JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE **8** (1997) 849–853

Influence of sterilization upon a range of properties of experimental bone cements

E. J. HARPER, M. BRADEN, W. BONFIELD*
IRC in Biomedical Materials, Queen Mary and Westfield College, Mile End Road, London, E1 4NS, UK

E. DINGELDEIN, H. WAHLIG
CORIPHARM GmbH & co., Lagerstraße 11-15, Dieburg, Germany

Bone cement, used to fix prostheses into the bone, must be sterilized prior to implantation. Two sterilization techniques, γ and β radiation, were investigated, examining the influence upon molecular weight, static and dynamic mechanical characteristics and rheological properties. A number of experimental cements were studied prepared from methylmethacrylate (MMA) co-polymers, either single powders or powder blends, mixed with MMA monomer. It was found that with both γ and β radiation, there was a decrease in molecular weight of all powders, including a MMA/styrene co-polymer, in relation to the radiation dose. This fall in molecular weight resulted in a drop in tensile strength, Young's modulus and strain to failure of all cements tested. However, the deterioration in mechanical strength was highlighted by the dynamic testing. Fatigue lives of cements after testing in tension–tension, at 2 Hz under load control and irradiated with 25 kGy γ radiation, displayed significant decreases. This result indicated the utmost importance of conducting such tests upon experimental bone cements prior to *in vivo* use. The rheological time profiles of curing cements were also found to be influenced by 25 kGy γ radiation, with a reduction of complex viscosity after sterilization.

1. Introduction

Bone cement is primarily used to fix implants into the bone. Most commercial cements are based upon the polymer poly(methylmethacrylate) (PMMA). Pre-formed beads of PMMA or an MMA co-polymer are mixed in surgery with MMA monomer. A chemical reaction takes place between the benzoyl peroxide in the polymer and the *N*, *N*-dimethyl-*p*-toluidine in the monomer, resulting in the polymerization of the MMA to form a hardened material [1].

Because the bone cement is to be inserted into the body, it must be sterilized before use. The powder and monomer are treated in different ways: this investigation is concerned with the powder component alone. There is a choice of methods available, which are used by bone cement manufacturers. The powder can be exposed to γ or β radiation or ethylene oxide (EtO) gas. There are advantages and disadvantages of each method. Irradiation is a convenient and relatively quick procedure and γ radiation, in particular, is widely used to sterilize a number of medical implants. However, it is well known that radiation results in a change in the properties of polymeric materials [2, 3], often with a deterioration in mechanical characteristics. In contrast, EtO gas sterilization does not result in damage to polymers to such an extent, but the procedure is not so quick and convenient. A long period of degassing, up to 50 days [4], may be required for a 40 g packet of bone cement powder.

A considerable amount of research has been conducted to investigate the degradation of ultra-high-molecular-weight polyethylene medical implant material after γ radiation [5, 6]. Although there have been many studies into the effects of γ radiation upon PMMA polymer [7–11], there are very few published investigations concerning PMMA bone cement. In this current study, the mechanical and rheological properties of a number of experimental acrylic bone cements have been investigated. Bone cement *in vivo* experiences millions of stress cycles each year and fatigue failure has been cited as one of the causes of implant loosening [12]. Therefore, both static and dynamic mechanical characteristics have been determined for one of the cements, to assess the influence of γ sterilization upon the two modes of testing.

---

*Author to whom all correspondence should be addressed.
Selected paper from the 13th European Conference on Biomaterials, Göteborg, Sweden.

0957–4530

2. Materials and methods

2.1. Materials

Six different polymer powders or polymer powder blends were investigated. Four single co-polymer powders were investigated; (1) MMA/styrene, (2) MMA/methacrylate (MA), (3) MMA/butylmethacrylate (BMA), and (4) MMA/2-ethylhexylmethacrylate (2EHA). The two powder blends investigated, (5 and 6), included either the MMA/styrene co-polymer or the MMA/MA co-polymer, respectively. The powder component was mixed by hand in air with methylmethacrylate monomer for approximately 30 s to produce a bone cement dough. Benzoyl peroxide present in the powder mixture and dimethyl-*p*-toluidine in the monomer reacted together to produce the chemical reaction. The bone cement dough was either injected into a mould to produce mechanical test specimens, or placed on the rheometer plate and used to investigate the handling properties. In order to study the effects of γ and β radiation, powders (1–4) were subjected to a range of doses of radiation, while powder blends (5) and (6) were irradiated using 25 kGy γ radiation. It is important to note that (5) and (6) included 10 wt % zirconium dioxide in order to enable a direct comparison to Palacos® R cement. The properties of Palacos® R (E. Merck, Darmstadt, Germany) were measured as an example of a widely used commercial cement. It is sterilized using EtO gas.

