Injectable, Bioactive Two-solution Bone Cements (η-TSBC) with Strontium Substituted Hydroxyapatite Microspheres

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Statement of Purpose: We have developed two-solution bone cement containing cross-linked polymethylmethacrylate (PMMA) nanospheres (η-TSBC) for the applications of vertebroplasty and kyphoplasty [1]. However, PMMA bone cements lack the ability to form chemical bonds with the living bone tissue. Lately, focus has been on developing bioactive cements using hydroxyapatite (HA) and strontium as filler materials, since HA is a natural bone mineral component and strontium is known to stimulate bone formation and acts as a good contrast agent [2]. In this study, bioactivity of η-TSBC containing strontium-calcium hydroxyapatite (SrCaHa, 50% strontium substitution) and strontium hydroxyapatite (SrHA, 100% strontium substitution) microspheres was investigated *in vitro* by evaluation of their apatite forming ability in simulated body fluid (SBF).

Methods: The η-TSBCs were prepared as described by Rodrigues et al. [1] at a polymer to monomer ratio of 1:1 and cross-linked PMMA nanospheres to linear PMMA ratio of 1.5:1. The SrHA and SrCaHa microspheres (2-5 μm in diameter) were synthesized as described by Zhang et al. [3] and added to the polymer phase at concentrations of 0 (controls), 10, 20, and 30% w/v. Three half inch square samples of 1 mm thickness were prepared per cement composition. SBF was prepared as described by Kokubo et al.[4] and all of the cement samples were immersed in SBF for a period of 4 weeks at 37°C (pH 7.4). Scanning electron microscopy (SEM) was used to evaluate apatite formation on the sample surface before and after immersion in SBF, while energy dispersive x-ray (EDX) and fourier transform infrared spectroscopy (FTIR) was used to determine the composition of apatite formed. The thickness of apatite layer was measured from the SEM micrographs using the ImageJ software by NIH.

Results: The bioactivity of η-TSBC was evaluated based on its ability to form apatite when immersed in SBF for a period of 4 weeks. Figure 1(a) shows the SEM micrographs and EDX spectra of the 0, 10, 20 and 30% SrCaHa samples before being immersed in SBF. The EDX spectra show the presence of primarily carbon and oxygen peaks (Figure 1(b)), as expected, since the cement surface primarily consists of PMMA. After being soaked in SBF for 4 weeks the control cements did not show any surface apatite formation as seen from Figure 1(a,b), indicating the lack of bioactivity. However, the 10, 20, and 30% SrCaHa containing η-TSBCs showed apatite formation after 4 weeks in SBF. The EDX spectra of 10, 20 and 30% SrCaHa cements also showed presence of calcium and phosphorus peaks, along with an increase in oxygen atomic percentage indicating formation of calcium phosphate (hydroxyapatite, Figure 1(a, b)). No significant differences were observed in the atomic percentage of calcium, phosphorus and oxygen between the three compositions of SrCaHa cement. The FTIR spectra of the apatite layers formed on 10, 20, and 30% SrCaHa cements, Figure 1(c), also showed presence of the 1080 cm^{-1} peak belonging to the P-O stretch and the bands in the region of 490 to 630 cm^{-1} belonging to the O-P-O bend, confirming the presence of phosphate groups. A decrease in apatite thickness with increasing SrCaHa concentration was observed (Figure 1(d)). A similar set of experiments were performed on the cements containing 10, 20, and 30% SrHA microspheres, and the preliminary results indicate formation of apatite on those surfaces as well, indicating that inclusion of both types of microspheres does impart bioactive properties to η-TSBC.

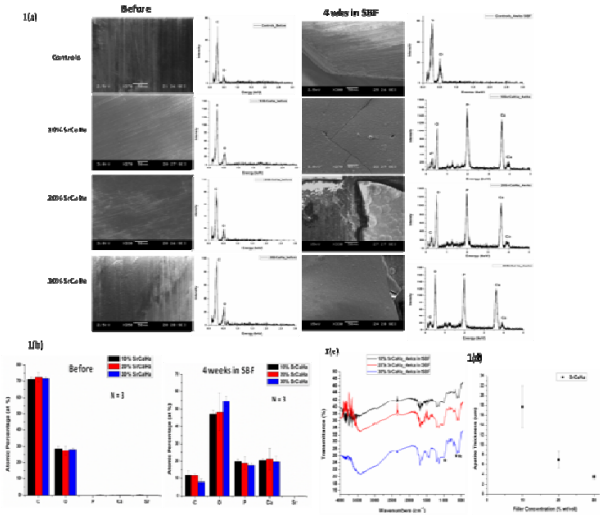

Figure 1. (a) SEM micrographs and EDX spectra of 0, 10, 20, and 30% SrCaHa cement samples before and after 4 weeks submersion in SBF. All compositions show apatite formation after 4 weeks in SBF. (b) The elemental content analysis from the EDX spectra of all SrCaHa cement compositions before and after 4 weeks submersion in SBF, showing presence of calcium and phosphate after immersion in SBF. (c) FTIR spectra of the apatite layer formed on 10, 20, and 30% SrCaHa samples showing presence of a peak at 1080 cm^{-1} and bands in the region of 490 to 630 cm^{-1} belonging to the phosphate group. (d) Graphical representation of the apatite layer thickness as a function of the SrCaHa concentration.

Conclusions: This work demonstrated that addition of SrCaHa or SrHA microspheres to η-TSBCs improved bioactivity in comparison to the control cements. Apatite formation was observed on all of the cement compositions. Future work encompasses determination of the mechanism behind the formation of apatite by cements containing SrHA and SrCaH microspheres and whether the mechanism of apatite formation affects the apatite thickness.

References: 1) Rodrigues D.B.C. et. al., *JBMR-B*, 2009; 92B:13-23. 2) Hernandez L.et.al., *J.Mater Sci: Mater.Med*, 2009; 20: 89-97. 3) Zhang C. et. al., *Langmuir*, 2009; 25:13591-13598. 4) Kokubo T., Takadama H., *Biomaterials*, 2006; 27:2907-2915.