

## Crosslink Density Is Reduced and Oxidation Is Increased in Retrieved Highly Crosslinked Polyethylene TKA Tibial Inserts

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### Abstract

**Background** The wear resistance of highly crosslinked polyethylene depends on crosslink density, which may decrease with in vivo loading, leading to more wear and increased oxidation. The relationship among large and complex in vivo mechanical stresses, breakdown of the polyethylene crosslinks, and oxidative degradation is not fully understood in total knee arthroplasty (TKA). We wished to determine whether crosslink density is reduced at the articular surfaces of retrieved tibial inserts in contact areas exposed to in vivo mechanical stress.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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**Questions/purposes** (1) Does polyethylene crosslink density decrease preferentially in regions of the articular surface of thermally stabilized crosslinked polyethylene tibial components exposed to mechanical stress in vivo; and (2) what is the ramification of decreased crosslink density in TKA in terms of accompanying oxidation of the polyethylene?

**Methods** From May 2011 to January 2014, 90 crosslinked polyethylene tibial components were retrieved during revision surgery as a part of a long-standing implant retrieval program. Forty highly crosslinked polyethylene tibial inserts (27 posterior-stabilized designs and 13 cruciate-retaining designs) retrieved for instability (15 cases), stiffness (11), infection (six), aseptic loosening (four), pain (two), and malposition (two) after a mean time of 18 months were inspected microscopically to identify loaded (burnished) and unloaded (unburnished) regions on the articular surfaces. Swell ratio testing was done according to ASTM F2214 to calculate crosslink density and infrared spectroscopy was used according to ASTM F2102 to measure oxidation.

**Results** The region of the tibial insert influenced crosslink density. Loaded surface regions had a mean crosslink density of 0.19 (95% confidence interval [CI], 0.18–0.19) mol/dm<sup>3</sup>, lower than the other three regions (loaded subsurface, unloaded surface, and unloaded subsurface), which had crosslink densities of 0.21 (95% CI, 0.21–0.22;  $p < 0.01$ ) mol/dm<sup>3</sup>. Peak oxidation levels were higher in loaded regions with a mean oxidation index (OI) of 0.67 (95% CI, 0.56–0.78) versus unloaded regions with a mean OI of 0.36 (95% CI, 0.27–0.45;  $p < 0.01$ ). Peak oxidation levels were higher in annealed samples with a mean OI of 0.66 (95% CI, 0.52–0.81) versus remelted samples with a mean OI of 0.40 (95% CI, 0.34–0.47;  $p < 0.01$ ).

**Conclusions** The results suggest that the crosslink density decreases and accompanying oxidation is driven

predominantly by contact stress conditions. If crosslink density continues to decrease with continued loading over time, crosslinked polyethylene may not provide a clinical advantage over conventional polyethylene in the long term for TKA. Therefore, we will continue to collect longer term retrievals to evaluate mechanical property changes in crosslinked polyethylenes.

**Clinical Relevance** Although we found a decrease in crosslink density and increase in oxidation in the tibial inserts, the degree of oxidation does not suggest, for now, a reason for concern in these early retrievals. The OI values of the tibial inserts in this study were lower than the critical oxidation level (OI > 3) reported in the literature where polyethylene may lose mechanical properties and have the compromised ability to withstand mechanical loading.

## Introduction

Highly crosslinked ultrahigh-molecular-weight polyethylene (crosslinked PE) was developed to reduce wear and particle-induced osteolysis in THA [26, 31] and has successfully reduced the frequency of osteolysis after THA into the second decade [8, 17]. The use of crosslinked PE in TKA continues to increase with the 2015 Annual Report of the Australian Joint Replacement Registry reporting an increase from 7% of primary TKAs in 2003 to 49% in 2014 of TKAs [1]. However, after more than 10 years using crosslinked PE as a bearing material for TKA, it remains unclear whether crosslinked PE provides a clinical advantage over conventional polyethylene [36]. The 2015 Annual Report of the Australian Orthopaedic Association National Joint Replacement Registry found a lower rate of revision in patients implanted with crosslinked PE tibial inserts [1]. In contrast, clinical reports with mid-term followup such as those from the Kaiser Implant Registry [18] demonstrated no benefits or differences in revision surgery rates between TKAs with crosslinked PE versus conventional polyethylene inserts [19, 20, 28]. In a recent short-term implant retrieval study comparing retrieved crosslinked PE and conventional polyethylene TKA inserts, Liu et al. found no difference in polyethylene surface damage between the two materials [24]. However, surface damage does not preclude the possibility that a difference in wear and creep might still exist [34].

Crosslinked PE is manufactured using ionizing radiation, which improves wear resistance by increasing crosslink density [16, 31], but also produces free radicals that have been implicated in oxidative degradation [9, 38]. Free radical oxidation results in decreased molecular weight and loss of mechanical properties. To decrease the potential for oxidative degradation, heating the polymer to above its melting point (“remelting”) or to just below that

temperature (“below-melt thermal annealing”) is a step added postirradiation to reduce the free radicals. However, retrieved crosslinked PE tibial inserts demonstrate increased oxidation levels at the articular surfaces after *in vivo* implantation regardless of whether they were either remelted or annealed after crosslinking, a phenomenon not observed with pristine, never implanted inserts [13, 14, 25].