2.2. Molecular weight analysis

The measurements were determined using gel permeation chromatography (GPC) performed at the Rubber and Plastics Research Association (RAPRA) Technology Ltd, Shawbury, Shropshire, UK. Sample solutions of polymer powder components (1–4) were prepared by dissolving 20 mg in 10 ml tetrahydrofuran. A small amount of 1,2-dichlorobenzene was added to the solvent as the internal marker and the solution was thoroughly mixed. The solutions were filtered through a 0.2 μm polyamide membrane and injected through a crosslinked polymer gel column. The GPC system was calibrated with polystyrene, therefore results were expressed as the "polystyrene equivalent" molecular mass.

2.3. Mechanical testing

After the initial mixing, the doughy mixture was transferred to the syringe body of a cement gun. At approximately 2 min after initial mixing, when the cement had reached the appropriate viscosity, the mixture was injected through the nozzle into the PTFE mould. The mould was placed under 1.4 MPa pressure for 15 min until curing had occurred. The dumb-bell specimens produced were either used for tensile or fatigue testing, conforming to half-size ISO 527 multi-purpose test specimen, 75 mm in total length, with a gauge length of 25 mm.

The tensile testing was conducted using a crosshead speed of 5 mm min^{-1} employing an Instron Testing Machine, Model 6025™ at ambient temperature. The force exerted and displacement of the specimen was monitored until failure giving a maximum tensile strength, Young's modulus and strain at failure. At least five specimens, prepared from powders (1–6), before and after irradiation, were tested and the means and standard deviations were calculated.

The fatigue testing was conducted using a MTS 810™ testing machine, again until failure occurred. The fatigue testing was performed at ambient temperature under load control and a frequency of 2 Hz using a sinusoidal loading pattern. The specimens were cycled in tension–tension with an upper stress of 22 MPa and a lower stress of 0.3 MPa. The number of cycles to failure were recorded for at least five specimens prepared from the polymer blend containing the MMA/MA co-polymer (6), before and after 25 kGy γ radiation. The data were represented using survival probability curves displaying the degree of scatter of the fatigue lives.

2.4. Rheology measurements

Changes in rheological properties, as a result of 25 kGy γ radiation, of the two cements prepared from the polymer blends containing either the MMA/styrene co-polymer (5) or the MMA/MA co-polymer (6) were investigated. The doughy mixture was monitored continuously from 1 to $\sim$6 min after initial mixing until rapid curing occurred, using a Physica rheometer, RHEOLAB MC100 with US 200 Software. A "plate–plate" system was employed with an oscillating frequency of 2 Hz and an amplitude of 0.05%. A number of rheological parameters including complex viscosity, torque, loss and storage moduli were calculated and plotted against time.

3. Results

3.1. Molecular weight changes

The GPC analysis revealed that the values of M_w and M_n of powders (1–4) were reduced by γ and β radiation to a similar extent in proportion to the original size of the molecular weight. The values of polydispersity were also decreased, but the shape of the molecular weight distributions were not altered. Fig. 1 shows the linear reduction in M_w of powders (1) and (2) with radiation dose.

3.2. Changes in mechanical properties

Tensile strengths, Young's moduli and strains to failure of cements prepared from powders (1–6) all exhibited similar reductions following γ or β radiation, given in Table I. The values displayed are the mean of at least five specimens, with standard deviations shown in brackets. The tensile strengths of cements prepared from powders (1) and (2) are shown in Fig. 2 in relation to radiation dose. Fatigue resistance of the cement prepared from powder blend (6) experienced a large decrease after γ radiation at a dose of 25 kGy. Cycles to failure of the cement, before and after radiation, resulting from testing in tension–tension to 22 MPa are shown in Fig. 3 along with Palacos® R for comparison.

