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The influence of sterilization technique and ageing on the structure and morphology of medical-grade ultrahigh molecular weight polyethylene

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The effects of four sterilization treatments (gamma radiation in nitrogen, electron-beam radiation, ethylene oxide gas, and no sterilization) on the structure and morphology of ultrahigh molecular weight polyethylene (UHMWPE) were monitored as a function of ageing time in air for a period of 1.5 y. Characterization techniques employed include differential scanning calorimetry, density gradient column, transmission electron microscopy, and small-angle X-ray scattering. Ethylene oxide gas does not affect the structure of the polymer. Both forms of radiation lead to measurable alterations of the material's structure, including an increase in crystallinity, an increase in density, and the enhancement of lamellae crystalline stacking. Most changes in structure occur in the first few months with little differences observed upon subsequent ageing in air. The sharpness of the crystalline–amorphous boundaries decreases with time for irradiated UHMWPE and is believed to be linked to the oxidation of the polymer. © *1998 Chapman & Hall*

1. Introduction

Ultrahigh molecular weight polyethylene (UHMWPE) possesses a unique structure and properties which have resulted in its having been the most widely used material for replacing damaged or diseased cartilage in total joint replacements for the last 35 y [1–4]. Both the structure and superior properties of UHMWPE are a direct consequence of its molecular weight which averages $3–6 \times 10^6$ g mol^{-1}. Owing to the extremely long nature of the polymer chains, packing becomes difficult, leading to a material with lower crystallinity, lower density, and more entanglements than commercial high-density polyethylenes. A microstructure results consisting of long molecular chains folded into disperse crystalline lamellae connected by tie molecules. It is this "composite" structure, along with its high entanglement density, which provide UHMWPE with the properties of a good bearing material: excellent toughness, good resistance to fatigue, reduced wear, low abrasion, and a low coefficient of friction.

While UHMWPE remains the best material choice to replace articulating cartilage, it is also the "weak link" in joint replacements. Serious long-term degradation and mechanical damage can occur *in vivo* [5]. The generation of polyethylene debris can result from pitting, delamination, and wear, and can in turn lead to osteolysis [6–8]. Thus, UHMWPE may lead to the premature failure of an implant.

There are many variables inherent in the presurgical life of an implant (see Fig. 1) which can explain the failure of some implants but not others. The first consideration is the choice of a starting resin; all resins must be medical grade UHMWPE but may vary in their molecular weight and additives present. Table I lists some typical resins and their properties. Once a resin has been chosen, a processing technique must be selected: compression moulding, ram extrusion or direct compression moulding. Compression moulding and extrusion produce bars or rods of polymer from which implant parts must be machined. The machining step is eliminated in direct compression moulding, as the resin is moulded directly into final implant part form. After the implant part is obtained, it must be sterilized before it can be placed in the body. There are a number of sterilization treatments that can be employed, including gamma radiation in air, gamma radiation in an inert atmosphere, ethylene oxide gas, and gas plasma. Finally, the polymer can sit on the shelf for any amount of time (in air, inert gas, or vacuum), as there is currently no FDA protocol, before it is implanted. Thus, the presurgical variables consist of resin, processing method, sterilization, and ageing time and environment.

There have been numerous studies [9–12] linking the problems associated with UHMWPE implants with their sterilization. Orthopaedic components machined from UHMWPE are typically sterilized by

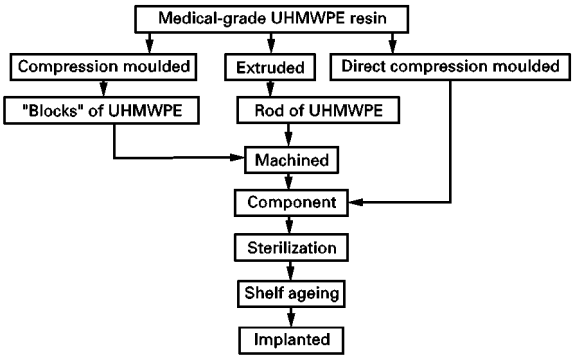

Figure 1 Flow chart depicting the presurgical life of an UHMWPE implant part.

