Mechanical properties of hydroxyapatite reinforced poly(ethylmethacrylate) bone cement after immersion in a physiological solution: influence of a silane coupling agent

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PEMA–based bone cement has previously been shown to possess many advantages over traditional PMMA cements. One of these is the option of adding up to 40 wt % HA without a decrease in static mechanical strength, thus providing the potential for enhanced bioactivity. Bone cement, *in vivo*, is subjected to an aqueous environment and therefore, it is important to understand the influence of this upon the mechanical integrity of experimental cements. In this current investigation the static and dynamic properties of PEMA cement, with and without 30 wt % untreated and silanated HA, were examined after periods of immersion in Ringer's solution. A commercial PMMA cement was also tested in a similar manner. Relatively small changes in static mechanical properties were observed after 12 weeks storage for the PEMA cements, the largest change being for the PEMA cement reinforced with silanated HA. The PMMA cement exhibited the largest change in static strength with a decrease of 16.6%. In contrast to these results, the fatigue properties of the PEMA cements were found to decrease significantly after storage in Ringer's solution, again with the largest changes to the PEMA cement reinforced with silanated HA. This effect was attributed to the reduction in efficiency of the silane coupling agent in the presence of water. The fatigue resistance of the PMMA cement was not reduced after immersion in a saline environment.

1. Introduction

The majority of prostheses are fixed in place using poly(methylmethacrylate) (PMMA) bone cement, acting as a filler between the implant and the bone. Although widely used, PMMA does not possess the ideal mechanical and biological characteristics required and when implants eventually become loose, bone cement has been implicated [1, 2]. The bone cement investigated in this study offers several advantages over PMMA based bone cement and its properties have been well documented [3–8]. The main advantage over traditional bone cement is in its much higher ductility, which is greater than 50% strain to failure, compared to approximately 2–3%. Thus, the experimental cement, prepared from poly(ethylmethacrylate) (PEMA) powder and n-butylmethacrylate monomer, provides a suitable matrix for hydroxyapatite addition. This approach increases the potential for enhanced bioactivity and control of mechanical properties.

The water absorption behavior of this cement has previously been studied [7], but no mechanical effects were monitored. In this investigation, the influence of storage in Ringer's solution upon both static and dynamic mechanical characteristics has been studied. Although Ringer's solution replicates the balance of mineral salts found in body fluids, it is not designed to represent the exact conditions of bone cement *in vivo*. It does, however, provide information on the stability of the PEMA cement in contact with a medium resembling body fluids.

2. Materials and methods

2.1. Materials

The bone cement used in this study consisted of a polymeric phase of poly(ethylmethacrylate) (PEMA) powder (Bonar Polymers, Co. Durham, UK), mixed with a monomer of n-butylmethacrylate (nBMA) stabilized with 0.01% quinol (Aldrich Chemicals, Dorset, UK). The initiator of the reaction included in the polymer component was benzoyl peroxide and the accelerator, N,N-dimethyl-p-toluidine (Aldrich Chemicals, Dorset, UK) was added to the monomer. The hydroxyapatite (HA) used to reinforce the PEMA bone cement was supplied by Plasma Biotal, Derbyshire, UK. A portion of the HA powder was treated with a silane coupling agent, 3-trimethoxysilylpropylmethacrylate (Union Carbide,

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Somerset, UK). The silanation was carried out using a 70/30 acetone-water mixture with 5 wt % coupling agent with respect to HA powder. The HA powder was washed and dried prior to addition to the polymer powder. The HA, either untreated or silanated, was added to the PEMA powder to obtain a weight fraction of 30%. The PMMA cement used as a comparison was a commercially available, low viscosity cement containing barium sulfate. The physiological medium used for the investigation was full strength Ringer's solution with a phosphate buffer.

2.2. Methods

Specimens for tensile and fatigue testing were prepared by adding the monomer to the polymer powder, mixing with HA where appropriate, maintaining a 2 : 1 polymer to monomer weight ratio. Molds were filled with the cement mixture at dough time and subjected to a pressure of 1.4 MPa for approximately 20 min. The samples produced were half-size ISO 527 multi-purpose dumbbell test specimens, as used in a previous fatigue characterization of this experimental cement [8]. With the exception of specimens to be used as controls, the samples were placed in Ringer's solution in a water bath at 37 °C. The specimens stored in Ringer's solution were weighed periodically throughout the 12 week immersion period.