This increased oxidation has been linked to decreased crosslink density at the articular surface of tibial components [35]. In a TKA, contact between the nonconforming surfaces of the metallic femoral component and PE tibial component results in a highly complex stress distribution including compressive and tensile stresses at the articular surface and shear stresses beneath the surface under the center of the contact area [5–7, 15]. However, the relationship among these large and complex *in vivo* mechanical stresses, breakdown of the PE crosslinks, and oxidative degradation is not fully understood in TKA.

We therefore wished to determine whether crosslink density is reduced at the articular surfaces of tibial inserts in contact areas exposed to *in vivo* mechanical stress. To do so, we identified damaged regions on the articular surfaces of retrieved crosslinked PE tibial components microscopically and compared the crosslink density and oxidation in these regions with unloaded regions at and near the articular surface. In so doing, we hoped to answer the following specific questions: (1) does PE crosslink density decrease preferentially in regions of the articular surface of thermally stabilized crosslinked PE tibial components exposed to mechanical stress *in vivo*; and (2) what is the ramification of decreased crosslink density in TKA in terms of accompanying oxidation of the PE?

## Materials and Methods

From May 2011 to January 2014, 90 crosslinked PE tibial components were retrieved. PE tibial components were only included in this study if the retrievals were placed in the  $-18^{\circ}\text{C}$  freezer within 6 months after revision surgery, leaving 40 crosslinked PE tibial inserts (27 posterior-stabilized designs and 13 cruciate-retaining designs) to be analyzed for this study. No differences in patient demographics or implant design were found between the population of implants that were included in this study and those that were not. *Ex vivo* oxidation occurs and correlates with shelf time between retrieval and analysis [32]. It has been previously recommended that only retrieved implants stored within a freezer less than 6 months after revision surgery should be analyzed to avoid the confounding effects of *ex vivo* oxidation [13]. Clinical and

demographic information were gathered from the patients' medical records (Table 1). Reasons for revision surgery were instability (15 cases), stiffness (11), infection (six), aseptic loosening (four), pain (two), and malposition (two), with mean in vivo implantation of 18 months (SD  $\pm$  14 months; range, 2–72 months). Components were cleaned and stored in  $-18$  °C freezers as part of a long-standing, institutional review board-approved implant retrieval program. Three tibial inserts were made of XLK polyethylene (manufactured by DePuy Inc, Warsaw, IN, USA), seven were made of XLPE polyethylene (Smith & Nephew Plc, London, UK), 17 were made of X3 polyethylene (Stryker Corp, Kalamazoo, MI, USA), and 13 were made of Prolong polyethylene (Zimmer Inc, Warsaw, IN, USA). Twenty-three of the 40 crosslinked PE tibial inserts were irradiated and remelted (XLK, XLPE, and Prolong), and 17 were sequentially irradiated and annealed (X3). None of the tibial inserts included the addition of antioxidants to scavenge free radicals within the polymer. The resins, sterilization modalities, crosslinking modalities, and postirradiation processes for all the retrieved inserts were determined (Table 2).

**Table 1.** Demographic data for the patients from whom the cross-linked polyethylene inserts were retrieved

Variable	Values (mean $\pm$ SD)
Length of implantation (months)	18 $\pm$ 14 (range, 2–72)
Body mass index (kg/m <sup>2</sup> )	30 $\pm$ 5 (range, 20–45)
Age at revision (years)	64 $\pm$ 10 (range, 36–85)
Number of females (%)	25 (63%)

**Table 2.** The implant properties of the crosslinked polyethylene inserts

Manufacturer (crosslinked PE trade name)	Resin	Sterilization modality	Crosslinking modality	Postirradiation process	Number retrieved (%)
Stryker, Kalamazoo, MI, USA (X3)	GUR 1020	Gas plasma	Gamma irradiation 30 kGy in 3 steps (90 kGy Total)	Sequential annealed	17 (42.5%)
Zimmer, Warsaw, IN, USA (Prolong)	GUR 1050	Gas plasma	E-beam irradiation 65 kGy	Remelted	13 (32.5%)
Smith & Nephew, Memphis, TN, USA (XLPE)	GUR 1020	Ethylene oxide	Gamma irradiation 75 kGy	Remelted	7 (17.5%)
DePuy, Warsaw, IN, USA (XLK)	GUR 1020	Gas plasma	Gamma irradiation 50 kGy	Remelted and annealed	3 (7.5%)

PE = polyethylene.

