FOREIGN BODY RESPONSE TO AN ORTHOPEDIC IMPLANT WITH A ZWITTERIONIC POLYMER COATING: IN VIVO RABBIT MODEL PILOT STUDY

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1. Objective

The goal of this study was to validate the efficacy of a hydrophilic coating on a novel implantable device in an *in-vivo* rabbit model.

2. Motivation: Implant

Our group has **developed a passive orthopedic implant for use in the ECRL-to-FDP tendon-transfer surgery** for patients suffering from a cervical spinal cord injury (SCI) [1,2].

Standard of Care (A) :

- All four FDP tendons are rerouted to the ECRL muscle, coupling the movement of all four fingers (Figure 1(A)).
- The coupled finger movement greatly limits the patient's grasping ability, reducing their independence and quality of life.

Implant-based surgery (B) :

- Passive implantable mechanism is placed between the FDP tendons during the standard of care surgery (Figure 1(B)).
- The implant improves the transmission of forces and movement between the muscle and FDP tendons, enabling superior finger adaptation to an object's shape during grasping.

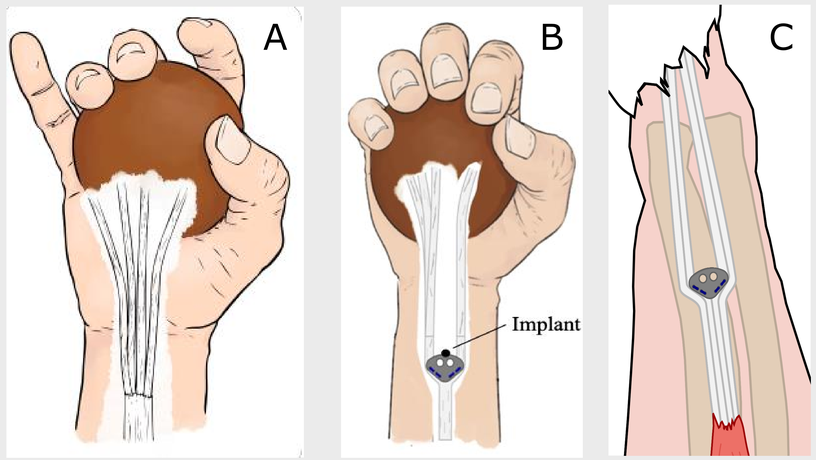


Figure 1. (A) The surgical standard of care and (B) the implant-based surgery to restore grasping function for patients. (C) The EDC tendon rabbit model to evaluate the implant's functionality in a biological system.

3. Motivation: New Zealand Rabbit Model

- Any device implanted in the human body is subject to the foreign body response and fibrotic encapsulation which can affect device functionally.
- **Hydrophobic coatings** can be applied to the surface of a device to reduce non-specific protein adsorption and the subsequent foreign body response.
- The New Zealand Rabbit's EDC tendons are ideal models to mimic the FDP tendons in humans [3] (Figure 1C).
- **Our group conducted a three-week survival trial, implanting the implant between tendons I/II and III/IV of the extensor digitorum communis (EDC) tendon bundle of the New Zealand white rabbit with varying coated and uncoated implants to determine its effect on the foreign body response.**

4. Methods: Coating Application and Rabbit Implantation

- A pilot study of n=4 rabbits was conducted to compare the effect of coated (n=2) vs uncoated implants (n=2).
  - Coated implants were coated with a novel hydrophilic zwitterionic coating of poly(sulfobetaine methacrylate) (pSBMA) using methods previously established [4]
  - The pSBMA coating has previously been found to create an 87-93% reduction in non-specific protein adsorption to the surface of implant material when tested in vitro [5]
  - All implants were then sterilized with ethylene oxide.
- Throughout the study the following post-operation or rehabilitation care protocol was followed:
  - Week 1: Animals received bandage changes daily and were maintained in respective cages.
  - Week 2: Animals were no longer receiving bandage changes and were allowed time daily to move about in a larger pen set up.
  - Week 3: In addition to the large pen time, the animals also participated in daily passive range of motion exercises on their implanted limb.

