J Mater Sci: Mater Med (2006) 17:1127–1132
DOI 10.1007/s10856-006-0539-2

Characterization of a novel calcium phosphate composite bone cement: Flow, setting, and aging properties

M. L. Roemhildt · S. D. Wagner · T. D. McGee

Received: 22 March 2005 / Accepted: 9 February 2006

Abstract The flow, setting, and aging characteristics of a newly developed calcium phosphate/calcium aluminate composite orthopaedic cement were studied. The effect of vibration on the flow of the cement paste was studied and found to greatly enhance placement. The setting times of this cement were dependent on temperature and decreased with increasing temperatures. At 37°C, the working and setting times were 6.3 ± 0.3 and 12.8 ± 0.4 minutes, respectively.

Hydration and conversion of the cement phases continued while specimens were stored under simulated, physiological conditions. A cumulative increase in mass of $8.23 \pm 0.65\%$ was observed over a 14 month test period. During this time, the cement was found to expand slightly, $0.71 \pm 0.39\%$. X-ray diffraction was used to characterize the crystalline phases present during hydration and conversion. The calcium aluminate in the cement hydrated and formed calcium aluminate chloride hydrates, while no changes were observed in the ß-tricalcium phosphate during the testing period.

M. L. Roemhildt (✉)
Department of Orthopaedics and Rehabilitation, 95 Carrigan Drive, University of Vermont, Burlington, VT 05403, USA
e-mail: maria.roemhildt@med.uvm.edu

S. D. Wagner
Department of Veterinary Clinical Sciences, Iowa State University, Ames, IA 50011, USA
e-mail: sdwagner@iastate.edu

T. D. McGee
Department of Materials Science and Engineering, Iowa State University, Ames, IA 50011, USA
e-mail: tmcgee@iastate.edu

1 Introduction

Poly(methyl-methacrylate), PMMA, cements are widely used in orthopaedic repair and joint replacement surgery despite well documented shortcomings including the exothermic setting reaction, lack of direct bonding at the cement-bone interface, cement breakdown over time, and effect of cement particulate debris. Much research has focused on attempting to improve characteristics of PMMA cement, while other efforts seek to develop new cements to replace PMMA cements. Several calcium phosphate cements have been developed and are being investigated for orthopaedic applications [1–7]. Hydroxyapatite and ß-tricalcium phosphate (ß-TCP) have favorable tissue responses; the interface between bone and these ceramics can occur without the formation of an intermediary, soft tissue layer [8, 9]. Present calcium phosphate cements are generally brittle and have poor mechanical properties. Although efforts continue to improve this class of cement, present mechanical properties are insufficient for load-bearing applications [10, 11].

In addition to biocompatibility and adequate mechanical properties, a bone cement should have flow properties to allow proper placement and an appropriate setting time so that cement placement can be verified before closure of the wound. If the projected use of a bone cement includes load-bearing applications, it should be stable in the physiological environment and provide enduring strength.

PMMA bone cement is typically placed with the application of pressure. The applied pressure increases the flow of the cement and promotes filling of the void space. With pressure, PMMA cement is forced into cavities of trabecular bone. The resulting mechanical interlocking between the cement and natural, surface interstices of the bone increases initial stabilization [12]. However, the procedure to implant PMMA cement in long bones decreases blood

supply to the surrounding bone which may be detrimental to the overall health of the bone [13]. In PMMA bone cement, shrinkage results following polymerization and has been found to increase loosening of the implanted prosthesis [12].

In previous work, Osteoceramic cement (OC-cement), a novel, composite bone cement containing calcium phosphate and calcium aluminate was developed [14, 15]. In this cement, calcium phosphate is incorporated for biological activity while calcium aluminate provides high, long-term strength. The result is a hydraulic cement wherein setting may be controlled through the use of additives. The cement achieves a compressive strength of 70 MPa within 4 hrs and values of 100 MPa are maintained after 32 wks aging under simulated physiological conditions [15].

