Improvement of the mechanical properties of acrylic bone cements by substitution of the radio-opaque agent

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Acrylic bone cements become radio-opaque by the addition of an inorganic compound, commonly $BaSO_4$ or ZrO_2. However, the use of these additives has some negative effects such as loss of mechanical properties, risk of release and bone resorption. The use of the monomer 2,5-diiodo-8-quinolyl methacrylate (IHQM), which shows adequate polymerization and radio-opacity properties, is proposed as a new X-ray opaque, methacrylate iodine-containing agent. The aim of this study is to determine the effect of this new radio-opaque agent on the mechanical properties of acrylic bone cements. The addition of the iodine-containing methacrylate provides a statistically significant increase in the tensile strength, fracture toughness and ductility, with respect to the barium sulphate-containing cement. This effect can be attributed to the fact that the use of a radio-opaque monomer eliminates the porosity associated with the barium sulfate particles, which show no adhesion to the matrix. However, some reinforcing effect must also be attributed to the iodine-containing monomer, since the tensile and fracture toughness values reached are even higher than those shown by the radiolucent cement.

1. Introduction

Bone cements have been used with encouraging results for a number of years in orthopaedic surgery for the fixation of artificial joints. They usually become radio-opaque by the addition of an inorganic compound, commonly $BaSO_4$ or ZrO_2. However, their effect can be considered as detrimental for the mechanical properties of bone cements. The presence of these fillers tends to increase the density of the cement, depending on the curing pressure, but this effect is not significant on porosity, and it plays a minor role on shrinkage [1]. The effect of radio-opacifiers on bone cements was taken into account very early on. It is usually accepted that $BaSO_4$, in amounts of about 10% in weight, reduces the tensile strength [1–3], flexural strength [4] and fracture toughness [5].

When the fracture surface of bone cement containing a radio-opacifier is observed at high magnification in the scanning electron microscope, it can be noticed that there is no adhesion between the polymerized poly(methyl-methacrylate) (PMMA) and the filler particles [6, 7]. This suggests that the filler particles will behave like pores when a tensional state of stress is applied to the cement [8].

There is also evidence that the release of the radio-opacifier particles in the surrounding tissues can have detrimental effects. If they enter the joint space they may cause damage to the articulating surfaces, with a marked increase in the production of polyethylene wear debris [9–11].

On the other hand, recent studies have shown that the addition of radio-opaque agents to PMMA enhance the macrophage–osteoclast differentiation and therefore they may contribute to the bone resorption of aseptic loosening [12]. Specifically, bone cement containing barium sulfate is likely to be associated with more osteolysis than that containing zirconium dioxide. Furthermore, these agents evoke a significant pathological response in the surrounding tissue. Barium sulfate has also been shown to intensify the release of inflammatory mediators in response to PMMA particles [13].

Taking into consideration these serious drawbacks, it makes sense to search for an alternative to the traditional radio-opaque agents. A possible approach is to introduce radio-opaque monomeric units during polymer synthesis. Monomers, having covalently bound halogen atoms such as iodine or bromine, that possess radio-opaque properties, can be copolymerized in small quantities with other monomers that constitute the bulk of the implant. In this line, some iodine methacrylates are being developed successfully for different clinical applications, such as endovascular prostheses [14–18]. Recently, Davy *et al.* have prepared polymer beads based on the copolymers methyl methacrylate/methacrylic monomers containing the group triiodobenzoate, and they have used them to prepare cold-cure systems with good mechanical properties [19].

The approach adopted in this study is to confer radio-opacity to acrylic bone cements by introducing an X-ray opaque iodine-containing methacrylate into the liquid phase of the bone cement. In this work the 2,5-diiodo-8-quinolyl methacrylate (IHQM), is proposed as the new radio-opaque agent. In previous works it was observed that the incorporation of this monomer produced a decrease of the peak temperatures and a slight increase of the setting time. The radio-opacity of the resulting cements was confirmed using a clinical X-ray standard instrument and was found to be good even for cements containing 5 wt % of IHQM in the liquid phase. The radiographic image presented a contrast similar to the metallic wire used as a control. Furthermore, implantation studies in rats showed that there is no chronic inflammatory response [20, 21]. The aim of this study is to determine the effect of this new radio-opaque agent on the mechanical properties of acrylic bone cements.

