Research and Development Report: Production of Fine Particulate Ultra High Molecular Weight Poly(ethylene) for Biological Response Studies

H. D. Leigh,* P. Taylor, A. Swaney, and J. Black

Departments of Bioengineering and *Ceramic Engineering, Clemson University, Clemson, South Carolina

Interest in biological responses to particulate biomaterials has produced a need for well-characterized submicron ultra high molecular weight poly(ethylene) (UHMWPE) debris. A new technique, cryogenic attrition, is described as well as a characterization of an initial ca. 65% submicron preparation of UHMWPE, termed *grind S*. Production of submicron particles from a common commercial medical grade of primary UHMWPE "grain" produces fractions with different densities, apparently reflecting the presence of crystalline and amorphous phases. Further process optimization and debris characterization is planned with eventual distribution of material as an interlaboratory comparison material for biological response experiments.

INTRODUCTION

Since Willert's original proposal[1] in 1972 that wear debris generated during the clinical life of a total joint replacement prosthesis may play a role in mediating loosening secondary to osteolysis, there has been an interest in exploring biological response to particulate biomaterials. While concern originally focused on poly(methyl) methacrylate (PMMA) debris released by the "bone cement" mantle, occasional adverse clinical experiences with noncemented joint replacements in the 1980s[2,3] have aroused interest in the role played by particulate ultra high molecular weight poly(ethylene) (UHMWPE) released from the articulating femoral–acetabular interface.

Experiments[4,5] exploring cellular response to UHMWPE have been hampered by the difficulty of obtaining adequate quantities of debris in appropriate sizes. Typically, wear debris is simulated by using primary UHMWPE grain, as fabricated (size range: 20 to 200 μm[5]), or by dental burr reduction of solid UHMWPE, yielding a smallest size fraction with a mean size near 16 μm.[4] Since the upper size limit for routine phagocytosis by mononuclear phagocytes, as determined *in vitro*,[6] is thought to be in the 3 to 7 μm range, despite occasionally reported possibly larger intracellular objects,[7] and recent studies have reported large volumes of intracellular submicron particles in tissues associated with revision of failed uncemented total joint replacements,[8,9] it appears that the challenge particles currently in use are probably too large in size (mean diameter) by a factor of 10 to 100 and thus too massive by a factor between 10^3 and 10^6.

For this reason, we undertook an effort to produce quantities of characterized submicron UHMWPE particles. This report describes our efforts to date and the characteristics of an initial submicron particulate fraction, termed *grind S*.

PROCEDURES AND RESULTS

We elected to use an attrition technique, rather than more conventional ball milling, for comminution of UHMWPE. The attritor mill has an advantage over ball and other types of mills in that the milling is independent of the density of the material being milled and is able to produce large quantities of fine particles rapidly. The typical attritor is an open or closed cylindrical vessel containing milling media which is stirred around a vertical axis by motor-driven continuously rotating bars. The milling action occurs by attrition of the surface of the particles impinged by the grinding media. The attritor used (Union Process Company, Akron, OH, Model 01 HD) has a 500 mL chamber and a multiprong agitator, both coated with poly (tetrafluoro) ethylene.

The initial trials were carried out using spherical alumina media (6 mm, Union Process Co.) in methanol. The UHMWPE selected was a conventional medical grade of primary grain (GUR 415, Hoescht–Celanese, Houston, TX) with a mean size of 80 μm (Figs. 1 and 2, [right curve]). Forty grams of UHMWPE was ground for 24 h. Particle size distributions (determined on a Horiba Capa 700) of the milled UHMWPE when compared to the unmilled UHMWPE (Fig. 2) appeared to demonstrate that 50% of particles were <4 μm in size. However, scanning electron micrographs (SEMs) of the milled

Requests for reprints should be sent to Prof. Jonathan Black, 301 Rhodes Engineering Research Center, Clemson University, Clemson, SC 29634-0905.

