AWARD NUMBER: W81XWH-16-1-0794

TITLE: Design and Validation of Implantable Passive Mechanisms for Orthopedic Surgery

PRINCIPAL INVESTIGATOR: Ravi Balasubramanian

CONTRACTING ORGANIZATION: Oregon State University
Corvallis, OR 97331-8517

REPORT DATE: OCTOBER 2019

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
OCTOBER 2019	Annual Report	09/30/2018 – 09/29/2019

4. TITLE AND SUBTITLE
Design and Validation of Implantable Passive Mechanisms for Orthopedic Surgery

5a. CONTRACT NUMBER
W81XWH-16-1-0794

5b. GRANT NUMBER
MR150091

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Ravi Balasubramanian

E-Mail: ravi.balasubramanian@oregonstate.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Oregon State University
Attn: Clem LaCava,
541-737-2373
308 Kerr Administration Bldg
Corvallis, OR 97331-8517

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The long-term goal of this research is to advance orthopedic surgery by designing implantable passive mechanisms (IPMs), such as artificial insertable rods and tendon networks, for enhancing and functionalizing the attachments of muscle to tendon(s) and bone and creating superior and customizable movement and force transmission. The specific objective of this work is to design, fabricate, and validate a biocompatible IPM that enables the surgical construction of a differential mechanism using existing biological tendons in order to improve the routing of forces and movements between muscle and tendons in the tendon transfer surgery for high median-ulnar nerve palsy. The key findings in this period relating to the project goals are as follows: (1) design and fabricate the implant using biocompatible materials; (2) develop a non-fouling coating for the implant; (3) validate the implant biomechanical function and coating using biomechanical simulations, human cadaver experiments, and cadaver and live animal experiments.

15. SUBJECT TERMS
Orthopedic surgery, biomechanics, biomaterials, implant design, non-fouling coating, robotics, cadaver, live-animal trials.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	41	19b. TELEPHONE NUMBER *(include area code)*

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1. INTRODUCTION:

The subject of this research is to advance orthopaedic surgery by designing implantable passive mechanisms (IPMs), such as artificial insertable rods and tendon networks, for enhancing and functionalizing the attachments between muscle to tendon(s) and bone. When used in place of the current surgical practice of direct suture repair to attach muscle to tendon(s) bone, the IPM will enable superior and customizable force and movement transmission using the patient's natural musculature without external power or control input. This work will design these implants so that the mechanism may be surgically constructed *in situ* by using the existing biological tendons maximally. The purpose of this research is to design, fabricate, and validate a biocompatible IPM that enables the surgical construction of a differential mechanism using existing biological tendons in order to improve the routing of forces and movements between muscle and tendons in the tendon transfer surgery for high median-ulnar nerve palsy. The scopes of the research are to (1) design and fabricate the implant using biocompatible materials, (2) develop a non-fouling coating for the implant, (3) validate the implant biomechanical function and coating using biomechanical simulations, human cadaver experiments, and live-animal experiments.

2. KEYWORDS:

Orthopaedic surgery, biomechanics, biomaterials, implant design, non-fouling coatings, robotics, cadaver, live-animal trials

3. ACCOMPLISHMENTS:

What were the major goals of the project?
The primary goal of this project is to develop implantable passive mechanism for orthopaedic surgery

Here are the subtasks that were identified in the approved Statement of Work for Year 3:

Specific Aim 1: To design, fabricate, and validate a miniature biocompatible rod for lateral insertion between two biological tendons.

Task 1.3

- 1.3P: Test and revise the design for the second cadaver experiment setup (months 20—21)
- 1.3Q: Procure second set of cadavers (month 13)
- 1.3R: Coordinate with clinical partners the metrics of success for cadaver studies (month 16)
- 1.3S: Conduct cadaver experiments (months 17-18)
- 1.3AA: Conduct live-animal pilot study (months 19—22 and 24—28)
- 1.3BB: Revise set-up design (months 22—23 and 28—30)
- 1.3 DD: Analyze data (months 22—24, 28—30, and 34—36)
- 1.3 EE: Feedback results to Tasks T1.1 and T1.2 (month 22—24, 28—30, and 34—36)

Specific Aim 2: To validate if an immobilized dense brush of sulfobetaine (SB) polymer to implanted components inhibits fibrosis and reduces interaction with surrounding tissue.

Task 2.1

- 2.1J: When ideal surface treatment is found, work with OSU team in Task 1.1 to apply coatings to implant design (months 25—30)
- 2.1G: When ideal surface treatment is applied to implant design, test implant in vivo (months 30—36)

Task 2.2

- 2.2C: Implant in mice (months 17—22)
- 2.2D: Harvest implants and fix samples (months 18—23)
- 2.2E: Embedding, staining, and sectioning (months 19—23)
- 2.2F: Histological analysis and measurement by microscopy (months 20—24)

What was accomplished under these goals?
Based on the tasks listed above for this year's annual report, the following tasks were achieved:

Tasks 1.3

- **1.3P: Test and revise the design for the second cadaver experiment setup**
    - The experimental setup for the cadaveric experiment was conducted this past year. This protocol was tested on the Utah-MIT robotic hand to validate the design. This test was valuable since it showed us that we needed to passively abduct the interosseous tendons to give the hand a posture that facilitates grasping of spherical objects. For the same reason, we also abduct the thumb. The implants are attached between the Flexor Digitorum Profundus (FDP) tendons of the four fingers and the motors simulating the donor muscle that actuates them. To summarize:
        - Flexor Digitorum Profundus (FDP) tendons - active force control by donor muscle via implant network
        - Flexor Pollicis Longus (FPL) tendon - active force control
        - Extensor Digitorum Communis (EDC) tendons - active control for resetting posture between trials only
        - Extensor Pollicis Longus (FPL) tendon - active control for resetting posture between trials only
        - Interosseous tendons - Passive tensioning for setting hand posture only.
        - Abductor Pollicis Longus tendon - Passive tensioning for setting hand posture only.
    - The protocol involves the robotic/cadaveric hand specimen grasping a spherical object that is connected by means of a stem to 6-axis force sensor. This instrumented ball is then mounted to an AdeptSix 300 robotic arm. Using the robotic arm, we can place the instrumented ball in such a location that makes it possible for the hand to grasp the ball. Then, we move the ball to different locations per our protocol. Figure 1 provides an imaged of the setup with cadaveric hand.

Figure 1: Image our actual experimental setup shows the AdeptSix 300 robot in the foreground, with the instrumented ball mounted to its end-effector. It is covered in plastic to safeguard it from human tissue contamination. The hand is mounted to our setup using the Agee WristJack with its tendons actuated by the frame-mounted motors in the background. CamJam adjustable rope anchors are used to passively tension the interosseous and Abductor Pollicis tendons.

- **1.3Q: Procure second set of cadavers (month 13)**
    - Here, we compare the contact performance of the two fingers in each of the two cases.
- **1.3R Coordinate with clinical partners the metrics of success for cadaver studies (month 16)**
    - Characterization of Grasp Quality Grasp quality is characterized by 4 metrics [Valero-Cuevas and Santello (2015), Roa et al. (2017)]:
        1. Disturbance resistance: immobility of the object being grasped to external perturbation
        2. Form/Force closure: ability to move the grasped object in any direction
        3. Zonotope of grasp quality: net wrench applied on object by the hand
        4. Stability: Any transients that appear because of perturbation decay to zero in a finite time constant.
    - These metrics are quantified in case by way of two experiments. First, we measure the yield strength of the grasp. We can then measure the zonotope of contact forces applied by the hand on the instrumented ball.

- Grasp yield strength

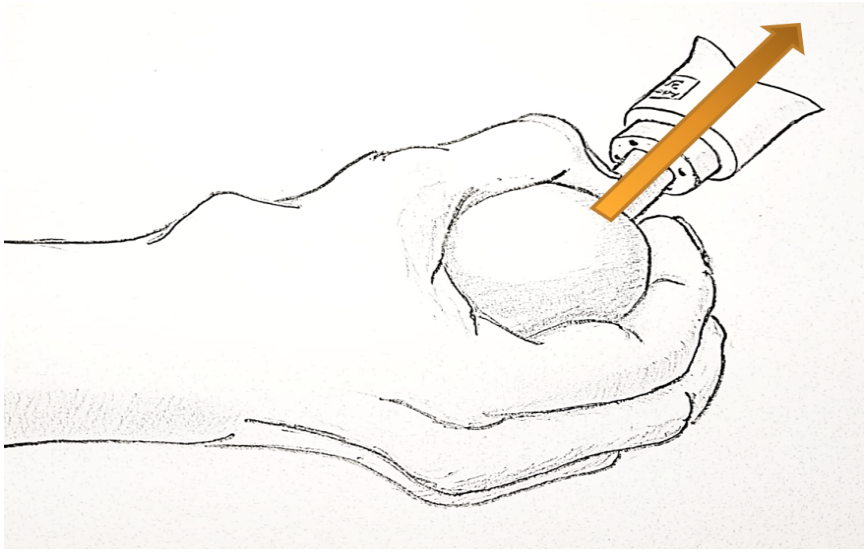


Figure 2: Measuring the work it takes to pull the object away from the grasp of the hand specimen enables us to quantify grasp strength. The object is pulled out in a direction roughly perpendicular to the palm as depicted by the orange arrow.

- For this, we program the robotic arm to position the instrumented ball, so the hand may grasp the object. Now, the robotic arm pulls the instrumented ball out of the grasp of the hand in a direction roughly perpendicular to the palm (as depicted by the orange arrow in *Figure 2*. The instantaneous force and torque applied on the ball, F(s), is measured by the 6-axis force sensors. The amount of work done is computed then computed using the following formula:

$$\boldsymbol{W} = \int_{\boldsymbol{C}} \boldsymbol{F(s)} \cdot \boldsymbol{ds}$$

  A greater amount of work done to remove the ball from the hand implies an increased grasp strength. This experiment tests the disturbance resistance of the grasp.

