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Evaluation of two novel aluminum-free, zinc-based glass polyalkenoate cements as alternatives to PMMA bone cement for use in vertebroplasty and balloon kyphoplasty

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Abstract Vertebroplasty (VP) and balloon kyphoplasty (BKP) are now widely used for treating patients in whom the pain due to vertebral compression fractures is severe and has proved to be refractory to conservative treatment. These procedures involve percutaneous delivery of a bolus of an injectable bone cement either directly to the fractured vertebral body, VB (VP) or to a void created in it by an inflatable bone tamp (BKP). Thus, the cement is a vital component of both procedures. In the vast majority of VPs and BKPs, a poly(methyl methacrylate) (PMMA) bone cement is used. This material has many shortcomings, notably lack of bioactivity and very limited resorbability. Thus, there is room for alternative cements. We report here on two variants of a novel, bioactive, Al-free, Zn-based glass polyalkenoate cement (Zn-GPC), and how their properties compare to those of an injectable PMMA bone cement (SIMPL) that is widely used in VP and BKP. The properties determined were injectability, radiopacity, uniaxial compressive strength, and biaxial flexural modulus. In addition, we compared the compression fatigue lives of a validated synthetic osteoporotic VB model (a polyurethane foam cube with an 8 mm-diameter through-thickness cylindrical hole), at 0–2300 N and 3 Hz, when the hole was filled with each of the three cements. A critical review of the results suggests that the performance of each of the Zn-GPCs is comparable to that of SIMPL; thus, the former cements merit further study with a view to being alternatives to an injectable PMMA cement for use in VP and BKP.

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1 Introduction

Vertebral compression fractures (VCFs)—a common complication of severe osteoporosis—commonly occur at the T6-L5 levels, have a high incidence, exert many deleterious repercussions on patients, and the economic ramifications are serious. For example, in the United States, there are ~750,000 new cases per year [1]; in Sweden, patients suffer a marked drop in a quality of life index [2], and in the European Union countries, the associated annual direct costs are ~$440 million [3]. When the pain (usually, acute or chronic back pain) due to VCFs is not severe, a conservative treatment, usually, back bracing, is employed [4]. However, in cases where the pain has proved to be refractory to conservative treatment, a surgical option is usually offered. Currently, this option consists of either vertebroplasty (VP) or balloon kyphoplasty (BKP). These treatments involve the injection of a bolus of a viscous bone cement paste either directly into the cancellous core of the fractured vertebral body, VB (VP) or into a void created in the fractured VB by an inflatable bone tamp (BKP). Thus, in both procedures, the injectable bone cement used is a critical element [5, 6].

Three chemistries of injectable bone cements are used in VP and BKP [7]. These are (1) a PMMA bone cement

brand that is approved for use in cemented total joint replacements (TJRs) (Surgical Simplex®P; Stryker-Howmedica-Osteonics, Mahwah, NJ, USA) but with extra amounts of radiopacifier(s) manually blended with the cement powder, thereby raising the radiopacifier content (defined as the ratio of the mass of the radiopacifier to the total cement powder mass), from 10% to, typically, 30%; (2) PMMA bone cement brands specifically formulated for VP or BKP (thus, the radiopacifier content is high, typically 30% of the cement powder mass) (for example, KyphX®HV-R™; Medtronic Spinal and Biologics, Sunnyvale, CA, USA); (3) calcium phosphate, CaP, materials (for example, KyphOs FS™; Medtronic Spinal and Biologics); and (4) a glass ceramic particle reinforced-bis-GMA composite material (CORTOSS®; Orthovita, Inc., Malvern, PA, USA). Each of these cement types has its share of shortcomings [7]. A PMMA bone cement is characterized by, for example, exothermic polymerization [7] (exotherms of as high as 70°C have been reported in the center of the bone bed, in cemented TJRs, when some brands are used [8]); lack of bioactivity and osteoconductivity [7]; neurotoxicity and cytotoxicity of the liquid monomer [7]; and very limited resorbability [7]. CaP cements are very difficult to inject and have poor radiopacity and low compressive strength [7]. CORTOSS® is not resorbable and has been found to be toxic to mesenchymal stem cells from sheep [9].