The objective of the present research is to gain fundamental knowledge regarding the properties of OC-cement. This includes characterization of flow properties of the cement paste, study of the effect of temperature on cement setting, and analysis of physical and crystalline phase changes in the cement during aging under simulated, physiological conditions. OC-cement paste exhibits dilatent flow; the resistance to flow is increased as the rate of shear increases. The cement is similar to Portland cements in that it flows better under light vibration. Therefore, the effect of vibration on the flow of the cement was studied to aid in effectively placing the cement. While the cement paste sets within minutes to form a rigid mass, mineralogical changes are expected to continue over a much longer period of time, which were observed with X-ray diffraction (XRD).

2 Materials and methods

2.1 Cement preparation

OC-cement was prepared from powders of ß-TCP (33 wt%, Fluka Chemicals, Neu-Ulm, Switzerland) and calcium aluminate (66 wt%) and combined with a calcium chloride solution to control setting as previously described [15]. Calcium aluminate with a molar ratio of calcium to alumina of approximately 0.82 to 1.00 was used. This cement contained mainly CA, CA_2, with small amounts of $C_{12}A_7$ and alumina: where C = CaO and A = Al_2O_3. Calcium chloride solution (2M), prepared from calcium chloride (Fisher Scientific, Fairlawn, NJ) and de-ionized water, was used to control the setting properties. The dry cement components were combined with the hydration solution, mixed for one minute to form a uniform paste, and vibration was applied with a hand massager for 45 seconds at high speed to aid in mixing and removal of entrapped air.

2.2 Setting

Working and setting times were determined using a procedure similar to that used for calcium phosphate cements and dental cements [2]. Working time indicates the end of moldability without damage to the developing cement structure [16]. The setting time was defined as the point beyond which it was possible to handle the cement without damaging the cement [16]. Because of the small sample size and the rapid rate of setting of OC-Cement, the standard test procedure for measuring working and setting time with Gillmore needles and heavy masses was unsuitable (ASTM C266-03). Initial experiments with the Vicat needle (ASTM C191-04), were not as versatile or sensitive as a simple manual test utilizing a tapered semi-microspatula with a thickness of 0.5 mm and a 1 mm radius at its apex (#21-401, Fisher Scientific). The working time was measured as the time when the cement paste no longer consolidated following withdrawal of a microspatula inserted to a depth of 5 mm. The setting time was measured as the time at which the cement could bear a microspatula pressed perpendicularly against its surface with a force of approximately 75 g without appreciable indentation (<0.2 mm). Setting times were measured at temperatures ranging from 10–40°C where the cement ingredients and surroundings were maintained at the indicated temperature.

2.3 Flow

The consistency of the prepared cement was that of a thick paste. To measure the flow of the OC-cement, procedures by Katsumura et al. and the American Dental Association Specification No. 8 for zinc phosphate dental cement were followed with appropriate modifications [17, 18]. The cement was placed in a syringe with an inner diameter of 0.8 cm and a disc was prepared using 0.5 ml of cement. The cement disc was placed on a smooth glass plate. An additional glass plate and weight (120 g total) were placed on top of the cement disc for 20 minutes. For the vibrated condition, immediately after disc formation, vibration with a hand massager was applied to the lower glass plate for the designated time. In general, the cement flowed outward between the plates in a radial manner. The diameter of the cement disc was measured initially, immediately after vibration, and subsequently at five-minute increments using a digital micrometer. The mean disc diameter of each trial was calculated from three measurements taken at 60° increments. The mean diameter for each condition was determined from 10 trials.

2.4 Characterization of set OC-cement

Specimens, 12 mm diameter ×16 mm height, were prepared for testing. Cylindrical, acrylic molds were filled with cement paste, ends of the mold were covered with small acrylic plates

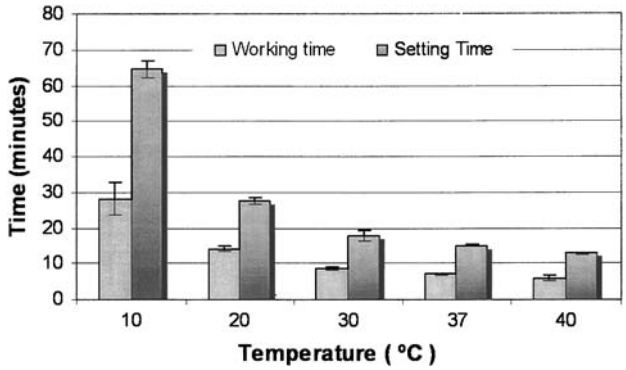

Fig. 1 Setting of OC-cement (mean ± SD, $n = 6$)

and secured before placing in a water bath maintained at 37°C to set. Twenty minutes after setting, the specimens were removed from the molds and placed in small containers filled with lactated Ringer's solution (Abbott Laboratories, North Chicago, IL). Samples were stored at 37°C until evaluation at a range of intervals from 1 hour after setting up to 24 months.