- Contact Force Zonotope

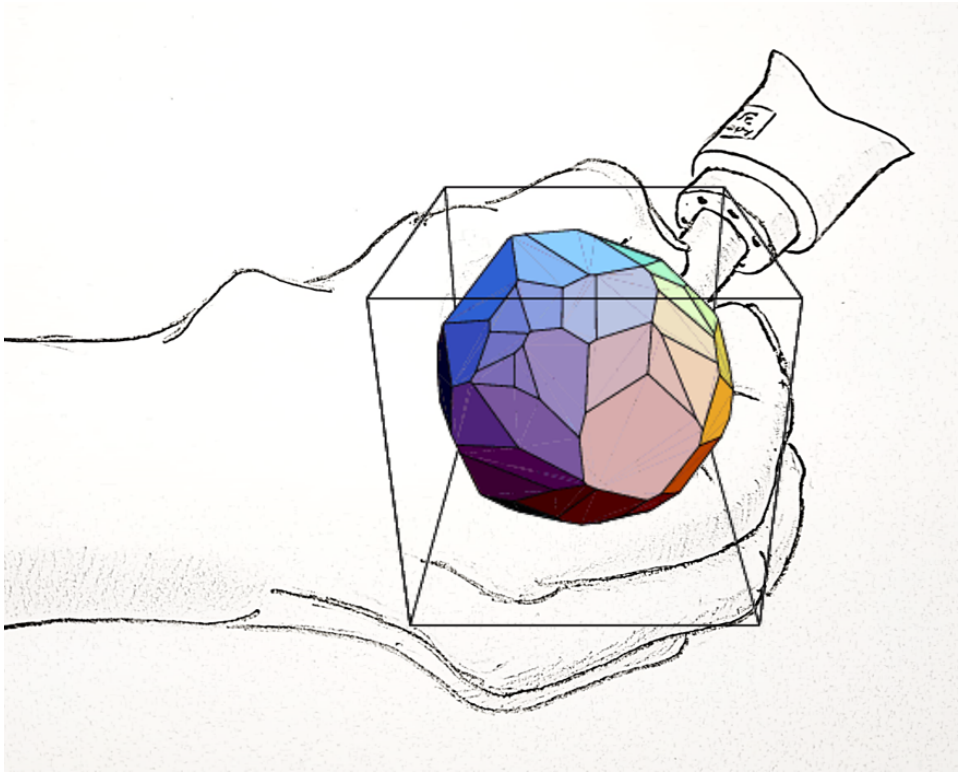


Figure 3: The zonotope of the contact forces applied by the hand on the instrumented ball is superimposed on top of the ball. This is produced by applying small perturbations of equal magnitude in all directions and computing the Minkowski sum of the resulting wrench vectors measured using the force sensor.

- The second experiment involves computing the zonotope of contact force of the hand on the instrumented ball. Once the ball has been grasped by the hand specimen, the robotic arm is programmed to apply several small perturbations of equal magnitude in all directions. By measuring the contact wrench (combined force and torque, each in 3 dimensions) applied by the hand on the instrumented ball for each direction of perturbation, we can construct a zonotope by performing an n-way Minkowski sum (also called dilation). This produces a convex polyhedron of contact forces. The volume of the largest sphere that can be fit inside this convex polyhedron is a metric to quantify grasp quality - a larger volume equated to a better grasp as well as improved force/form closure. Additionally, we can also measure the instantaneous wrench to check for stability of the grasp - a faster decay of transients equates to a more stable grasp that can adapt to different perturbations.

- We have designed the setup for instrumented ball mounted to the robotic arm. A stainless-steel ball with dimensions like a tennis ball is attached to the 6-axis force sensor (ATI Mini45 F/T Sensor) by way of a shaft to extend the reach of the ball. This assembly is then mounted on to the AdeptSix 300 robotic arm using a custom manufactured mounted. This requisite parts for the setup are currently being procured/manufactured.

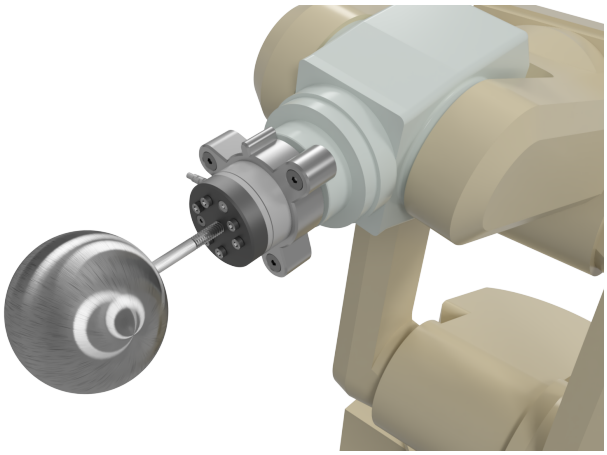


Figure 4: CAD model render of the ball, instrumented with a 6-axis force sensor, and attached to the robotic arm. The shaft between the force sensor and the ball extends the reach of the ball and allows the hand to grasp the object without disturbing the sensor apparatus.

- **1.3S: Conduct cadaver experiments**

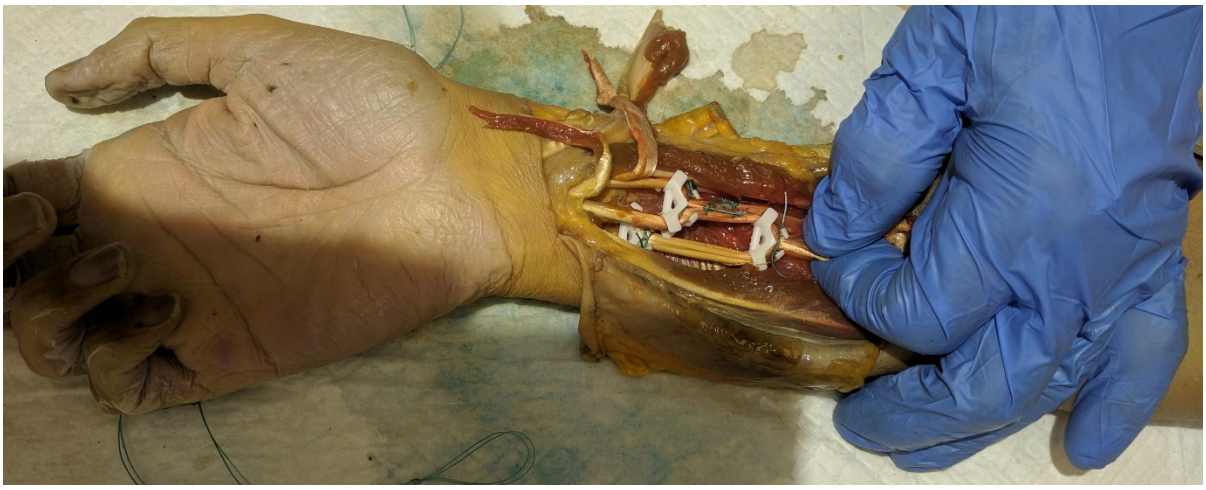


Figure 5: The image depicts a nearly complete cadaver dissection, with the network of three implants visualized. The first implant is clearly visible and is attached to the FDP tendons of the index and middle fingers. The second implant, which connects to the FDP tendons of the ring and little fingers, is below the middle finger FDP tendon and the first implant. The third implant is the one closest to the surgeon's hand (wearing blue gloves) and transmits force to the first two implants as needed.

- Our expert hand surgeon prepared the cadaver specimens for this second study in much the same way as the previous study. But, this time, we used a network of three implants between the FDP tendons and the donor muscle. One implant attached to the FDP tendons of the index and middle fingers. The second implant attached to the FDP tendons of the ring and little fingers. The third and final implant attaches to the first two implant and the donor muscle.

Figure 6: The cadaver hand specimen is mounted to our setup. The active tendons are wired to are motors which simulate muscles. The passive tendons are anchored to provide tension for posture. Then the instrumented ball on the robotic arm is used to test grasp.

- We then extracted the tendons through the tissue mounted it to our setup. The experiments finalized in Task 1.3R with the clinical partners were performed with and without the implant network, with the simple surgical case without the implants serving as a baseline. We were able to collect a wealth of data which we shall analyze and publish to a peer-reviewed journal in the near-future.

- **1.3AA: Conduct live-animal pilot study (months 19—22 and 24—28)**
  - Live-animal pilot study has conducted in the beginning of the month 25.
  - Total 12 freedom ranger chickens were utilized in the experiment. They were divided into four groups:
  - Strut implant group (4 chickens)
  - V-shape implant group (4 chickens)
  - Disk implant group (2 chickens)
  - Sham group (2 chickens)
  - Some chickens had Y-shaped tendon bifurcation which is perfect for this study. On the other hand, some chickens had almost parallel bifurcation that is not preferable.
  - Implants are mostly inserted to the chickens which have more Y-shaped tendon bifurcation.
  - The rest are used for disk implant and sham group.

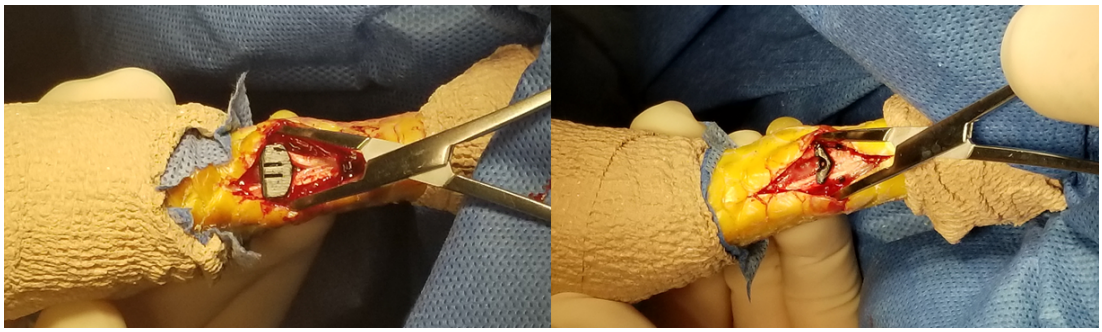


Figure 7: Strut (left) and V-shape (right) implant inserted on the bifurcation in the chicken model. Implant were manufactured from 3D printed RPU-70 and sterilized with ethanol.

- The functional electrical stimulation protocol designed in the previous year (2017-2018) was adopted for this study. Figures 8-10 illustrate the experimental setup.

Figure 8: Left pelvic limb of the chicken rigidly fixed and mounted with force transducers interfacing the splinted lateral and medical toes to measure toe tip forces and observe the interplay between the coupled toes.