The foregoing brief critique shows that there is room for improvements in the field of injectable bone cements for use in VP and BKP, with some recent work being reported on modified/alternative formulations of PMMA bone cements and CaP cements [10–14]. In the evaluation of these new formulations, the traditional methods of characterization involve determinations of properties of the cement per se (for example, radiopacity, injectability, rheological behaviour, and quasi-static compressive strength) and of biomechanical measures (such as compressive stiffness) of constructs (herein defined as osteoporotic VBs or motion segment unit(s) from animal model spines or from cadaveric spines that are fractured and then augmented using simulated VP or BKP and the test cement). While the former determinations are important, they are not sufficient because they provide information about the cement in isolation from the VB. The drawbacks of using animal model spines or cadaveric spines for ex vivo biomechanical studies are well known [15]. To supplement determinations of cement properties, we have reported on determinations using a validated synthetic osteoporotic VB augmentation model (hereafter referred to as "the augmentation model") comprising a polyurethane (PU) cube with a through-thickness cylindrical hole filled with the test cement [15].

In previous work, we highlighted the potential of Al-free, Zn-based glass polyalkenoate cements (GPCs) for use in orthopaedic applications [16, 17]. We suggest here that GPCs also have potential for use as injectable bone cements in VP and BKP because of properties such as: setting without significant heat evolution, ability to adhere to the mineral phase of bone, and mechanical properties that are comparable to those of bone [16, 17]. In the present study, we posed two hypotheses. The first was that each of four germane cement properties (injectability, radiopacity, uniaxial compressive strength, and biaxial flexural modulus) of two novel Al-free, Zn-based GPCs (based on two different glass formulations) were not significantly different from the corresponding value for a PMMA bone cement that is widely used in VP and BKP. The second was that the life of the augmentation model when it was filled with either of the two Zn-based GPCs and subject to cyclical compressive loading was not significantly different from that when the model was filled with the PMMA bone cement.

2 Materials and methods

2.1 Materials

The compositions of the PMMA bone cement (herein designated SIMPL) and the two novel, bioactive, Al-free, Zn-based GPCs (herein designated Zn-GPC A and Zn-GPC B) are given in Table 1. In producing the glass powders used for the Zn-GPCs, the relevant amounts of analytical grade strontium carbonate, calcium carbonate, zinc oxide, and silica (Sigma–Aldrich, Dublin, Ireland) were weighed out in a plastic tub, thoroughly mixed in a ball mill for 1 h, and then dried in vacuum oven, at 100°C, for 1 h. Following this, the glass batches were transferred to platinum crucibles in which they were fired (1480°C; 1 h), and then the glass melts were quenched in water, after which the resulting grits were dried, ground, and passed through a sieve to retrieve a powder with mean particle size of <25 μm (for Zn-GPC A) or of <45 μm (for Zn-GPC B). The two poly(acrylic) acids were supplied as aqueous solutions (Advanced Healthcare Limited, Kent, UK) and each was then freeze-dried, ground, and passed through a sieve to retrieve a powder with mean particle size of <90 μm. A total of 10 wt% tri-sodium citrate, TSC (Reagecon, Shannon, Ireland), supplied in <90 μm particle size, was added to the glass phase prior to mixing to extend the setting times of these cements.

2.2 Determination of injectability

Injectability was determined using a method reported in the literature for CaP cement [12, 18]. For SIMPL, the powder (25.5 g) and the liquid monomer (12.8 ml) were mixed in a polymeric bowl open to ambient laboratory air, for

