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Oxidation resistance and abrasive wear resistance of vitamin E stabilized radiation crosslinked ultra-high molecular weight polyethylene

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ABSTRACT: The effect of gamma radiation on the oxidation and wear resistance of ultra-high molecular weight polyethylene (UHMWPE) has been extensively studied since these properties are critical for the longevity of UHMWPE components of total joint replacement prostheses. While gamma radiation increases wear resistance of UHMWPE, the free radical generated in the lamellar regions by radiation must be stabilized before oxidative degradation occurs as the polymer ages. Initially, post-radiation melting conducted to quench free radicals but this treatment also decreases its mechanical properties. Recently, it has been replaced by incorporation of Vitamin E into UHMWPE to combat oxidative degradation. In this study, we assessed wear resistance of Vitamin E stabilized UHMWPE under abrasive wear conditions and oxidation resistance by shelf-aging irradiated components for 2 years. Equilibrium swelling experiments showed that Vitamin E decreased crosslink density, which affected wear resistance, but oxidation resistance was better preserved with increasing concentration of Vitamin E. © 2016 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2016**, *133*, 44125.

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INTRODUCTION

One of the most successful polymeric biomaterials used in orthopedic implants since 1962 is ultra-high molecular weight polyethylene (UHMWPE), which is a common bearing material paired with a ceramic or metallic counterface in total joint replacement prostheses. There have been three primary factors that affect the long-term performance of UHMWPE in this biomedical application—oxidation resistance, wear resistance, and resistance to mechanical damage.[1]

It has been well established that oxidative degradation occurs with aging of gamma radiation sterilized UHMWPE implants, irradiated to a dose of 25–37 kGy.[1–6] Ionizing radiation of UHMWPE results in crosslinking and chain scission in the amorphous regions and the formation of free radicals in the lamellar regions of this semicrystalline polymer. Over time, the free radicals are believed to migrate to lamellar surfaces, where the presence of dissolved air (oxygen) in the amorphous regions can induce oxidation that can further result in chain scission. This slow oxidative degradation has been shown to cause delamination wear, cracking, and mechanical damage to UHMWPE components.[7,8] It also accelerates the generation of particulate wear in joint components.[9] The association of gamma radiation in air and aging can be attributed to chain scission since initially the resistance of UHMWPE to wear increases upon gamma radiation due to a high ratio of crosslinking to chain scission with limited oxidative chain scission. This initial increase in crosslinking indicated that it increases resistance of UHMWPE to wear and leads to the development of highly crosslinked UHMWPEs (HXLPEs), which were subjected to higher radiation doses of gamma or electron beam radiation (50–100 kGy dose range), not as a final sterilization step of the packaged implant but as a processing step for molded sheets and rods of UHMWPE, prior to the fabrication of the implant. Then the obvious problem was that there would be a higher concentration of free radicals trapped in the lamellar regions, which would lead to even higher oxidation than gamma sterilization doses. In order to quench free radicals the first generation of HXLPEs were subjected to post-radiation melting or annealing close to the melting temperature prior to machining of the implant, packaging, and sterilization using methods that did not involve ionizing radiation, such as ethylene oxide sterilization. Post-radiation treatments removed the concern of oxidation due to irradiation and also high wear rate of the implant since HXLPEs have shown a high resistance to wear in laboratory tests[10,11] as well as in early clinical studies.[12,13]

A major drawback of HXLPEs is that both the radiation dose as well as the post-radiation heat treatments decreased several mechanical properties, such as tensile elongation,[10,11,14–17]

ultimate tensile strength,[10,11,14] J-integral fracture toughness,[14] and resistance to fatigue crack propagation.[18–20] While irradiation has been unavoidable due to its large increase in wear resistance, post-radiation treatments to reduce free radical content in irradiated HXLPEs can be avoided by incorporation of a stabilizer, such as Vitamin E or other biocompatible antioxidants.[21–28] Vitamin E can either be blended into the UHMWPE resin prior to molding[29] or diffused into the implant after radiation.[30] The advantage of the latter over the former process is that it was shown that Vitamin E can decrease the formation of crosslinks in the amorphous regions by scavenging free radicals before crosslinking can occur. It was shown that with increasing concentration of Vitamin E, there was increased suppression of crosslinking, leading to higher wear rates in a laboratory multidirection pin-on-disk wear test in which the Vitamin E stabilized HXLPE disks with varying concentration of Vitamin E were articulated against smooth CoCr disks. While such pristine, smooth CoCr surfaces serve well to obtain relative wear resistances, in the clinical situation, there often are scratches on the metallic counterface due to the presence of bone shards or other hard, third body particulates.