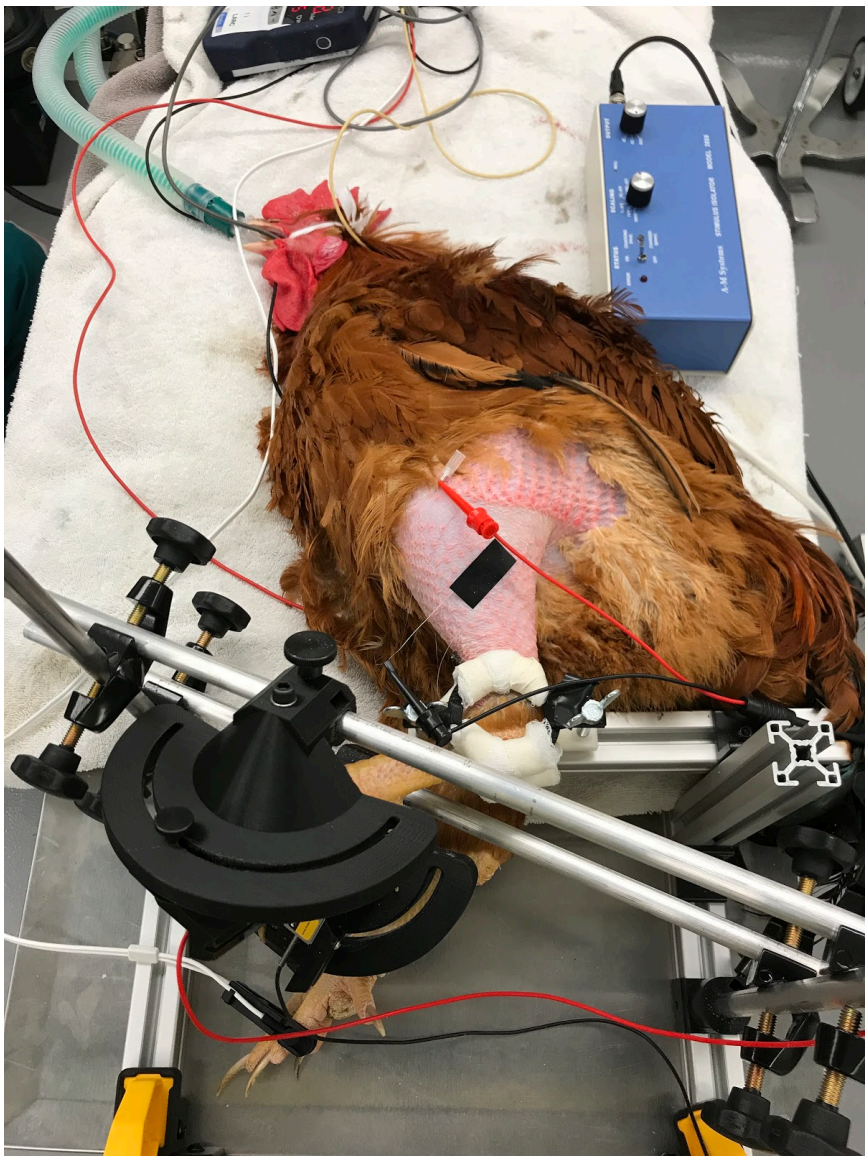


Figure 9: Left pelvic limb of the chicken rigidly fixed and stimulating electrodes inserted into the EDL muscle to induce controlled toe extension.

Figure 10: Motion capture environmental with chicken foot and retroreflective markers to measure the range motion.

- **1.3BB: Revise set-up design (months 22—23 and 28—30)**
  - No major changes revisions were made to the set-up
- **Subtask 1.3CC: Conduct live-animal experiments (months 31-34)**
  - Live animal experiments have been postponed due to the timing of Dr. Jennifer Warnock's, project Co-PI and veterinary surgeon, current medical leave. Specifically, surgeries for live-animal experiments were planned for this quarter. However, Dr. Warnock had to take an unexpected medical leave during this time and will not return to work until the first week of August. Therefore, we must forgo surgeries this quarter and will conduct the planned studies as soon as Dr. Warnock's schedule becomes clear.

- **1.3 DD: Analyze data (months 22—24, 28—30, and 34—36)**
  - FES protocol was completed in April of 2019, data analysis has yet to be completed.
- **1.3 EE: Feedback results to Tasks T1.1 and T1.2 (month 22—24, 28—30, and 34—36)**
  -
- **2.1G: When ideal surface treatment is applied to implant design, test implant in vivo (months 30—36)**
  - The ideal surface treatment has been achieved and prepared samples passed the required tests including protein adsorption, cytotoxicity and endotoxicity.

- The team is beginning to process the data to start writing papers on this work.

- The teams are working on re-scheduling chicken surgeries to test the coated implants in vivo due to Dr. Warnock's medical leave.
- Though not tested in vivo, we conducted mechanical Testing of RPU 70 with the non-fouling coating from the University of Washington partners and sterilized with ethylene oxide (EtO)
    - The goal of these tests was to confirm that after coating the implant material and sterilization, the stress-strain curve would be like that of Figure 11.

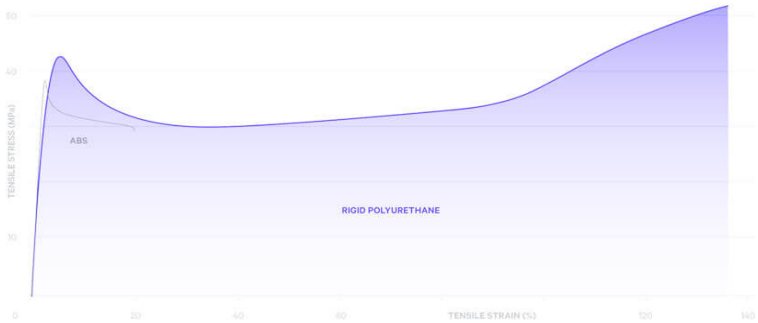


Figure 11: RPU 70 Stress Strain curve
Source:https://www.carbon3d.com/materials/rpu-rigid-polyurethane/

- All specimens used for testing followed the guidelines of ASTM standard D638-14 type 1 geometry. Specimens for tensile tests consist of a uniform thickness of 3 mm and follow type 1 guidelines for all other dimensions besides the overall length of the specimen due to additive manufacturing restrictions. These restrictions only allowed the overall length of the specimen to be 150 mm long thus causing the specimen grip lengths to be shortened by 7.5 mm on each side. The overall geometry and dimensions are specified in figure 12 and Table 1.

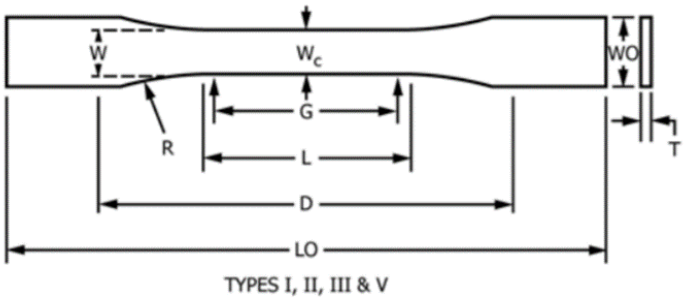


Figure 12: Specimen Geometry for ASTM D638-14

Table 1: Specimen Dimensions for Type I and Type II in terms of mm [7]

Dimensions (see drawings)	7 (0.28) or under	
	Type I	Type II
W—Width of narrow section[E,F]	13 (0.50)	6 (0.25)
L—Length of narrow section	57 (2.25)	57 (2.25)
WO—Width overall, min[G]	19 (0.75)	19 (0.75)
WO—Width overall, min[G]	...	...
LO—Length overall, min[H]	165 (6.5)	183 (7.2)
G—Gage length[I]	50 (2.00)	50 (2.00)
G—Gage length[I]	...	...
D—Distance between grips	115 (4.5)	135 (5.3)
R—Radius of fillet	76 (3.00)	76 (3.00)
RO—Outer radius (Type IV)	...	...

- A total of 10 specimens were initially supposed to be tested, with 2 specimens per each variation. These variations consist of 2 specimens coated with a non-fouling coating (C) , 2 specimens coated with ethylene oxide (E) , 2 specimens coated with non-fouling and ethylene oxide (CE) , and 4 baseline specimens (no coating applied)(R) .
- Specimens were tested on an Instron 5567 lead screw driven universal testing machine with a 30 kN load cell and tensile grips to support ASTM D638 Type 1 coupons, as shown in figure 3. Samples are set to a preload of 0-5 N. All tests were ran until full tensile failure of the specimen. Instron Bluehill® software is used to create a test method that elongates the sample at a rate of 5 mm/minute until a drop in load indicates that the sample has failed.

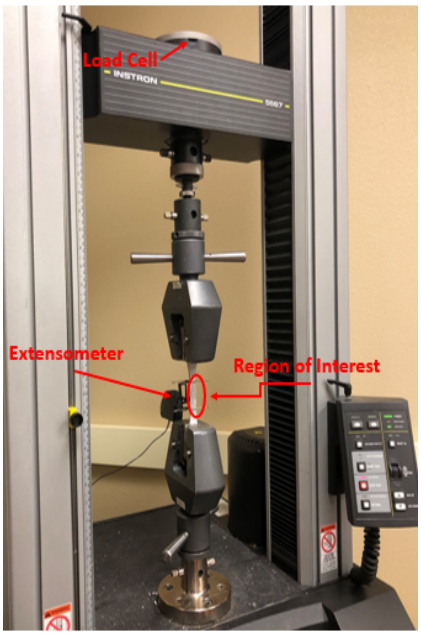


Figure 13: Experimental Setup

- To collect strain data, an Instron 2630-115 axial extensometer was used with a 2" gauge length and a +50%/-5% measurement range. The extensometer is clipped onto the back side of the specimens, opposite of the field of view of the DIC cameras to mitigate any negative interactions between the two measurement methods. The load data is collected using the load cell on the tensile tester. If the specimen elongates past the +50% measurement range of the extensometer, the grip will be quickly reset by hand, in between DIC images being taken, and the strain data will be corrected in post-processing to produce seamless data well past the 50% point.
- Data analysis
    - The results presented include both "engineering" and "true" values. Engineering data is taken directly from the measurement of the extensometer and load cell, where the engineering stress is the load divided by the original cross-section area. The "True" stress strain curve is obtained using the following equations:
        - $True\ Stress = Engineering\ Stress * (1 + Engineering\ Strain)$
        - $True\ Strain = ln(1 + Engineering\ Strain)$
- These "True" values account for the changing cross-section as the sample elongates, and that is why the "true" failure strength is usually much higher than the engineering strength. The elastic modulus is calculated using the engineering data, where its value is taken as the value of the slope of the stress-strain curve in the region between 0.00125 and 0.0025 m/m strain. The separate stress-strain response for each test is presented below
- The results from the conventional testing methods are outlined in Table 2

Table 2: Material properties for various RPU treatments

Sample	Elastic Modulus (GPa)	Yield Stress (MPa)	Yield Strain (m/m)	Fail Strength (MPa)	Fail Strain (m/m)	True Fail Strength (MPa)	True Fail Strain (m/m)	Percent Elongation (%)
R1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R2	1.50	34.8	0.048	27.7	0.355	37.6	0.304	35.5
R3	1.52	34.6	0.048	27.5	0.405	38.6	0.340	40.5
R4	1.38	34.3	0.048	28.1	0.367	38.4	0.312	36.7
CE1	0.306	5.5	0.0104	5.5	0.0104	5.6	0.0104	1.04
CE2	0.447	9.3	0.021	9.3	0.021	9.5	0.0208	2.10
E1	0.645	14.4	0.046	13.7	0.829	25.06	0.604	82.9

E2	0.664	14.7	0.047	13.9	0.877	26.1	0.630	87.7
C1	0.666	8.5	0.0181	8.5	0.0181	8.7	0.0180	1.82
C2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

- Untreated implant results
  - The first series of tests was conducted on the non-treated samples. These were labeled R2, R3, and R4, where "R" stands for "regular" (sample R1 was used to validate the test method and did not produce useable data). The stress-strain data from these tests are presented in Figures 14-17.