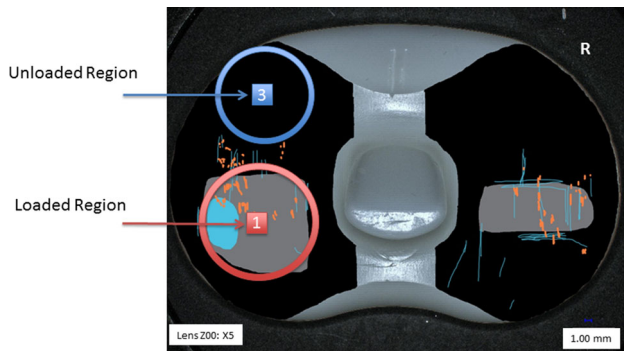
## Identification of the Regions to Be Tested

The articular surface of each tibial insert was photographed using a digital microscope (Keyence VHX-2000; Keyence Corp, Osaka, Japan) with high dynamic range mode. The presence of seven damage modes (burnishing, pitting, scratching, third-body debris, abrasion, deformation, and delamination) were then identified under a light stereomicroscope at magnifications between  $\times 10$  and  $\times 32$ . The regions on which they were present were manually replicated onto the digital images using Photoshop CS2 software (Adobe Systems, San Jose, CA, USA) to quantify the area of damage for each mode on both medial and lateral plateaus. This damage mapping technique has been described in more detail elsewhere [10, 24]. Burnishing was the most prevalent damage mode on the PE articular surface and was considered the in vivo-loaded contact area with the surface of the metallic femoral component while the insert had been implanted in the patient. For each retrieved insert, the center of the burnished area on the medial plateau was used to locate the loaded surface region (Region 1 in Fig. 1), and the largest area with minimal damage on the same plateau was considered the unloaded surface region for comparison (Region 3 in Fig. 1). Sub-surface loaded and unloaded regions (Regions 2 and 4, respectively, in Fig. 2) were located 3 mm underneath the corresponding surface regions. For all 40 inserts, it was possible to identify large enough loaded and unloaded regions from within which samples for crosslink density and oxidation measurements could be made. We hypothesized that crosslink density would be decreased at the surface of tibial inserts exposed to mechanical stress. To test this hypothesis, we chose to measure changes in crosslink density and oxidation in the medial compartment of the tibial inserts because the medial condyle is more likely exposed to higher loads [29]. If we did not find a correlation using the medial compartment, it would be

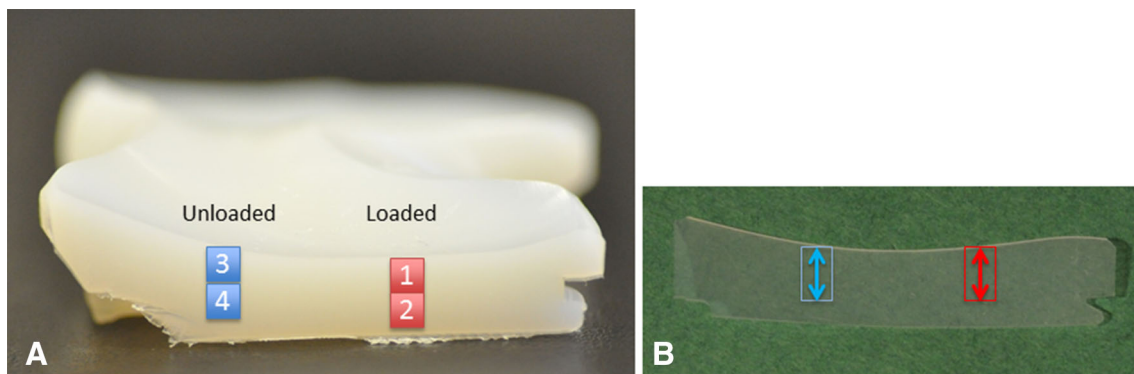
unlikely that we would find a correlation analyzing the lateral compartment.

### Measurement of Crosslink Density

Crosslink density was measured by using a gravimetric swell ratio test according to ASTM standard F2214. Three millimeter  $\times$  3 mm  $\times$  3-mm cubes were cut using a razor



**Fig. 1** A photograph shows a retrieved tibial insert with a damage map overlaid on the articular surfaces. Gray areas in the damage map are locations of burnishing damage, orange are locations of pitting damage, and light blue are locations of scratching damage on the tibial surfaces. Damage maps were used to identify loaded (burnished) and unloaded regions on the PE tibial inserts. Region 1 on the map shows the location where a loaded PE cube (3  $\times$  3  $\times$  3 mm) was cut for crosslink density testing, and Region 3 shows the location for an unloaded surface cube. These regions correspond to those in Figure 2.



**Fig. 2A–B** Photographs show a retrieved tibial insert showing the location where samples were collected for crosslink density analysis (A) and oxidation analysis (B). (A) A photograph showing a sagittal view of a tibial insert. Cubes of polyethylene were cut from different regions of the insert for crosslink density analysis. Regions were defined as the loaded surface (red square 1), loaded subsurface (red square 2), unloaded surface (blue square 3), and unloaded subsurface (blue square 4) of the tibial insert. (B) A photograph shows a 200- $\mu$ m thin slice of PE cut from the medial compartment of the tibial insert, which was used to measure peak oxidation of the PE. This slice was cut immediately adjacent to sagittal section of the tibial component

blade from the four identified regions (loaded surface region, loaded subsurface region, unloaded surface region, and unloaded subsurface region; Fig. 2) in the medial plateau of each tibial insert. The PE cubes were then immersed into 25 mL of xylene (Fisher Scientific, Pittsburgh, PA, USA) at 130  $^{\circ}$ C for 2 hours. The masses of each cube before and after the heating treatment were recorded for calculation of swell ratio and crosslink density according to ASTM standards D2765 and F2214 [2, 3].

