Enhanced Injectability of Self-Setting Calcium Phosphate Cements

Rosenberg, Aron; Palazzolo, Robert; Tofighi, Aliassghar; Chang, Jerry
ETEX R&D, Cambridge, MA, USA

Statement of Purpose:

Calcium phosphate cements (CPCs) have demonstrated efficacy in fracture repair and bone void filling applications such as distal radius, tibial plateau, and calcaneous fractures.[1] CPCs have also been shown to be effective carriers for bioactive molecules such as rh-BMP-2.[2] Their flowability and self setting properties are desirable for minimally invasive surgery (MIS), but their use has been limited because current formulations are prone to injection blockage due to separation of the liquid and solid phases. Additionally, current methods for preparing CPCs are cumbersome and require many steps to transfer the CPC into syringes, increasing preparation time and risk of contamination. Research to improve injectability has primarily relied upon polymer additives as viscosity modifiers to prevent phase separation, but these may alter performance and impact biocompatibility and bioactivity.[3] An alternative method to simplify preparation and enhance injectability of a conventional CPC is presented which uses standard syringes and connectors to apply high-shear mixing and thereby augment flow characteristics.

Methods:

Two CPC precursors; an amorphous calcium phosphate (ACP) (with Ca/P<1.5) and dicalcium phosphate dihydrate (DCPD) seeded with apatite (10-25% w/w) were prepared using a low temperature double decomposition technique. The two powders were mixed at a 1:1 ratio and milled in a high-energy ball mill for 3 hours. The resulting powder was filled into a syringe and connected to a second syringe filled with saline by means of a luer connector.[Figure 1] The saline was injected into the powder at a liquid to powder ratio of 0.5:1 and the mixture was then passed back-and-forth between the syringes until a uniform paste was formed (approximately 5 passes). The same cement mixed (with the same L/P) in a bowl with a spatula and then transferred into a syringe was used as a control. Materials were tested for chemical composition (FT-IR, XRD, and Ca:P atomic ratio) and performance characteristics (injection force and yield, working time, hardening rate, compressive strength, and resistance to washout).

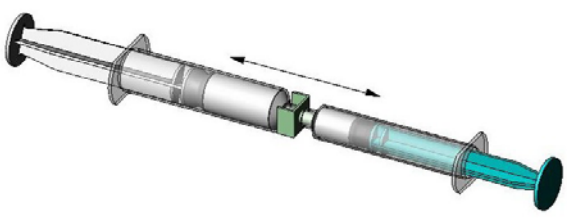

Figure 1: Syringe to Syringe Mixing System

Results:

Syringe mixing reduced preparation time from two minutes to one minute, and the cement was deliverable through a 16 gauge needle with less than 3kgf force. A 50% reduction in injection force relative to bowl mixed was observed. Syringe mixing also increased the percentage of CPC delivered. The delivered amount was less than 90% for bowl mixed cement but was 100% for syringe mixed cement. Syringe mixed cement could be stored for up to 6 minutes at room temperature and remixed while retaining full injectability. The mixing did not affect the hardening rate, compressive strength, or resistance to washout of the CPC, nor did it change the chemical composition. The injectable cement hardened in less than 5 minutes at 37 C, achieved a compressive strength of 30 MPA in 2 hours and could be injected directly into a water bath without loss of material.

Conclusions:

These results demonstrate a simple solution to a long standing issue of CPC injectability. Cement prepared and delivered using the syringe to syringe mixing method provides ease of use and improved injectability over traditional bowl mixing methods. Furthermore, there is no compromise in performance characteristics such as setting time or compressive strength, nor is there any chemical modification due to additives. The self-contained mixing and delivery device is also intuitive, faster, and reduces risk of contamination because the entire mixing process is contained. These findings demonstrate an opportunity to expand CPC usage for MIS.

References:

[1] Larsson S. et al, Clin. Orthopaedics & Rel. Res. 395:23-32, 2002.
[2] Li R.H. et al, J. Orthopedic Res. 21:997, 2003.
[3] Leroux L. et al, Bone 25:2, 31S–34S, 1999.