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Tensile properties of a bone cement containing non-ionic contrast media

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The addition of contrast media such as $BaSO_4$ or ZrO_2 to bone cement has adverse effects in joint replacements, including third body wear and particle-induced bone resorption. Ground PMMA containing particles of the non-ionic water-soluble iodine-based X-ray contrast media, iohexol (IHX) and iodixanol (IDX), has, in bone tissue culture, shown less bone resorption than commercial cements. These water-soluble non-ceramic contrast media may change the mechanical properties of acrylic bone cement. The static mechanical properties of bone cement containing either IHX or IDX have been investigated. There was no significant difference in ultimate stress between Palacos R® (with 15.0 wt% of ZrO_2) and plain cement with 8.0 wt% of IHX or IDX with mass median diameter (MMD) of 15.0 or 16.0 μm, while strain to failure was higher for the latter ($p < 0.02$). The larger particles (15.0 or 16.0 μm) gave significantly higher ($p < 0.001$) ultimate tensile strengths and strains to failure than smaller sizes (2.4 or 3.6 μm). Decreasing the amount of IHX from 10.0 wt% to 6.0 wt% gave a higher ultimate tensile strength ($p < 0.001$) and strain to failure ($p < 0.02$). Scanning electron microscopy (SEM) showed the smaller contrast media particles attached to the surface of the polymer beads, which may prevent areas of the acrylate bead surface from participating in the polymerization. In conclusion, the mechanical properties of bone cement were influenced by the size and amount of contrast medium particles. By choosing the appropriate amount and size of particles of water-soluble non-ionic contrast media the mechanical properties of the new radio-opaque bone cement can be optimized, thus reaching and surpassing given regulatory standards.

Introduction

Acrylic bone cement is widely used throughout orthopedics. The cement fills the space between an implant and the surrounding bone and thereby distributes the stresses evenly over the bone–implant interface. Adding contrast media to the cement enables defects in the cement mantle, cement position, the number and type of cracks to be seen and the detection of bone resorption around the cement at an X-ray examination. The common radio-opaque contrast media in acrylic bone cement are barium sulfate ($BaSO_4$) and zirconium dioxide (ZrO_2). These additives are hard ceramic particles that, if released from the main cement body, can reach the joint interface and get entrapped in the ultra high molecular weight polyethylene (UHMWPE) component, scratching the metal component and causing third body wear, which has been demonstrated amongst others in pin-on-disc studies [1] and clinically [2]. Scratches on the metal component increase the wear rate of the UHMWPE articulating surface dramatically, with a marked increase in the production of polyethylene wear debris [1, 3]. If contrast media particles enter the tissue interface, they may cause osteolysis in the bone bed either by stimulating osteoclast activity [4–6] or through an inflammatory reaction causing increased joint fluid pressure [7]. Additionally, it has been shown that cement containing $BaSO_4$ causes more bone cell resorption than ZrO_2 and that cement containing any of the available commercial contrast media cause more bone resorption than plain cement [4, 6, 8]. The inclusion of particles into polymers also leads to reduced mechanical properties due to stress concentrations around these particles [9]. Properties such as tensile strength, ductility and fatigue strength are reduced while the Young's modulus is increased. Topoleski [10] suggested that $BaSO_4$ and ZrO_2 have different influences on the fatigue crack

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propagation rate of bone cement. These differences could be caused by the differences in size, shape and behavior of the two contrast media.

