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Compressive fatigue properties of a commercially available acrylic bone cement for vertebroplasty

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Abstract

Acrylic bone cements are widely used for fixation of joint prostheses as well as for vertebral body augmentation procedures of vertebroplasty and balloon kyphoplasty, with the cement zone(s) being subjected to repeated mechanical loading in each of these applications. Although, in vertebroplasty and balloon kyphoplasty, the cement zone is exposed to mainly cyclical compressive load, the compressive fatigue properties of acrylic bone cements used in these procedures are yet to be determined. The purposes of the present study were to determine the compressive fatigue properties of a commercially available cement brand used in vertebroplasty, including the effect of frequency on these properties; to identify the cement failure modes under compressive cyclical load; and to introduce a screening method that may be used to shorten the lengthy character of the standardized fatigue tests. Osteopal®V was used as the model cement in this study. The combinations of maximum stress and frequency used were: 50.0, 55.0, 60.0, 62.5 and 75.5 MPa at 2 Hz; and of 40.0, 55.0, 60.0, 62.5 or 75.5 MPa at 10 Hz. Through analysis of nominal strain-number of loading cycles results, three cement failure modes were identified. The estimated mean fatigue limit at 2 Hz (55.4 MPa) was significantly higher than that at 10 Hz (41.1 MPa). The estimated fatigue limit at 2 Hz is much higher than stresses commonly found in the spine and also higher than that for other acrylic bone cements tested in a full tension-compression fatigue test, which indicates that tension-compression fatigue testing may substantially underestimate the performance of cements intended for vertebroplasty. A screening method was introduced, that may be used to shorten the time spent in performing compressive fatigue tests on specimens of acrylic bone cement for use in vertebral body augmentation procedures.

Highlights

- Compressive fatigue properties of a commercially available acrylic bone cement brand used in VP were determined.
- Three failure modes were found, the details of which depend on applied frequency and stress.

- The estimated mean fatigue limit at a frequency of 2 Hz was significantly higher than that at 10 Hz.
- Full tension-compression fatigue testing may underestimate the cements' performance in vertebroplasty.
- A screening method is introduced that may be used to shorten the duration of compressive fatigue tests.

Keywords

Acrylic bone cement; vertebroplasty; compressive fatigue properties

1. Introduction

Acrylic bone cements based on poly(methyl methacrylate) (PMMA) are widely used in total joint replacements (TJR) as well as in vertebral augmentation procedures known as vertebroplasty (VP) and balloon kyphoplasty (BKP), used for pain relief and fracture stabilization in the spine. The use of these types of cements in TJRs dates back to the 1960s (Charnley 1960) and in the spine to the 1980s, when they were introduced as a treatment for hemangioma (Galibert et al. 1987). In all the aforementioned applications, the bone cement is subjected to repeated mechanical loading, and, thus, its fatigue properties are important to the long-term success of the implant. Whereas the fatigue properties of acrylic bone cements used in TJRs have been extensively investigated (Charnley 1960; Lewis 2003), there are very few reports on the fatigue properties of acrylic bone cements used in VP and BKP, despite the fact that the composition of the cements may differ substantially. In particular, the amount of radiopacifier, commonly BaSO₄ or ZrO₂, is much higher in cements intended for use in VP and BKP. Since, in VP and BKP, a very high level of visualization of the cement is necessary, a radiopacifier content of the cement of between 30 and 45 wt% (of the powder mass), is used rather than the 9 – 15 wt% used in cements for TJRs, and this difference could be of importance as far as fatigue performance of the cement is concerned (Galibert et al. 1987; Lewis 2006). To the best of the present authors' knowledge, there are only four peer-reviewed reports available on the fatigue

