Vitamin E can be used to hinder scissioning in radiation cross-linked UHMWPE during high-temperature melting

Brinda N. Doshi,[1] Jun Fu,[1,2] Ebru Oral,[1,2] Orhun K. Muratoglu[1,2]

[1]Harris Orthopedic Laboratory, Massachusetts General Hospital, Boston, Massachusetts 02114
[2]Department of Orthopaedic Surgery, Harvard Medical School, Boston, Massachusetts 02115
Correspondence to: E. Oral (E-mail: eoral@partners.org)

ABSTRACT: High-temperature melting (HTM) of ultrahigh molecular weight polyethylene (UHMWPE) was shown to improve its elongation and toughness. This was believed to be due to increased scissioning and increased diffusion of polymer chains. It was hypothesized here that the toughness of previously radiation cross-linked UHMWPEs could also be improved by HTM. To test this hypothesis, the wear resistance, tensile mechanical properties, and Izod impact strength of radiation cross-linked virgin (no additive) and antioxidant-blended (with vitamin E) UHMWPEs were tested. The results suggested that although the impact strength of cross-linked UHMWPEs could be improved significantly by HTM, the wear resistance was decreased. Thus, this procedure can be optimized to be especially suited in high-stress applications, such as total knee replacements with lessened wear concerns. © 2015 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2015**, *132*, 42735.

INTRODUCTION

High-temperature melting (HTM) of ultrahigh molecular weight polyethylene (UHMWPE) consolidated first into total joint implant preforms (oversized versions of medical implants to be subsequently machined into final implant form) has been shown to improve elongation without sacrificing ultimate break stress.[1] This improvement was attributed partly to the increased chain mobility of the polymer at high temperatures above the melting point.[1] Because of the extremely high molecular weight of this specialized polymer, its consolidation is possible only through melt-state fusion via compression molding or ram extrusion.[2] Although this process results in integrated solid forms, which are viable as implant materials, the intergranular fusion is only partially complete, and the material retains a memory of the intergranular boundary.[3] By HTM, the diffusion of polymer chains through the grain boundary can be enhanced. An additional effect of HTM is chain scissioning, which can be quantified by the formation of terminal vinyl groups.[4] The amount of these functional groups can be controlled by the temperature of melting as well as duration and can be used subsequently to cross-link the polymer. The combined effects of chain scissioning and increased chain mobility at high temperature enable the elimination of structural and fusion defects and, thus, result in improved toughness.[1]

Currently used compression-molded UHMWPE without HTM is cross-linked after consolidation by exposure to ionizing irradiation.[5,6] Radiation cross-linking was shown to decrease the wear rate of UHMWPE implant bearing surfaces,[7] also resulting in a significant decrease in wear debris-induced periprosthetic osteolysis.[8] In the amorphous phase of this semicrystalline polymer, cross-linking occurs by the recombination of free radicals initiated by radiation.[9] But, some free radicals are trapped in the crystalline regions[10] and, over time, react with diffused oxygen and cause oxidative degeneration in the material.[11,12] The elimination of the residual free radicals in the crystalline regions by the melting of crystals prior to implantation[6] or the incorporation of antioxidants (most commonly vitamin E) into the cross-linked polymer[13] are two methods that are effective in improving the oxidation resistance of cross-linked materials *in vitro*[14–17] and *in vivo*.[18,19]

Despite increasing wear resistance, high-dose radiation cross-linking (50–100 kGy) of UHMWPE followed by melting of the crystalline regions to eliminate residual free radicals for long-term oxidative stability resulted in reduced fatigue strength, and the increased risk of fatigue damage modes became a concern, especially in high-stress applications.[20–22] Thus, there is a need to improve the toughness of cross-linked UHMWPE bearing surfaces without sacrificing their wear and oxidation-resistant properties. The effects of HTM, which have significantly
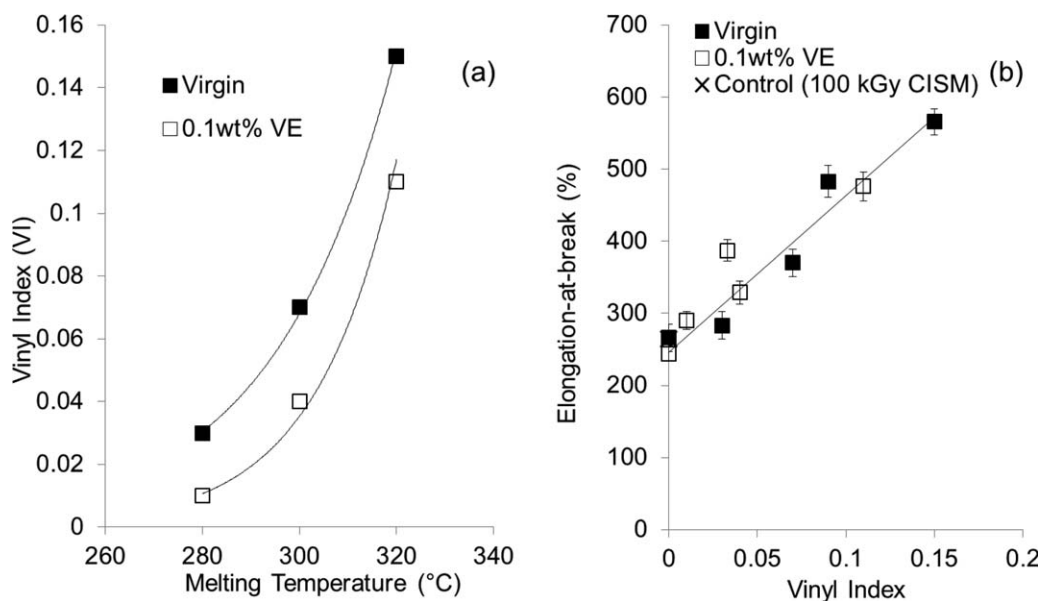
Figure 1. The (a) vinyl index as a function of increasing melting temperature and (b) elongation-at-break as a function of the vinyl index of irradiated and HTMed virgin and vitamin E-blended UHMWPEs. Control was 100 kGy-irradiated virgin UHMWPE conventionally melted at 170°C.