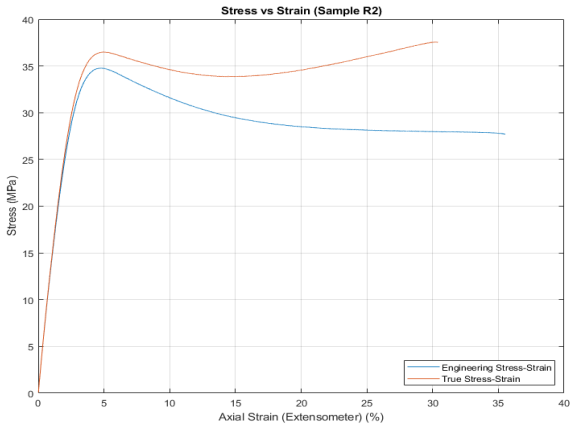


Figure 14: Stress-Strain Behavior for Regular (uncoated) Sample R2

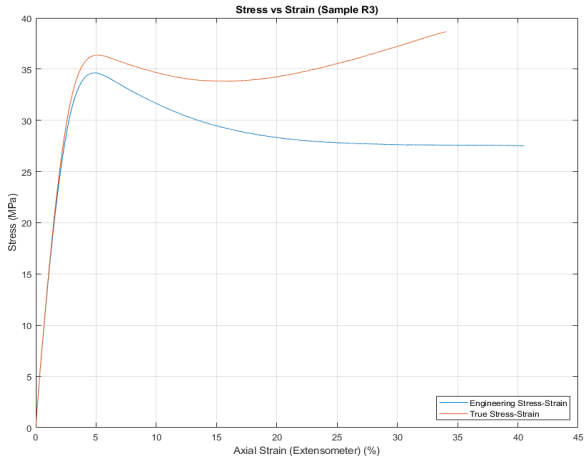


Figure 15: Stress-Strain Behavior for Regular (uncoated) Sample R3

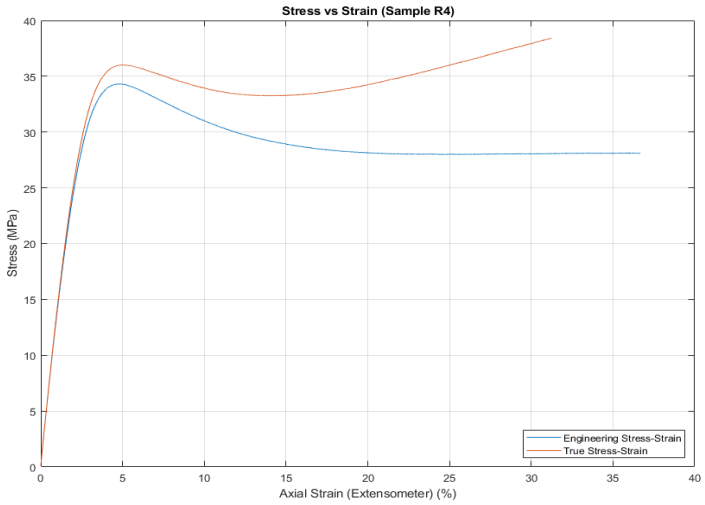


Figure 16: Stress-Strain Behavior for Regular (uncoated) Sample R4

- As shown, these samples fail around 35-40% elongation, and reach a maximum stress of around 35 MPa at the yield point. Yielding is consistently followed by a strain softening region where the stress decreases to around 27 MPa and stays there until failure. There is little to no strain hardening behavior after the strain softening region. These untreated samples have the highest elastic modulus values.

o Implants treated with Ethylene Oxide (EtO)

- Samples with just EtO treatment are labeled E1 and E2. The analyzed stress-strain data from these tests give the behavior shown in Figures 17 and 18.

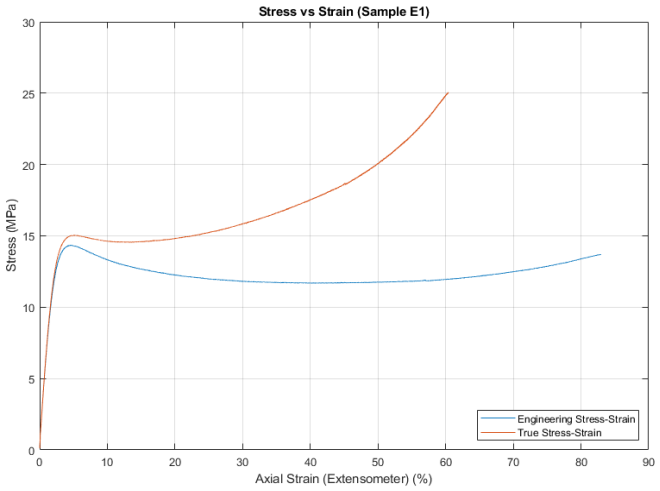


Figure 17: Stress-Strain Behavior for sample E1(just EtO)

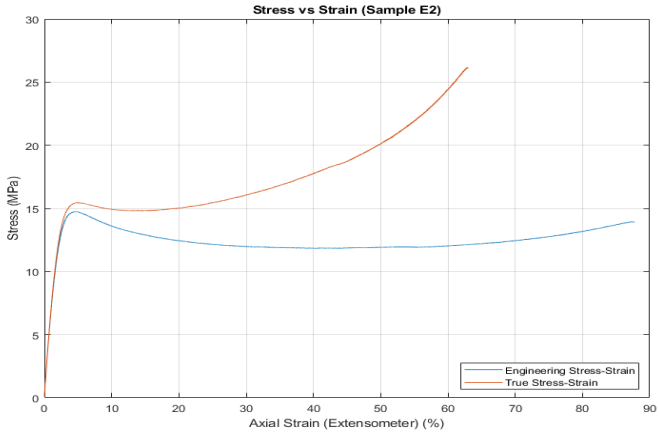


Figure 18: Stress-Strain Behavior for sample E2 (just EtO)

- These tests showed very ductile behavior, with enormous plastic deformation, and elongations approaching 100%. In fact, these tests elongated so much that the extensometer had to be re-set during the test, and strain data was corrected during post-processing. These samples yield consistently just below 15 MPa. The post-yield behavior includes both a strain-softening and strain-hardening region, where the stress decreases from yield to about 12 MPa, then hardens to a failure stress of just below 15 MPa - like the yield stress.

- Implants treated with non-fouling coating
  - The sample with just the non-fouling coating is labeled C1 and the analyzed stress-strain data from this test gives the behavior shown in Figure 19

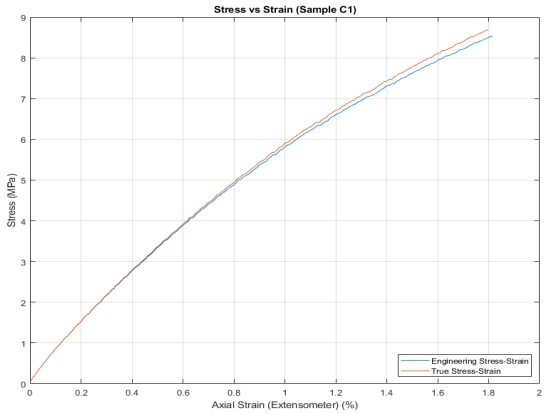


Figure 19: Stress-Strain Behavior for sample C1 (just Non-Fouling)

- This sample provided the most brittle behavior out of all the tests that were conducted. The material failed before reaching a yield point. The C1 sample only elongated to 1.8% before failure, and only reached a stress of

about 8.5 MPa. This treatment is not good for the mechanical properties of the material.

- Implant treated with both non-fouling and EtO
  - Samples with both the non-fouling coating and EtO treatment are labeled CE1 and CE2. The analyzed stress-strain data from these tests yielded the behavior shown in Figures 20 and 21

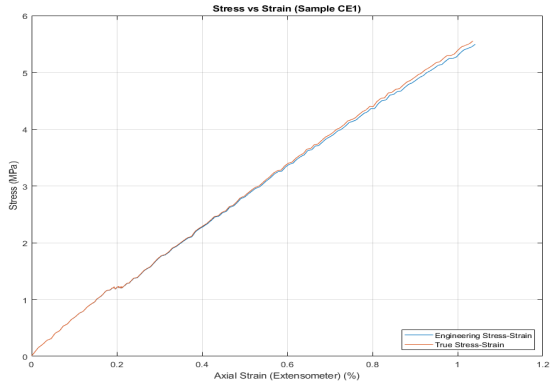


Figure **20**: Stress-Strain Behavior for sample CE1 (non-fouling and EtO)

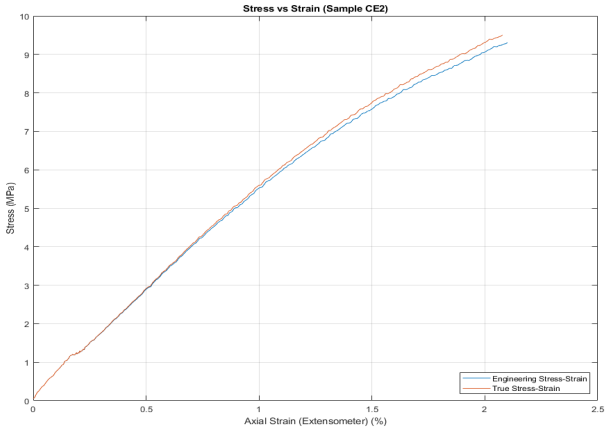


Figure **21**: Stress-Strain Behavior for sample CE2 (non-fouling and EtO)

- These tests showed extremely brittle behavior, with little or no plastic deformation. As seen by the shape of the stress-strain curves, the samples elongate through the elastic region, but quickly fail in a brittle fashion before reaching the yielding point. These samples have an elastic modulus much lower than that of the un-treated samples, as shown in Table 2. They

are shown to be much weaker, as they consistently fail at a stress below 10 MPa.

- Fractured coupons
  - The pattern of the fracture varies between the different sample treatment methods. These patterns refer to the angle of the crack with respect to the width of the coupon, and the number of cracks that form. These patterns are shown in Figures 22-25.
    - The regular samples violently fractured and showed two cracks at large angles.

