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Isolation and Characterization of Wear Debris Generated in Patients Wearing Polyethylene Hylamer Inserts, Gamma Irradiated in Air

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ABSTRACT: Hylamer polyethylene was used in the early 1990s to make hip-joint components. Clinical experience has shown that these components, if sterilized by gamma rays in the presence of oxygen, are easily affected by wear,

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which then leads to osteolysis. The authors analyzed polyethylene wear particles in seven patients who had received Hylamer polyethylene implants sterilized by gamma rays in air and had suffered prosthetic loosening. The results were compared to those of six controls, who had received traditional polyethylene implants, sterilized by the same method. The frequency distribution of globular and fibrillar particles was similar in both groups (38.5% in Hylamer, 45.2% in controls). The globular particles in the Hylamer samples had a mean area of $0.12 \mu\text{m}^2$, which was significantly lesser than that of the controls ($0.30 \mu\text{m}^2$). The width of fibrillar particles in the Hylamer samples was significantly lesser than that of the controls. Therefore, the two materials, despite undergoing the same type of sterilization, produced different types of wear, due to their different properties. In conclusion, the difference in the morphology of Hylamer polyethylene wear particles in comparison with PCA might have caused a more intensive biological response, early and massive osteolysis, and therefore, early loosening.

KEY WORDS: polyethylene, wear, Hylamer, scanning electron microscopy.

INTRODUCTION

Despite the recognized success and a worldwide acceptance of total joint arthroplasty, wear is a major obstacle in the longevity of implanted ultra-high-molecular-weight polyethylene (UHMWPE) components. There are many variables that affect the wear of a polyethylene bearing *in vivo*, including its chemical structure, and the method of manufacturing and sterilization [1]. With the aim of reducing wear, in 1991 a modified UHMWPE, known as Hylamer, was patented by Li and Howard from E.I. Du Pont de Nemours and Company (Wilmington, DE, USA) and marketed by the DePuy-DuPont Orthopedics joint venture. Hylamer is a hot isostatically pressed UHMWPE, with an extended-chain crystalline morphology and thicker lamellae (200–500 nm vs. 10–50 nm of the traditional one) and higher crystallinity (65–71% vs. 50–55%) [2–4]. Hylamer, compared with the traditional UHMWPE, claimed to have double the elastic modulus, increased compressive and tensile strengths and a greater resistance to crack propagation and creep [5]. Based on favorable preclinical evaluations, Hylamer was preferentially selected by surgeons for use in younger patients or those who were expected to be quite active.

Some studies confirmed this expectation both *in vitro* [6,7], and *in vivo* [8,9], whereas others discarded it. Since 1996, some authors have discussed early loosening [10–13]. Among the likely explanations for this disagreement is the sterilization method used. Hylamer polyethylene for Duraloc has been sterilized by different methods. Implants manufactured between 1992 and 1993 were sterilized by gamma irradiation

in air. Gamma irradiation in a nitrogen atmosphere followed by vacuum-packaging was introduced at the end of 1993. Since 1995 implants have been sterilized by gas plasma, without gamma irradiation.

Gamma irradiation has been known to generate various radicals with differing mobilities that, on reacting with oxygen, lead to progressive oxidation, alteration in the crystalline portion of the polymer, and deterioration in its mechanical properties. Therefore, the presence of oxygen in the sterilization process, as well as in the storing or implanting atmosphere (dissolved in biological liquids) leads to a damage in the material quality. The sensitivity to oxidation of the material increases along with a higher degree of polyethylene crystallinity. Due to this reason, as demonstrated in the laboratory wear tests [14,15], Hylamer polyethylene sterilized by gamma rays in the presence of oxygen has a poor resistance to wear. This was confirmed by simulation tests [16] that showed a decrease in the wear properties in Hylamer after irradiation in air, in Hylamer after irradiation in a low oxygen package, and in conventional UHMWPE after irradiation in air respectively. Further support was provided by subsequent studies that suggested shelf life might also be correlated with the extent of wear [17].

