INTERCALARY REPLACEMENT OF CANINE FEMORA USING A NEW BIOACTIVE BONE CEMENT

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We have developed a bioactive bone cement (BA cement) consisting of Bis-GMA resin and bioactive glass powder. It has high compressive and tensile strengths, a low curing temperature and its bioactivity allows it to bond directly with bone.

We operated on the 18 femora of nine mongrel dogs for intercalary replacement of part of the bone by a metal prosthesis using either PMMA cement or BA cement for fixation. Three dogs were killed at each of 4, 12 and 26 weeks after surgery for the evaluation of fixation strength by a push-out test and for histological examination by Giemsa surface staining and SEM.

Fixation strengths with PMMA cement at 4, 12 and 26 weeks after surgery were 46.8 ± 18.9, 50.0 ± 24.7, and 58.2 ± 28.9 kgf (mean ±SD), respectively. Those with BA cement were 56.8 ± 26.1, 67.2 ± 19.2, and 72.8 ± 22.2 kgf, respectively. Fibrous tissue intervened between bone and PMMA cement but BA cement had bonded directly to bone at 12 and 26 weeks. This suggests that BA cement will be useful in providing long-lasting fixation of implants to bone under weight-bearing conditions.

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The bone cements currently used in orthopaedic surgery are derived from polymethylmethacrylate (PMMA) (Black 1988). Their uses include the fixation of biomaterials such as artificial joints to bone, the filling of bone defects (Harrington 1981) and as a drug-delivery system (Buchholz, Elson and Heinert 1984; Downes et al 1990). Since 1970, many successful results have been reported of total hip replacement (THR) using PMMA cement (Charnley 1970, 1972; Yamamuro 1983), but there have also been many failures of fixation (Eftekhar 1987; Retpen et al 1992) and the apparent incidence of aseptic loosening has increased (Stauffer 1982; Garcia-Cimbrel and Munuera 1992).

The fixation strength of PMMA cement to bone is mainly dependent on mechanical interlocking (Friedman et al 1993), but it is known that a fibrous tissue layer intervenes between cement and bone (Freeman, Bradley and Revell 1982; Jasty et al 1990); PMMA cement never bonds directly to bone. Other problems with PMMA cement include the biological response (Thomson et al 1992), leakage of the monomer of methylmethacrylate (Gentil et al 1993) and a high curing temperature (Leeson and Lippitt 1993) which damages cell activity (Jones and Hungerford 1987). In addition, the wear debris from high-density polyethylene (HDP), PMMA cement and metal may be taken up by macrophages in fibrous tissue (Willert, Bertram and Buchorn 1990; Manley and Serekian 1994; Shanbhag et al 1994). Chemical mediators released from these macrophages and other cells may then lead to osteolysis and aseptic loosening (Spector et al 1990; Goodman et al 1991; Quinn et al 1992; Chiba et al 1994).

Because of these problems, some surgeons have employed porous-surfaced materials designed for bone ingrowth (Freeman and Tennant 1992; Santavirta, Gristina and Konttinen 1992), and others have used bioactive surface coatings such as hydroxyapatite to provide direct bonding to bone (Lemons 1988; Bloebaum et al 1991; Søballe et al 1991). None of these methods completely overcomes the disadvantages of PMMA cement (Wixson, Stulberg and Mehlhoff 1991; Tanzer et al 1992; Hozack et al 1993).

We have developed a bioactive bone cement (BA cement) (Kawanabe et al 1993) which bonds directly to bone with high strength and has a low curing temperature. We now report a comparison of the strength of fixation of
metallic prostheses to bone using either BA cement or PMMA cement under load-bearing conditions.

**MATERIALS AND METHODS**

**Cements.** BA cement consists of CaO-SiO<sub>2</sub>-P<sub>2</sub>O<sub>5</sub>-CaF<sub>2</sub> glass powder (Nippon Electric Glass Co Ltd, Otsu, Japan) and bis-phenol A glycidyl methacrylate resin (Bis-GMA) (Bowen 1963; Krause, Park and Straup 1989). The glass powder, with an average particle diameter of 3 μm, was treated with silane couplings. Two types of paste of BA cement were prepared for fixation. Type-A paste consisted of glass powder, Bis-GMA resin and toluisin. Type-B paste comprised glass powder, Bis-GMA resin and benzoyl peroxide. The two pastes were packed and sterilised separately. In use they are kneaded together for about one minute, and then harden within five minutes at a curing temperature below 50°C. BA cement bonds to rat tibia directly in vivo (Kawanabe et al 1993) and its compressive strength is approximately 180 MPa; this is approximately twice the strength of PMMA cement. We compared BA cement with CMW1 cement (CMW Laboratories Ltd, Devon, UK), which is commonly used in clinical practice.

**Implant preparation.** A segmental femoral replacement prosthesis (Fig. 1) was made of SUS316L stainless steel, which is often used clinically. It has a cylindrical spacer unit with a smooth surface, 16 mm in diameter and 40 mm long, between fixation units with roughened surfaces for insertion into femoral medullary canals. These units are 5 mm in diameter and 30 mm long. The spacer unit can be separated into two parts at a Morse taper junction; the parts can be reunited easily and tightly.

