Europium Stearate Additives Delay Oxidation of UHMWPE for Orthopaedic Applications

A Pilot Study

Luis A. Gallardo MS, Ilenia Carpentieri PhD,
Michel P. Laurent PhD, Luigi Costa PhD,
Markus A. Wimmer PhD

Published online: 10 December 2010
© The Association of Bone and Joint Surgeons® 2010

Abstract

Background Ultrahigh-molecular-weight polyethylene (UHMWPE) is used as an articulating surface in prosthetic devices. Its failure under various mechanisms after oxidation is of utmost concern. Free radicals formed during the sterilization process using high-energy irradiation result in oxidation. Europium, an element of the lanthanide family, has a unique electron configuration with an unusual lack of preference for directional bonding and notable bonding to oxygen. Because of this, it currently is used in studies for stabilization of polymers such as polyvinyl chloride.

Questions/purposes We asked whether europium stearate could enhance the oxidation resistance after irradiation in nitrogen of UHMWPE.

Methods Conventional nonirradiated and gamma-irradiated in nitrogen UHMWPE were compared with

polyethylene doped with 375 ppm and 3750 ppm europium(III) stearate under the same treatment conditions. Chemical characterization was performed by Fourier transform infrared (FTIR) microspectroscopy using 200- μ m thin films. The oxidation of doped samples with time was compared with that of conventional samples using accelerated oven aging. The types of oxidation products were identified by FTIR and quantified per material and treatment condition as indications of the oxidation level and mechanism.

Results The generation rate of hydroperoxides and ketones was decelerated proportionally with concentration of europium stearates. The oxidative mechanism appeared similar to that of conventional polyethylene with the same types of measurable end products as ketones and hydroperoxides. Yet, the rate of generation of the latter appeared to be slowed down by the action of europium stearate.

Conclusions Europium stearate mixed in UHMWPE decelerated the oxidation reactions triggered by gamma irradiation in nitrogen, seemingly without major alteration of the oxidation mechanism.

One or more of the authors (MPL) received funding from the Grainger Foundation (Chicago, IL). Student travel funds (LAG) have been made available through a Provost Award for Graduate Research and funds from the Bioengineering Department, Graduate College, and the Graduate Student Council of the University of Illinois at Chicago.

This work was performed at Rush University Medical Center, Chicago, IL; and Università degli Studi di Torino, Turin, Italy.

L. A. Gallardo, M. P. Laurent, M. A. Wimmer (✉)
Department of Orthopedic Surgery, Rush University Medical
Center, 1653 W Congress Parkway, Chicago, IL 60612, USA
e-mail: markus_a_wimmer@rush.edu

L. A. Gallardo, M. A. Wimmer
Department of Biomedical Engineering, University of Illinois
at Chicago, Chicago, IL, USA

I. Carpentieri, L. Costa
Dipartimento di Chimica, Università degli Studi di Torino,
Turin, Italy

Introduction

The number of cases of musculoskeletal system disorders associated with aging has increased as a consequence of technologic and medical practice improvements that have prolonged life expectancy. Therefore, the number of total joint arthroplasties (TJAs) has increased [28] and is expected to continue that trend in coming years [28]. Currently more than 600,000 TJAs are performed each year in the United States [28]. It is estimated that by 2030, they will exceed four million per year [28].

The prostheses used in TJAs are subject to challenging environments, variable loads, and wear regimes that can lead to failure [4]. Some joint implants consist of a metal or ceramic component articulating against UHMWPE [18, 20]. Degradation of this polymer leading to implant failures related to fatigue, wear, and others [20, 26, 42] can be accelerated or exacerbated as a result of oxidation of the polymer during storage and service [4, 11, 18, 31–37].

An additive to the polyethylene traceable in body fluids through lanthanide elements has been suggested to allow direct quantification of wear volume [17, 23]. Lanthanides were proposed primarily because of their high specificity using mass spectrometry and their absence in mammals [17].