2.4.1 Physical changes

The mass and diameter of OC-cement specimens were recorded at intervals from 1 hour after setting to 14 months. The diameter of each specimen was measured using a micrometer, taking readings from the same location at each time point. After being rinsed with deionized water, specimens were blotted dry with filter paper before the mass was measured to an accuracy of ±0.001 g using a precision balance. Specimens were returned to storage vials following measurement.

2.4.2 Mineralogical changes

Mineralogical changes of OC-cement after setting and during aging were analyzed using x-ray diffraction (XRD). Hydrated cement specimens that had aged under simulated physiological conditions were quenched in acetone to stop hydration, then crushed and ground to powder less than 250 μm in diameter using a mortar and pestle. Scans were performed on a Scintag XI diffractometer (Scintag Inc., Cupertino, CA) at 45 kV, 40 mA using Ni-filtered CuK_a radiation ($\lambda = 0.1542$ nm). Data was collected using a stepwise scan ($1°2\theta$ min^{-1}, step 0.020°, count time 1.2 s, $2\theta = 10$–70°). Phases were identified using JCPDS diffraction data [19].

2.5 Statistical analysis

Mean and standard deviation (SD) are presented for the experimental data. The Student's *t*-test was used to assess whether the observed differences between the means of different groups were statistically significant with a *p*-value less than 0.05 considered significant.

3 Results

3.1 Setting

The working and setting times of OC-cement are dependent on cement composition, the presence of additives, and the mixing environment. The working and setting times were evaluated from 10–40°C and found to be temperature dependent (Fig. 1). The working time decreased progressively: 28.2, 14.2, 8.6, 6.3, and 4.4 min, with increasing temperature. Similarly, the setting time decreased: 64.4, 27.5, 17.92, 12.8, and 10.2 min, as the temperature increased.

An Arhenius plot of In time vs. absolute temperature^{-1} in Fig. 2 shows high correlation and approximately the same slope for both the working and setting times. The slopes of the regressions lines are equal to δH/R, therefore δH of −42 kJ/mole was calculated for the setting reaction.

3.2 Flow

For OC-cement, the mean diameter of a standard cylinder, under a standard load, without vibration increased from 0.938 ± 0.720 to 1.395 ± 0.218 cm, 49%, over the 20 minute