The tensile testing was conducted on an Instron testing machine, Model No. 6025™ at ambient temperature. Samples which had been stored in Ringer's solution were kept moist throughout testing. A clip on Instron 472™ extensometer with a 25 mm gauge length was used to measure the extension of the specimen upon loading. The cross-head speed employed was 5 mm/min and maximum tensile strength, (σ_{max}), Young's Modulus (E) and strain at maximum strength $(\varepsilon_{\sigma max})$ or failure (ε_f) were calculated. At least five specimens were tested for each cement in all conditions.

The fatigue testing was conducted on a Bionix 858™ MTS electrohydraulic testing system. The specimens were cycled in tension–tension, at a frequency of 2 Hz until failure. The stress pattern used was 0.3–15 MPa for each cement. Ten specimens of each cement were tested and the fatigue lives are represented on graphs with the logarithm of life as the abscissa and as ordinate, $\log(1/(1-F))$, where F represents the median rank. Values of median rank are assigned to the fatigue life of each sample obtained from a table of median ranks [9].

2.3. Scanning electron microscopy

Electron microscopy was carried out using a JEOL 6300™ scanning electron microscope (SEM). Fracture surfaces of both the tensile and fatigue failures were examined using an accelerating voltage of 10 kV at a wide range of magnifications.

3. Results

3.1. Weight change

The change in weight of the cement specimens has been calculated as a percentage change from the weight of specimens 24 h after manufacture and plotted against time of storage, Fig. 1. It can be seen that the weight of the PMMA cement increased by the largest amount, followed by the 30 wt % HA-PEMA cement, 30 wt % sil. HA-PEMA cement and unfilled PEMA cement. The largest changes in weight of the PEMA cements occurred within one week from manufacture, the PMMA cement took approximately eight weeks to reach equilibrium. The cements stored in the dry environment at 37 °C all decreased in weight by a similar amount, each losing approximately 0.4 wt %. This equilibrium was reached after eight weeks of storage.

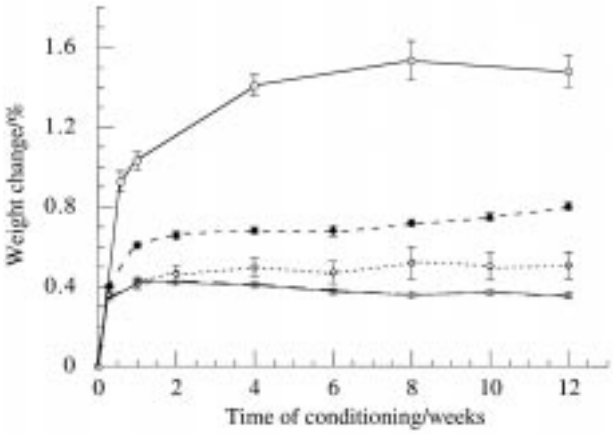


Figure 1 Change in weight of PEMA bone cement, with and without HA, in comparison to PMMA bone cement: ——+—— unfilled PEMA; – –◆– – 30 wt % untreated HA; ——⊖—— PMMA; – –◇– – 30 wt % silanated HA.

3.2. Changes in tensile properties after storage

The results of the tensile tests are displayed in Fig. 2a to c. Each point represents the mean of five tests and the error bars, the standard deviation. The mechanical properties obtained for the cements after storage for one week in air at 37 °C are shown in Table I and have been plotted at the zero week time point in Fig. 2a to c to show changes due to the immersion medium. The percentage change in tensile characteristics after storage in Ringer's solution compared to the results measured in air after one week are shown in Table II. Changes which are statistically significantly different are indicated.

The strength of the PEMA cements dropped by 10–15% within the first week compared to those tested in air. However, after 12 weeks immersion the strengths were higher, the unfilled cement not being significantly different to the strength after one week. The Young's modulus showed similar decreases after one and 12 weeks of storage in Ringer's solution. The strain values for the PEMA cements were obtained at maximum strength since the strain to failure values were out of the range of the extensometer and not thought to be a relevant value. In general, the strain increased after the period of immersion. The exception to this finding was the strain result for the 30 wt % HA-PEMA cement after 12 weeks immersion, which remained the same.

