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Influence of two changes in the composition of an acrylic bone cement on its handling, thermal, physical, and mechanical properties

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Abstract This study is a contribution to the growing body of work on the influence of changes in the composition of an acrylic bone cement on various properties of the curing and cured material. The focus is on one commercially-available acrylic bone cement brand, Surgical Simplex®P, and three variants of it and a series of properties, namely, setting time, maximum exotherm temperature, activation energy and frequency factor for the polymerization reaction, diffusion coefficient for the uptake of phosphate buffered saline, at 37 °C, ultimate compressive strength (UCS), plane-strain fracture toughness, fatigue life (under fully-reversed tension-compression stress), hardness (H) and elastic modulus (both determined using quasi-static nanoindentation), and the variation of the storage and loss moduli with frequency of the applied force in a dynamic nanoindentation test. It was found that (a) a 68% reduction in the volume of the activator, *N*,*N* dimethyl-4-toluidine, relative to the total volume of the liquid monomer (the amounts of all the constituents in the powder and of the hydroquinone in the liquid monomer remaining unchanged) led to, for example, a significant decrease in the rate of the polymerization reaction, at 37 °C (c′) and a significant increase in H; and (b) the elimination of the pre-polymerized poly (methyl methacrylate) beads in the powder (the amounts of all the other powder constituents and those of the liquid monomer remaining unchanged) led to, for example, a significant drop in c′ and a significant increase in UCS. Thus, these findings suggest a strategy for optimizing the composition of an acrylic bone cement.

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Introduction

Acrylic bone cement is widely used in orthopaedic surgery; specifically, for anchoring total joint replacements (especially, primary hip implants in many European countries [1] and primary knee implants in the US [2]) as well as in the stand-alone augmentation of osteoporotic vertebral compression fractures (vertebropasty and kyphoplasty) [3]. Although there are a large number of commercially-available acrylic bone cement brands that are used in these procedures, there are many similarities in composition between them. For example, all of them have pre-polymerized poly (methyl methacrylate) [PMMA] beads in the powder and, in most of them, the activator of the polymerization reaction is *N*,*N*-dimethyl-4-toluidine (DMPT) [4]. There are issues with these two reagents. Pre-polymerized PMMA beads in the cement powder act as polymerization sites and influence the rate of the polymerization process [5], although they do not influence thermal or chemical necrosis [6]. To the best of the authors' knowledge, only Madigan et al. [7] have reported on the influence of the amount of pre-polymerized PMMA beads on cement properties, but only three properties (setting time, t_{set}, maximum exotherm temperature, T_{max}, and ultimate compressive strength, UCS) were determined.

It has been suggested that the residual DMPT concentration in cement mantles of retrieved cemented hip arthroplasties, even after 10 year post implantation, is high

enough to be of concern [8], and, if the DMPT leaches out of the mantle, it may produce many deleterious effects in the patient, such as cytotoxicity of cell replication [9] and damage to chromosomes [10]. Thus, the options are either to replace DMPT with an alternative agent or to minimize its content. There have been many detailed characterizations of cements that include alternative activators, examples being 4,4-dimethylamino benzydrol [11], *N*,*N*-dimethylamino-4-benzyl oleate [12], and *N*,*N*-dimethylamino-4-benzyl laurate [12]. In contrast, much less research attention has been given to the impact of a reduction in the DMPT content on cement properties. Studies on this topic are limited in the sense that, in some cases, a radiolucent cement was used [13–15] and, in others, a radiopaque cement was used but only a few properties were determined [7, 16, 17].

At this point in time, all cement brands in which DMPT is replaced with an alternative activator are experimental formulations in the sense that the relevant regulatory authority, such as the US Food and Drug Administration (FDA) and the UK Medical Devices Agency, has not approved them for clinical use. (The only exception is Duracem^{TM}3/Sulcem^{TM}3 (Sulzer Orthopaedics Ltd., Barr, Switzerland), in which the activator is 2-[4-dimethylamino)phenyl]ethanol [4].) Thus, for now, studies on the influence of the amount of the pre-polymerized PMMA beads and of the activator on cement properties should concentrate on cement brands that contain DMPT. Such an investigation is carried in the present study, with the cement brand used being one that is widely employed in cemented arthroplasty, vertebroplasty, and kyphoplasty [3]. For this purpose, a wide collection of properties of the curing and the cured cement, as a function of the aforementioned changes in cement composition, was obtained. These properties include a sizeable proportion of those whose values must be included in applications that manufacturers of acrylic bone cements submit to a regulatory agency for pre-market approval [18], as well as those whose values have been reported in only two studies [19, 20]. The study should serve as an illustration of a methodology for optimizing the composition of an acrylic bone cement.

Materials and methods

Materials

The commercial Surgical Simplex®P (Howmedica International, Limerick, Ireland) formulation and three variants of it were used (Table 1). For each variant, 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 (sieve opening, 180 mm) to obtain a homogeneous powder, which was then stored in a vacuum-wrapped plastic package. The liquid monomer was prepared by mixing all the reagents in a screw-top glass jar, which was then sealed tightly.

For the determination of the properties of the cured cement, the powder and the liquid monomer were mixed using an open-bowl technique (hand/manual mixing) in the ambient laboratory (temperature and relative humidity of 22 ± 1 °C and 55 ± 2%, respectively).