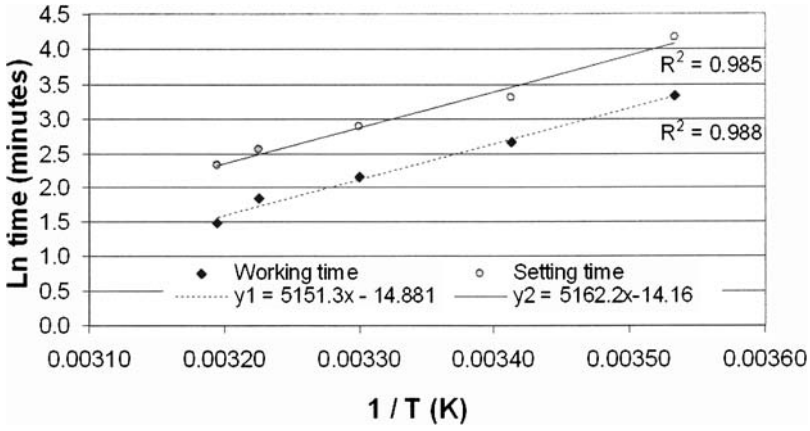

Fig. 2 Arhenius plot of OC-cement setting

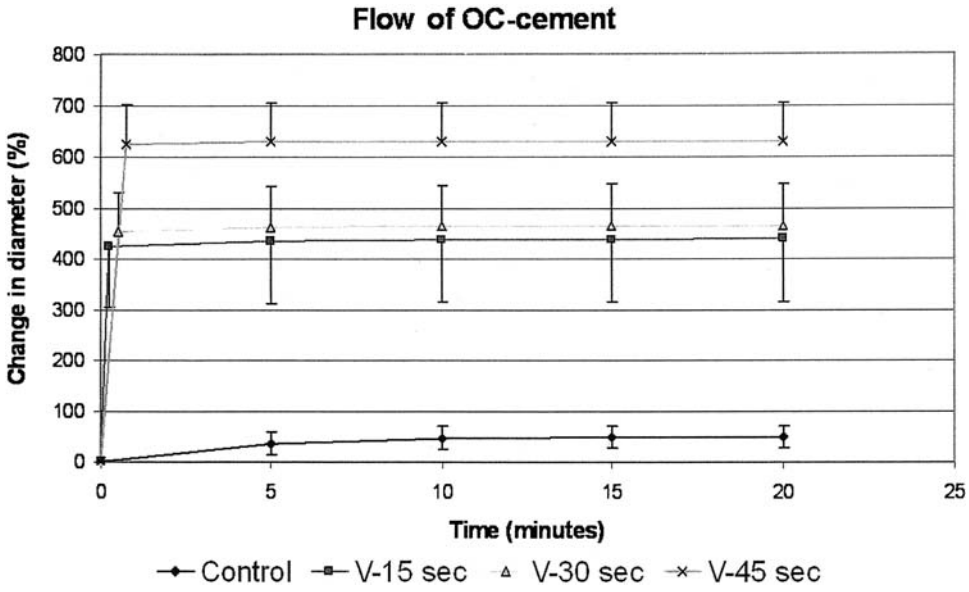

Fig. 3 Flow of OC-cement (mean ± SD, $n = 10$)

period. The greatest change took place during the initial 5 minute period (Fig. 3). OC-cement that had been vibrated showed an immense increase in mean diameter following vibration. Total increases in diameter over the 20 minute test period of 438%, 442% and 629% were found for OC-cement vibrated 15, 30, and 45 seconds, respectively (Fig. 3). Following vibration up to 20 minutes, there was an increasing trend in mean diameters 3.2%, 1.8%, and 0.9%, for the 15, 30, and 45 second vibration durations, respectively. However, these small changes in diameter following vibration were not statistically significant.

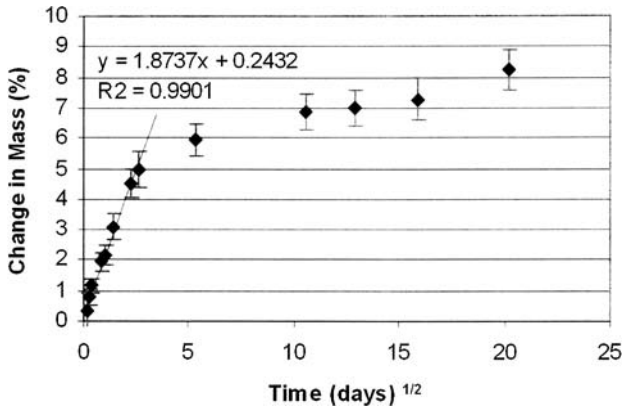

Fig. 4 Change in mass over time in OC-cement (mean ± SD, $n = 15$)

3.3 Changes in OC-cement during aging

3.3.1 Physical changes

Over a one-month period, the mass of the pellets was found to increase 5.95 ± 0.51% (Fig. 4). During the remainder of the experimental period the mass of cement pellets continued to increase, but at a slower rate. A total increase in mass of 8.23 ± 0.65% was observed after 14 months. This increase in mass is thought to be a result of absorption of water from the Ringer's solution that allows for continued hydration of calcium aluminate in the cement. The diameter of the same pellets increased 0.71 ± 0.39% over the 14 months period (Fig. 5).