Due to the growing concern, on September 26 2001, DePuy International Ltd sent a list of implant components incorporating Hylamer sterilized by gamma-irradiation in air to hospitals and clinics supplied with these components, and voluntary recall was begun. At our institute we checked all the 30 patients who had received Hylamer polyethylene implants sterilized in air. In 15 of these (50%) the presence of periprosthetic osteolysis and severe eccentricity of the metal head prompted the surgeon to recommend replacing the Hylamer polyethylene insert [18].

The aim of this study was to analyze the morphology of Hylamer polyethylene wear debris from these patients in comparison with wear debris from traditional polyethylene inserts sterilized by the same method.

MATERIALS AND METHODS

Patients

Tissue samples from joint capsules were obtained from seven patients with Hylamer inserts gamma sterilized in air (Duraloc cup, Depuy Orthopedics, Indiana, USA). The patients were undergoing hip prosthesis revision due to aseptic loosening (Group 1). For comparison, periprosthetic tissue was obtained from the capsules of six patients

Table 1. Details of the seven patients with Hylamer insert (Group 1) and six patients with traditional UHMWPE insert (Group 2).

| | Sex/Age | Side | Pathology | Years from last surgery | Fixation of the prosthesis | Shelf time (yrs) | Metal head diameter (mm) | Cup diameter (mm) |
|---------|---------|------|----------------------|-------------------------------|----------------------------------|------------------------|-----------------------------------|-------------------------|
| Group 1 | | | | | | | | |
| 1 | M/59 | R | Posttrauma arthrosis | 8.7 | Uncemented | 0.6 | 28 | 56 |
| 2 | M/63 | L | Hip dysplasia | 8.7 | Hybrid | 0.6 | 28 | 48 |
| 3 | F/63 | R | Hip dysplasia | 6.2 | Hybrid | 5.4 | 28 | 46 |
| 4 | M/71 | R | Coxarthrosis | 7.5 | Hybrid | 1.9 | 28 | 54 |
| 5 | F/54 | L | Coxarthrosis | 5.4 | Hybrid | 4.0 | 28 | 52 |
| 6 | F/67 | R | Coxarthrosis | 6.4 | Hybrid | 3.2 | 28 | 48 |
| 7 | F/51 | R | Hip dysplasia | 6.4 | Uncemented | 3.5 | 28 | 50 |
| Group 2 | | | | | | | | |
| 8 | M/58 | R | Arthritis | 10.7 | Uncemented | n.d. | 26 | 46 |
| 9 | F/65 | R | Coxarthrosis | 11.3 | Uncemented | n.d. | 32 | 52 |
| 10 | F/74 | L | Coxarthrosis | 11.0 | Uncemented | n.d. | 32 | 52 |
| 11 | F/75 | R | Femoral fracture | 10.2 | Uncemented | n.d. | 32 | 50 |
| 12 | F/55 | R | Hip dysplasia | 8.2 | Uncemented | n.d. | 26 | 44 |
| 13 | M/73 | R | Hip dysplasia | 16.9 | Uncemented | n.d. | 32 | 54 |

n.d.: not determinable.

with traditional UHMWPE (PCA cup, Stryker Howmedica, New Jersey, USA) sterilized by the same method (Group 2). The diagnosis of loosening was made on the basis of pain and radiographic findings. The preoperative radiographs were analyzed for any evidence of migration of the implant, the presence of radiolucent lines at the bone-implant interface and erosion, defined as localized resorption of bone, around the implant. Written informed consent was obtained from each patient for the procurement and analysis of the tissue. Details of the patients are provided in Table 1. The mean age of Group 1 patients was 61.1 years, with a mean time of 7.0 years since last surgery. The mean age in Group 2 patients was 66.7 years, with a mean time of 11.3 years from last surgery.

Isolation of Wear Debris Particles

Biopsy specimens were immediately fixed in 10% neutral buffered formalin and routinely embedded in paraffin. Microscope slides were prepared, stained with hematoxylin and eosin, and reviewed with the use of transmitted and polarized light (magnification 20×). Polyethylene particles were isolated following the method already described [19].

