Osteoconductive Bone Cements 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. A highly viscous, pre-mixed osteoconductive two-solution composite bone cement was synthesized that shows desirable rheological properties to reduce the chance of extravasation, and increased versatility to accommodate calcium phosphate (CaP) fillers. CaP fillers such as Hydroxyapatite, and Brushite have previously shown to detrimentally affect cement performance [1], however the developed composite cement can incorporate these 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. The two solution cement fully incorporates introduced fillers into the cement matrix due to the increased time it spends in the swelling phase.

Methods: *Synthesis:* The composite two-solution cement was prepared using protocols defined in previous studies [2]. The cement was studied with filler added formulations of 25/50% (wt/polymer wt) hydroxyapatite (HA), and 25/50% brushite. 10% Zirconium Oxide (ZrO_2) was added for radio-opacity. The different powder-to-liquid ratios are shown in Table 1. *Rheology:* Tests were performed using a Discovery HR-3 dynamic rheometer (TA Instruments, New Castle, DE). 0.5 mL of the cement was placed on 25 mm parallel plates with a geometry gap of 1000 +/- 300 µm. Strain sweeps were performed to detect the linear viscoelastic region. Frequency sweeps were performed from 100-0.1 Hz at 24 ^{o}C. *Contrast:* Cement was imaged with X-ray at 70 kV. *Mechanical Testing:* Compression testing was performed per ASTM standards [3]. 12x6 mm cylinders were prepared with the cements and loaded at 20 mm/min. The ultimate compressive strength was recorded. *Injectability:* Using custom-designed tools to deliver the cement simulating instrumentation employed in VP/KP, injection times were recorded for a 5mL volume of the composite cements.

Results: The results showed complete incorporation of the fillers in the cement. The cement properties were not deteriorated by the CaP fillers. *Rheology:* The presence of 25% filler caused an average increase of 4357.10 Pa.s at low shear, 307.83 Pa.s at medium, and 30.79 at high shear. 50 % filler had an average increase of 7077.87 Pa.s at low shear, 504.6 Pa.s at medium, and 51.04 at high shear. *Contrast:* Addition of 10% ZrO_2 significantly increased the contrast of the cements by an average optical density of 0.15. The fillers had no significant effect on contrast. *Mechanical Testing:* The cement strength increased with the addition of ZrO_2 and filler from 70MPa in cement with no filler to an average of 79MPa. *Injectability:* The injection times ranged from 3-9 minutes for the cements investigated.

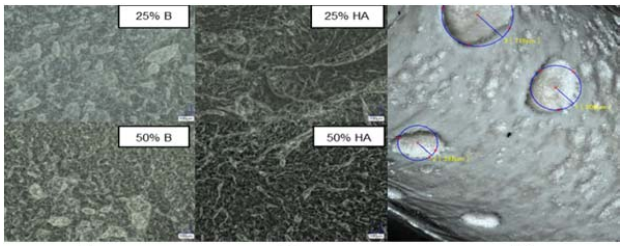

Figure 1. Two-solution composite bone cement with HA (B) and Brushite (A). The bioresorption of Brushite cement will lead to pore formation (C) and bone regeneration leaving the remaining acrylic scaffold for mechanical support.

Table 1. Static compressive tests showed no deterioration of the properties, but an increase in compressive strength with filler addition. Powder to liquid ratios (P:L) with the powder phase (P) further divided in PMMA:CaP.

Powder (P): liquid (L) ratio	PMMA: CaP	Compressive Strength (MPa)
0.9:1	N/A	80.9
1.2:1	4 (Brushite)	70.3
1.2:1	4 (HA)	83.9
1.4:1	2 (Brushite)	82.9
1.4:1	2 (HA)	84.7

Conclusions: CaP fillers were successfully introduced in the composite cements resulting in no detrimental effects on the material properties investigated. These novel cements were designed to allow for better bone interdigitation and integration within the cement. Also, these pre-mixed cements show desirable rheological properties showing shear-thinning for improved injectability and reduced risk of extravasation during injection. The versatility of the cement is a product of the increased time it is held in its swelling state. This allows for the complete integration of the filler into the cement matrix. The cement can be tailored to suit the application's requirement whether it is resorbability and interdigitation (Brushite cements) or increased bone growth (Hydroxyapatite cement). The brushite cements show potential for use in regenerative applications where the PMMA scaffold will provide strength as the brushite is resorbed. The composite cements will be studied for brushite degradation and tested in a porcine vertebroplasty model in future studies in order to assess efficiency of fracture augmentation.

References:

[1] Ishiguro S., J Orthop Surg 2010;18:346-351.
[2] Hasenwinkel JM, *J Biomed Mater Res* 47(1):36-45.
[3] ASTM F451-99a. 2007. West Conshohocken PA.