Telescoping Rod with Bioactive Glass Modification

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Abstract:

We will be analyzing whether the modification of a bioglass layer to a telescoping rod for pediatric patients will improve the mechanical properties and biocompatibility of the device. A telescoping rod is an adjustable rod consisting of multiple segments that allow for lengthening or retraction of the device. These rods are typically made of stainless steel or titanium and are implanted into the bones with a corkscrew-like anchor placed into the surrounding bone to provide structural support and stabilization. This type of implant is typically used in pediatric patients diagnosed with Osteogenesis Imperfecta, a brittle bone disease that makes patients more prone to fractures. We plan to add a bioglass layer to the surface of the implant in hopes of seeing better attachment to osteoblast cells and an improvement in the mechanical stability of the device. To test these aspects, we plan on conducting a pull-out test to assess the mechanical properties and a resazurin assay to compare the biocompatibility properties of the modification.

Background and Significance:

Osteogenesis Imperfecta (OI), commonly referred to as brittle bone disease, is a connective tissue disorder characterized by fragile bones, frequent fractures, bone deformities, and growth abnormalities. OI is diagnosed in approximately 1 in every 15,000 to 20,000 births, classifying it as a relatively rare disease [1] [9]. The severity of OI can vary widely, ranging from mild cases with minimal bone deformities and mild fragility of the bones to severe cases with life-threatening deformities and multiple fractures [2]. Primarily affecting pediatric patients, this condition requires frequent medical interventions to manage fractures and associated complications. Treating pediatric patients presents a unique challenge due to the continuous growth of their bones. Traditional treatment methods involve the use of telescoping rods, typically made of stainless steel or titanium, which provides structural support and stabilization to the bone. [6]

The primary function of the telescoping rod is to minimize the need for revision surgeries by adapting and growing alongside the patient's bones [6]. The rod consists of a male and female component that lengthens with the growth of the bone. Each component contains a corkscrew style nail at the end, which is attached to the proximal and distal epiphysis respectively. While the concept of a telescoping rod is inherently functional, several complications have been found such as migration, failure to telescope, rod fractures, growth plate lesions, rod bending, rotational issues, and infections [3]. Among the most common complications is the nail fixation component

of the rod migrating into surrounding muscles and tissues or failing to grow with the patient's growth. Surgeons suggest that improving the locking component of the telescopic implant is crucial to prevent potential migration of the nail from the bone [4]. The interface between the implant and the bone can sometimes lead to complications such as poor integration, mechanical failure, or infection. These complications require additional surgeries and medical intervention that could pose additional health risks to the patients.

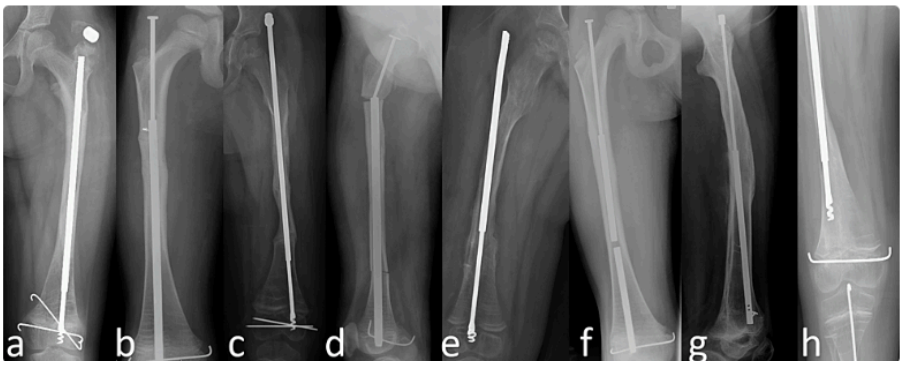

Figure 1: Complications seen in telescopic implant group. [5]

(a) Dislocation of the proximal locking screw; (b-c) migration into the abductor muscles; (d) fracture of the obturator part of the nail; (e) nail extraosseous; (f) fracture of the sleeve part of the nail; (g) limited telescoping of the implant with the locking hole system with K-wire; (h) limited telescoping of the corkscrew-tipped implant

Our research aims to address these challenges by modifying the surface of these telescoping rods with a bioactive glass layer. By incorporating a bioactive glass layer, we aim to enhance integration of the rod with the bone, leading to improved mechanical properties and stability of the device [7]. Enhancing the mechanical properties and biocompatibility of the telescoping rod provides significant benefits to many pediatric patients diagnosed with OI. Improved rod integration and stability could reduce the frequency of fractures, decrease the need for revision surgeries, and improve overall patient outcomes. Although our proposed modification does not provide any immediate cost savings, better integration and more stable implants could result in long-term cost savings by reducing the need for multiple surgeries and repeated hospital visits.