improved the impact toughness of UHMWPE without cross-linking, have not been studied for radiation cross-linked UHMWPE. In this study, we hypothesized that HTM of radiation cross-linked virgin and vitamin E-blended UHMWPEs would improve further the toughness of UHMWPE without sacrificing its wear resistance.

EXPERIMENTAL

To test our hypothesis stated earlier, we determined the tensile mechanical properties and Izod impact strength of virgin and vitamin E-blended UHMWPEs irradiated to 150 kGy with an electron beam and then subjected to HTM at 280, 300, and 320°C for 5 h. We also investigated the effects of HTM on the wear resistance, cross-link density, and crystallinity by using pin-on-disc wear testing, gravimetric swelling, and differential scanning calorimetry, respectively. A schematic describing the sample groups prepared for testing in this study is shown in Figure 1.

Preparation of Vitamin E/UHMWPE Blends Followed by Consolidation, Radiation Cross-Linking, and HTM
Vitamin E (D,L-α-tocopherol, DSM, Parsippany, NJ) was dissolved in isopropanol with a concentration of 20 g L^{-1}. Medical-grade GUR 1050 UHMWPE powder (Orthoplastics, Lancashire, UK; approximate molecular weight 6 million g mol^{-1}) was blended and stirred with the vitamin E/isopropanol solution to make a homogeneous blend with a concentration of 2 wt %. This blend was dried in a convection oven under vacuum at 60°C for 7 days and diluted with GUR 1050 powder to obtain a vitamin E concentration of 0.1 wt %.

The 0.1 wt % vitamin E blend or virgin resin was then placed in an aluminum mold and preheated under partial pressure (argon) at 194°C for 1.5 h. Further, the powder/mold assembly was transferred onto the preheated platen of a consolidation press (Carver, Wabash, IN) and consolidated at 20 MPa for 5

min. The polymer was cooled down under pressure to room temperature and then the pressure was released.

The consolidated pucks were irradiated with the 10-MeV electron beam in air (Iotron Industries USA, Columbia City, IN) at a rate of 50 kGy/pass, to a total dose of 150 kGy, at room temperature. These irradiated samples were then melted at 280, 300, and 320°C for 5 h in a preheated convection oven (Despatch Industries, Minneapolis, MN), under an atmosphere of nitrogen, and then cooled down at an average rate of ~2.5°C min^{-1} to 40°C. The 150 kGy-irradiated virgin and 0.1 wt % vitamin E UHMWPE materials, which did not undergo any HTM, were used as controls in this study. Virgin UHMWPE irradiated to 100 kGy was conventionally melted after irradiation, at 170°C for 4 h, and used as controls, denoted as "CISM" in this study.

All characterization samples in this study with the exception of section for FTIR were machined after removing the surfaces (about 1 mm) exposed to irradiation to minimize any effects of radiation-related oxidative effects.

Determination of Vinyl Index by Fourier Transform Infrared Spectroscopy
To quantify chain scissioning using the (terminal) vinyl index of the prepared UHMWPE materials, 1-cm cubes ($n = 3$ for each condition) were machined from all the experimental groups as described earlier. The cubes were then cut at the center and microtomed into 150-μm sections, by using a Leica manual microtome. The thin sections were scanned by using an LMA-500 FTIR microscope (Bio-Rad Laboratories, Natick, MA) from 400 to 4000 cm^{-1} from one edge of the thin section corresponding to a free surface of the cube along its depth at 500 μm increments.

The vinyl index was obtained by normalizing the area under the absorbance at 900 cm^{-1} (880–920 cm^{-1}) against that of the internal reference absorbance at 1895 cm^{-1} (1850–1985 cm^{-1}).

Measurement of Cross-Link Density by Gravimetric Swelling
Small cubes (approximately 3 mm^3, $n = 3$) were cut from all experimental groups and swollen in 25 mL xylene (Fisher Scientific, Waltham, MA) at 130°C in an oil bath (Fisher Scientific, Isotemp 3016HD) for 2 h to reach equilibrium swelling. The initial weight and xylene uptake were used to calculate the swell ratio and the cross-link density by using the density of the dry polymer as 0.94 g cm^{-3} and the density of xylene at 130°C as 0.75 g cm^{-3}. The cross-link density of the samples (d_x) was calculated using the following equations according to ASTM F2214 Standard Test Method for *In Situ* Determination of Network Parameters of Cross-linked UHMWPE:[23,24]

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

$$X = 0.33 + \frac{0.55}{q_{eq}} \qquad (2)$$

where, q_{eq} is the equilibrium swelling ratio, X is the interaction parameter, and the specific volume of xylene, V_1, was 136 cm^3 mol^{-1}.