Water-based solutions of two non-ionic iodine-based X-ray contrast media, iohexol (Omnipaque®) (IHX), *N*,*N*′ - bis(2,3 - dihydroxipropyl) - 5 - [*N*-(2,3-dihydroxipropyl)acetamido] - 2,4,6 - triiodoisophthalamide and iodixanol (Visipaque®) (IDX), 3,3′,5,5′-Tetrakis(2,3-dihydroxypropylcarbamoyl) - 2,2′,4,4′,6,6′ - hexaiodo - *N*,*N*′ - (2 - hydroxypropane - 1,3 - diyl)diacetanilide, are ex-tensively used in examination of blood vessels [11]. For example, in coronary arteriography with injection of a contrast medium bolus into arteries, or for urography or computed tomography (CT). These substances might also be used in its solid form, ground down to the required particle size. A bone resorption study [12], where osteoblast-like cells were co-cultured with bone cement particles containing the different radio-opaque agents IHX, IDX, $BaSO_4$ and ZrO_2, showed that IHX and IDX caused less bone resorption than $BaSO_4$ or ZrO_2, in PMMA. Furthermore, the cement particles containing ZrO_2 evoke a significant inflammatory reaction compared with that containing IHX and IDX in the surrounding tissue [13]. However, the effects IHX and IDX have on the mechanical properties need to be quantified. The present investigation considers the tensile properties when using IHX and IDX, in different particle sizes and weight percentages (wt %) in plain cement, using Palacos R® (containing 15.0 wt % ZrO_2) as control.

Materials and methods

Seven different batches (40 g) of cements were prepared (Table I). Palacos R® (containing 15.0 wt % ZrO_2) was used as the control and compared with plain cement (the basic Palacos R® formulation, but without ZrO_2) (from Biomet-Merck GmbH, Darmstadt, Germany) with IHX (from Nycomed Amersham Ltd., Oslo, Norway, ground and aerodynamically assorted particles by Bicema AB, Karlstad, Sweden) with mass median diameter (MMD) of 2.4 μm at 6.0, 8.0, 10.0 wt % and with MMD of 16.0 μm at 8.0 wt %. The wt % of contrast media mentioned is with reference to the powder ratio. Also, plain cement with IDX (same source and treatment as IHX) were prepared with MMD of 3.6 and 15.0 μm at 8.0 wt %. The particle distribution of all IHX and IDX batches were measured by laser diffraction using a Malvern Mastersizer 10 particle size analyzer. Prior to powder mixing, a modeling and radiophysical calculation was done to estimate the amount of contrast media necessary. For hip X-rays at the standard accelerating voltage of 70 kV, the X-ray attenuation (absorption) of IHX and IDX is similar to that for ZrO_2. For CT the absorptions of IHX and IDX are higher than that of ZrO_2. While our reference material, Palacos R®, contains 15.0 wt % of ZrO_2, the absorption exceeds that necessary and it has been reduced to 10.0 wt % in a newly released commercial bone cement based on the same formulae, thus 10.0 wt % or less was used in our study. Scanning electron microscopy (SEM) was performed on the IHX and IDX cement powder to observe the behavior of the water-soluble contrast media in PMMA.

The cements were pre-chilled according to the manufacturer's guidelines and were mixed under vacuum using the Optivac® (from Scandimed AB/ Biomet-Merck GmbH, Sjöbo, Sweden) mixing system [14]. The mixing procedure followed manufacturer's guidelines with 10 s of vacuum and then 30 s of mixing at approximately 1 Hz. Three minutes after the start of mixing, the cement was injected into eight half-size ISO 527 PTFE molds. After curing for 40 min under pressure, the specimens were ejected from the mold and then aged in saline at 37 ± 1 °C for a minimum of two weeks. After aging, any flash was removed using a sharp knife. The width and thickness of the gauge-section of the samples was measured using a dial micrometer and the cross-sectional area was calculated. Testing was performed on an Instron 8511 load frame with MTS TestStar II controller. Strain was measured using an Instron 2620-602 extensometer with gauge length of 25 mm. The specimens were loaded under displacement control at $2\,\mathrm{mm\,min^{-1}}$, load and extension data was collected at 25 Hz. The fracture surfaces were inspected and those specimens where the fracture surface contained pores with a diameter of more than 1 mm were excluded. The tensile stress was calculated by dividing the force by the cross-sectional area. The Young's modulus was based on the first 0.13 mm extension to give the initial slope and a regression analysis was performed. One-way ANOVA was used for statistical analysis of the ultimate strength, strain at failure and Young's modulus.