Figure 22: Regular untreated sample fracture

- The samples with just EtO elongated the most but failed at very low angles with one crack.

Figure 23: EtO sample fracture

- The sample with just the coating showed a single crack at a very low angle/ A large portion of this sample was broken off after the test, so it appears much shorter in the picture.

Figure 24: Non-fouling coating sample fracture

- The coating and EtO samples cracked at very low angles with one crack.

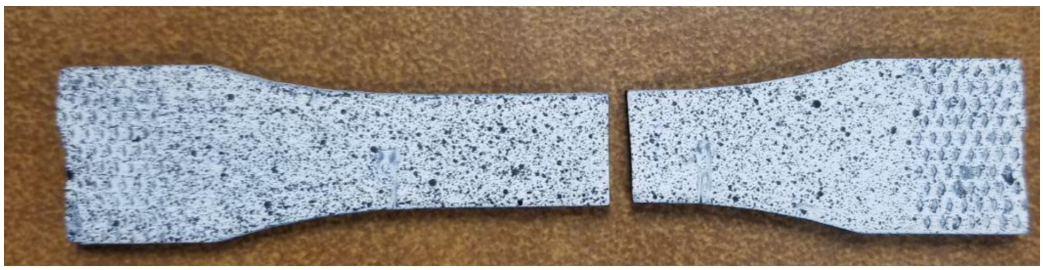


Figure 25: Non-fouling coating and EtO sample fracture

- The expected results of the regular (untreated) coupons were to be very similar to the properties found on Carbon's ®website. The percent elongation of RPU 70 is 80-120% according to Carbon®, while this study's coupons averaged 37.6% elongation. Many factors could cause this variance; temperature, humidity, deformation rate, print parameters, and coupon geometry are a few examples of uncontrolled variables.
- The EtO treated samples had the largest percent elongations of all coupons (~83 - 88%). The EtO treatment is done by permeating EtO gas on the sample for 12 hours. While there are no resources stating the effects of EtO on RPU 70, one study permeated polyethersulphone with CO2 and saw a 60% increase in percent elongation over the control [1].
- The results show that the non-fouling coating causes the RPU 70 to become brittle. However, this needs to be confirmed by running more tests. Two non-fouling coating samples were prepared for this study, but only one was tested because the other shattered during preparation. This may further strengthen the argument that the non-fouling coating causes the RPU 70 to become more brittle. While the non-fouling coating is a surface modification, it is likely that it affects the entire body. One theory is that the non-fouling coating changes the RPU 70 to more brittle behavior is that it decreases the number of crosslink bonds. Without any crosslink bonds the coupon acts as a linear polymer and becomes more brittle [2].
- The combination of the non-fouling coating and EtO had some of the lowest percent elongation of all the samples (1-2%). While it is difficult to make any strong conclusions, this helps promote the notion that the non-fouling coating changes the RPU 70 to become more brittle.
    - [1] Sanders, E. S., 1988, "Penetrant-Induced Plasticization and Gas Permeation in Glassy Polymers," Journal of Membrane Science, 37(1), pp. 63–80.
    - [2] Nielsen, L. E., 1969, "Cross-Linking–Effect on Physical Properties of Polymers," Journal of Macromolecular Science, Part C, 3(1), pp. 69–103.

- **2.1J: When ideal surface treatment is found, work with OSU team in Task 1.1 to apply coatings to implant design (months 25—30)**
    - Samples were prepared using the optimized ARGET ATRP protocol. Surface analysis tools including X-ray photoelectron spectroscopy, Atomic force microscopy and ellipsometer were used to make sure that the sample surface was successfully modified with the chosen non-fouling polymer i.e. PSBMA. Modified samples showed a protein adsorption as low as 4.7 ng/cm^2. The samples were

tested for cytotoxins and endotoxins. After the desired results were achieved, the coating protocol was used to modify the actual implant designs prepared by OSU.

- **2.2C: Implant in mice (months 17—22)**
  - With the optimized ARGET ATRP protocol, protein adsorption as low as 4.7 ng/cm2 was achieved. 10 male Balb/C mice were procured for the animal studies. All the animals were 8-10 weeks old. Two RPU disks were implanted in each mouse, one under the right shoulder and one under the left shoulder. Each animal received one coated disk and one pristine disk, distributed randomly. All the samples were implanted for four weeks.
- **2.2D: Harvest implants and fix samples (months 18—23)**
  - All the animals were euthanized and the samples were harvested after four weeks from the date of implantation. The harvested samples were then fixed using a zinc fixative for 24-36 hours, changing the fixative solution every 12 hours.
- **2.2E: Embedding, staining, and sectioning (months 19—23)**
  - the fixed samples were then embedded in paraffin wax. The sectioning and staining are under process. RPU is a very hard material, which is making it difficult to section them. The sectioning process is being optimized for RPU sectioning, while keeping the attached tissue intact.
- **2.2F: Histological analysis and measurement by microscopy (months 20—24)**
  - Histological analysis will be performed once the slides are sectioned and stained.

Describe the Regulatory Protocol and Activity Status (if applicable).

(a) Human Use Regulatory Protocols

No human subjects research will be performed to complete the Statement of Work.

(b) Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

TOTAL ACTIVITIES: 1

ACTIVITIES:

- Approval was obtained from the DoD and the USC for the human cadaver study titled "Design and Validation of Implantable Passive Mechanisms for Orthopedic Surgery"
- The activity involves the design, development, and validation of an implantable mechanism that will improve muscle and tendon movement.
- Tasks 1.3G—1.3S in the Statement of Work
- 26 cadavers will be used in the study.

(c) Animal Use Regulatory Protocols

TOTAL PROTOCOL(S): 2

PROTOCOL(S):

Protocol (1 of 2 total):
Protocol [ACURO Assigned Number]: MR150091.01
Title: Biomaterials Correlation of *In Vivo* Histology and *In Vitro* Cytokine Release
Target required for statistical significance: 8
Target approved for statistical significance: 8

Submitted to and Approved by:
UW IACUC (protocol number 3043-01) and USAMRMC Animal care and Use Review Office (ACURO)

Status: Active

Protocol (2 of 2 total):
Protocol [ACURO Assigned Number]: MR150091.02
Title: Experimental Validation of Implantable Passive Mechanism in Live Animals
Target required for statistical significance: 93
Target approved for statistical significance: 204

Submitted to and Approved by:
OSU IACUC (protocol number 4775) and USAMRMC Animal Care and Use Review Office (ACURO)

Status: Active

What opportunities for training and professional development has the project provided?
Training Opportunities:

1. Ravi Balasubramanian (PI)
    a. Consulted Dr. Vincent R. Hentz, hand surgeon, on implant design and testing protocols
    b. Consulted Dr. Christopher Allan, hand surgeon, on implant design, hand rehabilitation protocols, and testing protocols
    c. Mentored by Dr. Buddy Ratner, co-I and biomaterials experts, on implant design, material choice, and fabrication.
    d. Mentored by Dr. Francisco Valero-Cuevas, co-I and biomechanics expert, on biomechanical testing methods.

2. OSU graduate Students
    a. Trained by Dr. Ravi Balasubramanian, PI, and Won Suk You, post-doctoral fellow, on implant design, biomechanical testing, and project planning and management
    b. Learned about current clinical practices in hand rehabilitation from Dr. Christopher Allan, hand surgeon.
3. OSU undergraduate Students
    a. Trained on testbed design, testbed operation, implant design, implant fabrication, and biomechanical testing
4. UW Graduate Students
    a. Trained by Dr. Buddy Ratner, co-I, on surface characterization and modification, surface analysis, biocompatibility testing, polymer synthesis, and project planning and management
5. USC Graduate Students
    a. Trained by Dr. Francisco Valero-Cuevas, co-I, and Dr. Vincent R. Hentz, hand surgeon, on biomechanical testing and the use of robotic testbeds to prepare for cadaver experiments
6. All Participants
    a. Assisting in the cadaver studies at USC:
        i. Have undergone General Lab Safety (GLS) training as well as Bloodborne Pathogens (BBP) training to minimize the possibility of injury, and risk of transmission of bloodborne pathogens. These trainings have also provided insights into damage mitigation in the event of an accident or injury. The BBP program also provided an opportunity for the participants to get immunization for the Hepatitis-B vaccine.
    b. Assisting in live animal studies at OSU or UW:
        i. Trained in animal handling, postoperative monitoring, biomechanical experiments, sterile technique, live dissection/tenotomy, suturing techniques
        ii. Have completed OHSP-EH%S Animal Handler Training, Animal Welfare Education, and CITI Program curriculum groups “Working with the IACUC” and “Responsible Conduct of Research”
        iii. Have been cleared by the OHSP Occupational Medicine questionnaire

Professional Development Opportunities:

1. Research Conference Paper Presentations/Posters
    a. Military Health Systems Research Symposium 2019 (MHSRS 2019)
    b. Orthopaedic Research Society 2019 (ORS 2019)
    c. Northwest Biomechanics Symposium 2019 (NWBS 2019)
    d. OSU College of Engineering Graduate Research Showcase 2019

How were the results disseminated to communities of interest?
Results were disseminated through presentations and posters at research conferences, invited research seminars, and publications. Refer to the Training Opportunities and Professional Development Opportunities listed above.

What do you plan to do during the next reporting period to accomplish the goals?
During the next (and final) reporting period, the primary goals will be:

- To demonstrate and validate the performance of implantable passive mechanisms in creating differential actuation *in vivo*;
- To finalize implant designs, implant materials, and implant fabrication methods;
- To determine the ideal surface treatment to apply to the implant designs and test the implants *in vivo*;
- To demonstrate and validate the efficacy of the non-fouling coatings when applied to the implant designs and tested *in vivo*.

Here are the subtasks that were identified in the approved Statement of Work for Year 4:

Specific Aim 1: To design, fabricate, and validate a miniature biocompatible rod for lateral insertion between two biological tendons.

Task 1.3

- 1.3AA: Conduct live animal experiments (months 31—34)
- 1.3DD: Analyze data (months 22—24, 28—30, and 34—36)
- 1.3EE: Feedback results to Tasks T1.1 and T1.2 (month 22—24, 28—30, and 34—36)

Specific Aim 2: To validate if an immobilized dense brush of sulfobetaine (SB) polymer to implanted components inhibits fibrosis and reduces interaction with surrounding tissue.