### Measurement of Oxidation Index

Oxidation of the implants was measured using Fourier transform infrared spectroscopy (FTIR) following ASTM standard F2102 [4]. Sagittal 200- $\mu$ m slices were microtomed with a Leica SM2500 sliding microtome (Leica Microsystems, Wetzlar, Germany). Slices were cut from PE adjacent to the location where PE cubes were cut for crosslink density analysis (Fig. 2). FTIR analyses were performed on each slice with a PerkinElmer (Shelton, CT, USA) Spectrum 100 spectrometer connected to a Spectrum Spotlight 300 FTIR microscope. Scans were run from the articular surface to 6 mm beneath the surface of each insert using an aperture of 200  $\times$  200  $\mu$ m with 32 scans per 200- $\mu$ m interval. Oxidation index was then calculated from the spectrum as the ratio of the carbonyl peak area (centered near 1720  $\text{cm}^{-1}$ ) to the methylene vibration peak area (centered near 1370  $\text{cm}^{-1}$ ) according to ASTM standard F2102.

shown in A where cubes were cut for crosslink density analysis. Oxidation was measured with a FTIR microscope according to ASTM F2102. Thirty scans (200  $\times$  200  $\mu$ m) were taken from the articular surface to 6-mm depth to analyze the surface and subsurface of both loaded and unloaded regions. The red arrow shows the location of the 30 scans taken from the surface to the subsurface of the loaded regions (the location of the red arrow corresponds to the location of the red cubes 1 and 2 shown in A), and the blue arrow shows the location of the 30 scans taken from the surface to the subsurface of the unloaded regions (the location of the blue arrow corresponds to the location of the blue cubes 3 and 4 shown in A).

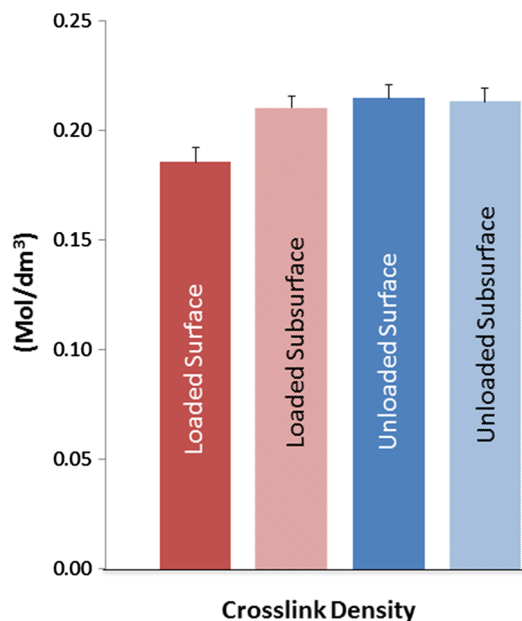
## Statistical Analyses

Descriptive statistics were calculated as means and 95% confidence intervals for continuous variables and frequencies and percentages for categorical variables. The effects of region (loaded surface region, loaded subsurface region, unloaded surface region, and unloaded subsurface region), postprocessing (annealing versus remelting), age, sex, body mass index (BMI), and length of implantation on crosslink density were assessed with repeated-measures generalized estimating equations (GEEs) with the insert treated as the repeated factor. Nonsignificant terms were removed from the model in order of decreasing *p* value. Two-way interactions among factors were investigated systematically, but none reached significance and therefore were not retained in the final model. Post hoc tests were adjusted for multiple comparisons with the Tukey-Kramer method. Profiles of oxidation index versus distance beneath the articular surfaces were examined visually. Differences in peak oxidation index with surface loading and annealing were assessed with GEEs paralleling the crosslink density analyses. All analyses were performed with SAS Version 9.3 (Cary, NC, USA) with a level of significance of  $\alpha = 0.05$ .

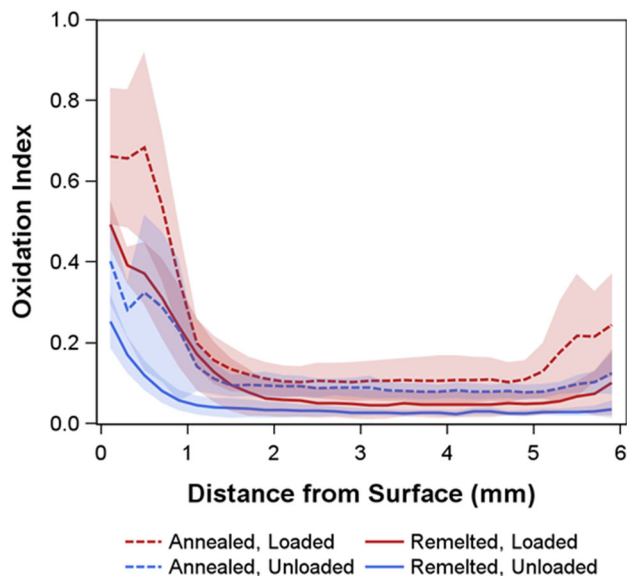
## Results

Region of the tibial insert articular surface influenced crosslink density ( $p < 0.01$ ). The loaded surface regions (Region 1 in Fig. 2) had a mean crosslink density of 0.19 (95% CI, 0.18–0.19) mol/dm<sup>3</sup>, whereas the other three regions (loaded subsurface, unloaded surface, and unloaded subsurface) had crosslink densities of 0.21 (95% CI, 0.21–0.22; Fig. 3) mol/dm<sup>3</sup>. Crosslink density was 0.01 (95% CI, 0.00–0.02) mol/dm<sup>3</sup> greater in females than males ( $p = 0.03$ ), but differences in crosslink densities were not associated with age ( $p = 0.12$ ), BMI ( $p = 0.07$ ), or length of implantation ( $p = 0.06$ ). The impact of the latter two factors was modest; the density only decreased 0.0006 mol/dm<sup>3</sup> for every 1-unit increase in BMI and only decreased 0.004 mol/dm<sup>3</sup> for every 1-year increase in length of implantation. Postirradiation processing (annealing versus remelting) did not influence crosslink density ( $p = 0.21$ ).