In this two part study, we evaluated the wear resistance of HXLPEs under abrasive conditions, meant to mimic wear more closely to clinical wear, in order to determine if Vitamin E preserved high wear resistance of HXLPEs. In the second part, we shelf-aged HXLPEs for two years to determine how differing concentrations of Vitamin E would preserve oxidation resistance.

EXPERIMENTAL

Compression molded UHMWPE billets of GUR 1050 (Ticona Inc, Bayport, TX) containing 0, 0.1, and 0.5 wt % α-tocopherol (synthetic Vitamin E) were provided by MediTECH Medical Polymers (Ft Wayne, IN). Blending of Vitamin E into UHMWPE powder is carried out by dissolving the appropriate amount of Vitamin E into ethanol and stirring until dissolution. The solution is then added to the UHMWPE with continuous stirring until the ethanol evaporates and the Vitamin E coats the UHMWPE resin powder. This is followed by compression molding at a temperature of 180 °C and an applied pressure of 5 MPa, followed by slow cooling to room temperature and then removal of the applied load. For each Vitamin E concentration, UHMWPE billets were gamma irradiated to a dose of 0, 30, and 100 kGy, respectively.

A Q1000 (TA instruments, New Castle, DE) differential scanning calorimeter (DSC) operating at a scan rate of 10 °C/min was used to measure the degree of crystallinity. Three specimens per group were subjected to DSC. Percentage crystallinity was obtained as $X_c = 100 \times \delta H / \delta H_f$, where δH is the area under the endotherm and δH_f is the heat of fusion of 100% crystalline PE (293 J/g).[31]

Equilibrium swelling experiments were performed on pre-weighed cubic samples of ~20 mg weight by immersing into xylene maintained at 135 °C using a silicone oil bath for a period of 3 h.[32] A total of six specimens per group were subjected to equilibrium swelling. The solvent swollen samples were sealed into pre-weighed glass vials and re-weighed. Swell ratio (q_{eq}), crosslink density (ν_d), and molecular weight between crosslinks (M_c) were calculated using the following three equations[10,32]:

$$q_{eq} = \frac{\text{Volume of xylene absorbed} + \text{Initial volume of sample}}{\text{Initial volume of sample}}$$

$$\nu_d = \frac{-\ln\left(1 - q_{eq}^{-1}\right) + q_{eq}^{-1} + \mathrm{X} q_{eq}^{-2}}{V_1 q_{eq}^{-1/3}}$$

$$M_c = (\nu \nu_d)^{-1}$$

where $V_1 = 136$ cm^3/mol, $\mathrm{X} = 0.33 + 0.55/q_{eq}$, and $\nu = 920$ g/dm^3.

Each billet was thereafter shelf-aged for a period of 2 years, along with unirradiated controls. The laboratory environment maintains a temperature of 20 °C and a relative humidity of 60%. Even if there were some periodic fluctuations in these values over a period of 2 years, the ageing conditions were identical for all groups of specimens since they were stored together and therefore we expect the results to be internally consistent. Fourier transform infrared (FTIR) spectroscopy was performed using a Nicolet Magna 860 spectrometer on thin sections of PE of 100–200 μm thickness, prepared using a Leitz Wetzlar sledge microtome. A total of six specimens per group were subjected to FTIR analyses. The FTIR beam was directed at the subsurface region where peak oxidation was located. The microtomed sections were polished with 360 grit emery paper followed by 600 grit emery paper to decrease the Fourier rippling effect. The transvinylene index, TVI, was defined as the ratio of the area under the 965 cm^{-1} transvinylene and 1900 cm^{-1} absorbances.[33,34] The oxidation index, OI, was defined as the ratio of the area under the 1740 cm^{-1} carbonyl and 1370 cm^{-1} methylene stretching absorbances.[35]