properties of acrylic bone cement alone intended for use in VP and BKP (Kurtz et al. 2005; Boelen et al. 2008; Lewis et al. 2009a; Köster et al. 2013). Kurtz *et al.* and Köster *et al.* did not report the fatigue limit but the other two studies found results for the mean fatigue limit at 1.5-2 million cycles (the fatigue limit is defined as the cyclic stress level that can be applied to the material without causing failure at 5 million cycles in ASTM F2118-03 (ASTM 2009)) of 6.8 – 10.4 MPa (95% confidence bounds 2.8 – 12.8 MPa) (Boelen et al. 2008; Lewis et al. 2009a), similar to previous reports on the mean fatigue limit of cements used in TJRs (8.1 – 13.1 MPa, 95% confidence bounds were not reported (Lewis and Austin 1994; Lewis and Mladsi 1998; Lewis 2000)). However, in the above mentioned studies, either fully-reversed tension-compression was applied (Kurtz et al. 2005; Boelen et al. 2008; Lewis et al. 2009a), as specified in the ASTM standard for fatigue testing of acrylic bone cement materials (ASTM 2009), or four-point bending (Köster et al. 2013), in accordance with the ISO standard for flexural fatigue testing of acrylic resin cements (ISO 2008).

The ASTM standard for fatigue testing of acrylic bone cement materials was developed for cements used in joint fixations. In the vertebral body, however, mainly compressive loads are experienced (Wilke et al. 1999; Lewis et al. 2009b), and a more relevant way of fatigue testing may be under compression loading. Furthermore, a previous study comparing cyclic zero-tension loading to tension-compression found that the effect of compression on the fatigue strength appeared negligible during fully reversed testing, indicating that cyclic compression only may give very different results (Gates et al. 1983). Moreover, the standardized number of run-out cycles of 5 million relates to testing of materials intended for joint and hip replacements, and may be less relevant for materials intended for VP and BKP (Lewis et al. 2008; ASTM 2009).

Purely compressive fatigue studies on acrylic bone cement (Serbetci et al. 2004) or PMMA (Rubiolo and Muar 1996; Rittel 2000) are also scarce and none has investigated the fatigue limit, nor vertebroplastic cements containing high amounts of radiopacifier. The only peer-reviewed report available on compressive fatigue properties of an acrylic bone cement intended for BKP is from a synthetic bone augmentation model, where the combined performance of

the cement/synthetic bone was evaluated, *i.e.* not the performance of the cement as a stand-alone material (Lewis et al. 2008). It was found that the acrylic cement/synthetic bone model survived one million cycles (run-out) under a compressive load of 3.4 MPa.

Due to the lengthy character of fatigue tests (the ASTM standard cites run-out at 5 million cycles, at a frequency of 2 Hz (ASTM 2009), thus, approximately 29 days of testing) there is incentive to use higher frequencies. However, the fatigue properties of PMMA may differ depending on the frequency; an increase in fatigue life has been observed with a higher frequency in tension-compression for some cement brands (Lewis 2003), whereas for other brands, the influence of the frequency on fatigue life was not significant (Lewis et al. 2003). However, where failure is mainly due to thermal softening, which may be the case under compressive loading (Rittel 2000), an increased frequency may lead to a decrease in fatigue life. Furthermore, there are no studies in the literature on the modes of cement failure in a fatigue test of acrylic bone cement, nor on a method that may be used to shorten the duration of fatigue testing on cement specimens.

The purposes of the present study were to 1) obtain the compressive fatigue properties of a commercially available acrylic bone cement used in VP, at test frequencies of 2 and 10 Hz, and hence determine the influence of frequency on these properties; 2) identify the failure modes of the cement; and 3) introduce a method that may be used to shorten the duration of compressive fatigue tests on acrylic bone cement specimens.

2. Materials and methods

The acrylic cement Osteopal®V (Heraeus Medical GmbH, Wehrheim, Germany), was used as the model cement in this study. This cement has been developed for use in VP and its powder constituents are poly(methyl acrylate, methyl methacrylate) beads, benzoyl peroxide, ZrO₂ (45 wt%), and chlorophyll; its liquid constituents are methyl methacrylate monomer, N,N di-methyl-p-toluidine, hydroquinone, and chlorophyll.

The cement was stored at room temperature. A spatula was used to manually mix the cement at room temperature, in a bowl, for 30 s, according to the cement manufacturer's instructions. The cement dough was then transferred into standard-sized moulds for compression tests on acrylic bone cements for TJRs (ASTM 2008), with the nominal dimensions of the specimen being 6 mm in diameter and 12 mm in height. The specimens were cured at room temperature and then pushed out of the moulds with a plunger.