Table 1 Compositions of the test cements

Cement	Composition
Surgical Simplex®P[a]	*Powder*[a]: 6.0 g of poly(methyl methacrylate); 30.0 g of methyl methacrylate–styrene copolymer (which included 0.68 g of benzoyl peroxide); and 15.0 g of $BaSO_4$. Total mass of powder: 51.0 g
	Liquid monomer[b]: 19.50 ml of methyl methacrylate; 0.50 ml of *N,N*-dimethyl-*p*-toluidine; and 75 ppm of hydroquinone. Total volume of liquid monomer: 20.00 ml
Zn-GPC A	4.0 g of particles of glass A (0.04 mol% of SrO; 0.12 mol% of CaO; 0.36 mol% of ZnO; and 0.48 mol% of SiO_2; mean particle size: <25 μm); 1.48 g of poly (acrylic) acid (weight–average molecular weight: 12,713 g mol^{-1}); 0.30 g of trisodium citrate dihydrate (particle size: <90 μm). Total mass: 5.78 g
Zn-GPC B	4.0 g of particles of glass B (0.04 mol% of SrO; 0.12 mol% of CaO; 0.36 mol% of ZnO; and 0.48 mol% of SiO_2; particle size: <45 μm); 1.48 g of poly(acrylic) acid (weight-average molecular weight: 80,800 g mol^{-1}); 0.15 g of trisodium citrate dihydrate (particle size: <90 μm). Total mass: 5.63 g

[a] Lot #: 4391 N 300906 2011-08, but an extra amount (11 g) of $BaSO_4$ was added to the powder

[b] Lot # 841CM 050372

30 ± 2 s, and then delivered into a cement gun from which some of the dough was extruded, without pressurization, into a 20 ml-syringe that has an opening of 2 mm (Miilipore, Bedford, MA, USA), filling it. (Thus, initial volume of cement, $V_i = 20$ ml.) Note that during the extrusion of the dough, the syringe was firmly gripped onto a metal clamp. For the Zn-GPCs, the powder constituents (5.78 g for Zn-GPC A and 5.63 g for Zn-GPC B) were mixed with 1.48 ml of distilled water on a glass plate, for 30 ± 1 s for Zn-GPC A or 20 ± 1 s for Zn-GPC B, after which the dough was quickly scooped into a 5 ml-syringe with an opening of 0.85 mm (Terumo Europe NV, Leuven, Belgium). (Note, in this case, V_i was 3.0 ± 0.5 ml.) As before, during the scooping of the dough, the syringe was firmly gripped onto a metal clamp.

For each cement, 5 ± 1 s after the dough was placed in the syringe, a 3 kg solid mild steel disc (diameter and thickness of 50 mm and 10 mm, respectively) was gently placed on top of the syringe's plunger, thus forcing the dough slowly and uniformly into a polymeric beaker positioned directly underneath the syringe for 10 ± 1 s, after which the test was stopped. This loading corresponds to the mean injection force recorded in injectability tests on CaP cements carried out using a universal materials testing machine [19].

Injectability (I) was defined as 100% (volume of cement dough extruded out of the syringe at the end of the test/the applicable value of V_i). For each of the cements, the tests were run in triplicate.

2.3 Determination of radiopacity

The radiopacity of a cement (R) was determined using the equivalent Al thickness method, per CEN ISO 4049 [20]. Disc-shaped specimens, approximately 12.25 mm in diameter, were prepared for each cement. The thickness was approximately 1.0 mm for the SIMPL and Zn-GPC A discs (1.00 ± 0.02 and 1.00 ± 0.08 mm, respectively) and 2.0 mm (1.97 ± 0.07 mm) for the Zn-GPC B discs. In the test, the cement specimen, an Al step-wedge (Al, 98.96 mass%; Mg, 0.55 mass%; Fe, 0.48 mass% alloy; Kerr, MI, USA) (with thickness of between 1 and 10 mm), and a lead-stop (15.0 mm diameter and thickness 3.0 mm) were exposed together in an X-ray machine (Planmeca Prostyle Intra X-ray machine; Roselle, IL, USA) at 66 kV and 8 mA. Focus-to-sensor distance was 400 mm and the exposure time was 0.32 s. The images were taken on dental X-ray occlusal-size film (Kodak ultra-speed DF-50; Eastman Kodak, NY, USA). The optical density was measured using a transmission densitometer (DT1405; R Y Parry Ltd., Berks, UK). R was calculated from the linear regression of the logarithm of the optical density on the Al thickness for the step-wedge image. For each cement, R was determined in triplicate.