Determination of Wear Rate by Bidirectional Pin-On-Disc Test
Cylindrical pins (9 mm diameter and 13 mm long, $n = 3$ each) were machined (Eastern Tools, Medford, MA) from all experimental groups (Figure 1). The pins were tested for wear with a cross-shear, rectangular pattern (5 × 10 mm) against polished CoCr discs at 2 Hz in undiluted, preserved bovine serum as a lubricant. The pins were cleaned and weighed before testing and at approximately every 0.16 million cycles (MC) after the first 0.5 MC until a total of 1.2 MC. The wear rate was determined by a linear regression of the weight loss as a function of number of cycles from 0.5 to 1.2 MC.[25]

Measurement of Izod Impact Strength
Samples with dimensions of 63.5 × 12.7 × 6.35 mm^3 ($n = 5$) were double notched according to ASTM F648 and ASTM D256 and were impact fractured with a pendulum at Orthoplastics. The energy loss of the pendulum after impacting to complete fracture was recorded as the impact strength of the samples. The impact strength was reported in kJ m^{-2}.

Measurement of Mechanical Properties Using a Tensile Tester
Type V samples ($n = 5$) were stamped out of 3.2 mm thin sections according to ASTM-D638 for all experimental groups as listed in Figure 1. These samples were tested in tension (Insight™, MTS, Prairie, MN) with a crosshead speed of 10 mm min^{-1}. The stress and strain were recorded at 100 Hz, and the gauge length was monitored using a laser extensometer. The ultimate tensile strength (UTS), yield strength (YS), and elongation-at-break (EAB) were calculated.

Measurement of Peak Melting Points and Crystallinity Using Differential Scanning Calorimetry
Small samples (3–5 mg) of all experimental groups (Figure 1) were placed in standard aluminum pans. The samples were then placed in the furnace of a TA 1000 differential scanning calorimeter (TA Instruments, Newark, DE) and heated from −20°C to 180°C at 10°C min^{-1}, cooled down to −20°C at −10°C min^{-1}, and heated again to 180°C at 10°C min^{-1} with a nitrogen flow of 5 L min^{-1}. The peak temperature was taken as the melting temperature (T_m) of the polymers. The percentage crystallinity was calculated by normalizing the integral from 20°C to 160°C of the first heating curve by the fusion heat of 100% crystalline polyethylene (291 J g^{-1}).

Student's *t*-test was conducted, and statistical significance was denoted as $P < 0.05$.

RESULTS

Chain Scissioning Quantified by the Vinyl End Groups
For the irradiated and high-temperature melted (HTMed) virgin and 0.1 wt % vitamin E-blended UHMWPEs, the vinyl index, which is a measure of the vinyl end groups (R—CH=CH$_2$) formed in the material,[1] increased significantly after HTM with increasing melting temperature [Figure 1(a)]. The irradiated and HTMed virgin materials showed higher vinyl index as compared with the 0.1 wt % vitamin E-blended UHMWPEs at the same HTM temperatures ($P = 0.002$ for 280°C, $P = 0.002$ for 300°C, and $P < 0.001$ for 320°C).

Mechanical Properties (Impact Strength, Elongation-at-Break, and Ultimate Tensile Strength)
The EAB increased linearly with vinyl index for both the irradiated virgin and vitamin E-blended UHMWPEs as a result of HTM [Figure 1(b)]. The HTM samples had significantly higher EAB than their non-HTM counterparts ($P < 0.001$ for all HTM temperatures). All of the irradiated and HTMed virgin and vitamin E-blended UHMWPEs except the UHMWPEs melted at 280°C had higher EAB than that of the 100 CISM control [$P < 0.05$; Figure 2(b)].

The impact strength of irradiated and HTMed virgin UHMWPE increased with increasing vinyl index up to a vinyl index of about 0.07 [Figure 2(a)] and with increasing EAB up to an EAB of approximately 400% [Figure 2(b)] and then decreased rapidly with a further increases in vinyl index and EAB. In contrast, for irradiated and HTMed vitamin E-blended UHMWPE, the impact strength continued to increase above these values. The impact strength of the irradiated virgin UHMWPE melted at 300°C and the vitamin E-blended UHMWPE melted at 300 and 320°C were significantly higher than that of 100 kGy CISM control ($P < 0.05$), and the impact strength of irradiated virgin UHMWPE melted at 320°C was significantly lower than that of 100 kGy CISM control ($P < 0.05$).