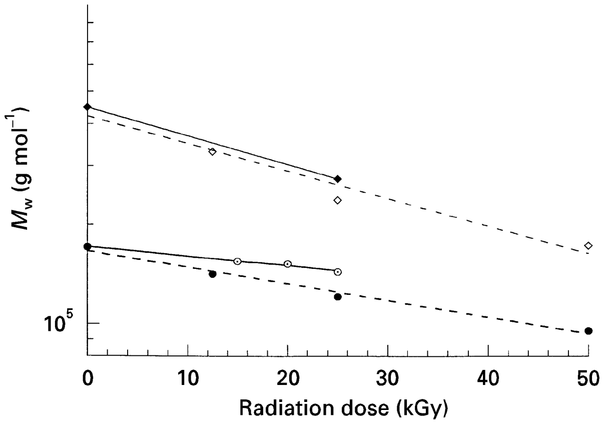

Figure 1 Influence of γ radiation dose upon the molecular weights of bone cements prepared from MMA/styrene co-polymer, cement (1) and MMA/MA co-polymer, cement (2). (—◆—) cement (1) γ, (—○—) cement (2) γ, (- -◇- -) cement (1)β, (- -●- -) cement (2) β.

3.3. Changes in rheological measurements

The complex viscosity, loss and storage modulus of cements prepared from powder blends (5) and (6) were both reduced as a result of 25 kGy γ radiation. The change in complex viscosity with time for cement (6) is given in Fig. 4.

4. Discussion

The decrease in molecular weight with respect to radiation dosage, illustrated in Fig. 1, is thought to be due to fracture or scission of the PMMA main polymer chain together, with decomposition of the side chain. Charlesby [2] reported, for PMMA, a relationship between molecular weight and γ radiation dosage, indicating that the number of fractures produced in the molecular chain is proportional to the radiation dose and that the fractures occur randomly. Cross-linking is not thought to occur, but there is a possibility that free radicals may be produced. These radicals become trapped and may cause subsequent degradation or recombination. However, the concentration of these radicals is very small and because the polymers in this investigation were tested within 1 month of irradiation they are unlikely to influence the properties of the polymer to any great extent.

The MMA/styrene co-polymer was expected to reduce the effect of the radiation upon the molecular weight and thus resultant bone cement properties. Poly(styrene) (PS) is known to cross-link upon exposure to radiation leading to an increase in molecular weight. The benzene ring provides radiation protection to molecules containing it, and when styrene units are included in a polymer chain they can assist in protecting neighbouring atoms from damage. However, when PS is irradiated in air at relatively low dose rates, oxidation can take place and chain scission may predominate over cross-linking [3]. The results of changes in molecular weight of the MMA/styrene co-polymer following radiation may not be a true reflection of what occurred, because some insoluble product is expected to form as a result of the cross-linking. This effect is unlikely, because the drop in molecular weight indicated by the GPC results was

TABLE I Static mechanical properties of experimental bone cements before and after irradiation

Powder component	Radiation dose (kGy)	Maximum strength (MPa)	Young's modulus (GPa)	Strain to failure (%)
(1) MMA/styr.	–	57.9 (2.12)	3.32 (0.08)	2.50 (0.28)
	25 (γ)	54.8 (3.01)	3.11 (0.20)	2.30 (0.27)
	12.5 (β)	58.7 (3.01)	3.23 (0.29)	2.51 (0.41)
	25 (β)	54.4 (4.60)	3.15 (0.22)	2.26 (0.35)
	50 (β)	51.1 (3.47)	3.22 (0.13)	2.32 (0.61)
(2) MMA/MA	–	54.1 (4.67)	3.45 (0.14)	2.20 (0.23)
	15 (γ)	52.5 (0.67)	3.12 (0.20)	1.86 (0.08)
	20 (γ)	49.2 (2.95)	3.22 (0.05)	1.72 (0.28)
	25 (γ)	52.5 (1.31)	3.46 (0.30)	1.93 (0.21)
	12.5 (β)	54.1 (2.66)	3.45 (0.01)	2.20 (0.06)
	25 (β)	50.4 (3.93)	3.48 (0.17)	1.86 (0.17)
	50 (β)	45.2 (7.34)	3.33 (0.12)	1.62 (0.33)
(3) MMA/BMA	–	55.1 (4.67)	2.95 (0.04)	2.97 (0.82)
	25 (γ)	47.2 (4.40)	2.83 (0.03)	2.28 (0.40)
(4) MMA/EHA	–	53.6 (2.00)	2.94 (0.20)	2.63 (0.32)
	25 (γ)	48.8 (4.12)	2.61 (0.11)	2.58 (0.72)
(5) Powder blend including MMA/styr.	–	49.2 (2.54)	3.25 (0.23)	2.35 (0.54)
	25 (γ)	48.3 (2.06)	3.26 (0.09)	2.28 (0.23)
(6) Powder blend including MMA/MA	–	51.2 (1.39)	3.83 (0.37)	2.46 (0.18)
	25 (γ)	48.9 (1.69)	3.42 (0.10)	2.22 (0.21)
Palacos® R	–	51.4 (3.47)	3.21 (0.18)	2.25 (0.32)
	20 (γ)	47.5 (2.47)	3.22 (0.23)	1.94 (0.20)
	25 (γ)	48.0 (1.17)	3.06 (0.12)	2.02 (0.11)
	12.5 (β)	50.9 (3.15)	3.04 (0.18)	2.37 (0.08)
	25 (β)	50.0 (4.38)	3.20 (0.11)	2.18 (0.37)
	50 (β)	42.9 (5.30)	3.05 (0.13)	1.91 (0.43)

