J Mater Sci: Mater Med (2010) 21:53–58
DOI 10.1007/s10856-009-3844-8

Evaluation of a novel radiopacifiying agent on the physical properties of surgical spineplex®

D. O'Brien · D. Boyd · S. Madigan · S. Murphy

Received: 26 June 2009 / Accepted: 27 July 2009 / Published online: 18 August 2009

Abstract Polymethlylmethacrylate (PMMA) is the most frequently used cement for percutaneous vertebroplasty and kyphoplasty. To aid visualisation during surgery cements are doped with radiopacifying agents such as Barium sulphate (Ba_2SO_4) or Zirconium Dioxide (ZiO_2). Mounting research suggests that these agents may impair the biocompatibility of the cements. However, incorporating an alternative radiopacifier agent with excellent biocompatibility would be a significant step forward. Bioactive radiopaque glasses incorporating elements such as strontium (Sr) and zinc (Zn), known to have beneficial and therapeutic effects on bone, are of great interest in this respect. In this study, the Ba_2SO_4 of the commercially available Spineplex® was incrementally replaced with a radiopaque therapeutic glass composition. The resulting effects on cement setting time, peak isotherm, ultimate compressive strength, Young's modulus (up to 30 days cement maturation) and radiopacity were evaluated. The substitution lead to an increase in cement setting time from 13.1 mins for Spineplex® to 16.6–18.3 mins for the glass substituted cements. The peak exotherm during curing was reduced from 74°C for Spineplex® to a minimum of 51°C for the fully substituted cement, indicating that reduced thermal necrosis in the in vivo setting is likely with these materials. Ultimate compressive strength and Young's modulus of each formulation showed no significant deterioration due to the substitution. Finally, the radiopacity of the substituted cements were reduced by up to a maximum of 18% in comparison to the control. However, the experimental formulations still maintained radiopacity equivalent to several millimetres of aluminium. As such the substituted cements had substantial equivalence to the Spineplex® control. In order to assess the clinical relevance of these findings further investigation is warranted.

1 Introduction

Percutaneous vertebroplasty (PVP) and kyphoplasty (KP) are surgical interventions designed to treat the pain associated with acute vertebral body compression fractures (VCFs) [1–4], such as those which are secondary to trauma due to osteoporosis of the spine, or insufficiency fractures secondary to osteoporosis or other lytic conditions. Both techniques require the percutaneous injection of a bone cement into the cancellous bone of the vertebral body via cannulas inserted through the pedicles of the specified vertebrae [5, 6]. Presently, acrylic bone cements (typically polymethylmethacrylate (PMMA)) are most frequently employed to stabilize such fractures [7].

Amongst the PMMA acrylic bone cements (ABCs) used, all include pre-polymerized poly (methyl methacrylate) (PMMA) beads, and either $BaSO_4$ or ZrO_2 particles as a radiopacifier, and most of them contain the accelerator is N,N dimethyl-*p*-toluidine (DMPT) [8, 9]. Whilst the side-effects associated with some of the cement constituents (monomer, activator, etc.) are debated in the literature [10] there is an ongoing concern regarding the suitability of the

D. O'Brien · D. Boyd (✉) · S. Murphy
Medical Engineering Design Innovation Centre (MEDIC), Cork Institute of Technology, Rossa Ave., Bishopstown, Co. Cork, Ireland
e-mail: daniel.boyd@cit.ie

S. Madigan
Stryker Orthopaedics, Raheen Business Park, Limerick, Ireland

radiopacifying agents $BaSO_4$ and ZrO_2 [11]. Certain reports have highlighted the deleterious effects, such as bone resorbtion [12], and degradation of mechanical properties [13] associated with standard radiopacifiers. Moreover, in the current paradigm where emphasis is placed on therapeutic and regenerative medicine in the context of biomaterials, it is clear that such radiopacifiers are contrary to preference. Thus, there is ongoing research on modifying the compatibility of commercially-available ABCs by altering compositions with potentially therapeutic radiopacifiers [14, 15].

