OsteoInk: Bioactive Bone Cements

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Statement of Purpose: Acrylic bone cements are used in a variety of orthopedic applications including vertebral decompression and implant augmentation. Acrylic cements are made of poly-methyl methacrylate (PMMA). However, they are bioinert with no ability to integrate with bone. Calcium phosphate (CaP) cements are used as bone void fillers because they can degrade and the residue can be used to create new bone in-vivo. However, simply mixing CaP into an acrylic cement paste at the time of surgery results in poor injectability and unsuitable mechanical strength for orthopedic applications [1]. Many acrylic cements can also contain an antibiotic mixed in the formulation. Our aim was to create a system that combines the mechanical strength of acrylic bone cements with the bioactive and resorptive nature of CaP and the prophylaxis of antibiotics. We achieved this by creating a two solution system and tuning the ratios of components in the material.

Methods: Two solution bone cements (TSBCs) are used by mixing two solutions together. Each solution contains the same amounts of polymer (PMMA), monomer (methyl methacrylate), and CaP. One solution contains the initiator of polymerization, benzoyl peroxide (BPO), and the other solution contains the activator of initiation, N,N-dimethyl p-toluidine (DMPT). The ratios of powder to liquid and PMMA to CaP were varied to determine formulations that exhibited useful characteristics for various surgical applications. Each solution was added to one chamber of a double-barrel cartridge and extruded through a static mixing nozzle when used. Mechanical, rheological, and injectability tests were performed to assess our material's characteristics. Toxicity studies were performed using ISO standards 10993-5 and 10993-12 with MC3T3-E1 cells. Bacterial proliferation assays and zone of inhibition testing were performed to assess the antibacterial efficacy of the cements.

Results: It was found that adding CaP to TSBC lowered the compressive strength a statistically significant amount in all samples above a concentration of 10% by mass of CaP (90 MPa in the control to around 70 MPa in the sample with the highest amount of CaP (40% by mass)). However, the mechanical strength of the cement is still above the ASTM standard of 70 MPa. Rheological results showed that CaP slightly increased the complex viscosity of TSBC by a significant amount at all concentrations and frequencies tested. Injectability tests demonstrated that high concentrations of powder in conjunction with high CaP content resulted in demixing and clumping, as expected. Toxicity studies indicated slight toxicity (grade 1) and over 70% cell viability. It was found that both chlorhexidine and chlorhexidine diacetate (antimicrobial compound) at concentrations above 2% were able to prevent bacterial proliferation by a minimum of 5 hours. A zone of inhibition up to 3mm was observed in cements with antimicrobials.

Conclusions: Our study showed that it is possible to combine an acrylic, calcium phosphate, and antimicrobial phase into one cement. The porosity created by the CaP phase allows for enhanced dispersion of the antimicrobial. Eventually, bone will grow into these pores and be supported by the remaining acrylic matrix. Making these additions while retaining suitable mechanical properties is possible due to the premixed nature of our two solution system. Since the solutions are premixed, the CaP, antimicrobials, and other additives have time to disperse within the acrylic matrix while it continues to swell. We also found that we can create cements with a range of properties including prophylaxis, degradability, and viscosity.

Technology: Our product portfolio consists of a range of two-solution bone cements including cements with antibiotics, contrast agents, and calcium phosphate, which come in regular, high, and low viscosities. The range of cements offered is wide enough to meet the needs of various orthopedic and restorative/plastic surgeries, but focused enough to be economically feasible. We will apply for a 510(K) based on our material's substantial equivalence to other Food & Drug Administration (FDA) approved devices and the results from our cellular toxicity studies and the animal studies that are currently being performed. Our technology is protected by a patent of which the founders of OsteoInk are the inventors. We also offer a metered dose injection system which removes operator variability during delivery.

Market: Millennium Research Group (MRG), a global authority on market intelligence for medical technology, predicts the global bone cement market to grow to over $700 million by 2016. Brazil, India, and China lead the growth due to their growing middle classes' increased access to healthcare. Reports to be published in the next year by Mayo Clinic will demonstrate the un-debatable efficacy of the usage of bone cement in hip arthroplasties versus increasingly popular press-fit procedures. Due to the reputation of the source, this will increase market growth and ultimately sales.

Commercialization Strategy: After Premarket Approval, manufacturing and sterilization will be outsourced to an appropriately certified business. Conferences which orthopedic and restorative/plastic surgeons attend serve as an excellent venue to market the product and the products will be purchased through the hospitals where they work. We are seeking an initial investment of $500,000. Based on an initial 0.1% market penetration (approximately 500 units sold the first year, with units selling at an average of $300 based on content), we will break even after 3 years. However, before year 3 we will seek further investment for increased manufacturing and marketing. We predict that as surgeons use and recommend our material, our market penetration will increase as seen with other brands. We are receptive to licensing the technology as a supplemental revenue source with the intent that the partnership(s) developed through such agreements will facilitate our eventual exit.

References: [1] Ryu, KS, et al. World Neurosurg 2010;73:408-411