, K. Oh, A. Klishko and B. Prilutsky (2019). Animal studies of the Skin and Bone Integrated Pylon with deep porosity for bone-anchored limb prosthetics with and without neural interface. Military Health System Research Symposium MHSRS-19-00758, Kissime, FL.

  Prilutsky, B., H. Park, K. Oh, J. P. Dalton IV, S. P. DeWeerth, M. Pitkin and A. Klishko (2019). Bidirectional Control of a Sensing Powered Transtibial Prosthesis during Walking in the Cat. Society for Neuroscience (to be presentation at the October Meeting).

  H. Park, E. Latash, Y. Morkov, A.N. Klishko, S.P. DeWeerth, A. Frigon, B. Prilutsky, Cutaneous Sensory
  Feedback from Paw Pads Affects Balance Control during Split-belt Treadmill Locomotion in the Cat, Journal of Experimental Biology 222(14, jeb198648) (2019).

**Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

**Other publications, conference papers, and presentations**. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

*Park H, Klishko AN, Oh K, Dalton JF, DeWeerth SP, Pitkin M, Prilutsky BI. Cat locomotion with a powered prosthesis* integrated with residua bone, skin, sensory nerves and muscles. In: Minisymposium of Society for Neuroscience Annual Meeting, San Diego, CA.

- **Website(s) or other Internet site(s)**
  *List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.*

Nothing to report

- **Technologies or techniques**
  *Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.*

Nothing to report

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

*Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.*

| Nothing to report |
|---|

- **Other Products**

*Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

| Nothing to report |
|---|

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

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

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."*

*Name:* *Mark Pitkin*
*Project Role:* *PI*
*Researcher Identifier (e.g. ORCID ID): L-7934-2017*

*Nearest person month worked: 5*
*Contribution to Project: Dr. Pitkin has directed all aspects of the project*
*Name: Grigory Raykhtsaum*
*Project Role: Director of Engineering*
*Nearest person month worked: 3*
*Contribution to Project: Mr. Raykhtsaum was responsible for development and manufacturing of the SBIP-PNI pylons for animal studies*
*Name: Charles Cassidy*
*Project Role: Investigator*
*Nearest person month worked: 0.1*
*Contribution to Project: Dr. Cassidy is a surgeon on the project performing two procedures in Year I.*
*Name: Boris Prilutsky*
*Project Role: Director of the Georgia Tech study*
*Nearest person month worked: 1*
*Contribution to Project: Dr. Prilutsky has directed development of the powered prosthesis for animal studies and the animal trials with SBIP-PNI in Year I.*
*Name: Hangue Park*
*Project Role: Investigator/Postgraduate student of Georgia Tech*
*Nearest person month worked: 10*
*Contribution to Project: Dr. Park developed the powered prosthesis for animal studies.*

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

**New active support**

Mark Pitkin, PI

a) Title of the project: R44 HD 090768 Large animal study on deeply porous transcutaneous pylon for direct skeletal attachment

b) Funding agency: NIH NCMRR
c) Project period: 09/26/2016 – 08/31/2019
d) Level (%) of effort in the project: 50%
e) Program Official: Louis A Quatrano
Email: quatranl@mail.nih.gov; Phone: (301) 402-4221 Fax: (301) 402-0832
f) The project is to develop and test new pylons and their implantation technique for direct skeletal attachment of leg prostheses. The goals are to increase integration of the pylons with skin and bone by developing new porous claddings with deep porosity and with Nano silver coating, developing technique of distraction implantation of pylons with side elements, and testing the Rolling Joint Foot and Ankle prosthesis with anticipation of minimizing bending moments from the pylon to the hosting bone.
g) There is no overlap with our current project

Grigory Raykhtsaum, Investigator/Director of Engineering
a) Title: R44 HD 090768 Large animal study on deeply porous transcutaneous pylon for direct skeletal attachment
b) Funding agency: NIH NCMRR
c) PI: Mark Pitkin
d) Project period: 09/26/2016 – 08/31/2019
e) Level (%) of effort in the project: 17%

Boris Prilutsky, PD for Georgia Tech study
a) Title: R01NS100928 Neural mechanisms of locomotion evoked by epidural stimulation of the spinal cord
b) Agency: NIH/NINDS
c) PI: Boris Prilutsky
d) Project Period: 07/15/2017-05/31/2022
e) Level of support: .12%
f) There is no overlap with our current project

**What other organizations were involved as partners?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

1. DaVinci Biomedical Research, 20 Maple St, Lancaster, MA 01523
   - *Financial support: MR150015 Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface*
   - *Facilities and personnel collaborating on animal studies with pigs.*

2. Advanced Manufacturing Products (ADMA), Hudson, OH
    - *Financial support: MR150015 Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface*
    - *Facilities and personnel for sintering titanium SBIP-PNI pylons with selected specifications for animal studies*
3. Georgia Institute of Technology, Atlanta, GA
    - *Financial support: MR150015 Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface*
    - *Conducting animals study with cats wearing powered prostheses following DSA*
4. T3 Labs, Atlanta, GA 30313
    - *Financial support: MR150015 Integration of the Residual Limb with Prostheses via Direct Skin-Bone-Peripheral Nerve Interface*
    - *Facilities and personnel collaborating on animal studies with cats.*

## 8. SPECIAL REPORTING REQUIREMENTS

### COLLABORATIVE AWARDS:

Nothing to report

### QUAD CHARTS: N/A

## 9. APPENDICES:

None