Glasses have an extensive clinical history as hard tissue biomaterials, due in particular to their ability to facilitate a direct bond with bone and tooth mineral via controlled surface modification in vivo [16], and their ability to upregulate specific genes associated with osteoneogenesis [17]. However, glass materials also form the basis for such implants as glass polyalkenoate cements and resin-modified polyalkenoate cements in dentistry where the glass composition is designed to impart bioactivity, whilst conferring inherent radiopacity of the implant [18–20]. Consequently, bioactive glass fillers have been used in BIS-GMA materials for implantation in the spine where such inclusion have been associated with the formation of a direct bond between bone and cement [21].

The authors have been engaged in the development and evaluation of novel bioactive glass compositions [22] which are capable of releasing therapeutic ions at clinically beneficial levels under physiological conditions [23]. The ions in question are strontium (Sr^{2+}) and zinc (Zn^{2+}); both of which are known to have potent beneficial effects on the metabolic activity of osteoporosis and as antibacterial agents respectively. Zn^{2+} has been shown to stimulate fracture healing by enhancing osteoblast differentiation [24] and increasing osteoblast DNA content [25]. Zn^{2+} ion release from biomaterials has also been shown to have antibacterial efficacy killing many bacterial strains commonly associated with infection after orthopaedic surgery [26]. Synergistically, Sr^{2+} has been shown to have a dual mode of action increasing bone formation by osteoblasts while simultaneously decreasing bone resorption by osteoclasts [27] and is currently in use as an osteoporosis treatment in the form of Strontium Ranelate [28].

Thus, the objective of this work is to incrementally replace the radiopacifying agent (Ba_2SO_4) of a commercial ABC (Spineplex®) with a radiopaque glass composition associated with excellent biocompatibility [22] and an ability to deliver clinically beneficial amounts of therapeutic ions into its local environment [23]. The effects of these substitutions on the physical properties, and radiopacity of the resultant ABCs is reported.

2 Materials and methods

2.1 Materials

2.1.1 Glass synthesis

A strontium–calcium–zinc–silicate glass formulation (Table 1) was synthesized. The glass was prepared by weighing out appropriate amounts of analytical grade reagents (Sigma-Aldrich, Dublin, Ireland) and ball milling for 1 h. The mixes were then dried in an oven (100°C, 1 h), then fired (1480°C, 1 h) in a Pt crucible and shock quenched into water. The resulting frit was dried, ground and sieved to retrieve a glass powder with a maximum particle size of 45 μm.

2.1.2 Acrylic bone cements (ABCs)

The compositions of the commercially-available cement (Surgical Spineplex®; Stryker, Limerick, Ireland) and three variant formulations are given in Table 2. For each variant formulation the powder was prepared by using a pestle to thoroughly mix all the constituents in a ceramic mortar and then passing the mixture three times through a fine sieve (180 m) to obtain a homogeneous powder, which was then stored in a vacuum-wrapped plastic package; and 2) the liquid monomer (methylmethacrylate: 19.5 mls/N,N-dimethylparatoulidine: 0.5mls/Hydroquinone: 1.5 mg) was prepared by mixing all the reagents in a screw-top glass jar, which was then sealed tightly.

2.2 Methods

2.2.1 Scanning electron microscop (SEM)

A Hitatchi TM-1000 SEM was used to examine the morphology and size of the BT112 glass and the Ba_2SO_4

Table 1 Glass composition (mol. fraction)

Glass	SiO_2	ZnO	CaO	SrO	NaO
BT112	0.40	0	0.10	0.20	0.30

Table 2 Compositions of cement powders (g)

Cement designation	PMMA (g)	MMA (g)	BaSO4 (g)	BT112 (g)
ABC (commercial spineplex®)	4.7	23.3	12	0
ABC 1	4.7	23.3	8	4
ABC2	4.7	23.3	4	8
ABC 3	2.7	23.3	0	12

radiopacifiers. Powders were adhered to double sided carbon tabs and images were generated using back scattered electrons at an accelerating voltage of 15 kV.

2.2.2 Cement mixing method

For the determination of all the properties of the cured cement, the respective powders (Table 2) were mixed with 20 ml of liquid monomer were mixed, in a polyethylene bowl, using an open-bowl technique (hand/manual mixing) in the ambient laboratory (temperature and relative humidity was recorded as 22 ± 1°C and 60 ± 20%, respectively).

