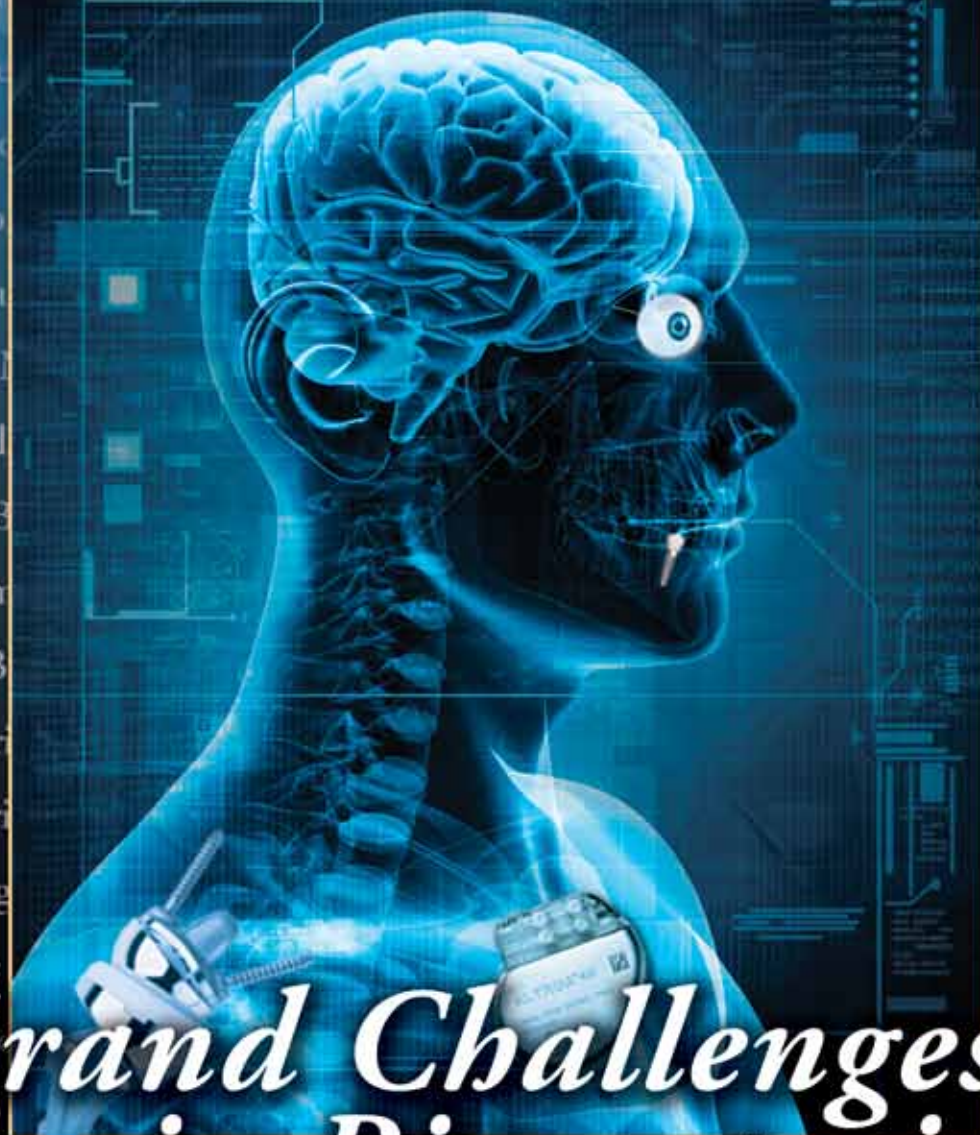


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New Low Modulus Bone Void Fillers For Osteoporotic Vertebral Fracture Fixation

K.H.M. Wong¹, P.K. Chu², K.D.K. Luk¹ and K.M.C. Cheung¹, K.W.K. Yeung¹

¹Department of Orthopaedics and Traumatology, The University of Hong Kong, Pokfulam, Hong Kong, China

²Department of Physics and Materials Science, City University of Hong Kong, Kowloon, Hong Kong, China

