DEVELOPMENT OF NEW BONE CEMENT

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Copolymers having 80/20 and 50/50 composition of PEMA and PMMA were respectively used instead of PMMA, and n-BMA was used instead of MMA monomer in the conventional bone cement. It was found that maximum exothermic temperature, generated from polymerization of the monomer in bone cement, was decreased from approximate 100-110°C. to approximate 50-60°C. The copolymer bone cement was also found to reduce brittleness problem of the PMMA bone cement. However, mechanical strength of the copolymer bone cements is still low even though they were reinforced with 0-40% by weight of hydroxyapatite. The 80/20 copolymer bone cement was found to have higher mechanical strength than the 50/50 copolymer bone cement though the 80/20 copolymer has lower PMMA composition. In addition, the monomer used as liquid component in bone cement tends to be the major influence on mechanical strength of the bone cement.

INTRODUCTION

Bone cement, here, means acrylic polymer used in hip joint replacement. Though it acts as an intermediary grout between implant or prosthesis and bone tissue, not as an adhesive, it is generally called *"bone cement"*. It is used to provide uniform distribution of stress between implant and bone, and designed to improve implant fixation. It was firstly introduced to orthopaedic surgery in the mid 1950's by Sir John charnley (1-2) and still using today. At the present, most total joint replacement surgeries including hip, knee, and ankle, use acrylic bone cement as a means of fixation of the prosthesis to the bone. Bone cements are often utilized in fixation of pathological fractures, and also in the repair of bone defects.

Bone cement generally composes of 2 components:- liquid and powder. The liquid is mainly *acrylic monomer* with trace of hydroquinone to prevent premature polmerization, and N,N-dimetyl-p-toluidine (DMPT) to promote cold curing. The powder is made up of a

fine *polymer powder, BPO initiator* to initiate polymerization of acrylic monomer and sometimes *radiopacifier* for X-ray inspectation. When the two components are mixed together, polymerization occurs and the mixture cures to *a rigid form of bone cement* in a short period of time (8-12 minutes after mixing) at room temperature.

In a typical operation, a metallic stem is secured in the medullary cavity of the femur by an in-situ polymerization of the bone cement and located in an ultra-high molecular weight polyethylene acetabular cup. While various combinations of alloys, ceramics and polymers have been utilized in the past twenty years as stems and cups, *polymethylmethacrylate* or *PMMA*, which is one of the most important acrylic polymers, had remained as an almost universal choice for bone cement.

However, the PMMA bone cement was found to have poor mechanical properties and high exothermic temperature which results in bone necrosis and reduction in blood pressure. In addition, in the long term orthopaedic implantation, mechanical mismatch in elastic deformation characteristics across the bone/cement/metal composite can result in fracture of the bone cement. It is no surprise therefore that instances of implant loosening have frequently been reported. According to Feith (3), 20% of all patients with total hip replacements would need a second operation within 10 years.

Similar data have been reported by other researchers and the possibility of cement breakdown has been highlighted as a contributory cause of this loosening. Then improvements in the properties of bone cement would have far-reaching consequences.There are in fact two major research initiatives in progress:
1) to eliminate cement completely by developing either bone growth into a porous metal stem or bone apposition at a bioactive surface
2) to reduce the exotherm and/or to improve the fracture toughness of existing acrylic bone cements.

Previous approaches to enhancing the mechanical properties of bone cement have been directed towards improving the existing PMMA cement rather than developing a new cement because of the time and expense required in finding a substitute and obtaining approval from federal regulatory agencies such as the DHSS and FDA. These attempted modifications, which have concentrated on improving the strength and stiffness mainly as a consequence of fibre reinforcement (4-7) have been shown to adversely affect distribution of load from the metal stem to the surrounding bone (6). For this reason,

the lower strengthening efficiency in a particulate composite would allow a better mechanical match with the surrounding materials (8-9).

Whilst most of investigators have tried to improve the mechanical properties of bone cement by various methods of reinforcement of the PMMA bone cement, Weightman et.al (10) have tried with a new, more ductile bone cement based on PEMA powder and n-butylmethacrylate monomer (n-BMA). It has been reported to have distinct advantages over the conventional PMMA bone cement, not only mechanically but also physiochemically and biologically. Unlike PMMA, the new cement is not irritant to soft tissue and less toxic to dental pulp (11-13) and has been shown to have a higher fracture toughness and superior fatigue life (14) as well as lower exotherm than the conventional PMMA bone cement. Unfortunately, the new bone cement was observed to have creep in certain prosthesses.