Determination of handling properties

t_{est} and T_{max} were determined, in ambient laboratory air (23 ± 1 °C), with all experimental steps and data treatment methods being as specified in ISO 5833 [21]. The thermocouple was connected to a temperature–time recorder (Eurotherm Chessel Recorder, Model #4102c; Eurotherm, Dublin, Ireland). For each cement, the test was run in duplicate.

Table 1 Compositions[a] of the cements

Cement set name	Powder (g)				Liquid monomer (mL)		
	Co-polymer[b]	PMMA[c]	$BaSO_4$	BPO[d]	MMA	DMPT	HQ[e]
I[f]	29.4	6.0	4.0	0.6	19.50	0.50	80[d]
II	29.4	6.0	4.0	0.6	19.84	0.16	80[d]
III	35.4	0.0	4.0	0.6	19.50	0.50	80[d]
IV	35.4	0.0	4.0	0.6	19.84	0.16	80[d]

[a] BPO: benzoyl peroxide; MMA; methyl methacrylate; HQ: hydroquinone

[b] PMMA-styrene (Molecular weight, MW = 306,000 g mol^{-1})

[c] Pre-polymerized beads (MW = 974,000 g mol^{-1})

[d] 75 wt% activity

[e] In ppm

[f] This is the current formulation of the commercially-available cement

Differential scanning calorimetry (DSC) tests

Prior to running the DSC tests on the cements, the differential scanning calorimeter used (DuPont 910; Instrument Specialists, Inc., Spring Grove, IL, USA) was calibrated for heat of fusion, using a high-purity-grade indium standard. For each cement, the powder and liquid monomer were hand mixed in a polyethylene bowl, and then 3 mg of that mixture was immediately transferred to the Al sample pan in the calorimeter and then heated, at a predetermined rate from its initial temperature to a final temperature of 200 °C.

An Arrhenius relationship was assumed between the rate constant for the polymerization of the cement (c) [in s^{-1}], and its temperature during the polymerization, T; thus, we can write

$$c = Z \exp [- Q/(RT)], \quad (1)$$

where Z is the frequency factor (in s^{-1}), Q is the activation energy (in J mol^{-1}), and R is the molar gas constant (= 8.314 J mol^{-1} K^{-1}).

All details regarding the use of the data in the thermogram obtained to compute c (and, hence, Q, and ln Z) have been given previously [22]. At each heating rate, Q and ln Z were obtained, from which the overall means of these parameters were calculated. (For each powder, triplicate DSC runs were performed at each of four heating rates of 5, 10, 15, and 20 K min^{-1}). The polymerization reaction rate at 37 °C (which is taken to be the temperature of the prepared bed in which the polymerizing dough is placed by the surgeon during a cemented arthroplasty) [c′] was then computed using Eq. 1 and the overall means for Q and ln Z.

PBS uptake tests

The gain in the mass of a circular cross-sectioned cement disc specimen (nominal diameter and length 2.80 and 8.00 mm, respectively), which was immersed in 40 mL of phosphate buffered saline, PBS (Gibco Invitrogen Corp., Grand Island, NY, USA) solution at 37 ± 0.5 °C, was monitored continuously until there was no significant increase; that is, process equilibrium was reached.

The early stages of the uptake (a zone over which M_t/M_∞ is linear, which, usually, is $M_t/M_\infty < 0.6$), is describable by a reduced form of an applicable solution to Fick's Second Law of Diffusion (Stefan's approximation), which is [23]

$$\frac{M_t}{M_\infty} = \frac{4}{L}\left(\frac{Dt}{\pi}\right)^{1/2}$$

where M_t and M_∞ are the mass gains of the specimen after time, t, in the PBS solution, and at the equilibrium stage, respectively. Thus, D (the diffusion coefficient) was computed from the slope of the linear plot of M_t/M_∞ versus $\sqrt{t}$. For each cement, three specimens were tested.

Determination of bulk mechanical properties

The ultimate compressive strength (UCS) was determined according to ISO 5833 [21] (molded solid cylindrical test specimens of nominal diameter and height of 6 and 12 mm, respectively), using a servohydraulic universal materials testing machine (Model 111, Instron, Inc., High Wycombe, Bucks, UK) at a cross-head speed of 20 mm min^{-1}. For each cement, five specimens were tested.

The plane-strain fracture toughness (K_{IC}) of each cement was determined using two different methods. In the first, ASTM D 5045 rectangular cross-sectioned compact tension (RCT) fracture toughness (K_{Ic}) specimens (nominal width, thickness, and crack length = 37.17, 14.87, and 14.87 mm, respectively) [24] were molded, allowed to cure in the mold for 2 h, after which they were removed from the mold, lightly sanded, and then aged in ambient laboratory air for 28 days. After that, the K_{IC} tests were performed on them, in ambient laboratory air, using a custom-built servohydraulic universal materials testing machine, under displacement control, with a cross-head speed of 10 mm min^{-1}. All other test procedures and data analysis methods (especially criteria regarding the validity of the results) followed were as given in ASTM D 5045. For each cement, five specimens were tested. The second method involved pouring the cement dough into a steel rectangular cross-sectioned mold (nominal dimensions of 65 mm × 25 mm × 3 mm), allowing the resulting specimen to cure in the mold for about 1 h, removing it and fabricating a double-torsion (DT) test specimen (nominal depth of the sharp groove down the center of the specimen = 1 mm). The K_{IC} tests were performed after various periods of aging (1 day, 14 days, 28 days) of the fabricated specimen in ambient laboratory air. In the test, the specimen was immersed in water, at 37 ± 2 °C, in an environmental chamber that was supported on a fixture [two 3 mm-diameter parallel rollers 20 mm apart (with the center-groove on the bottom face)] that was, in turn, held firmly in a servohydraulic universal materials testing machine (Instron Model 111, Instron, Inc., High Wycombe, UK). The specimen was then loaded, using two 3 mm-diameter ball bearings at the notched end, at a cross-head speed of 0.1 mm min^{-1}. For each cement, five specimens were tested for each aging time.