Task 2.1

- 2.1J: When ideal surface treatment is found, work with OSU team in Task 1.1 to apply coatings to implant design (months 25—30)
- 2.1G: When ideal surface treatment is applied to implant design, test implant *in vivo* (months 30—36)

Task 2.2

- 2.2E: Embedding, staining, and sectioning (months 19—23)
- 2.2F: Histological analysis and measurement by microscopy (months 20—24)

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
Significant contributions and products of this project in Year 3 in the principal disciplines:

1. Orthopaedic Surgery
    a. Introduces innovative alternatives in orthopaedic surgery for hand reconstructive interventions
    b. Expands the possibilities and options in surgical planning for patients who may be confined to limited surgical intervention options
    c. Establishes a better understanding of the functional outcomes for tendon transfer surgeries and other surgical interventions
2. Implant Design
    a. Develops new techniques for implant fabrication, such as 3D printing, while enabling the realization of micro-features
    b. Explores new biomaterials for implant fabrication, such as rigid polyurethane (RPU) and acrylate
    c. Introduces unique attachment methods between artificial implants and biological tissue (e.g., tendon)
3. Experimental Methods in Robotic and Cadaver Testbeds
    a. Develops new experimental methodologies for studying upper extremity biomechanics for advancing orthopaedic surgeries and understanding functional outcomes
    b. Provides insights into how the implants being developed in this project modify and improve force and movement transmission
    c. Introduces different perspectives in how to quantify and evaluate these modifications and improvements of force and movement transmission in the upper extremity for understanding the functional outcomes of surgical interventions
4. Experimental Methods in Live Animals
    a. Redefines the chicken pelvic limb model and the associated extensor digitorum longus (EDL) musculotendon unit as a feasible and appropriate animal model for tendon transfer surgery, specifically for surgeries that result in coupled musculotendon systems in humans like the flexor digitorum profundus (FDPs) tendons to the single donor extensor carpi radial longus (ECRL) muscle
5. Non-Fouling Coatings and Biomaterials
    a. Develops versatile non-fouling coatings that can be applied to an array of implant materials, which minimizing implant material selection and fabrication limitation when considering the compatibility of the coating
    b. Enables the possibility of implants that can slide with minimum friction between layers of connective tissues by increase protein resistance and minimizing adhesion formation during healing

What was the impact on other disciplines?

Significant contributions and products of this project in Year 2 in other disciplines:

1. Robotics
    a. Creates new opportunities of designing robotic devices that can be employed within the body
    b. Highlights the utility of using robotic testbeds as exemplar models for preliminary, translational studies in biomechanics for orthopaedic surgery in humans
2. Mechanism Design
    a. Demonstrates the possibilities of state-of-the-art mechanism designs for applications within the body – basically reengineering aspects of the musculoskeletal system for improved force and movement transmission

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Nothing to Report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

- In Year 3, after a series of chicken cadaver experiments, the team concluded that tendon stiffness due to calcification impeded differential action (See NWBS 2019 abstract). Considering this, the team has decided to use the chicken model to study biocompatibility and implant translation

Actual or anticipated problems or delays and actions or plans to resolve them

- Due to the unavailability of the veterinary surgeon due to medical leave live animal studies have been postponed until month 42 - 45 (i.e., the first quarter of Year 4)
    - Unavailability of the veterinary surgeon cannot be resolved; we must wait until month 42 - 45 to perform the next round of live animal studies

Changes that had a significant impact on expenditures

Nothing to Report.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

ACUP amendment approvals were obtained for changes in the number of animals required, changes in experimental protocols, and changes in the surgical procedure.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. PRODUCTS:

Publications, conference papers, and presentations

Journal publications

Nothing to Report.

Books or other non-periodical, one-time publications

Nothing to Report.

Other publications, conference papers, and presentations

Conference Papers/Proceedings

- J. Casebier, W. S. You, and R. Balasubramanian, "Validating the mechanical robustness of a passive implantable mechanism in the chicken extensor tendon model," *in Proceedings of the 11th Annual Meeting of the Military Health and Science Research Symposium*, Aug 2019
- W.S. You, J. Casebier, R. Balasubramanian, "Validation of chicken extensor model for a 3D printed force distribution implant," *in Proc. Northwest Biomechanics Symposium 2019*, Bozeman, MT, May 2019.
- H. Ling, K. L. Roberts, and R. Balasubramanian, "Restoration of key pinch strength using an implantable mechanism," in *Proceedings of the Annual Orthopaedic Research Society*, Feb 2019.
- W. S. You, J. Casebier, A. H. Le, and R. Balasubramanian, "Validation of passive implantable mechanisms in avian model," *in Proceedings of the Annual Orthopaedic Research Society*, Feb2019.

Website(s) or other Internet site(s)

Nothing to Report.

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Ravi Balasubramanian
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change
Contribution to Project:	No change
Funding Support:	No change

Name:	Jennifer Warnock
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change
Contribution to Project:	No change
Funding Support:	No change

Name:	James Sweeney
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change
Contribution to Project:	No change
Funding Support:	No change

Name:	Francisco Valero-Cuevas
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change

Contribution to Project:	No change
Funding Support:	No change

Name:	Buddy Ratner
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change
Contribution to Project:	No change
Funding Support:	No change

Name:	Forrest Ling
Project Role:	No change
Researcher Identifier (e.g., ORCID ID)	No change
Nearest person month worked:	No change
Contribution to Project:	No change
Funding Support:	No change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Nothing to Report.

What other organizations were involved as partners?
Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

Collaborative Awards:
Nothing to Report.

Quad Charts:
Attached to Report.

9. APPENDICES:

1. Conference papers/proceedings listed in Section **6 PRODUCTS** (pg. 39) are attached.

Validating the Mechanical Robustness of a Passive Implantable Mechanism in the Chicken Extensor Tendon Model

Background:

Previous work has shown that an implanted passive mechanism inserted between tendons successfully redistributes forces and movement within the human hand when compared with using direct sutures between the tendons in a tendon-transfer surgery [1]. This paper validates the mechanical strength and robustness of how the 3D-printed implants securely attach to the tendons through experiments with a chicken tendon model.

Specifically, the tendon transfer surgery for high median-ulnar palsy directly sutures all finger flexor tendons to a wrist muscle. This couples the movement of all four fingers making it difficult for fingers to adapt to varying object geometries. However, a miniature rod inserted between the flexor tendons creates a differential mechanism between the muscle and the fingers This enables all the fingers to move *differentially,* adapt to an object's shape while grasping, and create a more natural and secure grasp around an object even if all the fingers are actuated by only one muscle. This differential mechanism surgically created using the tendons and the rod *in situ* passively rotates and translates within the forearm to accommodate for each finger's movement. Thus, even if one finger has made contact with an object, the rotation of the implant enables the other fingers to complete closure around the object.

The chicken model is a good model to study this problem. This is because the extension of the chicken toes is driven by one muscle through a bifurcated tendon. Thus, this tendon structure mirrors the human tendon biomechanics after the current transfer surgery, where multiple digits are actuated by a single muscle. Previous work with live chickens showed that the implants attached to the tendon using sutures caused large scarring. To amend this, the implant was re-designed to use micro-spikes for attachment with the tendon. Also a non-fouling coating was added to the implant surface to reduce the foreign-body response. This paper demonstrates that 1) the micro-spikes securely attach the implant to the tendon in cadaveric chicken studies [2] and 2) the process for sterilization and applying the non-fouling coating does not weaken the 3D-printed implant structure. A live animal implantation study is currently underway to evaluate spike performance and surface modification effects in-vivo.

Methods:

Implants were manufactured from 3D printed rigid polyurethane (RPU 70 from *Carbon 3D*, Redwood City, CA), surface modified with a sulfobetaine (SB) polymer to reduce fibrosis, at the University of Washington, and ethylene oxide sterilized. The legs from a Freedom-Ranger chicken were severed below the elbow joint. Implants were mounted below the natural bifurcation of extensor digitorum longus (EDL) tendon, which is located at about the same height as the spur. The skin around the implant was removed and the legs were secured in a custom made mount and the EDL tendon was connected a DC motor (ServoCity 32 rpm Premium Planetary Gear motor w/ Encoder), with a force transducer (Futek LSB200 10lb) in-line. Each leg (n=2) underwent 5000 cycles where the first 2000 input was set to 8 N, which is the force need to fully extended the chicken extensor under no load. The next 2000 cycles at 12 N (safety factor of 1.5X), and the last 1000 at 20 N to test an *Extreme* force scenario (safety factor of 2.5X). After each study (full 5000 cycle), implants were dissected from the legs and visually checked for any wear or damage.

Results and Discussion:

Pulling force for the implants for the first chicken was 8.1 ± 0.4 N for 2000 cycles, 11.9 ± 0.7 N for 2000 cycles, and 20.9 ± 2.0 N for 1000 cycles. Pulling force for the second chicken was 8.7 ± 0.6 N for 2000 cycles, 12.7 ± 1.0 N for 2000 cycles, and 21.3 ± 1.3 N for 1000 cycles. In addition to these large tensile forces that the implants could withstand, the secure engagement between the microspikes and the tendon made it very difficult to remove the implant from the tendon after the cycle testing. This indicates that the spikes are an excellent attachment method. Furthermore, no visual signs of wear or damage were present on the implants following the experiment.

Conclusion:

This study shows that the implant with the non-fouling surface modification and ethylene oxide sterilization is capable of withstanding the forces and excursions of the chicken extensor tendon. Thus, the same implant design can be used in a live chicken study.

References:

[1] K. L. Mardula, R. Balasubramanian, and C. H. Allan, "Implanted Passive Engineering Mechanism Improves Hand Function after Tendon Transfer Surgery: a Cadaver-based Study," Hand, vol. 10, no. 1,pp. 116-122, Mar. 2015.

[2] W. S. You, J. Casebier, and R. Balasubramanian, "Validation of micro spikes for mounting an implant to a tendon," in Proceedings of the 42nd Annual Meeting of the American Society of Biomechanics, Aug. 2018.

VALIDATION OF CHICKEN EXTENSOR MODEL FOR A 3D PRINTED FORCE DISTRIBUTION IMPLANT

You, W.S., Casebier, J. and Balasubramanian, R.
Robotics and Human Control Lab, School of Mechanical, Industrial, and Manufacturing Engineering,
Oregon State University, Corvallis, OR USA
email: ravi.balasubramanian@oregonstate.edu, web: http://research.engr.oregonstate.edu/rhcs/

INTRODUCTION

In previous work, it has been shown that a 3D printed implantable passive mechanism inserted between two tendons successfully redistributes forces and movement within a human cadaver hand when compared to using direct sutures between the tendons in a tendon-transfer surgery [1]. However, before going for clinical trials, the in-vivo biomechanical benefit should be validated in a live animal model. The chicken model is a good model to test this as toes extension is driven by one muscle through a bifurcated tendon structure. This mirrors the biomechanics of human tendons after the current transfer surgery, where multiple digits are actuated by a single muscle. Dissection of the chicken leg revealed that a vital tendon in the chicken model was rigid due to calcification. To ensure this does not cause difficulties when implanting in live animals, the implants ability to attach to tendons and distribute forces between tendons must be tested.