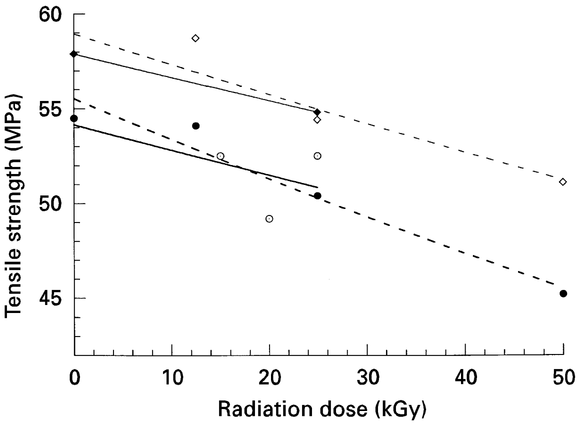

Figure 2 Influence of γ radiation dose upon the tensile strength of bone cements prepared from MMA/styrene co-polymer, cement (1) and MMA/MA co-polymer, cement (2). (—◆—) cement (1) γ, (—○—) cement (2) γ, (- -◇- -) cement (1)β, (- -●- -) cement (2) β.

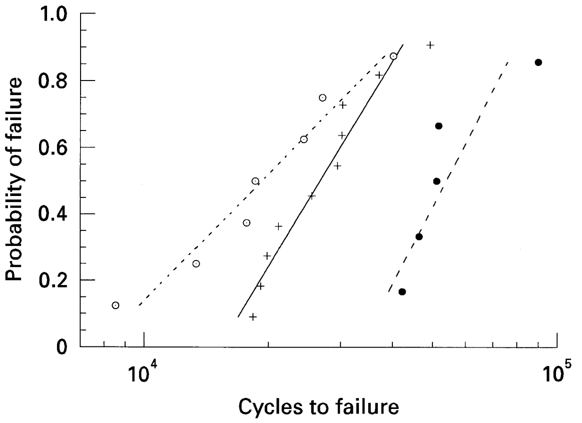

Figure 3 Fatigue characteristics of bone cement prepared from powder blend containing MMA/MA co-polymer, cement (6), before and after 25 kGy γ radiation, in comparison to Palacos® R. (- - -⊙- - -) Cement (6) γ, (—+—) Palacos, (- -●- -) cement (6).

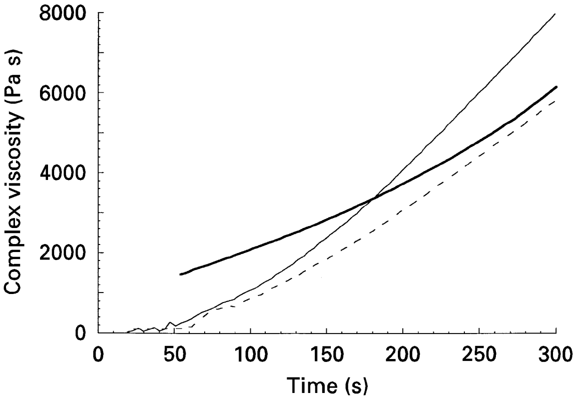

Figure 4 Viscosity profiles of bone cements prepared from powder blend containing MMA/MA co-polymer, cement (6), before and after 25 kGy gamma radiation, in comparison to Palacos® R. (———) Cement (6), (- - -) Cement (6) γ, (———) Palacos.

reflected in the fall in tensile strength shown in Fig. 2. The change in mechanical properties is discussed in more detail in a subsequent section. The lack of protection provided by the MMA/styrene co-polymer may be attributed to the relatively low proportion of styrene or due to the radiation occurring in air, causing oxidation and chain scission to take place in preference to cross-linking.