TABLE I Typical medical-grade UHMWPE resins with their molecular weights and additives. Calcium stearate is used as an additive to inhibit corrosion

Resin	Molecular weight (10^6 g mol^{-1})	Additives
GUR 1020	3–4	none
GUR 1120	3–4	Ca stearate
GUR 1050	5–6	none
GUR 1150	5–6	Ca stearate

irradiation with 25 kGy of ^{60}Co gamma rays. Such strong ionizing radiation is likely to have a detrimental effect upon the microstructure, such as entanglement density and tie molecules, that gives UHMWPE its needed properties for total joint replacement applications. Previous studies [13] have shown that high-energy photons, such as gamma rays, can generate free radicals in polymers through homolytic bond cleavage. These radicals have been shown to have long lifetimes, especially those generated in the crystalline regions of the polymer where they can diffuse at low mobility into the amorphous regions of the polymer, and can therefore continue to undergo chemical reactions for many months and beyond. This time-dependent free-radical reaction mechanism poses serious concern for the radiation degradation of polymers, especially in the presence of oxygen [14, 15] which has a high diffusional mobility and is very reactive with the radicals.

Previous work [16] has been reported in which a pilot study looking at the effects of gamma-radiation sterilization in air on the structure of UHMWPE was examined after ageing for 5 y in air. By studying material, some of which had been sterilized and some of which had not, from the same batch it was shown that a significant change in the structure occurred as a result of gamma radiation and subsequent 5 y ageing in air. While that study answered an important question, it also produced new questions: (1) when and at what rate during the 5 y did changes in structure occur, and (2) are there alternative sterilization techniques that exist that do not lead to the observed changes in structure and subsequent degradation of UHMWPE? This paper addresses these issues. Gamma radiation in nitrogen, electron-beam irradiation, and ethylene oxide gas have been examined as alternative sterilization techniques to gamma radiation in air. Structures were monitored over time for the first 1.5 y after sterilization to examine the evolution of microstructural changes that occur.

2. Materials and methods

2.1. Materials

Material used in this study was compression-moulded Hoechst GUR 1020 medical-grade UHMWPE supplied by Perplas Inc. (Bacup, UK) in bar form. Samples were machined to 1 cm diameter discs of 1 mm thickness and subsequently divided into four sterilization treatment groups: (a) gamma radiation, (b) electron-beam irradiation, (c) ethylene oxide gas, and (d) no sterilization. Gamma radiation (Raychem Corp., Menlo Park, CA) was performed in the Raychem Cobalt 60 Facility using the Gamma Beam 650 Irradiator. Samples were left in a laboratory nitrogen atmosphere prior to and during irradiation. Irradiation took place for 109 min at a dose rate of 43.5 min per kGy^{-1} resulting in a dose of 25.2 kGy. Electron-beam irradiation (Nicolet Imaging Systems, San Diego, CA) was performed using a 12 MeV electron beam and samples were irradiated with a dose of 25 kGy. Ethylene oxide gas (Sorex Medical, Salt Lake City, UT) samples were processed through a sterilization cycle using the following parameters: a temperature of 120 °C, a gas dwell time of 185 min and a gas concentration of 513 mg l^{-1}. Samples with no sterilization treatment served as a control group.

2.2. Differential scanning calorimetry

Differential Scanning Calorimetry (DSC) was performed on a Perkin–Elmer 007. Heating runs were conducted in which samples were heated from 80–180 °C at a rate of 5 °C min^{-1}. The sizes of the samples ranged from 2.9–3.1 g. Heats of fusion were obtained by integrating the area under the endothermic peak. Sample crystallinity was determined by comparing the heat of fusion for the sample to the heat of fusion for a fully crystalline polyethylene material (288 J cal^{-1}) [2]. Melting temperature is defined as the peak melting temperature. Two samples were run for each material tested, unless results were substantially varied, in which case a third sample was tested. All results reported are averaged over the number of samples examined.