The billets were machined into cylindrical pins of 20 mm length and 9 mm diameter. The counterface comprised CoCr discs ($R_a = 0.45$ μm), scratched along random directions using 320 grit emery paper in accordance with a previously established method.[36] A total of 4 pins and a soak control were used for all wear tests. A square wear path of 5 mm × 5 mm dimensions were digitized into an OrthoPod™ (AMTI, Watertown, MA) multi-directional wear tester operating at 1 Hz and with a constant applied load of 192 N (applied stress of 3 MPa, within the physiological stress of 2–5 MPa on the hip joint). A bovine serum (JRH Biosciences) lubricant was adjusted to contain 23 g/L protein, 20 m*M* EDTA, and 0.2% sodium azide. The serum was maintained at 37 °C using a recirculating water bath. Gravimetric weight loss per pin was determined approximately every 200,000 cycles for over 1 million cycles and converted into wear factor values, *k*.

Statistical analysis was conducted using ANOVA with Fisher's protected least significant difference *post hoc* test in which a *P*-value less than 0.05 was used to define significance.

RESULTS AND DISCUSSION

Crystallinity

The degree of crystallinity of the Vitamin E stabilized HXLPEs ranged from 47.1 to 47.9% but there was no statistically significant difference in the crystallinity for all Vitamin E concentrations and radiation dose (see Figure 1). A uniform crystallinity for all Vitamin E stabilized HXLPEs was essential since we did not want differences in crystallinity to affect wear or oxidation

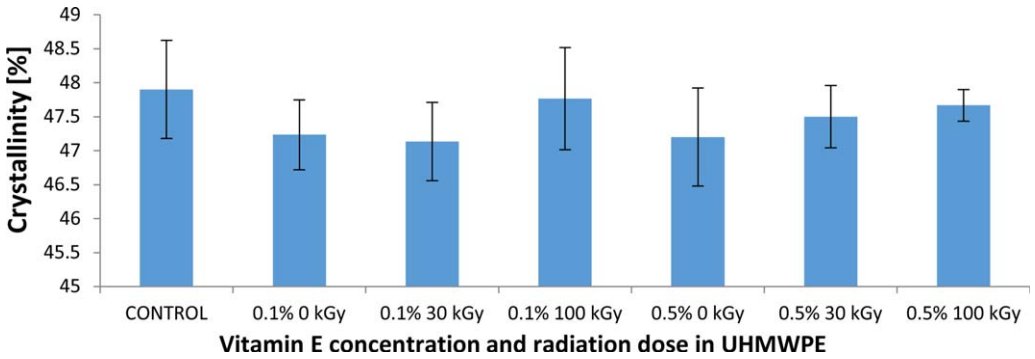

Figure 1. The degree of crystallinity of various groups of polyethylene including unirradiated UMWPE control and HXLPEs with various concentrations of Vitamin E and radiation dose (average ± standard deviation). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

rates, that is possible[37] and would complicate the analysis of the results. This also shows that over a concentration range of 0–0.5%, Vitamin E does not alter crystallization rates or mechanisms since all of the billets of Vitamin E stabilized HXLPEs were molded under identical conditions, but showed no statistically significant difference in crystallinity. If the nucleation and crystallization rate were affected by the presence of such low concentrations of Vitamin E, then we could have expected a systematic and statistically significant increase or decrease in the crystallinity with Vitamin E concentration, but this was not the case. Therefore, we conclude that Vitamin E could not have significantly altered the mode and rate of crystallization.