5. Methods: Histology

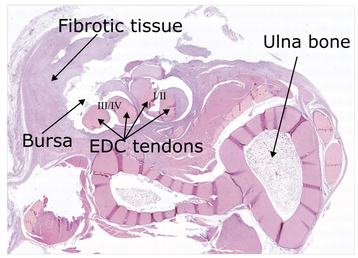
- Following euthanasia, the implant was surgically removed, the leg was set in formalin and then decalcified.
- The specimen was then sliced at the implant site, 3 mm proximal, and 3mm distal.
- Samples were mounted on slides and stained with a standard hematoxylin and eosin staining protocol.
- Legs were evaluated through ISO 10993-6 and a fibrosis measurement (FM) was made using ImageJ by dividing the area of the fibrosis by the area of the ulna bone to normalize across different rabbits [4].

6. Results and Discussion

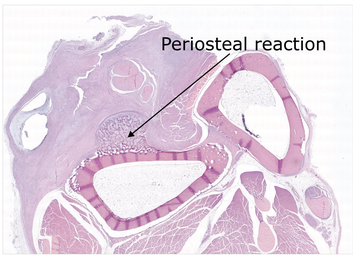
- For both groups, Histologic changes were most prominent at the device's location and reduced in severity 3mm proximal and distal to the implant.
- The device was contained within a fluid-filled pseudo-bursa apposed to the tendon and surrounded by an acquired fibrovascular scar capsule (Figure 1).
- Excessive lymphocytic, heterophilic, or granulomatous inflammation was not detected in any rabbits. No rabbits had microscopic signs of infection.
- **The two uncoated rabbits had a mean FM of 1.5 ± 0.28 while the coated rabbits had an FM of 0.645 ± 0.18 .**
- This reduction in FM shows that the coating decreased the development of fibrosis around the implant site.

7. Results and Discussion

Fibrosis measurement (FM)= (fibrosis area)/(ulna area)

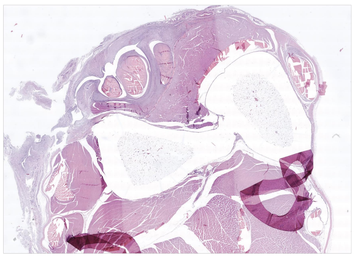


Uncoated Rabbit 1
FM=1.3



Uncoated Rabbit 2
FM=1.7

Coated Rabbit 1
FM= 0.52



Coated Rabbit 2
FM=0.77

Figure 2. Histology slides of the EDC tendon site of implanted rabbits. Top row shows rabbits implanted with uncoated implants. Bottom row shows rabbits implanted with coated implants. For uncoated rabbit 1, the bursa is clearly shown to have formed from the implanted device. Uncoated rabbit 2 notably shows a periosteal reaction. Both coated rabbits showed greatly reduced fibrotic tissue formation.

8. Conclusions and Further Study

- In this pilot study, it was shown that the hydrophobic coating on the implant greatly reduced the formation of scar tissue.
- These results concur with previous findings of the coating and further support its efficacy as a suitable coating for implantable devices [5].
- Future work will determine the coating effectiveness at larger timescales (3 months) in-vivo.

9. References

[1] Mardula, KL, et al. HAND. 2015;10(1):116-122.
[2] Mecwan M. M., et al; Biointerphases 2019, 14 (4), 041006.
[3] Lindsay EJ, et al. J Hand Surg Glob Online. 2022;4(1): 32-39
[4] Aithal, U. S, et al. J. Macromol. Sci. Part C Polym. Rev., 30(1): 43–105.
[5] Kaur, P, et al. University of Washington, 2022 Thesis.
[6] ISO, ISO 10993-6. 2016; 3.