

***In vivo* chemical alterations of tibial liners made from contemporary crosslinked UHMWPE**

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DISCLOSURE: Douglas Van Citters (5-DePuy Synthes, Medacta, RevBio, TJO), Joshua J. Jacobs (3B-Medtronic Sofamor Danek; 4-Implant Protection; 5-Medtronic Sofamor Danek, Nuvasive, Zimmer), Pourzal (5-Zimmer Biomet, Stryker; 8-Biotribology)

INTRODUCTION: The use of highly cross-linked UHMWPE (HXLPE) has successfully combatted early total knee arthroplasty (TKA) failure due to particle induced osteolysis. Nonetheless, studies have shown that *in vivo* oxidation of HXLPE components is related to the accelerated wear in TKA. Currently, there exist two generally accepted oxidation pathways: (1) a free radical mediated mechanism; and (2) an absorbed pro-oxidative species mechanism. The latter is believed to be affected by synovial fluid, which has a complex composition that varies among individuals. In this study, we are presenting a combined Fourier Transform Infrared spectroscopic imaging (FTIRI) and Raman spectroscopic mapping approach to generated spatial maps of full-depth oxidation profiles and absorbed organic constituents to better understand *in vivo* chemical alterations and its impact on wear and clinical outcomes.

METHODS: 13 retrieved tibial liners, with a minimum postretrieval shelf time, from 5 designs and 4 manufactures were analysed. The analysed liners included: NexGen, Zimmer (gamma barrier, N=2); Nexgen, Zimmer (prolong, N=4), Triathlon X3, Stryker (highly crosslinked/annealed, N=3), Sigma XLK, DePuy (N=2), Genesis, Smith & Nephew (XLPE, N=2) The average time *in situ* was 124.2 months (60.3, 197.5). Liners were cut in the sagittal plane of the medial condyle to expose a vertical cross-section. Thin sections (~200 µm thick) were removed parallel to the exposed cross-section using a microtome for FTIRI/Raman analysis. For FTIRI, a large field of view was achieved via mosaic mode for a full-depth scans reaching from the articulating surface to the backside. All imaging data were collected using an Agilent Cary 670/620 system with 2 cm⁻¹ spectral resolution (wavenumber range: 3750-900 cm⁻¹). Because absorbed species are of interest, devices were not extracted. Thus, the spatial distribution of the oxidation profile was calculated using the ester-insensitive ketone oxidation index (KOI), defined as the peak center of around 1715 cm⁻¹ (ketone peak) referenced against the peak center at 1368cm⁻¹. Data processing was done using CytoSpec software. Absorbed species were assessed by Raman micro-spectroscopy (Horiba) using a 10x objective and 532nm laser with ND filter set to 10%.

RESULTS: 12 of 13 liners, across all manufacturers and PE types, exhibited a strong subsurface oxidation band (hundreds of microns below the articulating surface) and an increased oxidation zone in the subsurface. The average maximum KOI was 0.89 ± 0.54 (range: 0.05 to 2.3). For comparison with the ASTM oxidation index based on the carbonyl band (1736cm⁻¹ vs. 1368cm⁻¹), the corresponding chemical images of one liner are showcased in **Figure 1**. The maximum oxidation was in most cases distributed heterogeneously within the oxidation band. The Raman data identified the occurrence of β-carotene infiltrates within the surface of 11 tibial liners. β-carotene is an antioxidant characterized by Raman peaks at 1005cm⁻¹, 1155cm⁻¹, and 1514cm⁻¹ (**Fig.2**). The β-carotene layer occurred in most cases as band at a depth 50-70 micrometers below the bearing surface. One Case (XLK, DePuy) exhibited a broader β-carotene band reaching from the surface several hundreds of micrometers into the liner. This liner did not exhibit an oxidation band.