Quasi-static compression testing was performed using a universal materials testing machine (AGS-X, Shimadzu, Kyoto, Japan), in order to determine the stress at zero cycles. The tests were performed according to ASTM F-451 (ASTM 2008) on 11 specimens.

The specimens intended for fatigue testing were examined visually and radiographically (Faxitron® HP Cabinet X-ray System, Faxitron Bioptics LLC, Tucson, AZ, USA) for defects, with specimens containing pores with diameter larger than 1 mm being rejected (Cristofolini et al. 2000). The rejection rate, *i.e.*, the number of discarded specimens as a proportion of the total number of manufactured specimens, (46%) was within the range previously reported (40 – 60%) (Lewis 2000; Boelen et al. 2008; Lewis et al. 2009a).

The fatigue tests were performed under ambient conditions in a dynamic material testing system (MTS® Axial 858 Mini Bionix®II, MTS Systems Corp., Eden Prairie, MN, USA). Each of the accepted specimens was subjected to a small pre-load of 20 N, followed by a constant-amplitude cyclic compression-compression load, at a frequency of 2 or 10 Hz. A frequency of 2 Hz is the prescribed, clinically relevant, frequency in the standard (ASTM 2009); a frequency of 10 Hz, on the other hand, was merely used in order to investigate a possible acceleration of the test. The applied compressive loads corresponded to maximum stress levels of 50.0, 55.0, 60.0, 62.5 and 75.5 MPa at the lower tested frequency; and of 40.0, 55.0, 60.0, 62.5 or 75.5 MPa at the higher frequency. A stress level of two-thirds of the quasi-static compression strength was chosen as the starting point and steps of 2.5 MPa were used to identify the relevant stresses (Little 1975; Lewis et al. 2009a). For each specimen, the load was

ramped up in a tapered sinusoidal manner during the first 20 cycles until the maximum load was reached. Run-out was taken to be 5 million cycles, as indicated by the standard for tension-compression testing of acrylic bone cements (ASTM 2009). Since failure could not be detected as a sudden decrease in load in all cases (at lower applied load, the specimen continued to deform over time but not in a catastrophic manner), failure was taken to occur at a nominal strain (calculated during testing from the load frame displacement) value of 15%, as vertebral compression fractures are detected at a vertebral height reduction of 15 – 25% (Schwartz and Steinberg 2005). Four specimens were tested at each combination of stress and frequency level, with the following exceptions for which three specimens were tested: 50.0 MPa and 2 Hz; 62.5 MPa and 2 Hz ; 62.5 MPa and 10 Hz. Additional fatigue data come from preliminary tests, with only one tested specimen at each stress level.

The test results were analyzed using the Olgive equation (Krause et al. 1988):

$$S = A + \frac{B-A}{1+\left(\frac{\log N_f}{C}\right)^D}, \quad (1)$$

where S is the applied stress (in MPa), N_f is the number of cycles to failure, and A , B , C and D are material constants. A corresponds to the lower asymptote of the curve (estimated fatigue limit), B is upper asymptote, C is the number of cycles at the inflection point of the curve, and D is related to the slope at the inflection point (Krause et al. 1988). The Levenberg-Marquardt non-linear regression method, available in the Curve Fitting Toolbox™ in MATLAB® (Version R2012a, The MathWorks® Inc., Natick, MA, USA) was used to estimate the values of the material constants in Eq. (1). IBM® SPSS® Statistics (Version 19, IBM Corp., Armonk, NY, USA) was used to make a statistical comparison of the log fatigue life at the two frequencies, using a t-test at each stress level (ASTM 2009). Shapiro-Wilk's test was first used to confirm normality of the data.

At each combination of applied stress and frequency, a two-term power function was used to analyze the cumulative nominal strain (up to a maximum strain of 15%)-versus-number of stress cycles, N (Curve Fitting Toolbox™ in MATLAB®, Version R2012a, The MathWorks® Inc., Natick, MA, USA). This function was

$$S = aN^b + c, \quad (2)$$

where a , b , and c are constants. Results from these analyses were used to identify cement failure modes.