2.2.3 Determination of setting time and peak exotherm

Setting time and maximum exotherm temperature were determined, in ambient laboratory air (22 ± 1°C), with all experimental steps and data treatment methods being as specified in ISO 5833 [38]. The thermocouple was connected to a temperature-time recorder (Eurotherm Chessel Recorder, Model #4102c; Eurotherm, Dublin, Ireland). For each of the 24 cements, the test was run in duplicate.

2.2.4 Determination of time dependant compressive strength and Young's modulus

The ultimate compressive strength (UCS) of cement compositions was determined according to ISO 5833 [38], whilst the modulus of was recorded (molded solid cylindrical test specimens of nominal diameter and height = 6 and 12 mm, respectively). Specimens (n = 5) of each compositions were incubated in tissue culture water at 37°C for 1, 7 and 30 days then tested using a universal materials testing machine (Model 5833, Instron, Inc., High Wycombe, Bucks, UK) at a cross-head speed of 20 mm min^{-1} which was equipped with a 5 kN load cell.

2.2.5 Statistical analysis

Compression and Young's modulus results were analyzed using Graphpad prism 4 software (Graphpad software Inc). Results are expressed as mean ± standard error of the mean. Analysis of the results was carried out using Student's *t*-test, with a significance level of $P < 0.05$.

2.2.6 Determination of radiopacity

Cement discs were produced in a similar fashion to the biaxial flexural strength discs. Once removed from their moulds the specimens were ground using 1200 grit silicon carbide paper until they were 1 mm thick (15 ± 0.2 mm diameter). The radiopacity of each material was determined by irradiating specimens alongside an aluminium step wedge (12 steps, 1 mm per step) at a distance of 400 mm under 60 kV and 2.5 mA. Specimens were exposed on an AGFA CR 85×/MD4.0 plate. The radiopacity of each specimen was determined by plotting a standard curve of SAL^2 versus thickness of aluminium. The corresponding SAL^2 value for each specimen was superimposed on the standard curve and the equivalent thickness of Aluminium was recorded.

3 Results

Figure 1 shows the morphology and approximate size differential between the radiopacifiers examined in this work. The particles of BT112 are typically in the range 0–45 μm and are of random morphology. Conversely the Ba_2SO_4 are demonstrable smaller particles (2–4 μm) which are present in agglomerated form in the powder.

The setting time (S_t) for surgical Spineplex® was recorded as 13.1 min, and its peak exotherm was 74°C. However, total replacement of Ba_2SO_4 with BT112 resulted in a 26% increase in S_t to 16.6 min and a 31% decrease in peak exotherm to 51°C.

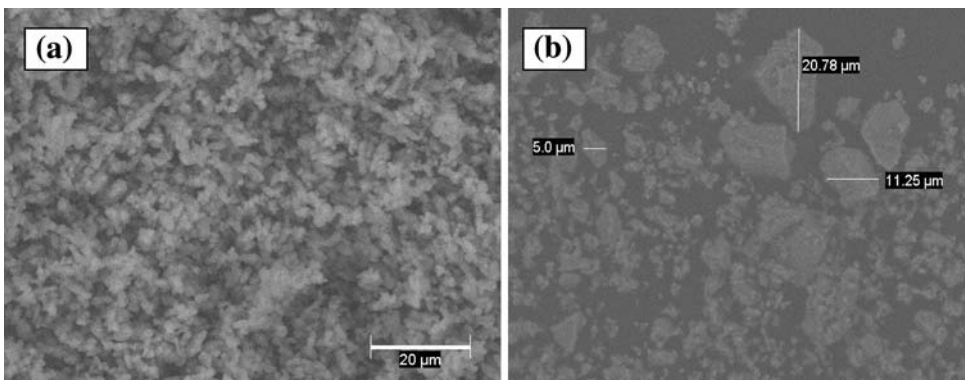

Fig. 1 SEM images of **a** Ba_2SO_4 at ×8000 and **b** BT112 at ×2000 powders used in this study

The UCS of the ABCs was not significantly altered as a result of the substitution, with the mean UCS of each group remaining above the threshold of 70 MPa as required for a load bearing orthopaedic cement [29]. Additionally the results confirm UCS of each ABC is not significantly altered up to 30 days.