In addition, lanthanides possess a unique chemistry attributable to their 4f electron shell that can be used toward polymer stabilization. The poor shielding properties of this shell cause it to be buried in the xenon-like core of the atom, giving lanthanides unusual chemical uniformity and no directional bonding preference [3]. This contrasts with d-transition metals for which the d-electron shell leads to strong directional bonding and reactivity that can make them pro-oxidants [16]. The Ln + 3 ion is a hard Lewis acid that strongly coordinates to oxygen in ligands and exhibits high coordination numbers (> 6). Consequently, lanthanides may be effective scavengers for oxygen-containing species, including radicals.

Ceria nanoparticles have been reported to have hydroxyl scavenging properties and to act as direct antioxidants by limiting the amount of oxygen species reaching neurons [37]. Lanthanide stearates act as thermal stabilizers for polyvinyl chloride, where it is believed they act as free-radical chain terminators and by inhibiting dehydrochlorination [29, 45]. An additive that similarly would improve the oxidative performance of UHMWPE is highly desirable. In combination with stearate it would constitute a readily dissolvable additive for the hydrophobic polymeric chain of UHMWPE adding to the fact that it is a successful

tracer [17, 23]. Thus, we asked whether UHMWPE doped with europium stearate, which was gamma-sterilized, would: (1) allow for FTIR spectral evaluation of the extent of oxidation without interference from stearate chains with the carbonyl bands; (2) have a decreased oxidation rate once the reaction is initiated; and (3) oxidize less than conventional UHMWPE producing lower concentrations of hydroperoxides and ketones after accelerated aging.

Materials and Methods

We conducted a pilot spectroscopic analysis of oxidation quantifying hydroperoxide and ketone concentrations on three single-sample groups of UHMWPE consisting of a nondoped control and UHMWPE doped with europium stearate at 0.35 and 3.5 mmol/L (Table 1). These concentrations were chosen based on literature data of calcium stearate and antioxidant addition to polyethylene [8, 38, 40, 41, 43, 44]. All three groups underwent simultaneous gamma irradiation (35.1 kGy) and thin-film accelerated aging (95°C), the latter adopted from previous studies [8, 15, 20].

We used a general factorial design of an experimental model based on ANOVA to examine the effect of doping and aging on the oxidation product concentration. This type of model is well suited to our limited number of samples because a level for a given factor is represented at each level of the other factors and thus is effectively replicated, reducing the number of actual replicates required [22]. The input variables were dopant concentration at three levels and aging time at five levels, yielding 15 conditions. The output variables were the ketone, free hydroperoxide, and hydrogen-bonded hydroperoxide concentrations, each analyzed separately. Single replicates were run. The data were fit to a model entailing four parameters: additive concentration (A), aging time (B), interaction A-B, and the intercept, leaving 11 degrees of freedom for the pooled

Table 1. Concentrations of oxidation products resulting for the various dopant concentrations, irradiation levels and aging durations. One replicate per condition (Cond 1–16)

	Cond 1	Cond 2	Cond 3	Cond 4	Cond 5	Cond 6	Cond 7	Cond 8	Cond 9	Cond 10	Cond 11	Cond 12	Cond 13	Cond 14	Cond 15	Cond 16
Europium(III) concentration (ppm)	0	0	0	0	0	375	375	375	375	375	3750	3750	3750	3750	3750	3750
Irradiation (kGy)	0.0	35.1	35.1	35.1	35.1	0.0	35.1	35.1	35.1	35.1	0.0	35.1	35.1	35.1	35.1	35.1
Aging (hr)	0	0	48	96	144	0	0	48	96	144	0	0	48	96	144	192
Oxidation Products Concentration (mmol/L)																
Ketone	0.2	2.5	7.2	16.0	39.6	1.5	2.7	5.2	10.0	25.5	0.5	2.9	3.4	5.3	8.2	15.0
Free hydroperoxide	0.0	0.0	8.4	13.8	16.7	0.0	0.0	5.5	10.4	15.7	0.0	0.0	2.0	5.7	9.0	12.1
Bonded hydroperoxide	0.0	0.0	9.3	24.8	52.4	0.0	0.0	2.8	12.5	34.5	0.0	0.0	−0.8	4.1	11.6	22.7

standard deviation. This statistical analysis is similar to least-squares fitting a line through a set of single-measurement points. We reported p values obtained by ANOVA using Design Expert, Version 6.0.6 (Stat-Ease, Inc, Minneapolis, MN, USA).

