Biocompatibility and Osteointegration of a Swelling Copolymeric Material for Bone Anchoring applications

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INTRODUCTION: Most conventional bone anchors are made of metals such as titanium and stainless steel with a higher modulus of elasticity than bone. This mismatch in modulus of elasticity may result in poor long-term fixation due to bone resorption. In addition, conventional bone anchors achieve their fixation to the bone using threads, and therefore, their resistance to pull-out forces is achieved by shearing the bone between the threads. Such anchors have poor fixation in low-density bone and when dislodged leave behind significant damage. To address these problems, porous swelling co-polymeric bone anchors, made of methyl methacrylate (MMA) and Acrylic Acid (AA), were introduced in the past [1]. These anchors closely match the mechanical properties of cancellous bone and achieve fixation through friction-based mechanism, an efficient fixation mechanism in low-density bone [2]. In addition, the radial stresses produced through swelling are expected to stimulate osteointegration into the porous structure of the swelling anchor. This work investigated the biocompatibility and osteointegration capability of the swelling bone anchor through an in-vitro cell study and in-vivo animal study.

METHODS: In-Vitro: The polymer resin was a combination of 80% MMA, 20% AA, and DEGDMA as the cross-linker agent. All the porous anchors were cylindrical (8mm dia.) and made of a solid core (5 mm dia.) and a porous sleeve around it. An *in-vitro* biocompatibility cell study was conducted on the porous swelling bone anchors. For this purpose, thin samples of the porous swelling copolymer (8mm dia. and 2mm length) were placed in the center of wells of different diameters (35 and 21.9 mm), and Mesenchymal stem cells (MSCs) combined with Fetal Bovine Serum (FBS) were added into each well. The cells were checked twice daily, and the media was changed four times over the period of seven days to ensure that cells had adequate room and nutrients for proliferation. Following the seven-day incubation period, microscopic images provided details of the cell's proliferation (Fig 1). In-vivo: With IACUC approval sheep were placed under general anesthesia and implants were placed into vertebral bodies of the lumbar spine (L2 to L5) in 12 sheep using a left lateral retroperitoneal transpsoatic approach under fluoroscopic guidance. For each sheep, one sample was press-fitted into each of the four vertebrae (L2 to L5). One sample was used for histology. The remaining three samples were used for mechanical testing. Two of them were swelling, and one, used as a reference, was non-swelling. All samples were 8 mm in diameter and 8 mm in length. The samples used for mechanical testing had a 2mm threaded metal rod in the center, which was used for performing pull-out tests. To date, six animals were sacrificed after 12 weeks and three after 24 weeks (Fig 2). After each sacrifice, the vertebrates were extracted, cleaned of soft tissues, and the cortical layer that covered the surface area above the implantation was removed. All vertebrae were imaged with micro-CT. Mechanical pull-out tests were then conducted on the vertebrae implanted with the mechanical samples (the one with the metal rod). The results of the mechanical pull-out tests and those obtained from the micro-CT provided data indicating biocompatibility and osteointegration.

RESULTS: In-vitro, the daily observation of the cells under a microscope (Magnification scale 4x) showed all the wells contained live and attached cells. There was no visually detectable change in the media after each observation. The small surface area in the 21.9mm diameter wells led to a high concentration of cell proliferation compared to the 35mm diameter well. The *in-vivo* results indicated that all the anchors had biocompatibility inside sheep vertebrates. Non-swelling anchors had a stable and higher fixation strength and a high level of bone ingrowth. The swelling anchors also showed levels of osteointegration, but lower fixation strength compared to non-swelling anchors (Table 1). The swelling property of the anchor created radial stresses that provided an initial friction-based fixation. For all the mechanical anchors after the pull-out test, it was observed that only solid cores were pulled out while the porous sleeves were left behind in the bone. Micro-CT image processing was conducted by thresholding the DICOM files. For all mechanical anchors, integration between the porous sleeve and the bone interface was observed.

DISUSSION: The cell study trial provided evidence of the biocompatibility of the porous anchor with stem cells. It was observed that increasing surface area allowed the cells to spread and stretch across the base of the plate. Although 35mm wells generally provide a more accurate ratio similar to implanting the material in sheep, information about the 21.9mm diameter wells is still valuable. Further to the *in-vitro* cell study results, the *in-vivo* results also indicated biocompatibility and osteointegration. For all the mechanical anchors, it was observed that solid cores were pulled out and porous sleeve remained inside the bone suggesting that due to osteointegration, the bone-implant interface was stronger than the interface between the solid core and porous sleeve of the implant. In addition to mechanical pull-out results, micro-CT results also indicated that the porous sleeve was highly integrated into the bone.

SIGNIFICANCE/CLINICAL RELEVANCE: Bone anchors such as suture anchors or interference screws made of, or augmented by the swelling co-polymeric material may provide an effective alternative to conventional anchors particularly in low density bone.

REFERENCES: 1. Siegler, S., et al., A porous swelling copolymeric material for improved implant fixation to bone. J Biomed Mater Res B Appl Biomater, 2023. 111(7): p. 1342-1350. 2. Sadighi, A., et al., Numerical analysis of the mechanical response of novel swelling bone implants in polyurethane foams. J Mech Behav Biomed Mater, 2023. 143: p. 105871.

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IMAGES AND TABLE:

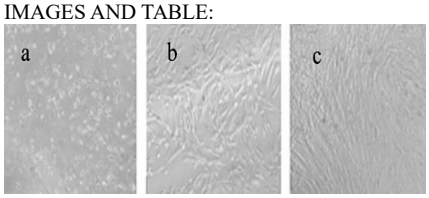

Figure 1. (a) 24hrs post sample introduction, (b) Day 7 post sample introduction in 35mm well, (c) Day 7 post sample introduction in 21.9mm well.

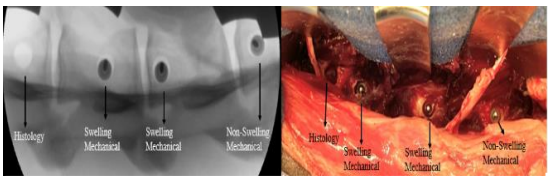

Figure 2. Implantation of the Swelling and Non-swelling bone anchors in sheep vertebrates

Type of anchor / Implant Duration	Average fixation strength (N)
Swelling mechanical \ 12 Weeks	216
Swelling mechanical \ 24 Weeks	381
Non-Swelling mechanical \ 12 Weeks	1093
Non-Swelling mechanical \ 24 Weeks	1220

Table 1. Average of the mechanical pull-out testing of the mechanical anchors with two postoperative sacrifice date of 12 and 24 weeks