FACTS AND FIGURES

Bio 1-Quickset injectable self-hardening resorbable bone void filler: Injectability, setting time, and compressive strength

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Introduction

Calcium phosphate ceramics are now well accepted as bone void fillers. Such calcium phosphates can also be used as a cement, so called CPCs (calcium phosphate cements). The primary advantage of injectable bone void filler over blocks, granules, or powders is the ability to custom-fill defects. Capable of hardening in situ, calcium phosphate cements can be injected or molded during surgery, and will lead to a complete filling of a defect, independent of size or shape, improving bone–implant contact [(1)]. Irregular bone defects can so be completely filled. It also allows for a minimally invasive approach of defect that are accessible under radioscopic control.

Injection of a resorbable bone void filler into an osseous defect may help to stabilize the fracture and to maintain osseous integrity as the substitute is resorbed and replaced by bone [(2)].

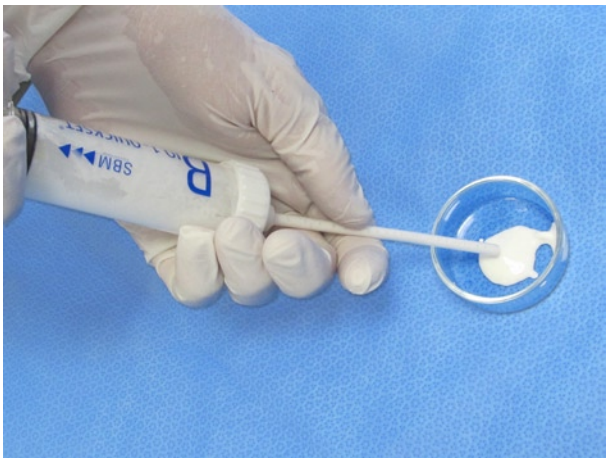

Figure 1: SBM Bio 1-Quickset injectable filler

The ability of calcium phosphate bone substitutes to act as a bone void filler has been documented in animal studies and human case series [(3)] [(4)].

These bony voids may be created surgically or result from traumatic injury. Clinical applications include:

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Treatment of primary metaphyseal bone defects and extremities (**with osteosynthesis**):

- distal radius fractures [5] [6] [7] [8] [9]
- calcaneus fractures [10] [11] [12] [13]
- proximal and distal tibia fractures [13]
- fibula fractures [13]
- proximal and distal femur fractures [13]
- proximal humerus fractures [13] [14]
- phalanx and metacarpals fractures [13]
- acetabulum fractures [13]
- tibial plateau fractures [15] [16] [17]
- hip fractures [18] [19]
- unstable trochanteric fractures [20] [21]
- femoral neck fractures [22] [23]
- acetabular reconstruction

Filling of bone cavities :

- removing benign cysts and tumors [24], including fibrous dysplasia, enchondroma and bone tuberculosis [13]
- iliac crest bone harvesting sites [13]
- post-traumatic bone defects [25]
- periodontal intraosseous defects [26] [27] [28] [29]

Injectable bone substitutes that set in situ are also suitable for screw fixation in low quality bone with a high risk of loosening [30] [18] [31] [32] [33].

Material and Methods

Development of injectable bone void filler implies both chemical and physical characterisation of the three main phases of the material:

- the components, i.e. the powders, liquids and eventual additives
- the injection time and the setting time of the paste into a solid material
- the properties of the end product.

During setting, a dissolution and precipitation reaction occurs in presence of a liquid, leading to the formation of calcium phosphate and sulfate crystals.

Material

Bio 1-Quickset is a self-hardening resorbable bone void filler that is injectable and biocompatible. It is made of pure beta tricalcium phosphate (β-TCP) and calcium sulfate hemihydrate (α-form CSH) powders, that sets to a solid material at body temperature when mixed with a saline solution (injectable sodium chloride).

Bio 1-Quickset closely resembles the mineral phase of bone and gradually remodels to bone via osteoclastic resorption and osteoblastic new bone formation [34] [35].