SEM was performed on the fracture surface of one specimen of each batch. The magnification ranged from 72× to 2500× with the majority of the pictures at 500–1500×. After testing, an X-ray investigation of the specimens was performed. Additionally a specimen of Simplex P® (Howmedica Inc., Rutherford, NJ, USA), another commercially available bone cement, was included. The set up simulated that of a normal hip X-ray, using a setting of 70 kV, 80 mAs and 113 ms, at a

TABLE I The different bone cement batches investigated. The content and particle size of iohexol (IHX) and iodixanol (IDX) were varied between batches

Cement formulation	Radio contrast media	Contrast media particle size/μm	Contrast media content /wt %
A	IHX	2.4	10.0
B	IHX	2.4	8.0
C	IHX	2.4	6.0
D	IHX	16.0	8.0
E	IDX	15.0	8.0
F	IDX	3.6	8.0
Palacos R®	ZrO_2	$d_{50} \sim 15$	15.0

distance of 1 m and with the specimens under 0.1 m of water to model the absorption of the human body. The image was recorded on a digital X-ray system.

Results

The amount and size of contrast medium particles in the cement have significant effects upon the mechanical properties. The results clearly demonstrate the importance of minimizing the amount of contrast medium at a given particle size. Increasing the content of IHX from 6.0 wt % to 10.0 wt % decreased the ultimate strength from 36.2 ± 2.5 (Mean ± S.D.) to 31.1 ± 1.1 MPa ($p < 0.0001$) and decreased the ultimate strain from 1.7 ± 0.2 to 1.5 ± 0.1% ($p < 0.02$). The larger particles of both water-soluble contrast media (16.0 and 15.0 μm) produced significantly stronger and more ductile cements than the cements with the small particles (Figs 1–2), for both IHX ($p < 0.0001$) and IDX ($p < 0.0001$). For both sizes, no significant difference was seen between IHX and IDX. When comparing the two water-soluble materials to Palacos R®, the large particle cements containing either IHX (16.0 μm) and IDX (15.0 μm) show similar ultimate strengths, while ultimate strains are significantly higher ($p < 0.01$ for IHX and $p < 0.02$ for IDX) than those for Palacos R®. Young's moduli (Fig. 3) were significantly higher for Palacos R® than for all other cement compositions ($p < 0.02$ for IDX with the larger particles and $p < 0.0001$ for all others). IDX (15.0 μm) had a significantly higher value of Young's modulus than IHX (16.0 μm) ($p < 0.0001$). SEM of the cement powder showed accumulation of the smaller contrast media particles upon the surface of the polymer beads (Fig. 4), with IHX showing more particles attached to the polymer surface than IDX. The SEM study of the fractured specimens (Figs 5–7) did not reveal any significant pattern for failure, except that the fracture surface on the specimens with the smaller contrast particles did, in some cases, show areas with conglomerates of more contrast media compared to the specimens with the larger particles. When observing the shape of the IHX and IDX particles on the fracture surfaces (Figs 5–6) a difference was seen, with the IHX particles being more spherical than the IDX particles. Such difference in shape of the particles was not observed in the cement powder before polymerization. Radiographically, Palacos R® had the highest absorption. The water-soluble cements all had somewhat less absorption than Palacos R® or Simplex P®, however, there were variations (Fig. 8).

Discussion

The higher strength and ductility of the water-soluble cement formulations containing the larger non-ionic contrast medium particles could be caused by several factors. Normally, larger particles increase the stress