Oxidation was highest at or near the surface and plateaued by 2 mm into the sample (Fig. 4). Peak oxidation levels were higher in loaded regions with a mean oxidation index (OI) of 0.67 (95% CI, 0.56–0.78) versus unloaded regions with a mean OI of 0.36 (95% CI, 0.27–0.45;  $p < 0.01$ ). Peak oxidation levels were higher in annealed samples with a mean OI of 0.66 (95% CI, 0.52–0.81) versus remelted samples with a mean OI of 0.40 (95% CI, 0.34–0.47;  $p < 0.01$ ). On average, loaded regions had 86%

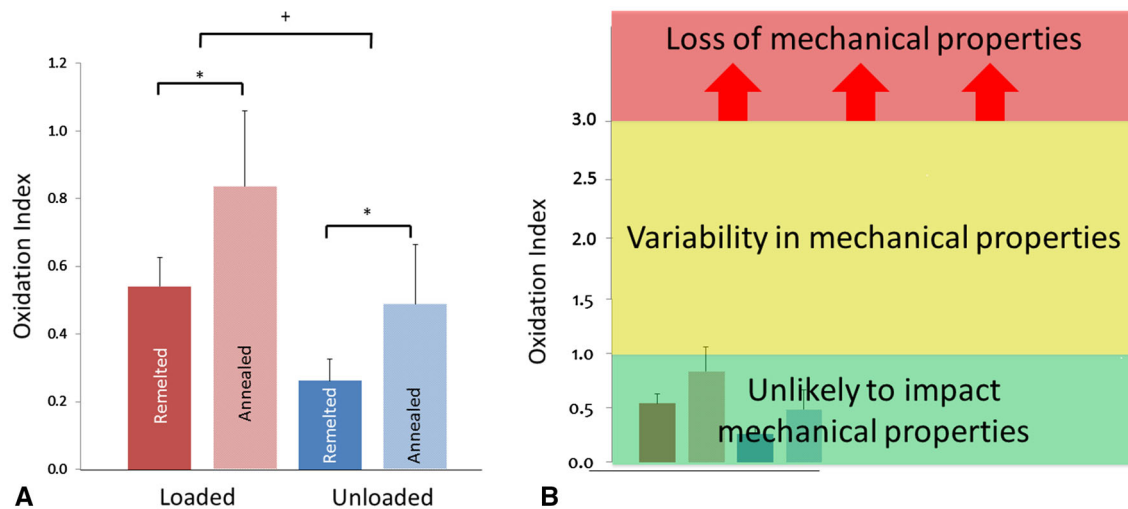


**Fig. 3** A bar chart showing the mean crosslink density in different regions on the retrieved tibial PE inserts. Crosslink density was significantly less at the loaded articular surface compared with the other regions ( $p < 0.001$ ).



**Fig. 4** A scatterplot showing the mean oxidation index (95% CIs in the shaded regions) at increasing distances from the articular surface of the tibial inserts. Peak oxidation occurred in the 1 to 2 mm closest to the articular surface.

higher peak OIs than unloaded regions, whereas annealed samples had 65% greater peak oxidation than remelted samples (Fig. 5). Differences in OIs were not associated with age ( $p = 0.72$ ), sex ( $p = 0.59$ ), BMI ( $p = 0.99$ ), or length of implantation ( $p = 0.07$ ). Again, the effect of length of implantation on OI appears modest; the OI



**Fig. 5A–B** (A) A bar chart showing differences in peak OI between remelted and annealed polyethylene tibial components in areas that were loaded or unloaded in vivo. Significant differences between remelted and annealed PEs are shown with an asterisk (\*). There was a significant difference in peak oxidation between loaded and unloaded groups (shown with +). The magnitude of the differences in peak oxidation between loaded and unload regions did not differ

significantly between remelted and annealed groups. (B) A bar chart displaying the same data shown in A, but the scale has been adjusted to show threshold values where OI levels correlate to mechanical property changes in PE. The threshold values were determined from published implant retrieval data evaluating in vivo oxidation and mechanical behavior of PE [21].

increased by only 0.07 for every 1-year increase in length of implantation, which is smaller than the other effect sizes.

