

The effect of antibiotic additions on the fracture properties of bone cements

Two commercially developed cements (Palacos and Zimmer) were tested for fracture toughness with and without gentamicin additions. Compact tension specimens were molded under standardized conditions and divided into four groups. Each group contained specimens of both plain and both antibiotic cements. One group was tested as zero-time controls. The remaining three groups were radiation sterilized. One group was tested as zero-time sterilization controls. Another group was tested after 2 months immersion in Ringer's lactate to elute gentamicin. The last group was tested after being implanted for 2 months subcutaneously in dogs. Comparison of the fracture toughness of the two zero-time groups showed no effect of radiation sterilization on any of the four types of cement. The results from both the group immersed in Ringer's solution and the group implanted in dogs showed no significant effect on fracture toughness with gentamicin additions. Both these groups, however, did have greater toughness values than the zero-time groups, probably caused by the more complete polymerization with time. Furthermore, the Palacos cement exhibited a greater toughness than the Zimmer cement. The results of this study demonstrate that the addition of gentamicin to bone cement is not deleterious to the fracture properties.

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The addition of antibiotics to poly[methyl methacrylate] (PMMA) bone cement has been used to treat surgical infection in total hip replacement (Buchholz et al. 1981, Carlsson et al. 1978). Concern remains, however, that such additions may weaken the mechanical properties of the cement. Previous studies have reported conflicting results on the effect of antibiotic additions (Lautenschlager et al. 1976a, Schurman et al. 1978, Buchholz & Engelbrecht 1970). In the present study, the techniques of fracture mechanics were used to investigate the effects of antibiotic additions by measuring the fracture properties of PMMA bone cements with and without the addition of antibiotics.

Fracture mechanics

One of the obvious characteristics of PMMA as it is used in orthopedic surgery is its flawed structure. Because the polymer must be allowed to polymerize *in situ* to provide a mechanical grout, it must be mixed in the operating room and packed or injected into the bone cavity prior to polymerization. Unfortunately, this results in a material with a significant degree of porosity in the form of air holes and foreign material such as blood entrapped in the cement. Likewise, the very nature of its application as a mechanical grout results in PMMA having a very rough surface in contact

with bone, resulting in many areas of stress concentration.

The question becomes, therefore, one of how to measure the mechanical properties of this material in a way which reflects the many imperfections present in its structure. One approach is to introduce a flaw (with a well-defined geometry) more severe than any inherent flaw in the material and then characterize the behavior of the material in the presence of this flaw. This approach is the basis for fracture mechanics studies. By testing a standardized specimen with a well-defined flaw oriented to insure fracture initiation from the flaw, it is possible to relate the applied loads and the flaw and specimen geometries to the stress field around the tip of the flaw. When this stress field reaches a critical value, commonly called the fracture toughness, catastrophic failure results. This critical value of fracture toughness is, in fact, a material property that reflects the material's resistance to fracture in the presence of a flaw. Once the critical fracture toughness is known, it can be applied to other conditions of geometry and flaw size to predict failure.

Material and methods

Two cements (Palacos-R™ and Zimmer™) were tested for fracture toughness with and without gentamicin additions. The Palacos-R with antibiotic had 0.84 g gentamicin sulfate premixed with 40 g powder by the manufacturer. Similarly, the Zimmer cement had 1 g gentamicin premixed. All cements were formed by the addition of 20 ml of liquid monomer. For the Palacos-R, all the monomer ampules were from the same batch, while for the Zimmer cement, ampules used for plain cement were from a different batch than those used for gentamicin cement. For both cement types, the powder in the plain cement was from a different batch than that in the gentamicin cement.

Compact tension specimens (Figure 1) were molded under standardized conditions of temperature ($25 \pm 1^\circ\text{C}$) and relative humidity (20 ± 2 per cent) and divided into four test groups, each of which contained specimens of both plain and both antibiotic cements. One group was tested as zero-time controls (allowing 2 weeks between molding the specimens and performing the testing). The remaining three groups were radiation sterilized with a 2.6 mrad