The UTS and the YS did not change with increasing vinyl index for both radiation cross-linked virgin and vitamin E-blended UHMWPEs [Figure 3(a,b)]. The UTS was lower for the CISM control as compared with all the sample groups ($P < 0.05$) except irradiated and HTMed virgin UHMWPE melted at 320°C ($P = 0.008$). Looking at the true stress–strain curves revealed that stress hardening occurred at somewhat higher strains for the HTMed UHMWPE and the ultimate true stress was higher [Figure 4(a,b)].
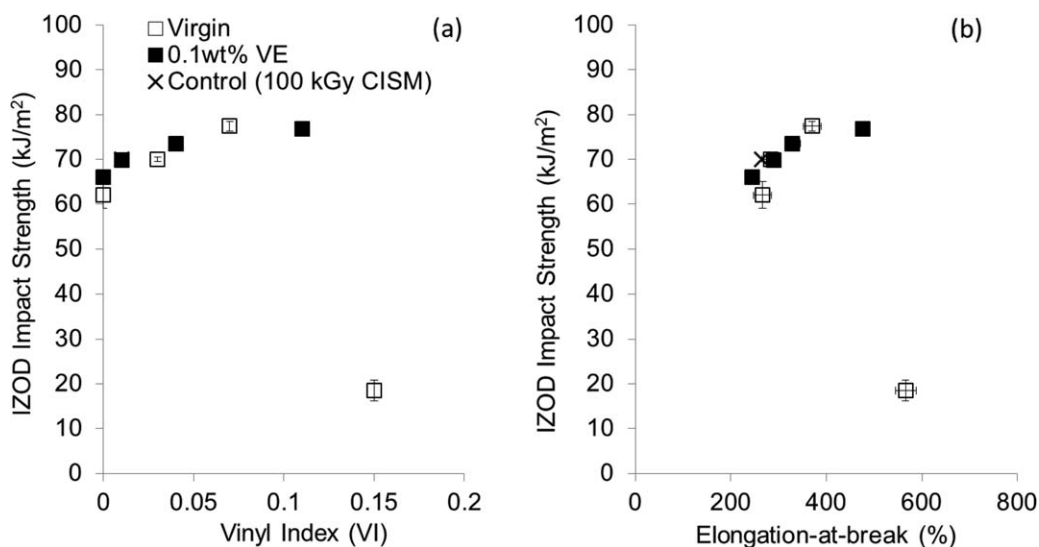
Figure 2. Impact strength as a function of the vinyl index (a) and elongation-at-break (b) for irradiated and HTMed virgin and vitamin E-blended UHMWPEs. Control was 100 kGy-irradiated virgin UHMWPE conventionally melted at 170°C.

Effect of Chain Scissioning on Cross-Link Density

The cross-link density decreased linearly with increasing vinyl index for irradiated and HTMed virgin and vitamin E-blended UHMWPEs [Figure 5(a); $R^2 = 0.99$]. The virgin UHMWPEs had lower cross-link density as compared with the vitamin E-blended UHMWPEs at the same melting temperatures [Figure 5(a); $P = 0.04$, 0.0001, and 0.03 for 280, 300, and 320°C, respectively].

Crystallinity and Peak Melting Temperature

The crystallinity of irradiated and HTMed virgin UHMWPEs showed no correlation with vinyl index [Figure 5(b)]. In contrast, the crystallinity of the irradiated and HTMed vitamin

E-blended UHMWPEs showed a slight positive correlation with vinyl index [Figure 5(b)].

The peak melting temperature of the radiation cross-linked materials was lower after HTM for both the virgin and the vitamin E-blended UHMWPEs for all HTM temperatures ($P < 0.01$). However, the peak melting temperature did not have a strong correlation with vinyl index [Figure 5(c)].

Wear Resistance

The wear rates of irradiated virgin and vitamin E-blended UHMWPEs were higher after HTM [Figure 6(a); $P > 0.05$ except for virgin UHMWPE HTMed at 320°C]. Only the wear rates of irradiated UHMWPEs melted at 320°C were significantly higher than that of virgin 100-kGy CISM ($P < 0.05$).
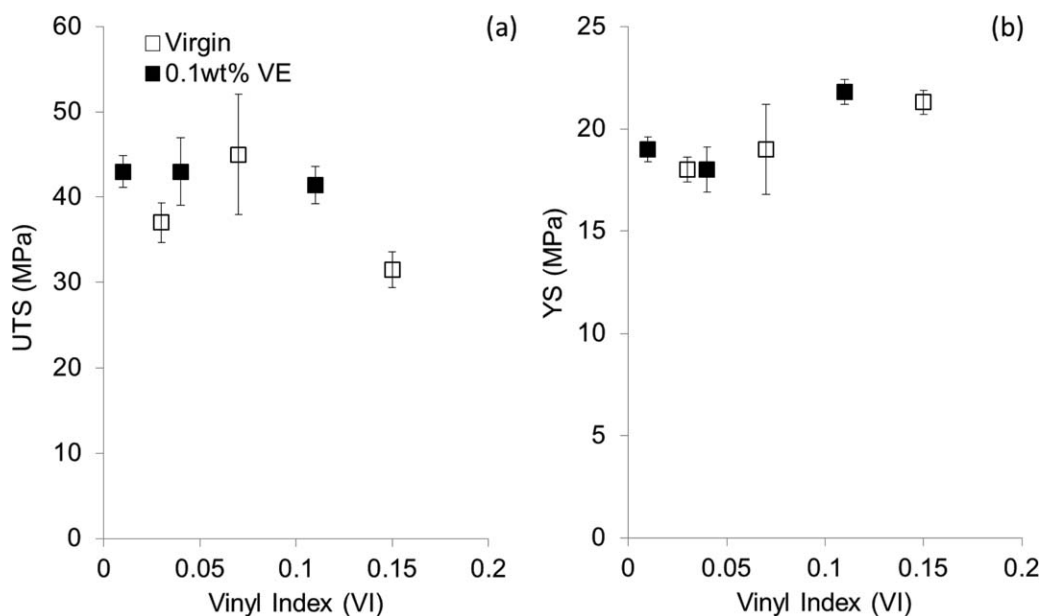