2.4 Determination of uniaxial compressive strength

Uniaxial compressive strength (UCS) was determined per ISO 9917 [21]. Spilt-ring steel moulds (4 mm in diameter and 6 mm in height) were filled to excess with freshly-mixed cement and then covered with acetate sheet. The moulds were then sandwiched between 2 stainless steel plates, clamped, and incubated in distilled water at 37 ± 1°C, for 1 h. The moulds were then removed from the clamps. Flash around the moulds was removed using a grinding wheel (100 rpm) and 1200 grit silicon carbide paper, which ensured that the specimens had flat, parallel ends. Specimens were then aged in distilled water, at 37 ± 1°C, for 1, 7, 30 and 90 days, and tested wet at a crosshead displacement rate of 1 mm min^{-1} in a servo-hydraulically driven materials testing machine (Model 4082; Instron Ltd., High Wycombe, Bucks, UK). For each cement, five specimens were tested.

2.5 Determination of biaxial flexural modulus of cement

The method used to determine the biaxial flexural modulus (E_b) was a modification of that described by Williams et al. [22]. Specimen preparation was the same as for the uniaxial compression test specimens, except that rubber moulds of diameter and thickness 12 and 2 mm, respectively, were used to prepare test specimens. Similarly, all the details regarding the incubation and aging of the test specimens were the same as for the uniaxial test specimens. In the test, the specimen was simply supported on a jig comprised of a support base that had three equally spaced ball bearings (diameter = 1.5 mm) and was loaded, using a loading platen (1.5 mm-diameter ball), at 1 mm min^{-1} (Instron Model 4082) at its center. E_b was then computed from the expression for the slope of the plot of applied load versus deflection of the center of the specimen, as given by Higgs et al. [23], with the Poisson's ratio of the cement taken to be 0.30 [24].

2.6 Augmentation model

The augmentation model comprised a PU foam cube (25 mm sides) into which a centrally located 8 mm-diameter through-thickness cylindrical hole was drilled and then the hole was completely filled with a bolus of cement (Fig. 1). Thus, the volume fraction of the cement in the cube (volume of cement/volume of cube) (V_c) of 8% is within the range of the cement fill, which was defined as (injected volume of cement (= 1.0–8.5 ml [25, 26])/(volume of VB in the T6-L5 levels (= 29.4 ml [27]))), typically used in VP and BKP.

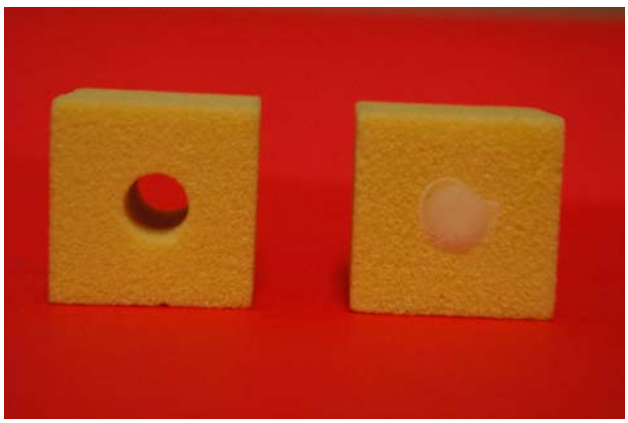

Fig. 1 Photographs of the synthetic osteoporotic vertebral body augmentation model, with the centrally located through-thickness cylindrical hole empty and completely filled with a bolus of injectable bone cement

2.7 Cement mixing methods for augmentation model

For the SIMPL specimens used in the compression fatigue life tests, the powder (51.0 g) and the liquid monomer (25.5 ml) were mixed in a polymeric bowl open to ambient laboratory air (temperature and relative humidity of 22 ± 1°C and 59 ± 1%, respectively), for 30 ± 2 s, and then delivered into a cement gun from which it was extruded, without pressurization, into the hole in the PU cube to fill it. Excess cement dough was scraped off from the top of the filled cube to produce a fill pattern flush with the foam, which facilitated visualization of the cement cylinder during a test; for example, to observe when a crack first appears.