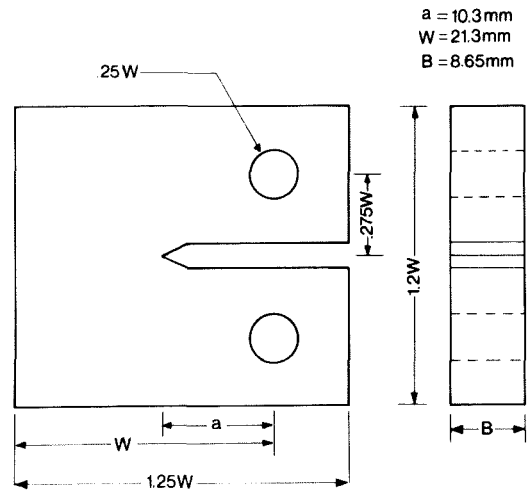


Figure 1. Dimensions of the compact tension specimen.

dose. One group was tested as zero-sterilization controls (again allowing approximately 2 weeks from mixing until testing). Another group was tested after immersion for 2 months in Ringer's lactate to elute gentamicin. Within this group, the four types of cement specimens were separated and immersed in individually sealed glass containers. The last group was tested after being implanted for 2 months subcutaneously in adult mongrel dogs. Eight dogs were used, with each dog receiving either eight or nine specimens, three to five of which contained antibiotic.

To insure that gentamicin was being eluted from the immersed and implanted specimens, samples of the Ringer's lactate and samples of the dog's blood were periodically drawn and tested for gentamicin content, using a standard radioimmunoassay technique.

All mechanical testing was performed on an MTS servo-hydraulic system at a rate of 5 mm min^{-1} (Figure 2). Two-month specimens were tested within 24 h of being removed from either the Ringer's solution or the dogs. Load versus displacement graphs were monitored continuously during the test and maximum load at fracture was used to calculate fracture toughness from a standard stress intensity equation relating load, geometry and fracture toughness for the compact tension specimen geometry [ASTM Standard E399-81T].

Results

Comparison of the calculated fracture toughnesses for the two zero-time groups showed no

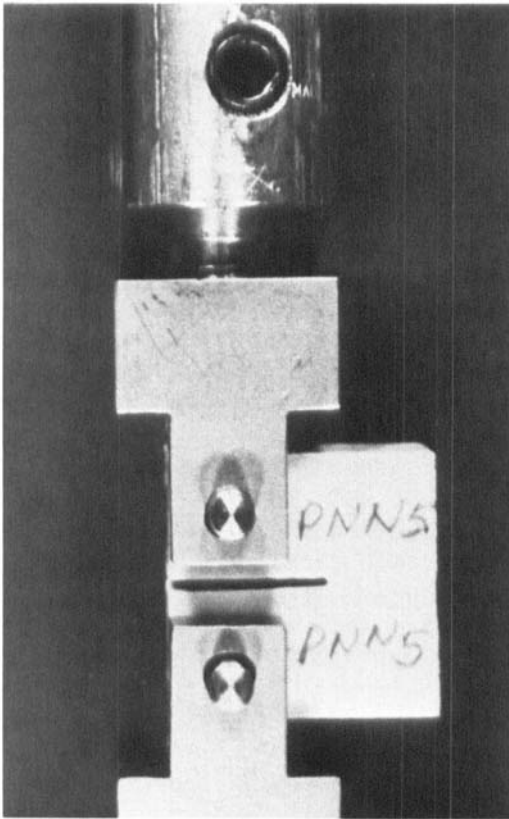


Figure 2. Clevis and pin grips for loading the PMMA specimen. A universal joint was included in the load train to insure alignment.

significant effect ($p < 0.05$) of radiation sterilization on any of the four types of cement (Table 1). In fact, no significant difference was found between any of the Palacos-R zero-time results. That is, no initial effect on fracture

toughness was found due to the addition of antibiotic to Palacos-R cement. For the Zimmer cements, however, the zero-time fracture toughness results were significantly ($p < 0.01$) greater for the cement containing gentamicin than for plain Zimmer cement.

The results for both the group immersed in Ringer's lactate for 2 months and the group implanted *in vivo* for 2 months were significantly higher than the zero-time results for all four cement types. No significant difference was found between any of the 2-month results for Palacos-R cement. No significant difference existed between the immersed and implanted Palacos-R groups, nor between the plain Palacos-R cement and the Palacos-R containing antibiotic. The significant difference found between plain Zimmer and Zimmer with antibiotics in the zero-time groups was no longer evident in either of the 2-month groups. However, a significant difference existed between the results for the specimens immersed in Ringer's and the results from the specimens implanted in dogs for both the plain Zimmer cement and Zimmer cement with antibiotics.