Figure 3. (a) Ultimate tensile strength (UTS) and (b) yield strength (YS) of irradiated virgin and vitamin E-blended UHMWPEs post HTM as a function of the vinyl index. Control was 100 kGy-irradiated virgin UHMWPE conventionally melted at 170°C.
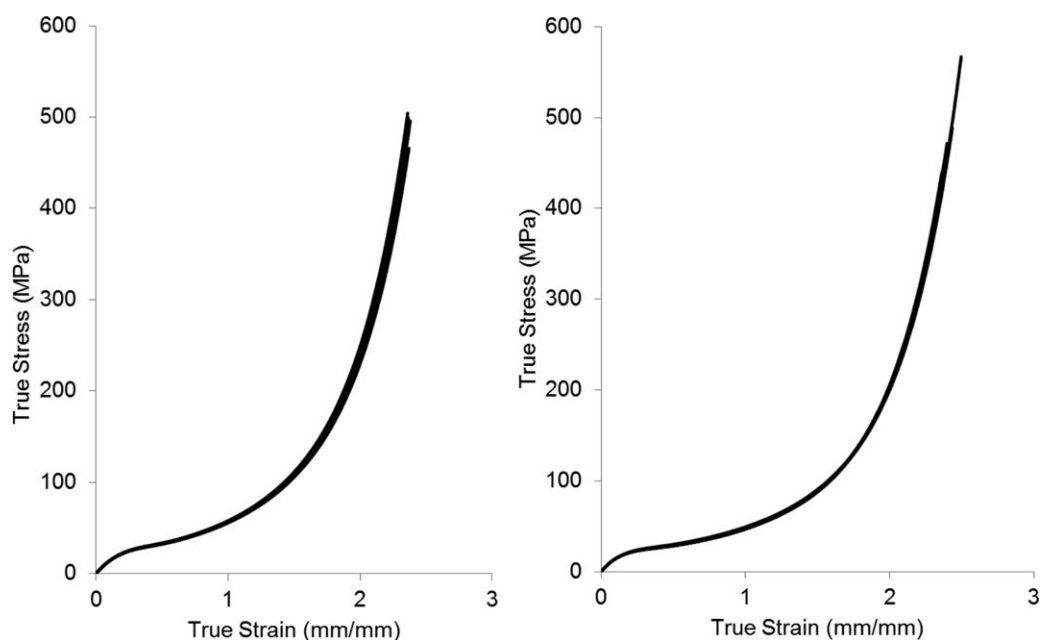
Figure 4. True stress–strain curves of control (a) and irradiated vitamin E-blended UHMWPEs after HTM at 300°C for 5 h (b). Control was 100 kG-irradiated virgin UHMWPE conventionally melted at 170°C.

The wear rates increased with increasing EAB for irradiated and HTMed virgin and vitamin E-blended UHMWPEs [Figure 6(a)]. Also, the correlation of the wear rate with EAB for irradiated and HTMed materials was very different from that of UHMWPE radiation cross-linked after HTM, which was not dependent on EAB [Figure 6(b)].[26]

DISCUSSION

The improved *in vivo* wear resistance of virgin, radiation cross-linked UHMWPE irradiated to 100 kGy and postirradiation melted at 150°C–170°C was shown to decrease wear-related problems clinically.[8] In this method, radiation cross-linking was used to decrease the wear rate, and the postirradiation melting
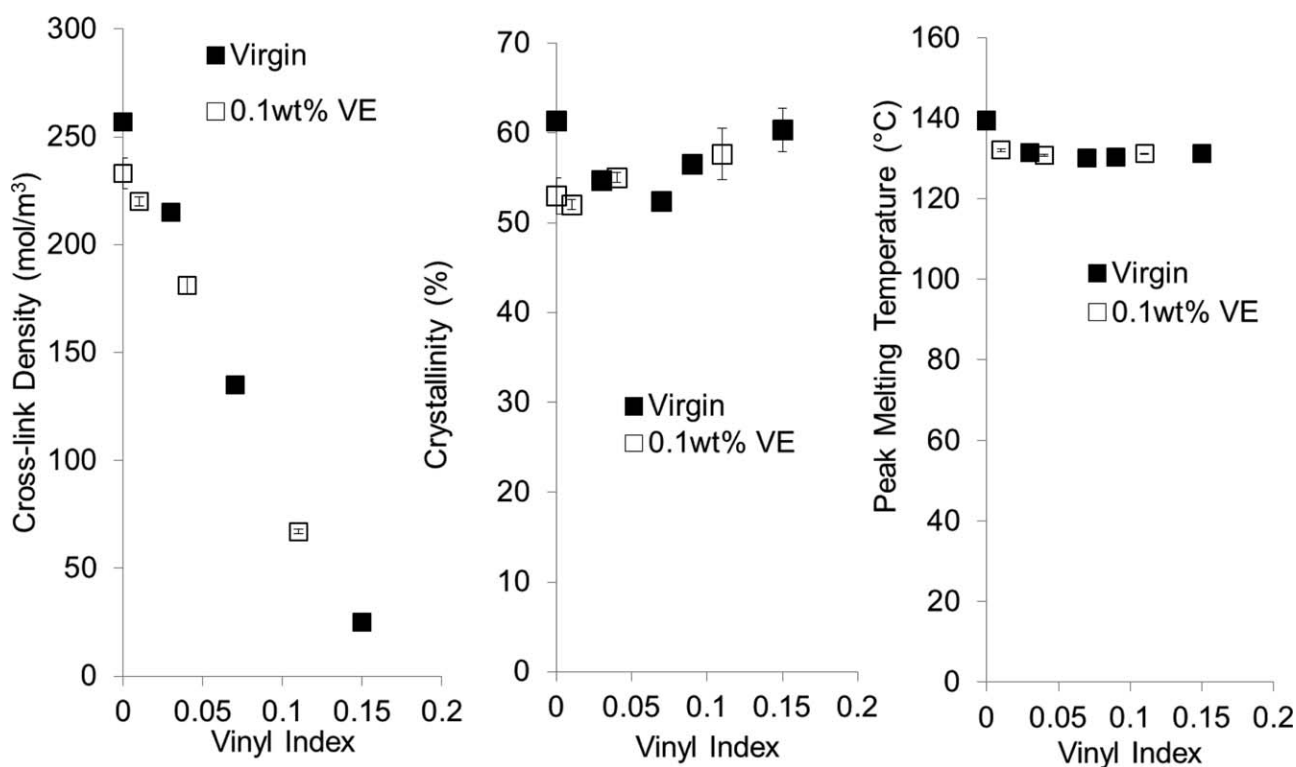