3. Results and discussion

The quasi-static compressive strength of Osteopal®V was found to be 87.8 ± 2.8 MPa, which serves as the stress level at zero cycles in Fig. 1. This result is similar to the previously reported strength (97.5 ± 8.7 MPa) of hand-mixed Osteopal® (Lewis 2000), a similar formulation to Osteopal®V but with lower amount of radiopacifier (6 wt% of powder instead of 45 wt%).

The $S-N_f$ results and the Olgive equation [Eq. (1)] fit to these results are shown in Fig.1, while the estimated values of the Olgive equation parameters are given in Table 1. The fatigue strengths presented here (55.4 MPa at 2 Hz) are lower than previous findings for acrylic cement under compression (CMW1®); the fatigue strength was found to be 71 MPa at 2Hz for the CMW1® cement, by extrapolation of the regression curve to 1 million cycles (Serbetci et al. 2004). However, the cement composition differs (CMW1® is aimed for prosthesis fixation and contains, *e.g.*, 9% BaSO₄ and higher relative amounts of activator and initiator) – which will influence the molecular structure and hence the mechanical properties. The mean fatigue life of different cement brands in tension-compression has in fact been found to differ substantially (Lewis 2003). However, the fatigue strengths found in our study as well as the one on CMW1®, are substantially higher than those found for acrylic bone cements tested at 2 Hz in fully reversed tension-compression fatigue, both those developed for fixation of TJR's as well as those developed for VP. In fact, mean fatigue limits of 8.1 – 13.1 MPa (Lewis and Austin 1994; Lewis and Mladsi 1998; Lewis 2000)) have been found for cements used in TJR's and mean fatigue limits of 6.8 – 10.4 MPa (95% confidence bounds 2.8 – 12.8 MPa) (Boelen et al. 2008; Lewis et al. 2009a) for cements developed for VP. In particular, the estimated fatigue limit at 2 Hz of a similar cement to Osteopal®V was found to be 11.0 MPa, when tested in a fully reversed tension-compression fatigue test (Lewis 2000). Osteopal® (the cement

used in the aforementioned study) has a lower amount of ZrO_2 compared to Osteopal®V, but is from the same cement brand and contains the same chemical components. Unfortunately, there are no data available comparing the fatigue strengths of commercial cements from the same producer containing different amounts of radiopacifier. One study (Kurtz et al. 2005), performed under tension-compression fatigue, on different cements containing 10, 30 and 36 wt% BaSO_4 found that the cement containing 30 wt% BaSO_4 gave somewhat better fatigue properties than the cement containing 10 wt%, while the cement containing 36 wt% performed worse than both of the other formulations. However, while the cements containing 10 and 30 wt% BaSO_4 were both commercial formulations, they came from different brands (the formulations were Simplex®P and KyphX HV-R, respectively). Furthermore, the cement containing 36 wt% BaSO_4 was an experimental formulation, based on Simplex®P, and it was hypothesized that agglomeration together with a less homogenous distribution of the radiopacifier in the cement affected the properties negatively. Hence, the effect of the amount of radiopacifier on the mechanical properties of acrylic bone cement remains inconclusive, although it is unlikely that the effect is as large as the difference found here in fatigue properties between cements tested under tension-compression and compression-compression. Although there are no data on the performance of the exact same cement composition in fully reversed tension-compression fatigue, the much higher estimated fatigue limit found in this study compared to the previously published data, could indicate that tension-compression fatigue testing may substantially underestimate the performance of cements intended for vertebroplasty. Moreover, as previously mentioned, Gates *et al.* (Gates et al. 1983) found that the effect of compression appeared negligible during fully reversed testing by comparing cyclic zero-tension loading to tension-compression.

The fatigue limits presented here are substantially higher than stresses typically experienced by vertebral bodies during many normal daily activities (for example, at L4-L5, stress ranges from 0.1 MPa, while lying supine, to 2.3 MPa, while lifting 20 kg, bent over with round back (Wilke et al. 1999)). Furthermore, mechanical testing of human vertebral trabecular bone, in the thoracic-lumbar

region, indicates that their compressive strength ranges from 0.05 – 14.0 MPa (mean ultimate stress values of 0.05 MPa (Keller 1994; Follet et al. 2010) – 7.0 MPa (Augat et al. 1998) and mean yield stress values of 0.1 – 14.0 MPa (Nazarian et al. 2008) have been reported). However, most of the tested vertebrae in these studies were not divided into healthy bone or underlying pathologies, *e.g.*, osteoporotic or metastatic bone. Hence, the authors expect the fatigue limits found in this study to be far higher than what is actually required in vivo, where the main indication for vertebroplastic treatment is for osteoporotic fractures. This suggests that, in a fractured vertebral body augmented using VP, the likelihood of fatigue of the cement zone is very low.