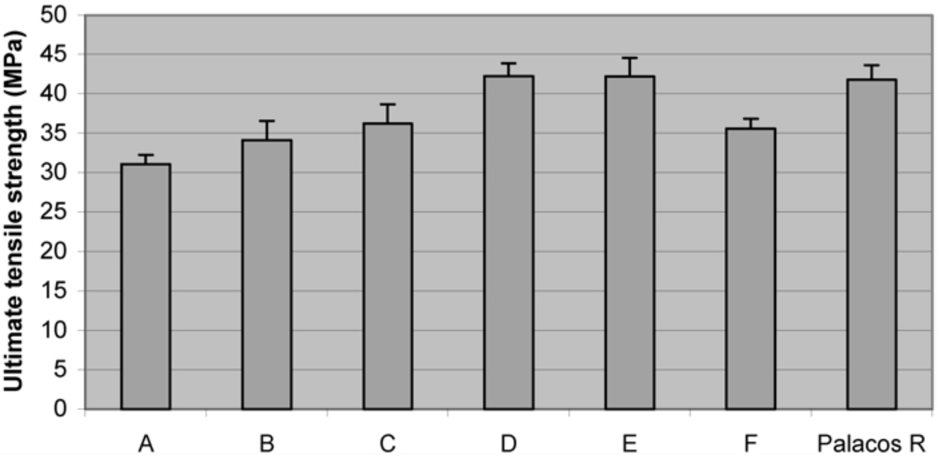

Figure 1 Ultimate stress in MPa with standard deviation. A, B, C, D, E and F refer to the different bone cement batches in Table I.

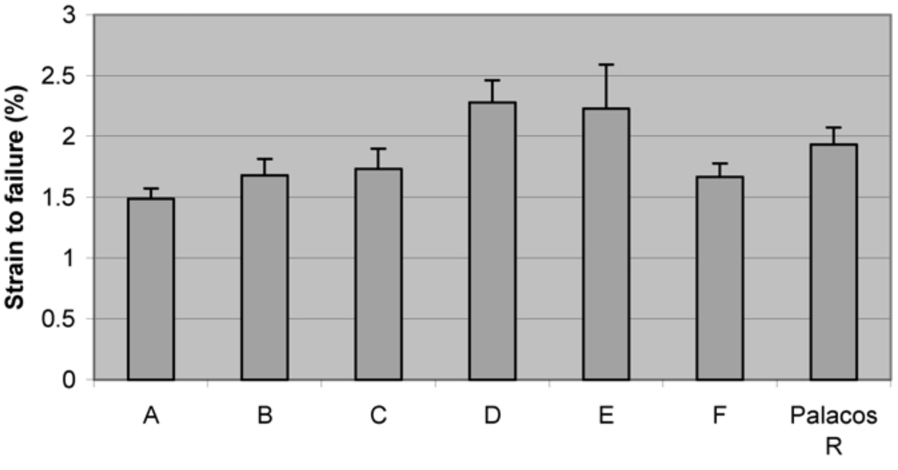

Figure 2 Strain to failure in % with standard deviation. A, B, C, D, E and F refer to the different bone cement batches in Table I.

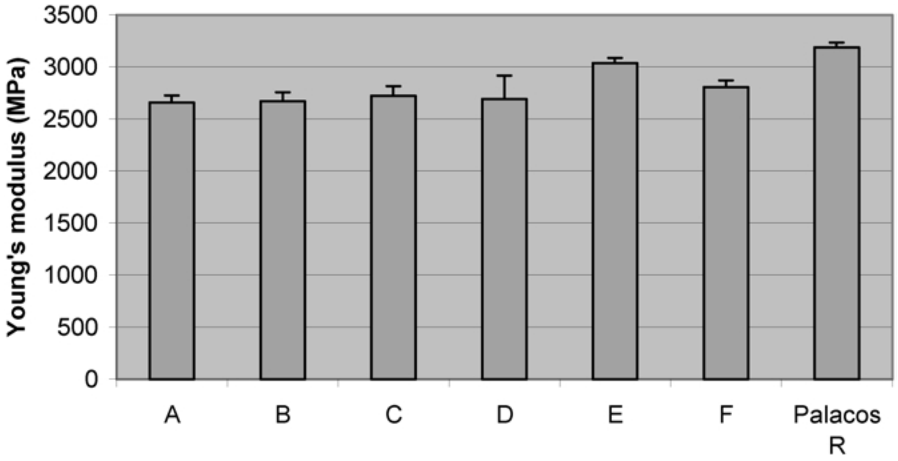

Figure 3 Young's modulus in MPa with standard deviation. A, B, C, D, E and F refer to the different bone cement batches in Table I.