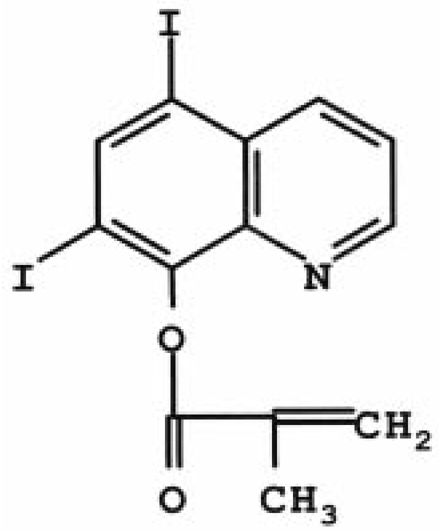

Figure 1 Chemical structure of IHQM.

2. Materials and methods

2.1. Materials

IHQM (5% w/w, dissolved in liquid phase) was synthesized as follows: 3.97 g of 2,5-diiodo-8-hydroxyquinoline (Aldrich) were dissolved in tetrahydrofurane at room temperature in the presence of triethylamine (Scharlau) as catalyst (1.38 ml). Methacryloylchloride (Aldrich), previously distilled, was added dropwise to the solution with constant stirring. The reaction mixture was allowed to proceed for 48 h at room temperature. Triethylamine hydrochloride was removed by filtration and the solvent was extracted by rotary evaporation. After drying over magnesium sulfate the excess of methacryloyl chloride was distilled off at reduced pressure. The product 2,5-diiodo-8-quinolyl methacrylate (Fig. 1) was a greenish solid soluble in polar solvents such as acetone and chloroform, and slightly soluble in monomethyl methacrylate (MMA). It was characterized by Fourier transform infrared (FTIR) and nuclear magnetic resonance (NMR) spectroscopies [21].

The three cement formulations studied were: radiolucent cement (RL-cement), $BaSO_4$ containing cement (BS-cement) and IHQM containing cement (IHQM-cement). PMMA beads (RHOM, Plexigum) were mixed with either MMA (Merck) or a mixture of MMA/IHQM (5 wt % in the liquid phase) depending on the formulation prepared, in a solid : liquid ratio of 2 : 1. The activator used was *N*,*N*-dimethyl-4-toluidine (Merck, 1 wt % in the liquid phase) and the initiator was benzoyl peroxide (Merck, 2 wt % in the solid phase) in all cases. For the preparation of the conventional radio-opaque cement (BS-cement) 10 wt % of $BaSO_4$ (Panreac) was added to the solid phase.

2.2. Experimental methods

The particle size of the $BaSO_4$ powder was measured by means of laser diffraction (Microtrac Particle Size Analyser SRA150, Leeds & Northrup, North Wales, PA). The powder had been previously dispersed in ethanol in an ultrasonic bath.

The mechanical tests were carried out in a servo-hydraulic testing machine (MTS Bionix 858). In all cases the specimens were molded in vacuum and stored in air for 1 month before testing.

The compression tests were performed according to the ASTM F451 standard for acrylic bone cements on cylindrical specimens (6 mm diameter, 12 mm height) at a cross-head speed of 20 mm min^{-1}. Six to 12 specimens were tested for each series and their compressive strength was determined.

Tensile specimens were molded and tested according to ISO 527 standard using an extensometer and at cross-head speed of 1 mm min^{-1}. Ten to 14 specimens were tested for each material. The parameters measured were the tensile strength, modulus of elasticity in tension and strain to fracture.

