DoD Grant Sample

FOCUS AREA | The proposed research outlined in this proposal seeks to address the PRORP ARA Focus Area pertaining to osseointegration (OI) and identifying the best practice to address failure of percutaneous OI prosthetic limbs. In the past ten years, significant progress has been made in the development of prosthetic limbs. State-of-the-art prostheses are electrically powered and controlled using muscle sensors placed over the residual limb of the user. These devices are heavy, uncomfortable, dependent on batteries, and most significantly, they lack proprioceptive feedback (a person's ability to know the position and movement of their body at any given time). As a result, users rely primarily on vision to know the position and orientation of their prosthesis. Surveys have reported this over-dependence on vision as one of the largest contributors to prosthesis abandonment (Peerdeman, 2011). To solve this, PSYONIC proposes to create a biointegrated prosthesis that connects to the patient's residual tendons and bone (**Fig. 1**). This will be accomplished by developing an anatomically accurate (biomechanically and anthropometrically), osseointegrated, artificial tendon-driven prosthesis; initially to replace a human finger. **The contributions of this project are significant because it will be the first prosthesis that enables users to control their prosthesis directly from their muscles, battery-free, with proprioception, in a biomechanically natural way.** PSYONIC has a patent pending on this technology (Akhtar, 2021).

RESEARCH IDEA | The proposed research outlines the development of an anatomically, biomechanically, and anthropometrically accurate, osseointegrated, artificial tendon-driven prosthesis for amputees. The proposed prosthesis would be a significant improvement over current state-of-the-art prostheses, providing a battery-free, biomechanically natural way for users to control their prosthesis while preserving inherent proprioception in the residual muscles.

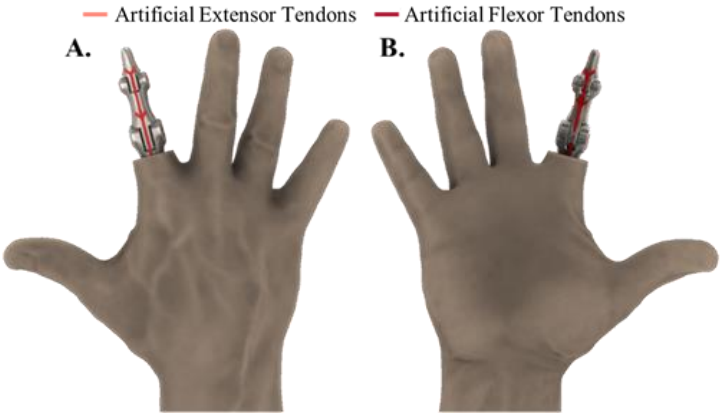

Figure 1. Concept rendering for proposed osseointegrated, artificial tendon-driven prosthesis. (A) Posterior and (B) anterior view of implanted finger prosthesis into real-view hand.

Osseointegration Systems Although OI is relatively new in the clinical setting, in 2019 Resnik et al. showed that in a national sample, 41% of veterans with upper limb loss would already consider receiving OI (Resnik, 2019). Currently, the only clinically available prosthetic OI systems are the Integrum OPRA (Hoellwarth, 2020), OrthoDynamics ILP (Frolke, 2017), and Osseointegration Group of Australia OPL (Haque, 2020) systems. These systems have been used for lower extremity amputations, and the majority of finger OI research, such as Lundborg et al. (Lundborg, 1996), Manurangsee et al. (Manurangsee, 2021), and Sierakowski et al. (Sierakowski, 2010), also use similar techniques. However, these have limited applicability to certain amputation levels. A novel finger OI system has been developed by Manrique et al. (Manrique, 2017) that applies to all amputation levels but suffers from issues with stress shielding.

Artificial Tendon Systems (ATS) To date, there is no ATS that can replace or attach an external prosthesis to existing tendons (Melvin, 2011). Fully implanted artificial tendons made of polyester that biologically integrate with the tendon have been reported, such as OrthoCoupler (Melvin, 2011, Melvin, 2016, Melvin, 2009) and the commercially available Neoligaments Poly-Tape (Abdullah, 2015); however, these systems are limited to repairing limbs that are still present. In most situations of tendon repair, a tendon transfer is performed, however, cannot be used with external prostheses (Gardenier, 2020).

RESEARCH STRATEGY | The proposed project consists of an ATS, infection mitigation system (IMS), and prosthesis component, implanted using a novel OI technique. We have derived scalable biomechanical models from our own preliminary cadaver tests and use them as a baseline for the proposed work. Testing will be conducted on cadaveric human finger models with at least ten cadavers (five male, five female). Computation of RMSE and R^2 values will be used to validate the accuracy of results. Low RMSE values and R^2 values higher than 0.7 will be used to indicate a strong fit to the data (Kaliki, 2008, Akhtar, 2017). Statistically significant differences ($p<0.05$) between models and experimental values will be determined using a 3-way repeated measures ANOVA (DIP angle, PIP

angle, grip strength). The expected outcome of the proposed project is a partial hand prosthesis ready for clinical testing that: 1) grants people with partial hand amputations a full ROM and the ability to perform highly dexterous activities with fine motor control; 2) restores proprioception in the device replacing the amputated limb; and 3) reduces prosthesis abandonment. These outcomes have the potential to greatly improve the functionality of prosthetic devices and overall, drastically improve users' quality of life. To accomplish this, we propose the following specific aims:

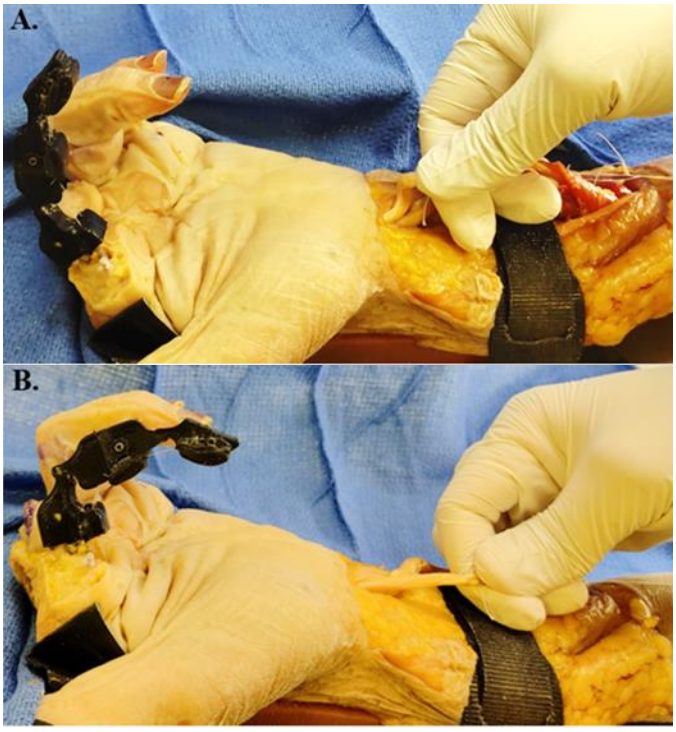

Figure 2. Human cadaver prosthesis motion. Actuation of implanted finger prosthesis from (A) neutral position to (B) flexed position.

Aim 1. Develop an OI abutment that reduces stress shielding and ATS that creates a robust and biological connection between the external prosthesis and residual muscles/tendons. Preliminary mechanical testing will characterize the strength of our devices without tissue integration/OI. OI abutment mechanical testing will be conducted under normal finger loading conditions, represented by uniaxial tension, compression, and shear loading. We will also perform in-vitro OI testing on the abutment to identify its OI capacity and quantify its resulting mechanical strength. Results will be compared to both the preliminary mechanical testing data and data from traditional OI techniques found in literature. ATS mechanical testing will entail cycle tests to identify the point and mode of failure. We will also test the in-vitro biocompatibility of the ATS to identify its tissue integration capacity.

Proposed Methods A novel OI technique is proposed, consisting of a hybrid design based on Manrique et al. (Melvin, 2011) with an intramedullary press-fit rod made from a titanium mesh. Initially, the OI abutment will be analyzed using FEA to characterize the optimal combination of intramedullary rod dimensions and screw orientation to prevent stress shielding under normal finger loading conditions. Stress shielding induced by improper force distribution between the implant and bone interface can lead to bone resorption and improper bone remodeling (Piao, 2014). Preliminary OI abutment mechanical testing will then be conducted by implanting the abutments into cadaveric specimens and identifying the maximum loads withstood under uniaxial compressive, tensile, and shear loading. These tests will serve as controls and will be applied with successive increase until the observed loading is similar to the maximum loads identified in the FEA models or until total failure of the abutment/bone. In-vitro OI testing will then be conducted following procedures laid out in Sivolella et al. (Sivolella, 2016). SEM and gene expression will be used to examine stem cell commitment to the OI abutment. Subsequent mechanical testing will be performed and compared to the preliminary OI abutment mechanical testing.

The ATS will then be constructed based on OrthoCoupler (Melvin, 2011, Melvin, 2016, Melvin, 2009) and mechanically tested in-vitro through fatigue testing using experimental protocols outlined by Melvin et al. (Melvin, 2011). After meeting the FDA requirement of 10^7 cycles, a new ATS will be implanted into a cadaveric specimen. Protocols for these experiments have previously been documented by Greenwald et al. (Greenwald, 1994) and Sapienza et al. (Sapienza, 2012). The objective of these experiments is to characterize the finger's ROM (dependent on tendon excursion) and grip strength (dependent on tendon load). Both experiments will be repeated on several fingers and cadavers, each with a new ATS. The results will be compared to previously completed cadaver testing of the unimpaired finger. The ATS will then be subjected to in-vitro biocompatibility testing by creating a biological assay comprising human tenocytes and collagen cells to which the ATS will be suspended. After a set period of time, the ATS will be removed, and histological analysis will be performed using methods outlined by Melvin et al. (Abdullah, 2015). Ingrowth and deposition of collagen and tenocytes will be evaluated. Human tenocyte proliferation within the ATS fibers and without scar tissue formation will provide convincing evidence into the viability of the ATS in-vivo.