## Discussion

The use of crosslinked PE tibial inserts in TKA continues to increase [1], despite a two- to four fold greater cost [36] and limited data demonstrating a clinical advantage when using crosslinked PE compared with conventional PE [19, 27]. Crosslinked PE has been accepted as the gold standard in hip arthroplasty [22], but as a result of different mechanical loading paradigms between hip and knee replacements, it is unclear if crosslinked PE will degrade in TKAs to a greater extent than in THAs. Therefore, we sought to measure polyethylene crosslink density and oxidation levels in a large series of crosslinked PE tibial inserts retrieved during revision surgery to determine whether deleterious changes occur in the material properties of crosslinked PE in TKA as a result of in vivo use. We found both decreased crosslink density and increased oxidation at the articular surface of retrieved PE tibial inserts in burnished areas exposed to in vivo loading. Furthermore, these changes between the loaded surface region and both the loaded subsurface region and unloaded surface region were consistent regardless of whether the PE was remelted or sequentially annealed as part of the fabrication process. Thermally annealed crosslinked inserts showed higher peak oxidation than remelted inserts, which is likely explained

by residual free radicals that are reduced but not completely eliminated with the annealing treatment method [23], although the remelted inserts did not show any greater loss in crosslink density.

There are limitations to this work. First, an inherent limitation to any retrieval study is that the study is retrospective for which certain variables cannot be controlled and that the implants in this study by definition have failed and may not reflect well-functioning devices. Another limitation is the short length of implantation (an average of 18 months), in so much as the longer term regional differences in crosslink density or oxidation will likely be more consequential to the in vivo performance of the bearings. Third, the method for measuring crosslink density required  $3 \times 3 \times 3$ -mm cubes, which did not allow us to evaluate crosslink density breakdown with the same precision as FTIR. Therefore, we were unable to determine whether chain scission was occurring throughout the cube of PE or just at the articular surface. Fourth, we were limited by a relatively small sample size, which limited our ability to examine other important factors. For example, within the population of 23 inserts that had been remelted after irradiation crosslinking, we were unable to (given the sample sizes available) investigate whether the magnitude of irradiation, type of irradiation used (electron beam versus gamma), polyethylene resin, or terminal sterilization method may have affected our oxidation or crosslink density measurement results. Fifth, we did not evaluate crosslink density or peak oxidation on the backside of the

inserts. Although the backside surfaces can experience large contact stresses and therefore might also demonstrate decreases in crosslink density, we felt that the variability in insert thicknesses (and therefore contact stresses), differences in tibial tray locking mechanisms, the potential for mechanical damage to the backside during the separation of the insert from the tibial tray, and differences in the articular constraint between the insert articular surface and femoral component would confound our ability to reach meaningful conclusions. Finally, our results may not be germane to polyethylene tibial inserts that contain antioxidants or were mechanically annealed to reduce free radical concentrations.

Our results are consistent with the mechanical breakdown of crosslinks in the loaded regions of crosslinked PE inserts. Surface tensile stresses in the PE may be the culprit, because they are maximum at the trailing edges of the contact area as it sweeps back and forth across the surface during flexion-extension [5]. These stresses are quite low below the surface, consistent with the little loss of crosslinking and little oxidation at subsurface regions. It has been suggested that lipids absorbed from the synovial fluid *in vivo* could initiate and accelerate oxidation of UHMWPE even in the absence of detectable residual free radicals [33]. However, if this were the predominant mechanism for material degradation, we would have expected to find reduced crosslink density at the unloaded articular surfaces, not just the loaded surfaces. We did not find a difference in crosslink density values between remelted and annealed materials, which may be the result of the large size of the PE cubes required to test density. Chain scission might only be a surface phenomenon, occurring in the same area closest to the articular surface in which we observed the peak oxidation index (Fig. 4). If we could have measured crosslink density on the same dimensional scale as oxidation index (200- $\mu\text{m}$  regions instead of 3-mm regions), we may well have found crosslink density differences between the remelted and annealed materials. Although trends existed relating crosslink density changes to patient demographics (BMI and length of implantation), the decreases in crosslink density for meaningful increases in BMI or length of implantation were quite small, and, therefore, no clinically relevant conclusions should be drawn regarding these relationships.

The clinical implications of the decrease in crosslink density observed in the loaded region, although difficult to discern, can be considered in light of wear simulator studies that reported both wear rate and crosslink density so that changes in density could be directly related to wear rate. For example, McKellop and colleagues [26] established the positive effects of increased crosslink density on improved wear resistance using a hip simulator. Combining their measured crosslink density versus wear rate

relationship with the decreased crosslink density measured in the loaded regions of our retrieved tibial inserts (from 0.21 mol/dm<sup>3</sup> to 0.19 mol/dm<sup>3</sup>) would suggest a nearly twofold increase in wear rate, almost back to that of conventional polyethylene material. No similar data exist for knee simulator studies, and comparing hip and knee wear is not direct to be sure. However, our retrievals showed a dominant damage mode of burnishing, consistent with the same abrasive mechanism that dominates in hip wear, so we believe a prediction of markedly more wear is justified. Although no clinical implications were attributed to wear in our short-term retrievals, if crosslink density were to continue to decrease with continued loading over time, crosslinked PE may not provide a long term clinical advantage over conventional PE for TKA.