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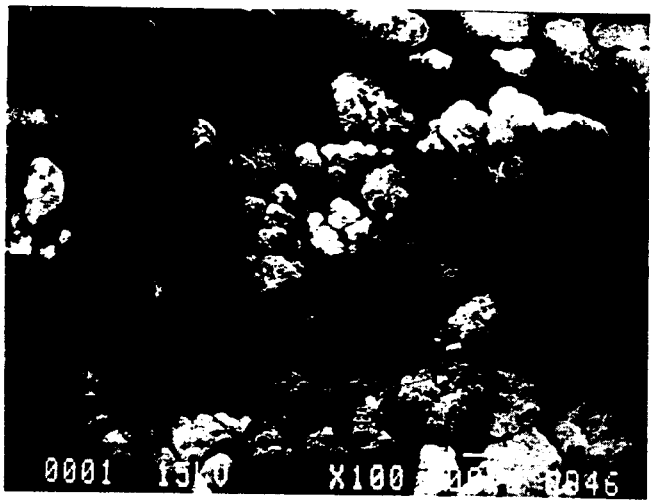

Figure 1. As-received UHMWPE (GUR 415).

UHMWPE (post 200 Å Au coat over Cu foil/Al stub) (Fig. 3), showed that each particle had apparently been deformed into a very large plate-like structure rather than being comminuted to a fine size. The apparent error in determination of the particle size distribution was a direct consequence of this particle shape, since the Horiba, a particle size analyzer which utilizes centrifugal sedimentation combined with photodensitometry, in common with other Stokes Law (sedimentation) instruments, utilizes the *minimum* cross-sectional area of particles being measured.

In light of the observed gross plastic deformation and of the common perception that wear debris can be released *in vivo* by an essentially brittle fatigue mechanism,[10] it was decided to attempt to produce brittle fracture by the introduction of liquid nitrogen to the attritor during grinding. The liquid nitrogen was poured in until steady temperature was reached (minimum boiling) and was "topped up" from time to time. This produced a four-phase milling milieu (UHMWPE, Al_2O_3, gaseous and liquid nitrogen) in contrast to the more usual two-phase situation in cryogenic milling.[7] The cryogenic milling procedure successfully produced fine particulate material after milling times ranging from 30 min to 8 h. The fine particulate was separated from the milling media by a wash flotation process at room temperature. The final successful protocol and its product are termed *grind S*.

The alumina media and milled UHMWPE were mixed with various water:methanol solutions and vigorously stirred to cause the alumina to sink and the UHMWPE to float. The alumina was repeatedly washed to remove all of the adherent UHMWPE. The UHMWPE was then beneficiated into "fine" and "coarse" fractions by a gravitational separation technique (1 h settling which removed all particles ca. >10 μm from suspension). SEMs of the fine UHMWPE (Fig. 4) and number fraction distribution (Fig. 5) show the presence of a significant number of very small particles (ca. 35% < 0.25 μm, 50% < 0.7 μm, ca. 65% < 1 μm). Note that these particles are similar in size to fine "subgrains" seen in as-received UHMWPE (Fig. 1) which appears to be made up of balls of agglomerated submicron particles, which together form a cauliflower-like grain. Further, the shape (horizontal flattening) of the number distribution curve between 0.7 and 5 μm suggests that two distinct particle populations are present: a submicron one and a larger one, consistent with observations (by SEM) of apparent aggregates (Fig. 4).

The fine fraction was examined by electron dispersion spectroscopy (EDS) and showed only a uniform background with a single resolvable chlorine peak. This reflects the use of Hank's balanced salt solution as a final suspension agent. Differential thermal analysis (DTA)