For the fatigue tests, test specimen configuration and size, specimen preparation, specimen examination and, hence, selection for testing, and test procedures were all as detailed in ASTM F 2118–03 [25]. The specimens were subjected to a fully-reversed sinusoidal (tension-compression) cyclic

load, corresponding to a stress of ± 15 MPa, at a constant frequency of 2 Hz. The number of specimens rejected as a proportion of the total number of specimens molded were 45, 40, 45, and 45% for Cements I, II, III, and IV, respectively. For each cement, 12 specimens selected at random from the accepted specimens were tested, as recommended by Lewis and Sadhasivini [26]. The cycles to fracture, N_f, results were analyzed using the three-parameter Weibull method. A nonlinear minimization method contained in a commercially-available software (Matlab® Version 6.0, The MathWorks, In., Natick, MA, USA) was used to obtain estimates of (i) N_o (the minimum or guaranteed fatigue life), (ii) β (the Weibull shape factor), and (iii) N_a (the Weibull characteristic fatigue life). These estimates were then combined to compute an overall index of the material's fatigue performance, known as the Weibull mean, N_{WM}. [27], which is given by

$$N_{WM} = N_o + (N_a - N_o)\,\Gamma[1 + 1/\beta], \quad (3)$$

where Γ is the gamma function.

Thus, N_{WM} reflects both the magnitude of the fatigue life (i.e., N_o and N_a) and the variability or degree of scatter of the N_f results (i.e., β).

Quasi-static and dynamic nanoindentation tests

Molded specimens (nominally 45 mm × 12 mm × 5 mm bars) were stored in PBS, at 37 °C until they reached equilibrium mass (this took 23 ± 1 d) before the tests were performed using a commercially-available nanoindentation instrument (TriboIndenter®; Hysitron, Inc., Minneapolis, MN).

In the quasi-static test, the indenter was driven into the surface of the specimen at a constant loading rate of 30 μN s^{-1} until a peak load (P_m) of 260 μN was reached. The values of the hardness, H, and elastic modulus, E, were calculated using the Modified Slopes Method, MSM [28]. Further details about specimen preparation, the performance of the test, data acquisition, and the treatment of the data using MSM to obtain H and E for acrylic bone cement specimens have been given previously [19, 20]. For each cement specimen, the indenter load (P)-versus-indentation depth (h) measurements were made at 36 points on its surface that were selected (using an optical microscope that is housed in the nanoindentation instrument) to ensure that they were widely dispersed. Three specimens per cement were tested.

In the dynamic test, the indenter was driven, under computer control, toward the surface of the specimen, at a constant rate of 10 nm s^{-1}, until it contacted the surface. After contact, a small, constant oscillatory load of 15 μN, at a selected frequency, ω, was imposed. The values of the storage modulus (E′) and loss modulus (E″), at a given value of ω, were determined assuming that the head assembly of the instrument may be modeled as a simple damped harmonic oscillator [29]. Further details of specimen preparation, performance of the test, data acquisition, and the treatment of the data using the aforementioned model to obtain E′ and E″ for acrylic bone cement specimens have been given previously [20]. For each specimen, the values of the following parameters were obtained from the E′-versus-ω and E″ -versus-ω curves: maximum E′ and the ω at which it occurred; and minimum E″ and the ω at which it occurred. Three specimens per cement were tested.

Validation nanoindentation tests

Quasi-static and dynamic nanoindentation validation tests were performed on three specimens of poly (methyl methacrylate, PMMA (the polymer on which acrylic bone cement is based [Perspex®; Plastico, Inc., Memphis, TN]. Results of these tests and comments on them have been presented previously [19, 20].

Characterization of powders

The particle size distributions of the powder in Cement I (which is the current formulation of Surgical Simplex®P) and in the old formulation of Surgical Simplex®P were determined using a laser diffraction system (Sympatec Particle Size Analyzer, Model HDD200; Sympatec GmbH, Golar, Germany), while their morphologies were obtained using an environmental scanning electron microscope (Model XL30; Philips), operated at an acceleration voltage of 15 kV. All tests were run in triplicate.

Statistical analysis

The results for the cement properties were statistically analyzed using one-way ANOVA, with the Bonferroni correction (SAS®Version 8.02; SAS Institute Inc., Cary, NC, USA), with a value of $P < 0.05$ taken to be significant.