The E values of the ABCs examined illustrate that no significant changes occur as a result of the substitution of Ba_2SO_4 for BT112, and as observed with the compressive strength the mean E of each is not significantly altered as a function of incubation time up to 30 days.

The radiopacity (as a function of equivalent thickness of aluminum) of surgical Spineplex® was recorded as 7.32 mm. The complete replacement of Ba_2SO_4 with BT112 resulted in a 13% decrease in radiopacity to 6.34 mm.

4 Discussion

The results associated with the S_t and peak exotherm indicate a beneficial effect associated with the substitution Ba_2SO_4 with BT112. Firstly, the increased setting times associated with the substitution can be deemed advantageous in the context of current surgical procedures where delivery of cement under fluoroscopy is a function of the S_t of the cement. Presently, procedures must be performed as quickly as possible to prevent the premature hardening of the cement within the delivery system which can lead to suboptimal placement/underfilling of vertebrae [30]. The optimal S_t for such cements is regarded to be 15 min. approx. [31], such that incidences of extravasation and errant deposition of the cement in the vertebral body can be avoided. Indeed, it should be pointed out that working times of up to 18 min are preferable given current surgical practices. From this perspective the results (Table 3) presented herein demonstrate an improvement in the working time of surgical Spineplex® from 13.1 min, which seems to be suboptimal based on current opinion [31], to between 16.6 and 18.3 min when BT112 is substituted into the formulation.

Further to the improvements in S_t, the formulations ABC1, ABC2 and ABC3 have peak exotherms considerably lower than that of the control material ABC, in fact a reduction from 74 to 51°C is reported for ABC3 (Table 3). The literature pertaining to the effect of the exotherm is conflicted. Some authors report that the high curing exotherm associated with PMMA has palliative effects as a result of damage to intraosseous neural tissue [32], whilst others have demonstrated (in a baboon model) only a few segments of necrotic bone present in augmented vertebrae [33]. Nevertheless, the general consensus in the literature is that achieving the lowest possible exotherm is an important feature in the development of novel cements [31, 34]. As such the reduction in peak exotherm associated with ABC1, ABC2, and ABC3 is a positive finding and indicates that reduced thermal necrosis is likely to be associated with the experimental materials in vivo.

From a mechanical standpoint the literature pays significant attention to compressive strength and modulus of the material [31]. Injectable bone cements must allow for immediate reinforcement of the augmented vertebrae, with concomitantly sustained strengths for the life of the implant; the preferred UCS for such materials is in the range 70–100 MPa [21]. Figure 2 illustrates that bone cement compositions examined in this work are all of the order required for successful performance of vertebral cements. Furthermore, the substitutions had no significant effect on the performance of the materials as compared with the commercial control indicating substantial equivalence between the materials. Some statistically significant results were obtained for UCS (Table 4) when BT112 doped

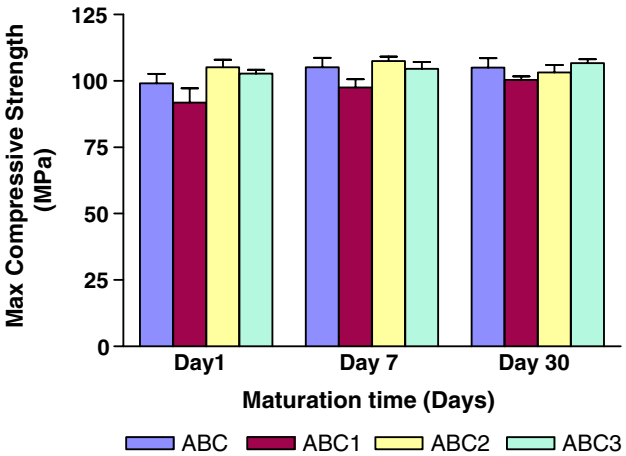

Fig. 2 UCS as a function of composition and maturation time

Table 3 Setting times (S_t) and peak exotherm values for cements

Cement designation	S_t (min)	Peak exotherm (°C)
ABC (commercial spineplex®)	13.1	74
ABC 1	17.9	63
ABC2	18.3	64
ABC 3	16.6	51