For the Zn-GPC specimens used in the compression fatigue life tests, the powder constituents (5.78 g for Zn-GPC A and 5.63 g for Zn-GPC B) were mixed with 1.48 ml of distilled water on a glass plate, for 30 ± 1 s for Zn-GPC A or 20 ± 1 s for Zn-GPC B, after which the dough was quickly scooped into a 5 ml-syringe (Terumo), using a spatula, from which the dough was extruded, without pressurization, into the hole in the PU foam cube. To fill the hole, this procedure was repeated once. The final steps were the same as for the SIMPL specimens.

2.8 Compression fatigue life testing of augmentation model

After preparation of an augmentation model, it was cured in ambient laboratory conditions for 20 ± 1 min, after which it was immersed in PBS solution (Invitrogen Corp., Chicago, IL, USA), at 37 ± 1°C, that was contained in an environmental chamber fitted to a servohydraulically driven custom-built universal materials testing machine (Fig. 2), for 24 ± 1 h. After that, the cyclic axial compressive load (0–2300 N) was applied normal to the longitudinal axis of the cement cylinder, consistent with the clinical situation of a VP- or BKP-augmented VB [26, 28, 29], at a frequency of 3 Hz. For each specimen, testing continued until either a crack was first observed in the cement cylinder or "run-out" occurred, whichever was first. (Run-out was defined as no cracks seen in the cement cylinder after 1 million loading cycles.) The specimen was inspected visually for cracks at intervals of 4 h. For each cement, six specimens were tested.

2.9 Statistical analysis

The I and R results were analyzed using the Kruskal–Wallis test (SAS® Version 9.1; SAS Institute Inc., Cary, NC, USA), while the UCS and E_b results were analyzed using both the Kruskal–Wallis test and ANOVA, with the Bonferroni correction, and the 95% confidence limits for

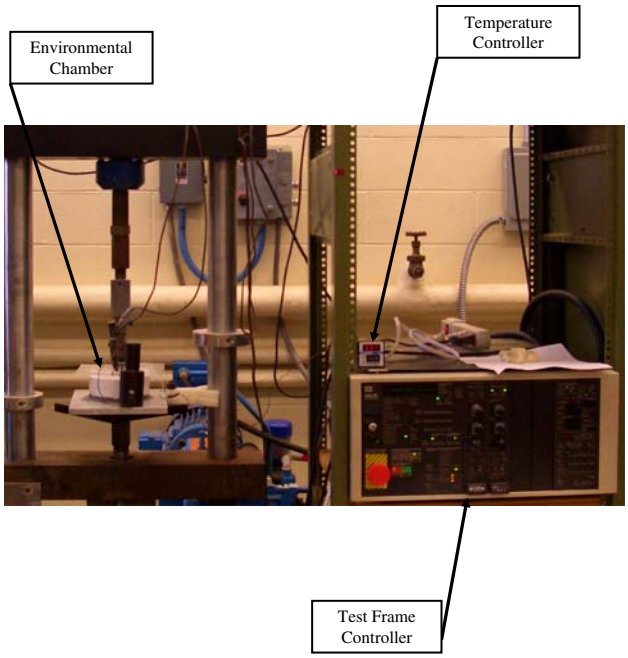

Fig. 2 Photograph of the set-up for the compression fatigue life tests

the differences between population means method (SAS® Version 9.1). Significance was denoted at the 5% level.

3 Results

3.1 Injectabilities, radiopacities, uniaxial compressive strengths, and biaxial flexural moduli of cements

These results are given in Table 2. While there was no significant difference in the injectabilities of Zn GPC-A and Zn GPC-B, each cement was significantly less injectable than SIMPL (Kruskal–Wallis; $Pr > \chi^2 = 0.0008$). There was no significant difference in the radiopacities of Zn-GPCA and Zn-GPC B; however, each of these cements was significantly more radiopaque than SIMPL ($Pr > \chi^2 = 0.0008$).