The PMMA cement exhibited a decrease in strength after one week storage and a further drop after 12 weeks

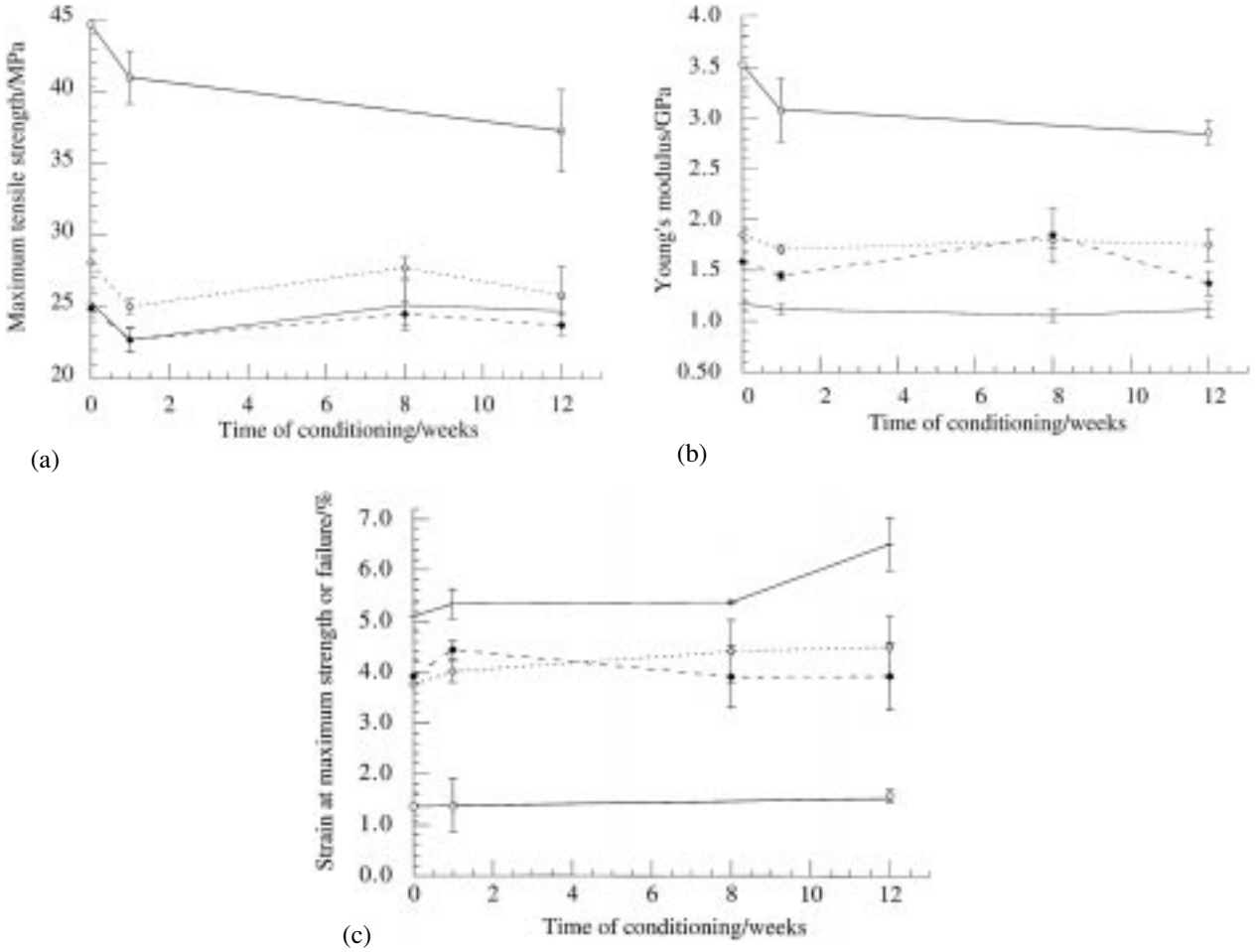


Figure 2 Influence of storage in Ringer's solution upon (a) tensile strength, (b) Young's modulus or (c) strain at maximum strength or failure: ——+—— unfilled PEMA; – –◆– – 30 wt % untreated HA; – –◇– – 30 wt % silanated HA; ——⊖—— PMMA.

TABLE I Mechanical properties after one week storage in air at 37 °C

Cement tested	σ_{max}/MPa	E/GPa	$\varepsilon_{\sigma max}$ or ε_f/%
Unfilled PEMA	25.3 (0.95)	1.17 (0.056)	5.10 (0.24)
30 wt % HA-PEMA	24.9 (0.22)	1.72 (0.083)	3.92 (0.33)
30 wt % sil.HA-PEMA	28.1 (0.75)	1.85 (0.082)	3.76 (0.16)
PMMA	44.7 (4.3)	3.53 (0.28)	1.36 (0.27)

storage. After the period of immersion, the cement was less compliant with an increase in strain to failure.

