

Detrimental effect of aging on the endurance of bone cement

An in vivo and in vitro study in rabbits

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We investigated the effect of aging on the compressive strength of bone cement under in vivo and in vitro conditions. Cement molds were implanted in the dorsum of rabbits and other molds were kept under stable conditions and in darkness. Comparative measures taken at 15 days and 1, 3, 6, 12 and 24 months showed lower endurance of the implanted molds ($p < 0.001$). A reactive capsule surrounded the bone cement in vivo

up to the 3rd month, its cellularity increased, and then almost disappeared by 1 year. Macrophages and foreign body cells reappeared at 2 years, indicating a "chemical aging" effect in the in vivo environment. Our findings suggest that aging may play an important role in the amelioration of the mechanical properties of bone cement.

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Extensive bone cement research (Jones and Hungerford 1987) led to the innovation of a second generation cementing technique, including careful debridement and pressure application (Lidgren 1988), and to third generation methods which involved vacuum mixing or centrifuging, chilling and augmenting the quantity of the cement (Burke et al. 1984, Wixson et al. 1987, Lindgren et al. 1987, Wang et al. 1993, Ioannidis et al. 1992, 1994).

However, there is little information on degradation or the aging of this polymer, and none following the introduction of the new methods for preparing bone cement. We compared the compression endurance of cement prepared using third generation techniques and aged under either in vivo or in vitro conditions.

Material and methods

Test molds of radiopaque bone cement, CMW-1, of standard viscosity were formed inside syringes of 1-cm diameter and were subsequently cut to a height of 2 cm for compression testing which requires that cylindrical molds with a diameter to height ratio of 1:2. The use of syringes with moderate pressure to form the molds had the advantage of preventing air bubbles. To obtain a longer working time and augment

compression strength, the cement was prechilled to 4 °C and vacuum mixed using 2 commercial batches (Ioannidis et al. 1994). For the in vivo experiments, 24 white New Zealand rabbits, weighing 2–2.5 kg were used. 4 molds were implanted under the subcutaneous tissue of the dorsum of each rabbit under aseptic conditions. The location was chosen to avoid exposing the molds to mechanical stress. For the in vitro study, an equal number of molds were made from the same mixture of bone cement used for the implanted molds. The in vitro molds were stored in sealed boxes at room temperature under low humidity and darkness, thus matching the in vivo conditions, as much as possible. 8 of the in vitro molds were tested 2 hours after formation; no in vivo molds were studied at this time point. 4 in vitro and 4 in vivo molds from killed rabbits were assessed at 15 days and 1, 3, 6, 12 and 24 months. The in vivo molds were taken from the rabbit's dorsum together with the surrounding soft tissue. Soft tissues underwent histologic examination, with one sample from each time point being evaluated 'en bloc' with the bone cement. Molds were tested in compression till failure using an Instron machine, 1 ton at a speed of 25 mm/min.

The Wilcoxon paired criterion was used for statistical analysis.

Table 1. Cumulative results of bone cement testing in compression endurance (mean and SD; MPa)

Time	In vivo		In vitro	
2 h	0	0	65	1
15 days	63	1	72	1
1 month	76	1	81	1
3 months	83	1	87	1
6 months	83	1	85	1
12 months	78	1	85	1
24 months	71	2	84	1

Results

Compressive testing of molds maintained and aged *in vivo* and *in vitro* demonstrated that at all time points, *in vitro* molds had greater endurance than *in vivo* ones ($p < 0.001$). The only exception was at 6 months when the difference was not statistically significant (Table 1). On the other hand, both groups demonstrated an increase of their endurance up to the third month. The magnitude of the increase of compressive strength was statistically significant for both groups (*in vitro*: 65 to 87 Mpa; *in vivo*: 63 to 83 Mpa; $p \leq 0.001$).

From 3 to 24 months there was a difference in the behavior between *in vivo* and *in vitro* molds. *In vitro* molds showed a small drop in compressive endurance (87 to 83 Mpa), while *in vivo* molds showed a larger decrease in endurance (83 to 71 Mpa; $p < 0.001$). It is noteworthy that at 15 days, the *in vivo* group showed less endurance than the *in vitro* group at 2 hours

The molds aged *in vivo* were always encased by a well-defined layer of fibrous tissue. Macroscopically it had a synovial like appearance, when separated from the bone cement. Microscopic examination using hematoxylin-eosine showed the following: At 15 days and 1 month after implantation, the surrounding tissue was highly cellular, although necrotic at some sites (Figure 1). The cells that were recognized included lymphocytes, macrophages, multinuclear eosinophils and characteristic foreign body giant cells. The latter were in active phagocytosis of micro-particles, presumably bone cement. At 3 and 6 months, the tissue was less cellular and at 1 year, an acellular fibrous tissue surrounded the bone cement, suggesting quiescence (Figure 2). Increased cellularity with the reappearance of macrophages, lymphocytes, giant cells and occasional histiocytes was observed at 2 years (Figure 3).

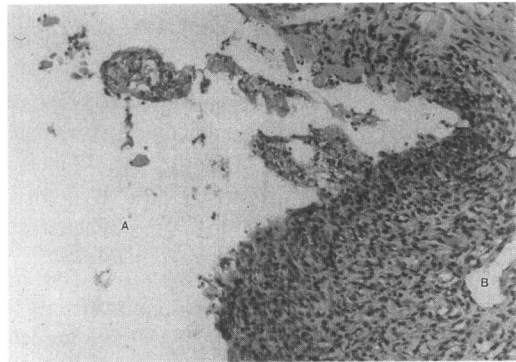


Figure 1. 1-month-old in vivo specimen of bone cement plus surrounding tissue. Note extremely cellular reactive tissue (B) in contact with the cement (A). (HE x100).