Europium(III) stearate was synthesized by reacting europium(III) nitrate with sodium stearate in water. After boiling the mixture under reflux for 2 hours, it was cooled, and the resulting europium stearate was filtered and eluted with water until the pH of the effluent was neutral. The europium stearate residue was dried in a porcelain dish by lyophilization for at least 24 hours. The obtained europium(III) stearate was mixed with nascent polyethylene powder in the presence of ligroin, a petroleum ether in which the additive is soluble, providing good miscibility with the polyethylene powder. Subsequently, the solvent was removed from the nascent polyethylene powder by rotary evaporation. Two batches were mixed, one with 375 ppm and another with 3750 ppm of europium stearate, corresponding to concentrations of 0.35 and 3.5 mmol/L, respectively. The control material was nondoped UHMWPE of the same resin lot.

Consolidation was performed through slab compression molding by Orthoplastics Ltd (Bacup, Lancashire, UK) followed by machining into rectangular prisms with final dimensions of 80 mm × 30 mm × 25 mm. Two prisms per condition were gamma-irradiated in a nitrogen atmosphere at a dose of 35.1 ± 0.5 kGy (3.51 ± 0.05 Mrad) and two remained virgin. The prisms then were vacuum-packaged using a three-layer foil for shelf storage purposes. A fully automated RM2265 rotary microtome by Leica Microsystems Inc (Wetzlar, Germany) was used in the trimming mode to obtain thin films, 200 ± 15 µm thick with an area of 25 mm × 30 mm, perpendicular to the surface of the prism.

To accelerate the oxidation reactions in irradiated UHMWPE, the thin films were placed in an oven with airflow at $95 \pm 1^\circ\text{C}$ [8]. They were extracted from the oven briefly to collect spectra at 48-hour intervals.

FTIR spectra were collected at 32 scans per point from 400 to 4000 cm^{-1} and then normalized for chemical analysis of the films. A PerkinElmer Spotlight 2000 FTIR Microscope System (Shelton, CT) with imaging, autoimage, autofocus, and autoadjustment of the aperture capabilities was used. To minimize the interference bands that arise in FTIR spectra, both surfaces of the thin films were treated with ultrafine grit sand paper. The samples also were placed at an angle with respect to the plane perpendicular to the incident ray to diffract the light incident on the surface. Spectra were normalized at the 2020 wave-number CH_2 twisting peak, which has been shown to remain relatively unaffected by the changes in the polymer structure induced by thermal, high-energy, or mechanical treatments [5, 8, 31].

The height of this peak was set to 0.05 units of absorbance, which would correspond to a 100-µm thin film [8, 15]; the base of this peak was zeroed at 2100 cm^{-1} [8]. This consistent treatment for all samples allowed for quantitative comparison of the concentration of all species of interest [8].

After normalization, the spectra were processed through spectral subtraction using PerkinElmer Spectrum and Thermo Grams Suite software. Current spectroscopic technology obtains high signal-to-noise ratios and wave number specificities that consent spectral subtraction. Subtracted spectra allow effects of particular treatments on independent species to be evaluated independently [40]. Therefore, it currently is believed that oxidized species concentrations at particular processing stages are best quantified when using subtractions of normalized FTIR spectra [5, 8]. This technique has been used in the science of luminescence [14], biochemistry, organic chemistry, and polymer science [5, 7–9].

The contribution of the doping agent to the spectra was observed by subtracting the nonirradiated nondoped sample (virgin) spectrum from the nonirradiated doped sample spectrum. This procedure isolates the effect of the additive. The resulting spectrum was compared with the spectrum of pure europium stearate powder and the contributed peaks were located with respect to those of carbonyls and the normalization band.