There was little difference between the influence of γ and β radiation. β radiation is produced by high-energy electron beams and its effects decrease with specimen thickness. The polymer powders were irradiated in relatively small batches and time was allowed for the radiation to penetrate fully. γ radiation or X-rays are electromagnetic waves and more penetrative than β radiation, depending largely on atomic number rather than amount of irradiated substance. γ radiation is, therefore, more convenient than β radiation, with a shorter time required for a particular dose and lower sensitivity to the size of material to be irradiated.

The microstructure of the bone cements produced in this investigation was two-phased, consisting of the pre-polymerized polymer beads within a newly formed PMMA matrix. The bone cements prepared from powders (5) and (6) and Palacos® R also contained zirconia in the interbead matrix. Failure could therefore occur through either phase. Bhambri and Gilbertson [13] found fatigue crack propagation proceeded through both phases. This result was confirmed by scanning electron microscopy of fracture surfaces of all the cements examined in this study. The radiation damage influenced only the pre-formed polymer beads; the newly polymerized PMMA matrix was formed after the irradiation and is not thought to be influenced to a large extent. It is possible that the effectiveness of the benzoyl peroxide present in the polymer beads was damaged upon irradiation, resulting in a reduction in the degree of polymerization. However, this effect would not be expected to produce such changes in mechanical properties that were observed. Therefore, differences in mechanical properties were assumed to be the direct result of a reduction in molecular weight of the polymer beads. Fig. 2 shows a similar trend in tensile strength as found for molecular weight. It is important to note that the highest molecular weight polymer powder, MMA/styrene co-polymer, produced the highest cement strength. It is sometimes stated that tensile strength and elongation are independent of molecular weight above a critical minimum value between 100 000 and 200 000 [1]. This conclusion does not appear to be the case with bone cements tested in this investigation and Table I shows the tensile strength, Young's modulus and strain to failure were higher with larger molecular weights.

Although a decrease in static mechanical properties did occur, in comparison to the deterioration in fatigue resistance, it was comparatively small. At 25 kGy γ radiation, the drop in tensile strength for the powder-blended cement containing MMA/styrene co-polymer, was only 1.8%, and for the powder-blended cement containing MMA/MA co-polymer, the decrease was 4.5%. In contrast, Fig. 3 shows the drop in number of cycles of cement (6) was considerable, the change in median fatigue life was from 51 115 to 18 583, a decrease of 64%. Similar changes were found for the powder-blended cement containing MMA/styrene co-polymer, not reported here. The high sensitivity of fatigue resistance to molecular weight has been reported by several investigators [6–8]. Kim *et al.* [7] attributed differences to the degree of chain entanglement and strength of the craze preceding the growing crack. At higher molecular weights the polymer chains are longer and more tangled and thus able to resist the growth of cracks. Once a chain is long enough to span a craze effectively, a further increase in molecular weight does not provide much advantage. However, with cyclic loading, the molecular chains disentangle and this is easier at low molecular weights. Increases of fatigue resistance with molecular weight of PS were investigated by Foden *et al.* [14]. The dependence of the resistance of the polymer to alternating load upon molecular weight was attributed to a number of reasons. Firstly, at higher molecular weight, the density of chain ends, which act as a potential source of microcracks, is reduced; secondly, intermolecular bonding increases at higher molecular weight; and finally, higher molecular weight allows a greater degree of chain orientation in regions of plastic deformation near tips of microcracks. It is important to note that prior to γ sterilization, the fatigue median cycles of failure of cement (6) at 51 115 was significantly higher than that of Palacos® R at 27 906. Palacos® R is sterilized using EtO gas which does not produce a reduction in mechanical properties.