3.3. Changes in fatigue properties after storage

The results of the fatigue testing for the filled and unfilled PEMA cement specimens tested before storage, in either air or Ringer's solution for 12 weeks, are given in Table III as both Weibull medians and means, according to the guidelines outlined in Johnson [9]. When the distributions are skewed, these two values are not the same, as in the case for the unfilled PEMA, 30 wt % HA-PEMA and PMMA cements. Statistical differences between the lives of the cements have been calculated using the Mann Whitney U-test [10]. The results of all the fatigue testing lives to failure are displayed on the Weibull plots in Fig. 3a and b.

All the PEMA cements possessed much reduced fatigue resistances after storage in Ringer's solution.

TABLE II Change in tensile properties after 12 weeks storage in Ringer's solution

Cement tested	Time of storage/weeks	Change in σ_{max}/%	Change in E/%	Change in ε_f or $\varepsilon_{\sigma max}$/%
Unfilled PEMA	1	− 10.3*	− 4.3	+ 4.7
	12	− 2.2	− 4.9	+ 28.2*
30 wt % HA-PEMA	1	− 8.8*	− 8.7*	+ 13.3*
	12	− 4.8*	− 13.4*	− 0.47
30 wt % sil.HA-PEMA	1	− 10.9*	− 7.7*	+ 6.8
	12	− 8.2*	− 5.1	+ 20.2*
PMMA	1	− 8.3*	− 12.7*	+ 1.5
	12	− 16.6*	− 19.0*	+ 16.9*

TABLE III Fatigue properties of the PEMA and PMMA cements after storage in air or Ringer's solution

Cement Tested	Cycles to failure			
	Weibull median		Weibull mean	
	Air	Saline	Air	Saline
Unfilled PEMA	56 494 $	12 474 $	63 671	16 692
30 wt % HA-PEMA	18 782 $ *	3232 *	19 592	3948
30 wt % sil.HA-PEMA	52 277 *	5358 *	52 277	5358
PMMA	125 729	168 572	172 898	185 002

* No significant difference $p > 0.05$
$ significant difference $p < 0.01$

The unfilled cement retained the highest Weibull median of cycles to failure, followed by the 30 wt % sil. HA-PEMA cement and the 30 wt % HA-PEMA cement, the same order as the tests in air. There was no significant difference between the unfilled PEMA cement and 30 wt % sil. HA-PEMA cement, whereas the 30 wt % HA-PEMA cement possessed significantly lower fatigue lives than the unfilled PEMA cement. There was no significant difference in the fatigue lives of the PMMA cement, whether tested after storage in air or Ringer's solution, in contrast to its static tensile properties. There was, however, slightly less scatter in the fatigue lives to failure after the storage in Ringer's solution. The range of fatigue lives after testing in air was 21 397–449 558 compared to 44 019–409 547 in Ringer's solution. This result indicated that the presence of water in the cement leads to less sensitivity to flaws and voids.

3.4. Scanning electron microscopy

Selected fracture surfaces of the specimens after fatigue testing are shown in Figs 4–6. Fig. 4a shows the magnitude of HA pull-out on a 30 wt % HA-PEMA fracture surface and Fig. 4b demonstrates the lack of bonding between the ceramic HA particles and the cement. After coating the HA powder with silane coupling agent there was less particle debonding on the fatigue fracture surfaces, Fig. 5a. This is demonstrated more clearly in Fig. 5b, showing the increased adhesion between HA particle and cement matrix. After immersion in Ringer's solution the fatigue fracture surfaces of