Results and discussion

Handling properties

The mean t_{set} and T_{max} values for all the cements (Table 2) are lower than the maximum limits, as stipulated in ISO 5833 [21] (except for t_{set} for Cement II). Differences seen in these results for Cement I (which is the current

Table 2 Summary of the values of the properties of the cements

Property	Cement I	Cement II	Cement III	Cement IV
Setting time, t_{set} (min)	11.2 ± 1.5	17.2 ± 1.5	9.3 ± 1.5	12.0 ± 1.5
Maximum exotherm temperature, T_{max} (°C)	71 ± 2	66 ± 2	76 ± 2	59 ± 2
Overall estimate[a] of activation energy, Q (kJ mol^{-1})	245 ± 19	211 ± 15	234 ± 22	263 ± 20
Overall estimate[a] of frequency factor, ln Z (Z in s^{-1})	92 ± 8	75 ± 7	81 ± 9	90 ± 7
Computed polymerization reaction rate,[b] c′ (s^{-1})	$(5.3 \pm 2.6) \times 10^{-2}$	$(1.6 \pm 1.3) \times 10^{-3}$	$(6.0 \pm 2.0) \times 10^{-5}$	$(7.1 \pm 4.0) \times 10^{-6}$
Diffusion coefficient, D (10^{-12} m^2 s^{-1})	4.84 ± 0.56	4.28 ± 0.20	8.98 ± 0.40	4.82 ± 0.54
Ultimate compressive strength, UCS (MPa)	88 ± 2	85 ± 3	100 ± 8	92 ± 2
Fracture toughness, K_{IC} (MPa$\sqrt{m}$), via RCTS[c]	1.71 ± 0.05	1.60 ± 0.02	1.70 ± 0.10	1.74 ± 0.07
- via DTS[d] (1 day[e])	2.14 ± 0.25	2.06 ± 0.21	2.37 ± 0.20	2.16 ± 0.22
- via DTS (14 days[e])	2.35 ± 0.24	2.13 ± 0.20	2.41 ± 0.23	2.27 ± 0.27
- via DTS (28 days[e])	2.48 ± 0.24	2.47 ± 0.13	2.93 ± 0.33	2.32 ± 0.26
Weibull minimum fatigue life, N_o (cycles)	4,367	426	1,214	400
Weibull characteristic fatigue life, N_a (cycles)	20,900	14,580	39,050	28,910
Weibull modulus, β	1.65	1.21	1.37	1.14
Weibull mean fatigue life, N_{WM} (cycles)	19,153	13,713	36,074	10,373
Hardness, H (MPa)	163 ± 9	187 ± 11	190 ± 13	197 ± 16
Elastic modulus, E (GPa)	3.59 ± 0.24	3.82 ± 0.22	3.66 ± 0.21	3.68 ± 0.09
Maximum storage modulus, E_h' (GPa)	6.17 ± 0.02	6.14 ± 0.01	6.18 ± 0.02	6.17 ± 0.02
Frequency at maximum storage modulus, ω_h (Hz)	137 ± 2	138 ± 3	136 ± 3	137 ± 2
Minimum loss modulus, E_l''((kPa)	390 ± 3	387 ± 2	391 ± 1	388 ± 2
Frequency at minimum loss modulus, ω_l((Hz)	81 ± 2	80 ± 1	81 ± 2	81 ± 2

[a] Calculated from all the estimates at all four heating rates

[b] Computed using Eq. 1, the overall means and standard deviations of Q and ln Z, and T = 310 K (37 °C)

[c] Rectangular cross-sectioned compact tension test specimens

[d] Double-torsion test specimens

[e] Aging time, in ambient laboratory air

formulation of Surgical Simplex®P) and those reported in the literature for hand-mixed old formulation of Surgical Simplex®P [4, 30, 31] are regarded to be marginal. Assuming that the ambient temperature of the room in which the tests were about the same in all cases, this finding suggests that, for these two formulations, differences in the powder particle size distribution (Fig. 1; for Cement I, this distribution is bimodal, with mean of 13.14 ± 0.12 μm, whereas for the old formulation, the distribution is unimodal, with mean = 30.49 ± 0.57 μm) exerted less influence on the handling properties than does similarity in morphology (Fig. 2).

Kinetics of polymerization

Typical DSC thermograms are presented in Fig. 3, while the whole collection of Q and ln Z estimates is given in Table 2. Across the range of heating rates used, the overall mean and standard deviations of Q and ln Z were higher than those reported for the old formulation of Surgical Simplex®P, which is the only commercially-available acrylic bone for which these values are reported in the literature. For this cement, the overall mean and standard deviation of Q and ln Z values, as computed from the estimates given at heating rates of 5, 10, and 20 K min^{-1} [32], were 203 ± 48 kJ mol^{-1} and 70 ± 17, respectively. For a given parameter, the difference in the estimates given by Yang et al. [32] and in the present work is attributed to two factors. The first, and, possibly the major reason, is the difference in the powder particle size distribution of the powders in the Simplex®P used in the present study compared to that used by Yang et al. [32]. (It is assumed that Yang et al. [32] used the old formulation.) The second factor is the difference in the method used to compute the baseline in the thermogram, which, almost invariably, is sloping (The method used will affect the values of the relevant areas of the thermogram that are used to compute c.)