Crosslink Density

Equilibrium swelling experiments showed that the swell ratio systematically increased with increase in Vitamin E, regardless of radiation dose (see Table I). As expected, the high radiation dose led to a lower swell ratio due to the formation of a denser crosslinked network. The crosslink density decreased with increasing Vitamin E content. For the 30 kGy dose, the crosslink density was 6% lower for the HXLPE containing 0.1% Vitamin E and 28% lower for the HXLPE containing 0.5% Vitamin E compared to the HXLPE with no Vitamin E present. And consequently, the molecular weights between crosslinks were 7% and 39% higher, respectively. At the 100 kGy dose, the crosslink density was 24% lower for the HXLPE containing 0.1% Vitamin E and 59% lower for the HXLPE containing 0.5% Vitamin E compared to the HXLPE with no Vitamin E present. As a consequence, the molecular weights between crosslinks were 26% and 139% higher, respectively. Thus, 0.5% Vitamin E content substantially affected crosslink density and molecular weight between crosslinks at both radiation dose, but more so at the higher radiation dose. Such a suppression of crosslinking by the incorporation of Vitamin E has been previously reported, but for lower concentrations.[29] One must note however that the equilibrium swelling method has a few limitations. It requires the polymer to be heated and for the lamellae to melt in order to swell. This means that the free radicals trapped within the lamellar regions would get released and then form additional crosslinks since the macromolecules would have high mobility in solution. Thus equilibrium swelling counts crosslinks that are formed during the swelling process in addition to the actual crosslinks that are present in the amorphous regions of the polymer at room temperature. A previous study demonstrated modeling of a solid-state deformation method to measure crosslinks but the solid-state deformation process is rate dependent so such a method would only be useful if it were to be standardized.[32] It must also be noted that the presence of differing amounts of Vitamin E in the polymer would also affect the additional crosslinks formed during the swelling process since their ability to scavenge free radicals in solution prior to the formation of additional crosslinks would be enhanced at higher concentration of Vitamin E. Thus, the equilibrium swelling would not only provide a higher number of crosslinks than there are in the polymer but they would also preferentially provide a higher crosslink density at lower concentrations of Vitamin E than higher concentrations.

Wear Resistance

The highest wear rate was observed in control, non-irradiated GUR 1050 UHMWPE with a wear factor value of 3.01×10^{-6} mm^3/Nm (see Figure 2). Under conditions of abrasive wear,

Table I. Swell Ratio, Crosslink Density, and Molecular Weight between Crosslinks for UHMWPE Irradiated to 30 and 100 kGy Dose, respectively, Containing 0, 0.1, and 0.5 Weight % Vitamin E

Radiation dose (kGy)	Vitamin E (%)	Swell ratio	Crosslink density (mol/dm^3)	Molecular weight between crosslinks (g/mol)
30	0	5.19 ± 0.37	0.079 ± 0.010	11,741 ± 1372
	0.1	5.41 ± 0.23	0.074 ± 0.005	12,547 ± 865
	0.5	6.32 ± 0.28	0.057 ± 0.004	16,299 ± 1201
100	0	2.74 ± 0.28	0.262 ± 0.055	3653 ± 804
	0.1	3.08 ± 0.09	0.200 ± 0.011	4619 ± 273
	0.5	4.35 ± 0.30	0.107 ± 0.014	8714 ± 1021

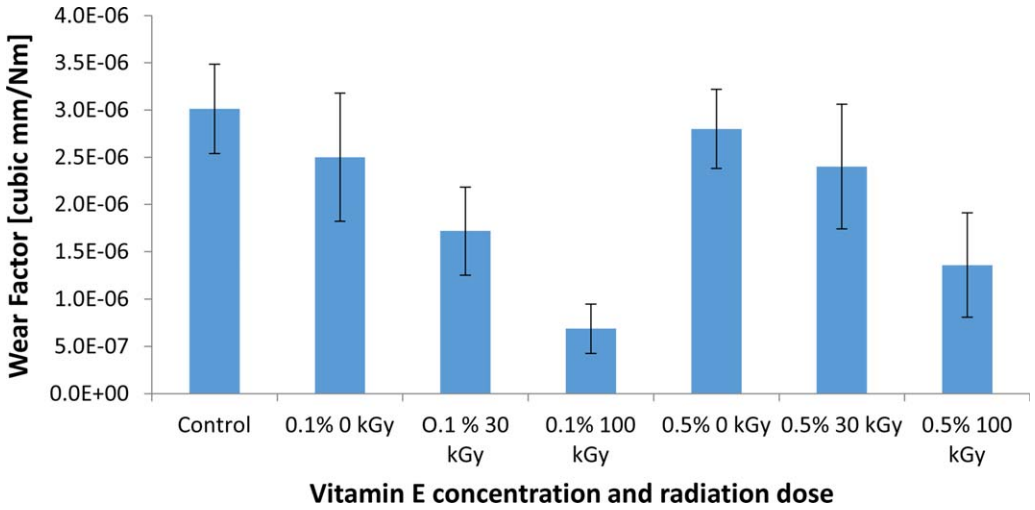

Figure 2. Wear factor of control, unirradiated polyethylene containing no Vitamin E, and various groups of radiation crosslinked polyethylene containing varying weight percentages of Vitamin E (average ± standard error). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