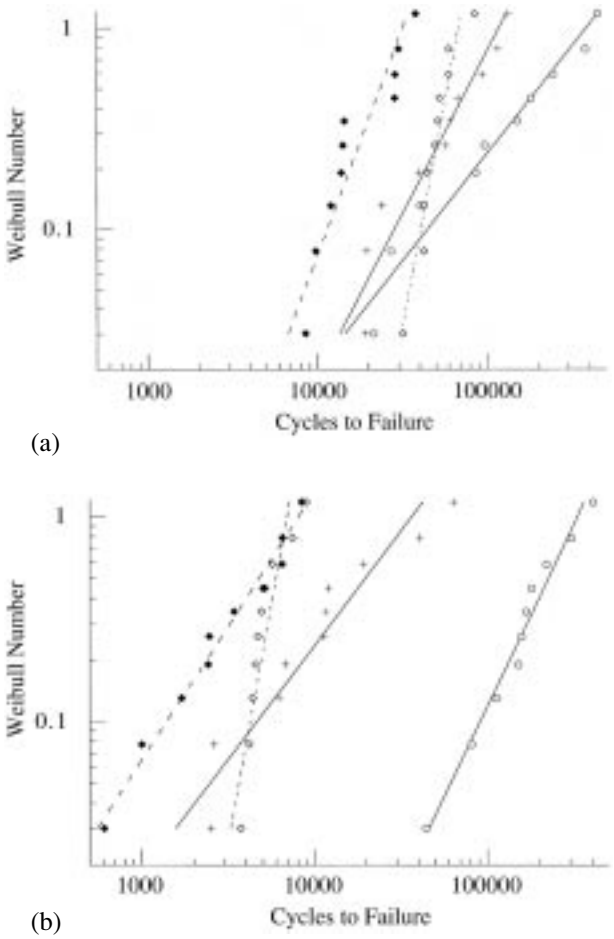


Figure 3 Fatigue lives of bone cement cycled 0.3–15 MPa at 2 Hz, after storage in (a) air at room temperature or (b) Ringer's solution at 37 °C: ——+—— unfilled PEMA; – –◆– – 30 wt % untreated HA; – –◇– – 30 wt % silanated HA; ——⊖—— PMMA.

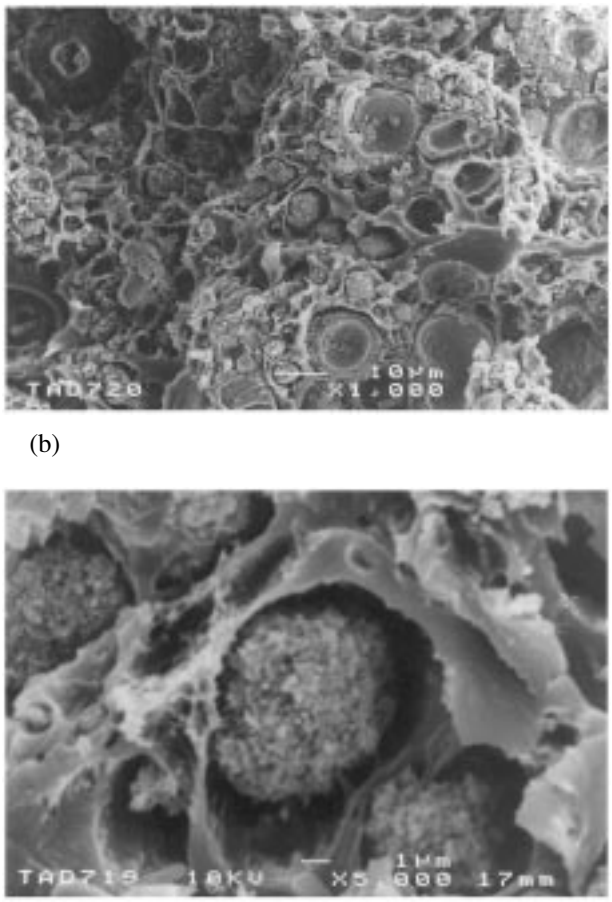
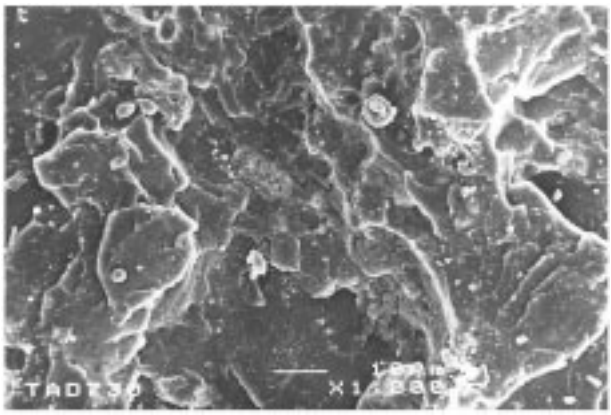
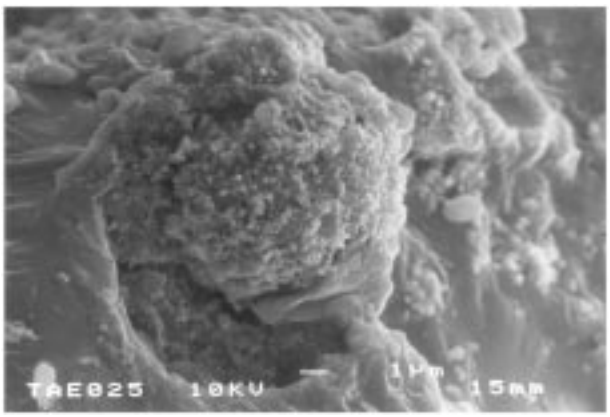


