


CLINICAL DEVICE-RELATED ARTICLE

MPC-grafted highly cross-linked polyethylene liners retrieved from short-term total hip arthroplasty: Further evidences for the unsuitability of the MPC method

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Abstract

An analysis is presented of four short-term retrieved highly crosslinked polyethylene (HXLPE) hip liners grafted with 2-methacryloyloxyethyl phosphorylcholine (MPC) on their bearing surfaces, which were recently commercialized as a new generation of artificial hip joints. Straightforward evidences by X-ray photoelectron spectroscopy (XPS) confirmed that the MPC layer peeled off on the bearing surface of all short-term liners in both main wear and nonwear zones. Analyses by Fourier-transform infrared spectroscopy with attenuated total reflection assessed the extent of surface oxidation and revealed the type of oxidative species. Electron spin resonance analyses, which compared retrievals and as-received samples, revealed the presence of different species of alkoxy CO[•] radicals. This study suggests that MPC grafts on polyethylene do not offer any additional protection from oxidation and can delaminate prematurely after short-term in vivo exposure.

KEYWORDS

alkoxy radical, oxidation, phosphorylcholine, polyethylene, total hip arthroplasty

1 | INTRODUCTION

Phospholipids stacked in a series of superposed bilayers on the cartilage surface are hydrophilic, fully hydrated at physiological pH, and act as a solid lubricant at the bearing interface of human joints (Guerra et al., 1996; Kumar et al., 2001). Depriving of such lipid bilayers the cartilage surface results in a two- to threefold increase of the self-mated friction coefficient as compared to lipid-covered cartilage surfaces (Pawlak et al., 2012). Hence, the presence of phospholipid bilayers is crucial in increasing wettability and reducing surface friction in articular cartilage. These basic concepts of joint physiology have recently inspired a man-made technological path to reproduce the same tribophysics of the human cartilage into artificial hip joints (Moro et al., 2004). Invoking a biomimetic approach, Kyocera Medical got

approval from the Japanese Ministry of Health, Labor, and Welfare in 2011 and successively commercialized HXLPE hip liners grafted at their bearing surfaces with a thin layer of 2-methacryloyloxyethyl phosphorylcholine (MPC). MPC is a methacrylate monomer with a phospholipid polar group as side chains, which, grafted onto the HXLPE liner, was intended to provide the same functionality of the phospholipid layers stacked on top of the human cartilage. The newly conceived liners were presented as a new generation of artificial hip joints capable to reduce friction and to prevent aseptic loosening (Kyomoto et al., 2007; Kyomoto et al., 2017). Thanks to their biocompatibility, MPC grafting were successfully applied to various devices, such as soft contact lenses (Goda & Ishihara, 2006), stents (Iwasaki & Ishihara, 2012), guide wires (Lewis, 2000), cardiopulmonary bypasses (Rubens & Mesana, 2004), and ventricular assist devices (Iwasaki & Ishihara, 2012).

Intuitiveness makes it easy even for nonexperts to understand the phospholipid graft concept, and this has so far been the main reason for a successful story telling by the maker on MPC-grafted liners. However, at second glance, several conceptual inconsistencies might appear in this specific application. First, diseased joints, especially those of rheumatoid patients or those developing infection, might experience pH values lower than the physiological one since the buffering function of synovial fluid is missing or insufficient (Goldie & Nachemson, 1970; Treuhaft & McCarty, 1971). However, the difference between pH of joint fluid in normal and rheumatoid patients seems to be quite small. Even in a mildly acidic environment, phospholipids easily undergo disruption of hydrogen bonding between the hydrophilic phospholipid head and hydrophobic tails, which make their structure unstable (Wang et al., 2015). Accordingly, the structure of MPC grafted on HXLPE liners is expected to be pH sensitive and to chemically degrade exactly in the same way osteoarthritic cartilage phospholipids do in diseased joints (Pawlak et al., 2012). Second, unlike native joint interfaces, the mating surfaces of artificial hip joints are scarcely lubricated, lack synovium-derived lubricin molecules, and thus locally experience high stress concentrations in a lack of lateral hydrodynamic conditions (Jay & Waller, 2014; Stewart, 2010; Zhu, Marin, Sugano, & Pezzotti, 2017). The combination of such detrimental circumstances makes the scenario much more complex than the ideal picture so far proposed for a lubricated MPC-grafted liner. For these reasons, we have been skeptic toward the early optimism that accompanied hip simulation and early radiographic tests, which claimed the enhanced hydrophilicity and superior frictional performance for MPC-grafted polyethylene liners (Kyomoto et al., 2007; Moro et al., 2014; Takatori et al., 2015).