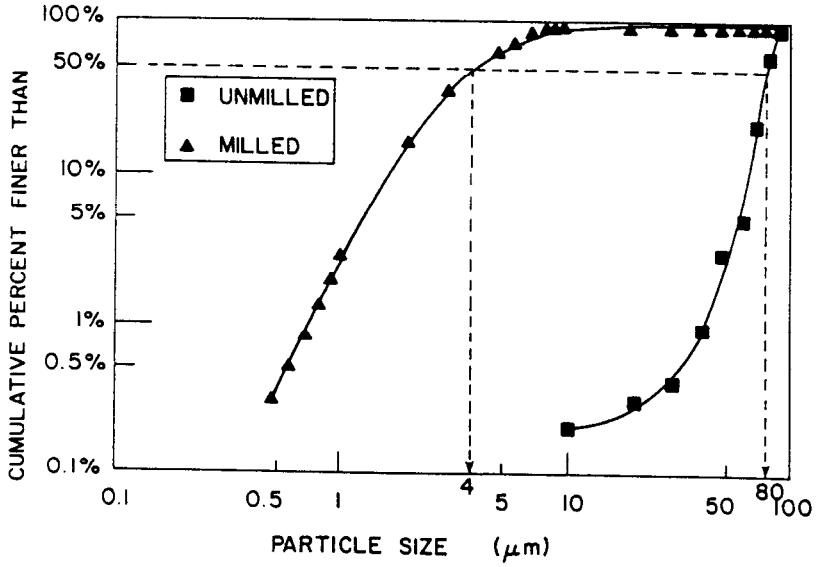

Figure 2. Particle size distributions of UHMWPE (GUR 415) as-received (right) and after milling at ambient temperature (left).

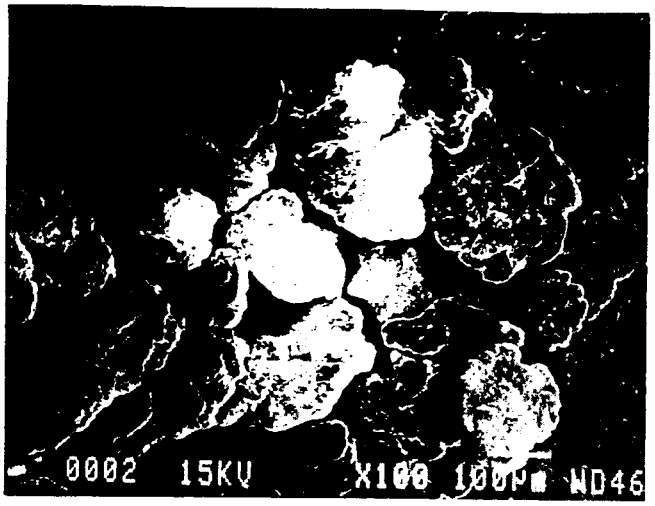

Figure 3. UHMWPE (GUR 415) milled at ambient temperature (SEM).

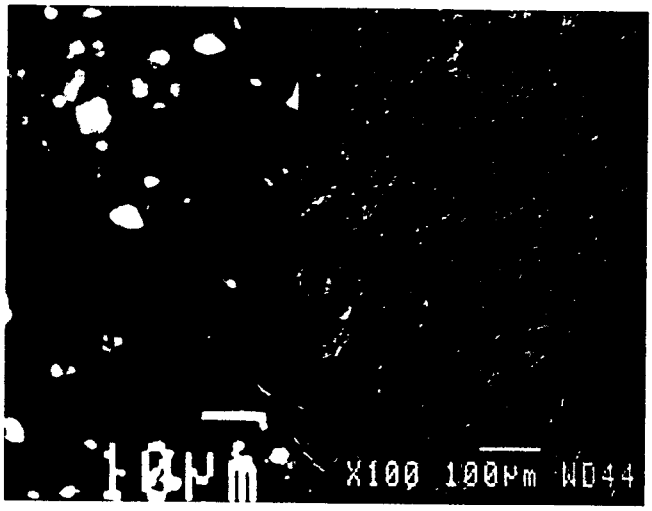

Figure 4. SEM appearance of fine fraction of *grind S:* cryogenically milled UHMWPE (GUR 415).

indicated a single melting point at 154°C, suggesting that only UHMWPE was present. This was confirmed by Fourier transform infrared spectroscopy (FTIR) which failed to show any spectra not referable to UHMWPE.