Table 4 Radiopacity of each composition (expressed as equivalent thickness of aluminum)

Cement designation	Equivalent thickness of aluminiumm (mm))
ABC (commercial spineplex®)	7.32
ABC1	6.52
ABC2	6.00
ABC3	6.34

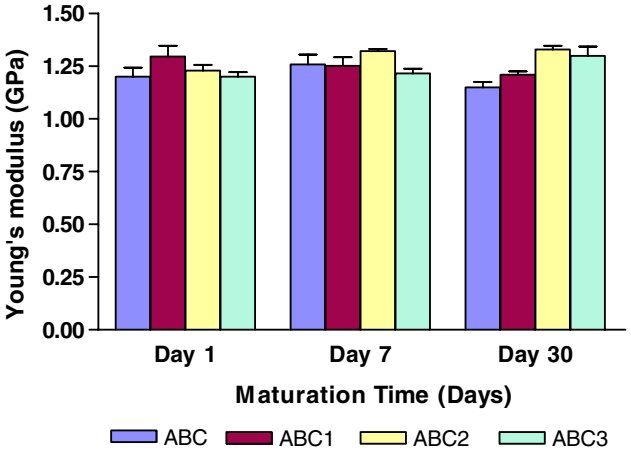

Fig. 3 Young's modulus as a function of composition and maturation time

Table 5 Statistically significant differences within the UCS results

Compression	*P* value	Comment
Day 30 ABC1 V Day 30 ABC3	0.0133	ABC3 has greater UCS
Day 7 ABC1 V Day 7 ABC2	0.0263	ABC2 has greater UCS

cements are compared. The explanation for such differences however remains unclear. In respect of the stiffness of the cements examined the results (Fig. 3 and Table 5) show that no significant change in modulus occurs between the commercial control and experimental formulations. However as with UCS data some significant differences in E were recorded between experimental groups. Nevertheless the data clearly illustrates biomechanical equivalence between the experimental materials and the commercial control. The effect of cements on vertebral stiffness post augmentation has induced considerable debate in the literature. Data available in the literature point toward vertebral augmentation resulting in increases in overall stiffness of the vertebral body [35–38], others report decreases in overall stiffness [39], whilst other literature indicates no change in stiffness of the vertebral body post-augmentation [40]. The variations reported are likely due to a number of factors including variation in method (prophylactic or fracture stabilization), region of the spine, percentage fill, and natural variations in bone quality. Irrespective of this data however, and on the basis of the performance of the experimental bone cements versus the commercial control it can be inferred that the compositions ABC1, ABC2 and ABC3, comprising a therapeutic filler, will demonstrate a level of performance comparable to the commercial control.

Aside from the properties already discussed however, it is important to state that the pre-requisite property for injectable bone cements is high radiopacity. This is required such that the surgeon can clearly monitor cement flow and prevent extravasation during surgery. In this work the standard radiopacifier Ba_2SO_4 was incrementally replaced with BT112 bioactive glass and the radiopacity of each formulation was recorded. It was found (Table 6) that such substitutions did negatively impact on the radiopacity of the cement, and in the most extreme case (ABC2) reduced the radiopacity of the cement by 18% versus the commercial control. However, it should be pointed out that the radiopacity of the experimental cement had a radiopacity equivalent to several millimeters of aluminum and as such have sufficient radiopacity for successful roentgenographic guided placement of the cement.

Table 6 Statistically significant differences between moduli

Young's modulus	*P* value	Comment
Day 7 ABC2 vs. Day 7 ABC3	0.0022	ABC2 has greater E
Day 30 ABC vs. Day 30 ABC2	0.0006	ABC2 has greater E
Day 30 ABC vs. Day 30 ABC3	0.0202	ABC3 has greater E
Day 30 ABC1 vs. Day 30 ABC2	0.0012	ABC2 has greater E
Day 1 vs. Day 7 ABC2	0.0128	Day 7 has greater E
Day 1 vs. Day 30 ABC2	0.0157	Day 30 has greater E

Additionally it should be pointed out that during experimentation it was noticed that the substitutions of Ba_2SO_4 for BT112 resulted in a striking transient colour transformation (from white (ABC) to bright blue (ABC1-3)) during the dough time of the cement. The colour change also became more striking as more glass was incorporated at the expenses of Ba_2SO_4. The reason for this change is unclear at present but will be evaluated in future work.