In a previous paper (Tone, Hasegawa, Puppulin, Pezzotti, & Sudo, 2018), we examined short-term retrievals and found that in none of three studied samples of retrieved MPC-grafted liners, detectable MPC graft remained on the bearing surfaces although two samples yet contained remains of MPC polymer in their rim zones. We suggested that the MPC graft might have quickly disappeared from the bearing surface under *in vivo* loading, which is more severe than the *in vitro* one. In this study, we examined four additional short-term retrievals and sought a confirmation of our previous results, while also looking for further clarifications of the mechanism of MPC peeling off. Similar evidences were obtained by different research group on short-term retrievals (Nakasone et al., 2015), consistent with our previous studies (Sugano et al., 2016; Tone et al., 2018) in reporting the quick disappearance *in vivo* of the grafted polymer. Despite such a body of evidences on the tribological insignificance of the MPC technology in ameliorating the performance of artificial hip joints, the MPC-grafting approach continued to receive official appreciations (<https://www.businesswire.com/news/home/20180625005394/en/>).

In this study, we analyzed four HXLPE MPC-grafted retrieval liners in comparison with three as-received samples of the same type. The main purposes of this investigation were to evaluate whether the MPC layer had any role in reducing wear or, at least, if it remained on the surface after short-term *in vivo* exposure; and, to detect whether

or not oxidation or other structural modifications occurred during service. Such evaluations are crucial in the evaluation of the MPC-grafting technology, and it is hoped that the additional scientific evidences shown in this paper will contribute to clarify the real suitability of the MPC method in hip arthroplasty. In addition, this study shall hopefully trigger evaluation criteria based on more rigorously scientific arguments and clinical evidences, and promote a better transparency toward the end-user patients.

2 | EXPERIMENTAL PROCEDURES

2.1 | Investigated samples

A set of four retrieved MPC-grafted HXLPE liners were analyzed, which were manufactured by Kyocera Medical under the commercial name Aquala[®] (clinically introduced in Japan since 2011 for total hip arthroplasty). Three new liners of the same type were also studied for comparison. All samples are listed in Table 1 together with their geometrical characteristics and clinical information. The Aquala[®] liners were manufactured by compression molding ultra-high molecular weight polyethylene (UHMWPE) (GUR1020) bar stock gamma-ray irradiated with 50 kGy in N₂ gas and then annealed at 120°C for 7.5 h in N₂ gas for crosslinking. According to the maker, the HXLPE liner surface was preliminary coated with benzophenone and immersed in an aqueous MPC solution. Then, the liners was subjected to photo-induced graft polymerization on their surface by means of ultraviolet irradiation (5 mW/cm (Kumar et al., 2001) for 10–360 min at 60°C) using a Toshiba D-35 filter that permitted the passage of ultraviolet light in the narrow wavelength interval of 350 ± 50 nm. Finally, the MPC grafted HXLPE specimens were gamma-sterilized with a dose of 25 kGy in N₂ gas atmosphere (Kyomoto et al., 2007). As a control, one nongrafted sample manufactured by the same maker was also studied (simply labeled as UHMWPE, henceforth).

In Table 1, the as-received liners and the retrievals are labeled as Samples AR1–AR3 and Samples R1–R4, respectively. The as-received samples were 32 mm (one sample) and 36 mm (two samples) in their inner diameter. Of the four retrievals, two had an inner diameter of 40 mm and two of 32 mm. All samples lasted in the human body for a period between 1 and 2 years. The retrieved liner was cleaned with washing saline and stored with 70% ethanol in refrigerator. The causes of revision after total hip arthroplasty were reported that instability, aseptic loosening, infection, and periprosthetic fracture were four major reason (https://connect.ajrr.net/hubfs/Campaigns/All%20Annual%20Reports/AAOS_AJRR_2019_Annual_Report_FINAL.pdf?hsCtaTracking=1d80e9fa-66fe-4525-a5cb-15c30ec19a1f%7C8becda93-a51e-41cc-bcfa-ca9130c1add6; <https://jsra.info/pdf/THA-20180331.pdf>

). Aseptic stem loosening and cup loosening sometimes occur if the initial fixation stability of implant is not adequate. All pristine and retrieved samples were observed under a laser microscope (VKX200K series, Keyence, Osaka, Japan) both in their main wear and nonwear zones (MWZ and NWZ, respectively). The MWZ was assumed to lie at an azimuthal angle of 30° from the perpendicular line at the

TABLE 1 Geometrical and clinical information about the pristine and retrieved liners investigated in this study

Implant type	Clinical information	Internal diameter	Maker	Resin
As-received sample AR1 MPC/UHMWPE	—	32 mm	Kyocera Medical	GUR1020
As-received sample AR2 MPC/UHMWPE	—	36 mm	Kyocera Medical	GUR1020
As-received sample AR3 MPC/UHMWPE	—	36 mm	Kyocera Medical	GUR1020
Retrieval sample R1 MPC/UHMWPE	68 years old man 1 year and 11 months Stem aseptic loosening	40 mm	Kyocera Medical	GUR1020
Retrieved sample R2 MPC/UHMWPE	80 years old female 1 year and 9 months Infection	32 mm	Kyocera Medical	GUR1020
Retrieval sample R3 MPC/UHMWPE	53 years old woman 1 year and 2 months Cup aseptic loosening	32 mm	Kyocera Medical	GUR1020
Retrieved sample R4 MPC/UHMWPE	69 years old man 1 year and 11 months Stem aseptic loosening	40 mm	Kyocera Medical	GUR1020

geometric center of the bearing surface, while the NWZ was taken in a zone of the bearing surface closer to the rim and belonging to an unloaded region of the liner. For comparison, pristine samples were also observed in the corresponding zones.