Briefly, other consecutive slices, 20 μm thick, were obtained from the same block of paraffin used to provide the slices for microscopy. These slices were carefully released from the surrounding excess paraffin and placed directly onto a polycarbonate filter (25 mm diameter) with a pore size of 0.2 μm (Millipore, Isopore TM, membrane filters, Ireland). The filter was then placed onto a polypropylene holder (Swinnex, 25 mm, Millipore), xylol was added to dewax and the slices were then rehydrated. Finally, it was digested with sodium hypochlorite. After flushing with water many times, the filters were dried in a dust-free environment.

Chemical Characterization of the Particles

The chemical identification of the wear particle was performed using micro-Raman spectroscopy. Being a nondestructive method, the polycarbonate filters were analyzed by micro-Raman spectroscopy before the SEM analyses. A Jasco NRS-2000C instrument was used. The micro-Raman spectrometer consisted of an argon ion laser (Innova Coherent 70) using the 488 nm line focused through a microscope objective at 100 \times magnification; the laser power was ca. 10 mW. The beam spot of the laser was ca. 1 μm . All the spectra were recorded in backscattering conditions with 5 cm^{-1} spectral resolution using a frozen nitrogen CCD detector (Princeton Instruments Inc). For each filter, the spectra of twenty different wear particles were recorded in the polyethylene fingerprint region (from 1000 to 1600 cm^{-1}) [20].

SEM Analysis

The filters were cut with a razor blade into rectangular pieces of about 8 \times 12 mm^2 encompassing the filter center at one end. Mounted on the SEM holders by a biadhesive tape, the fragment edges were electrically connected to the holder by silver glue. The samples were gold sputtered in an Edwards S150B apparatus and examined horizontally in a Cambridge Stereoscan 200 electron microscope operated at 10 kV. Micrographs were taken at 10,000 \times magnification.

Morphological Analysis of Particles

The SEM micrographs were digitized. Seven scanning electron micrographs were chosen in such a way that each captures an area of 90 μm^2 and represents typical filter fields. Quantification of debris was performed for the biologically most active fraction, with a dimension of lesser than 5 μm [21].

In the seven prechosen fields the particles were counted, and the average number of particles was determined for all the fields. The particles were then outlined on each micrograph and analysis was performed using image analysis software (Qwin, Leica). Only separate particles were selected. Agglomerates and particles partially obscured by other particles were omitted. The size, shape, and area of the particles were characterized using a series of predefined terms, such as area, perimeter, length calculated as $\text{perimeter} + \sqrt{(\text{perimeter} \times \text{perimeter} - 16\text{area})/4}$, and width calculated as $\text{perimeter} - \sqrt{(\text{perimeter} \times \text{perimeter} - 16\text{area})/4}$, equivalent circle diameter (diameter of a circle with the same area as particle), aspect ratio (length/breadth) and roundness ($\text{perimeter}^2/4\pi \times \text{area}$) as per ISO/DIS 17853. Roundness is a measure of how closely the particle resembles a circle with a perfect circle having a value of 1. The number of particles per volume of tissue (area of the histological section \times 20 μm thickness) was calculated.

Statistical Analysis

Comparisons between the mean values of the number of particles and their shape descriptions were made by Student's *t*-test, or the Kolmogorov–Smirnov test according to the variance of data. The deviation between the observed frequencies in the two groups was calculated by the chi-square test. The correlations were tested by applying the linear regression method.

RESULTS

Histology

Sections of the newly formed joint capsule were characterized by the presence of a fibrous layer of variable thickness, many mononuclear phagocytes and sometimes a few giant cells (Figure 1). The intensity and the morphological appearance of the cellular infiltrate directly correlate the degree and the size of wear particles: particles smaller than 6–8 μm are phagocytosed by histiocytes. Bigger particles, such as plastic flakes, elicit giant-cell reaction. Giant cells were present only in some of Group 1 samples (Figure 2). Ingested particles cannot be morphologically characterized due to their small size. Furthermore, polarized light makes the particle very bright and its outline is not perfectly definable for a subsequent study based on morphological parameters. Surprisingly, two out of six Group 2 samples did not show any detectable wear particles either at 20 \times or 40 \times magnification.