2.3. Density gradient column

Density was measured on a density gradient column (DGC) according to ASTM D1505-85 standard [17]. Specimens were 1 mm thick sections (to include the entire thickness of the sample discs) with volumes ranging between 10 and 15 mm^3 depending on the shape used. Two samples were investigated for each material studied. Sample density was determined by submerging the specimens in a density gradient column of isopropanol and distilled water containing calibrated density floats. Before insertion into the DGC, each sample was wetted for 15 min in a 50/50

solution of isopropanol and water. Each sample was then gently placed in the column and allowed to reach equilibrium for 10 min before a reading was taken. Density measurements were taken at a temperature of 22.5 °C.

2.4. Transmission electron microscopy

Specimens were prepared for transmission electron microscopy (TEM) by staining the UHMWPE with chlorosulphonic acid (99% concentrated) to cross-link and stabilize the amorphous regions of the polymer [18]. After staining at 60 °C for 9 h, acetone (at 0 °C) and subsequent distilled water rinses, were performed. Following drying at 60 °C for 30 min, samples were embedded in epoxy resin and cured for 24 h at 60 °C. A nominal thickness of 65 nm was obtained through ultramicrotomy with the use of a diamond knife. Specimens were placed on carbon-coated substrates and then post-stained in 2% uranyl acetate solution for 3 h to enhance contrast further in the TEM. A Jeol 100 CX operating at 80 kV was utilized to characterize the morphology of the prepared samples.

2.5. Small-angle X-ray scattering

Small-angle X-ray scattering (SAXS) experiments were conducted at the NIST beamline X23A3 at the National Synchrotron Light Source at Brookhaven National Laboratory (Upton, NY). The experimental details of this system are described elsewhere [19]. Specimens consisted of the entire 1 cm diameter, 1 mm thick discs and were probed by 10 keV photons. Data were placed on an absolute scale and were desmeared according to the method given by Lake [19, 20].

3. Results

3.1. Differential scanning calorimetry

Fig. 2 shows crystallinities as a function of time for each of the four sterilization treatments. It can be seen that both forms of irradiation sterilizations lead to an initial increase in crystallinity when compared with the non-sterile control. EtO sterilization does not appear to affect crystallinity. It appears that the entire increase in crystallinity occurs initially (within the first 3 mon) and that crystallinity remains stable for the next year and beyond. Thus, ageing in air does not appear to lead to changes in the crystallinity of UHMWPE, regardless of sterilization treatment.

Similar results are found for the peak melting temperature. The results for melting temperature as a function of time are presented in Table II. Both forms of irradiation sterilization lead to an increase in melting temperature of approximately 2 °C, while EtO does not alter the melting point of UHMWPE. Once again, ageing in air does not appear to be a factor, as the melting temperatures remain relatively constant for a year and beyond.

3.2. Density gradient column

Density results for the four sterilization treatments as a function of ageing time in air are given in Table III.

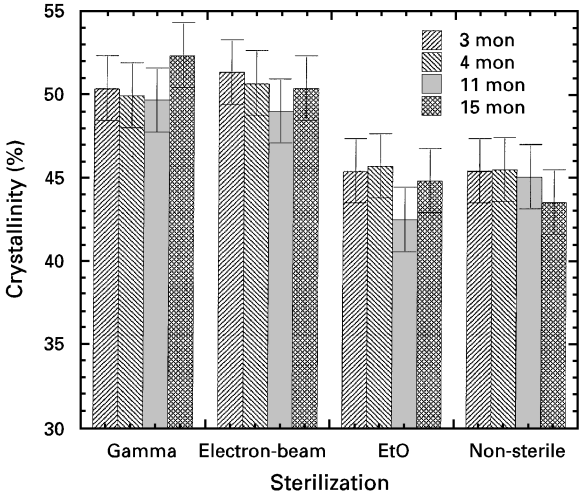

Figure 2 DSC results showing per cent crystallinity as a function of ageing time for all four sterilization treatments. Both forms of irradiation lead to an increase in the crystallinity of the polymer. EtO does not affect crystallinity. Ageing in air does not appear to be a factor as most changes occur by 3 mon.