As a consequence of these findings, further study has continued in this area to address this weakness. Behiri et al. (15) found that introduction of hydroxyapatite powder with PEMA produced the increases in Young's modulus and yield stress and also the decreases in elongation to fracture. In addition, mechanical property improvement of the bone cement has been attempted by using a new bone cement based on EMA/MMA copolymer powder and n-BMA monomer instead of PEMA bone cement as in the present study.

MATERIALS AND METHODS

Poly(ethyl-co-methyl)methacrylate or *PEMA-co-PMMA* powder supplied by Bonar Polymer Ltd. together with *hydroxyapatite powder* supplied by Plasma Biotal Ltd., *silane coupling agent* (3-Trimethoxy-silylpropylmethacrylate or A-174) supplied by Union Carbide Ltd., and *Interox BP50FT* supplied by Peroxid Chemie Ltd. were starting materials for the present study.

A portion of the supplied hydroxyapatite was surface treated with various percentages of silane coupling agent (A-174), by dissolving the silane in a 30/70 water/acetone mixture and mixing the liquid with hydroxyapatite to obtain a slurry. Acetone and water were then partially removed from the slurry at 100°C, and the silane consequently condensed on surface of the hydroxyapatite by heat treatment at 125°C for 2 hours. The treated hydroxyapatite was then filtered, washed, dried and then sieved through a 60 mesh screen. Existent of silane on the hydroxyapatite surface was confirmed by FT-IR spectra, and the silane content was determined by weight-loss analysis.

A composition range of reinforced copolymer bone cements was obtained by using 80/20 PEMA-co-PMMA or 50/50 PEMA-co-PMMA as starting material. Prior to mixing, a known quantity of the copolymer powder containing 1.5% w/w benzoylperoxide was replaced and physically blended with an equal weight of hydroxyapatite. In this way a range of reinforcement concentrations in the powder was investigated. The 2:1 ratio of copolymer powder (either with or without reinforcement) and monomer containing 2.5%v/v N,N-dimethyl-p-toluidine and traces of hydroquinone were mixed in a beaker until the dough state was reached and subsequently transferred into a standard tensile test aluminum specimen mould (ISO/DIS 6239-40) under a compression pressure of 100 psi at room temparature for 25 min. The tensile specimens had a thickness of 3 mm and had a total length of 75 mm while the parallel test sections in the centre of the specimens had a reduced width of 4.5 mm and a length of 40 mm. The tensile tests were performed in a Lloyd 500 testing machine at a cross head speed of 5 mm mm^{-1} using an extensometer V/25 to measure displacement.

Doughing time and exothermic behavior of various bone cements were investigated according to ASTM F451-76. For the doughing time investigation, start a stopwatch at the onset of combining all the powder and liguid components, and read all subsequent times from this stopwatch. Approximate 1.5 minutes after the onset of mixing, gently probe the mixture with a surgically gloved finger. Take visual notice as to the formation of fibers between the surface of the mix and the finger as it leaves the surface. Repeat this process of probing from that time on at 15-second intervals until the gloved finger separates cleanly. Denote the time at which this is first observed as the *doughing time*.

For exothermic behavior investigation, gently pack approximate 25 g of the dough, within 1 minute after dougning time, into a mould for exothermic temperature test (ASTM F451-76). Continue measuring the time from the onset of mixing and continuously record the temperature until cooling is oberved. Report the maximum temperature recorded to the nearest 1°C. From the continuous time versus temperature curve, setting time of the bone cement is the time when temperature of the polymerizing mass is $(T_{max} + T_{ambient})/2$, where T_{max} is the maximum temperature and $T_{ambient}$ is the ambient temperature of 23 ± 2°C. Report the setting time to the nearest 15 second.