With a few exceptions, aging time did not have a significant influence on UCS of any of the three cements, the exceptions being 90 d versus 7 d for SIMPL, 90 d versus 1 d for Zn-GPC A, and 90 d versus 1 d and 90 d versus 30 d for Zn-GPC B ($Pr > \chi^2 = 0.0019$–0038). For each aging time (1) UCS of Zn-GPC B was significantly greater than that of Zn-GPC A ($Pr > \chi^2 = 0.0021$–0.0052) and (2) UCS of either of these cements was significantly lower than that of SIMPL ($Pr > \chi^2 = 0.0019$–0.0033). As an illustration of this point regarding the influence of aging time, the results of the ANOVA of the UCS results obtained after aging time of 30 d are presented in Table 3. For SIMPL, Zn-GPC A, and Zn-GPC B, the highest mean value of UCS was achieved after 30, 30, and 90 d aging, respectively.

With a few exceptions, aging time did not have a significant influence on E_b of any of the three cements, the exceptions being 90 d versus 7 d for SIMPL, 90 d versus 1 d for Zn-GPC A, and 90 d versus 1 d and 90 d versus 30 d for Zn-GPC B ($Pr > \chi^2 = 0.0010$–0.0043). For each aging time: (1) E_b of Zn-GPC B was significantly greater than that of Zn-GPC A ($Pr > \chi^2 = 0.0044$–0.0082), and (2) E_b of either of these cements was significantly lower than that of SIMPL ($Pr > \chi^2 = 0.0019$–0.0032). As an illustration of this point regarding the influence of aging time, the results of the ANOVA of the E_b results obtained after aging time of 30 d are presented in Table 3. For SIMPL, Zn-GPC A, and Zn-GPC B, the highest mean value of E_b was achieved after 7, 90, and 90 d aging, respectively.

3.2 Compression fatigue life test results and damage profiles

For each of the augmentation models in the three study sets: (1) the foam cube suffered distortion within the first 100–110 cycles of the cyclic loading. (This distortion, herein designated the initial foam cube distortion, amounted to linear longitudinal and lateral strains of $\sim -35\%$ and $\sim +5\%$, respectively); (2) there was a small change in this distortion as the test progressed; (3) the foam cube did not suffer breakage (Fig. 3); (4) there was no debonding of the cement cylinder from the foam cube (Fig. 3); and (5) run-out was achieved. (Note that, because there were no differences in the results when any of the three cements were used, a typical model result when Zn-GPC B was used is presented in Fig. 3, as an illustration.) The last-mentioned point means that the probability of the cement cylinder in each of the models surviving 1 million loading cycles at 2300 N was 100%. The absence of debonding in the models suggests that the extent to which interdigitation fingers are created in the model is the same regardless of the cement used.

4 Discussion

A balanced comparison of the Zn-GPCs and SIMPL, in terms of cement properties, should involve consideration of three points. First, while it is true that the most widely used injectable bone cement in VP and BKP is a PMMA bone cement (for example, SIMPL), ideally, the value of a given cement property should be viewed against a limit/threshold, as stipulated in a testing standard. However, there are no testing standards for determining any properties of injectable bone cements for use in VP and BKP. This situation means that, for a given property, the discussions of

Table 2 Summary of the injectability results, radiopacitity results, the uniaxial compressive strengths, and biaxial flexural moduli of the cements

Cement property	SIMPL	Zn-GPC A	Zn-GPC B
Injectability (%)	100.0 ± 0.0	6.3 ± 0.2	6.3 ± 0.3
Radiopacity (equivalent thickness of Al for 1 mm-thick specimens, in mm)	1.02 ± 0.08	2.70 ± 0.05	2.40 ± 0.04
Uniaxial compressive strength (MPa)			
After 1 d aging[a]	95.7 ± 5.9	26.8 ± 1.1	63.4 ± 2.8
After 7 d aging[a]	98.0 ± 2.2	37.6 ± 3.3	63.4 ± 5.2
After 30 d aging[a]	116.6 ± 1.7	39.1 ± 3.6	62.5 ± 7.6
After 90 d aging[a]	92.4 ± 2.3	23.4 ± 1.2	75.4 ± 9.5
Biaxial flexural modulus (MPa)			
After 1 d aging[a]	1,000 ± 210	180 ± 60	390 ± 80
After 7 d aging[a]	1,190 ± 90	210 ± 30	430 ± 70
After 30 d aging[a]	1,140 ± 120	240 ± 30	390 ± 70
After 90 d aging[a]	900 ± 160	290 ± 70	550 ± 70