TABLE II Peak melting temperatures as a function of time for all four sterilization treatments determined by DSC

	Peak melting temperature (°C ± 0.4 °C)				
	4 mon	11 mon	13 mon	15 mon	16 mon
Gamma	133.45	133.53	133.66	133.07	133.73
Electron-beam	133.75	133.21	133.51	133.33	133.46
EtO	131.44	131.69	132.32	131.86	131.91
Non-sterile	131.30	131.74	131.72	131.53	132.13

TABLE III Densities as a function of time for all four sterilization treatments determined by DGC

	Densities (g ml^{-1} ± 0.001 g ml^{-1})		
	2 mon	14 mon	17 mon
Gamma	0.939	0.939	0.941
Electron-beam	0.939	0.940	0.940
EtO	0.935	0.933	0.934
Non-sterile	0.935	0.933	0.933

These results are similar to those found for crystallinity and melting temperature. An initial increase in density is observed for both forms of irradiation sterilization when compared to the non-sterile control material. These increases are approximately equal to 0.006 g ml^{-1}. Ageing in air, similar to the DSC findings, does not appear to affect the density values for all four materials.

3.3. Transmission electron microscopy

Transmission electron micrographs of gamma-irradiated and EtO-sterilized UHMWPE aged for 10 mon are shown in Fig. 3. Both gamma and electron-beam irradiation lead to a more ordered structure evinced by the appearance of lamellar stacks, as seen in Fig. 3a

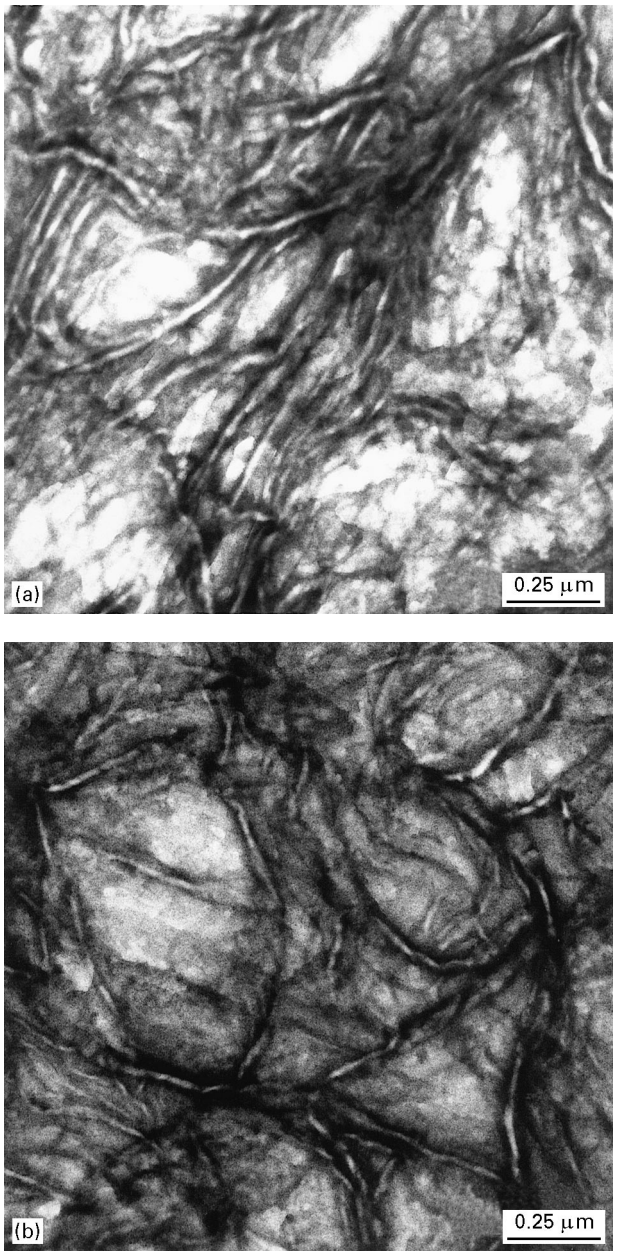

Figure 3 Transmission electron micrographs showing a (a) gamma irradiated and (b) EtO gas sterilized sample after 10 months ageing in air. Irradiation leads to a more lamellar structure.

for the gamma-irradiated material. Lamellar thickness does not appear to change and is of the order of 50 nm for all samples. EtO (Fig. 3b) does not appear to alter the microstructure and it looks identical to the non-sterile polymer. Although micrographs for only one ageing time are shown here, time did not have an effect on the morphologies observed.