RESULTS AND DISCUSSION

1. Curing Behavior of Various Bone Cements

Table 1 and figures 1-2 show respectively curing behavior of PMMA, PEMA, 80/20 and 50/50 PEMA-co-PMMA bone cements. Exotherm or maximum exothermic temperature of the bone cements was found to be 100-110°C when using MMA monomer as the liquid component, but decreased to 50-60°C when using n-BMA monomer instead. Setting time of the bone cement was observed to be increased with the decrease of polymer-monomer wettability. especially in the case of 50/50 copolymer & n-BMA bone cement, of which setting time was observed to be the highest. However, setting time of both 80/20 and 50/50 copolymer bone cements was found to be decreased with addition of 1.0% by weight of Interox BP50 FT, i.e. the BPO mixed with 50% by weight of Dicyclohexyl Phthalate, a non-reactive plastising powder.

Table 1 Curing Behavior of Various Bone Cements

Polymer	Monomer	%Added BP50FT	Maximum Temp. (°C)	Setting Time (min)	Ambient Temp. (°C)
PMMA	MMA	0	111.1	3.25	24.8
80/20 P supplied by EMA-co-PMMA	MMA	0	102.3	5.25	27.5
PEMA	BMA	0	56.5	8	30.1
80/20 PEMA-co-PMMA	BMA	0	49.6	16	28.8
		1.0	63.8	6.8	32.3
50/50 PEMA-co-PMMA	BMA	0	41	44	28.6
		1.0	49	14.2	32.1

Exotherm Profile of Various Bone Cements
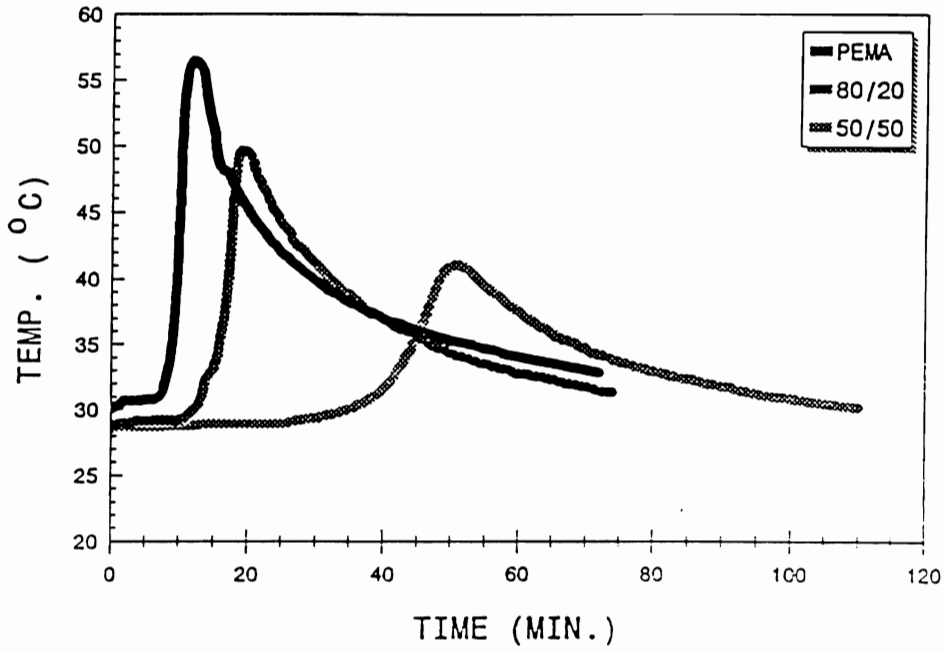
n-BMA MONOMER
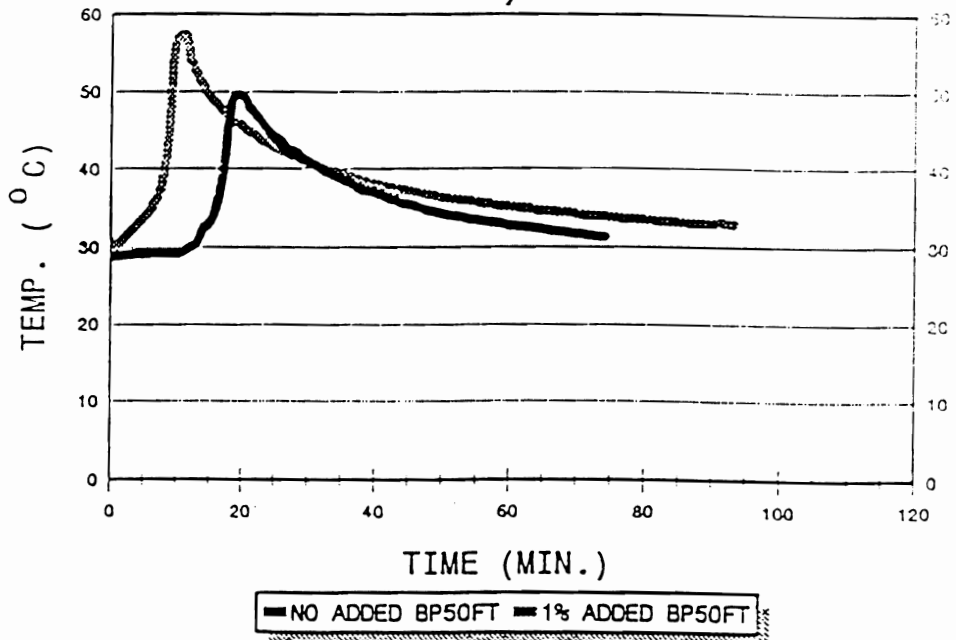
Figure 1   Curing behavior of various bone cements

