The Incorporation of Tissue-promoting Alginate into ACL Interference Screws for Bone Re-growth

Katherine J. Davis, Aaron J. Huser, Cole R. Kreofsky, Dana C. Nadler, Joseph R. Poblocki
Department of Biomedical Engineering, University of Wisconsin-Madison
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Abstract

The objective of this project was to develop a novel ACL interference screw that not only secures a graft in place, but incorporates a material intended to promote bone tissue growth. This material is composed of a mineralized alginate scaffold that mimics natural matrix environment. Using this material along with the selected growth factors in an interference screw may greatly improve recovery and longevity of the graft. A potential solution has been developed that utilizes a structurally sound thermoplastic while optimizing the amount of mineralized alginate scaffold present in the screw. Preliminary work has been done testing the feasibility of the fabrication process for this type of biphasic screw using model materials. Comparative mechanical testing was completed to ensure that the structural integrity of the screw had not been compromised by the addition of alginate. A controlled study was performed with purely thermoplastic screws, screws containing 2% of cross-sectional area alginate pocket cutouts, and screws containing 5% of cross-sectional area alginate pocket cutouts. Experimental data suggests a maximum of 2% of cross-sectional area alginate pockets can be incorporated while still maintaining a mechanically sound screw.

1. Introduction

There are 90,000 annual ACL reconstructive surgeries worldwide. Interference screws are used during these surgeries to secure a graft in the femur and tibia. The interference (or wedge) screw is utilized to hold a replacement ligament/tendon in a drilled bone hole while tissues heal. The screws lack "heads" so they do not protrude out of the drilled hole. A hollow socket extends down the middle of the screw almost to the tip and is in the specific shape of a driver to allow torque application during surgery.

Current interference screws are comprised of either metal or a partially biodegradable polymer, however the polymer screws are growing in popularity. All screws introduce foreign materials into a patient and both metal and degradable screws have their disadvantages. The metal screws can cause lacerations to the graft, may require second surgeries for removal, and may be problematic during MRI scans of the knee. The disadvantages of the biodegradable screw are that they may fracture during the implantation or there may be adverse reactions to the material.

Most notably, current polymer screws do not promote bone re-growth, subsequently leaving voids and scarring in the tissue once the screw has fully degraded. It has been shown that, because tendon-to-bone healing occurs by bony in-growth, it is possible that healing could be improved by adding exogenous bone-growth factors (Anderson et al., 2001; Rodeo et al., 1999). A favorable means by which growth factors can be transplanted is by utilizing alginate hydrogel due to its ability to act as a biocompatible scaffold for bone cells (Alsberg et al., 2003).

A design has been created that integrates a structural thermoplastic with a bioactive alginate matrix. The purpose of this study was to examine the effects of removing various amounts of structural poly (Lactic-co-Glycolic) Acid (PLGA) to be replaced with mineralized alginate for the sake of promoting bone re-growth and minimizing scar formation. The goal was to create a screw that maximizes the alginate osteo-inductive material while still maintaining its structural integrity.

2. Methods

2.1 Design

The novelty of this design lies in its biphasic nature. Ideally, for tissue in-growth and bone formation, the interference screw would be solely comprised of mineralized alginate, however, because of the structural limitations of the alginate that would severely impair the mechanical integrity of the overall design. Therefore this design incorporates PLGA, a much stiffer, stronger screw that still exhibits degradable properties while promoting tissue growth with the presence of mineralized alginate. The PLGA copolymer that will ideally be used for this purpose will have a lactide to glycolide ratio of approximately 85:15. The large amount of lactide gives the screw mechanical strength, while the glycolide portion increases degradation rate. The ideal composition will degrade at a rate that complements the rate of bone regrowth, while still providing enough strength to secure the graft until the new bone can fully handle associated loads. Interference screws composed entirely of PLGA are mainly be replaced by fibrous and fatty tissue at the bone tunnel site once degraded (Bach *et al*., 2002), while this design would foster new bone tissue to grow onto the alginate scaffold.

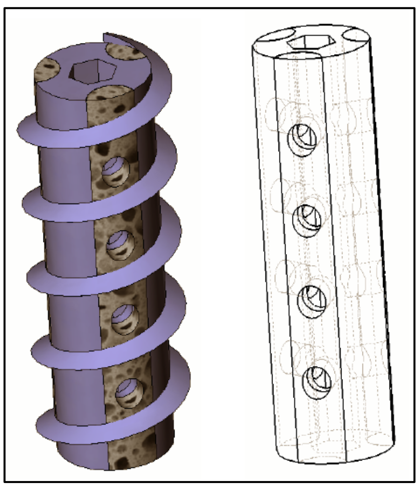

Figure 1: Schematic of the biphasic interference screw design. The thermoplastic is purple and alginate is porous grey.