3.4. Small-angle X-ray scattering

The Lorentz-corrected intensity as a function of the scattering vector, $q(=4\pi/\lambda \sin \varphi$ where 2φ is the angle of the scatter and λ is the photon wavelength) is shown in Fig. 4 for all four sterilization treatments at 1 and 11 mon ageing. It can be seen that both sterilization and ageing time do not affect the position (q) at which the peak occurs. This peak can be used to find the long period, d, of the polymer (where the long period refers to the width of the crystalline plus the amorphous region in an ideal crystalline–amorphous–crystalline layered structure) by applying Bragg's law such that $d = 2\pi/q$. Values for d of the order of 50 nm are obtained. Sterilization treatment and ageing time were found to influence the intensity of the small-angle X-ray scattering. It can be seen that both forms of irradiation result in a decrease in scattering intensity and that this decrease is more pronounced after ageing for 11 mon in air.

4. Discussion

The sterilization of UHMWPE can greatly influence the structure of the polymer, depending on the treatment employed. Ethylene oxide gas sterilization does not appear to alter the UHMWPE microstructure. Ionizing irradiation, on the other hand, significantly changes the polymer, regardless of the form of the irradiation (gamma or electron-beam).

Radiation creates free radicals in polyolefins and these free radicals undergo a combination of cross-linking and chain-scission reactions [13, 14]. Which of these mechanisms dominates has been shown to be influenced by the environment in which irradiation takes place. Streicher [10] has shown that for UHMWPE, cross-linking dominates when the polymer is irradiated in nitrogen, while chain scission dominates when the material is irradiated in air [10]. This is due to the fact that oxygen is extremely reactive with the free radicals produced by irradiation, forming peroxides which can break down and lead to further radical production, so that the total number of free radicals generated and the total extent of chain scission, are greatly increased.

Results for the present study indicate that chain scission is the dominant mechanism that occurs when UHMWPE is exposed to irradiation sterilizations in an inert environment and then subsequently exposed to ageing in air. This evidence for chain scission is manifested in the DSC, DGC, and TEM results. Scission of the long chains in UHMWPE results in shorter, more mobile chains which are able to pack together more easily into a denser, more crystalline, lamellar structure. Although gamma irradiation was performed in nitrogen and electron beam irradiation occurred in vacuum, the material has thus appeared to undergo chain scission. This is most likely a consequence of the polymer's exposure to air (oxygen) following irradiation or oxygen present initially as a result of processing. Oxygen has a high diffusivity and can readily enter the material and react with the long-lived radicals that have not had the opportunity to cross-link while the polymer was in an inert environment.

Ageing in air does not appear strongly to affect the structure of UHMWPE subsequent to sterilization. Results from DSC, DGC, and TEM indicate that the alteration of the polymer's structure accompanying radiation primarily occurs within the first 2–3 mon of irradiation and that subsequent ageing in air has little or no effect. A similar trend has been seen in previous work which examined the oxidation of UHMWPE

