A Clinically Relevant Oxidation Model for UHMWPE and its Comparison to Retrievals

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Introduction In cross-linked polyethylene (UHMWPE) with no antioxidants, irradiation and melting eliminates free radicals to impart oxidation resistance. But there are incidences of oxidation in long term retrievals [1] and in those stored on the shelf after retrievals [2]. Current in vitro aging is unable to reproduce these changes. Squalene, a lipid known to absorb into polyethylene *in vivo* [3], can initiate oxidation in the absence of free radicals [4]. To develop a clinically relevant aging model incorporating synovial fluid lipids, we absorbed four lipids into UHMWPE before accelerated aging. We compared oxidation levels, profiles, and products, to those of retrievals. **Methods** *Individual* lipid emulsions were prepared using 0.25 wt. % of each of cholesterol, cholesteryl linoleate, cholesteryl stearate, and squalene Tween 20 or Tween 80 as emulsifier. A *mixed-lipid* emulsion was made by mixing the individual emulsions. A 65-kGy irradiated/ melted Prolong™ (48 months *in vivo*), and two 100-kGy irradiated/melted Longevity™ (44 & 120 months *in vivo*) were used. Cubes (1 cm) of 100 kGy and melted GUR1050 UHMWPE were doped at 40°C in the individual emulsions (5-6 weeks), pure squalene (1 day) or the mixed-lipid emulsion (3 weeks) to achieve 1-3 mg absorption. One set doped in pure squalene at 40 °C for 11.5 weeks had 17 mg. They were analyzed before and after aging at 5 atm of O_2 and 70 °C for 14 days. Thin sections (150 µm) were analyzed using Fourier Transform Infrared Spectroscopy (FTIR) at every 100µm along the depth. A carbonyl or oxidation index was calculated by normalizing the area under 1740 cm^{-1} (1685-1780 cm^{-1}) to that at 1370 cm^{-1} (1330-1390 cm^{-1}) before and after extraction with boiling hexane, respectively. **Results** Retrievals showed subsurface oxidation (not shown). The MOI were 0.1 ± 0.03, 0.2 ± 0.05, and 0.6 ± 0.03 for the 120 month Longevity, 44 month Longevity and the Prolong, respectively. The cause of oxidation in irradiated/melted retrievals is not known. Oxidation is not related to in vivo duration; but, there is sometimes significant oxidation in the short term such as that in the 48-month Prolong. The carbonyl profiles of retrievals showed mainly ester compounds (1736 cm^{-1}; Fig 1) and some ketones (1717 cm^{-1}). These variable results suggest an influence of the in vivo environment on oxidation.

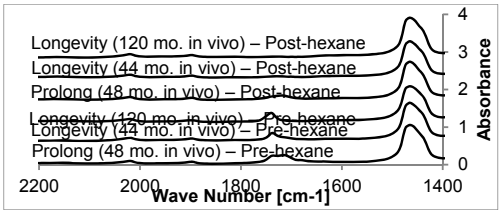
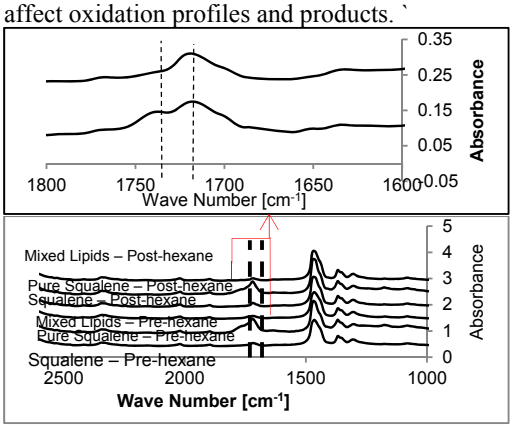


Figure 1. Overlay of FTIR absorbance spectra before and after hexane extraction. These correspond to the location of the retrievals' maximum carbonyl indices.

Samples aged *in vitro* in the presence of lipids showed surface maxima, with the exception of pure squalene doped samples, which showed subsurface peaks (not shown). All of the lipids initiated oxidation in UHMWPE in clinically meaningful concentrations of 1-3 mg, which were based on previously observed lipid absorption in retrievals [5]. Samples aged in the presence of mixed lipids showed oxidation maxima at the surface with MOI of 0.8 ± 0.09. The carbonyl profiles before hexane extraction comprise both polymer oxidation and extractable lipids, those after extraction comprise only oxidation. The profiles of mixed lipid-doped and accelerated aged UHMWPEs showed peaks at 1736 and 1717 cm^{-1}, suggesting that different lipids may act synergistically to change the products of oxidation. Interestingly, samples doped with pure squalene at 40°C for a longer period of time showed both subsurface oxidation profiles and esters and ketones as oxidation products (Fig 2), supporting that (1) squalene may be a major contributor to oxidation *in vivo*; (2) changes in the diffusion and oxidation rates of the absorbed lipids in UHMWPE can significantly affect oxidation profiles and products. `



Therefore, the investigation into the mechanisms and rates of oxidation is crucial in predicting the rate of degradation of total joint implants *in vivo*.

Conclusions The incorporation of synovial lipids into aging models showed promise in replicating oxidation levels, profiles and products observed in long-term highly cross-linked retrievals.

References 1. Currier et al. JBJS 92A: 2409-18 (2010); 2. Muratoglu et al. JBJS 92A: 2809-16 (2010); 3. Costa et al. Biomaterials 22:307-15 (2001); 4. Oral et al. JBMR 100B:742-51 (2012); 5. Rowell et al. ORS (2011).