Statement of Purpose: Cement augmentation by using polymethylmethacrylate (PMMA) is a commonly used treatment for patients with osteoporotic vertebral fractures. However, adjacent level fracture after surgery due to the mismatched mechanical properties between PMMA and the osteoporotic cancellous bone is a concern¹. Indeed, the stiffness of PMMA bone cement is about seven to ten times higher as compared with that of osteoporotic vertebral cancellous bone. Furthermore, tissue necrosis after operation has been reported, since its polymerization is chemically exothermic, thereby potentially damaging the surrounding tissues. Other concerns associated with the use of conventional PMMA are monomer toxicity, non-resorbable and non-bioactive properties in which these unsatisfied factors may jeopardize the integration of biomaterial and host bone in the long-term. Alternatively, someone has developed calcium phosphate cement (CPC), as CPC contains more advanced osteoconductivity². However, the major problem of CPC is that its inferior mechanical properties are insufficient to match the clinical needs. Hence, the development of new bone substitutes is essential and attractive in clinical point of view. Hence, our group has fabricated novel bone substitutes comprised of polycaprolactone (PCL) and magnesium (Mg) with a wide range of compressive moduli and enhanced osteoblastic activity for vertebral cement augmentation. This paper aims to report the mechanical characteristics, *in-vitro* and *in-vivo* properties of the new bone substitute. **Methods:** The bone substitutes were prepared by incorporating 0.1-0.6g silane-treated Mg micro-particles into 1g PCL. Their mechanical properties were evaluated by compression test, whereas the cytocompatibility and osteogenic differentiation properties were studied by direct cell culture, MTT and ALP assays, respectively. The *in-vivo* response was studied in rat model for 6 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: The compressive moduli of the composites with 0.1g and 0.6g Mg were 1-fold and 3-fold higher than PCL, respectively (as shown in Fig. 1). Also, they were about 5-fold and 2-fold lower than PMMA. The cell viabilities of all new composites were higher than 100% as compared to the control. The ALP activities of PMMA were significantly lower on days 3, 7 and 14 as compared to the new composites and pure PCL, whereas higher ALP activities were significantly found on day 14 of the new composites with 0.1g Mg. The percentage of bone volume change of all the samples along the implantation period was shown in Fig. 2. Significant new bone formation was found on new bone substitutes with 0.1g Mg after post-operation 1 to 8 weeks as compared with the control. However, less bone was found on the

substitute with 0.6g Mg. The bone formation effect was visualized by the 3D uCT reconstruction images in Fig.3.

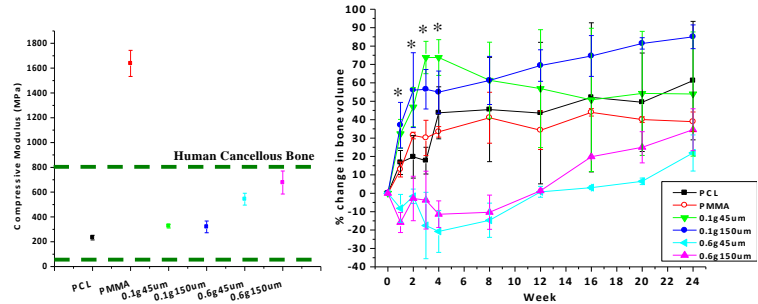


Fig. 1 (Left): Compressive moduli of the PCL-Mg composites as compared to PMMA & PCL (Green dotted line: range of human cancellous bone moduli).

Fig. 2 (Right): The percentage change of bone volume during the implantation period.

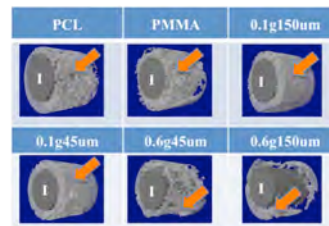


Fig. 3 The 3D uCT images of PCL, PMMA and PCL-Mg composites after 2 months of operation. Orange arrows indicated the newly formed bone and 'I' indicated the implants.

Discussion & Conclusions: The results of *in-vitro* tests suggested that the new composites were well tolerated by bone cells and osteoconductive. In *in-vivo* experiment, new bone formation found in the composite with 0.1g Mg was significantly higher than that of PMMA at the early time points. It indicated the new bone substitutes could promote fast bone healing as compared to the conventional PMMA. However, high dosage of Mg might weaken the new bone formation *in-vivo*. Additionally, various compressive moduli of the new composites can be adjusted by incorporating various amounts of Mg into the material matrix in which these new substitutes are mechanically similar to the cancellous bone (50-800MPa)³. Hence, they potentially help reduce the post-op complications while using PMMA. In summary, we prove that the mechanical properties of the newly developed bone substitutes can be individualized according to patient's need. Also, the new composites are radiopaque, biodegradable and injectable that benefit for clinical applications.

References: 1. S. Larsson et al (2002) Clin Orthop Relat Res 395:23-32. 2. DK. Ahn et al (2009) J Korean Orthop Assoc 44:386-90. 3. X. Banse et al (2002) J Bone Miner Res 17:1621-28.

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