Quantification of hydroperoxide and ketone peaks was chosen as an oxidation level indicator because these are the easiest peaks to detect through FTIR. The reaction between free radicals in UHMWPE and oxygen generates hydroperoxides. The same reaction and the decomposition of hydroperoxides engenders the formation of ketones and carboxylic acids during thermal degradation. Although all three are products of postirradiation oxidation, the latter are the species responsible for backbone scission and therefore backbone degradation [7], yet hydroperoxides and ketones are products of oxidation commonly reported to estimate UHMWPE oxidation level [2, 5–7, 9, 10, 15, 20, 30]. To obtain the amount of these products generated during aging alone, the spectrum collected from each irradiated material before aging was subtracted from the corresponding spectrum after aging. The differential concentration was quantified by using the corrected height of the resulting peaks at 3550 cm^{-1} , 3415 cm^{-1} , and 1718 cm^{-1} . Their heights were converted to concentrations using the Beer-Lambert law: $\text{Concentration} = \frac{\text{Absorbance}}{\epsilon \cdot b} \left[\frac{\text{Mol}}{\text{L}} \right]$, where b is the unit thickness chosen for normalization (100 µm [8]) and ϵ is the extinction coefficient [8, 21, 39] of each species.

To investigate the rate of oxidation during aging, and thus the stabilization performance of the additive with time, the concentrations of the aforementioned products were calculated at 48-hour intervals until substantial concentrations were achieved (144–192 hours).

Results

The contribution of the europium stearate to the FTIR spectra of UHMWPE was confined to an increase in the band located at 1545 cm^{-1} . The outstanding peak at 1545 cm^{-1} (Fig. 1) is the band attributable to stretching of the carboxylate anion structure of the europium stearate. This is the only predominant waveband contributing to the spectrum of the mixture. It was ruled out that the infrared absorption bands for the europium stearate additive interfered with those associated with the oxidation products or used for normalization because there was no contribution

of the additive to the FTIR spectra in the vicinity of the ketone, hydroperoxide, or CH_2 twisting peaks. The peak at 1545 cm^{-1} increased consistently with increasing concentration of the additive (Fig. 2) achieving a height of 0.0074 absorbance units for the europium stearate sample doped with 375 ppm and 0.0389 absorbance units for the one doped with 3750 ppm.

Irradiated samples showed signs of oxidation in the FTIR spectra after aging (Table 1), all consistently higher ($p < 0.001$) in nondoped than in doped samples at each time (Fig. 3). Oxidation consisted of generation of free hydroperoxides (3550 cm^{-1}), hydrogen-bonded

Fig. 1 The contribution of the additive (A) to the spectra obtained by subtracting the spectrum of a nondoped virgin UHMWPE (B) from the spectrum of europium(III) stearate doped virgin UHMWPE (C) was a carboxylate anion peak at 1545 cm^{-1} .

Fig. 2 The carboxylate anion peak at 1545 cm^{-1} increases proportionately with concentration from 375 ppm (A) to 3750 ppm (B).

Fig. 3 Conventional and 3750 ppm europium stearate-doped UHMWPE showed generation of free hydroperoxides, hydrogen-bonded hydroperoxides, and ketones during aging (48, 96, and 144 hours), all consistently higher in nondoped than in doped samples at each time. Spectral subtractions are shown.

hydroperoxides (3415 cm^{-1}), and ketones (1718 cm^{-1}). Ketone concentrations were higher for nondoped UHMWPE than UHMWPE doped with 375 ppm and than 3750 ppm of europium stearate ($p < 0.001$) in all aging times (48, 94, and 148 hours). The same was found for free hydroperoxide and bonded hydroperoxide concentrations.

The concentration of each oxidized product increased ($p < 0.001$) in each sample after every aging cycle, but acceleration was lowest in the doped material. The acceleration of the oxidation reaction was not initiated in UHMWPE doped with 3750 ppm until after 48 hours of aging; thus, there was no increase during this period for this condition and thus the latter effect was not present. Although acceleration in the formation of hydroperoxides and ketones was observed for all conditions, a reduction in the rate was observed for the doped samples when compared with the nondoped control (Fig. 4). Increased additive concentration reduced the absolute concentration of ketones and hydroperoxides and reduced the rate of acceleration of the reaction (Fig. 4). It was observed that the sample doped with 3750 ppm was less oxidized and degraded slower than the sample doped with 375 ppm and the latter was less oxidized and degraded slower than the control.

Irradiation affected all samples similarly bringing about the generation of ketones at concentrations of 2.5 mmol/L for nondoped, 2.7 mmol/L for doped at 375 ppm, and 2.9 mmol/L for doped at 3750 ppm. Similarly, a vinyl group (peak at 908 cm^{-1}) that was not evident for nonirradiated samples was measurable with heights of 0.0066, 0.0063, and 0.0069 absorbance units for nondoped, doped at 375 ppm, and at 3750 ppm samples correspondingly.