To date, there is only speculative data on the strength of the mineralized alginate. With respect to the strength of the screw, the properties of the alginate are considered negligible and not added to the strength of the thermoplastic. Incorporating the weaker mineralized alginate into this design is achieved by creating axial "pockets" through the thermoplastic screw shaft (Figure 1). Three semi-circular cavities in our design are embedded in the thermoplastic, located along the circumference of the screw. This location was chosen because the alginate will be in direct contact with surrounding bone tissue between the threads, thus maximizing the alginate-tissue interface. In addition, the alginate pockets are almost completely surrounded by PLGA, and so will not have to be responsible for any direct support. Finally, these permit in-growth of the tissue to surround the plastic as degradation occurs (Hunt *et al*., 2005). Lastly, this design compliments the possibility for addition of mineralized alginate in-situ into the driver cavity. This scenario includes more osteoconductive material in the driver cavity which is usually void immediately following surgery. The growth holes between alginate pockets and driver cavity would allow better distribution of the alginate's tissue-promoting growth factors.

2.2 Biomaterials

This biphasic screw will provide structural support and bioactivity in a biological environment. The mineralized alginate portion of the screw is a made from hydrogels. The hydrogel is three-dimensional polymer scaffold and acts as a natural extra-cellular matrix (ECM); subsequently promoting cell proliferation and tissue re-growth. The pseudo-ECM, comprised of growth factors, metabolites and other materials, brings cells together and controls tissue structure with the ultimate goal of replacing the natural tissue that was lost or damaged (Lee and Mooney, 2001). Mineralized alginate is commonly used in several applications of tissue engineering. More over, mineralization holds a rigid form and thus can easily remain in the pocket design described previously.

Thermoplastics are synthesized polymers and some exhibit mechanical properties comparable to metals currently being used for interference screws. These thermoplastics, as suggested by the name, can be cast in liquid form and then allowed to cool into desired dimensions, making their possible application quite diverse. An exceptionally important feature of some thermoplastics is their ability to degrade over time under biological settings. More specifically, the resulting monomers from degradation can be removed naturally by the body.

The thermoplastic considered for the structural portion of the screw was poly(lactic co-glycolic acid) (PLGA). Depending on the makeup of enantiomers present, the mechanical properties and degradation rate of the plastic will vary. In addition, the ratio of lactic to glycolic acid also affects the mechanical properties and degradation rate of the polymer plastic. While poly(glycolic acid) (PGA) degrades faster than both poly(lactic acid) (PLA), the copolymer composition of the resulting PLGA does not have a linear relationship to the degradation rate.

Due to the high expense of PLGA, other model thermoplastics needed to be used for preliminary testing. The model material chosen was poly-caprolactone (PCL) as it exhibits similar mechanical properties to that of PLGA (Table 1) and has a low melting point for ease of screw of fabrication.

	Young's Modulus (GPa)*	**Yield Stress (MPa)**	**Maximum Shear Stress (MPa)****
PLGA	**1.4-2.8**	**41.4-55.2**	**14**
PCL	**0.21-0.34**	**20.7-34.5**	**7**

Table 1: Comparison of mechanical properties between PLGA and PCL
***Properties depend on molecular weight, crystallinity, porosity, etc.**
****Shear Stress approximated used Tresca's criterion** $\left[\tau_y \leq \frac{\sigma_y}{2}\right]$

2.3 Cost

The most influential factor of material cost will be that of the thermoplastic. PLGA is currently very expensive and the majority of the costs incurred lie here. The one time cost of the mold, alginate plug and driver amounted to less than $10. A current estimation of the mineralized alginate was not available at the time of this publication.

2.4 Fabrication

A mold for our study was fabricated from stock aluminum rodding, where a hole was drilled out and tapped to create the interference screw shape. The process of creating a model screw began by preparing a mineral oil bath as a heat source for controlled heating of the metal mold. Once the mineral oil reached 70° C, the mold, filled with PCL beads was placed in the bath. As the PCL melted and compressed, more PCL beads were added to completely fill the mold with molten PCL. Next, the driver shaft was inserted to fully displace the thermoplastic into the distal threads and create the shaft. The mold was then removed and quenched in a cold water bath. The cooled PCL product was screwed out of the mold and the shaft was removed, resulting in the finished solid screw design. The fabricated screws used for this study were 1 inch in length and 3/8 inches in diameter, which is similar in size to a surgical interference screw used in a large adult. To further create the alginate pockets, drill bits were used to bore out three equally spaced pockets on the peripheral shaft. The sum of the three pocket areas equaled either 2% or 5% of the total cross sectional area (including driver cavity area).