Fig. 1 Summary of the fatigue test results, where N_f is number of cycles to failure. Fits to Eq. (1) are shown as continuous curves, and the dotted curves represent the 95% confidence limits.

Table 1. Estimates of the parameters in the Olgive equation [Eq. (1)]. (Mean values with 95% confidence limits in parentheses.)

Frequency [Hz]	A	B	C	D
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2	55.37 (52.87; 57.87)	87.66 (80.07; 95.25)	2.23 (1.99; 2.47)	6.18 (2.73; 9.62)
10	41.13 (38.42; 43.85)	88.10 (82.14; 94.07)	2.58 (2.44; 2.72)	6.05 (4.26; 7.83)

The statistical analysis of the fatigue results is shown in Fig. 2. Significant differences ($p < 0.05$) were found between 2 and 10 Hz at stress levels of 55.0 and 60.0 MPa. However, at 62.5 and 75.5 MPa the differences between 2 and 10 Hz were no longer significant ($p > 0.05$). The estimated mean fatigue limit, at 2 Hz (maximum compressive stress 55.4 MPa) is much larger than that obtained at 10 Hz (41.1 MPa). The significantly higher fatigue limit observed when the frequency was decreased, is diametrically opposed to the findings of a previous work (Lewis et al. 2003). However, Lewis *et al.* tested their cement formulations in a fully reversed tension-compression set-up, which may affect the performance of the cements. In fact, large thermal effects, due to an increased frequency, have been shown to have a negative influence on the compressive fatigue properties (Rittel 2000). Rittel also showed that a slight increase in the maximum applied load caused a radical increase in temperature, whereas a rise of the frequency from 10 to 15 Hz only resulted in a minor temperature change. Hence, where failure is mainly due to thermal softening, *e.g.*, at high loads, the frequency effect may be less pronounced, and vice versa, in accordance with our results. It should be noted however, that the tested material in Rittel's study was a commercial PMMA which is likely to be different from a vertebroplastic PMMA cement, in terms of, *e.g.*, molecular weight, additives and porosity (Vallo et al. 1998), which might have an effect on the heat dissipation from the material. Furthermore, in Rittel's study it was never clarified whether the introduction of a thermocouple into the PMMA specimen may have affected the fatigue results.

Fig. 2 Statistical comparison of the log fatigue life at the two frequencies, at a significance level $p = 0.05$ (ASTM 2009)

The nominal strain versus N results obtained are shown in Figs. 3 and 4 for specimens tested at 2 and 10 Hz, respectively. Specimens that survived all the way to run-out are indicated with a ring and arrow pointing upwards. In both Figs. 3b and 3c, failure for three out of four specimens occurred after $2.5 \cdot 10^4$ and 3000 cycles, respectively, as noted by the arrows.

a)

b)

c)

d)

e)

Fig. 3 Summary of the nominal strain-versus-number of stress cycles (N) results, obtained at a frequency of 2 Hz and a stress of a) 50.0 MPa, b) 55.0 MPa, c) 60.0 MPa, d) 62.5 MPa and e) 75.5 MPa. Grey circles correspond to data points for tested specimens and continuous black curve is the mean curve from the fit of Eq. (2) to the results. The insets show photographs of typical specimens after fatigue testing for each stress level. The ring with an upwards-pointing arrow indicates that the specimen survived all the way to run-out. The arrows indicate that the specimens survived longer than the highest value shown on the N axis.

a)

b)

c)

d)

e)

Fig. 4 Summary of the nominal strain-versus-number of stress cycles (N) results, obtained at a frequency of 2 Hz and a stress of a) 40.0 MPa, b) 55.0 MPa, c) 60.0 MPa, d) 62.5 MPa and e) 75.5 MPa. Grey circles correspond to data points for tested specimens and continuous black curve is the mean curve from the fit of Eq. (2) to the results. The insets show photographs of typical specimens after fatigue testing for each stress level. The ring with an upwards-pointing arrow indicates that the specimen survived all the way to run-out.