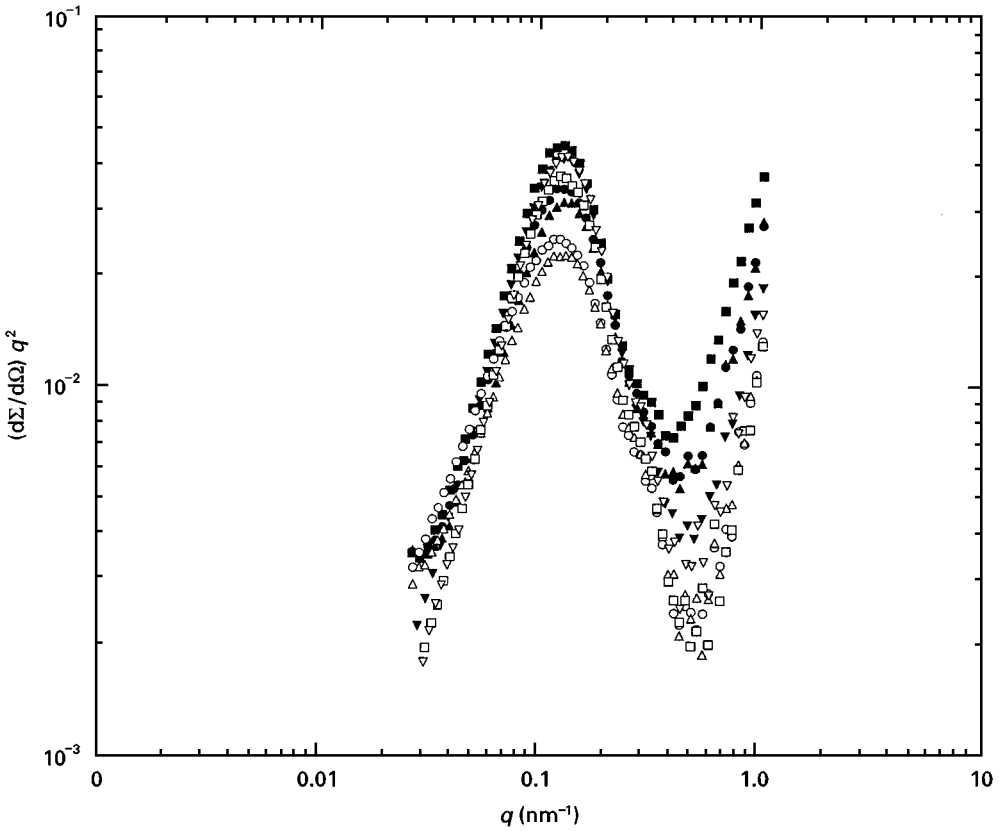

Figure 4 A plot of the Lorentz-corrected scattering intensity versus q for all four sterilization treatments at (●, ▲, ■, ▼) 1 and (○, △, □, ▽) 11 mon. Both forms of irradiation lead to a decrease in scattering while EtO gas has no effect. Ageing in air augments the effects that are observed. (●, ○) Gamma, (▲, △) electron-beam, (■, □) EtO, and (▼, ▽) non-sterile treatments.

after the same sterilization treatments and subsequent ageing [21]. While oxidation was found to increase with time, indefinitely, subsequent to irradiation sterilization, the most significant oxidation occurred in the first 2.5 mon.

A noticeable change over time is, however, observed in the SAXS data. Irradiation is seen to lead to a decrease in scattering intensity (Fig. 4) and this decrease becomes more pronounced as the polymer ages in air. Scattering in UHMWPE occurs at the boundaries of the crystalline and amorphous regions as a change in electron densities is present there. A decrease in scattering suggests that either there are fewer of these boundaries present or that these boundaries are becoming less sharp. Results from DSC and TEM indicate that the number of boundaries is not less and thus they are most likely becoming more diffuse. A possible explanation for this behaviour is that as the material oxidizes, the oxygen diffuses to and starts attacking the boundaries between the crystalline and amorphous regions. Because oxidation continues to increase over time for irradiated UHMWPE, the attack of the boundaries and concomitant decrease in observed scattering intensity will increase with time as well.

5. Conclusion

The sterilization employed can determine whether the structure and morphology of medical-grade UHMWPE will be altered. EtO sterilization does not appear to change UHMWPE while both gamma and electron-beam irradiation lead to significant changes in the structure of the polymer. Ionizing radiation causes an increase in crystallinity, an increase in melting temperature, an increase in density, and a more ordered lamellar microstructure to form. These changes are seen to occur in the first few months after sterilization and ageing in air, and subsequent ageing does not have a significant effect. Irradiation is also seen to lead to a decrease in SAXS intensity and this decrease becomes more pronounced with ageing. It is believed that this is suggestive of the crystalline–amorphous boundaries losing their sharpness in response to the oxidation of the material.

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