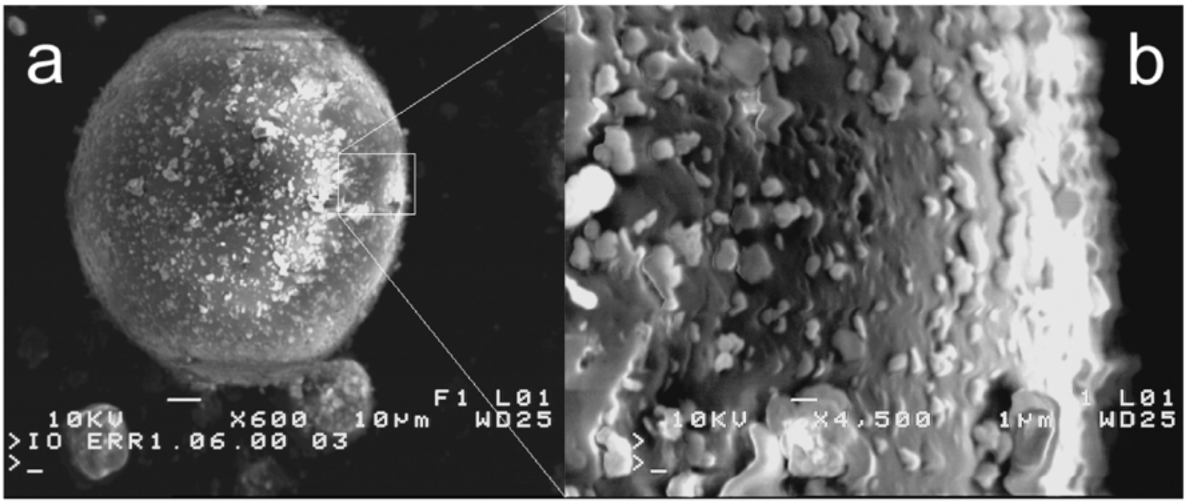

Figure 4 SEM of polymer beads with 10.0 wt % iohexol at a mean particle size of 2.4 μm. Marker bar for (a) is 10 μm and for (b) is 1 μm.

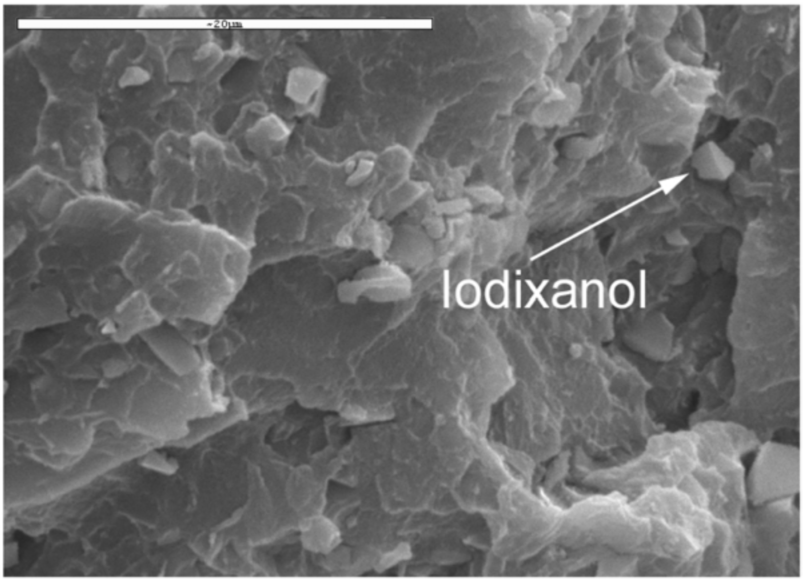

Figure 5 Fracture surface of plain cement containing contrast media particles of iodixanol at a concentration of 8.0 wt % with a mean particle size of 3.6 μm. Marker bar is 20 μm.

concentration and thus reduce the strength and ductility. In this study where the contrast media particles were mixed with the PMMA powder, SEM showed the smaller particles coating the PMMA polymer beads, which can explain the lower mechanical strength for the specimens with smaller particles of either contrast medium. The explanation would be that the total surface area for the small particle batches is much larger than that of the larger particle batches, due to the greater number of particles in this fraction. A surface energy effect also

