Using Nanotechnology To Improve The Performance Of Acrylic Bone Cements

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INTRODUCTION

In recent years, there has been an emergence of a new technology, popularly known as nanotechnology or nanoscience. This broad area of technology encompasses the fabrication, detection and manipulation of small structures in the range of one nanometer up to 100 nanometers, including biological molecules, ultrafine synthetic powders or nanostructured composite materials. In January, 2000, President Bill Clinton unveiled the National Nanotechnology Initiative (http://www.nano.gov/) to promote and support research on nanotechnology. Thereafter, several federal agencies such as the National Science Foundation, U.S. Department of Energy, U.S. Department of Defense, National Aeronautics and Space Administration and the National Institute of Health have begun to initiate and support research in this new field. In June, 2000, the National Institute of Health conducted a workshop entitled "Nanoscience and Nanotechnology: Shaping Biomedical Research" held at NIH, Bethesda, MD where several areas of applicability of nanotechnology in the healthcare sector were outlined.

We have used an aspect of nanotechnology to improve the performance of acrylic bone cement. We have developed a new nanocomposite polymethyl methacrylate (PMMA) bone cement with improved fatigue properties for application in the fixation of total joint replacement prostheses. All commercial cements contain approximately 10% weight of 0.5-3 μm size barium sulfate or zirconium oxide particles. These particles are radiopacifiers, which enable orthopedic surgeons to monitor the implanted cement using x-ray radiographs. This is necessary since cements are known to fail due to fracture, resulting in implant loosening and requiring revision surgery.

Early fracture of cement has led to several studies[1-4] that focus on the possible reasons for cement fracture. Topoleski et al[1] and Demian et al[2] have shown that agglomeration of radiopacifier particles is associated with cement fracture. Improvement in their dispersion can therefore lead to increase in fracture toughness of bone cement. In these studies, the 1-3 μm size barium sulfate particles were substituted with 100 nm size barium sulfate particles in a commercial bone cement. It was hypothesized that smaller radiopacifier "nanoparticles" could be more uniformly dispersed in the cement and would thus have the potential to improve its fracture toughness. Recent advances in nanotechnology have led to the commercial availability of "nano-sized" barium sulfate powder particles, making it possible to explore the effect of particle size on dispersion and fracture toughness of cements. Our preliminary fatigue tests showed that the "nanocomposite" cement had a substantially longer fatigue life than the currently used "microcomposite" cement.

MATERIALS AND METHODS

All tests were performed on CMW1 bone cement (Johnson&Johnson/Depuy, Warsaw, IN) since the powder component of these cements do not contain pre-mixed barium sulfate powder. The 100 nm size barium sulfate powder was purchased (Sachtleben, Duisburg, Germany) and mixed into CMW1 cement in a quantity that was equal to that of regular barium sulfate powder. All cements contained 10% weight barium sulfate. The nano-sized barium sulfate powder contained 2% weight of sodium citrate to prevent particle agglomeration. Radiolucent PMMA cement, in which no barium sulfate was added, served as a control. All samples were prepared using a standard vacuum mixing technique.

Fatigue tests were performed on an Instron 8511 servo-hydraulic testing machine in the laboratory of Professor Lisa Pruitt, Department of Mechanical Engineering, University of California at Berkeley. Prior to testing, the specimens were soaked in room temperature water for 2 days. During testing, the specimens were maintained at 37°C using a recirculating water bath. The pre-notched specimens were fatigued in load

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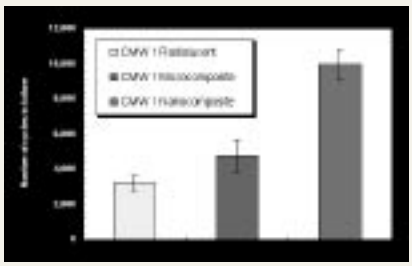

Figure 1. Fatigue life of radiolucent, microcomposite, and nanocomposite cements

control with an R-ratio (minimum load to maximum load) of 0.03 and stress amplitude of 15 MPa at a frequency of 2 Hz. Specimens that failed at the grips were discarded. Sample size ranged from 6-10. A JEOL 6320FV field emission low voltage scanning electron microscope (LVSEM) at the Center for Materials Science and Engineering at the Massachusetts Institute of Technology, Cambridge, MA was used to examine all fracture surfaces. In addition, ultra-small angle x-ray scattering (USAXS) at the UNICAT synchrotron x-ray beamline[5] of the Advanced Photon Source, Argonne National Laboratory, Argonne, IL was used to quantify the dispersion of radiopacifier particles in the microcomposite and nanocomposite PMMA cements. Sheets of 0.5mm thickness of each type of cement were subjected to USAXS using 10 kEV x-rays and a beam cross-sectional area of 2mm x 0.6mm. The x-ray scattering curves were analyzed using Porod's law[6] to characterize the surface area to volume ratio (specific surface area) of dispersed radiopacifier particles as well as voids within the PMMA matrix. A reduction in the specific surface area of radiopacifiers detected by USAXS would imply particle agglomeration. Thus USAXS can be used for quantitative comparison of well-dispersed and poorly dispersed radiopacifier particles within the cement. USAXS is advantageous in comparison to imaging methods in that the experiment estimates the average specific surface area over a relatively large sampling volume of approximately 1 mm^3.