5 Conclusions

The collection of results indicate that it is possible to substitute the conventional radiopacifier Ba_2SO_4 from surgical Spineplex® and replace it with a glass known to therapeutic capabilities and that such substitutions will:

1. increase the S_t of the cement.
2. reduce the peak exotherm associated with cement curing.
3. not significantly alter the biomechanical properties (UCS and E) of the cement.
4. reduce radiopacity, though still leaves the cement highly radiopaque.

However, further research will be necessary to evaluate the fracture toughness of the experimental cement compositions, as well as their biocompatibility particularly the ion release profiles (Sr^{2+} and Zn^{2+}) from the experimental cement compositions.

References

1. Weill A, Chiras J, Simon JM, Rose M, SolaMartinez T, Enkaoua E. Spinal metastases: indications for and results of percutaneous injection of acrylic surgical cement. Radiology. 1996;199:241–47.
2. Mathis JM, Barr JD, Belkoff SM, Barr MS, Jensen ME, Deramond H. Percutaneous vertebroplasty: a developing standard of care for vertebral compression fractures. Am J Neuroradiol. 2001; 22:373–81.
3. Deramond H, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results. Radiol Clin North Am. 1998;36:533–46.
4. Garfin SR, Reilley MA. Minimally invasive treatment of osteoporotic vertebral body compression fractures. Spine J. 2002;2:76–80.
5. Soin A, Kapural L, Mekhail N. Imaging for percutaneous vertebral augmentation. Tech Reg Anesth Pain Manag. 2007;11:90–94.
6. Carlier RY, Gordji H, Mompoint DM, Vernhet N, Feydy A, Vallee C. Osteoporotic vertebral collapse: percutaneous vertebroplasty and local kyphosis correction. Radiology. 2004;233: 891–8.
7. Jasper LE, Deramond H, Mathis JM, Belkoff SM. Material properties of various cements for use with vertebroplasty. J Mater Sci: Mater Med. 2002;13:1–5.
8. Lewis G. Properties of acrylic bone cement: state of the art review. J Biomed Mater Res. 1997;38:155–82.
9. Breusch SJ, Kuhn KD. Bone cements based on polymethylmethacrylate. Orthopade. 2003;32:41–50.
10. Demian HW, McDermott K. Regulatory perspective on characterization and testing of orthopedic bone cements. Biomaterials. 1998;19:1607–18.
11. Wang JS, Diaz J, Sabokbar A, Athanasou N, Kjellson F, Tanner KE, et al. In vitro and in vivo biological responses to a novel radiopacifying agent for bone cement. J R Soc Interface. 2005;2:71–8.
12. Sabokbar A, Fujikawa Y, Murray DW, Athanasou NA. Radioopaque agents in bone cement increase bone resorption. J Bone Joint Surg Br Vol. 1997;79B:129–34.
13. Bhambri SK, Gilbertson LN. Micromechanisms of fatiguecrack initiation and propagation in bone cements. J Biomed Mater Res. 1995;29:233–7.
14. Lewis G, Xu J, Madigan S, Towler MR. Influence of strontia on various properties of surgical Simplex P acrylic bone cement and experimental variants. Acta Biomater. 2007;3:970–9.
15. Hernández L, Fernández M, Collía F, Gurruchaga M, Goñi I. Preparation of acrylic bone cements for vertebroplasty with bismuth salicylate as radiopaque agent. Biomaterials. 2006;27:100–7.
16. Bohner M, Lemaitre J. Can bioactivity be tested in vitro with SBF solution? Biomaterials. 2009;30:2175–9.
17. Hench LL. Genetic design of bioactive glass. Amsterdam: Elsevier Sci Ltd; 2009.
18. Shah PMM, Sidhu SK, Chong BS, Ford TRP. Radiopacity of resin-modified glass ionomer liners and bases. J Prosthet Dent. 1997;77:239–42.
19. Dabsie F, Gregoire G, Sixou M, Sharrock P. Does strontium play a role in the cariostatic activity of glass ionomer? Strontium diffusion and antibacterial activity. J Dent. 2009;37:554–9.