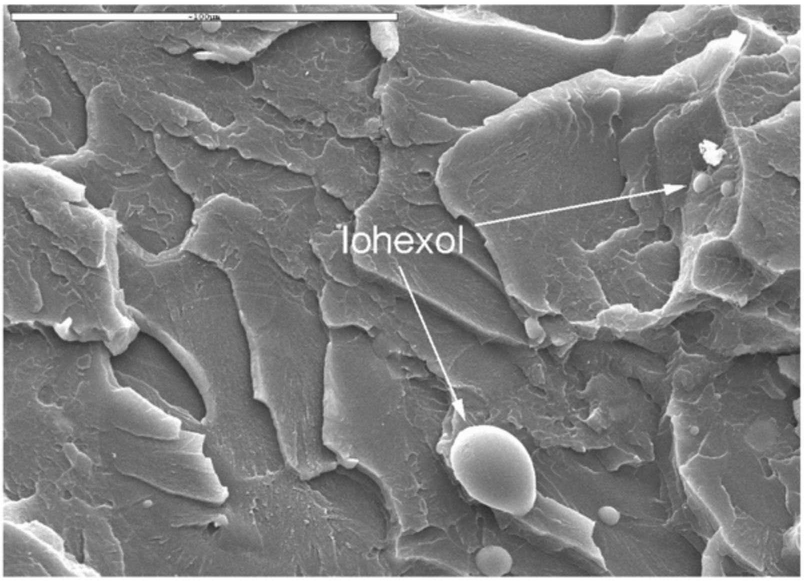

Figure 6 Fracture surface of plain cement containing contrast media particles of iohexol at a concentration of 8.0 wt % with a mean particle size of 16.0 µm. Marker bar is 100 µm.

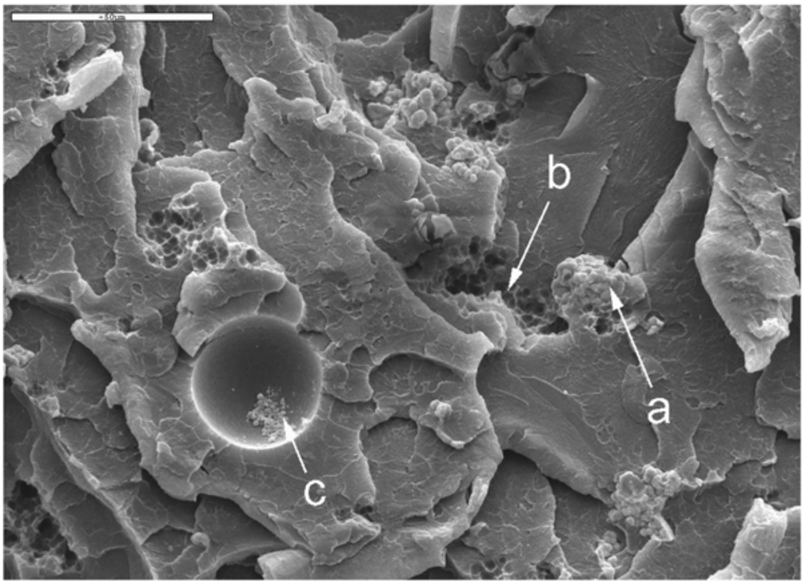

Figure 7 Fracture surface of Palacos R® with (a) ZrO_2 particle, (b) imprint of ZrO_2 particle and (c) residue of ZrO_2 powder. Marker bar is 50 µm.

occurs, with smaller particles having a higher surface energy than larger particles, which leads to a higher attraction-force, thus the small contrast media particles stick to the surface of the polymer beads, coating the beads. The polymerization of the monomer which joins the beads together into a polymer mass may be disrupted because of these two effects. During polymerization, the developing chains join onto the PMMA beads, and if the contrast medium is attached to the beads a point defect will occur. This finding is in agreement with several other studies [9, 15, 16]. Potentially there is an optimal particle size (Fig. 9) where the surface area/energy effect is minimized, yet the particles are small enough to minimize stress concentrations in the polymer.