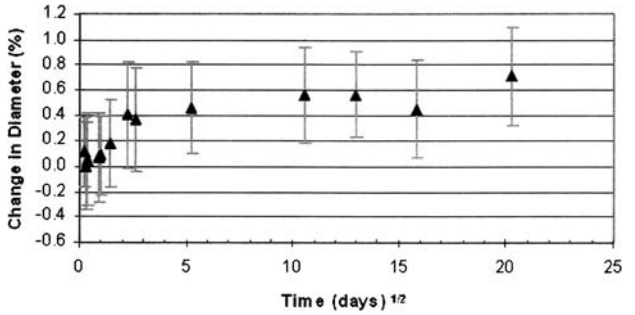

Fig. 5 Change in diameter over time in OC-cement specimen (mean ± SD, $n = 15$)

3.3.2 Changes in phase composition

X-ray diffraction (XRD) scans were collected at 1, 5, 7, 14, 28 days, 6, 14 months, and 2 yrs. Figure 6 shows a compilation of XRD scans for all times, with the major characteristic peaks of each phase marked. Cement notation is used to identify the phases present: C = CaO, A = Al_2O_3 and H = H_2O.

Although the OC-cement sets within 15 minutes of preparation, changes in the mineralogical composition occur over a much longer time due to the continued hydration of calcium

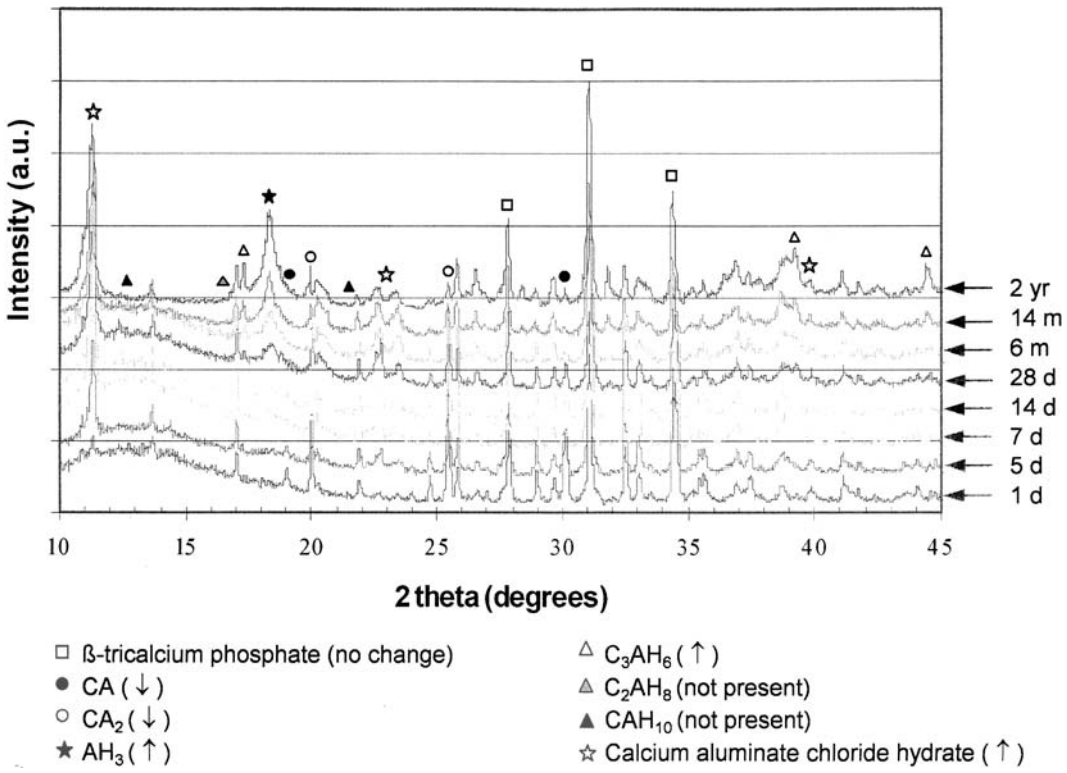

Fig. 6 Compilation of XRD scans of OC-cement aged 1 day up to 2 years. Intensity is shown in arbitrary units (a.u.)