Characteristics of PBS uptake

Typical mass gain, M_t-versus time in PBS (t) and M_t/M_∞ plots are given in Fig. 4. The computed values of D (Table 2) cannot be compared to relevant literature results

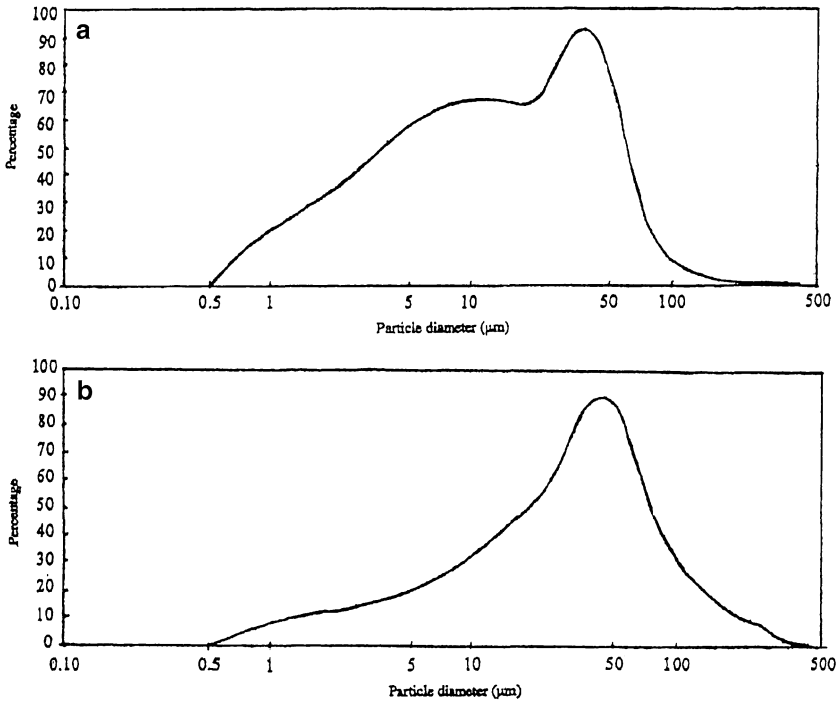

Fig. 1 The particle distribution of the powder in (**a**) Cement I (which is the new formulation of Surgical Simplex®P); and (**b**) the old formulation of Surgical Simplex®P

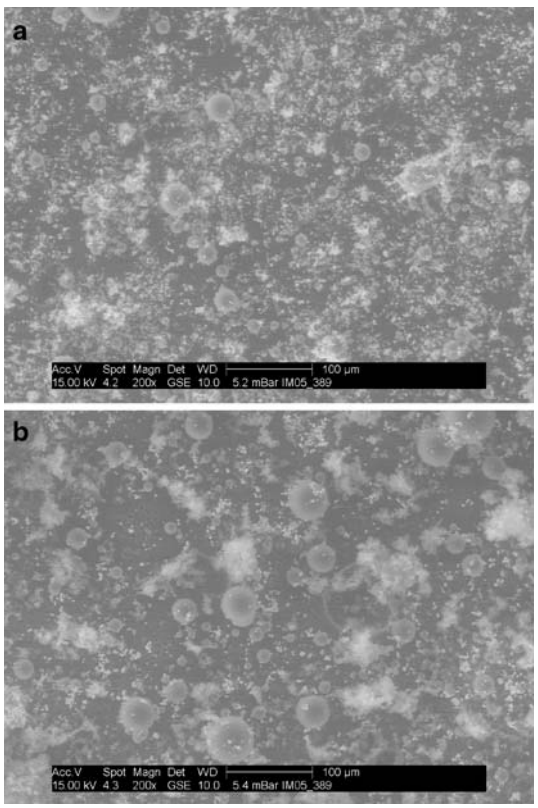

Fig. 2 (**A**) The morphology of the powder in Cement I (which is the new formulation of Surgical Simplex®P) (**B**) The morphology of the powder in the old formulation of Surgical Simplex®P

as the present authors are not aware of any for hand-mixed Simplex®P or another commercially-available cement brand, in PBS or in a comparable medium, at 37 °C. The

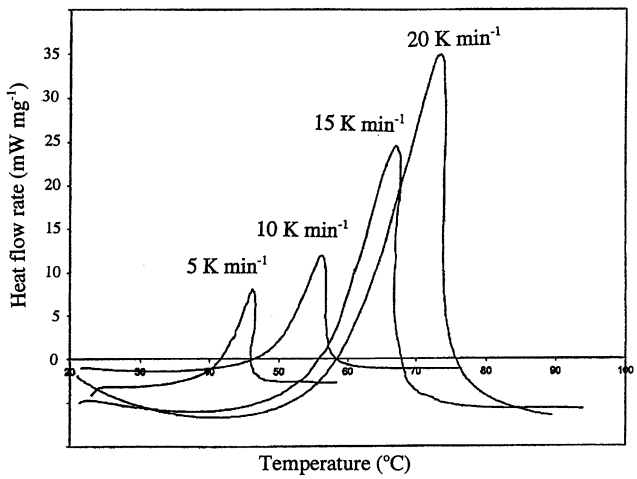

Fig. 3 Typical thermograms obtained from the DSC tests

present D results are, on the whole, higher than are given in the literature for a hand-mixed experimental cement that contained 10% p/p $BaSO_4$, in 0.9% NaCl solution, at 37 °C ($(1.61 \pm 0.22) \times 10^{-12}$ m^2 s^{-1} [33].)