Effect of Interox BP50FT Addition

50/50

TEMP. (^{O}C)

TIME (MIN.)

■ NO ADDED BP50FT ■ 1% ADDED BP50FT

n-BMA MONOMER

80/20

TEMP. (^{O}C)

TIME (MIN.)

■ NO ADDED BP50FT ■ 1% ADDED BP50FT
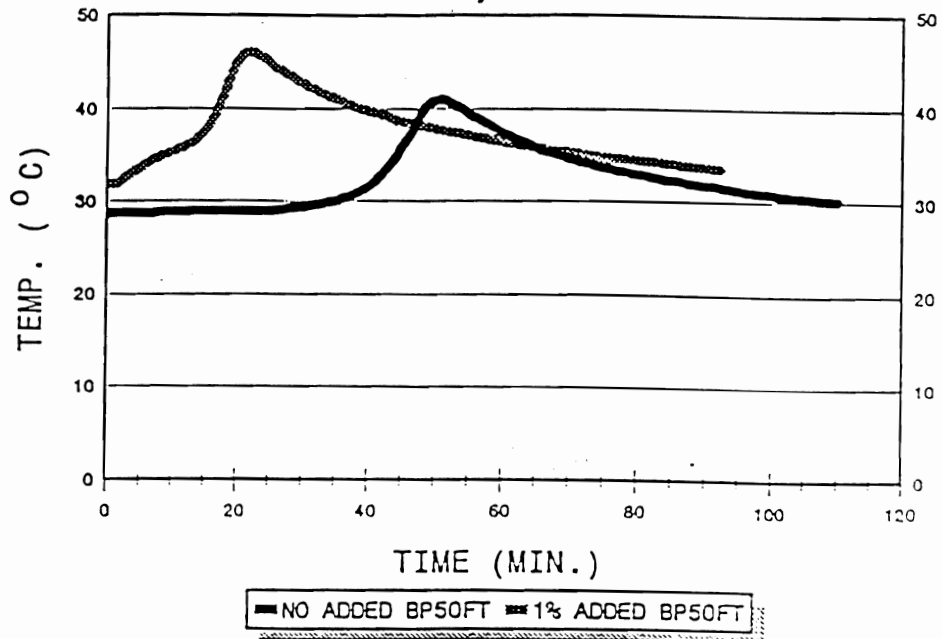
n-BMA MONOMER