Aim 2. Develop a feasible and robust IMS through the OI abutment and at the site that the artificial tendons interface between the internal and external environments of the body. IMS feasibility will be assessed by its ability to be constructed in the OR. IMS robustness will be assessed by its ability to sustain the mechanical forces incurred by normal joint motion and without negatively impacting the prosthesis' biomechanics. IMS construction in the OR will be observed and feedback from a hand surgeon will be collected to provide insight into areas for improvement. Mechanical testing will be conducted to characterize the durability of the system as being dependent on the applied tendon force and tendon excursion. These tests will determine if the IMS will fail or inhibit the prosthesis' ability to return mechanical functionality to the cadaveric finger models (i.e. achieve normal ROM and grip strength as in an unimpaired finger). The results of this task will be vital to preventing infection in-vivo.

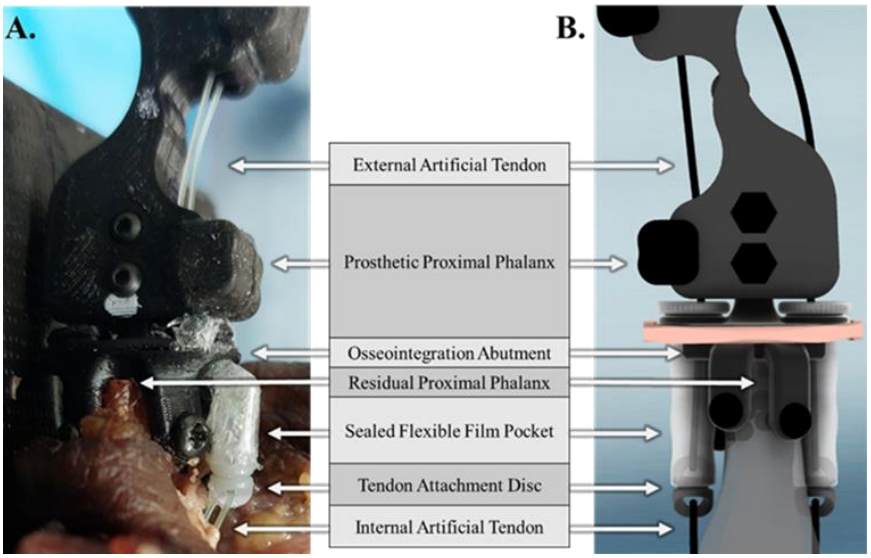

Figure 3. Proposed infection mitigation system. (A) Proposed IMS constructed and tested within the human cadaver model. (B) CAD model for the proposed system.

Proposed Methods IMS construction feasibility in the OR will be evaluated by at least 5 different hand surgeons. Design changes will be implemented to address each hand surgeons' areas of concern. Two successive rounds of extensive and exhaustive mechanical testing of the IMS will then be conducted using protocols documented by Greenwald et al. (Greenwald, 1994) and Sapienza et al. (Sapienza, 2012). The first round of tests will identify if full tendon translation and loading can be accomplished without IMS failure or negative impact to prosthesis ROM and grip strength. The tests will be expanded to include all flexor and extensor tendons in the human finger model and results will be compared to the unimpaired cadaver finger. To ensure a proper safety factor is obtained, IMS cycle testing will be conducted until failure to grant us insight into its maximum loading capacities and failure mode. After meeting the FDA requirement of 10^7 cycles, we will move on to in-vivo environments to test its infection mitigation capacity.

IMPACT | The proposed project intends to create an innovative prosthesis for the 1.6 million Americans living with the loss of a limb and specifically the 515,000 Americans with finger amputations (Ziegler-Graham, 2008). For these amputees, their current prosthetic options are both limited and over-priced for the technology available. This project aligns with PSYONIC's overall vision of lowering the barrier of access to advanced prosthetic technology by creating a next-generation prosthesis that is affordable for all amputees.

By creating an artificial tendon-driven finger prosthesis, users will be able to regain their sense of proprioception, allowing them to perform highly dexterous movements and fine motor control. By implementing osseointegration, users will be able to gain osseoperception, allowing them to feel sensations from what they touch. We intend to design this prosthesis initially to replace a human finger; successful implementation of the technology outlined in this application can then be applied to prostheses of all parts of the body, including upper and lower extremity amputations. Providing people with amputations a seamless, biologically integrated prosthesis, will greatly improve their quality of life and reduce prosthesis abandonment.

MILITARY BENEFIT | During the conflicts in Afghanistan and Iraq (2001-2006), 5.2% of all serious injuries and 7.4% of all major limb injuries in the US military included major limb amputation (Swiontkowski, 2009). The proposed technology outlined in this proposal is relevant to the needs of military personnel as it will repair, restore, preserve, and maintain sensory system function after a military member has sustained a combat related injury requiring limb amputation. This technology will provide veterans the option of regaining full functionality of their lost limbs and improve their quality of life.