For the study of the fracture toughness of bone cements, compact tension (CT) specimens were molded (Fig. 2), according to the ASTM E399 standard [22, 23]. After preliminary tests it was assessed that 6-mm thickness specimens ($B = 6$ mm, $W = 23$ mm and $a = 11.35$ mm) would ensure plane strain conditions at the tip of the crack. Seven to 12 specimens were tested for each series. A sharp crack was introduced in the CT specimens by means of a razor blade [22]. The samples were tested at a cross-head speed of 1 mm min^{-1}. Load versus displacement graphs were registered and the

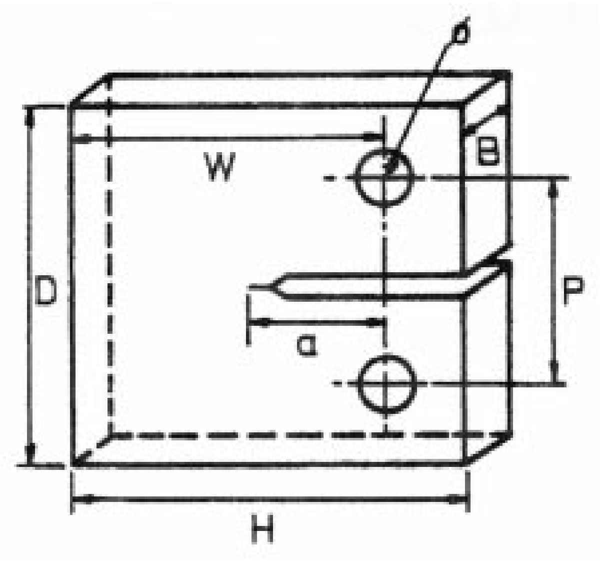

Figure 2 CT test specimens in accordance with ASTM E399 standard.

maximum load at fracture was measured from each test and used to calculate the fracture toughness [22, 23].

The statistical analysis of the results was carried out by analysis of variance (ANOVA) and Fisher multiple comparison test.

After testing, representative fracture surfaces were sputter coated with a layer of gold and examined in the scanning electron microscope (SEM).

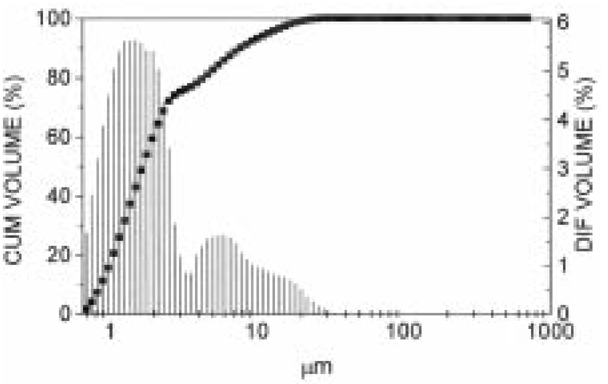

Figure 3 Particle size distribution of the $BaSO_4$.

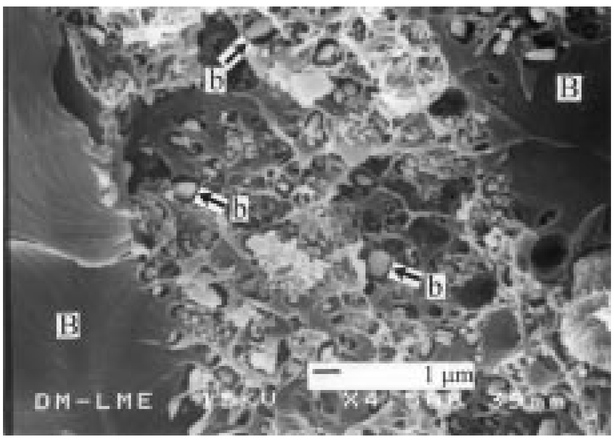

Figure 4 Fracture surface of a barium sulfate-containing cement. It can be seen that a very good continuity exists between the PMMA beads (B) and the matrix. In contrast, the barium sulfate particles (b) do not adhere to the surrounding polymeric matrix.