Figure 4 Fatigue fracture surface of 30 wt % untreated HA-PEMA cement at two magnifications (a) × 1000 and (b) × 5000.



(a)



(b)

Figure 5 Fatigue fracture surface of 30 wt % silanated HA-PEMA cement at two magnifications (a) ×1000 and (b) ×5000.

the 30 wt % sil. HA-PEMA cement, (Fig. 6), displayed greater evidence of particle pull-out than after storage in air (Fig. 5a).

4. Discussion

4.1. Weight change

The weight loss after storage in air for 12 weeks of all the bone cements studied was found to be approximately 0.4 wt %, a similar value to that obtained by Hailey *et al.* [11] for PMMA cement. An equilibrium appeared to have been reached after 8–10 weeks. It has been reported [12–14], and is widely accepted, that PMMA bone cement contains up to approximately 2 wt % residual monomer following room temperature polymerization. The loss in weight of the cement specimens after storage in air at 37 °C can therefore be attributed to the release of some of this residual monomer. Smith and Bains [14] concluded from an investigation into residual monomer in PMMA bone cement, that the total residual methylmethacrylate could be considered as the sum of two parts, one of which was extractable and one of which was not. The extractable part was associated with the surface of the material, which did not reach such high temperatures upon polymerization as the internal part of the material, and the non–extractable part referring to the molecules trapped in the long polymer chains. Therefore, the loss in weight can be assumed to be associated with the surface monomer.

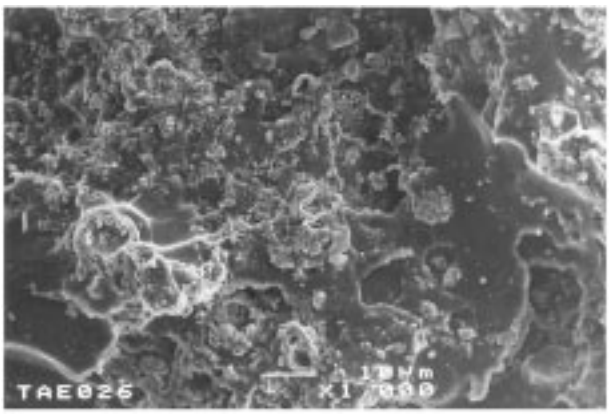


Figure 6 Fatigue fracture surface of 30 wt % silanated HA-PEMA cement after immersion in Ringer's solution for 12 weeks.

When the specimens were stored in the Ringer's solution, their weights were found to increase. Two processes were occurring in the specimens, that of monomer extraction and that of water uptake by diffusion into the polymer. Therefore, the actual change in weight of the specimens was the combination of increase in weight due to the water and loss in weight due to leaching of the monomer. This implies that the total amount of water absorbed was greater than the change in weight measured. The amount of MMA monomer loss from PMMA-based bone cement has been shown previously to be greater when the cement was stored in an aqueous environment compared to air [11] since the monomer is slightly soluble in water. The amount of nBMA monomer lost from the cement samples would be less due to its lower extractability in saline [4].

The 30 wt % HA-PEMA cement increased in weight by the largest amount after storage in Ringer's solution and had still not reached equilibrium by 12 weeks. This is in agreement with a water absorption study by Deb *et al.* [7] which showed that the equilibrium uptake of water with 40 wt % untreated HA in PEMA cement was higher than the unfilled PEMA cement. This study also showed a reduction in uptake when the HA was silane coated. In the current investigation, the unfilled cement and 30 wt % sil. HA-PEMA cement reached equilibrium after only one week of immersion. The largest increase in weight occurring with the 30 wt % HA-PEMA cement has been attributed to the presence of the HA powder which is able to absorb considerable amounts of water onto its surface. When the HA was present in the PEMA cement, the water was able to bond to the hydroxyl groups available at the HA-cement interfaces, via hydrogen bonding. In addition, the presence of the filler may have introduced impurities, which provided sites for water absorption. The presence of the silane coupling agent inhibited the ability of the HA powder to absorb water by producing a hydrophobic surface upon the HA, thus less weight change was observed. The PMMA cement gained significantly more water than the PEMA cements after 12 weeks immersion, 1.5 wt % compared to 0.8 wt % for 30 wt % HA-PEMA cement. In addition to this effect, the PMMA cement took much longer to reach equilibrium, which occurred after eight weeks compared to one week