There was no consistent trend with regard to the influence of the two compositional variables investigated on D (Tables 2, 3). Two mechanisms have been proposed for the diffusion of a fluid into a polymeric material; namely, infiltration of the fluid into the free spaces in the material (such as micro-voids in the case of an acrylic bone cement) and molecular interaction of available hydrogen bonds at the hydrophilic sites [34]. It is unclear from the present findings if either of these mechanisms is applicable to the

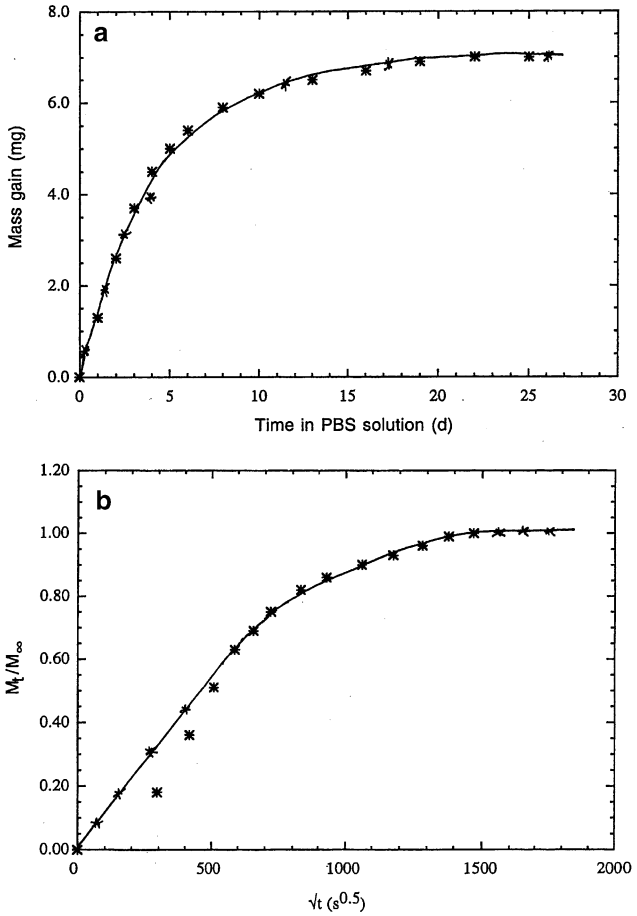

Fig. 4 (**a**) Typical full PBS absorption plot (mass gain, M_t, versus time in PBS, t); (**b**) Plot of Mt/M_∞ versus $\sqrt{t}$, obtained from (a)

cements studied or if another mechanism is more appropriate. Whatever mechanism applies, the influence of the compositional changes on it is not straightforward. However, an examination of these issues is outside the scope of the present study.

Bulk mechanical properties

The UCS values (Table 2) for all the cements exceed the minimum limit of 70 MPa, as stipulated in ISO 5833 [21] and are within the range given in the literature for hand-mixed old formulation of Surgical Simplex®P (which is comparable to Cement I) [4, 35, 36].

The K_{Ic} results (Table 2), as obtained using the RCT specimens, are within the range given in the literature for hand-mixed old formulation of Surgical Simplex®P (which is comparable to Cement I) [35–38]. The present K_{IC} results using the DT specimens are comparable to that given by Beaumont and Young [39] for hand-mixed old formulation Surgical Simplex®P (2.10 MPa $\sqrt{m}$), which, to the best of the authors' knowledge, is one of only two literature reports in which acrylic bone cement was the subject. (The other one is by Buckley et al. [40] on vacuum-mixed CMW™3 cement, tested in water, at 37 °C.) The present K_{IC} results, obtained after 28 d aging in ambient laboratory air, were 33–72% higher when DT specimens were used compared to when RCT specimens were. This difference may be attributed to differences in two aspects. First, the RCT and DT specimens were tested in ambient laboratory air and in water, at 37 °C, respectively. (It is accepted that water has a plasticizing influence on the mechanical properties of acrylic bone cements; for example, Beaumont and Young reported that the mean K_{IC} of Surgical Simplex®P when DT specimens were tested in air and in water were 1.85 and 2.10 MPa $\sqrt{m}$, respectively [39].) Second, for a given testing medium, a specimen geometry effect on K_{IC} of acrylic bone cements has been noted in the literature, with the comparison being between results obtained using single-edge notched three-point bend (SENB) and DT specimens in one study [39] and between RCT, SENB, and chevron-notched short rod specimens in another [41]. With these points in mind, the real difference in the present results using RCT and DT specimens may not be as large as indicated. For a given cement, the K_{IC} values obtained using the DT specimens were not influenced by maturation ($P = 0.147$–0.697). This is in agreement with the results for another quasi-static fracture property (work-of-fracture, WOF) of hand-mixed old formulation of Surgical Simplex®P (which corresponds to Cement I) that increased from 502 J m^{-2} after 7 d in air at 21 °C to 513 J m^{-2} after 21 d in that medium [42]. In other words, the present results and those for WOF indicate that ambient laboratory air does not act as a plasticizer for the cement. While detailed comments on the relative strengths and shortcomings of these two types of specimens when used to determine K_{IC} of an acrylic bone cement is outside the scope of the present study, it is useful to point out one important distinction in tests using these specimens that may help to explain the difference in the values noted above. This is that the stress intensity factor (and, hence, K_{IC}) is independent of and dependent on crack length in DT and RCT specimens, respectively.