3. Results and discussion

The particle size distribution of the $BaSO_4$ powder as obtained by laser diffraction is represented in Fig. 3. SEM observations suggested that the size of the particles ranged between 0.1 and 3 μm (Fig. 4), and therefore the particles larger than these values detected by laser diffraction were probably agglomerates.

The results obtained for the compressive strength (σ_c), tensile strength (σ_t), modulus of elasticity in tension (E_t), total strain (ε) and fracture toughness (K_{IC}) are shown in Table I.

The addition of the iodine-containing methacrylate provided a statistically significant increase in the tensile strength, fracture toughness and ductility, with respect to the barium sulfate containing cement. This effect can be attributed to the fact that the use of a radio-opaque monomer eliminates the porosity associated to the barium sulfate particles, which show no adhesion to the matrix, as supported by SEM analysis of the fracture surfaces (Fig. 4).

SEM evaluation of the tensile fracture surfaces of the different cement formulations revealed that the IHQM-containing cement (Fig. 5) had a homogeneous appearance, which is an indication of a good copolymerization of the radio-opaque monomer with the MMA. In contrast, in the BS-cement specimens (Fig. 6), the presence of barium sulfate particles in the interbead matrix can contribute to its weakening, since there is a significant void volume associated to this inorganic filler. In addition, large agglomerates of barium sulfate were observed. The occurrence of these agglomerates is

TABLE I Mean (SD) values of the compressive strength (σ_c), tensile strength (σ_t), modulus of elasticity in tension (E_t), total strain (ε) and fracture toughness (K_{IC}) of radiolucent cement (RL-cement), barium sulfate-containing cement (BS-cement) and iodine-containing cement (IHQM-cement)

	RL-cement	BS-cement	IHQM-cement
σ_c (MPa)	101.1 (3.0)	105.3 (2.8)	103.6 (3.7)
σ_t (MPa)	42.5 (2.4)	36.3 (3.8)	45.1 (2.0)
E_t (GPa)	2.4 (0.07)	2.5 (0.04)	2.5 (0.08)
ε (%)	2.5 (0.2)	2.0 (0.3)	2.5 (0.2)
K_{IC}(MPa m$^{1/2}$)	1.18 (0.08)	1.22 (0.03)	1.35 (0.12)

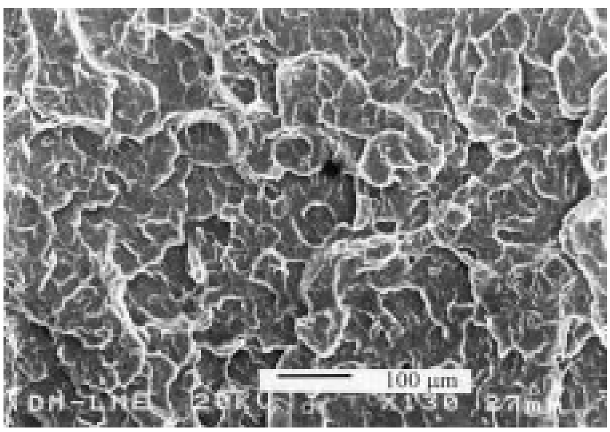

Figure 5 Fracture surface of a tensile specimen of the IHQM-containing cement.

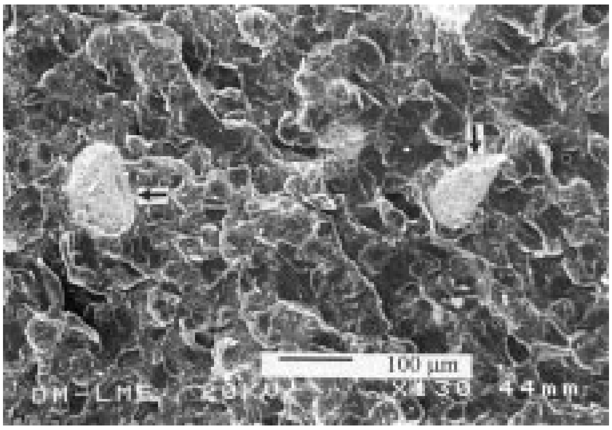

Figure 6 Fracture surface of a tensile specimen of the $BaSO_4$-containing cement. Some barium sulfate agglomerates are indicated by arrows.