Figure 5. Cross-link density (a), crystallinity (b), and peak melting temperature (c) as a function of the vinyl index for irradiated and HTMed virgin and vitamin E-blended UHMWPEs.
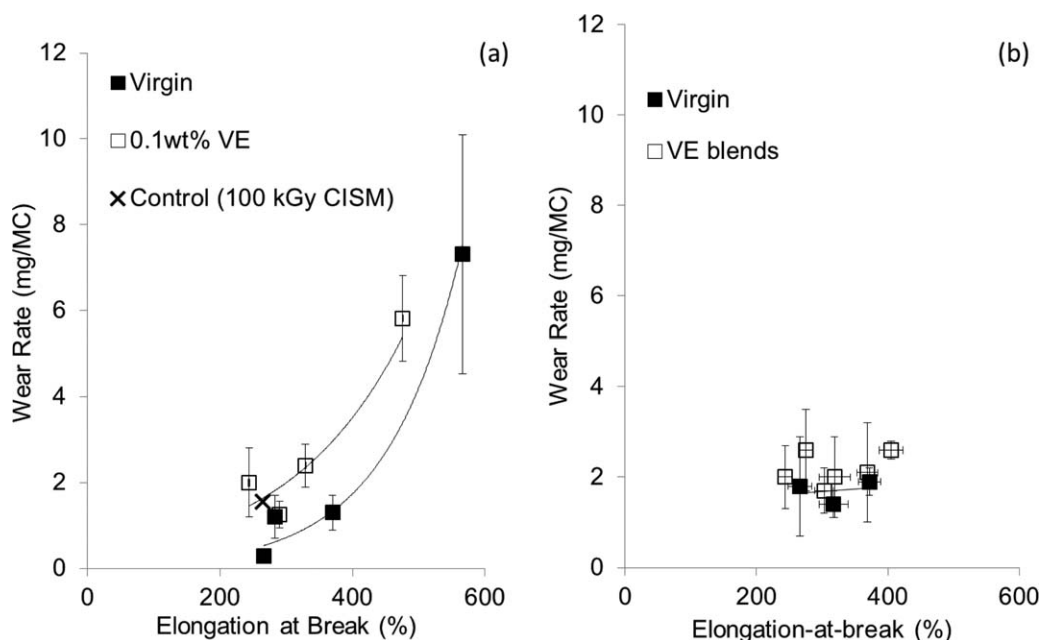
Figure 6. Wear rate of (a) 150 kGy-irradiated virgin and vitamin E-blended UHMWPEs after HTM and (b) HTMed virgin and vitamin E-blended UHMWPE followed by irradiation to 150 kGy as a function of the elongation-at-break. Control was 100 kGy-irradiated virgin UHMWPE conventionally melted at 170°C.

was used to eliminate the detectable residual free radicals remaining in the crystalline domains after irradiation[10] to prevent long-term oxidation. The mid-term clinical success of this material has instituted this level of cross-linking and resultant wear resistance as a benchmark when developing newer materials. Thus, we used 100 kGy-irradiated virgin UHMWPE with postirradiation melting at "conventional temperatures" (150°C–170°C) as a control in this study.

Recently, antioxidant stabilization (mostly by vitamin E and lately also by the synthetic hindered phenol Covernox[TM]) has been introduced into clinical practice to eliminate the need for postirradiation melting for long-term oxidative stability.[13,27] Because vitamin E can act as a free-radical scavenger, it can hinder cross-linking of UHMWPE when present during irradiation. Thus, a raised radiation dose is used with vitamin E-containing UHMWPEs to achieve similar cross-link density and wear resistance to that of virgin, 100 kGy-irradiated UHMWPE.[28] The UHMWPE containing 0.1 wt % vitamin E was irradiated to 150 kGy because of this reason.

We have defined HTM as melting above 200°C to differentiate this method from conventional temperatures (150°C–170°C) used during the manufacturing of clinically available implants as described earlier. For unirradiated and uncross-linked UHMWPE, it was shown previously that HTM improved the elongation and toughness without compromising wear resistance when performed in the range of 280°C–320°C.[1] These consequences were attributed partly due to chain scissioning resulting in vinyl end groups.[1] Although vinyl end groups do occur in UHMWPE at a low concentration and have been discussed with respect to causing Y-shaped cross-links,[29] the significant increase in their presence after the HTM process[1] suggested that this process was largely responsible for their pro-

duction. In addition, increases in vinyl end groups have been observed in linear polyolefins because of chain scissioning during extrusion due to high shear and was accompanied by oxidation.[30] In this case, HTM in inert gas led to controlled chain scissioning without oxidation.

The goal of this study was to use HTM on vitamin E-blended, radiation cross-linked UHMWPE to improve its toughness. Our approach was to melt 0.1 wt % vitamin E-blended and 150 kGy-irradiated UHMWPE at 280, 300, and 320°C for 5 h. To control for the effect of vitamin E, we also used virgin, 150 kGy-irradiated UHMWPE melted at the same temperatures. All samples used in this study are outlined in Table I.