2.5 Experimental Design

Mechanical tests were performed to validate the screw creation technique; PCL models were used for the testing. The tests consisted of simple compression in the axial plane, simple compression in the radial plane, and insertion torque. Three different PCL screw specimens with triangular shafts were used for comparison: solid screws, screws with 2% of the cross-sectional area removed to form three alginate pockets, and screws with 5% of the cross-sectional area removed to form three alginate pockets. The pockets were not filled with alginate for the testing, because it was assumed that the mineralized alginate would add a negligible amount of structural support to the screw. Three samples of each specimen ($n = 3$) were used to perform the tests; therefore, a total of twenty-seven screws went through the various testing.

The simple axial and radial compression tests were performed on the MTS® Sintech 10/GL which consists of the two flat, circular plates: one which is stationary and holds the sample and one which applies the force in the desired plane. The data was recorded through the computer using TestWorks 4.0 (Software Research, Inc., San Francisco, CA) and saved for data analysis. Before performing the axial tests the tip of the screws were removed to allow the screws to stand upright on the compression plate. The plate slowly applied more and more force until the screw failed. The radial tests followed the axial tests. The tips of the screws were removed so that the weakest part of the screw, the body which has the driver volume removed, was subjected to the testing. The screws were laid on their sides, with their threads perpendicular to the compression plates. The plate exerted force upon the screw until the machine hit its limit, 10,000 ft·lb.

A Lo-Torq Machine® torque analysis instrument was used to perform insertion force tests. The instrument required that the object being tested must have a diameter of .25 inches and a length of at least three inches. Additionally, it was recommended that grips of the Lo-Torq Machine® not directly grasp the PCL screw because the grips would slip. Therefore, the test was performed by inserting the screw into the mold and then inserting the driver into the screw. The mold was placed into the grips and the driver was placed into a chuck, which was secured in the grips. In order to acquire the most sensitive data, the machine was set at the lowest range for torque, 500 in·lb. The test was run and the maximum torque values for each sample were recorded.

3. Results

An example of axial compressed data from each sample type can be found in Figure 2. The mean maximum axial compressive force prior to failure was 146.9 ± 5.9 ft·lb for the 0% group, 142.6 ± 4.8 ft·lb for the 2% group, and 109.1 ± 8.5 ft·lb for the 5% group as can be shown in Figure 3. There was no significant difference between the 0% group and the 2% group (P = .097); however, there was a significant difference between the 2% group and the 5% group (P = .008).

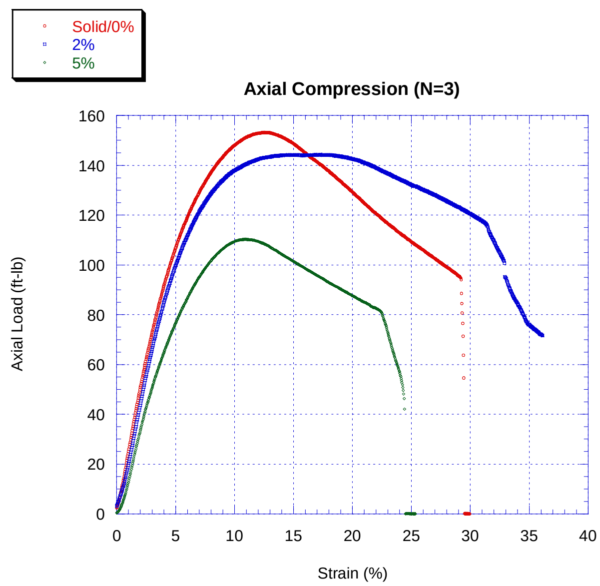

Figure 2: Axial load vs. strain testing of 0% (control), 2%, and 5% pockets-area screws.