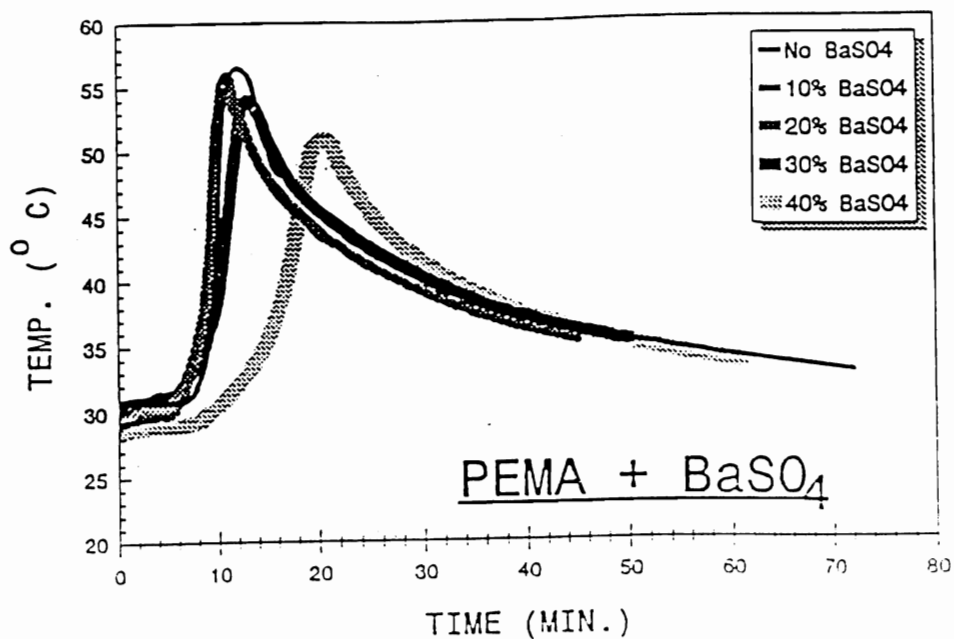**Figure 2 Effect of BP50FT on curing behavior of copolymer bone cements**

2. Effect of Reinforcement on Curing Behavior of Various Bone Cements

Table 2 and figure 3 show effect of BaSO4 addition on curing behavior of various bone cements. It was observed that maximum exothermic temperature gradually decreased with the increased amount of BaSO4 addition, but the setting time remarkably increased with the increased amount of BaSO4 addition, especially when the BaSO4 addition exceeded 30% by weight for PEMA bone cement and exceeded 20% by weight for 80/20 copolymer bone cement, as shown in Table 2 and figure 3. These results may by considered as the effect of wettability or BPO extraction efficiency of the monomer. Therefore, addition of Interox BP50FT was expected to improve curing capability of the bone cement.
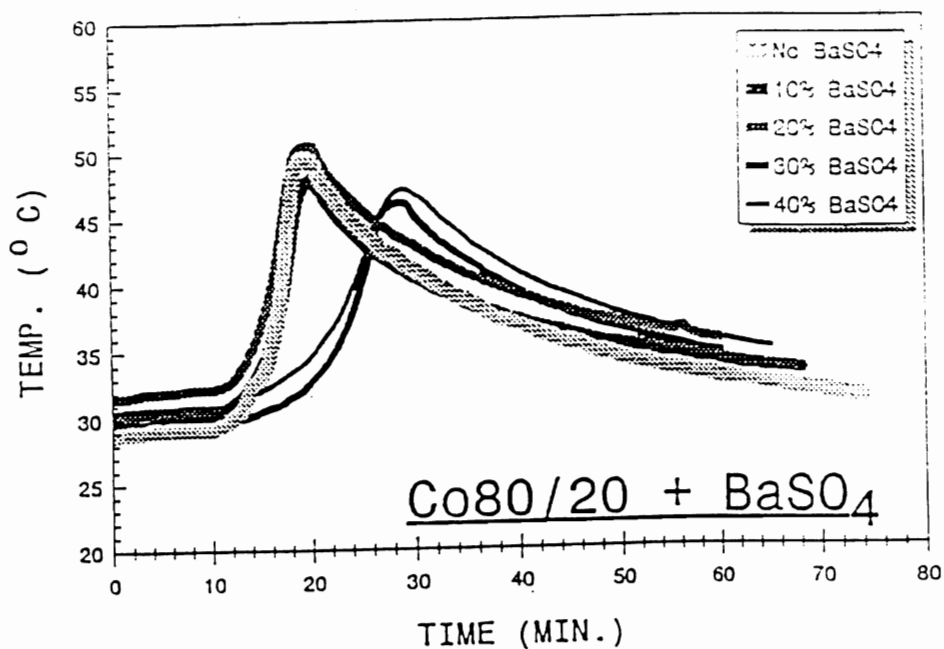
Table 2 Effect of BaSO4 Addition on Curing Behavior of Various Bone Cements