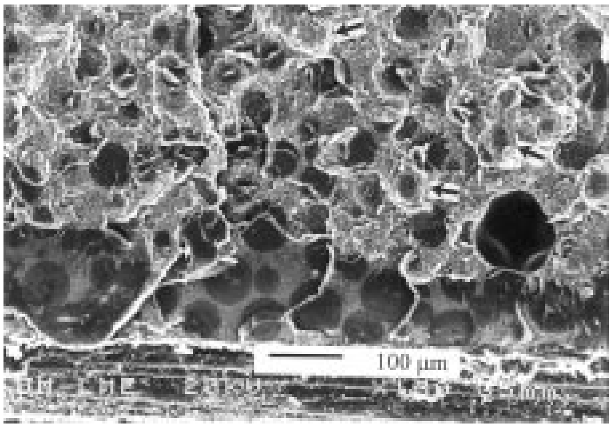

Figure 8 Fracture surface of a CT specimen of the $BaSO_4$-containing cement. Some PMMA beads not fractured but surrounded by the crack that propagates through the interbead matrix are indicated by arrows.

referred to in the literature as one of the causes of the decrease of the tensile properties of the cement [24, 25].

When comparing the RL-cement with the IHQM-cement, it is observed that there is a statistically significant increase in both the tensile strength and the fracture toughness. This indicates that the enhancement produced by the addition of the radio-opaque monomer is due not only to the elimination of the problems associated with the presence of barium sulfate, but also to some reinforcing effect, which must be attributed to the iodine-containing monomer. On the other hand, in relation to the fracture toughness results, it must be pointed out also that, in contrast with some results from the literature [5] the differences between the RL-cement and the BS-cement are not statistically significant.

Figs 7 and 8 show the fracture surfaces of CT specimens corresponding to the IHQM-cement and the BS-cement, respectively. For the IHQM-cement, the crack shows flat propagation, with both the PMMA particles and the interbead matrix being fractured. However, in the BS-cement the crack propagates preferentially through the interbead matrix. In fact, the roughness observed in some zones is produced by the fact that the PMMA beads are surrounded by the crack which propagates through the matrix, weakened by the $BaSO_4$ particles.

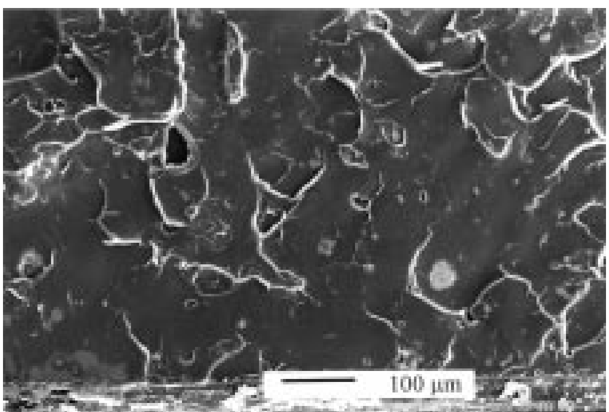

Figure 7 Fracture surface of a CT specimen of the IHQM-containing cement.

To conclude, after having assessed the enhancement of the mechanical properties of the acrylic bone cement achieved by substituting the barium sulfate by the iodine containing monomer, it is important to focus the attention in further investigations on the fatigue properties of this new bone cement formulation, since they are clinically relevant. This is even more significant when considering that it is known that $BaSO_4$ improves the fatigue crack propagation resistance of the acrylic bone cements [26]. In this line, it has to be mentioned that further studies in this direction are being carried out in our laboratory.

Acknowledgments

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