DISCUSSION: This study highlights the heterogeneity of oxidation profiles of HXLPE liners across manufacturers, both first and second generation with various degrees of cross-linking. Imaging revealed a complex oxidation progression scenario that likely results from a competitive interplay between the absorption of anti- and pro-oxidative species, which could affect the mechanical property of these liners. Interestingly, the liner without oxidation exhibited the strongest β-carotene signal at the surface. The cause of *in vivo* oxidation is multifactorial warranting further research. The chemical state of wear debris generated from chemically altered surfaces also needs to be considered with respect to its bio-reactivity. Also, future studies will include liners with antioxidant-doped polyethylene, to determine how these materials alter chemically *in vivo*.

SIGNIFICANCE: This study is highly clinically relevant with respect to the potential occurrence of delayed osteolysis (*i.e.*, time *in vivo*: >10 years) in the long run. The *in vivo* oxidation will deteriorate the material's properties and accelerate material loss during articulation. Liner oxidation can also lead to the on-set of delamination (**Fig. 3**) resulting in gross wear and subsequent failure due to instability or laxity. No current lab-based accelerated aging experiments can reproduce the *in vivo* oxidation profiles shown here suggesting a much more complex mechanism.

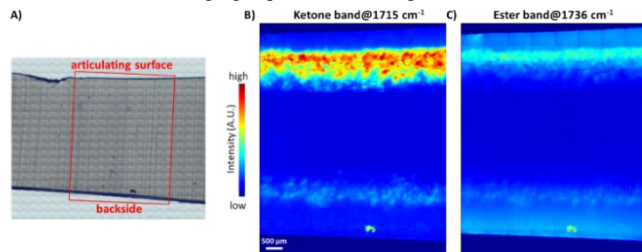


Figure 1 The FTIR spectroscopic characterization of a liner with time in vivo of 107.5 months and a maximum KOI of 0.88: A) The light microscopic image of the cross-section sample. FTIRI was performed on the red-boxed area. Chemical images of the B) KOI and C) ASTM method. A higher subsurface oxidation band was evident at both the articulating surface and the backside. By using the ketone band for imaging, the heterogenous nature of the subsurface oxidation can be appreciated, while the ester band-based image is more evenly distributed and narrower in width. It also has a transition zone from the surface and backside, whilst it is not the case for KOI band. It should be noted that the chemical map should not be compared directly with each other because the color scale is not global.

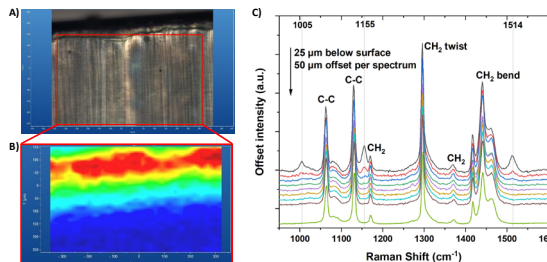


Figure 1 The Raman micro-spectroscopic mapping of absorbed chemical constituent in the liner articulating surface. A) The light microscopic image of a zoomed-in area (red-boxed) of the same sample using the Raman microscope with polarized light. Different birefringent patterns can be seen from the image. The measured point density was 27×27 array at the total region-of-interest of 400×640 µm². B) Using the characteristic β-carotene peak at 1155 cm⁻¹, a strong β-carotene band can be visualized right below the articulating surface. Several consecutive point spectra were plotted in a stacking fashion in C) to demonstrate the spectral difference of a liner between areas with and without β-carotene. The rest of the labelled peaks are the characteristic vibrational modes for HXLPE.

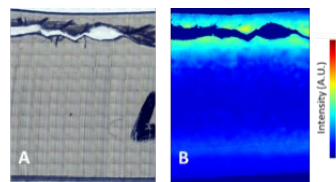


Figure 3 The FTIR spectroscopic characterization of a liner with time in vivo of 123.1 months and a maximum KOI of 2.3. Prominent subsurface delamination can be observed, and highest oxidation can be found along the subsurface crack.