The collection of the N_f results and the estimates of the Weibull parameters for all the cements are presented in Fig. 5 and Table 2, respectively. There is a clear demarcation in the value of N_{WM}, with that for Cement III being between 88 and 248% higher than that for any of the others.

Nanomechanical properties

Previously reported results from PMMA (Perspex®) [19, 20] validated the methods and data analysis procedures followed in the quasi-static and dynamic nanoindentation

Table 3 Results[a] of the ANOVA, with Bonferroni post hoc, tests

Property	Cement I versus Cement II	Cement III versus Cement IV	Cement I versus Cement III	Cement II versus Cement IV
t_{set}	NS; 0.060	NS; 0.214	NS; 0.333	NS; 0.074
T_{max}	NS; 0.130	S; 0.014	NS; 0.130	NS; 0.073
c'	S; < 0.001	S; <0.001	S; <0.001	S; <0.001
D	NS; 0.178	S; <0.001	S; <0.001	NS; 0.180
UCS	NS; 0.100	NS; 0.062	S; 0.012	S; 0.003
K_{IC} (RCT)	S; 0.002	NS; 0.242	NS; 0.673	S; 0.003
K_{IC} (DT; 1 d)	NS; 0.599	NS; 0.153	NS; 0.147	NS; 0.483
K_{IC} (DT; 14 d)	NS; 0.154	NS; 0.403	NS; 0.697	NS; 0.379
K_{IC} (DT; 28 d)	NS; 0.937	S; 0.012	S; 0.039	NS; 0.282
ln N_f	NS; 0.067	NS; 0.288	NS; 0.114	NS; 0.100
H	S; <0.001	S; 0.045	S; <0.001	S; 0.003
E	S; <0.001	NS; 0.744	NS; 0.171	S;<0.001
E_h'	NS; 0.915	NS; 0.929	NS; 0.911	NS; 0.901
ω_h	NS; 0.913	NS; 0.948	NS; 0.965	NS; 0.927
E_l''	NS; 0.954	NS; 0.917	NS; 0.925	NS; 0.918
ω_l	NS: 0.922	NS; 0.968	NS; 0.943	NS: 0.961

[a] NS: difference in mean values is not significant; S: difference in mean values is significant. The numbers are the *P* values

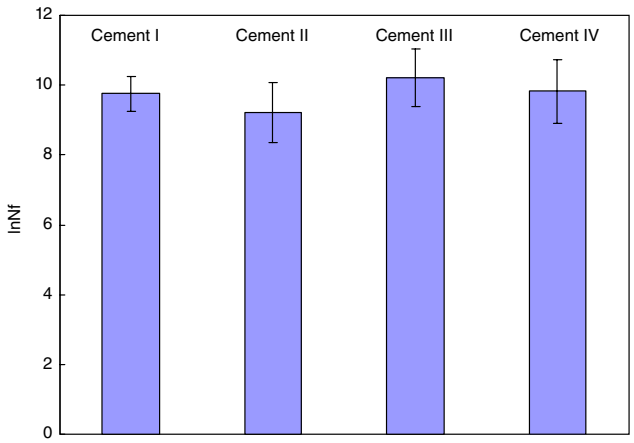

Fig. 5 Summary of the fatigue test results, expressed as ln N_f

tests. (The E value obtained, 3.89 ± 0.14 GPa, is within the range reported in literature reports [43–45]. The storage modulus-ω results were similar to those reported by White et al. [46] for a commercially-available PMMA (Plexiglas®)).

In the quasi-static tests, the Modified Slopes Method (MSM) was used, rather than the original Oliver and Pharr Method (OOPM) [47], because, for a synthetic or a natural biomaterial, Lewis et al. [19] have shown that while there is no significant difference in the H (or E) values determined using these two methods, MSM is preferable because it is less complex—only the P–h measurements and values of constants that depend on the geometry of the indenter used are needed, whereas, when the OOPM is used, there is a critical input (the indenter tip area function), whose computation can be both problematic and challenging. A typical P–h plot for the cements, obtained in the quasi-static tests, is given in Fig. 6, with the collection of E and H values for the cements being given in Table 2.

In the dynamic tests, each specimen was tested over an ω range of clinical relevance; that is, from slow normal walking (1 Hz) to traumatic impact loading (200 Hz), in steps of 1 Hz. The pattern of the viscoelastic behavior is essentially the same for all the cements (Fig. 7), with the values of some key properties being given in Table 2.