Our hypothesis tested positive. The increase in the impact strength of irradiated virgin and vitamin E-blended UHMWPEs after HTM [Figure 2(a,b)] was attributed, in large part, to the marked increase (up to 2.2-fold) in the EAB [Figure 1(b)]. Similar to uncross-linked UHMWPEs, this increase in elongation may be due to an increase in the chain scissioning with HTM. Chain scissioning, as measured by the formation of terminal vinyl groups and the vinyl index, increased with HTM temperature [Figure 1(a)]. Another effect of HTM is the increased diffusion of the polymer chains. Although this effect may not be as prevalent for cross-linked UHMWPE as it is for uncross-linked

Table I. The Parameters Used in Preparing the Samples Used in This Study

Antioxidant concentration	Radiation dose (kGy)	Melting temperature (°C)
–	150	280, 300, 320
0.1 wt %	150	280, 300, 320

UHMWPE because of the reduced mobility of cross-linked chains, it is still expected to play a role because cross-linking takes place only in the amorphous phase of the polymer when irradiated in the solid state.

Impact strength increased with increasing EAB up to approximately 400% for virgin UHMWPE [Figure 2(b)], after which it decreased rapidly, suggesting a vinyl index threshold [Figure 2(a)], beyond which the toughness decreases. The contrasting lack of decrease of impact strength for vitamin E-blended UHMWPE up to an EAB of 480% [Figure 2(b)] can possibly be explained by the interference of vitamin E in chain scissioning. The vinyl index is lower for vitamin E-blended UHMWPE [Figure 1(a)], undergoing the same melting conditions as virgin UHMWPE, for which there may be several reasons. The extent of chain scissioning may be the same in both types of polymers, but vitamin E may be interfering with the formation of terminal vinyl groups after chain scissioning by scavenging the free radicals formed. On the other hand, chain scissioning may be decreased because of the action of vitamin E, which would then decrease the formation of vinyl groups. The second mechanism is supported by the EAB values for vitamin E-blended UHMWPE being lower than those of virgin UHMWPE [Figure 1(b)] and also by literature wherein hindered phenolic antioxidants were shown to decrease degradation in polymers even in the absence of oxidation.[31,32]

In contrast to the drastic changes in EAB, the UTS [Figure 3(a)] and YS [Figure 3(b)] did not change significantly with increasing HTM temperature, suggesting that the effects of HTM were predominantly in the amorphous domains of the semi-crystalline network. This was corroborated both by the steady decrease of cross-link density [Figure 5(a)] and by the small changes in the crystallinity [Figure 5(b)] and peak melting temperature [Figure 5(c)] with increasing vinyl index. It should be mentioned that the incorporation of vitamin E by itself was found to affect neither the crystallinity nor any of the tensile mechanical properties of UHMWPE significantly.[33] The increase in crystallinity in UHMWPEs with the highest vinyl index [Figure 5(b)] is presumably due to local recrystallization of shorter chains, which can result from increased chain scissioning.[34,35] Nevertheless, this disruption of the network did not affect the strength of the material significantly at this level of scissioning.

For radiation cross-linked UHMWPE melted at conventional melting temperatures (150°C–170°C), wear is dependent strongly on cross-link density (molecular weight between cross-links[36]) and EAB[37]; therefore, the increase in the wear rate after HTM for both the virgin and the vitamin E-blended UHMWPEs [Figure 6(a)] was attributed to the increased chain scissioning and the accompanying decrease in the cross-link density with HTM [Figure 5(a)]. The similar dependence of cross-link density on vinyl index for virgin and vitamin E-blended UHMWPEs suggested that the chain scissioning followed a similar mechanism. The wear behavior of the irradiated and HTMed UHMWPEs in this study was in contrast to previously published results on HTMed, then irradiated UHMWPEs [Figure 6(b)], which did not show a dependence on EAB or cross-link density.[38]

Based on our results, there may be a window of processing parameters for HTM, which may offer an improvement in tough-ness even for cross-linked UHMWPE despite a decrease in cross-link density. Only when the processing temperature was increased to 320°C was the detrimental effect of chain scissioning predominant on the wear resistance [Figure 6(a)] and impact strength in the case of virgin UHMWPE (Figure 2). It seems that a viable alternative implant material can be developed by melting irradiated at high temperatures UHMWPEs by controlling the vitamin E content and melting temperature to optimize the toughness and wear resistance desired in specific applications.

CONCLUSION

HTM of radiation cross-linked virgin and vitamin E-blended UHMWPEs showed improved impact strength as compared with irradiated UHMWPEs melted at conventional temperatures. The incorporation of vitamin E hindered the chain scissioning that is a resultant of HTM and enabled a larger process temperature window. A terminal HTM step of radiation cross-linked antioxidant-blended UHMWPE can be used as a feasible alternative manufacturing method in applications, which require higher toughness but may not require extremely low wear rates.

REFERENCES

1. Fu, J.; Ghali, B.; Lozynsky, A.; Oral, E.; Muratoglu, O. K. *Polymer* **2010**, *51*, 2721.

2. Kurtz, S. In UHMWPE Biomaterials Handbook; Kurtz, S., Ed.; Elsevier: New York, **2009**; pp 7–19.

3. Buckley, C. P.; Wu, J.; Haughie, D. W. *Biomaterials* **2006**, *27*, 3178.

4. Satti, A.; Andreucetti, N; Quijada, R; Sarmoria, C; Pastor, J; Valles, E. *J. Appl. Polym. Sci.* **2010**, *117*, 290.