Methods

Injectability

For the purpose of injectability testings, the bone void filler was introduced in a commercial syringe (Plastipak, Becton Dickinson, Frankin Lake, New Jersey, USA) with a volume capacity of 20 ml, 24 mm of internal diameter and a nozzle diameter of 2.4 mm, and was extruded manualy. The injectability was measured by comparing the amount of the substitute before and after extrusion from the syringe.

Figure 2: extrusion from the syringe

Injection time and setting time

The powder was mixed with saline solution during 30 seconds. The viscosity was then measured using a rotative viscosimeter (Tve-05s, Lamy Rheology, Champagne Au Mont d'Or, France) at 100 rpm, every thirty seconds during ten minutes.

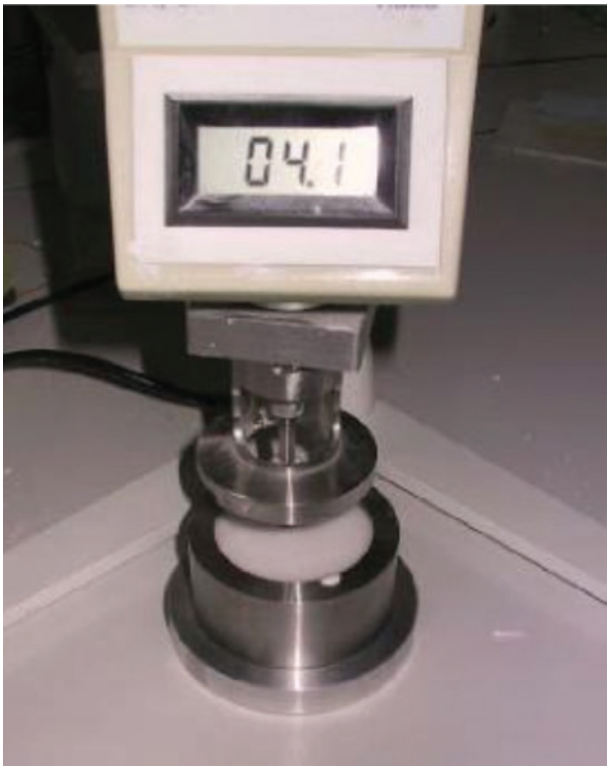

Figure 3: Setting times measurements set-up

Compressive strength

Mechanical strength was evaluated in terms of compressive strength (CS) and measured in an Universal Testing Machine (LR30K, Lloyd instruments, Bognor Regis, West Sussex, UK) at a cross-head speed of 0.5 mm/min until fracture.

Six specimens were tested, sized 18.9 mm in diameter and 17.5 mm in heigth (heigth-to-diameter ratio almost equal to 1). The compressive strength (Pascal) is the force (Newton) applied to the cross section (m^2).

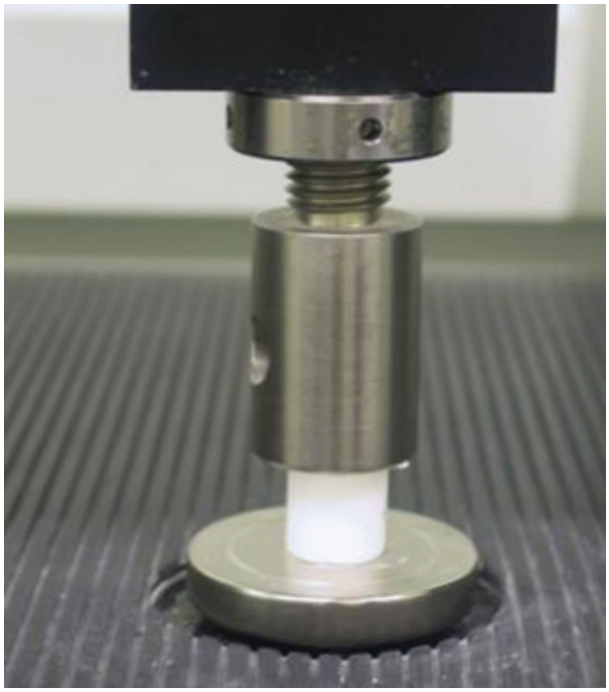

Figure 4: Compression testing set-up

Results

Injectability

The injectability is defined as the relative amount of mixture which can be extruded from the syringe, according to the equation below [36]:

$$INJ = \frac{(M_{before} - M_{syringe}) - (M_{after} - M_{syringe})}{M_{before} - M_{syringe}} \times 100$$