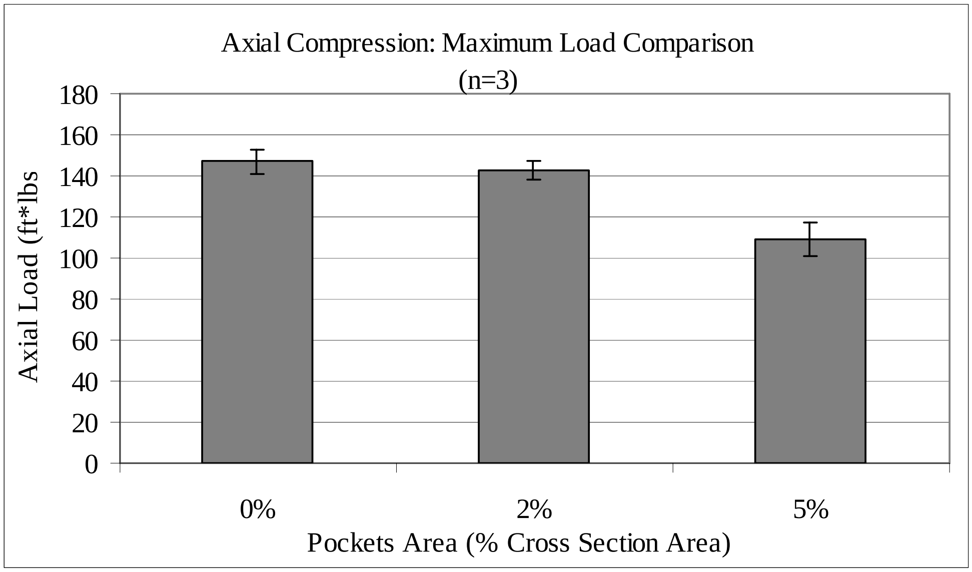

Figure 3: Axial load administered to 0% (control), 2%, and 5% pockets-area screws.

The results taken from the radial compression experiment are slightly different. Failure was defined as the point at which the hollow driver shaft collapsed. Therefore, the mean maximum radial compressive force prior to failure was 201.3 ± 13.6 ft·lb for the 0% group, 149.6 ± 17.6 ft·lb for the 2% group, and 173.4 ± 12.2 ft·lb for the 5% group as can be shown in Figure 4. There was no statistical significance between any of the groups (P = .17 and P = .12, respectively).

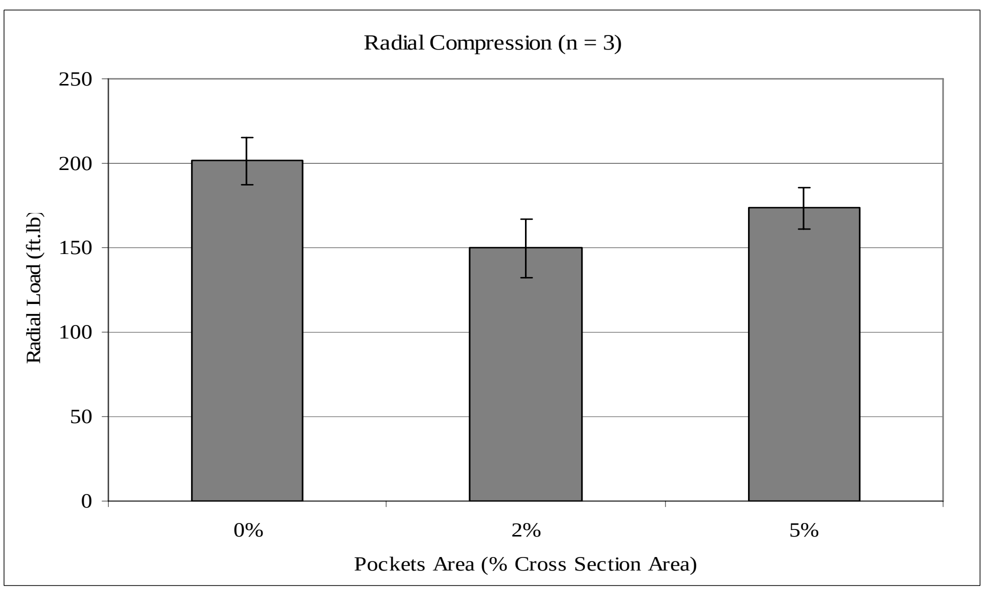

Figure 4: Radial load administered to 0% (control), 2%, and 5% pockets-area screws.

Finally, the mean maximum insertion torque prior to failure was 65.3 ± 3.8 in·lb for the 0%, 37.8 ± 2.6 in·lb for the 2% group, and 30.3 ± 16.8 in·lb for the 5% group as can be shown in Figure 5. There was a significant difference between the 0% group and the 2% group (P = .016), but no difference significant difference between the 2% and the 5% group (P = .503).

