Bioactive Glass-Collagen Scaffolds for Treating Infected Bone

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Statement of Purpose: Traumatic bone fractures, such as those sustained on a battlefield, often produce open wounds that become infected. During the course of the infection, bone tissue is destroyed. These infections can be especially difficult to clear and may require local antibiotic therapy[1]. Poly(methylmethacrylate) has historically been used to deliver antibiotics to bone. However, this material does not encourage regrowth of bone and must be surgically removed. Therefore, there is a need for a material which both delivers antibiotics and can regenerate bone tissue.

To meet this need, microspheres have been created that are composed of a bioactive glass. These microspheres are loaded with antibiotics to mitigate the infection. The microspheres are subsequently loaded into cross-linked collagen gels. The bioactive glass-collagen composite is a material that can be applied at the site of a seriously infected bone wound. The purpose of this study is to demonstrate that these materials inhibit bacterial growth and encourage the growth of bone marrow-derived stem cells (MSCs).

Methods: A sol-gel method is used to create the bioactive glass. This low-temperature process has previously been shown to effectively encapsulate of antibiotics such as vancomycin in a glassy matrix[2-4]. A water-in-oil emulsion process is used to create vancomycin-loaded microspheres[5]. The effectiveness of the eluted drug was tested against *Staphylococcus aureus* (ATCC #25923). The microspheres were mixed with a collagen solution (Advanced Biomatrix) and crosslinked using carbodiimide. The time to gelation, adhesiveness, and mechanical properties of the glass-collagen composite were quantified dynamically with a Stable Microsystems TA.XT*Plus* Texture Analyzer. Primary MSCs were collected from canine cadavers and grown on the bioactive glass-collagen composites.

Results: Microspheres prepared by this method are polydisperse and have diameters ranging from approximately 1-50 µm (Fig. 1A). SEM micrographs show that these particles often have a core-shell morphology (Fig 1B). The shell consists of the bioactive glass, while the core contains poly(n-vinylpyrrolidone), a template used during microsphere synthesis (Fig. 1 C-E). The elution of vancomycin from these microspheres was shown to inhibit *S. aureus* for up to 5 days *in vitro* (Fig. 1F). The microspheres were loaded into a collagen solution, which could be gelled within 5 minutes using a carbodiimide crosslinking agent. Additionally, these gels demonstrated adhesion to the acrylic probe of the texture analyzer. MSCs proliferated on gels both with and without bioactive glass microspheres.

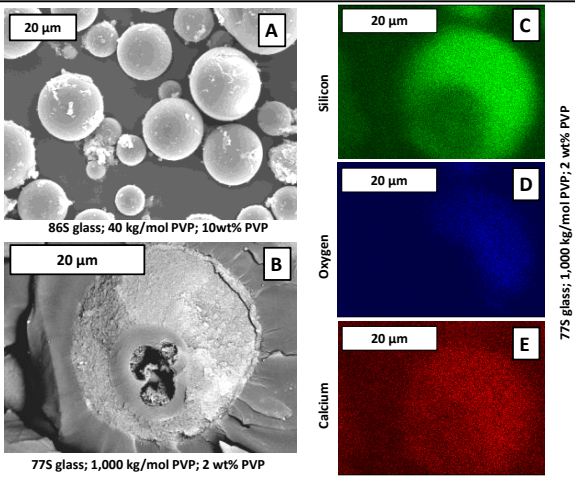

Figure 1. (A) Scanning electron micrographs (secondary electron signal) of bioactive glass microspheres. (B) Backscattered electron micrograph of cross-section of a microsphere, demonstrating hollow morphology. Elemental maps of the microsphere show that it contains the elements of bioactive glass, silicon (C), oxygen (D), and calcium (E)

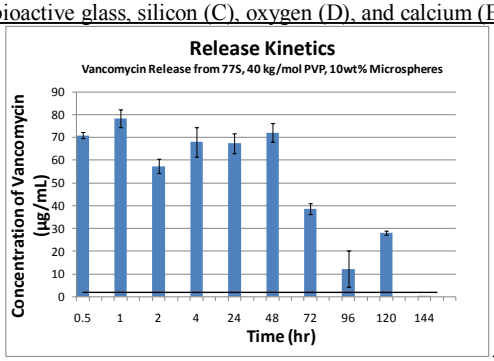

Fig. 2 A zone of inhibition study shows that vancomycin released from microspheres inhibits *S. aureus* for up to 5 days.

Conclusions: This study demonstrates that bioactive glass-collagen composites can be used to deliver antibiotics and encourage growth of MSCs. These materials can be used to treat infected wounds while providing a surface for bone regeneration.

References:

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