**Animal experiments.** We operated on nine mongrel dogs of average weight 12.5 kg (9 to 16) under general anaesthesia after the intramuscular injection of ketamine (15 mg/kg) and atropine sulphate (0.5 mg). After standard skin sterilisation with 70% ethanol and povidone iodine, a straight incision of about 12 cm was made on the lateral side of the leg and the femur exposed. After resection of 40 mm of the central diaphysis of the femur, the medullary canal of the remaining segments was reamed. The distal part of the prosthesis was then fixed to the distal segment and the proximal part to the proximal segment using either PMMA cement or BA cement. After the cement was well cured and each part of the prosthesis fixed completely, the parts of the prosthesis were combined at the Morse taper junction. The operating field was washed with physiological saline and closed in layers. During the operation, 2 g of piperacillin sodium was administered intravenously; bleeding was minimal.

In each dog, both femora were operated on using PMMA cement on one side and BA cement on the other, so that the cemented prostheses should bear weight equally when the treated dogs stood or ran. No postoperative immobilisation or support was used, but the dogs were restricted to their cages for the first two weeks after surgery, and then allowed to take outdoor exercise.

Three dogs were killed at 4, 12 and 26 weeks post-operatively by an intravenous overdose of pentobarbital and the proximal and distal segments of the femora with the cemented prostheses were removed. This provided six PMMA cement-fixed prosthetic components and six BA cement-fixed components at each postoperative stage. The management of the dogs and the experiments were carried out according to the guidelines for animal experiments at Kyoto University.

**Mechanical tests.** The shape of the reamed intramedullary canal of the femur affects the results of push- or pull-out tests if the implants are pushed or pulled en bloc. We therefore cut the cemented femora into thin discs for the push-out test, to minimise the influence of the shape of the canal. One section of the retrieved femur was cut into six discs, each 5 mm in thickness, using a band saw (BS-3000, Exakt, Hamburg, Germany); these were numbered I, II, III, IV, V and VI from the metaphysis toward the diaphysis (Fig. 2). Mechanical push-out tests (Dai et al 1991) were performed on these discs.
performed on discs II, IV and VI using an Instron-type machine (Autograph 500, Shimadzu, Japan). During the test the bony cortex of the bone-cement-prosthesis composite was held while the metal rod of the machine, 4 mm in diameter, pushed the metallic part of the composite disc strictly axially at a cross-head speed of 0.5 mm/s. The specimens were kept moist with physiological saline at room temperature.

The failure load was recorded as the minimum load which caused failure of the fixation of the prosthesis to bone. PMMA cement was found to have an interface with intervening fibrous tissue but BA cement had bonded directly with bone, so that the areas of the interfaces could not be calculated precisely. We regarded the failure load of the push-out test as the fixation strength.

Data were analysed using one-factor ANOVA and post-hoc testing (Fisher’s protected least significance) (Gagnon et al 1989; Haycock et al 1992), using a statistical application (StatView4.0, Abacus Concepts Inc, Berkeley, California) for Macintosh (Quadra 800, Apple Computer Inc, Cupertino, California). A p value of < 0.05 was accepted as statistically significant.

Histological examination. We performed histological examination on the alternate discs numbered I, III and V. The specimens were fixed in 10% phosphate-buffered formalin solution, dehydrated in serial concentrations of ethanol, and then embedded in 2-hydroxyethyl methacrylate (Oken-Metholate G, Oken-shoji Co Ltd, Tokyo, Japan). Undecalcified 200 μm-thick sections were made using a band saw and grinding machine (BS-3000 and MG-4000, Exakt, Hamburg, Germany). The specimens were studied after Giemsa surface staining by light microscopy and by SEM using a back-scattered electron detector (X-650, Hita-chi, Tokyo, Japan).

RESULTS

Clinical results. The fixation of the metal prostheses and femora with either cement was satisfactory under weight-bearing conditions during free exercise; all the dogs were able to run without limping from their first outdoor exercise.

Histological findings. The histological examination of specimens at four weeks after surgery showed fibrous tissue already intervening at the interface between PMMA cement and bone; many pores were seen in the PMMA cement itself (James et al 1992). At the same follow-up BA cement specimens also showed intervening fibrous tissue at the cement-bone interface and there were a few pores in the BA cement itself. At 12 and 26 weeks after surgery, the fibrous tissue at the interface with PMMA cement showed a tendency to become thicker, but BA cement had bonded to bone with no intervening fibrous tissue on examination by light microscopy and SEM (Figs 3 to 5).