Polymer	Monomer	%BaSO$_4$	Exothermic Temp. (°C)	Setting Time (min)	Ambient Temp. (°C)
PMMA	MMA	0	111.1	3.25	24.8
		5	109.5	3.5	21.1
		10	111	4.2	26.2
		15	103.5	5	21.9
		20	81.6	3.75	23.6
80/20 Copolymer	MMA	0	102.3	5.25	27.5
		5	100	5	28.7
		10	103.5	5	27.6
		20	102	5.25	28.4
		30	114.4	5.9	28
		40	113.1	6.25	28.1
PEMA	BMA	0	56.5	8	30.1
		10	56	9.2	29.4
		20	54.2	10	29.8
		30	54	10.5	30.3
		40	50.8	16.5	28.3
80/20 Copolymer	BMA	0	49.6	16	28.8
		10	48	17	30.1
		20	50.6	16	31.5
		30	46.2	24	29.4
		40	47.2	24	30.5
50/50 Copolymer	BMA	0	41	44	28.6

Effect of BaSO₄ Addition upon Exotherm Profile

n-BMA MONOMER

n-BMA MONOMER

Figure 3   Effect of BaSO₄ addition upon curing behavior of Bone Cements

3. Mechanical Properties of Various Bone Cements

Tensile specimens according to ISO/DIS 6239/1 and bending specimens according to ASTM D790-40 were prepared and left for complete curing in an oven at 37°C for one month. Tensile properties as well as bending properties were then investigated with Universal Testing Machine Lloyd 500, and the result was shown in Tables 3-4 and figure 4. Tensile strength as well as bending strength of the 80/20 copolymer bone cements was observed to be higher than those of the 50/50 copolymer bone cements, though the 50/50 copolymer contains higher PMMA content. This may be the result of insufficient BPO extracted from the 50/50 copolymer powder. Consequently, tensile strength of the 50/50 copolymer bone cements was observed to be increased with the addition of the Interox BP50FT, but still lower than that of the 80/20 copolymer cements as shown in Table 5.

It was also observed that mechanical strength of the 80/20 copolymer cements was similar as that of PEMA, but strain to failure of the copolymer cements tends to be lower than that of the PEMA cements. Therefore, mechanical strength of the 80/20 copolymer cements is expected to be improved by reinforced with hydroxyapatite particle which should be further studied.

Table 3 Tensile Properties of Various Bone Cements

Polymer	Monomer	Tensile Strength (MPa)	%Strain at max. load	Tensile Modulus (GPa)
Tested at C.U.				
PMMA	MMA	47.13 +/- 4.20	1.14 +/- 0.19	3.19 +/- 1.09
80/20	MMA	48.77 +/- 4.33	2.26 +/- 0.45	3.45 +/- 0.42
Copolymer	BMA	12.26 +/- 1.55	3.71 +/- 0.83	0.83 +/- 0.24
PEMA	BMA	25.32 +/- 0.25	4.73 +/- 0.41	1.20 +/- 0.10
50/50 Copolymer	BMA	9.82 +/- 0.25	1.82 +/- 0.88	1.19 +/- 0.29
Note : Tested with Lloyd 500 & Extensometer V/25, 2.5 kN (5mm / min) Without BP50FT addition				
Tested at QMW				
PMMA	MMA	26.57 +/- 6.27	0.75 +/- 0.37	3.02 +/- 0.11
80/20 Copolymer	BMA	16.44 +/- 0.88	3.28 +/- 0.30	0.91 +/- 0.07
PEMA	BMA	19.84 +/- 0.87	4.29 +/- 0.35	0.83 +/- 0.07
50/50 Copolymer	BMA	No data	No data	No data
Note : Tested with Instron 6032 & 60 psi clip on extensometer, 1 kN load cell (5mm/ min) Without BP50FT addition				

Table 4 Bending Properties of Various Bone Cements

Polymer	Monomer	Bending Strength (MPa)	Bending Modulus (MPa)
PMMA	MMA	81.64 +/- 16.80	1798.0 +/- 347.8
PEMA	BMA	27.72 +/- 5.34	676.6 +/- 143.2
80/20 Copolymer	BMA	29.27 +/- 4.64	748.7 +/- 123.9
50/50 Copolyme	BMA	22.83 +/- 1.49	772.6 +/- 103.0

Note : Tested at C.U. with Lloyd 500,2.5 kN load cell(1 mm/min)
        Without BP50FT addition

Table5 Effect of BP50FT and/or HAP addition upon Tensile
        Properties of Various Bone Cements