Innovation:

Our proposed design is to introduce a bioactive glass coating to the telescoping rod in hopes of seeing little to no migration of the rod from structural bone supports. Bioactive glass has been shown to enhance protein adsorption to the surface of a material with surrounding bone

cells [13] and is already FDA-approved so it is not a new technology. However, the addition of bioactive glass to a telescoping rod has not been performed yet. There have been studies using this compound on other orthopedic bone anchoring implants, that we could see similar results to.

A current issue with telescoping rods is they are commonly used in already brittle bones that are prone to fracturing, which already makes implants more susceptible to migration from the host tissue [14]. While the telescoping rod does provide greater structural support and the prevention of fractures, the long term stability of the device could still be improved. If the telescoping rod had better protein adsorption and tissue integration with the bone cells this would theoretically improve the mechanical stability of the device. However, there is the possibility that this added bioactive glass coating could result in protein adsorption to surrounding tissues more so than surrounding bone, which would be a mechanical mismatch and could have negative effects.

Approach:

Specific Aim 1: *We will assess whether our telescoping rod will have improved mechanical properties due to tissue integration in comparison to the control. We will perform a pull-out test to test how much tensile force the tissue integration can withstand before it disconnects from the connection site.*

Hypothesis 1: Our telescoping rod will have increased strength, toughness, and yield strength compared to controls.

Methods:

We hypothesize that the rod with the bioglass implant on it will have increased tissue integration compared to the rod without the bioglass. Increased tissue integration means that the rod will be more stable in its position and therefore less likely to shift, fracture, or fail [7]. This is extremely important when dealing with orthopedic implants because they are exposed to significant loads and are therefore susceptible to failure. This hypothesis can be tested using in-vivo testing using the bone implant with and without the bioglass. We would then perform a pull-out test on the implant to determine how much force would be required to displace the rod from its original position.

Pull-out tests determine the amount of force required to disconnect a fully integrated implant from its connection point. We will perform this test on the rod both with and without the bioglass to determine if the bioglass shows a significant increase in the strength of the

connection between the implant and connective tissues. The point of the bioglass is to promote tissue integration and increase the mechanical properties and stability of the connection point [7], so we are expecting to see a significant increase in the disconnection force. One study performed pull-out testing to analyze the biomechanical property differences between degradable calcium alloy and standard stainless steel screws. The study was done using 40 adult rabbits implanted with 48 alloy screws and 32 stainless steel screws in the tibiae with follow-ups at two, four, six, and eight weeks [12]. In this case, the pull-out testing was done at different time intervals because one screw is biodegradable, which would not be necessary for our device modification. However, even though our device is a telescoping rod and not a screw, our test could be modeled similarly in order to test the tissue integration strength of our modified device.

In order to model it as closely to humans as possible, we will conduct in-vivo animal testing and would want to choose an animal that closely mimics the performance in a human body. Larger animals such as a sheep, pig, or dog are preferable due to their similar bone size and density to humans. Research shows that dogs and pigs most closely mimic human bone density, while sheep are typically suitable for senile osteoporosis studies [10]. Since puppies have similar bone densities to humans and mimic growth that would be seen in adolescents we concluded that this would be the best animal to use[10]. One study performed testing on twelve puppies, analyzing the results for hydroxyapatite coated(HA) telescoping rods, which is very similar to our modification [8]. We propose to use twelve puppies - six being tested with the standard telescoping rod, and six being tested with the bioglass coated rod. Each group will include three males and three females of the same breed, with the rod implanted in the back left leg. We will allow six weeks after implantation for proper healing and tissue integration before conducting a pull-out test. The puppies will receive sedation and pain medication during the healing process and will be humanely euthanized intravenously after the study to minimize suffering [15].

Results:

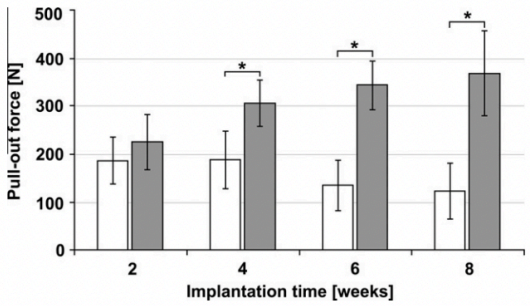

Figure 2: Pull-out testing results [12]

Mean peak pull-out force of standard stainless steel(white bars) and bioglass coated(grey bars) rods and standard deviation at different implantation periods. (* indicates a significant difference $P<0.05$)

The tensile force to extract the modified rod would exceed that needed for the original rod, however our results would only be done at six weeks and not the other implantation times. There is a potential risk for bone fractures due to such strong tissue integration, which is especially important to avoid since the purpose of a telescoping rod is to prevent fractures during growth.

