Introduction: Polymethyl methacrylate (PMMA) has been used for over four decades as a bone cement for fixation of total joint replacement (TJR) prostheses to peri-prosthetic bone tissue. It is well known that failure of bone cement due to fracture leads to aseptic loosening of the implant, requiring early revision surgery to replace the cement and implant. Early fracture of PMMA based bone cement has motivated several studies [1-3] to determine the cause of its mechanical failure. Topoleski et al [1] and Demian et al [2] have shown that agglomeration of radiopaque particles of barium sulfate act as flaws or defects in PMMA and can reduce its fracture toughness. In this study, the 1-3 µm size barium sulfate radiopacifier particles were replaced by average 0.07 µm (or 70 nanometer) size alumina filler particles to form a "nanocomposite" bone cement. The choice of alumina was based on a recent study that showed that "nano-sized" alumina promotes osteoblast adhesion while inhibiting fibroblast function, which can potentially improve bonding of cement to bone [4]. More importantly, a reduction in particle size has the potential for reducing the formation of large agglomerates of particles in cement, thereby improving its fracture properties. Both uncoated and acrylic precoated alumina particles were examined since precoating is expected to further reduce particle agglomeration. The results of this study show that the use of nano-sized, precoated alumina particles as a filler prevents agglomeration and consequently improves the mechanical properties of PMMA bone cement.

Methods: Barium sulfate (Mallinckrodt Inc) was purchased and added to prepolymerized, radioopaque PMMA powder in a weight fraction identical to that of commercially available cement. Alumina nanoparticles (Nanophase Technologies Inc), both uncoated and acrylic coated, were purchased and added to prepolymerized PMMA powder using identical volume fractions as that of barium sulfate containing commercial PMMA cement. A JEOL 6320FEV low voltage scanning electron microscope (LVHRSEM) operating at 1keV and an accelerating distance of 3mm was used to examine the filler particles. Thereafter, each pre-polymerized powder containing filler particles was mixed with MMA monomer using the vacuum mixing technique and cured in molds to prepare tensile test specimens. The cured cements were initially subjected to ultra-small angle x-ray scattering (USAXS) at the UNICAT beamline of the Advanced Photon Source, Argonne National Laboratory. These experiments provided the average inter-particle or inter-agglomerate distance between adjacent filler particles present in the cured cements. An Instron 4201 tensile tester was used to perform ASTM 638 standard tensile tests on all cement samples to determine their ultimate stress, ultimate strain and work-of-fracture (defined by the area under the stress-strain curve). A minimum of 4 specimens were tested for each cement type as required by ASTM standards. Student's two-tailed t-test for unpaired samples was performed to determine statistical significance of the results.

Results: Low voltage SEM experiments showed that the barium sulfate particles used in commercial bone cements were approximately 0.5-3µm in diameter although smaller size particles were also present in small quantities (see Figure 1). In the case of alumina particles, a majority of particles were less than 0.2µm in size, indicating a substantially smaller size of alumina particles compared to barium sulfate. USAXS experiments provided the average inter-particle or inter-agglomerate distance present between the strongly scattering filler particles in the cured cements. In the case of barium sulfate filled cements, the inter-agglomerate distance was greater than 5 µm while the maximum resolution of the USAXS instrument. In contrast, the inter-agglomerate distance between adjacent nanoparticles in coated alumina was well within the measurement range of USAXS. The center-to-center inter-agglomerate distance measured was approximately 0.2-0.1µm indicating good particle dispersion in the cement. The ASTM standard tensile tests showed a statistically significant increase (p<0.05) in the ultimate tensile stress, ultimate tensile strain and work-of-fracture upon substitution of barium sulfate with coated alumina particles (see Table 1). There was no statistically significant difference between these properties for uncoated alumina cements when compared to barium sulfate cements (p>0.05). It should be noted that the replacement of barium sulfate particles with nano-sized alumina did not substantially affect the handling characteristics and setting times of the cements.

Discussion: A combination of morphological (SEM, USAXS) and mechanical tests showed that coated, nano-sized alumina filler particles increased the mechanical properties of PMMA bone cement over that of cement containing an equal volume fraction of barium sulfate particles. The work-of-fracture of cements containing coated alumina particles was 70% higher than cements containing barium sulfate, and 35% higher than cements containing uncoated, nano-sized alumina particles. The most likely reason for the increase in mechanical properties is the improved dispersion of coated, nano-sized particles in bone cement compared to that of uncoated alumina particles of the same size and the micrometer size barium sulfate particles. It has been shown that the 1-3µm diameter barium sulfate particles form 47-197µm size agglomerates which can reduce resistance to fracture of PMMA [2]. The USAXS results, which showed a larger than 5µm center-to-center inter-agglomerate distance in barium sulfate cements is in agreement with this report since this distance is expected to be greater than (assuming no contact between adjacent agglomerates) or equal to (assuming contact between agglomerates) the average diameter of adjacent agglomerates. The cements containing coated alumina nano-particles had a 0.2-0.1 µm inter-agglomerate distance, indicating that these particles were well dispersed with average agglomerate sizes of 0.2 µm or less. The primary reason for good dispersion is precoating of the particles which is expected to prevent contact, and consequently agglomeration, between the hard alumina particles. These results show that PMMA bone cement containing precoated, nano-sized alumina particles as a filler has the potential for improved mechanical performance in TJR prostheses.

Figure 1: Low Voltage SEM micrographs of barium sulfate particles (left) and coated alumina nano-sized particles (right) (20,000x, bar = 1µm)

<table>
<thead>
<tr>
<th>Cement Filler</th>
<th>Ultimate Stress [MPa]</th>
<th>Ultimate Strain [%]</th>
<th>Work-of-Fracture [MJ/m³]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium sulfate</td>
<td>44.7 +/- 6.1</td>
<td>8.5 +/- 1.9</td>
<td>2.16 +/- 0.83</td>
</tr>
<tr>
<td>Alumina</td>
<td>48.8 +/- 2.7</td>
<td>9.0 +/- 1.0</td>
<td>2.43 +/- 0.45</td>
</tr>
<tr>
<td>Coated Alumina</td>
<td>56.0 +/- 2.7</td>
<td>11.5 +/- 1.7</td>
<td>3.74 +/- 0.88</td>
</tr>
</tbody>
</table>

Table 1: Mechanical properties of PMMA cements containing various fillers

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