This paper explores the effects tendon calcification has 1) on the ability of the micro-spike to securely hold to tendon and 2) on implant's ability to distribute forces between tendons.

METHODS

Implants were manufactured from 3D printed rigid polyurethane (RPU70, Carbon 3D®). The legs from freedom ranger chickens were severed below the elbow joint and implants were mounted below the natural bifurcation of extensor digitorum longus (EDL) tendon. Legs were secured in a custom-made mount with the skin around the implant removed and the EDL tendon connected to a DC motor (32 rpm Premium Planetary Gear motor w/ Encoder, Servo City®), with a force transducer (Futek LSB200) in-line.

To test the micro-spikes attachment method, each leg (n=2) underwent 5000 cycles (Table 1). The initial 2000 was at 8 N as this is force needed to fully extend the chicken extensor unloaded. The next 2000 cycles were at 12 N (safety factor of 1.5X), and 1000 at 20 N to test an extreme force scenario (safety factor of 2.5X). After each study (full 5000 cycles), implants were dissected from the legs and visually checked for any wear or damage.

No	Cycle	Avg. Pulling Force (N)	Std. (N)
1	2000	8.1	0.4
	2000	11.9	0.7
	1000	20.9	2.0
2	2000	8.7	0.6
	2000	12.7	1.0
	1000	21.3	1.3

Table 1: Pulling force to test mechanical robustness

The implant's ability to distribute forces in a calcified tendon network was tested kinematically. A webbing connection between the outside and middle toes was severed based on the result from a simulation showing force distribution was not possible with this webbing [2]. The lateral toe was splinted, and reflective markers were placed at the knuckle, toe tip, and in line with the leg. (Fig. 1). Marker movements were measured with the OptiTrack motion capture system. Legs (n=2) were pulled at 8N and 12N. Implants were removed, and the test was repeated for the control case.

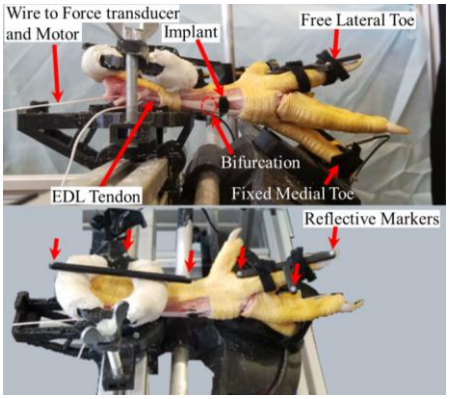


Figure 1: Experimental setup to validate of chicken extensor model for a force distribution implant.

RESULTS AND DISCUSSION

The implant was able to withstand cyclical testing and the micro-spike attachment made removing them from the tendons extremely difficult; proving that the spikes make a secure attachment even on a calcified tendon.

The force distribution test showed no significant difference in movement capability between the implanted and control cases. As predicted, this is due to mineralization on the tendon negating the implant's ability to rotate; an essential for distributing forces between the toes. Even though this shows that the chicken extensor model is not suitable for testing differential action, the chicken model serves to ensure that the implant is biologically sound before moving on to another animal model without a mineralized tendon.

CONCLUSIONS

This study provides the required tests to help pave the way for clinical testing. The spikes proved to be an effective attachment method to test the implants biocompatibility in the chicken model. Tendon calcification caused the chicken model to be ineffective for validation of force distribution, but will help in better defining the criteria for another animal model.

REFERENCES

1. Raja SC, et al. *Proceedings of Tetrahand World Congress*, Nottwil, Switzerland, Abstract 36, 2018.
2. Casebier J, et al. *Proceedings of the 44th Annual Meeting of the Veterinary Orthopedic Society*, Snowbird, Utah, USA, Abstract 17, 2019.

ACKNOWLEDGEMENTS

This work was supported by NSF CBET 1554739 and DoD CDMRP.

Restoration of Key Pinch Strength using an Implantable Passive Mechanism

Hantao Ling, Kai L. Roberts, Ravi Balasubramanian
Oregon State University, Corvallis, OR
lingh@oregonstate.edu

Disclosures: None.

INTRODUCTION: In the United States, approximately 17,700 new cases of spinal cord injury occur each year, with 58.7% resulting in some degree of tetraplegia[1]. The loss of functional strength associated with these injuries decreases an individual's autonomy and increases their dependence on caregivers and family members. For the tetraplegic population, restoration of key pinch grasp is vital for returning to activities of daily living, such as zipper manipulation, inserting and removing plugs into wall outlets, and inserting cards into an ATM[2]. A common surgery used to restore key pinch grasp, in cases with complete functional loss, is the brachioradialis (BR) to flexor pollicis longus (FPL) tendon transfer surgery, which has been shown to improve key pinch strength from 0 kg to 2 kg[3]. While this procedure is successful in restoring key pinch ability, functional key pinch strength is significantly lower than the 9 kg produced by a healthy population[4]. A possible improvement to this procedure will utilize tendon routing and an implantable passive mechanism (IPM) to more fully restore functional strength. Previously, these devices have shown the ability to improve hand function following nerve damage and increase foot arch support through muscle force amplification for individuals with adult-acquired flatfoot deformity[5].

For the tetraplegic, this IPM can be used to improve key pinch grasp in two scenarios: (1) when a BR to FPL tendon transfer surgery is required to restore key pinch grasp and (2) when the FPL is responsive but lacks strength. In the first scenario, an IPM would be used in conjunction with a modified version of the BR to FPL surgery to better restore strength of the key pinch grasp. The second scenario requires the development of a novel surgery to implement the IPM with a single weakened musculotendinous system. The objective of this study is to conduct a proof-of-concept experiment of the tendon transfer scenario to determine the force-scaling capabilities of an IPM in an animal model.

METHODS: A New Zealand white rabbit wrist extensor model (n = 1) was used to evaluate the force-scaling capabilities of an IPM in a control and implant condition. The control condition was created by dissecting out the lateral digital extensor (LDE) tendon and transecting it just distal of its muscle-tendon junction. Vectran rope was sutured to the proximal end of the transected tendon and was routed from the forelimb to a pulley on a custom testbed, which allowed the rope to freely hang off the edge of the table. The rabbit forelimb was positioned and secured on the testbed in 100° elbow extension and 165° wrist extension. Once positioned, another Vectran rope was secured just distal of the fifth metacarpophalangeal joint and attached to a miniature S-beam load cell (Futek), which was used to measure toe force. A 500 g mass was secured to the loose end of the free-hanging rope. The weight was lowered by hand, and the subsequent forces produced at the fifth metatarsal were recorded for 5 seconds at 1000 Hz.

The implant condition was created by first suturing a 3D printed rigid polyurethane IPM to the transected LDE tendon. The common digital extensor (CDE) tendon was then dissected out as proximal to its insertion point as possible and routed through the IPM. A Vectran rope was sutured to the distal end of the CDE tendon and routed to the testbed pulley, where it hung freely. The same procedure used in lowering the weight and recording data for the control condition was used for the implant condition. Three trials were conducted for each condition for a total of six trials.

For preliminary statistical analysis, an independent t-test was performed to determine if the force output results of the implant condition differed from the control condition. Significance was set at $p = 0.05$.

RESULTS: Preliminary findings indicate that IPMs have the potential to increase functional strength in tendon transfer scenarios. The 1.52 ± 0.127 N of force produced by the fifth metatarsal in the implant condition was significantly greater than the 0.931 ± 0.052 N produced in the control condition ($p < 0.0001$). This difference results in an average mechanical advantage produced by the IPM of 1.63.

DISCUSSION: The aim of this study was to evaluate the force-scaling capabilities of an IPM in a rabbit forelimb tendon transfer model. The addition of the IPM scaled up the force output of the fifth metatarsal toe by 1.63 times when compared to the non-implanted case. These results suggest that IPMs have the potential for restoring higher levels of functional strength than traditional tendon transfer surgeries in the tetraplegic population. Furthermore, the results of this study indicate that the rabbit wrist extensor model is an effective workspace for evaluating IPMs and their associated surgical procedure. Despite the encouraging findings of this study, the experiment was conducted on a single rabbit forelimb. Larger sample sizes are needed to determine the true force-scaling capabilities of IPMs.

SIGNIFICANCE/CLINICAL RELEVANCE: Functional weakness following spinal cord injury is a life-long disability that can be partially restored through traditional tendon transfer surgeries. The successful development of a force-scaling IPM allows patients lacking functional strength to return to more activities of daily living than current treatment options.

REFERENCES: [1] National Spinal Cord Injury Statistical Center 2018, UAB; [2] Smaby et al. 2004, JRRD; [3] Hamou et al. 2009, JHS; [4] Mathiowetz et al. 1985, APMR [5] Pihl et al. 2016, JOR;

ACKNOWLEDGEMENTS: Jennifer Warnock and Lindsay Benage; NSF CBET 1554739; CDMRP-NIRA Award No. W81XWH-16-1-0794

IMAGES AND TABLES:

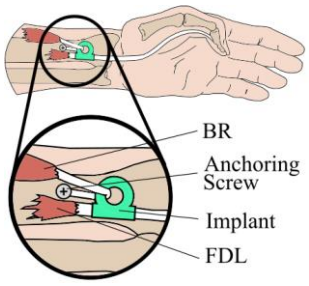


Figure 1. Illustration of a force-scaling implantable passive mechanism in a modified BR to FDL tendon transfer.

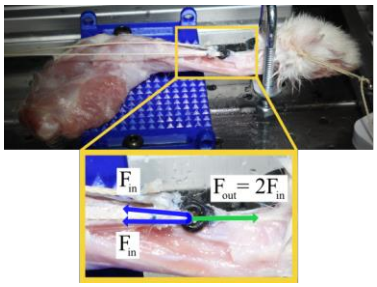


Figure 2. Rabbit forelimb mounted on custom testbed (top) and implanted force-scaling device (bottom).

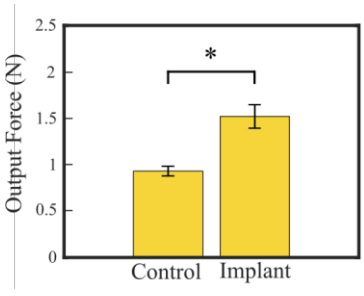


Figure 3. Mean force generated at fifth metatarsal during tendon tensioning (3 trials, n = 1).