20. Glass-ionomer fluoride release to adjacent caries *Dental Abstracts* 2009; **54:** 149.
21. Erbe EM, Clineff TD, Gualtieri G. Comparison of a new bisphenol-a-glycidyl dimethacrylate-based cortical bone void filler with polymethyl methacrylate. Eur Spine J. 2001;10:S147–52.
22. Boyd D, Carroll G, Towler MR, Freeman C, Farthing P, Brook IM. Preliminary investigation of novel bone graft substitutes based on strontium-calcium-zinc-silicate glasses. J Mater Sci: Mater Med. 2009;20:413–20.
23. Murphy S, Boyd D, Moane S, Bennett M. J Mater Sci: Mater Med 2009; **in press**.
24. Jenni BJL, Popp R, Goldstein AS. JEffect of soluble zinc on differentiation of osteoprogenitor cells. Biomed Mater Res A. 2007;81A:766–9.
25. Chen D, Waite L, Pierce W. In vitro effects of zinc on markers of bone formation. Biol Trace Elem Res. 1999;68:225–34.
26. Boyd D, Li H, DA T, Towler M, Wall J. The antibacterial effects of zinc ion migration from zinc-based glass polyalkenoate cements. J Mater Sci: Mater Med. 2006;17:489–94.
27. Zhu L-L, Zaidi S, Peng Y. Induction of a program of gene expression during osteoblast differentiation with strontium ranelate. Biochem Biophys Res Commun. 2007;355:307–11.
28. Bonnelye E, Chabadel A, Saltel F, Jurdic P. Dual effect of strontium ranelate: stimulation of osteoblast differentiation and inhibition of osteoclast formation and resorption in vitro. Bone. 2008; 42:129–38.
29. International Standard 5833:2002. Implants for surgery acrylic resin cements. Geneve, Switzerland: International Organization for Standardization.
30. Chavali R, Resijek R, Knight SK, Choi IS. Extending polymerization time of polymethylmethacrylate cement in percutaneous vertebroplasty with ice bath cooling. Am J Neuroradiol. 2003; 24:545–46.
31. Lewis G. Injectable bone cements for use in vertebroplasty and kyphoplasty: state of the art review. J Biomed Mater Res B Appl Biomater. 2006;76B:456–468.
32. Deramond H, Wright NT, Belkoff SM. Temperature elevation caused by bone cement polymerization during vertebroplasty. Bone. 1999;25:17S–21.
33. Kovacic J, Lieberman IH, Togawa D, Bauer TW, Brodke D, Reinhart MK. The behavior of polymethylmethacrylate during kyphoplasty and vertebroplasty in the primate spine—a gross and histologic analysis. Spine J. 2003;3:79.
34. Heini PF, Berlemann U. Bone substitutes in vertebroplasty. Eur Spine J. 2001;10:S205–13.
35. Lim TH, Brebach GT, Renner SM, Kim WJ, Kim JG, Lee RE, Andersson G. B. J, An HS. Biomechanical evaluation of an injectable calcium phosphate cement for vertebroplasty; 2002.
36. Heini PF, Berlemann U, Kaufmann M, Lippuner K, Fankhauser C, van Landuyt P. Augmentation of mechanical properties in osteoporotic vertebral bones–a biomechanical investigation of vertebroplasty efficacy with different bone cements. Eur Spine J. 2001;10:164–71.
37. Belkoff SM, Mathis JM, Jasper LE, Deramond H. The biomechanics of vertebroplasty. The effect of cement volume on mechanical behavior. Spine. 2001;26:1537–41.
38. Molloy S, Mathis JM, Belkoff SM. The effect of vertebral body percentage fill on mechanical behaviour during percutaneous vertebroplasty. Spine. 2003;28:1549–4.
39. Belkoff SM, Mathis JM, Erbe EM, Fenton DC. Biomechanical evaluation of a new bone cement for use in vertebroplasty. Spine. 2000;25:1061–64.
40. Higgins KB, Harten RD, Langrana NA, Reiter MF. Biomechanical effects of unipedicular vertebroplasty on intact vertebrae. Spine. 2003;28:1540–7.