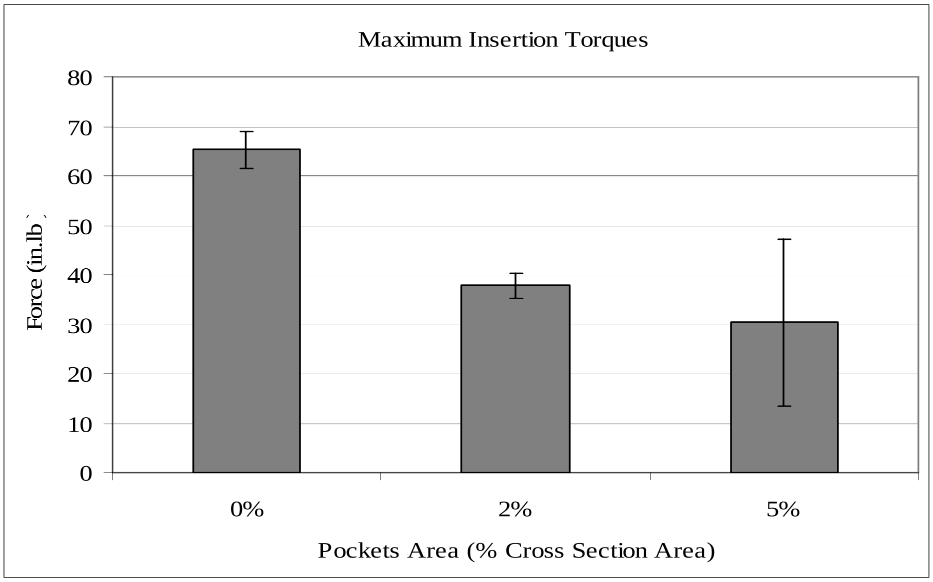

Figure 5: Maximum insertion torques of 0% (control), 2% and 5% pockets-area screws.

4. Discussion

Overall the solid screw of PCL performed the most effectively in all the mechanical testing. However, this design does not incorporate the addition of alginate and therefore is not an option. In the axial compression test, the 2% and 5% of cross-sectional area of PCL removed acted comparable to the solid screws. In the radial compression test, there was a significant difference seen between the solid screws and those with area removed. This may be caused by the placement of the alginate holes close to the perimeter and there is also a reduced cross-sectional area which increases the amount of stress acting on the screws.

Due to the ductile nature of the thermoplastic, it will first fail in shear. Thus the insertion torque analysis was deemed most important. Also, insertion torque values are reported for ACL reconstruction surgeries while values are not available for the stresses a screw experiences once inserted. A larger difference was seen between the solid screw and 2% in the insertion torque test because material was removed. Although not seen with the solid screws and 2% alginate pockets, the 5% alginate pocket screws yielded unusable inconsistent data, perhaps from the extra attachments (chuck), ill-defined failure points or user error.

The objective of this study was to develop and test a biodegradable ACL interference screw with a novel structure that allows for incorporation of mineralized alginate with growth factors. Several prototypes of the aforementioned screw designs were fabricated and tested in compression and torsion. The mechanical testing data shows that removal of material from the PCL solid screw design changes the mechanical properties. Although the differences due to alginate pockets were significant in most tests from the solid screws, they do not necessarily mean the alginate pocket designs have insufficient strength. Using PCL as a model material, it was assumed that the quantitative mechanical properties were not great enough to be safely used in ACL reconstructions. Thus, the data from PCL merely suggests trends in mechanical behavior by thermoplastic screws with similar molecular properties to PCL, such as PLGA (our final design material).

Important assumptions can be made through the use of PCL. Because of its similar mechanical properties to PLGA, the behavior of the experimental screws can be correlated to our ultimate material. It is important to note, however, that PLGA has mechanical properties an order of magnitude above those of PCL. Therefore, the results do extend to PLGA, but there could potentially be more alginate added into the final design.

The results presented in this paper indicate that pockets of bioactive mineralized alginate could be added to biodegradable interference screws without compromising the mechanical integrity of the structure. This means adding a novel component to current screw materials that would speed recovery times and better prevent re-injuries, benefiting a huge number of people every year. While these results show feasibility, an investment must now be made into further development of this design with PLGA and customized molds. This would allow for optimization of alginate incorporation as well as degradation studies.

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