Discussion

Despite recent material improvements, in particular by crosslinking through irradiation [18], postgamma irradiation oxidation of UHMWPE is still a concern. Its oxidative decay is a well-known phenomenon that progresses throughout the implant's life cycle. Free radicals created during polymer production and sterilization become sites for oxidation [20]. Oxygen is entrapped in the polymer and diffuses into it during production, shelf life, and use in amounts large enough to allow propagation of oxidation [6, 18, 20]. Oxidation accelerates wear and may lead to pitting, delamination, and fracture of the liner resulting from embrittlement and loss in fatigue properties [19]. Efforts have mixed antioxidants, like alpha-tocopherol, with polyethylene to preserve the mechanical properties through oxidation scavenging mechanisms that substantially slow down oxidation reactions [8, 24–26, 38, 40, 41, 44]. However, lanthanides also have been used for polymer

Fig. 4A–C The formation of (A) ketones, (B) free hydroperoxides, and (C) bonded hydroperoxides accelerate in time during accelerated in irradiated UHMWPE. Acceleration was lower for doped UHMWPE when compared with conventional UHMWPE.

stabilization and thus we asked whether UHMWPE doped with europium stearate, which was gamma-sterilized, would: (1) allow for FTIR evaluation of the extent of oxidation without interference from stearate chains with the carbonyl bands; (2) have a decreased oxidation rate; and (3) oxidize less than conventional UHMWPE after accelerated aging.

Our study has some limitations. First, this is a pilot study to document and understand an effect through single-sample groups. Although the observed effect was strong, a replicate study would increase statistical confidence. Second, the study used an aging procedure that is

capable of accelerating the oxidative reactions taking place in irradiated UHMWPE during shelf aging and obtains reasonably similar oxidation to retrieved components [20], but it involves temperatures high enough to decompose hydroperoxides and is incapable of capturing the complex degradation process of polyethylene in the human body [1, 12, 13, 20]. Similarly, the materials were treated under specific conditions; thus, we did not attempt to predict the performance of UHMWPE doped at any concentration, under any treatment conditions, nor *in vivo*. Rather, the study compares samples undergoing an oxidative challenge to observe an antioxidant effect and performance under these conditions, yet we would expect similar effects under similar treatments of a europium-doped UHMWPE. Third, although the spectra of all samples showed the same types of oxidation products throughout the oxidative challenge, the actual mechanism cannot be elucidated based solely on these end products; however, it appears to be similar to the documented mechanism for UHMWPE. Fourth, although the similar ketone and vinyl concentrations among samples after irradiation suggest the additive did not prevent the action of ionizing radiation, the degree of crosslinking should be measured to determine the effect of radiation.

Postirradiation concentrations of oxidized species were lower for UHMWPE doped with europium stearate than conventional UHMWPE suggesting the additive interfered with the formation of these species. Oxidation of UHMWPE induced by ionizing radiation has been documented [5–9, 14, 15, 18–21]. High energy-induced secondary macroalkyl radicals react with oxygen-producing peroxy macroradicals (ROO•), which extract hydrogen from nearby molecules creating a new alkyl macroradical (R•) [18]. If the latter migrates along the molecule, a free hydroperoxide is formed [18]. If instead it reacts with oxygen immediately, hydrogen-bonded hydroperoxides result [18]. Both of these were observed in all of our aged samples yet at a decreasing concentration with increasing additive. During accelerated aging, because it is performed at temperatures at or greater than 70°C, the hydroperoxides can easily decompose to form ketones [18]. In all samples of this study, this thermoxidation resulted in formation of hydroperoxides as the first oxidized products of oxidation followed by ketones. Ketone formation does not only rely on decomposition of hydroperoxides; they are formed from macroalkyl radicals and oxygen as well [11, 18], which explains the trace level of ketones found in our virgin material.