[a] In distilled water, at 37 ± 1°C

Table 3 Results of the ANOVA, with Bonferroni post hoc, tests on the results for the uniaxial compressive strength after aging time of 30 d in distilled water, at 37 ± 1°C (UCS/30), and for the biaxial flexural modulus after aging time of 30 d in distilled water, at 37 ± 1°C (E_b/30)

Property	Zn-GPC A vs. SIMPL			Zn-GPC B vs. SIMPL			Zn-GPC A vs. Zn-GPC B		
	Difference between means	Simultaneous 95% confidence limits	Outcome[a]	Difference between means	Simultaneous 95% confidence limits	Outcome[a]	Difference between means	Simultaneous 95% confidence limits	Outcome[a]
UCS/30	−77.45	−86.00; −68.89	S	−54.06	−62.61; −45.50	S	−23.39	−31.95; −14.84	S
E_b/30	−901	−1041; −762	S	−751	−891; −612	S	−150	−290; −11.00	S

[a] S: difference between means is significant

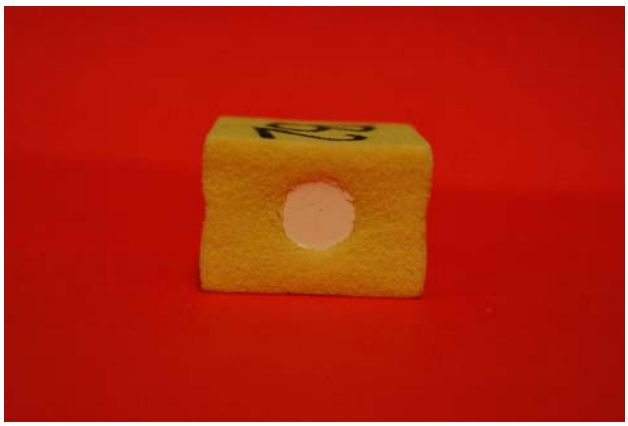

Fig. 3 Photograph of an augmentation model (cement used: Zn-GPC B) after 1 million load cycles in the compression fatigue life test

the values for different cements should be cautious. To apply this suggestion in the present case, it is safe to say that, on the basis of the injectability results, SIMPL is more attractive, while on the basis of the radiopacity results, the Zn-GPCs are more attractive. As far as the UCS results are concerned, it may be that the Zn-GPCs are more attractive because their strengths are closer to that of osteoporotic cancellous bone, taken to be 0.5–5.8 MPa [30]. (This value is for cancellous bone taken from the femoral heads of patients with osteoporosis, but all the indications are that these values are applicable to cancellous bone from vertebral bodies of osteoporotic patients [31].) With regard to the E_b results, it may be that a value close to that of osteoporotic vertebral cancellous bone (taken to be 50–420 MPa [30], with the same caveat as stated above for the strength values) may be desirable as this may reduce modulus mismatch between the cement and the bone and, hence, reduce the potential for compression fractures of VBs adjacent to VB(s) augmented using VP or BKP [32]. If these postulates regarding UCS and E_b are accepted as being plausible, then, the Zn-GPCs are more attractive than SIMPL.

The second point is that properties of the Zn-GPCs are comparable to those of some cements that are now used in VP and BKP. For example, UCS of Zn-GPC B, after 1 d aging in distilled water at 37°C, is 63.4 ± 2.8 MPa (Table 2), a level that is about the same as that for KyphOs FS™ (Medtronic Spinal and Biologics, Sunnyvale, CA, USA), a CaP cement that is approved for BKP in Europe (61 ± 6 MPa after 1 d in water, at 37°C [33].