for the unfilled PEMA cement. The reason for this difference is due to the higher availability of the carbon to oxygen double bonds in the poly(methylmethacrylate) molecules compared to the poly(ethylmethacrylate) and poly(n-butylmethacrylate).

4.2. Changes in tensile strength

The trends observed in the water uptake behavior of the cements were reflected by the changes in the mechanical properties measured. During storage in an aqueous environment, two processes occur simultaneously: first, post-curing of the cement and leaching of the residual monomer, both effects reducing the amount of monomer in the cement and, second, uptake of water. The largest increases in weight of the PEMA cements, found after only one week storage in Ringer's solution, reflected the largest decreases of tensile strength, demonstrated by Fig. 2a. After 12 weeks, the loss of strength of the unfilled PEMA cement was only 2.2% compared to a decrease of 10.3% after one week. The 30 wt % HA-PEMA cement dropped 4.5% compared to 8.8%, after one week, and the 30 wt % sil. HA-PEMA cement by 8.2%, compared to 10.9% after one week. The other static results showed, in general, the secant modulus was lowest and the strain at maximum strength was highest after the 12 weeks conditioning in the Ringer's solution. This increase in compliance was attributed to the presence of the water in the polymer acting as an internal plasticizer. The observed changes in strength may be due to the water not actually reducing the strength of the bonds within the polymer, but allowing the chains to slip over each other more easily, thus reducing the stiffness and increasing the ability of the cement to extend prior to failure. After storage in Ringer's solution, the poly(n-butylmethacrylate) (PBMA) matrix was more ductile resulting in a rougher surface when examined using SEM. The increase in strength of the PEMA cements from 1 to 12 weeks immersion may be due to the water being redistributed during this time and/or due to the post-curing that occurred. The largest decrease in strength of the PEMA cements, after 12 weeks, was obtained with the cement reinforced with silanated HA, a result discussed later in relation to the fatigue strength. In contrast to these results, the PMMA cement, which took longer to reach the equilibrium of water sorption, decreased in strength from 1 to 12 weeks, with an 8.3% decrease after one week to 16.6% after 12 weeks. The secant modulus and strain to failure showed similar trends to those for the PEMA cements, with a decrease in stiffness and increase in ductility after a period of immersion in Ringer's solution.

Therefore it was found that the changes in static mechanical properties of the PEMA cement after 12 weeks immersion in Ringer's solution were relatively small and less than those of the PMMA cement. No investigations have been reported on the effect of Ringer's solution upon the tensile properties of PMMA bone cement, however related studies on the stability of PMMA cements are briefly summarized. Kusy [15] found the tensile strength and Young's modulus of PMMA cement dropped by 50 and 25% respectively after 10 months conditioning in water at 37 °C and Lee *et al*. [16] observed a 7% drop in compressive strength after 6 months in saline at 37 °C. In contrast, Hailey *et al*. [11] observed increasing work of fracture values for a PMMA cement after storage in Ringer's solution up to 600 days and Nguyen *et al*. [17] measured an increase in fracture toughness when testing a PMMA cement in Ringer's solution compared to air.

4.3. Changes in fatigue strength

The influence of HA addition upon the fatigue strength of PEMA cement has been reported previously [8] and was shown to decrease the resistance to cyclic loading. However, when the HA particles were treated with a silane coupling agent, the fatigue characteristics of the reinforced cement were improved, reflected in an increase in the Weibull median lives to failure [18]. These results are shown in Fig. 3a and Table III. This increase in fatigue resistance has been attributed to the greater adhesion of the HA particles to the polymer when the coupling agent is present. Fig. 4a shows a fatigue fracture surface of PEMA cement reinforced with untreated HA particles and extensive HA particle pull-out can be observed. Fig. 4b shows an individual HA particle on the fracture surface and the lack of adhesion between ceramic and matrix. When the coupling agent was present, fewer HA particles were found on the fatigue fracture surface, (Fig. 5a). The most energetically favorable fracture path is through the matrix, above and below the reinforcing particle. Fig. 5b shows a silanated HA particle which was pulled-out of the matrix upon failure with some matrix still attached to its surface.