As shown in Figs. 3 and 4, the nominal strain is highly affected by the frequency and the stress level. The nominal strain- N dependence is, essentially, logarithmic for all specimens tested at 2 Hz and 50.0 MPa; for all specimens tested at 10 Hz and 40.0 MPa; and for a few specimens tested at 2 Hz, 55.0 and 2 Hz, 60.0 MPa (Figs. 3 and 4). The lattermost results may indicate a change in failure mode in these cases (relative to the modes for specimens tested at 2 Hz but at 50.0 MPa, 62.5 MPa, and 75.5 MPa). This is further supported by the large variations in N_f for specimens tested at 2 Hz, 55.0 MPa and 60.0 MPa, as compared to that of the other stress levels, as seen in Fig. 2.

Based on the adjusted coefficients of determination, R^2_{adj} , the power functions were overall slightly better at describing the evolution of the strain over N for fatigue tests performed at 2 Hz than at 10 Hz (Table 2), except for the lowest stress level at 10 Hz which had values of R^2_{adj} comparable with that of the 2 Hz

specimens (average R^2_{adj} of 99.2% and 98.9%, for 2 and 10 Hz, respectively). Note that in Fig. 3c, the mean fit curve was created from only three of the specimens, as the strain- N behavior for one of them deviated substantially from the others.

The logarithmic dependence is also reflected in the b -values, which are in the order of 10^{-1} , see, *e.g.*, b -values for 50.0, 55.0 or 60.0 MPa in Table 2a or 40.0 MPa in Table 2b. At these stress levels, the a -values are also similar, having an order of 10^{-3} . At higher stress levels at 2 Hz, the increase in strain is more sudden, but not as catastrophic as for the specimens tested at 10 Hz and stress levels of 55.0 MPa, 60.0 MPa, 62.5 MPa, and 75.5 MPa. As seen in Table 2, the b -values for these stress levels – connected to an exponential increase in strain at failure – are a factor 20 higher compared to the stress levels associated to strain- N curves resembling a logarithmic increase in strain. The a -values for the former curves are much smaller, in the order of 10^{-15} , than the latter.

Three different failure modes of the acrylic bone cements were found in this study, as indicated by specimen shape after testing, values of N_f at the different stress levels, and the shape of the strain- N curves. For the lowest stress levels (50.0 and 40.0 MPa for 2 and 10 Hz, respectively), the specimens were slightly deformed but the cylindrical shape the specimens had from the start was still maintained, as seen in the inset in Fig. 3a. The same shape was found for a majority of the specimens tested at 2 Hz and 55.0 MPa (Fig. 3b). This specimen shape was connected to strain- N curves indicating a logarithmic increase in strain, see, *e.g.*, Fig. 3a. The failure mode of the 2 Hz specimens tested at 62.5 and 75.5 MPa corresponded to pronounced barreling (see insets in Figs. 3d and. 3e). One of the specimens tested at 2 Hz, 60.0 MPa was found to have this shape after testing as well. Strain- N curves with an exponential increase in strain at failure were associated to this specimen shape, see, *e.g.*, Fig. 3d. In contrast, the failure of the specimens tested at 10 Hz at stress levels of 55.0 MPa or higher, had a more rapid exponential increase in strain at failure, see, *e.g.*, Fig. 4b, and gave a torus-like bulging of the specimens, as seen in the inset of the same figure. A similar failure mode has previously been reported to occur for PMMA under compressive fatigue loading, hypothetically caused by a lack of uniform heat

distribution in the specimens (Rittel 2000). In that study, fatigue tests were performed at frequencies of 3, 10 and 15 Hz, but it is not clear whether the localized bulging of the specimens was found for all frequencies. Rittel also observed that a small increase from $0.40\sigma_y$ to $0.44\sigma_y$ (where σ_y is the yield strength) in maximum stress level, caused the specimen core temperature to double, and consequently gave a sudden failure of the specimen. However, Rittel tested PMMA, not acrylic bone cement; as such, the findings in the present study cannot be directly compared to those of Rittel. Nonetheless, the influence of the frequency and stress level on the failure mode found in this study could be explained by the same kind of thermal heating during fatigue cycling. However, the temperature distribution within the specimens needs to be studied in more detail in order to investigate this behavior thoroughly.