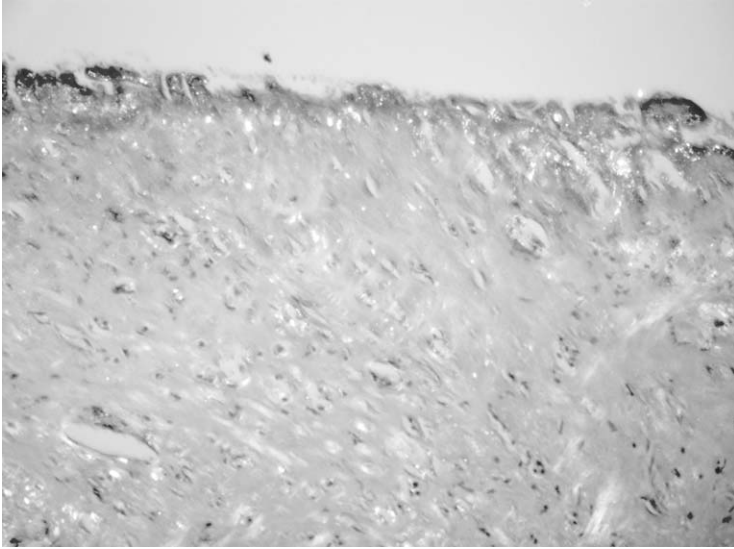


Figure 1. Slide of joint neocapsule sample of traditional polyethylene insert. Mainly histocyte reaction to small polyethylene particles (H-E 20 \times , pol).

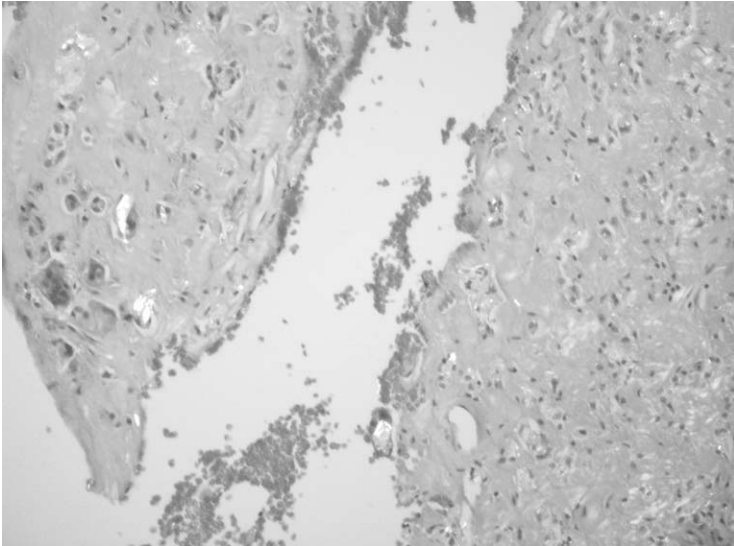


Figure 2. Histological slide of joint neocapsule of case no. 2. Varying sizes of microscopic polyethylene wear particles can be seen. The biggest particles prompt giant-cell reaction (H-E 20 \times , pol).

Chemical Characterization of the Particles

Figure 3 shows the Raman spectra of debris from Hylamer inserts (Figure 3(a)), a PCA wear particle (Figure 3(b)), and pure UHMWPE (Figure 3(c)). All the spectra reordered show that the debris was polyethylene particles and no signs of impurities were found. The debris spectra show the presence of polyethylene bands at 1068 and 1131 cm^{-1} (C–C stretching), 1170 cm^{-1} (CH_2 rocking), 1295 cm^{-1} (C–H twisting), 1370 cm^{-1} (CH_2 wagging), 1416 , 1440 and 1460 cm^{-1} (CH_2 bending).