Polymer	Monomer	% BP50FT	% HAP	Tensile Strength (MPa)	%Strain at max. load	Tensile Modulus (GPa)
PMMA	MMA	0	0	47.13 +/- 4.20	1.14 +/- 0.19	3.19 +/- 1.09
PEMA	BMA	0	0	25.32 +/- 0.25	4.73 +/- 0.41	1.20 +/- 0.10
		0.5	0	27.82 +/- 0.35	4.79 +/- 0.44	1.44 +/- 0.35
		1	0	27.04 +/- 1.30	4.66 +/- 0.60	1.35 +/- 0.29
		2	0	25.86 +/- 0.62	5.08 +/- 0.41	1.19 +/- 0.19
80/20 Copolymer	MMA	0	0	48.77 +/- 4.33	2.26 +/- 0.45	3.45 +/- 0.42
	BMA	0	0	12.26 +/- 1.55	3.71 +/- 0.83	0.83 +/- 0.24
		1	0	26.21 +/- 1.61	3.97 +/- 0.56	1.60 +/- 0.19
		2	0	18.43 +/- 0.38	4.34 +/- 0.59	1.30 +/- 0.24
		1	20	21.91 +/- 1.29	4.20 +/- 0.40	1.49 +/- 0.44
		1	30	22.87 +/- 0.24	3.83 +/- 0.31	2.21 +/- 0.66
		1	40	06.10 +/- 0.44	4.46 +/- 0.58	0.41 +/- 0.14
50/50 Copolymer	BMA	0	0	09.82 +/- 0.25	1.82 +/- 0.88	1.19 +/- 0.29
		0.5	0	10.06 +/- 0.63	3.45 +/- 0.48	0.78 +/- 0.22
		1	0	10.59 +/- 1.28	4.67 +/- 1.08	0.87 +/- 0.72
		2	0	15.50 +/- 1.13	4.18 +/- 1.02	1.20 +/- 0.27

Note: Tested at C.U. with Lloyd 500 & Extensometer V/25 (5mm/min)

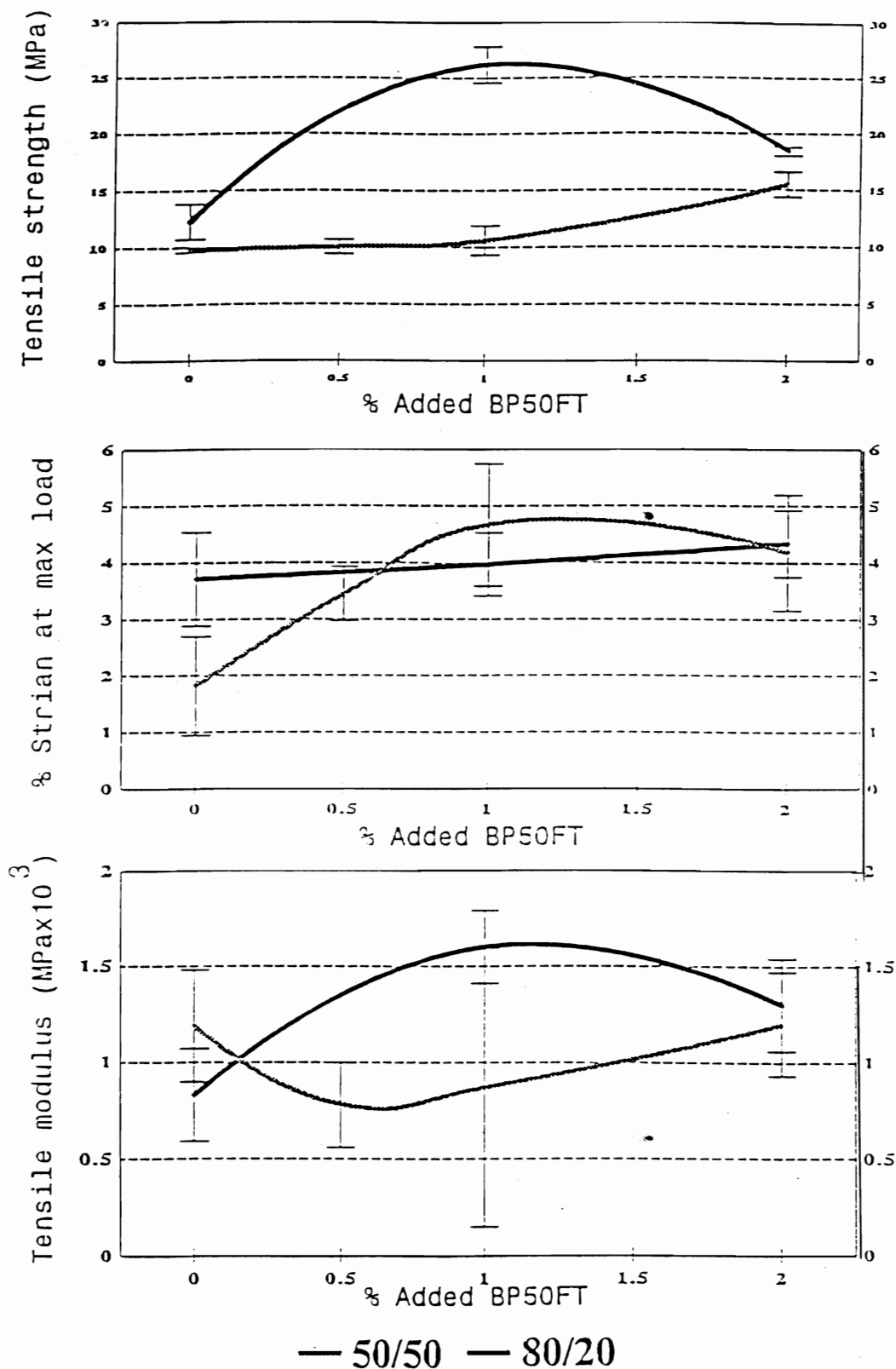# Effect of BP50FT Addition on Tensile Properties