It could be debated as to whether the present nominal strain- N results (Figs. 3 and 4) are due solely to elastic and plastic strain resulting from the applied loads, or if creep plays a role. Generally speaking, highly cross-linked polymers, such as PMMA, have a good creep resistance (Kaiser 1989). Several investigators have studied the creep behavior of acrylic bone cements, as summarized in the review by Lewis (Lewis 2011). It has previously been shown that the creep is faster when the cement is loaded under tension rather than under compression, and that a higher stress level will result in a higher creep rate (Verdonschot and Huiskes 1995). Moreover, an increasing temperature in the core of the specimen is likely to lead to higher creep strains. However, neither the creep rate nor the specimen temperature was investigated in the present study. Hence, the influence of creep strain on the strain- N behavior of vertebroplastic cements under purely compressive loading should be clarified in future studies.

Table 2. Summary of the estimates of the coefficients in Eq. (2), obtained from analysis of the mean strain-versus- N results for a) 2 Hz and b) 10 Hz.

a)

2 Hz	a	b	c	$R^2_{adj} [\%]^1$
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50.0 MPa	$1.1 \cdot 10^{-3}$	$2.6 \cdot 10^{-1}$	$9.4 \cdot 10^{-3}$	100
55.0 MPa	$2.8 \cdot 10^{-3}$	$3.8 \cdot 10^{-1}$	$-2.1 \cdot 10^{-3}$	99.9
60.0 MPa	$7.4 \cdot 10^{-3}$	$3.1 \cdot 10^{-1}$	$-1.5 \cdot 10^{-2}$	99.8
62.5 MPa	$4.7 \cdot 10^{-15}$	5.2	$2.1 \cdot 10^{-2}$	100
75.5 MPa	$1.6 \cdot 10^{-15}$	6.7	$2.5 \cdot 10^{-2}$	99.9

b)

10 Hz	<i>a</i>	<i>b</i>	<i>c</i>	R^2_{adj} [%]¹
40.0 MPa	$1.3 \cdot 10^{-3}$	$2.2 \cdot 10^{-1}$	$4.8 \cdot 10^{-3}$	100
55.0 MPa	$1.7 \cdot 10^{-18}$	5.8	0	98.9
60.0 MPa	$2.0 \cdot 10^{-16}$	5.4	$1.5 \cdot 10^{-2}$	100
62.5 MPa	$2.7 \cdot 10^{-16}$	5.4	$1.9 \cdot 10^{-2}$	100
75.5 MPa	$9.7 \cdot 10^{-17}$	6.9	0	100

¹ R^2_{adj} : coefficient of determination, adjusted for degrees of freedom.

Given the cost associated with running fatigue tests, there is incentive to identify or develop methods that may be used to shorten the duration of these tests, without degrading the quality of the results. Here, a screening method is presented that may be used to identify relevant fatigue testing conditions, such as the stress level that approximates to the cement's fatigue limit. The best estimates of curve fitting parameters *a* and *b* (for each strain-*N* curve), for all cycles until failure or run-out were used. In addition, curve fits on strain-*N* results obtained up to 300 cycles were performed, using the same method as previously described. The specimens were divided into three groups based on visual inspection of their shape, together with an assessment of their strain-*N* curves: type 1 being the type of specimens seemingly unaffected by the loading (slightly deformed specimens; Fig. 3a); type 2 having the barrel shape (Fig. 3e); and type 3 with a torus-like bulging (Fig. 4b). The relationship between b^2 and a^2 , mapping the three types of specimens, is shown in Fig. 5. In the left-hand graph of Fig. 5, showing fits of strain data up to 300 cycles, the type 1 specimens barely overlap those of type 2, however, it is impossible to discriminate the type 3