A reduction in the oxidation acceleration rate proportional to additive concentration was observable in doped samples. Unlike ketones and as a result of their thermal instability, hydroperoxides have free radical formation capabilities and thus are responsible of oxidation

propagation [18], which can be clearly observed in the acceleration of the reaction of all the samples. Because the oxidation products observed in this study for all samples, doped and nondoped, were of the same nature, it seems like this additive does not alter the nature of the oxidation reaction mechanisms involving formation of free hydroperoxides, hydrogen-bonded hydroperoxides, and ketones followed by decomposition of hydroperoxides into ketones and other carbonyls [18], yet the acceleration rate was also decreased in the presence of europium stearate.

Europium stearate does not interfere with the normalizing peaks or those measured for oxidation in the FTIR spectra; thus, measuring ketone and hydroperoxide peaks remains a valid indication of oxidation level in the presence of europium stearate. The effect of the additive was contained to an identifiable vibration at 1545 cm⁻¹ distant from bands of interest.

The stabilizing effect of lanthanides has been attributed to their unique electron configuration of their outer shell [29, 45], although it appeared to us that the carboxylate anion is also directly involved in the mechanism. An interesting observation obtained during the analysis of the spectra of the samples under different treatment combinations was that wavebands related to stearate underwent a decrease of vibration energy after irradiation and aging. This consumption of the carboxylate anion has been documented previously in high-density polyethylene with other stearate additives that delay oxidation of the polymer [27]. It is reasonable to assume that europium(III) stearate chains undergo a structural transformation during irradiation. This change possibly could be a reduction to europium(II) with the liberation of stearate chains. This speculation would be consistent with reported data showing that lanthanides and stearates act symbiotically to prevent polymer oxidation [29].

This pilot study suggests the addition of europium(III) stearate to UHMWPE leads to an increase in the oxidation resistance of the polymer, confirming the hypothesis. Despite not being immune to oxidation with time, the doped material exhibited reduced hydroperoxide and ketone generation rate when compared with an irradiated, nondoped control material. Such a synergistic antioxidant action by europium with stearates along with biocompatibility and tracing capabilities could offer potential clinical applications for orthopaedic implants, possibly even implants doped with other antioxidants. Additional studies are needed to further develop the observations made in this pilot study. These should include a larger number of samples per condition that should be aged on the shelf, according to ASTM, and in air at 95°C. Similarly, higher irradiation doses should be used and the induced crosslinking studied. Derivatization would allow better isolation of the products.

Acknowledgments We thank Joachim Kunze for providing his expertise for the development and application of the mixing technique for the additive into the nascent powder. We also thank Orthoplastics for their support in sample processing. Finally, we thank all members of the Inorganic, Physical and Material Chemistry Department in the University of Turin for their invaluable contributions and expertise.