Figure 4   Effect of BP50FT on mechanical properties of various bone cements

CONCLUSION

Exothermic temperature as well as brittleness of the conventional PMMA bone cement could be reduced by replacement of MMA monomer with n-BMA monomer in the bone cement mixture. Either exothermic temperature or brittleness of the bone cement cannot be reduced by replacement of PMMA powder with 80/20 PEMA-co-PMMA powder in the PMMA bone cement (using MMA monomer as the liquid commponent). Whereas the both can be reduced with either PEMA or PEMA-co-PMMA bone cement (using n-BMA monomer as the liquid component), but mechanical strength of the bone cements is still lower than that of the PMMA bone cement even reinforced with particulate hydroxyapatite. Thus the monomer used as liquid component in bone cement tends to be the major influence on both mechanical strength and exotherm of the bone cement.

ACKNOWLEDGEMENT

REFERENCES

1. J. Charnley : J. Bone Joint Surg., 42 B (1960), 28.
2. J. Charnley : J. Bone Joint surg., 46 B (1964), 518.
3. R. Feith : Acta Orthop. Scand. Suppl., 161 (1975), 1.
4. A. Knoell. H. Maxwell and C. Bechtol : Ann. Biomed. Eng., 3 (1975), 225.
5. R.M. Pilliar, et al.: J. Biomed. Mater. Res., 10(1976), 893.
6. T.M. Wright and P.S. Trent : J. Mater., Sci., 14 (1979), 503.
7. T.M. Wright and R.P. Robinson : J. Mater. Sci., 17 (1982), 2463.
8. A. Murakami, J.C. Behiri and W. Bonfield : J. Mater. Sci., 23 (1988), 2029
9. W. Bonfield : Biocompatability of Tissue Analogs, 2 (1985), 89, edited by D.F. Williams (CRC Press, Boca Raton, Florida).

10. B. Weightman, M.A.R. Freeman, P.A. Revell and M. Braden :
    J. Bone Joint Surg., 69B (1987), 558.
11. European Application Number ; 8 (1985), 152, 524.
12. W.D. Schwartz and M. Braden : J. Dentistry, 1 (1973), 179.
13. M. Braden, R.L. Clarke, G.J. Pearson and W. Cambell Keys.:
    Brit Dent. J., 141 (1976), 269.
14. M.P. Patel, K.W.M. Davy and M. Braden : Biomaterials, (1987),
    53.
15. J.C. Behiri, M. Braden, S.N. Khorasani, D. Wiwattanadate and
    W. Bonfield : Bioceramic, vol.4 (1991) 301, edited by W.Bonfield,
    G.W. Hastings and K.E. Tanner.