It is well-known that the Raman spectrum is related to the morphology of polyethylene; in fact, some bands are typical of the crystalline phase and others of the amorphous phase [22]. From a qualitative point of view the debris appears to be of similar, but less crystallinity than the pure UHMWPE. In the debris spectra the bands prevalently due to crystalline phase (1416 , 1295 and 1131 cm^{-1}) are less intense and the marker bands of amorphous polyethylene (1460 and 1440 cm^{-1}) are more intense.

Morphological Analysis of Particles

At high magnification ($10,000\times$), the submicron and micron-sized particles were easily identified on the background polycarbonate filter

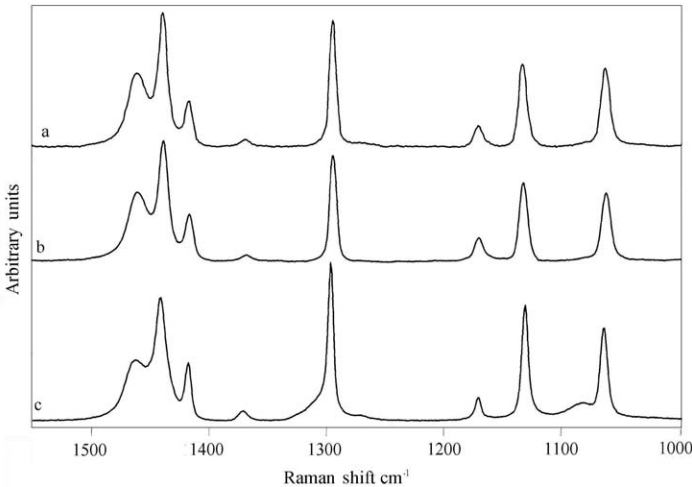


Figure 3. Raman spectra of: (a) isolated wear particle from Group 1; (b) isolated wear particle Group 2; (c) UHMWPE control powder.

containing the uniform, dark holes. The SEM images showed that the isolation processes removed cell debris from the PE particles (Figures 4 and 5). The distribution of particles on the filter was irregular; some areas of the filter were devoid of particles, others were overcrowded. Before selecting the seven representative fields, the percentage of consecutive fields not suitable for reading was assessed on each filter, either because they were empty or because they were too full. The number of fields that were discarded and the number of empty fields were not different for each sample examined (Chi-square test, 0.581).

The number of particles per cm^3 of tissue in Group 1 ranged from 9.02 to 56.79×10^9 (mean 20.54) and in Group 2 from 9.03 to 15.37×10^9 (mean 13.02). The values of the mean were not statistically different due to their small number and wide dispersion (Kolmogorov–Smirnov $p=0.5391$), but they were indicative of a tendency toward a greater number of particles in Group 1. No correlation was observed between the number of particles and implant duration, patients' weight, or shelf life of the polyethylene implant (time elapsed between sterilization by gamma rays and implantation).



Figure 4. SEM image of submicron-sized polyethylene particles isolated from tissues of a patient of Group 1.

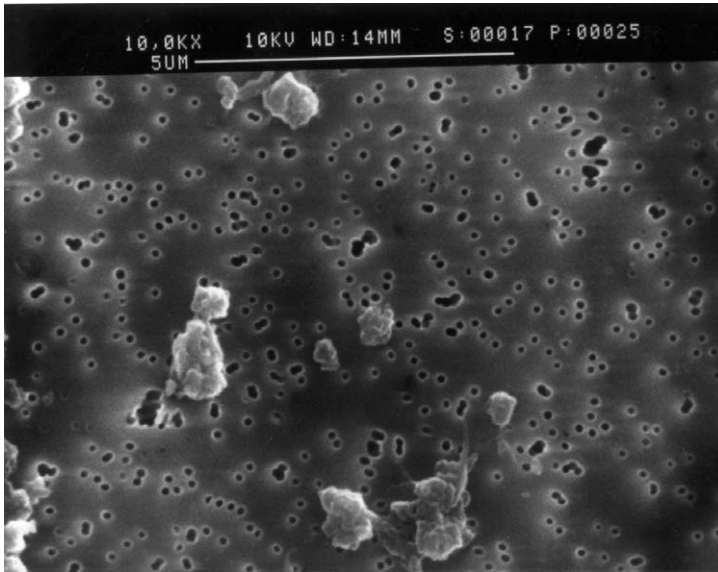


Figure 5. SEM image of submicron-sized polyethylene particles isolated from tissues of a patient of Group 2.

