Semi-resorbable PMMA-Brushite composite bone cement for spinal augmentation

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Statement of Purpose: Spinal augmentation techniques including Kyphoplasty and Vertebroplasty have come under much scrutiny, due to the mixed results in the literature. One main complication often reported is extravasation of the bone cement resulting in pulmonary embolism formation. We have synthesized a highly viscous, pre-mixed osteoconductive composite bone cement with desirable rheological properties to reduce the chance of extravasation, and increased versatility to accommodate calcium phosphate (CaP) fillers. The goal of this innovative approach is to introduce bioactivity to the bone cement enhancing integration with cancellous bone for successful augmentation of fractured vertebrae. A Brushite-PMMA composite cement is envisioned as a semi-resorbable material which can augment the fractured vertebrae and provide a scaffold for bone regeneration.

Methods: *Synthesis:* The composite two-solution cement was prepared using protocols defined in previous studies [1]. The 1.65:1 (powder:liquid) Brushite cement was selected as the most suitable for spinal augmentation. [2] *Resorption:* Mass-loss experiments were performed in order to study the Brushite release over time and track developed porosity. The cement samples were placed in Hank's simulated salt solution at 37°C with continuous shaking. Samples were dried prior to weighing at the different time points. Microscopy (Keyence VHX) was used to visualize the pores. *Mechanical Testing:* Mechanical tests (MTS Bionix) were performed per ASTM standards before and after immersion, the duration was derived from the mass-loss tests. [3] The tests included compression, flexural, and fracture toughness experiments. *Cell Studies:* Following ISO standards, cell viability was addressed. [4] Toxicity and cell differentiation were studied via direct contact with the cement. MC3T3-E1 mouse pre-osteoblast fibroblasts were used. Alkaline phosphatase (ALP) assay was used to stain for osteoblast differentiation.

Results: *Resorption:* The results showed a mass-loss plateau of 65% for the Brushite cement within 2 weeks. The pure acrylic cement had a 17% decrease in mass. Pore formation is clearly seen in Figure 1 (left). Pore sizes reached up to 750 microns. *Mechanical Testing:* The cement strength was retained after the 2 week immersion with the values shown in Table 1. *Cell Studies:* The cells were 91% viable after direct contact with the cement. Cell differentiation was also found not to be hindered by the cement. Fig 1 (middle) shows the 6-well plate stained for ALP activity which is indicative of osteoblast differentiation.

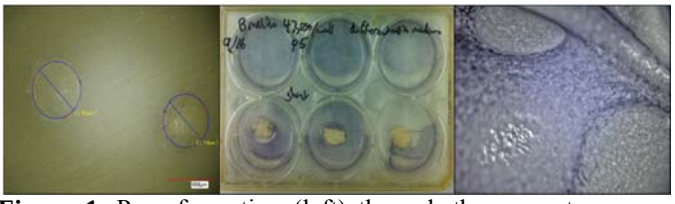

Figure 1. Pore formation (left) through the cement can create a scaffold to promote bone growth. Cell differentiation (middle) was viable after contact with the cement. (right)

Table 1 Mechanical tests showed the Brushite cement retained its strength post-immersion.

Brushite Cement	Before Immersion	After Immersion
Compressive Strength σ_c (MPa)	75.6 ± 3.0	101.1 ± 4.5
Compressive modulus E_c (GPa)	1.8 ± 0.3	2.6 ± 0.2
Flexural Strength σ_f (MPa)	60.1 ± 1.9	45.3 ± 3.4
Flexural Modulus E_f (GPa)	3.3 ± 0.2	2.1 ± 0.1
Strain to Failure ε_f (%)	3.0 ± 1.2	2.4 ± 0.3
Fracture toughness K_{IC} ($MPam^{0.5}$)	1.4 ± 0.1	1.3 ± 0.1

Conclusions: The Brushite cement was found to be stable post-resorption even with the presence of pores. Within 2 weeks the cement can be able to accommodate cells as it forms a scaffold for bone growth. The calcium and phosphate from the Brushite can enhance osteoblast activity. The tests showed no toxic effects due to residual monomer and cell differentiation was sustained. These novel cements were designed to allow for better bone interdigitation and integration within the cement. The Brushite cement shows potential for use in regenerative applications where the remaining PMMA scaffold will provide strength as the Brushite is resorbed. The Brushite cement will be studied with micro-CT to visualize bulk porosity, and future studies can incorporate cell cultures with mechanical testing.

References:

[1] Hasenwinkel JM, *J Biomed Mater Res* 47(1):36-45.
[2] Aghyarian S., et al., *J Biomat App 29: 688*
[3] ASTM F451-99a. 2007. West Conshohocken PA.
[4] ISO 10993-5:2009