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A Novel Biodegradable Injectable Polycaprolactone-Magnesium Composite for Vertebral Fracture Fixation

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Introduction:
Currently developed bone substitutes such as calcium-based bone cements have tried to overcome the clinical complications found in PMMA cement augmentation for osteoporotic spinal fracture¹. However, their undesired mechanical properties potentially jeopardize surgical outcomes including adjacent level fracture². To serve as an ideal bone substitute, it should be biocompatible, resorbable, osteoconductive and osteoinductive³. Hence, our group has fabricated a novel bone substitute comprised of polycaprolactone (PCL) and magnesium (Mg) with a wide range of compressive moduli and enhanced osteoblastic activity for vertebral cement augmentation. This study aims to report the mechanical characterizations, in-vitro and in-vivo properties of the new bone substitutes.

Methodology:
The new bone substitutes were prepared by incorporating 150µm silane-treated Mg particles to PCL in the ratios of 0.1:1 and 0.6:1, respectively. A 7-day simulated body fluid (SBF) immersion test was conducted to test the bioactivity of the new bone substitutes by viewing under scanning electron microscopy (SEM) and the surface composition was checked by using energy dispersive x-ray spectroscopy (EDS). Their mechanical properties were then evaluated by compression test prior SBF immersion and a 2-month SBF immersion so as to gauge the mechanical properties of the composites upon degradation. The cytocompatibility was studied by direct cell culture using green fluorescent protein osteoblast and MTT assay using pre-osteoblasts MC3T3-E1, and the osteoblastic differentiation property was measured by ALP assay using MC3T3-E1 as well. The in-vivo response was evaluated by rat model for 2 months. The animals were monitored and examined by Micro-CT at respective time points. Commercial PMMA and pure PCL were served as the controls.

Results:
After 7 days of SBF immersion, calcium and phosphate deposition was detected on the hybrids rather than the control. The pre-degraded compressive moduli of the composites with 0.1g and 0.6g Mg were 37% and 190% higher than that of PCL, respectively (Figure 1). Furthermore, they were about 4-fold and 1-fold lower than that of PMMA. After 2 months of degradation, the compressive moduli of all the composites could be maintained (Figure 2). It indicates that the mechanical properties of new composites will not minimize during first 2 months of immersion. The cell viabilities of all new composites were higher than 100% as compared with the control. The specific ALP activities of PMMA were significantly lower on days 3, 7 and 14 as compared to the new composites and pure PCL, whereas significantly higher ALP activities were found on day 14 of the composite with 0.1g Mg (Figure 3). Figure 4 exhibits the percentage change of bone volume on the samples during the implantation period. Significant new bone formation was found on the new composites with 0.1g Mg after 1 week of post-operation as compared to the PMMA and PCL, whereas bone loss was detected on the composite with 0.6g Mg.
Discussion:
The results of in-vitro studies suggested that the new composites were well tolerated by bone cells. In addition, the specific ALP activities suggested that the composites with 0.1g Mg possessed higher osteoblastic activities as compared to PMMA and PCL. This can be correlated with our previous studies with the use of different concentrations of Mg supplemented medium, which suggested that culture medium with addition of low concentration of Mg ions was able to enhance the osteoblastic differentiation properties. This explained why higher ALP activity was found on composites with 0.1g Mg but not on the composite with 0.6g Mg. Consistent results were also obtained in in-vivo studies. New bone formation found in the composite with 0.1g Mg was significantly higher than that of the PMMA and PCL especially at early time points (from week 1 to week 8 of post-implantation). It indicated that the new composites with smaller amount of Mg incorporation could promote rapid bone formation as compared to the conventional PMMA whereas bone loss was found once the amount of Mg incorporation increased. Hence, the amount of Mg should be carefully controlled. Moreover, an apatite layer was found on the composites but not on PCL after 7 days of SBF immersion. This illustrated that the composites were bioactive. Various compressive moduli of the new composites can be adjusted by incorporating different amounts of Mg particles into the material matrix in order to adjust their mechanical properties similar to that of cancellous bone (50-800MPa). Hopefully, they can potentially help reduce the post-op complications found in cement augmentation using PMMA. Additionally, their mechanical properties can be maintained for 60 days which indicated that they maybe able to provide sufficient support for bone healing. However, longer immersion time is still needed in order to show that the mechanical support is enough before complete bone healing.

Conclusion:

Our new bone substitutes were found to be bioactive, biocompatible, osteoconductive and having sufficient mechanical properties as compared to conventional PMMA. Hence, the new composites may substitute the currently used PMMA for vertebral augmentation in the future.

References:

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