Table 2. Percentage distribution of granules and fibrils in the two groups.

| | % Granules | % Fibrils |
|---------|------------|-----------|
| Group 1 | 38.5 | 61.5 |
| Group 2 | 45.2 | 54.8 |

Chi-square test $p = 0.048$

On the whole, in both groups, 1099 particles were measured and observed under the SEM; they were classified into two groups:

- Granules with an aspect ratio of 2 or less;
- Fibrils of any length and aspect ratio greater than 2.

Table 2 shows the distribution of the two types of particles. The difference was just within statistical significance.

For each morphology, standard shape descriptions were calculated and measured. A preliminary statistical analysis was performed to test whether the metal head-size (not uniform in Group 2) might affect the mean result. The Student *t*-test showed that all parameters measured in the two 26 mm cases were not significantly different from the four

Table 3. Size and shape descriptors of globular particles.

| | No. of measured particles | Area μm^2 | Perimeter μm^2 | Length μm^2 | Width μm^2 | Aspect ratio | Roundness | Equivalent diameter μm^2 |
|----------------|---------------------------|----------------------|---------------------------|------------------------|-----------------------|-----------------|-----------------|-------------------------------------|
| Group 1 | 318 | 0.12 ± 0.23 | 1.11 ± 0.96 | 0.35 ± 0.31 | 0.22 ± 0.17 | 1.53 ± 0.43 | 1.25 ± 0.09 | 0.30 ± 0.26 |
| Group 2 | 123 | 0.30 ± 0.54 | 1.97 ± 1.17 | 0.63 ± 0.39 | 0.37 ± 0.22 | 1.76 ± 0.40 | 1.30 ± 0.08 | 0.53 ± 0.31 |
| <i>p</i> value | | **<0.000 | *<0.000 | *<0.000 | *<0.000 | *<0.000 | *<0.000 | *<0.000 |
| | | S | S | S | S | S | S | S |

**p* value Student *t*-test.

***p* value Kolmogorov–Smirnov.

Table 4. Size and shape descriptions of fibrillar particles.

| | No. of measured particles | Area μm^2 | Perimeter μm | Length μm | Width μm | Aspect ratio | Roundness | Equivalent diameter μm |
|----------------|---------------------------|----------------------|-------------------------|----------------------|---------------------|-----------------|-----------------|-----------------------------------|
| Group 1 | 509 | 0.70 ± 0.91 | 4.66 ± 3.99 | 2.05 ± 1.93 | 0.28 ± 0.16 | 7.67 ± 6.97 | 2.96 ± 2.06 | 0.80 ± 0.49 |
| Group 2 | 149 | 1.14 ± 2.21 | 4.76 ± 4.50 | 1.98 ± 2.07 | 0.39 ± 0.29 | 4.97 ± 3.56 | 2.16 ± 1.04 | 0.96 ± 0.73 |
| <i>p</i> value | | **0.207 | *0.802 | *0.708 | **<0.000 | **<0.000 | **<0.000 | **0.207 |
| | | NS | NS | NS | S | S | S | NS |

**p* value Student *t*-test.

***p* value Kolmogorov–Smirnov.

32mm cases. This allowed us to consider them as a uniform group with respect to Group 1. The granular particles had a smaller area and a more regular shape in Group 1 than in Group 2. All parameters measured and calculated were significantly different in Group 1 compared to Group 2 (Tables 3 and 4). The significance of the differences was calculated by the Student *t*-test or Kolmogorov–Smirnov test depending on the variance of values.

The mean size of fibrillar particles was also smaller in Group 1 compared to Group 2, although the marked dispersion of data makes the difference statistically insignificant.