References

1. ASTM Standard F2003-2002 Standard Practice for Accelerated Aging of UHMWPE After Gamma Irradiation in Air. West Conshohocken, PA: ASTM International; 2002. Available at: www.astm.org. Accessed October 5, 2007.
2. ASTM Standard F2102-2006e1 Standard Guide for Evaluating the Extent of Oxidation in UHMWPE Fabricated Forms Intended for Surgical Implants. West Conshohocken, PA: ASTM International; 2006. Available at: www.astm.org. Accessed March 17, 2009.
3. Atkins PW, Overton TL, Rourke JP, Weller MT, Armstrong FA. *Shriver & Atkins Inorganic Chemistry*. 4th ed. New York: Freeman and Co; 2006.
4. Batchelor AW, Chandrasekaran M. *Service Characteristics of Biomedical Materials and Implants. Series on Biomaterials and Bioengineering*. Vol 3. London, England: Imperial College Press; 2004.
5. Bracco P, Brach del Prever EM, Cannas M, Luda MP, Costa L. Oxidation behaviour in prosthetic UHMWPE components sterilised with high energy radiation in a low-oxygen environment. *Polymer Degradation and Stability*. 2006;91:2030–2038.
6. Coote CF, Hamilton JV, McGimpsey WG, Thompson RW. Oxidation of gamma- irradiated ultrahigh molecular weight polyethylene. *J Appl Polym Sci*. 2000;77:2525–2542.
7. Costa L, Brach del Prever EM. *UHMWPE for Arthroplasty*. Torino, Italy: Edizioni Minerva Medica; 2000.
8. Costa L, Carpentieri I, Bracco P. Post electron-beam irradiation oxidation of orthopaedic ultra-high molecular weight polyethylene (UHMWPE) stabilized with vitamin E. *Polymer Degradation and Stability*. 2009;94:1542–1547.
9. Costa L, Luda MP, Trossarelli L, Brach del Prever EM, Crova M, Gallinaro P. Oxidation in orthopaedic UHMWPE sterilized by gamma-radiation and ethylene oxide. *Biomaterials*. 1998;19:659–668.
10. Edidin AA, Herr MP, Villarraga ML, Muth J, Yau SS, Kurtz SM. Accelerated aging studies UHMWPE: I. effect of resin, processing, and radiation environment on resistance to mechanical degradation. *J Biomed Mater Res*. 2002;61:312–322.
11. Edidin AA, Villarraga ML, Herr MP, Muth J, Yau SS, Kurtz SM. Accelerated aging studies UHMWPE: II. virgin UHMWPE is not immune to oxidative degradation. *J Biomed Mater Res*. 2002;61:323–329.
12. Feller RL. *Accelerated Aging: Photochemical and Thermal Aspects*. Marina del Rey, CA: Getty Conservation Institute; 1994.
13. Hemmerich KJ. General aging theory and simplified protocol for accelerated aging of medical devices. *Medical Plastics and Biomaterials Magazine*. 1998;July:16–23.
14. Jacobson K. Oxidation of ultrahigh molecular weight polyethylene (UHMWPE) part 2: critical examination of the total luminescence intensity (TLI) method for determining hydroperoxides. *Polymer Degradation and Stability*. 2006;91:2133–2139.
15. Jacobson K, Costa L, Bracco P, Augustsson N, Stenberg B. Effects of microtoming on oxidation of ultra high molecular weight polyethylene (UHMWPE). *Polymer Degradation and Stability*. 2001;73:141–150.
16. Khabbaz F, Albertsson AC. Rapid test methods for analyzing degradable polyolefins with a pro-oxidant system. *J Appl Polym Sci*. 2001;79:2309–2316.
17. Kunze J, Wimmer MA. A tracer method to determine extremely low wear rates of ultrahigh molecular weight polyethylene. *J ASTM International*. 2006;3:JA1100253. Available at: www.astm.org/digital_library/journals/jai/pages/JA1100253.htm. Accessed November 4, 2010.
18. Kurtz SM, ed. *UHMWPE Biomaterials Handbook: Ultra High Molecular Weight Polyethylene in Total Joint Replacement and Medical Devices*. 2nd ed. San Diego, CA: Academic Press; 2009.
19. Kurtz SM, Mazzucco M, Rimnac CM, Schroeder D. Anisotropy and oxidative resistance of highly crosslinked UHMWPE after deformation processing by solid-state ram extrusion. *Biomaterials*. 2006;27:24–34.
20. Kurtz SM, Muratoglu OK, Evans M, Edidin AA. Advances in the processing, sterilization, and crosslinking of UHMWPE for total joint arthroplasty. *Biomaterials*. 1999;20:1659–1688.
21. Lacoste J, Carlsson DJ. Gamma-, photo-, and thermally-initiated oxidation of linear low density polyethylene: a quantitative comparison of oxidation products. *J Polym Sci Part A Polym Chem*. 1992;30:493–500.
22. Montgomery DC. *Design and Analysis of Experiments*. 6th ed. New York, NY: John Wiley & Sons; 2004.
23. Ngai V, Wimmer MA, Kunze J. Rare earth stearates for wear determination of UHMWPE bearings. *Wear*. 2009;267:679–682.
24. Oral E, Greenbaum ES, Malhi AS, Harris WH, Muratoglu OK. Characterization of irradiated blends of alpha-tocopherol and UHMWPE. *Biomaterials*. 2005;26:6657–6663.
25. Oral E, Wannomae KK, Hawkins N, Harris WH, Muratoglu OK. Alpha-tocopherol-doped irradiated UHMWPE for high fatigue resistance and low wear. *Biomaterials*. 2004;25:5515–5522.
26. Oral E, Wannomae KK, Rowell SL, Muratoglu OK. Migration stability of alpha-tocopherol in irradiated UHMWPE. *Biomaterials*. 2006;27:2434–2439.
27. Osawa Z, Kurisu N, Nagashima K, Nakano K. The effect of transition metal stearates on the photodegradation of polyethylene. *J Appl Polym Sci*. 1979;23:3583–3590.
28. Paxton EW, Inacio M, Slipchenko T, Fithian DC. The Kaiser Permanente national total joint replacement registry. *Permanente J*. 2008;12:12–16.
29. Peng Z, Bin H, Su Q, Qu J. Study on the mechanism of rare earth PVC stabilizer. *J Rare Earths*. 2003;21:328–330.
30. Premnath V, Harris WH, Jasty M, Merrill EW. Gamma sterilization of UHMWPE articular implants: an analysis of the oxidation problem. *Biomaterials*. 1996;17:1741–1753.
31. Roy PK, Surekha P, Rajagopal C, Choudhary V. Comparative effects of cobalt carboxylates on the thermo-oxidative degradation of LDPE films. *J Appl Polym Sci*. 2007;103:3758–3765.
32. Roy PK, Surekha P, Rajagopal C, Choudhary V. Thermal degradation studies of LDPE containing cobalt stearate as pro-oxidant. *eXPRESS Polym Lett*. 2007;1:208–216.
33. Roy PK, Surekha P, Rajagopal C, Choudhary V. Degradation behavior of linear low-density polyethylene films containing prooxidants under accelerated test conditions. *J Appl Polym Sci*. 2008;108:2726–2733.
34. Roy PK, Surekha P, Raman R, Rajagopal C. Investigating the role of metal oxidation state on the degradation behaviour of LDPE. *Polym Degrad Stabil*. 2009;94:1033–1039.
35. Roy PK, Surekha P, Raman R, Rajagopal C, Choudhary V. Effect of cobalt carboxylates on the photo-oxidative degradation of low-density polyethylene: Part I. *Polym Degrad Stabil*. 2006;91:1980–1988.
36. Sakoda H, Fisher J, Lu S, Buchanan F. The effect of accelerated aging on the wear of UHMWPE. *J Mater Sci Mater Med*. 2001;12:1043–1047.