During the separation process, a significant quantity of the fine white material recovered from the milling process was found to sink in water after prolonged standing. Since this material had a density >1 g/cm^3, it was initially thought to be something other than UHMWPE, which is generally reported to have a density in the range of 0.926 to 0.934 g/cm^3.[11] The sediment material was analyzed by DTA and was found to have the same melting point and pattern as the unmilled UHMWPE. Selected area diffraction patterns obtained on transmission electron microscope (TEM) samples of this milled fraction and unmilled UHMWPE were found to be the same.

It been calculated that the density of fully crystalline poly(ethylene) is 1.01 g/cm^3.[12] It is also known that the crystals of poly(ethylene) may grow as large as 1 μm.[12] This suggests that the fine (dense) material found in *grind S* may be completely or nearly completely crystalline UHMWPE.

Additional material (before sedimentation) from *grind S* was mixed with a 50 wt% water:methanol solution (density = 0.881 g/cm^3). The specimens clearly separated into two components, one of which sank and one of which floated. This result, taken with the previous observations, indicates that the fine UHMWPE exists in at least two density forms. Again referring to the SEM micrograph of the as-received UHMWPE (Fig. 1), it seems likely that the as-received grain is composed of at least two components: (1) a dense highly crystalline phase, and (2) an amorphous phase bonding the high density crystals together. Since both of these types of material may be released during *in vivo* wear processes, biological activity studies of particulate UHMWPE may need to address

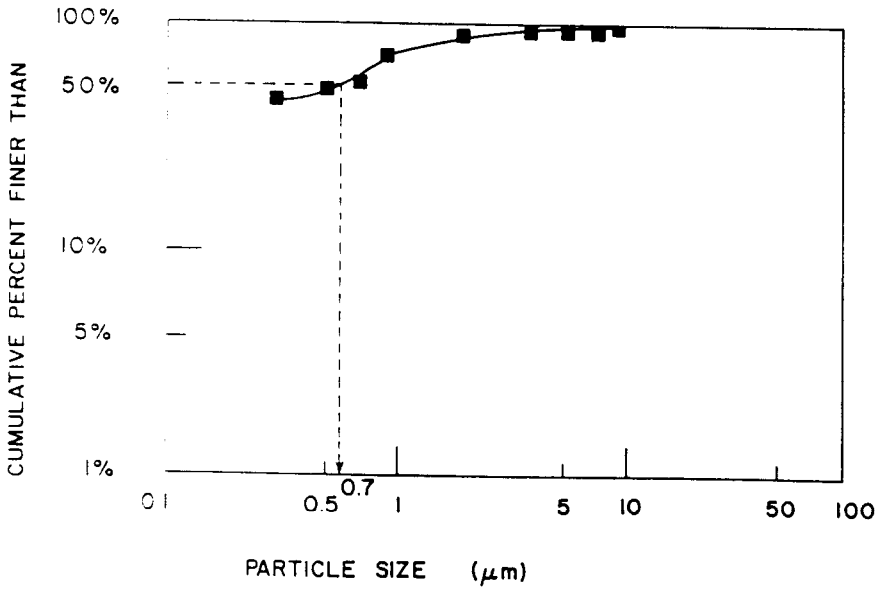

Figure 5. Particle size distribution of fine fraction of *grind S:* cryogenically milled UHMWPE (GUR 415).

both particle size and degree of crystallinity of challenge materials.

FUTURE PLANS

Further studies of cryogenically attrited UHMWPE are underway to refine the production process and to characterize the resulting particles more fully. Subsequent to informal working group meetings held at the 1991 meetings of the Orthopaedic Research Society (March, Anaheim, CA) and Society for Biomaterials (May, Scottsdale, AZ), it is planned that well-characterized specimens of these materials be made available in the future to other investigators for use as common factor or interlaboratory comparison materials in experiments examining biological response to particulate biomaterials.

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