After 12 weeks storage in Ringer's solution, the fatigue strength of the PEMA cements, both filled and unfilled, exhibited a large decrease, shown in Table III. The unfilled PEMA cement specimens failed in a different manner compared to those tested in air. The fracture surfaces of the specimens stored in Ringer's solution were very smooth, with no bead pull-out. The result of immersing the specimens in Ringer's solution appeared to make the PBMA matrix less able to deform upon cyclic loading. The process of bead pull-out to produce a roughened surface is energy absorbing, so it is not surprising that a smooth surface was produced when the fatigue resistance was lowered. The cyclic loading resulted in a higher strain rate in the PEMA cement specimens, compared to the static loading. At the higher strain rate, the PBMA matrix acted in a more brittle manner, as the water did not appear able to act as a plasticizer.

The Mann-Whitney U-test results showed there was no significant difference between the fatigue lives of the unfilled PEMA cement and the 30 wt % sil. HA-PEMA cement after storage in Ringer's solution, which was the same as the result of the tests in air. In contrast to the results obtained for the specimens tested in air, the Mann-Whitney U-test showed there was no significant difference between the Weibull medians of the 30 wt % HA-PEMA and 30 wt % sil. HA-PEMA cements. The difference is due to the larger decrease in fatigue lives obtained for the 30 wt % sil. HA-PEMA cement specimens, the Weibull median dropped from 52 277 to 5358 cycles to failure, which is a 90% decrease. In

comparison, a decrease from 63 671 to 12 474 was obtained for the unfilled PEMA cement and a drop from 18 782 to 3232 for 30 wt % HA-PEMA cement, corresponding to losses of 80% and 83% respectively. The decreases obtained in tensile strengths for these specimens stored for 12 weeks in Ringer's solution were only 2.2% for the unfilled PEMA cement, 4.8% for the HA filled cement and 8.2% for the silanated HA filled cement. The largest drop in tensile strength and fatigue lives of the 30 wt % sil. HA-PEMA cement was surprising, since the increase in weight of this cement was less than that of the cement filled with untreated HA, 0.5 wt % compared to 0.8 wt %. The micrograph in Fig. 5c shows that there was a greater presence of HA on the fatigue fracture surface compared to the specimens fatigued after storage in air, (Fig. 5a). This result, along with the decrease in tensile strength, implies that the silane coupling agent was not as effective in the presence of Ringer's solution, due to either dissolution or hydrolysis of the coupling agent in the presence of water and/or the mineral salts. This observation was confirmed by a study by Dupraz *et al*. [19] investigating the stability of a variety of silane treated HA powders. The results showed only approximately 50% of a coating, similar to the one used in this study, remained after five days of water extraction at 37 °C. Although the presence of the coupling agent upon the HA in the PEMA cement resulted in the largest decrease in fatigue strength, there was a very small scatter in the fatigue lives obtained. This finding is reflected by the steep gradient of the Weibull curves shown in Fig. 3a and b. A narrow distribution of failure for a bone cement is a desirable quality and is an advantage over a bone cement displaying much wider scatter.

The PMMA cement did not exhibit any significant change in fatigue strength after immersion in Ringer's solution. Previous results reporting upon the influence of an aqueous medium upon the dynamic properties of acrylic bone cement are not in complete agreement. Migliaresi *et al*. [12] found an increase in creep resistance after a period of immersion in water, whereas Shen *et al*. [20] observed a large fall in fatigue properties with the presence of sorbed water. This reduction in fatigue resistance in the presence of water was attributed to lower resistance to craze initiation, thus enabling fracture to occur more easily. It should be noted, however, that these investigations were conducted using water as the aqueous medium and in this present study Ringer's solution was used.

5. Conclusions

The maximum tensile strength of unfilled PEMA cement was not altered upon immersion in Ringers solution, whereas the fatigue properties were significantly reduced. When a silane coupling agent was present upon the HA particle surface, the fatigue resistance of the reinforced PEMA cement was increased when tested in air but was considerably lowered after storage in Ringer's solution. Immersion of PMMA cement resulted in a reduction in tensile strength, but the fatigue resistance was not changed.

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