37. Schubert D, Dargusch R, Raitano J, Chan SW. Cerium and yttrium oxide nanoparticles are neuroprotective. *Biochem Biophys Res Commun*. 2006;342:86–91.
38. Shibata N, Tomita N. The anti-oxidative properties of alpha-tocopherol in gamma-irradiated UHMWPE with respect to fatigue and oxidation resistance. *Biomaterials*. 2005;26:5755–5762.
39. Stuart B. *Infrared Spectroscopy: Fundamentals and Applications*. Hoboken, NJ: John Wiley and Sons; 2004.
40. Teramura S, Sakoda H, Terao T, Endo MM, Fujiwara K, Tomita N. Reduction of wear volume from ultrahigh molecular weight polyethylene knee components by the addition of vitamin E. *J Orthop Res*. 2008;26:460–464.
41. Tomita N, Kitakura T, Onmori N, Ikada Y, Aoyama E. Prevention of fatigue cracks in ultrahigh molecular weight polyethylene joint components by addition of vitamin E. *J Biomed Mater Res*. 1999;48:474–478.
42. Toohey KS, Blanchet TA, Heckelman DD. Effect of accelerated aging conditions on resultant depth-dependent oxidation and wear resistance of UHMWPE joint replacement bearing materials. *Wear*. 2003;255:1076–1084.
43. Utsumi M, Nagata K, Suzuki M, Mori A, Sakuramoto I, Torigoe Y, Kaneeda T, Moriya H. Effects of calcium stearate addition of ultrahigh molecular weight polyethylene in direct compression molding. *J Appl Polym Sci*. 2003;87:1602–1609.
44. Wolf C, Krivec T, Blassnig J, Lederer K, Schneider W. Examination of the suitability of alpha-tocopherol as a stabilizer for ultra-high molecular weight polyethylene used for articulating surfaces in joint endoprostheses. *J Mater Sci Mater Med*. 2002; 13:185–189.
45. Zheng Y, Cai W, Fu M, Wang C, Zhang X. Rare earth stearates as thermal stabilizers for rigid poly(vinyl chloride) *J Rare Earths*. 2005;23:172–177.