Discussion:

Using animals to test orthopedic implants is difficult because there will always be a difference in bone density, body mass, and bone quality. There is also no animal that perfectly models human bone, so results seen in animal testing may not be comparable to results in human testing [11]. Additionally, there is the possibility that using a coating could stunt the growth of the bone containing the implant [8]. Whatever the results may be, it is important to know that the results would still be different in humans because our physiology is different, and there would most likely be a greater bone density difference because OI deals with brittle bones.

Specific Aim 2: *We will assess the cell viability of the bioglass by observing the reduction of resazurin and resorufin. We will perform a resazurin assay to compare the bioglass with human osteoblasts against controls.*

Hypothesis 2: The bioglass will present as non toxic to the osteoblasts and therefore be compatible with its environment when implanted.

Methods:

Cytotoxicity is key in the evaluation of whether the material is toxic to cells in the body and is observed via in vitro testing. Our hypothesis is that the bioglass will be non toxic to osteoblasts and will not induce cytotoxicity. This hypothesis will be tested by measuring the cell viability through observing the reduction of resazurin. The bioactive glass will be tested with human osteoblasts (bone-forming cells) which is essential in orthopedic applications. Various assays can be used to measure the viability of the cells but one of the most common is the Resazurin Assay. These biological tests will be performed adhering to ISO 10993. Culture mediums with bioglass particles will be added to the osteoblast cells cultured Dulbecco's modified Eagle's medium. After the incubation period, the medium will be removed and replaced with a new culture medium and resazurin, then incubated for 24 hours at 37 °C. A color change from the original blue to red will indicate the presence of healthy, active osteoblasts. Resazurin solution is a

non-toxic, blue dye that is added to the culture medium. Viable cells will convert it to resorufin which presents as a pink die, and the amount of living cells in each test can be compared based on the brightness of its color. This test allows for real-time observations of the cells' interaction with the materials [11]. ALP tests measure the enzyme alkaline phosphatase, which is produced by osteoblasts to indicate healthy activity. After the cells undergo testing conditions, the presence of ALP will be measured using the BCIP/NBT assay.

Results:

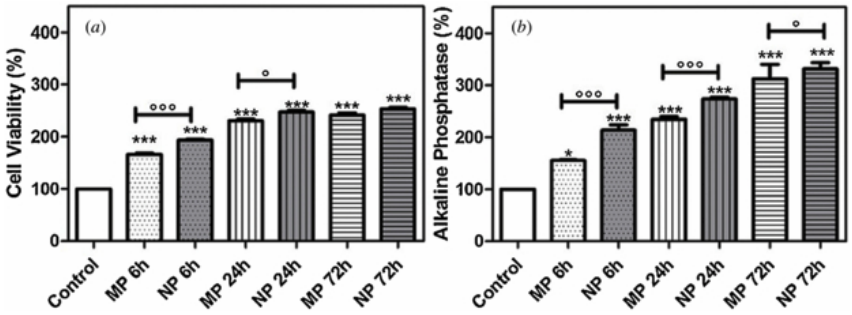

Figure 3: Cell Viability and ALP Activity Results. [11]

(a) Cell Viability and (b) ALP activity of BGMP and BGNP after 6, 24, and 72 hours of culture measured by resazurin assay. (*) Symbolizes notable differences to the control and (°) symbolizes notable differences between MP and NP at a significance level of 0.05%.

The resazurin assay showed a higher mitochondrial osteoblast viability for both bioactive glass micro and nano particles compared to the control by showing cell viability percentage versus time, thus both forms of bioactive glass particles are biocompatible. Additionally the ATP testing showed alkaline phosphatase presence in the culture cells by showing increased ATP percentage over time [11].

Discussion:

For orthopedic implants, tissue integration is key for successful patient outcomes. Good tissue integration will help prevent foreign body response complications after implantation. The material's biocompatibility determines whether or not it will integrate with the tissue. From the results of this experiment, we have reason to believe that the bio active glass will support tissue integration and have decreased risk for foreign body response after implantation, which is hopeful for post-operative outcomes.

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