there was no statistically significant difference ($P > 0.05$, ANOVA) in wear rate of the non-irradiated UHMWPE samples regardless of Vitamin E concentration. For a Vitamin E concentration of 0.1 wt %, the wear rates of the 30 kGy and 100 kGy HXLPEs were lower than the wear rate of control UHMWPE by 43% and 77%, respectively. For a vitamin E concentration of 0.5 wt %, there was no statistically significant difference in wear rate of the 30 kGy irradiated UHMWPE and control UHMWPE. However, the wear rate of 100 kGy-irradiated UHMWPE with 0.5 wt % Vitamin E was 55% lower than the wear rate of control UHMWPE. This indicated that an increase in Vitamin E content affects wear rates of HXLPEs not merely under conditions in which the articulation is against smooth, pristine CoCr counterfaces,[29] but also under abrasive conditions that are often observed clinically. It suggests that if a large Vitamin E content is desired to combat oxidation due to free radicals associated with other external sources such as cyclic loads[38] or infiltration of the implant with oxidizing species,[39] then the UHMWPE must be subjected to higher radiation doses in order to counter the effects of reduced crosslink density and wear resistance. A larger radiation dose would however imply a larger reservoir of free radicals in the lamellar regions of HXLPEs, thereby requiring more Vitamin E. Therefore, alternate crosslinking processes[25] or alternate antioxidants, which do not suppress crosslinking to such a large extent,[40] may be preferred to conventional irradiation of HXLPEs at room temperatures containing Vitamin E. It must be recognized that the type of wear investigated in this study was primarily the generation of particulate wear and did not investigate other modes of wear such as those related to fatigue processes like delamination wear. Such wear modes would require more knee-like articulation, so the results of this study can only be interpreted in terms of slowing the rate of generation of wear particles of UHMWPE under hip-like articulation involving a multidirectional wear pattern. While the wear pattern was simplified to a square pattern and in reality the gait cycle of patients involves a pseudo elliptical wear pattern, the results of this study can only be interpreted in terms of ranking of the materials rather than predicting the relative magnitude of wear rates clinically.[41]

Oxidation Resistance

The transvinylene index, TVI, for 0, 30, and 100 kGy irradiated UHMWPE, regardless of Vitamin E content, showed an increase with radiation dose (see Figure 3). Although there were small differences measured in the TVI between various samples irradiated to an identical dose, the average TVI for 30 kGy and 100 kGy dose was 0.067 ± 0.004 and 0.242 ± 0.009, and was negligibly low for unirradiated controls (see Figure 3). The ratio of TVIs for the 100 kGy irradiated HXLPEs to that of 30 kGy was 3.6 while the ratio of radiation dose was 3.33, which show the correspondence between radiation dose and the formation of tranvinylene unsaturations in the otherwise linear UHMWPE macromolecules.

As expected, the oxidation index for UHMWPE without Vitamin E demonstrated a statistically significant increase with irradiation dose (see Figure 4). There was measurable oxidation in the non-irradiated control samples as well, probably due to

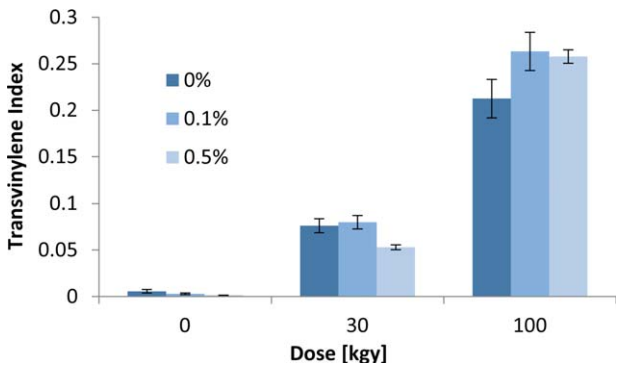

Figure 3. Transvinylene indices of polyethylene containing various weight percentages of Vitamin E and irradiated to 0, 30, or 100 kGy (average ± standard error). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