DISCUSSION

This study was aimed at assessing the morphology of submicroscopic wear particles released by Hylamer polyethylene sterilized in the presence of oxygen compared with those released by traditional polyethylene sterilized by the same technique. Optical microscopy of the histological slides of Group 1 tissue confirmed the typical wear reaction by polyethylene particles, albeit with the unusual presence

of a huge large-sized debris, presumably originating from delamination processes, with subsequent recruitment of giant cells. Observation of Group 2 slides showed four cases of a typical reaction to polyethylene wear products, with intra- and extra-cellular particles, whereas in two cases no evident signs of wear were visible. Conversely, in all samples, including the ones that were negative by optical microscopy, a large amount of particles were isolated by the process of digestion on the filter. This confirms the observations of a previous study that there is submicroscopic polyethylene wear even when particles are not visible under the optical microscope [23]. The phenomenon of osteolysis that cannot be explained by observing periprosthetic tissues under the optical microscope might be explained by this etiological factor.

Chemical characterization by Raman-Laser spectroscopy enabled to ascertain the purity of the particles and, even more, the total absence of organic residue (that might have falsified subsequent SEM morphology analysis).

Data on the number of particles isolated from periprosthetic tissues provide important information, because the extent of organism response depends on both the size and the number of the particles [21]. The estimation made by counting the particles isolated on the filter ($20 \times 10^9/\text{cm}^3$ of tissue in Group 1 and $13 \times 10^9/\text{cm}^3$ of tissue in Group 2) is only an indicative value, since the count can be performed correctly only if the particles are not overlapping, and that leads to an inevitable selection of measurement fields. In addition, the need to examine filters at high magnification ($10,000\times$), so as not to neglect the particles smaller than a micron, makes examining the entire surface of the filter impractical. The method used for counting particles is similar to the one used by other authors [24,25], even if it is not precise; probably the best way to determine the number of wear particles is the electronic count [26,27]. It should also be pointed out that in the present study only tissue samples from the neocapsule were analyzed. Preliminary tests to assess the distribution of particles within these samples were encouraging and confirmed that if the harvesting area was at least 1 cm^2 , there was no significant difference from area to area. However, it is known that the particles are not only located in the neocapsule, on the contrary, the concentration of particles may be higher in samples retrieved from sites around the proximal part of the femoral component than in the joint capsule or the acetabular membrane [28]. Therefore, the number of particles is only an indicative value, not an absolute one.

Another limitation of the analysis may be that in Group 2 the diameter of the metal head was not 28 mm, as in Group 1. Both types

of heads in Group 2 (26 and 32 mm) are, however, considered to be pejorative compared to the 28 mm head [29], at least with regards to the amount of debris produced. However, despite this, there was less debris produced in Group 2 subjects. The difference in follow-up between the two groups may also be a limitation. However, the patients of Group 2 should have been penalized by a longer follow-up, but the amount of wear debris produced was less compared to Group 1 patients.

With regards to morphological assessment, it should be underlined that great care is to be taken in interpreting the measurements provided by the image analysis system. In particular, second order measures (length and width) can be calculated by different algorithms according to the geometry of the object. The recurrent shapes in polyethylene debris are basically circular for the granule and elongated for the fibril. Polygonal shapes are observed in negligible amounts. That is why we chose to calculate the length and width of particles by the above-mentioned formula, which gives the length of the longest and shortest sides of a rectangle having the same area and perimeter as the measured object. Several image analysis softwares give output as length and width of the object calculated with different algorithms (Feret maximum and minimum are the measured distance between theoretical parallel lines that are drawn tangential to the particle profile and perpendicular to the ocular scale) and a not carefully assessed use of the analysis system output can lead to substantial errors. The results obtained in the analysis of the polyethylene wear debris produced in the two groups show that the percentage distribution of round and fibrillar particles was very similar in the two groups, with a slight tendency for the Hylamer group to produce more fibrillar particles (difference just within statistical significance). This result is in agreement with that of Scott [30], who carried out a semiquantitative evaluation of the different aspects of wear particles in six patients who had undergone removal of the Hylamer polyethylene inserts, sterilized by gamma rays in air, after a mean follow-up of 47 months. Despite a much shorter follow-up (47 months vs. 84) Scott's results are very similar to ours (36% round particles, 50% fibrillar, and the rest have different shapes). Conversely, the results of McKellopp's [31] simulator study indicate a prevalence of globular debris (up to 90%) for traditional polyethylene sterilized by gamma rays in air, even though the comparison is not easy since the author does not specify categorization criteria. This observation might indicate that the morphology of wear particles produced by the simulator may not perfectly match that of debris produced *in vivo*, but the question needs to be investigated by an appropriately planned experiment.