Where:

- INJ is the percentage of injectability,
- M_{before} is the weight of the syringe and the substitute before injecting,
- M_{after} is the weight of the syringe and the residual mixture after injecting,
- $M_{syringe}$ is the weight of the syringe.

Optimal β-TCP/CSH ratio achieves an injectabilty over 92%.

β-TCP/CSH ratio (%)	$M_{syringe}$ (g)	M_{before} (g)	M_{after} (g)	INJ (%)
47	14.29	22.31	14.66	95.4
50	14.25	24.08	14.99	92.5
50	14.17	23.97	14.45	97.1
55	14.23	25.06	18.11	64.2
55	14.08	27.78	17.07	78.2
60	14.23	26.36	21.50	40.1

Table 1: Injectability results

Injection time

Injection time is the delay after the powders and the liquid have been mixed and before the viscosity curve of the obtained paste show a deflexion.

The results obtained show that after 4 minutes the initial setting is too fast to allow injection. The mixture should be injected during the first three minutes after been mixed.

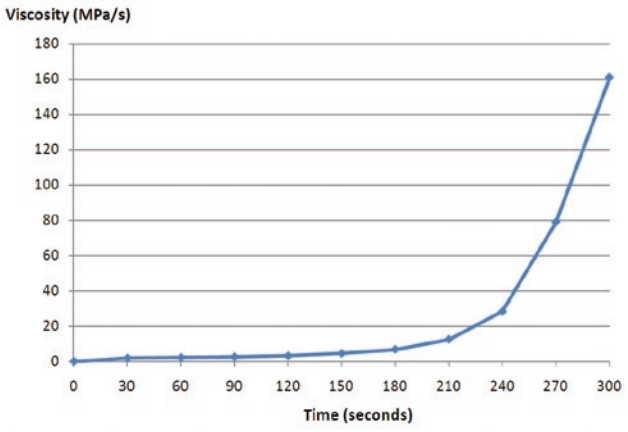

Figure 5: Injection time

The liquid-to-powder ratio (L/P) is the amount of liquid added to the powders. It plays a major role in the setting time. Excess liquid increases setting time.

Clinical experience has shown that high viscosity bone void fillers produce better clinical results, as compared to low viscosity bone void fillers [37] [38] .

Setting time

Setting time is the delay after the powders and the liquid have been mixed and before the mixture reach its maximal strength.

There are several factors influencing the setting and hardening of β-TCP based bone substitutes. Small particle size both accelerates the dissolution step, and thus the setting, and provides a stronger bone substitute [39].

Other factors that accelerate the initial dissolu¬tion of β-TCP are acidic pH [40], and increased temperature [41] [42] [43] [44].

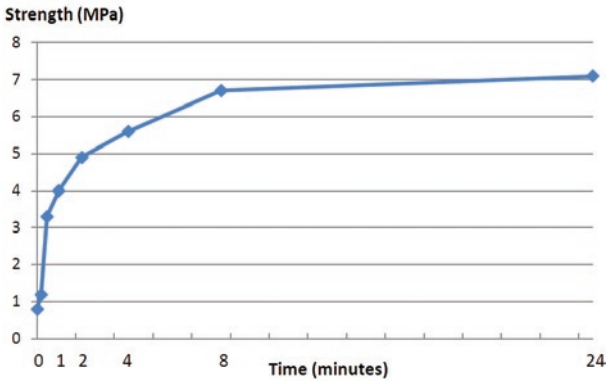

Figure 6: Setting time

Bio 1-Quickset achieves 94% of its maximal compressive strength 8 minutes after mixing.