aluminate phases and conversion reactions of the cement hydrates. The CA peak decreased rapidly within the first seven days. The CA_2 peak showed little change up to 28 days. A decrease was noted at six and 14 months while some CA_2 remained present up to two years. The change in CA and CA_2 peaks results from the hydration of these phases. The ß-TCP peak was not observed to change during the testing period. Of particular interest was the initial absence of the typical calcium aluminate hydration peaks: CAH_{10}, C_2AH_8, and C_3AH_6. Instead, the $CaCl_2$ in the hydration solution led to the formation of calcium aluminate chloride hydrates. There are multiple types and phases of calcium aluminate chloride hydrates and given that hydrate peaks often appear broad; at times less than six months it was not possible to resolve the peaks to determine which specific phases were present. Additional higher resolution scans collected between 11–12 degrees and 21.5–23.0 degrees 2? on the 14 months and two year samples found hydrate peaks consistent with a-$Ca_4Al_2H_{0.34}O_{6.34}Cl_{1.67}$ and $Ca_2Al(OH)_6Cl{\cdot}2H_2O$. Most likely, a solid solution exists as was reported for the calcium chloride aluminate hydrates studied by Poellmann and Kuzel [20]. At seven days, the presence of AH_3 was observed. After two years, the AH_3 peaks had become more prominent and sharpened. Small peaks corresponding to C_3AH_6 began to emerge after 28 days; over time, they became slightly larger and more defined.

4 Discussion

Results from flow experiments show that under specific conditions, OC-cement flows readily. Its unique flow properties could be advantageous for some applications. The dilatent nature of the cement could prevent cement from being forced deeply into trabecular bone, as frequently occurs with PMMA cement implanted with applied pressure. However, adapting to the differences in flow would require modifications to the typical PMMA cement placement procedure.

The setting time of OC-cement can be controlled through the use of a variety of additives. The calcium chloride solution used in this study resulted in a setting time of 12.5 to 13.5 min at 37°C. This conforms to the ASTM standards for setting and is similar to commercial PMMA bone cements [21, 22].

The increase in mass observed over time is due to the uptake of water and continued hydration of the calcium aluminate in the cement. Initially, this effect is likely diffusion controlled, as the percentage change in mass is linear with $\text{time}^{1/2}$ as is typical of diffusion-controlled reactions (Fig. 5). Then the change occurs at a slower rate.

OC-cement was found to expand slightly (approximately 0.7%) over the 14-month, test period. The hydration and subsequent conversion of the hydrated phases in calcium aluminate cement are both temperature and time dependent [23–25]. The variations in densities of the calcium aluminate phases present on hydration in OC-cement are believed to

play a role in the slight expansion observed. Whether this expansion could be a beneficial characteristic for *in vivo* applications is not yet known, but it may enhance stability and circumvent loosening. Although cement hydration reactions continued throughout the test period as observed with XRD, the system had not yet achieved equilibrium most likely due to simultaneous conversion reactions occurring in the cement. It is clear that OC-cement is a complex system and the details of conversion reactions require further study. Calcium aluminate cements are widely used in ordinary concretes for construction purposes and are known to continue to hydrate very slowly for years after placement. Calcium aluminate cements are stable in sea water with salt concentrations similar to body fluids [26]. With the mineralogical changes observed here, *in vivo* stability is anticipated although longer term studies, as well as, *in vivo* experimentation will be needed to verify this.

The characteristics of the setting time, flow, physical changes reported presently, and the previously reported long-term stability under physiological conditions appear suitable for a bone cement material. Calcium phosphate is a well accepted material for bone replacement.

Furthermore, porous calcium aluminate ceramics have been investigated for orthopaedic applications since the 1970's and have been found to be biocompatible when implanted in bone [27–29]. OC-cement combines calcium phosphate and calcium aluminate cement to form a novel biomaterial. Additional study including *in vitro* and *in vivo* tissue response is warranted to investigate host response to this material as well as the material's performance *in situ*.

Acknowledgment This study was supported in part by the Iowa State University Research Foundation.