The morphology of wear particles is a crucial factor in inflammatory response, as demonstrated by Laquerriere, who observed *in vitro* that at least for hydroxyapatite particles the needle shaped and small particles induced a larger production of some cytokines and of some metallo-proteinases [32–34]. These results were supported by Ren's studies on polyethylene particles; the elongated particles generated a significantly higher expression for the genes encoding mediators involved in tissue inflammation and osteoclastogenesis [35].

With regards to the size of particles produced by Hylamer, they were smaller than those produced by traditional polyethylene (area 0.12 vs. 0.30 μm^2 for granules and 0.70 vs. 1.14 μm^2 for fibrils). This difference was statistically significant only for round particles. The difference was not statistically significant for fibrillar particles, presumably due to the wide dispersion in the measurements of Group 2. Fibrillar particles of the same length were, however, thinner in Group 1 than in Group 2. The results obtained are comparable to those in the literature [30].

Size, as well as shape, of UHMWPE wear particles is a critical factor in macrophage activation. Particles in the size range 1–10 μm are proven to be five times less active than the 0.1–1 μm particles [36]. Smaller particles (range 0.1–15 μm) result in enhanced levels of cytokine secretion by macrophages [37]. Ingham proposed that the concentration of wear volume within a critical size range (0.2–0.8 μm) was critical in order to determine the biological response [38]. In fact, submicron particles are more readily engulfed by macrophages, and thus more likely to activate adverse cellular responses.

The reason for the difference in debris size between Group 1 and Group 2 may lie in a different effect that the same sterilizing procedure (gamma radiation at 2.5 megarad, with the components packaged in air) had on the two materials. It is now known that the oxygen that is present in the polyethylene when it is irradiated, or which diffuses into the material during shelf storage and/or during *in vivo* use, reacts with residual free radicals that are generated by the radiation [39,40]. The resultant chain scission reduced the molecular weight, leading to increased density, stiffness and brittleness, and reduced fracture strength and elongation to failure [41]. These changes, in turn, reduce the resistance to wear [42]. Because of its higher crystallinity, Hylamer was thought to be more oxidation resistant, due to the assumption that oxygen can diffuse less rapidly into crystalline regions [43]. On the contrary, Hylamer was more susceptible to oxidation than traditional polyethylene, due to the scarcity of amorphous regions. Oxidation occurs preferentially in amorphous regions, and therefore it is localized and concentrated in Hylamer, thus leading to more evident mechanical

failures [44]. Oxidation occurs not only at the time of sterilization or preimplantation preservation, but also continues *in vivo*, through enzymes and/or the reactive oxygen species produced by inflamed synoviocytes that can induce a breaking of the polymer chains and increase the level of exposure of the free radicals on polyethylene, perpetuating *in vivo* the oxidative degradation of the implant and increasing tissue responses around the implant [45].

CONCLUSION

In conclusion the amount of debris produced *in vivo* in total hip prostheses with Hylamer insert was greater than that produced by traditional polyethylene when the same method of sterilization was employed. The percentage of round and fibrillar-shaped submicroscopic debris was similar in both groups. Hylamer polyethylene, however, produced smaller particles than traditional polyethylene. Besides submicroscopic particles, there was also plenty of large flakes. Finally, the difference in amount and morphology of Hylamer polyethylene wear particles in comparison with PCA might have caused a more intensive biological response, early and massive osteolysis, and therefore, early loosening.

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