The third point to consider is that the results for other cement properties, as presented in previous relevant

literature reports, should be taken into account. For example, it has been reported that (1) the Zn-GPCs form amorphous CaP layers on their surfaces, suggesting that these cements are bioactive [34]; in contrast, SIMPL is not bioactive by nature [35] and (2) strontium ions are released from the Zn-GPCs [17] and these ions may contribute to the formation of healthy bone even in osteoporotic patients [36], whereas SIMPL makes no such contribution.

The case for the appropriateness and clinical relevance of the augmentation model employed in the present compression fatigue life testing is based on seven aspects, among which are (1) the similarity of some relevant mechanical properties of the foam to those of cancellous bone and of the mechanical properties of the model to those of fractured cadaveric VBs that are augmented using VP or BKP; (2) the value of V_c used in the present study (8%) being within the range used in VP and BKP; (3) the magnitude of the maximum applied load used (2300 N) translating to a stress that is within the compressive stresses measured on lumbar vertebrae during normal activities of daily living; and (4) the "run-out" point selected (1 million cycles) translating to an estimated in vivo time that is 110–201% longer than the period over which bone healing of a fractured VB augmented using VP is expected to occur. Expositions on these and the other three aspects have been given in a previous report [15]. Furthermore, the issue of the validation of the augmentation model as well as limitations of the compression fatigue life studies, namely, that (1) in the augmentation model, the cement cylinder was flush with the foam cube rather than being embedded in it and (2) the sample size was small, have been addressed in detail in a previous report [15].

The specimens in the compression fatigue life work were tested after aging in PBS, at 37 ± 1°C, for 24 ± 1 h. There are no standards for testing constructs; however, this aging time is considered appropriate in that this time is commonly used in ex vivo biomechanical tests in which compression fractures are created in osteoporotic cadaveric VBs and then augmented using simulated VP or BKP [37, 38]. Furthermore, the aging time used is consistent with clinical practice in which once the procedure is completed, the patient is made to remain rested for several hours [39]; in other words, the aging time used ensured that any mechanical properties determined for the augmentation model are a plausible reflection of the mechanical integrity of the VP- or BKP-augmented VB in a patient at the end of the first day post-procedure.

The study results do not support the first hypothesis but do support the second. Thus, the question as to whether or not a Zn-GPC has potential for use in VP and BKP, in place of SIMPL, must be resolved with the aid of a methodology that recognizes tradeoffs between properties. We suggest the use of a materials selection methodology that utilizes the weighting factor concept [40]. In this case, we used the following steps: (1) each of the four cement properties determined was assigned a weighting factor of 1.0; (2) the compression fatigue life was assigned a factor of 2.0, reflecting its comparatively higher significance; (3) the cements were ranked based on the performance on each property (best, second best, and third best performances are worth 10, 6, and 3 points, respectively). For I and R, the higher the value for a cement is the higher is its rank. Based on our discussion points on UCS and E_b given above, we decided that, for each of these properties, the closer the value for a cement is to that of osteoporotic cancellous bone, the higher is its rank. Using this scheme, SIMPL, Zn-GPC A, and Zn-GPC B have total weighted points of 42, 56, and 48, respectively. In other words, the overall performance of each of the Zn-GPCs is comparable to that of SIMPL.

Future work should include (1) manipulation of the composition of the Zn-GPCs to increase setting time without adversely affecting cement mechanical properties; (2) determination of the histological features relevant to bone remodeling and resorption when the Zn-GPCs are used in an animal model (for example, to fill bone voids surgically created in L2 of skeletally mature sheep spines); and (3) determination of the comparative compression fatigue life performance of the three cements used in the present study using osteoporotic cadaveric VBs, with compression fractures created and then augmented using simulated VP in one series and simulated BKP in the other.

5 Conclusion

On the basis of the results of the four cement properties determined as well as the predicate performance of the augmentation model in the compression fatigue life tests regardless of the cement used, each of the novel glass polyalkenoate cements evaluated has the potential of being used in vertebroplasty and balloon kyphoplasty, instead of a PMMA bone cement, and, therefore, merits further study.

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