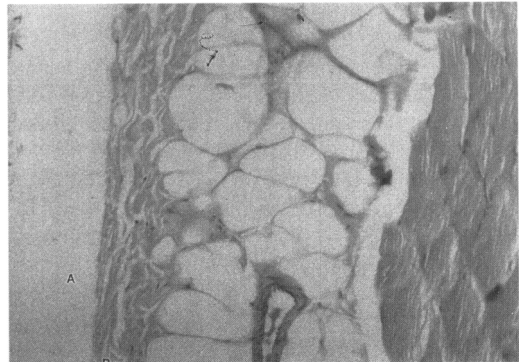


Figure 2. 1-year-old in vivo specimen. Note the practically acellular connective tissue (B) adjacent to the cement (A). (HE x100).

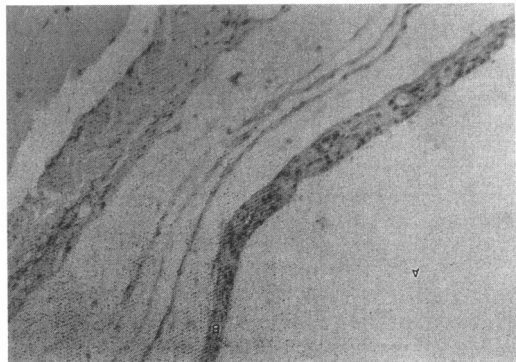


Figure 3. 2-year-old in vivo specimen. Note the resurgence of inflammatory and foreign body cells (A) around the cement (B). (HE x100).

Discussion

After Sir John Charnley (1964) popularized the use of bone cement for the fixation of prostheses, an effort to enhance its mechanical capabilities, as well as to invent better and stronger cements has continued. Nonetheless, few studies have addressed the effect of degradation or aging on bone cement.

Our findings indicate that there is an initial increase in compression endurance in both the *in vivo*-*in vitro* groups up to 3 months, when both groups reach their zenith in strength. This can be explained by the fact that approximately 20% of the polymerization process is achieved gradually after the initial preparation, ranging from 18 hours to 4 months (Haas et al. 1975, Marks et al. 1976, Rostoker et al. 1979, Wright et al. 1984, Bargar et al. 1986, Looney and Park 1986). In a study using a more accurate method to evaluate the state of polymerization (Electron Paramagnetic Resonance), Looney and Park (1986) demonstrated that there is a rapid increase in polymerization for the first 15 days which then fades up to 6 months. The latter is compatible with our results.

After the third month, the *in vivo* specimens were always found to be weaker than the *in vitro* counterpart. This suggests that the *in vivo* environment impedes the continuation of polymerization. Furthermore, it is noteworthy that the 15-day *in vivo* specimen tended to have lower endurance than the 2 hours measurement of the *in vitro* cement. Moreover, this measurement falls significantly below the A.S.T.M. lower limit of 70 Mpa for compressive endurance. If these findings can be applied to patients the indications for immediate postoperative mobilization of patients should be reevaluated.

The rest of the measurements of the *in vivo* group showed a statistically significant decline at each time period up to 2 year limit when they fall almost at the A.S.T.M. lower limit. On the other hand, the *in vitro* group presented a nonsignificant decrease in strength, and it was always greater than that measured *in vivo*.

Similar studies have yielded conflicting results. Jaffee et al. (1974) found no difference after immersion of the tested specimens in bovine serum at 37° for 2 years, while Freitag and Cannon (1976) found an increased fracture toughness with time. Recent reports with conventional preparations of bone cement showed an adverse effect of time on strength. Although several studies have shown a decrease in endurance with time compatible with our findings, the cement molds were not tested in a true biologic environment (Lidgren et al. 1987, Looney and Park 1986). On the other hand, an equally diminished endurance was found in both compression and tension after im-

plantation of the molds in the spinal muscles of rabbits for 6 and 16 months (Kon 1981), while in a similar experiment Rostoker et al. (1979) found significantly reduced flexion endurance at both 16 and 26 months.

We found a fall in compression endurance of 15% after 2 years. Similarly, Eyerer and Jin (1977) reported about a 10% reduction of compression endurance with time. This decrease was observed despite the use of third generation preparation methods which are known to augment cement endurance (Lidgren et al. 1987, Wixson et al. 1987, Wang et al. 1993) and increase compression up to 18% (Ioannidis et al. 1992, 1994). Although we can exclude photochemical and thermal effects on degradation, the effects of chemical aging were not controlled in our study. The fact that cement absorbs about 0.5 mg/cm² water from its surface or the possible influence of weak bases and acids may explain, in part, both the delay in polymerization and the fall in endurance (Clough and Gilley 1985).

The initially increased cellularity, including macrophages, lymphocytes and eosinophils together with the areas of focal necrosis can be attributed to the surgical trauma and the effort of the organism to get rid of local cement debris. By 1 year the mold was encased by an acellular membrane of fibrous tissue and glycoproteins or glycocalyx, the production of which is a well-known response to foreign bodies (Black 1988, Linder and Carlsson 1986). A surprising finding, however, was that reactive cells, including macrophages, lymphocytes, giant cells and occasionally histiocytes, reappeared after 2 years. Since bone cement attracts macrophages (Rostoker et al. 1979, Freeman et al. 1982, Linder and Hansson 1983, Levack et al. 1989), their presence was not alarming. On the other hand, the presence of giant cells and histiocytes is a clear indication of foreign body reaction. However, our findings cannot distinguish whether this is in response to the entire cement mass in the form of hypersensitivity or to particles resulting from the aging of the cement.

Our findings indicate that bone cement ages with a significant reduction in compression endurance in the biological environment. Furthermore, the reappearance of inflammatory and foreign body cells at a later stage raises significant questions as to the application of bone cement in joint replacement.

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