The amount of contrast media in acrylic bone cement should be minimized. This is clearly demonstrated by materials A, B and C (Figs 1–2). Material C (6.0 wt % IHX), which had the least contrast media, shows the highest ultimate stress and strain to failure, which both decreased with increasing amounts of contrast material. It was not the intention of this study to judge the minimum absorption needed in the cement. Palacos R® has 15.0 wt % ZrO_2, while Palamed [17], which is a recently released bone cement (Biomet-Merck GmbH), has 10.0 wt %. The good mechanical strength achieved, especially with the larger particle specimens compared to those of Palacos R®, can to a large extent be explained by the lower amount (8.0 wt %) of contrast medium in these cement formulations. The optimal particle size for IHX and IDX has to be further investigated and the mechanical properties, albeit already sufficient, should thus be improved further. X-ray investigation (Fig. 8) revealed that the two IDX specimens and the IHX at 10.0 wt % produced less X-ray absorption than Palacos R® but close to that of Simplex P®. Additional investigations should be carried out to find a suitable contrast level between the bone cement and its surroundings. We are currently developing standardized methods of comparing radiopacity in bone cements,

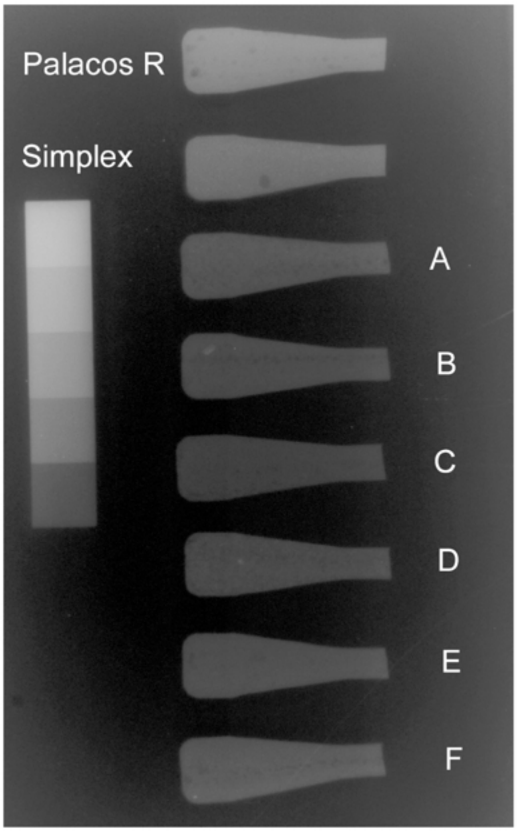

Figure 8 X-ray of specimens at 70 kV, 80 mAs and 113 ms, at a distance of 1 m with the specimen under 0.1 m of water, simulating body tissue. A, B, C, D, E and F refer to the different bone cement batches in Table I. To the left is an aluminum wedge, for X-ray attenuation comparisons.

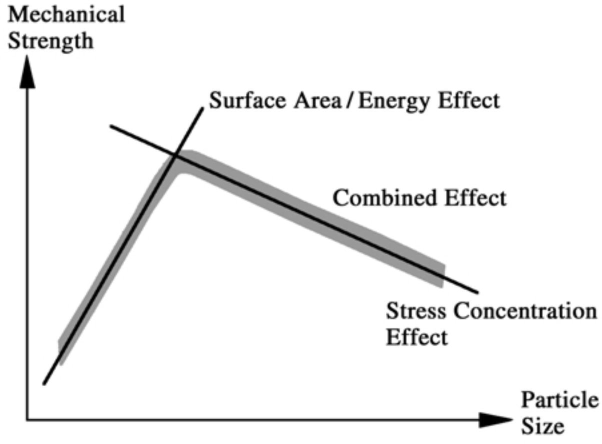

Figure 9 Schematic of the interaction between the surface energy and stress concentration effects and the particle size and their effect on strength.

using water as an absorbent media in a fixed setting simulating clinical situations.

Conclusions

The mechanical properties of bone cement were influenced by the size and amount of the IHX and IDX contrast medium particles. Water-soluble materials such as IHX and IDX will dissolve if released into tissue or joint space leaving the less damaging plain cement. Secondly they are *per se* not as abrasive as $BaSO_4$ or ZrO_2. By choosing appropriate size and amount of particles of water-soluble non-ionic contrast media the mechanical properties of radio-opaque bone cement can be optimized.

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