



## Evaluation of the ultrasonication process for injectability of hydraulic calcium phosphate pastes

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### ABSTRACT

This study examined the use of ultrasonication to improve the injectability of an aqueous calcium phosphate paste. Ultrasonication was applied to the paste through the plunger of the delivery syringe. A factorial design of experiments with three investigated factors, liquid to powder ratio (LPR) (38%, 39% and 40%), the size of the delivery syringe (5 and 10 ml) and the amplitude of the 20 kHz power ultrasonication (0–30  $\mu$ m), was used in this study. The volume fraction of the extruded paste was used to quantify injectability. Small injectability improvements were observed with an increase in LPR and decrease in syringe size, which is consistent with previously published results. The improvements due to ultrasonication were significant and remarkable. For example, when using the 5 ml syringe the injected volume fraction of the 38% LPR paste improved from  $63.4 \pm 2.3\%$  without ultrasonication to  $97.3 \pm 2.4\%$  with 30%. This result shows that ultrasonication is an effective solution to improve injectability.

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### 1. Introduction

The poor injectability of calcium phosphate (CaP) pastes is an important limitation in the use of such pastes as bone graft substitutes [1–6]. Recent studies have shown that the poor injectability results from separation of the liquid and solid particles under the injection pressure, eventually leading to a halt of the injection process [1–3]. Bohner and Baroud [1] postulated that there is competition between the filtration process and flow of the paste through the thin cannula. Specifically, the delivery pressure applied to the hydraulic paste forces flow of the paste itself but, at the same time, the liquid phase is more mobile than the particles and is expelled at a faster rate than the solid particles. Bohner and Baroud [1] demonstrated experimentally these observations using a calcium phosphate hydraulic paste and examined the relations between several parameters of the delivery process and the paste volume fraction extruded. Additionally, Habib et al. [2] investigated the water content and the distribution of paste left in the delivery syringe and of the extrudate. This study showed that a water gradient exists in the paste left in the syringe, with a higher water content near the syringe tip and a lower water content near the syringe plunger, suggesting that poor injectability is due to the formation of a plug on the plunger side.

Earlier research studies focused on the use of chemical additives to improve paste injectability and significant attention was given to examining the injectability of thick pastes and the required delivery force [4–6]. In particular, ionic modifiers such as trisodium citrate solution were added to the calcium phosphate paste to decrease the viscosity and, therefore, improve the paste injectability [4]. However, this strategy generally leads to very liquid pastes with poor cohesion, which may have dramatic consequences upon implantation, for example for vertebroplasty (risk of leakage). Alternatively, steric modifiers such as xanthan gum alter the interaction between the particles and enhance the injectability, partially due to the viscosity increase of the dispersing medium [5]. High viscosity dispersing liquids are less mobile and, therefore, reduce the filtration process. Injectability was accordingly improved by adding sodium glycerophosphate (NaGP), lactic acid, and glycerol [6]. Chitosan slightly improved injectability, as reported by Leroux et al. [6]. However, cost, sterilization, and biocompatibility are some of the main concerns when using such additives.

Beside chemical approaches, physical approaches have also been used to enhance injectability, for example by optimizing the particle size distribution (PSD) [1,5,7–9]. Bohner and Baroud [1] predicted that a decrease in mean particle size should improve injectability. This result was confirmed by Baroud et al. [5] and Gbureck et al. [7]. However, the mechanisms were slightly different. Whereas Baroud et al. [5] observed an increase in paste viscosity and yield stress with a decrease of in particle size,

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