Fig. 4 showed that the complex viscosity of the powder-blended cement containing MMA/MA co-polymer (6), was reduced by γ radiation at a dose of 25 kGy when compared at similar times to pre-irradiated material. A decrease in viscosity was also found for the powder-blended cement containing MMA/styrene co-polymer (5). This reduction in viscosity was attributed to the reduction in molecular weight of the polymer beads. Viscosity of a polymer, usually in solution, is often used to calculate the molecular weight and depends upon the ability of polymer chains to flow past each other. At higher molecular weight this process becomes more difficult as forces between chains are increased. The decrease in viscosity found with these cements was somewhat surprising because only the polymer beads were irradiated; the monomer which polymerizes to form the hardened cement was not affected. Although the viscosity of bone cement has not been extensively studied, there have been a few investigations [15, 16] and it is known that the viscosity setting profile is influenced by polymer powder size, shape, molecular weight, benzoyl peroxide content and composition. The experimental cements containing powders (5) and (6) were developed to possess excellent handling characteristics with low initial viscosity followed by a gradual, but not too slow, increase. The profile in Fig. 4 demonstrates this property in comparison to Palacos® R which has a much higher initial viscosity and slower increase with time.

5. Conclusion

Both γ and β radiation, at a dose suitable for sterilization of bone cement powder, caused the molecular weight of a number of MMA co-polymers, including one containing styrene, to decrease. This effect resulted in a decrease in a number of static mechanical properties, tensile strength, Young's modulus and strain to failure in relation to radiation dose. However, fatigue testing was more sensitive to the fall in molecular weights and bone cements displayed a large reduction in fatigue resistance following γ radiation. This result demonstrated the need to test experimental bone cements using dynamic as well as static methods. The rheological properties of bone cement were influenced by γ radiation demonstrated by the decrease in complex viscosity during curing. In summary, these results suggest that although the use of irradiation, either γ or β, is more convenient for sterilization, the deterioration in properties of the resulting bone cement was significant and would adversely affect *in vivo* performance.

Acknowledgements

The financial support of EPSRC and supply of polymer powders from Bonar Polymers Ltd, Co. Durham, UK is gratefully acknowledged. EC BIBOCHEM-Project PMH 4-CT 95-0147.

References

1. E. P. LAUTENSCHLAGER, S. I. STUPP and J. C. KELLER, "Functional Behaviour of Orthopaedic Biomaterials", Vol. 2, "Applications" (CRC Series in Structure Property Relationship of Biomaterials, Boca Raton, FL, 1987) p. 87.
2. A. CHARLESBY, "Atomic Radiation and Polymers" (Pergamon Press, London, 1960) p. 335.
3. J. E. WILSON, "Radiation Chemistry of Monomers, Polymers and Plastics" (Marcel Dekker, New York, 1974) p. 369.
4. MITAB, Sobo, Sweden, "EtO degassing investigation", private communication, June 1996.
5. V. PREMNATH, W. H. HARRIS, M. JASTY and E. W. MERRILL, *Biomaterials* **17** (1996) 1741.
6. W. L. SAUER, K. D. WEAVER and N. B. BEALS, *ibid.* **17** (1996) 1929.
7. S. L. KIM, M. SKIBO, J. A. MANSON and R. W. HERTZBERG, *Polym. Engng. Sci.* **17** (1977) 194.
8. J. A. SAUER, *Polymer* **19** (1978) 859.
9. J. A. SAUER and G. C. RICHARDSON, *Int. J. Fract.* **16** (1980) 499.
10. M. TANAKA, H. YOSHIDA and T. ICHIKAWA, *Polym. J.* **22** (1990) 835.
11. L. DONG, D. J. T. HILL, J. H. O'DONNELL, P. J. POMERY and K. HATADA, *J. Appl. Polym. Sci.* **59** (1996) 589.
12. T. A. GRUEN, G. M. MCNEICE and H. C. AMSTUTZ, *Clin. Orthop. Rel. Res.* **141** (1979) 17.
13. S. K. BHAMBRI and L. N. GILBERTSON, *J. Biomed. Mater. Res.* **29** (1995) 233.
14. E. FODEN, D. R. MORROW and J. E. SAUER, *J. Appl. Polym. Sci.* **16** (1972) 519.
15. W. R. KRAUSE, J. MILLER and P. NG, *J. Biomed. Mater. Res.* **16** (1982) 219.
16. K. L. MARKOLF, M. KABO, D. W. STOLLER, S. A. ZAGER and H. C. AMSTUTZ, *Clin. Orthop. Rel. Res.* **183** (1984) 246.

Received 5 May
and accepted 12 May 1997