Push-out tests. The mean fixation strengths by the push-out tests (Fig. 6) on PMMA bone cement at 4, 12 and 26 weeks after surgery were 46.8 ± 18.9, 50.0 ± 24.7, and 58.2 ± 28.9 kgf (mean ±sd) respectively, showing no significant statistical difference. With BA cement, fixation strengths for the same intervals were 56.8 ± 26.1, 67.2 ± 19.2, and 72.8 ± 22.2 kgf respectively. The fixation strength at 26 weeks was significantly greater than that at 4 weeks. At 12 weeks after surgery, the fixation strength of BA cement was greater than that of PMMA cement.

The relative fixation strengths of BA cement and PMMA cement were compared in numbered segments (Fig. 7). In segment II, consisting of cortical bone and residual cancellous bone, the fixation strength increased with time from 4 to 26 weeks after surgery. In segment VI, consisting almost entirely of cortical bone, the fixation strength of PMMA cement decreased with time; at 26 weeks it was half the value at 4 weeks. With BA cement in segment VI, the fixation strength at 26 weeks was three times greater than that of PMMA cement. In segment IV, intermediate between segments II and VI, the fixation strength of PMMA cement at 26 postoperative weeks was greater than that at 4 weeks.

DISCUSSION

We have previously reported the use of a bioactive glass powder-ammonium phosphate composite paste (Taguchi et al 1990) and a bioactive bone cement (BA cement) (Kawanabe et al 1993). The former cement bonded with rat tibia under unloaded conditions, but failed to fix the prosthesis to canine femur under weight-bearing conditions because of low mechanical strength (unpublished data). The BA cement used in this study bonded directly to bone in rat tibia under unloaded conditions, and had a higher compressive strength than the first-mentioned composite paste and PMMA cement. The bioactivity of BA cement is due to chemical bonding to bone via a Ca-P-rich layer (apatite layer formed on BA cement) (Kawanabe et al 1993).

In this study, we aimed to fix a segmental prosthesis to canine femora under weight-bearing conditions using the new bioactive cement and conventional PMMA cement. We showed that BA cement was clinically acceptable under weight-bearing conditions since the implanted dogs and those with PMMA cement were able to run at 4, 12 and 26 weeks after surgery. We have also shown that the mean fixation strength of BA cement increased with time under weight-bearing conditions while that of PMMA cement did not increase significantly with time. In the early stages, up to four weeks after implantation, mechanical interlocking is the main source of fixation strength with both cements and we found no significant difference between the fixation strengths of BA cement and PMMA cement. In the later stages, at 12 and 26 weeks after implantation, the BA cement had bonded to bone; by contrast PMMA cement never bonded to bone directly, and the fixation strength of BA cement was then higher than that of PMMA cement.

Failure at some part of the fixation will normally propa-
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Figure 3 – Giemsa surface staining of specimens at four weeks after implantation. Figure 3a – With PMMA bone cement a thin layer of fibrous tissue intervenes at the interface of PMMA bone cement (P) and bone (B). There are many pores (arrow) in the cement itself (×100). Figure 3b – With BA cement, there is a thin layer of fibrous tissue at the interface between cement (A) and bone (B), but some areas of the interface (*) lack this tissue. There are some pores in the cement itself (×100). Figure 4 – Giemsa surface staining of the specimens at 26 weeks after implantation. Figure 4a – With PMMA cement, there is thick intervening soft tissue (I) between the PMMA cement (P) and the bone (B) (×50). Figure 4b – The BA cement (A) has bonded directly to bone (B) (×100).

Figure 3

Figure 4

Figure 3a

Figure 3b

Figure 4a

Figure 4b

gate to other parts, meaning that the failure load of an interface should depend on its weakest segment. We therefore compared the fixation strength of different segments of the cemented prostheses. In the segment with most cancellous bone (segment II), the cement surface in contact with bone became porous. Tight interlocking was created and the bone ingrowth required to reach a stable and biocompatible condition should occur at the interfaces of bone and both PMMA cement and BA cement. We believe that the fixation strength at this segment was increased for this reason. In segments consisting mainly of cortical bone with little cancellous bone (segment VI), the fixation strength of PMMA cement was reduced by the thickening of the intervening fibrous tissue in the relative absence of interlocking, but the fixation strength of BA cement was increased by direct bonding to cortical bone which has a higher strength than cancellous bone.

Fixation to bone by a bioactive bone cement cannot be successful if the cement itself has a poor mechanical strength. The compressive and tensile strengths of BA cement (approximately 180 MPa and 36 MPa) are greater than those of conventional PMMA cement (approximately 80 MPa and 26 MPa).

Furthermore, the lack of intervening fibrous tissue at the interface of BA cement and bone at 26 weeks implies that osteolysis is unlikely to occur. This should reduce the incid-
ence of loosening of the fixation with BA cement in comparison with fixation with conventional PMMA cement.

**Conclusions.** A new bioactive bone cement consisting of bioactive glass powder and Bis-GMA resin became bonded to bone and successfully fixed metal prostheses to bone under weight-bearing conditions in animal experiments. Investigations confirmed the presence of strong fixation with no intervening fibrous tissue at the interface. These findings suggest that aseptic loosening of fixed biomaterials may be reduced by the use of this cement.

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