RESULTS

Fatigue tests showed that the nanocomposite CMW1 cement had a fatigue life of over a 100% longer than that of the microcomposite CMW1 cement containing regular barium sulfate (ANOVA-Bonferroni method, $p<0.05$), as shown in Figure 1. There was no statistically significant difference in the fatigue life of the radiolucent and microcomposite CMW1 cements for the number of samples tested.

LVSEM observation of fracture surfaces revealed the presence of 0.5-3.0 µm size barium sulfate particles in the microcomposite cement (Figure 2). In addition, LVSEM revealed uniform dispersion of the nanometer-sized barium sulfate, a result that is likely due to the addition of sodium citrate as an anticoagulant. There was a higher concentration of features associated with fracture in the nanocomposite cement (Figure 3). These were confined to the regions containing the barium sulfate nanoparticles, and were not observed in the regions of the pre-polymerized powder. X-ray radiographs of tensile

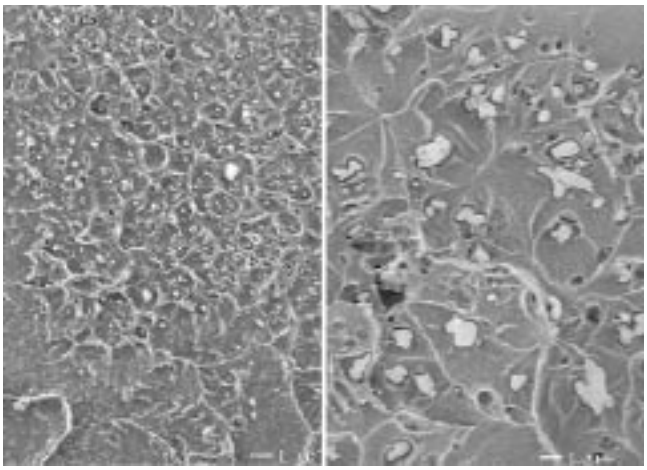

Figure 2. Low voltage scanning electron micrographs of nanocomposite (left) and microcomposite (right) fracture surfaces (Scale bar= 1 micron).

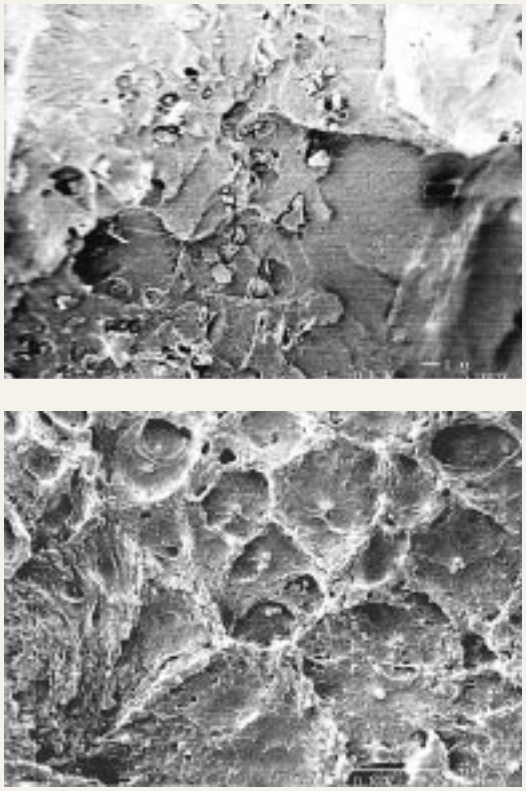

Figure 3. Low voltage scanning electron micrographs of fracture surfaces of microcomposite (top; magnification= 2,000x) and nanocomposite cement (bottom; magnification= 10,000x) (Scale bar= 1 micron).

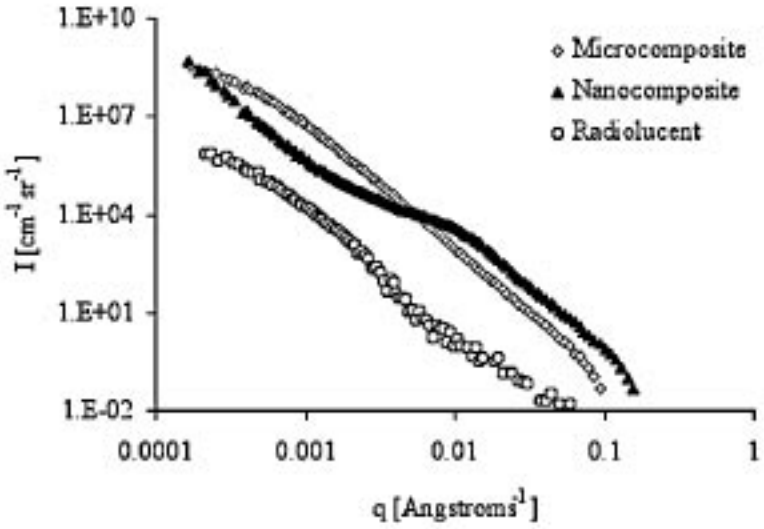

Figure 4. USAXS scattering curves for microcomposite, nanocomposite, and radiolucent cements.