Stability of the SBM Bio 1-Quicket performances was also evaluated by an accelerated ageing protocol:

- 1 year is equivalent to 6 weeks at 55°C
- 2 years is equivalent to 12 weeks at 55°C
- 5 years is equivalent to 28 weeks at 55°C

Delay (years)	Hardening time (min.'sec.'')
0	5'45'' (0'15'')
1	7'00'' (1'06'')
2	6'15'' (0'15'')
5	7'12'' (0'36'')

Table 2: Accelerated ageing setting time results

Compressive strength

The compressive strength is the applied force (MPa) at time where the first sign of crack appear on the sample (Figure 7).

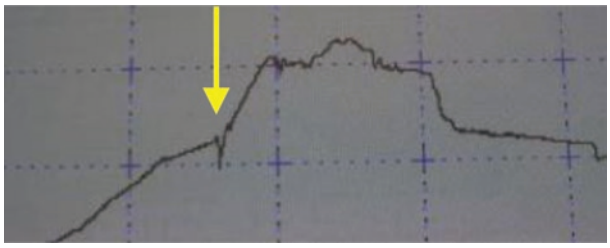

Figure 7: Typical compression testing curve

The observed mean compressive strength is 1537 N, that is equivalent to a maximum stress of 6 MPa. These results showed that the Bio 1-Quickset injectable bone void filler has a compressive strength similar to cancellous bone [45].

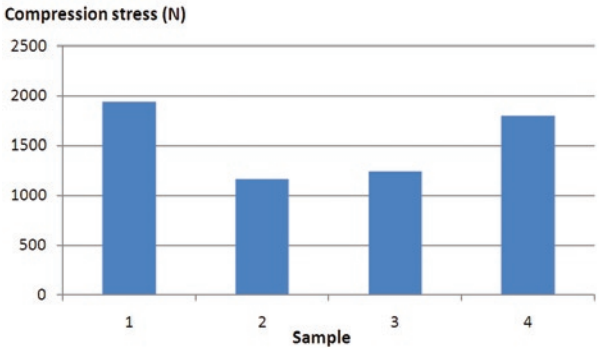

Figure 8: Mechanical characterization

Proportion of tricalcium phosphate

The compressive strength is directly correlated to the weight proportions of the powders. It was shown that the compressive strength could be controlled by varying the composition of the bone void filler. As the β-TCP content increases, the strength increases [46], but injectability decreases. Bio 1-Quickset β-TCP proportions have been determined for leading to an ideal compromise between injectability and compressive strength.

Temperature

The hydration reaction of β-TCP to CSH is temperature dependent and a higher compressive strength is obtained at 37 °C compared to room temperature (even if the final strength obtained at the end of the reaction is the same for both temperatures) [42].

Liquid-to-powder ratio

But the factor that affected the strength of the end product the most is liquid-to-powder ratio (L/P). The strength increased linearly with the decrease in added water [46]. The SBM Bio 1-Quickset powder is mixed with a saline solution at a L/P ratio of 0.30 mL.g-1 (range 0.28 to 0.37 mL.g-1 depending on conditioning).

Discussion

Bio 1-Quickset associates two well known bone substitutes. It allows for having good injectability and ease of use, and to limit the drawback of too fast absorption of the bone void filler. The defined 30 to 60 seconds mixing and 2.30 minutes injection times, allows for a simple and ergonomic use of the system.

In vivo studies have shown that this bone void filler is bioactive, resorbable, and osteoconductive [34] [35]. Thanks to our large background on β-TCP, mechanical strength characterization, surgical technique validation and according to the available scientific litterature, we can conclude that Bio 1-Quickset injectable self hardening resorbable bone void filler is suitable for the filling of bone defects with no mechanical stress. It is indicated for the filling of bony voids or gaps that are not intrinsic to the stability of the bony structure, like cysts or benign tumors.

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