References

1. W. E. BROWN and L. C. CHOW, in "Cement Research Progress," Westerville, Ohio, 1986, edited by P. W. Brown (American Ceramic Society) p. 352.
2. A. MIRTCHI, J. LEMAITRE and E. MUNTING, *Biomaterials* **11** (1990) 83.
3. M. HIRANO and H. TAKEUCHI, U.S. Patent No. 5,152,836 (1992).
4. Y. MIYAMOTO, K. ISHIKAWA, M. TAKECHI, M. YUASA, M. KON, M. NAGAYAMA and K. ASAOKA, *Biomaterials* **17** (1996) 1429.
5. J. LEMAITRE, A. MIRTCHI and A. MORTIER, *Sil. Ind. Ceram. Sci. Tech.* **52** (1987) 141.
6. B. R. CONSTANTZ, B. M. BARR and K. MCVICKER, U.S. Patent No. 5,053,212 (1991).
7. O. BERMUDEZ, M. G. BOLTONG, F. C. M. DRIESSENS and J. A. PLANELL, *J. Mater. Sci.: Mater. Med.* **5** (1994) 144.
8. M. JARCHO, *Clin. Orthop. Rel. Res.* **157** (1981) 259.
9. P. D. COSTANTINO, C. D. FRIEDMAN, K. JONES, L. C. CHOW, H. J. PELZER and G. A. SISSON, *Arch. Otol. Head. Neck. Surg.* **117** (1991) 379.
10. E. F. MORGAN, D. N. YETKINLER, B. R. CONSTANTZ and R. H. DAUSKARDT, *J. Mater. Sci.: Mater. Med.* **8** (1997) 559.
11. H. YAMAMOTO, S. NIWA, M. HORI, T. HATTORI, K. SAWAI, S. AOKI, M. HIRANO and H. TAKEUCHI, *Biomaterials* **19** (1998) 1587.
12. K. DRAENERT, Y. DRAENERT, U. GARDE and C. ULRICH, in "Manual of Cementing Technique" (Springer-Verlag, Berlin, 1999).
13. J. STURUP, L. NIMB and J. S. JENSEN, *Biomaterials* **16** (1995) 845.
14. T. D. MCGEE and M. L. ROEMHILDT, U.S. Patent No. 6,723,334 (2002).
15. M. L. ROEMHILDT, T. D. MCGEE and S. D. WAGNER, *J. Mater. Sci.: Mater. Med.* **14** (2003) 137.
16. F. C. DRIESSENS, J. A. PLANELL and F. J. GIL, in "Enclyclopedic Handbook of Biomaterials and Bioengineering" edited by D. Wise, D. Trantolo, D. Altobelli, M. Yaszemski, J. Gresser and E. Schwartz (Marcel Dekker, Inc., New York, NY, 1995) p. 171.
17. T. KATSUMURA, T. KOSHINO and T. SAITO, *Biomaterials* **19** (1998) 1839.
18. A. N. S. I. A. D. ASSOCIATION, *J. Amer. Dent. Assoc.* **96** (1977) 121.
19. Powder Diffraction File [Computer file] JCPDS-International Centre for Diffraction Data (Newton Square, PA, 1999).
20. H. POELLMANN and H. J. KUZEL, *Neues Jahrb Mineral* **5** (1988) 193.
21. T. KINDT-LARSEN, D. SMITH and J. S. JENSEN, *J. App. Biomaterials* **6** (1995) 75.
22. F451-95: Standard Specification for Acrylic Bone Cement, in "Annual Book of ASTM Standards" (American Society for Testing Materials, Conshohocken, PA, 1995).
23. A. CAPMAS, D. SORRENTINO and D. DADMIDOT, in "Calcium Aluminate Cements" edited by R. J. Mangabhai (E. & F. N. Spon., Cambridge, Great Britain, 1990) p. 65.
24. T. KOSMAC, G. LAHAJNAR and A. SEPE, *Cement and Concrete Res.* **23** (1993) 1.
25. H. F. TAYLOR, in "Cement Chemistry" (Thomas Telford, New York, NY, 1997).
26. H. G. MIDGLEY, in "Calcium Aluminate Cements" edited by R. J. Mangabhai (E.& F.N. Spon, Cambridge, Great Britain, 1990) p. 1.
27. S. NADE, L. ARMSTRONG, E. MCCARTNEY and B. BAGGALEY, *Clin. Orthop. Rel. Res.* (1983) 255.
28. J. AUTIAN and J. E. HAMNER, *J. Dent. Res.* **51** (1972) 880.
29. B. A. CARVALHO, P. K. BAJPAI and G. A. GRAVES, *Biomedicine* **25** (1976) 130.