Table 1. USAXS Specific Surface Areas for PMMA Bone Cements

Sample	Specific Surface Area (S) [cm^{-1}]
Radiolucent	6.16147×10^5
Microcomposite	2.39404×10^5
Nanocomposite	2.19348×10^6

specimens confirmed that both composite cements were radiopaque.

USAXS scattering curves were obtained by plotting the scattered intensity (I) vs (q) as shown in Figure 4, where:

$$q=(4\pi/\lambda)\sin\theta$$

such that θ equals one half of the scattering angle and λ is the wavelength of x-rays (=2.38 Angstrom). USAXS revealed a substantial scattering intensity due to the presence of both voids (radiolucent cement) as well as due to barium sulfate particles (Figure 4). The region of the scattering curve at $q > 0.008$ [Angstrom^{-1}] was curve fitted to a Power law function which is:

$$I(q)=Kq^{-4}$$

where $K=2\pi\Delta\rho^2(S/V)$

such that Δρ is the electron density difference between barium sulfate (or voids, in the case of radiolucent cement) and PMMA and (S/V) is the specific surface area of the scattering entity (radiopacifier or voids). The scattering invariant, Q, defined by the following equation was calculated for all cement samples using the area under the scattering curve, $q^2I(q)$ versus q:

$$Q=\int_0^\infty q^2I(q)dq$$

The invariant for an angular range of 0-q_{min} was calculated by fitting the low q region of the scattering curve using Guinier's Law [6] and for q_{max} – ∞ using Porod's Law. The specific surface area can then be defined as: $S/V=\pi(K/Q)$. Porod analysis showed that the ratio of the specific surface area for the nanocomposite and microcomposite cements respectively was 9.16 (Table 1).

DISCUSSION

The use of barium sulfate nanoparticles led to a substantial increase in the fatigue life of CMW1 at the chosen test conditions. All samples were pre-notched prior to cyclic loading thereby testing the resistance of the cements to crack propagation. It must be noted that the samples were screened using x-ray radiographs for the presence of large bubbles. All samples with visible bubbles in the anticipated path of crack propagation were discarded so that the results would reflect the toughening of cement due to radiopacifier size and dispersion alone. We also plan to perform tests for resistance to crack initiation for these new nanocomposite cements. If crack initiation is flaw driven, and if the major source of flaws is the agglomeration of radiopacifiers, we believe that the nanocomposite may have improved resistance to crack initiation as well.

This study also showed that USAXS is effective in quantitatively measuring the specific surface area of barium sulfate radiopacifiers dispersed within PMMA bone cement. It is expected that for the same volume (or weight) fraction, the nanometer size particles must have a total specific surface area that is 10 times larger than the micrometer size particles in bone cement since there would be a 1000 times more particles of $1/10^{th}$ of the diameter. The value of 9.16 is in excellent agreement with this calculation, considering that the inherent particle size distributions can alter the ratio of specific surface area. Agglomeration of particles would result in a reduction in specific surface area. USAXS therefore showed that both microcomposite and nanocomposite cement had relatively well-dispersed radiopacifier particles. In addition, USAXS was able to provide the specific surface area of voids.

This technique could be used to guide in the development of new mixing protocols with the objective of reducing voids since these flaws can also reduce the fracture toughness of cements. LVSEM confirmed the quantitative analysis provided by USAXS measurements by revealing fracture surfaces where particles were uniformly dispersed throughout the PMMA matrix. The large concentration of features associated with fracture of the nanocomposite suggests that there was extensive crack tip blunting, probably due to the large number of barium sulfate nanoparticles encountered by the propagating crack.

In conclusion, the fatigue performance of acrylic cements can be substantially improved by a uniform dispersion of

barium sulfate nanoparticles. However, there must be more rigorous testing under conditions that simulate *in vivo* loading and biological environments before these nanocomposite cements may be implemented in clinical practice.

ACKNOWLEDGMENTS

This study was supported by the Brigham Orthopaedic Foundation. We thank Peter Jemian and Jan Ilavsky for their assistance with USAXS measurements. The UNI-CAT facility at the Advanced Photon Source (APS) is supported by the University of Illinois at Urbana Champaign, Materials Research Laboratory (U.S. Department of Energy, the State of Illinois-IBHE-HECA, and the National Science Foundation), the Oak Ridge National Laboratory (U.S. Department of Energy), the National Institute of Standards and Technology (U.S. Department of Commerce), and UOP LLC. The APS is supported by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences, under Contract No. W-31-109-ENG-38.

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