Oxidation of PE can reduce mechanical properties and increase wear and the release of particulate debris, ultimately leading to periprosthetic osteolysis in patients with TKA [30, 37]. The higher oxidation in annealed crosslinked PE compared with remelted PE is consistent with the incomplete quenching of free radicals that occurs from the thermal treatment used in the fabrication process. Others investigators showed that both remelted and sequentially annealed crosslinked PEs oxidize *in vivo* [13, 35], particularly at the bearing surface with both sequentially annealed and remelted crosslinked PE exhibiting a positive correlation of oxidation with implantation time. We did not find an association with length of implantation, but this may be explained by the short time *in vivo* of our retrievals. Peak oxidation occurred in the 1 to 2 mm closest to the articular surface in areas that contacted the metallic femoral components (and hence were burnished). The level of oxidation, as measured by the OI, may have been insufficient in our short-term retrievals to have caused the necessary degradation of mechanical properties that would be accompanied by a meaningful decrease in wear resistance. Historical studies of conventional gamma sterilized in air polyethylene found that bearings with OIs of 1.5 or greater had little resistance to fatigue and frequently failed after an unacceptably short time *in vivo* [11, 12, 21]. The OIs of < 1 reported in our study are unlikely to have an impact on the mechanical behavior of the PE material (Fig. 5B) [12, 21].

Thus, the decrease in crosslink density and increase in oxidation in our retrieved crosslinked PE tibial inserts do not suggest, for now, a reason for concern. Nonetheless, the strong correlations that have been made in retrieved implants between peak oxidation and the length of time of implantation [13, 14] suggest that longer term retrievals must be analyzed to gain more clarity as to whether mechanical failure of the polymer (fracture or delamination) may become more likely with continued increases in oxidation levels at or below loaded regions of the articular

surface. Similarly, if crosslink density continues to decrease in the loaded regions of the tibial insert, the possibility exists for increased wear over time.

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## References

1. Anonymous. *Australian Orthopaedic Association National Joint Replacement Registry. Annual Report*. Adelaide: AOA; 2015.
2. ASTM International. *D2765-11 Standard Test Methods for Determination of Gel Content and Swell Ratio of Crosslinked Ethylene Plastics*. West Conshohocken, PA, USA: ASTM; 2006.
3. ASTM International. *F2214-02 Standard Test Method for In Situ Determination of Network Parameters of Crosslinked Ultra High Molecular Weight Polyethylene (UHMWPE)*. West Conshohocken, PA, USA: ASTM; 2008.
4. ASTM International. *F2102-13 Standard Guide for Evaluating the Extent of Oxidation in Polyethylene Fabricated Forms Intended for Surgical Implants*. West Conshohocken, PA, USA: ASTM; 2013.
5. Bartel DL, Bicknell VL, Wright TM. The effect of conformity, thickness, and material on stresses in ultra-high molecular weight components for total joint replacement. *J Bone Joint Surg Am*. 1986;68:1041–1051.
6. Bartel DL, Burstein AH, Toda MD, Edwards DL. The effect of conformity and plastic thickness on contact stresses in metal-backed plastic implants. *J Biomech Eng*. 1985;107:193–199.
7. Bartel DL, Wright TM, Edwards D. The effect of metal backing on stresses in polyethylene acetabular components. *Hip*. 1983;229–239.
8. Bragdon CR, Doerner M, Martell J, Jarrett B, Palm H, Multicenter Study Group, Malchau H. The 2012 John Charnley Award: Clinical multicenter studies of the wear performance of highly crosslinked remelted polyethylene in THA. *Clin Orthop Relat Res*. 2013;471:393–402.
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. Cottrell JM, Townsend E, Lipman J, Sculco TP, Wright TM. Bearing surface design changes affect contact patterns in total knee arthroplasty. *Clin Orthop Relat Res*. 2007;464:127–131.
11. Currier BH, Currier JH, Collier JP, Mayor MB, Scott RD. Shelf life and in vivo duration. Impacts on performance of tibial bearings. *Clin Orthop Relat Res*. 1997;342:111–122.
12. Currier BH, Currier JH, Mayor MB, Lyford KA, Van Citters DW, Collier JP. In Vivo oxidation of  $\gamma$ -barrier-sterilized ultra-high-molecular-weight polyethylene bearings. *J Arthroplasty*. 2007;22:721–731.
13. Currier BH, Van Citters DW, Currier JH, Carlson EM, Tibbo ME, Collier JP. In vivo oxidation in retrieved highly crosslinked tibial inserts. *J Biomed Mater Res B Appl Biomater*. 2013;101:441–448.
14. Currier BH, Van Citters DW, Currier JH, Collier JP. In vivo oxidation in remelted highly cross-linked retrievals. *J Bone Joint Surg Am*. 2010;92:2409–2418.
15. D’Lima DD, Chen PC, Colwell CW. Polyethylene contact stresses, articular congruity, and knee alignment. *Clin Orthop Relat Res*. 2001;392:232–238.
16. Endo M, Tipper JL, Barton DC, Stone MH, Ingham E, Fisher J. Comparison of wear, wear debris and functional biological activity of moderately crosslinked and non-crosslinked polyethylenes in hip prostheses. *Proc Inst Mech Eng [H]*. 2002;216:111–122.
17. Engh CA, Hopper RH, Huynh C, Ho H, Sritulanondha S, Engh CA. A prospective, randomized study of cross-linked and non-cross-linked polyethylene for total hip arthroplasty at 10-year follow-up. *J Arthroplasty*. 2012;27:2–7.e1.
18. Inacio MCS, Cafri G, Paxton EW, Kurtz SM, Namba RS. Alternative bearings in total knee arthroplasty: risk of early revision compared to traditional bearings: an analysis of 62,177 primary cases. *Acta Orthop*. 2013;84:145–152.
19. Kim Y-H, Park J-W. Comparison of highly cross-linked and conventional polyethylene in posterior cruciate-substituting total knee arthroplasty in the same patients. *J Bone Joint Surg Am*. 2014;96:1807–1813.
20. Kindsfater KA, Pomeroy D, Clark CR, Gruen TA, Murphy J, Himden S. In vivo performance of moderately crosslinked, thermally treated polyethylene in a prospective randomized controlled primary total knee arthroplasty trial. *J Arthroplasty*. 2015;30:1333–1338.
21. Kurtz SM. *UHMWPE Biomaterials Handbook*. 2nd ed. London, UK: Elsevier; 2009.
22. Kurtz SM, Gawel HA, Patel JD. History and systematic review of wear and osteolysis outcomes for first-generation highly cross-linked polyethylene. *Clin Orthop Relat Res*. 2011;469:2262–2277.
23. Kurtz SM, Manley M, Wang A, Taylor S, Dumbleton J. Comparison of the properties of annealed crosslinked (Crossfire) and conventional polyethylene as hip bearing materials. *Bull Hosp Jt Dis*. 2002;61:17–26.
24. Liu T, Esposito C, Elpers M, Wright T. Surface damage is not reduced with highly crosslinked polyethylene tibial inserts at short-term. *Clin Orthop Relat Res*. 2016;474:107–116.
25. MacDonald DW, Higgs G, Parvizi J, Klein G, Hartzband M, Levine H, Kraay M, Rinnac CM, Kurtz SM. Oxidative properties and surface damage mechanisms of remelted highly crosslinked polyethylenes in total knee arthroplasty. *Int Orthop*. 2013;37:611–615.
26. McKellop H, Shen FW, Lu B, Campbell P, Salovey R. Development of an extremely wear-resistant ultra high molecular weight polyethylene for total hip replacements. *J Orthop Res*. 1999;17:157–167.
27. Meneghini RM, Ireland PH, Bhowmik-Stoker M. Multicenter study of highly cross-linked vs conventional polyethylene in total knee arthroplasty. *J Arthroplasty*. 2015 Dec 12 [Epub ahead of print].
28. Minoda Y, Aihara M, Sakawa A, Fukuoka S, Hayakawa K, Tomita M, Umeda N, Ohzono K. Comparison between highly cross-linked and conventional polyethylene in total knee arthroplasty. *Knee*. 2009;16:348–351.
29. Mündermann A, Dyrby CO, D’Lima DD, Colwell CW, Andriacchi TP. In vivo knee loading characteristics during activities of daily living as measured by an instrumented total knee replacement. *J Orthop Res*. 2008;26:1167–1172.
30. Muratoglu OK, Bragdon CR, O’Connor DO, Jasty M, Harris WH. A novel method of cross-linking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties. Recipient of the 1999 HAP Paul Award. *J Arthroplasty*. 2001;16:149–160.
31. Muratoglu OK, Bragdon CR, O’Connor DO, Jasty M, Harris WH, Gul R, McGarry F. Unified wear model for highly crosslinked ultra-high molecular weight polyethylenes (UHMWPE). *Biomaterials*. 1999;20:1463–1470.