Validation of Passive Implantable Mechanism in Avian Model

Won Suk You, Justin Casebier, Anthony H. Le and Ravi Balasubramanian
[1]Oregon State University, Corvallis, OR, USA
ravi.balasubramanian@oregonstate.edu

INTRODUCTION: Implantable passive mechanism that reconfigure the mechanics of force and movement in-vivo have been shown in a previous study to be biomechanically advantageous [1]. For instance, in the case of high median ulnar palsy, the insertion of an artificial strut between the four-finger tendons allows for movement between digits to increase finger flexion during grasping tasks (Fig. 1a) when compared to the current surgical procedure. Initial embodiments of the implant used sutures to attach the artificial strut to the tendon. However, after implantation in an avian model, it was shown that the sutures induced severe trauma to the tendons which led to a fibrotic healing response and long-term scarring [2]. To overcome this issue, a new generation of implants were designed to replace sutures with micro spikes. This paper seeks to validate the effectiveness of these new implant to allow for differential action between the medial and lateral toe of an avian model when applying a force to the extensor tendon.

METHODS: Two different implant embodiments were validated in this study; the first design has spiked lined slots for the tendon to sit, preventing the tendon from disengaging (Fig.2b left). The second designs use the same methodology as the first design but adds a structural locking component to prevent any shifting of the implant on the tendon (Fig.2b middle). The effectiveness of the spikes was tested by cycling them on the flexor tendon for 5000 cycles [3]. Implants were manufactured using Carbon 3D®'s SLA 3D printer using Polyurethane (RPU 70). Implants were inserted distal of the first bifurcation of the extensor tendon in the chicken and the webbing between the center toes and outside toes was removed to allow for similarity to the human's tendon network. Surgeries were performed by Dr. Jennifer J. Warnock DVM, (Oregon State University, College of Veterinary Medicine) (Fig.2b right). Legs were mounted on a custom-made test bed that allowed for the measurement of both kinetic and kinematic data collections. Kinetic data was measured by securing the medial and lateral toes of the chicken to two separate force sensors in a neutral position while the extensor tendon attached to another force sensor in series with a linear actuator was pulled to 12 newtons [4]. Kinematics data was collected by securing the medial toe of the left leg and lateral toes of the right leg while the leg was pulled to full extension (12 N) and the movement of the opposite toe was tracked with respect to the tarsometatarsal bone using Optitrack®'s motion capture system. Implants were then removed from the legs and the same tests were conducted as two control cases.

RESULTS: A total of 7 cases of cadaver tests were conducted using 5 chicken legs (two right legs and three left legs). Legs of approximately 5 months old freedom rangers were used for this experiment. As shown in the top portion of Table 1, the results of collected kinematic data show that the V-shape implant can improve 23%, 500%, 72% of maximum extension angle, abduction angle, and toe tip movement respectively when the lateral toe was fixed and medial toe was allowed to move. On the other hand, the strut implant case in the right leg and both v-shape and strut implant cases showed decreased range of motion comparing to the control cases. In kinetic data collection result, except decrease of medial toe tip force of left leg with strut implant (-34%), implant cases in both in right and left leg, generated significantly higher toe tip forces (as small as 32% (left leg, v-shape, medial toe) and as big as 711% (left leg, strut, lateral toe)) than control cases (Table 1 lower).

DISCUSSION: In kinematic data collection, it was expected to see improved range of motion in the implanted cases and isometric toe tip forces were expected to be similar before and after the implants were inserted. However, the chicken cadaver test showed the opposite result when comparing to the expected result. Since the control cases were conducted a day implanted cases due to a technicality problem, the most probable reason for this result is the tendon property change in the control cases caused by repeated freezing and thawing. The secondary suspected reason is the damage inflicted on the tendons when removing implants from cadaver legs due to the spikes tearing into the tendons. To overcome the limitation of this work, the effectiveness of these v-shape and strut implants will be evaluated via a live chicken study which is planned to be conducted in the near future.

SIGNIFICANCE/CLINICAL RELEVANCE: The passive implantable mechanisms have never before been used in orthopedic surgery and the implants help overcome the drawbacks in the current suture-based surgical paradigm, the purpose of this work is to explore the possibility of using suture-less implants in orthopedic surgery and provide better hand function to affected patients.

REFERENCES:
1. Homayouni et al. IEEE Transactions on Biomedical Engineering, 62(9), 2208-2214, 2015.
2. Le et al. Proceedings of 44th VOS Conference, Snowbird, Utah, 2017.
3. You et al. Proceeding of the 42nd ASB Conference, Rochester, MN, 2018.
4. Gilbert et al. Journal of biomedical materials research. 19(5), 601-605, 1985.

ACKNOWLEDGEMENTS: This work was supported in part by the Office of the Assistant Secretary of Defense for Health Affairs, through the Joint Program Committee 8 (JPC8), Clinical and Rehabilitative Medicine Research Program (CRMRP), Neuromusculoskeletal Injuries Research Award (NIRA), Funding Opportunity Number: W81XWH-15-JPC-8/CRMRP-NMSIRA, under Award No. W81XWH-16-1-0794. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

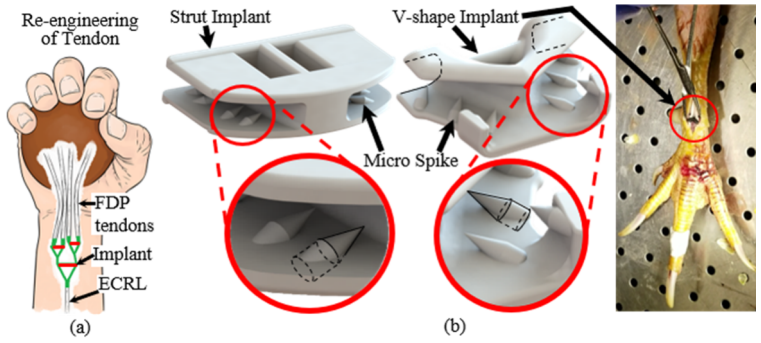


Figure 1. Depiction of (a) tendon re-engineering using implants and (b) Strut (left), V-shape (middle) implant, and inserted V-shape implant in a chicken cadaver leg.

Kinematic data collection			Extension angle (°)	Abduction angle (°)	Teo tip movement (mm)
Right Leg	Implanted	V-shape (n=1)	3.99±0.086	2.56±0.034	4.68±0.068
		Strut (n=1)	2.04±0.20	0.897±0.096	0.722±0.078
	Control (n=1)		3.24±0.054	0.426±0.14	2.72±0.15
Left Leg	Control (n=1)		19.19±0.42	25.9±0.97	29.7±0.86
	Implanted	V-shape (n=2)	6.43±1.06	8.22±0.90	10.8±1.41
		Strut (n=1)	16.35±0.58	16.7±0.40	19.9±0.55
Kinetic data collection			**Lateral toe tip force (*N*)**	**Medial toe tip force (*N*)**	**Tendon pulling force (*N*)**
Right Leg	Implanted	V-shape (n=1)	1.46±0.023	0.173±0.0046	11.78±0.20
		Strut (n=1)	1.67±0.030	0.751 ±0.021	11.96±0.25
	Control (n=1)		0.443±0.091	0.0354±0.241	11.92±0.25
Left Leg	Control (n=1)		0.419±0.021	0.551±0.088	11.91±0.26
	Implanted	V-shape (n=2)	2.84±0.033	0.728±0.041	11.65±0.22
		Strut (n=1)	3.40±0.062	0.362±0.0097	11.93±0.30

Table 1. Results of chicken cadaver test in point of view of movement of MTP joint (upper), and isometric force generated by lateral and medial toe (lower)

Design and Validation of Implantable Passive Mechanisms for Orthopedic Surgery

ERMS number: DM153091; Task title: Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program Neuromusculoskeletal Injuries Research Award

Award #: W81XWH-16-1-0794

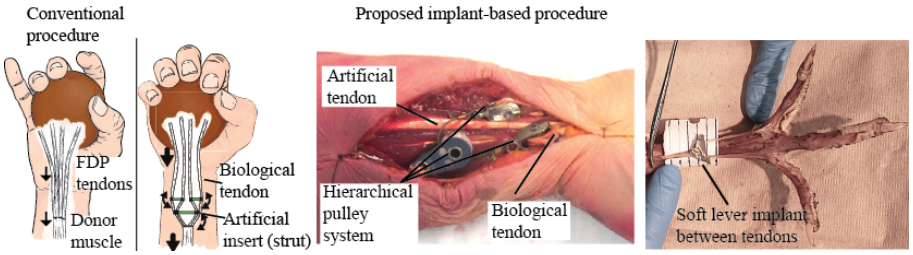
PI: Ravi Balasubramanian **Org:** Oregon State University **Award Amount:** $1.5 Million

Study/Product Aim(s)

- Advance orthopedic surgery by developing implantable passive mechanisms for attaching muscles to tendons and bone
- The implantable mechanism will enable customizable force and movement transmission inside the body based on patient's desired musculoskeletal action
- Expected benefits when compared with current suture-based paradigm: (i) Significantly better joint function; (ii) More surgical choices.

Approach

- Specific Aim 1: To design, fabricate, and validate a miniature biocompatible rod for lateral insertion between two biological tendons.. The validation will be performed through human cadaver and live animal experiments and biomechanical simulation.
- Specific Aim 2: Inhibit fibrosis and reduce interactions between tissue and the implanted mechanism with an immobilized brush of sulfobetaine (SB) polymer.



Preliminary work: Human and animal (chicken) cadaver experiments and biomechanical simulation studies show that the implant-based surgery enables significantly better hand function when compared with using the direct suture in orthopedic surgery

Timeline and Cost

Activities	CY 16	17	18
Specific Aim 1: Design, fabricate implant			
Develop evaluation metrics for implant			
Specific Aim 2: Develop non-fouling layer			
Pilot and full cadaver studies, live animal studies			
Estimated Budget ($K)	**$350K**	**$450K**	**$700K**

Updated: Corvallis, OR

Goals/Milestones

CY16 Goals – Design and fabrication of implantable passive mechanism (lever insert or artificial tendon network) and develop coating

- ❑ Identify the specifications for the implant in terms of strength, movement, fatigue, and biocompatibility requirements. Identify metrics for evaluating implant
- ❑ Conduct pilot cadaver study
- ❑ Develop non-fouling chemical coating

CY17 Goals – Validation of implant in cadavers and pilot study of coating

- ❑ Evaluate the implant in human cadavers (N = 6) in terms of hand function enabled in comparison to hand function enabled by current suture-based procedure.
- ❑ Conduct sensitivity analyses for design using biomechanical simulations
- ❑ Conduct pilot studies of biomaterial coating in mice (N=8)

CY18 Goals – Animal model trials

- ❑ Evaluate implant in live chicken toe-extensor system (N = 18)

Comments/Challenges/Issues/Concerns

- Clinical relevance in human surgery. Will seek advice from orthopedic surgeon.

Budget Expenditure to Date

Projected Expenditure: $1.5 Million Actual Expenditure: $1,367,206