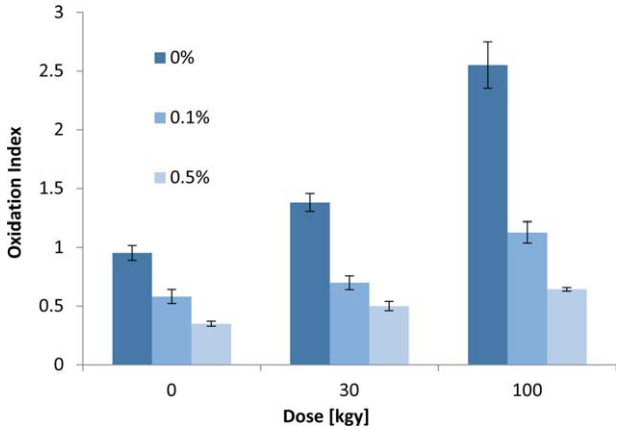

Figure 4. Oxidation indices of polyethylene containing various weight percentages of Vitamin E and irradiated to 0, 30, or 100 kGy (average ± standard error). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

thermal oxidation during processing. At all concentrations of Vitamin E, there was a statistically significant decrease in oxidation compared to the pure UHMWPE components. As expected, the oxidation index was higher in the 100 kGy dose UHMWPEs compared to the 30 kGy dose UHMWPEs for all concentrations of Vitamin E except for 0.5% Vitamin E dose, which showed no statistically significant increase in oxidation at the higher irradiation dose of 100 kGy. For the series of UHMWPEs with no Vitamin E, the oxidation index of 30 kGy HXLPE was 45% higher than the non-radiated UHMWPE and that of 100 kGy HXLPE was 168% higher. For the 0.1% Vitamin E series, the corresponding increases with radiation dose were 20% and 94% higher, respectively, and for 0.5% Vitamin E series, they were 43% and 84%, respectively. Clearly, the radiation dose increased oxidation in HXLPEs, regardless of Vitamin E content. However, when comparing UHMWPE with no Vitamin E and 0.1% Vitamin E and 0.5% Vitamin E UHMWPEs, respectively, for non-irradiated UHMWPE, thermal oxidation decreased by 39% for 0.1% Vitamin E content and 63% for 0.5% Vitamin E content. For 30 kGy irradiation, the oxidation in 0.1% Vitamin E and 0.5% Vitamin E HXLPEs was 49% lower and 64% lower, respectively, compared to HXLPE without Vitamin E and for 100 kGy, it was 56% and 75% lower, respectively. Thus, with increasing concentration of Vitamin E, there was greater oxidation induced in Vitamin E. So from the standpoint of oxidation resistance alone, Vitamin E was very effective in retarding oxidation over a span of two years of shelf aging. Most orthopedic implants are not stored in the shelf for such a long time before implantation, so these effects are expected to be much larger than for HXLPE components of total joint replacements. Also, *in vivo* oxidation is expected to be at a lower rate than shelf-aged HXLPEs.[1,2,42]

A limitation of this study is that it only focuses on shelf aging and does not measure *in vivo* oxidation. However, it is well known that oxidation via shelf aging is more aggressive compared *in vivo* oxidation.[1,2,42] Therefore, it can be anticipated that Vitamin E would be effective in imparting oxidation resistance in both environments. Another limitation of this study is that it conducts wear tests that investigate the generation of particulate debris as generated in hip articulation but does not investigate fatigue related wear, such as delamination wear produced in knee components. However, in both the oxidation and wear investigations, the ranking of oxidation and wear resistance with respect to radiation dose and Vitamin E content should be unchanged, at least for the application of UHMWPE in hip components of joint replacement prostheses.

CONCLUSIONS

The main conclusions of this study are that Vitamin E at a concentration range of 0.1–0.5% is effective in inducing oxidation resistance in HXLPEs. Second, radiation crosslinking induces high wear resistance in UHMWPE compared to non-crosslinked UHMWPE. Third, with increasing concentration of Vitamin E, there is a larger decrease in crosslink formation due to the free radical scavenging capability of Vitamin E, which can result in a lower resistance to wear. Thus, for conventional processing conditions, in which Vitamin E is blended into the UHMWPE resin prior to molding and crosslinking, a balance must be sought between inducing oxidation resistance and preventing suppression of crosslink formation which has consequences for its wear resistance in this clinically relevant application.

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