5. Kurtz, S. In UHMWPE Biomaterials Handbook; Kurtz, S., Ed.; Elsevier: New York, **2009**; pp 291–308.

6. Muratoglu, O. K.; Bragdon, C. R.; O'Connor, D. O.; Jasty, M.; Harris, W. H. *J. Arthroplasty* **2001**, *16*, 149.

7. Digas, G.; Karrholm, J.; Thanner, J.; Herberts, P. *Acta Orthop.* **2007**, *78*, 746.

8. Kurtz, S.; Gawel, H.; Patel, J. *Clin. Orthop. Relat. Res.* **2011**, *469*, 2262.

9. Dole, M. In The Radiation Chemistry of Macromolecules; Dole, M., Ed.; Academic Press: New York, **1972**; pp 335–348.

10. Bhateja, S.; Duerst, R.; Aus, E.; Andrews, E. *J. Macromol. Sci. Phys.* **1995**, *B34*, 263.

11. Costa, L.; Jacobson, K.; Bracco, P.; Brach, del Prever E. M. *Biomaterials* **2002**, *23*, 1613.

12. Kurtz, S. M.; Austin, M. S.; Azzam, K.; Sharkey, P. F.; MacDonald, D. W.; Medel, F. J.; Hozack, W. J. *J. Arthroplasty* **2010**, *25*, 614.

13. Bracco, P.; Oral, E. *Clin. Orthop. Relat. Res.* **2011**, *469*, 2286.

14. Oral, E.; Wannomae, K. K.; Hawkins, N. E.; Harris, W. H.; Muratoglu, O. K. *Biomaterials* **2004**, *25*, 5515.

15. Oral, E.; Christensen, S.; Malhi, A.; Wannomae, K.; Muratoglu, O. K. *J. Arthroplasty* **2006**, *21*, 580.

16. Rowell, S.; Oral, E.; Muratoglu, O. In Transactions of the 55th Annual Meeting of the Orthopaedic Research Society, Las Vegas, NV, **2009**.

17. Kurtz, S.; Dumbleton, J.; Siskey, R.; Wang, A.; Manley, M. *J. Biomed. Mater. Res.* **2008**, *90A*, 549.

18. Currier, B. H.; Currier, J. H.; Mayor, M. B.; Lyford, K.; Van Citters, D. W.; Collier, J. P. *J. Arthroplasty* **2007**, *22*, 721.

19. Currier, B.; Van Citters, D.; Currier, J.; Collier, J. *J. Bone Joint Surg. Am.* **2010**, *92*, 2409.

20. Ries, M.; Pruitt, L. *Clin. Orthop. Relat. Res.* **2005**, *440*, 149.

21. Tower, S. S.; Currier, J. H.; Currier, B. H.; Lyford, K. A.; Van Citters, D. W.; Mayor, M. B. *J. Bone Joint Surg. Am.* **2007**, *89*, 2212.

22. Rodriguez, J. *J. Arthroplasty* **2008**, *23*(7 Suppl. 1), 31.

23. Flory, P. Principles of Polymer Chemistry; Cornell University Press: Ithaca, NY, **1953**.

24. Gent, A. N.; Vickroy, V. V. *J. Polym. Sci. Part A-2 Polym. Phys.* **1967**, *5*, 47.

25. Bragdon, C. R.; O'Connor, D. O.; Lowenstein, J. D.; Jasty, M.; Biggs, S. A.; Harris, W. H. *J. Arthroplasty* **2001**, *16*, 658.

26. Fu, J.; Ghali, B.; Lozynsky, A.; Oral, E.; Muratoglu, O. K. *Polymer* **2011**, *52*, 1155.

27. Narayan, V. *Clin. Orthop. Relat. Res.* **2015**, *473*, 952.

28. Oral, E.; Godleski Beckos, C.; Malhi, A.; Muratoglu, O. *Biomaterials* **2008**, *29*, 3557.

29. Horii, F.; Zhu, Q.; Kitamaru, R.; Yamaoka, H. *Macromolecules* **1990**, *23*, 977.

30. Jabarin, S.; Lofgren, E. *J. Appl. Polym. Sci.* **1994**, *53*, 411.

31. Mariani, P.; Carianni, G.; La Mantia, F. *Polym. Degrad. Stab.* **2004**, *85*, 1003.

32. Kovarik, P.; Klein, E.; Schwarzova, M. *Chem. Papers* **1998**, *52*, 175.

33. Oral, E.; Malhi, A.; Muratoglu, O. In Transactions of the 52nd Annual Meeting of the Orthopaedic Research Society, San Diego, CA, **2007**.

34. Grood, E. S.; Shastri, L.; Hopson, C. N. *J. Biomed. Mater. Res.* **1982**, *16*, 399.

35. Wannomae, K.; Bhattacharyya, S.; Freiberg, A.; Estok, D.; Harris, W.; Muratoglu, O. *J. Arthroplasty* **2006**, *21*, 1005.

36. Muratoglu, O. K.; Bragdon, C. R.; O'Connor, D. O.; Jasty, M.; Harris, W. H.; Gul, R.; McGarry, F. *Biomaterials* **1999**, *20*, 1463.

37. Oral, E.; Greenbaum, E. S.; Malhi, A. S.; Harris, W. H.; Muratoglu, O. K. *Biomaterials* **2005**, *26*, 6657.

38. Fu, J.; Doshi, B.; Oral, E.; Muratoglu, O. *Polymer* **2013**, *54*, 199.