INTRODUCTION:
Periprosthetic osteolysis represents the most common long-term cause of failure after total hip arthroplasty (THA). Recent efforts to reduce the incidence of osteolysis include the introduction of highly crosslinked polyethylene. These promising new polyethylenes have demonstrated significantly reduced wear rates compared with conventional polyethylene in laboratory testing. Whether the use of these novel materials will have the intended biologic effect of reducing rates of osteolysis remains to be determined on many factors including the particle dose, the presence or absence of endotoxin, and the relative biologic response to the wear debris generated. The goal of our study is to determine the relative inflammatory potential of crosslinked and non-crosslinked polyethylene using an in vivo murine model.

METHODS:

Crosslinking
Ceridust 3615 high density polyethylene (CD) and GUR 1050 UHMWPE base resin were crosslinked via e-beam irradiation at 10 Mrad and 40 Mrad. The 40 Mrad dose was achieved by 4 sequential treatments of 10 Mrad to mitigate adiabatic heating.

Characterization of the Polyethylene Particles
CD particles and GUR 1050 were characterized in this study using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared spectroscopy (FTIR) to confirm chemical composition (Table 1). The Transvinylene Index (TVI) was used to confirm the degree of crosslinking (Table 2). Size distribution profiles were determined using scanning electron microscopy (SEM) and a commercial particle analyzer (LA-920, Horiba).

Endotoxin Testing
A standardized LAL endotoxin detection test (QCL-1000, Cambrex, Inc) was used to detect endotoxin levels in all samples. This chromogenic assay was modified according to previously published protocols to detect both bound and soluble endotoxin.1

In Vivo Osteolysis Experiments
The inflammatory response to crosslinked and non-crosslinked CD debris was quantified using an established murine calvarial model.2 All particles were washed in ethanol to remove endotoxins according to previously described protocols.3 CD particles were tested at 10, 25, and 40 mg/mL. Endotoxin-spiked titanium was used as a positive control.

All non-crosslinked CD particle-treated groups (10, 25, 40 mg/mL) demonstrated inflammatory profiles greater than vehicle alone. (p<0.05, Figure 1) When tested at 25 mg/mL, CD crosslinked at 10 Mrad demonstrated significantly higher inflammatory potential than non-crosslinked groups (p<0.05, Figure 2). The increased inflammatory potential noted for particles crosslinked at 40 Mrad compared with non-crosslinked CD approached, but did not reach statistical significance (p=0.07).

DISCUSSION:
CD debris was selected for in vivo analysis based on previous publications documenting that these particles demonstrate a size distribution profile similar to that found in polyethylene retrieved from hip simulators and failed THA.4-6 Although TVI and DSC data for irradiated CD were not found in the literature, the results obtained here for GUR 1050 are consistent with known values.

The biologic response to both vehicles tested (HA and mineral oil) were comparable (Figure 1). We introduced the use of mineral oil because the hydrophilicity of HA makes the resuspension of polyethylene debris incomplete and inconsistent, with some aggregation. Mineral oil proved to be an ideal, cost-effective alternative which yields improved consistency in application of polyethylene debris.

In this study we demonstrated that CD can be crosslinked at 10 and 40 Mrad without significantly changing the size distribution profile compared with non-crosslinked CD. The crosslinked CD particles also demonstrated the expected changes in melting point (Table 1) and TVI (Table 2) compared with non-crosslinked CD.

Our data suggest that the biologic activity effect of crosslinking alone on CD debris diminishes beyond a certain radiation dose (10Mrad). No further increase in biologic response was seen at 40 Mrad. However, it should be noted that while a dose of 10Mrad correlates to some of the highly crosslinked UHMWPE acetabular liners used in contemporary hip arthroplasty, we do not suggest that this same radiation dose necessarily correlates to the same degree of crosslinking in the CD particles tested.

When tested in vivo using an established murine calvarial model, we noted that crosslinked CD at 10Mrad was more inflammatory than an identical dose (25 mg/mL) of non-crosslinked CD debris (p<0.05). This suggests that crosslinked debris may be somewhat more inflammatory than non-crosslinked debris. Further study is needed to determine if similar findings would be noted comparing crosslinked and non-crosslinked UHMWPE used in modern THA.

REFERENCES:
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