32. Muratoglu OK, Wannomae KK, Rowell SL, Micheli BR, Malchau H. Ex vivo stability loss of irradiated and melted ultra-high molecular weight polyethylene. *J Bone Joint Surg Am.* 2010;92:2809–2816.
33. Oral E, Ghali BW, Neils A, Muratoglu OK. A new mechanism of oxidation in ultrahigh molecular weight polyethylene caused by squalene absorption. *J Biomed Mater Res B Appl Biomater.* 2012;100:742–751.
34. Pang H-N, Naudie DDR, McCalden RW, MacDonald SJ, Teeter MG. Highly crosslinked polyethylene improves wear but not surface damage in retrieved acetabular liners. *Clin Orthop Relat Res.* 2015;473:463–468.
35. Reinitz SD, Currier BH, Levine RA, Van Citters DW. Crosslink density, oxidation and chain scission in retrieved, highly cross-linked UHMWPE tibial bearings. *Biomaterials.* 2014;35:4436–4440.
36. Sakellariou VI, Sculco P, Poultsides L, Wright T, Sculco TP. Highly cross-linked polyethylene may not have an advantage in total knee arthroplasty. *HSS J.* 2013;9:264–269.
37. Schmalzried TP, Jasty M, Harris WH. Periprosthetic bone loss in total hip arthroplasty. Polyethylene wear debris and the concept of the effective joint space. *J Bone Joint Surg Am.* 1992;74:849–863.
38. Sutula LC, Collier JP, Saum KA, Currier BH, Currier JH, Sanford WM, Mayor MB, Wooding RE, Sperling DK, Williams IR. The Otto Aufranc Award. Impact of gamma sterilization on clinical performance of polyethylene in the hip. *Clin Orthop Relat Res.* 1995;319:28–40.