Effective elution of gentamicin from the bone cement specimens was evident from the results of the gentamicin radioimmunoassay from the samples of Ringer's solution and canine blood. For example, the measured concentrations of gentamicin varied from $22 \mu\text{g ml}^{-1}$ during the first week to $33 \mu\text{g ml}^{-1}$ during the eighth week in the 250 cc of Ringer's lactate in which 18 gentamicin-containing Palacos-R cement specimens were stored. Similarly, the concentration varied from $14 \mu\text{g ml}^{-1}$

Table 1. Fracture toughness results for the four test groups. (Values are mean \pm s.d. in units of $\text{MPam}^{3/2}$, with n = number of specimens tested)

	Zero-time		Two month	
	Not sterilized	Sterilized	In vitro	In vivo
Palacos-R	1.54 ± 0.13 ($n=9$)	1.56 ± 0.09 ($n=9$)	2.04 ± 0.09 ($n=9$)	2.02 ± 0.07 ($n=9$)
Palacos-R with gentamicin	1.60 ± 0.08 ($n=9$)	1.64 ± 0.05 ($n=9$)	2.08 ± 0.12 ($n=10$)	2.07 ± 0.12 ($n=10$)
Zimmer	0.92 ± 0.05 ($n=10$)	0.93 ± 0.05 ($n=8$)	1.50 ± 0.09 ($n=9$)	1.36 ± 0.06 ($n=9$)
Zimmer with gentamicin	1.16 ± 0.06 ($n=6$)	1.10 ± 0.07 ($n=7$)	1.56 ± 0.05 ($n=7$)	1.40 ± 0.07 ($n=7$)

during the first week to $18 \mu\text{g ml}^{-1}$ during the eighth week for 12 gentamicin-containing Zimmer specimens, again stored in 250 cc of Ringer's lactate. The measured gentamicin concentrations in blood samples taken from the eight dogs varied from a peak of $3\text{--}4 \mu\text{g ml}^{-1}$ in the first few days of implantation to values of less than $1 \mu\text{g ml}^{-1}$ near the end of the 2-month implantation.

Discussion

The addition of gentamicin sulfate to Palacos-R and Zimmer PMMA bone cements did not affect the fracture properties, even after 2 months of elution in Ringer's or *in vivo*. This conclusion must be considered in conjunction with previous work on the effect of antibiotic additions to bone cement, which has shown detrimental effects on the strength of PMMA with larger antibiotic additions (Nelson et al. 1978, Lautenschlager et al. 1976b). Schurman and colleagues (1978) studied the fatigue properties of Palacos-R cement with 1 g additions of gentamicin and found a significant reduction in the fatigue life of the cement caused by additions of the antibiotic. However, in an effort to examine uniform specimens, Schurman and co-workers considered data only from specimens which had pores less than 1 mm in diameter as measured on the resulting fracture surfaces. This resulted in data from specimens with significantly less porosity than cement material as it is commonly used in the operating room. Reducing the porosity by this means of data selection exaggerated any effect caused by antibiotic addition. That is, by reducing the size and, therefore, the stress concentration effect of the inherent flaws in the bone cement, the effect of introduced defects such as gentamicin additions was unrealistically magnified. Their results do emphasize, however, the need to examine the effect of antibiotic additions on cement centrifuged to reduce its inherent porosity (Burke et al. 1984).

The significantly increased toughness of Palacos cement compared to Zimmer is consistent with results from other studies comparing Palacos, Simplex-P, and Zimmer cements (Robin-

son et al. 1981, Davies et al. 1984). The superior properties of the Palacos cement over both Zimmer and Simplex-P are difficult to assess in terms of *in vivo* performance; however, given the incidence of cement fractures in clinical series reported in the literature (e.g., Weber & Charnley 1975, Stauffer 1982), any improvement in mechanical properties must be considered important.

The significant differences found in the toughness results of Zimmer cement with and without antibiotics in the zero-time groups was most likely due to batch-to-batch variation; both the monomer and powders used in the zero-time groups were from different batches. Previous testing of Zimmer cement has also yielded significant batch-to-batch variations and more data scatter than several other cement types tested (Robinson et al. 1981). But it should be noted that these zero-time differences were eliminated by 2 months as more complete polymerization occurred. The difference between the *in vitro* and *in vivo* Zimmer properties might be explained by the differences in temperature and/or environment. But why these factors should influence Zimmer and not Palacos cement is not known.

The increased toughness values found in all four types of cement after 2 months are consistent with compressive and tensile strength measurements made by other researchers as a function of time after mixing (Lautenschlager et al. 1976b, Nelson et al. 1978).

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