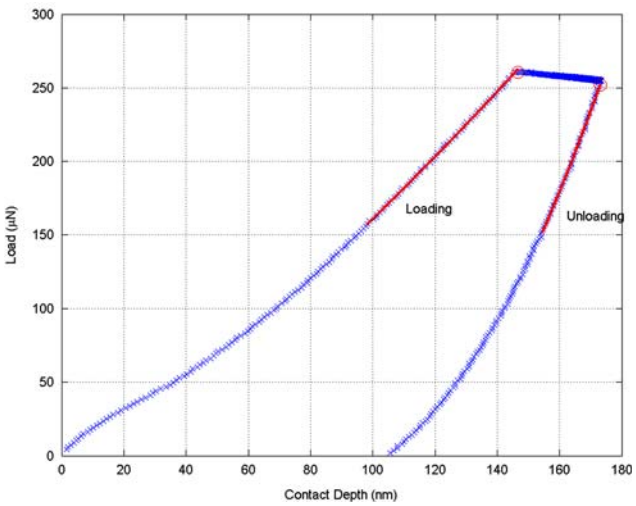

Fig. 6 A representative P–h plot, obtained in the quasi-static nanoindentation test

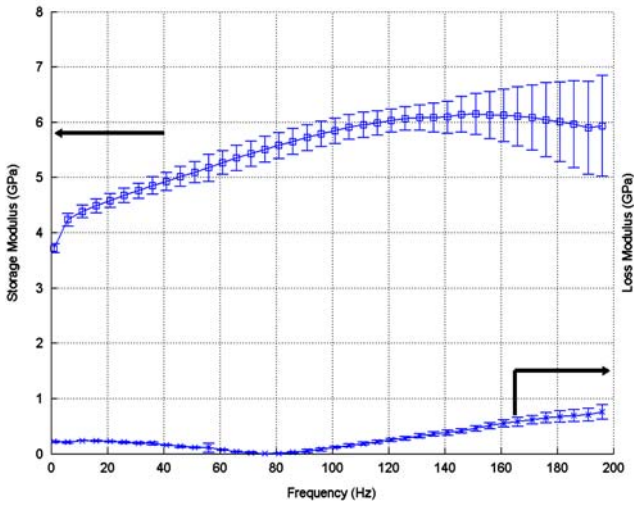

Fig. 7 Representative results for the variation of the storage and loss moduli with frequency

Two limitations of the determination of the nanomechanical properties are noted. First, they were made in air at ambient temperature. Clearly, measurements in situ (in an appropriate solution, such as simulated body fluid, at 37 °C) would be preferable. The second limitation regards the dynamic nanoindentation test method itself, in that (a) it is assumed that the test material displays linear viscoelastic characteristics and (b) the dynamic model used does not account for characteristics of other parts of the nanoindenter instrument (such as the head and base of the loadframe). These limitations may not be important in the present nanoindentation work, which is parametric; that is, in both the quasi-static and the dynamic tests, all the conditions used were the same for all the cement sets.

Trends in results and clinical relevance

The results of the ANOVA tests on the results are summarized in Table 3, from which the following consistent trends are seen. First, for a given ratio of the mass of the co-polymer in the powder, as a proportion of the total mass of the powder (COP), a decrease in the volume of DMPT, relative to the total volume of the liquid monomer (ACC) [Cements I versus II, and Cements III versus IV], produced no significant effect on t_{set}, UCS, K_{IC} (via DT specimens; after 1 or 14 d aging), ln N_f, E_h', ω_h, E_l'', and ω_l, but there was a significant decrease in c′ and a significant increase in H. Second, for a given ACC, an increase in COP [Cements I versus III and Cements II versus IV] produced no significant effect on t_{set}, T_{max}, K_{IC} (via DT specimens; after 1 or 14 d aging), ln N_f, E_h', ω_h, E_l'', and ω_l, but there were significant increases in UCS and H and a significant decrease in c′. These consistent trends point the way as to how to manipulate the composition of cement to achieve a specific goal as far as individual cement properties (or a collection of properties) are concerned. In other words, the present work could be regarded as an illustration of a methodology for optimizing the composition of an acrylic bone cement.

From the perspective of potential clinical relevance, arguably the most important finding in the present work is that the fact that both of the compositional changes lead to a significant decrease in c′, which may make cements with low ACC or high COP favorable for long-term anchoring of total join replacements [48]. Furthermore, the present study has relevance to cemented arthroplasties because the collection of properties determined represents a sizeable proportion of those that regulatory authorities, such as the FDA, require information about when cement manufacturers/suppliers apply for approval for cements for clinical use [18]. Having said this, two cautionary points are emphasized. The first is that there are other important properties that were not determined in this study, notably in vitro cytotoxicity, osteolytic potential, and biocompatibility. The second is that the true performance of a cement can only be obtained from well-designed, prospective, randomized, multi-centered, and long-term clinical trials in which the subjects in the study groups are matched (for age, sex, weight, and numbers) and all the variables (particularly, design of implant, method of mixing and delivery of the cement dough, and the implantation technique) are the same for the study groups except for the cement used.

Conclusions

The following are the main conclusions of the study:

- A 68% reduction in the volume of the activator of the polymerization reaction, DMPT, relative to the total volume of the liquid monomer (the amounts of all the constituents in the powder and of the hydroquinone in the liquid monomer remaining unchanged) led to a significant drop in the rate of the polymerization reaction of the cement and a significant increase in its hardness.
- The elimination of the pre-polymerized poly (methyl methacrylate) beads in the powder (the amounts of all the other powder constituents and those of the liquid monomer remaining unchanged) led to a significant drop in the rate of the polymerization reaction of the cement and a significant increase in the ultimate compressive strength of the cured cement.
- These findings suggest strategies for optimizing the composition of an acrylic bone cement.

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