specimens from the others. In the right-hand graph, showing fits of strain data until failure or all the way to run-out, the type 1 specimens are clearly distinguished from those of type 2 and 3, whereas the latter two types overlap. Thus, it is impossible to discriminate type 1 specimens, *i.e.*, specimens that will survive millions of cycles, from specimens that will fail more suddenly (type 2 and 3), unless the failure has already occurred. In the present study, at least 900 cycles, *i.e.*, the maximum number of cycles a type 3 specimen survived, were necessary to separate the type 1 specimens from the others (graph not shown). The method shows that, after just a few hundreds of cycles, it is possible to predict the stress and frequency level where specimens will survive millions of cycles, and the stress and frequency level where specimens will fail more suddenly. Thus, the results of the screening method indicate that a lower run-out limit could have been used for the compressive fatigue tests, rather than the standardized number of run-out cycles of 5 million. The screening method presented here needs to be applied to compressive strain-versus- N results obtained from a large collection of specimens fabricated from many cement brands used or developed for use in VP and BKP before its universality to this class of cements is established.

Fig. 5 Squared curve fitting parameters, a and b , for the three different specimen types: type 1, 2 and 3. To the left, the curve fittings were performed on nominal

strain data up to 300 cycles and to the right, strain data for all cycles until failure or run-out were included in the fits

Four limitations of the current study are recognized. First, in the fatigue tests, at each stress level, the number of specimens (3-4) tested was lower than what is specified in the standard (15) (ASTM 2009). However, more stress levels were tested here than what is specified in the standard, partly compensating for this. Second, in the fatigue tests, the higher frequency was used in this study to evaluate the feasibility of using accelerated testing conditions. However, it should be pointed out that 10 Hz is not considered a clinically relevant frequency. Third, in the fatigue tests, the specimens were tested in air at ambient temperature, rather than, as specified in the standard, immersed in a test solution at 37°C (ASTM 2009). Performing the fatigue testing in a test solution, *e.g.*, phosphate buffered saline, would more closely simulate the conditions the PMMA cements would experience in vivo. However, the influence of specimen conditions on fatigue life of acrylic bone cement specimens lacks clarity, with some workers reporting higher fatigue life for specimens tested in bovine serum at 37°C compared to testing in ambient air (Freitag and Cannon 1977), while the opposite trend was reported in studies that compared testing in room-temperature air and saline solution at 37°C (Johnson et al. 1989). The temperature of the test environment seems to have an effect; Johnson et al. showed an increase in fatigue life when the saline was at room temperature compared to 37°C (Johnson et al. 1989). Further studies of the compressive fatigue properties of acrylic bone cements, should include testing under wet conditions in an environmental chamber. Fourth, the chosen power function to the strain- N results (see Eq. (2)) slightly underestimates the b -values for the specimens tested at 10 Hz and stress levels of 55.0 MPa or above, mostly type 3 specimens. Hence, in Fig. 5, type 3 data points are expected to be more easily distinguished after failure, given a better curve fitting method. However, this would not affect the results shown in the left hand graph of Fig. 5, since here, most of the type 3 specimens had not failed. The two-term power function was chosen on the premise that this function was able to conform to all types of

strain data and was more straightforward to analyze and compare, given its relatively few fitting parameters.

4. Conclusions

The compressive fatigue properties of a commercially available acrylic bone cement developed for use in VP, and hence containing high amounts of radiopacifier, were evaluated for the first time. The estimated mean fatigue limit at 2 Hz (55.4 MPa) was much higher than that at 10 Hz (41.1 MPa). The estimated fatigue limit found here was approximately five times that of the compressive loading part of a similar cement tested in full tension-compression. This indicates that tension-compression fatigue testing may substantially underestimate the performance of cements intended for vertebroplasty, where the cements are mainly subjected to compressive loading. Concurrent with the fatigue tests, nominal strain-versus-number of loading cycles results were obtained. An analysis of these results showed that there were three cement failure modes, the details of which depend on frequency and applied stress. A screening method was introduced, that may be used to shorten the time spent in performing compressive fatigue tests on specimens of acrylic bone cement for use in vertebral body augmentation procedures. This involved analyzing power function curve fits to the nominal strain- N results. It was found that 900 cycles were sufficient to discriminate between specimens that will survive millions of cycles from those that will fail after just a few hundreds of cycles. Thus, the results obtained indicate that a lower run-out limit could be used for compressive fatigue testing of acrylic bone cements, rather than the standardized number of run-out cycles of 5 million.

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