2.2 | XPS analyses of liner bearing surfaces

The elemental chemistry of the surfaces of new and retrieved MPC-grafted HXLPE samples was analyzed by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using a device (JPS-9010MC/SP; JEOL, Tokyo, Japan) equipped with an Mg-K α radiation source at 10 kV (10 mA) at the anode. Both wide scan and narrow scan modes were applied with voltage steps of 1.0 and 0.1 eV, respectively. The dwell time was always 100 ms and the measurement angle 34°. The penetration depth is several nanometers and the measurement spot (probe) diameter is around several mm in XPS measurement. Emissions from carbon atoms (C1s region) at 284, 285.5, 286.5, and 288 eV were recorded, which related to C-C skeletal bonds in the UHXLPE structure, C-C-CN, C-CO (ether), and C=O (ester) bonds, respectively. Bonds related to nitrogen atoms (N1s) were monitored at 399 eV (N $_2$) and at 402–403 eV (–N $^+$ [CH $_3$] $_3$), while those related to phosphorus atoms (P2p) appeared at 132 eV as specific to the phosphorylcholine group in the MPC unit (–O–PO $^-$ [=O]–O–). XPS measurements were repeated three times per each investigated zone (MWZ, NWZ, Rim zone), namely $n = 9$ per each investigated sample. Each measurement involved scanning 40 times.

2.3 | ATR-FTIR spectroscopy on bearing surfaces

The functional-group vibrations of NWZ and MWZ of all the MPC-grafted HXLPE retrievals were examined by Fourier-transform

infrared spectroscopy with attenuated total reflection (ATR-FTIR). The measurements were performed on the bearing surfaces of all retrievals and pristine samples over a range of frequencies between 900 and 1800 cm $^{-1}$ by using the ATR-FTIR analyzer FT/IR-4700 type A (ATR PRO ONE; Jasco Co., Tokyo, Japan) with a spectral resolution ~4.0 cm $^{-1}$. The number of scans was 60 at $n = 5$ measurement locations for each studied sample. The probe size was >15 μ m. Oxidation products, namely, acyl peroxy, peroxy acid, esters, aldehydes, ketones, and carboxyl acids were searched for in the ATR-FTIR spectra at 1794, 1770, 1,744/1733, 1,724, 1,715, and 1,706 cm $^{-1}$, respectively (Chenery, 1997; Kurtz et al., 2001). The intensities of these bands were compared to the wagging signal of methylene chains at 1368 cm $^{-1}$. The so-called “oxidation index,” *OI*, was calculated from the ATR-FTIR spectra according to the following equation (Kurtz et al., 2001):

$$OI = \sum_i (I_{\text{carbonyl}})_i / I_{-\text{CH}_2-}$$

where *I* is the intensity of bands in the ATR-FTIR spectrum represented by the subscript (oxidative species and methylene chains at numerator and denominator, respectively).

2.4 | ESR analyses

Electron spin resonance (ESR) measurements were carried out at room temperature using a JES-TE300 (JEOL, Tokyo, Japan) with 9.3 GHz microwave, a power of 5.2 mW, and a center field of 332.0 mT (sweep width and time equal to 5.0 mT and 0.5 min, respectively). A standard specimen Mn $^{2+}$ /MgO was used as a marker. Samples were located in a quartz tube at a fixed position and sealed off after evacuation up to 10 $^{-2}$ Pa. The relative radical

concentration was calculated according to the spectral double integration method (Jahan & Durant, 2005). The amount of radicals per unit weight, R_a , was calculated according to the following equation:

$$R_a = \int \int g_i(B) dB^2 / \left[\left(\int \int g_{ref}(B) dB^2 \right) \times W \right]$$

where $g(B)$ is the first derivative of the absorption curve, B is the magnetic field, the subscripts i and ref refer to the measured sample and to the Mn^{2+}/MgO standard sample, respectively, and W is the weight of the polyethylene sample.

2.5 | Statistical analysis

The unpaired Student's t -test was utilized for statistical analyses. In the Results section, sample size, n , for each experiment are stipulated in the figure's insets. A p value $< .05$ was considered statistically significant and labeled with one asterisk. On the other hand, values of $p > .05$ were considered as statistically nonsignificant and labeled "n.s."

3 | RESULTS

Both pristine and retrieved samples were inspected by laser microscopy (Figure 1). The machining marks seen in the pristine liners all over the bearing surface (cf., Figure 1a,b for Sample AR1 and AR2, respectively) were clearly present in both NWZ and MWZ of the retrieved Samples R1 and R2 (Figure 1c/d and e/f, respectively). Regarding the retrievals Samples R3 and R4, we yet observed machining marks on their respective NWZs (Figure 1g,i, respectively), but such marks were partly erased in their MWZs (Figure 1h,j, respectively). Scratches occurred in vivo during implantation were visible in

all retrievals, but the overall amount of wear damage appeared to be low in all the studied samples.

Figures 2–4 show the XPS spectra (P2p, N1s, and C1s, respectively) of MPC-grafted HXLPE pristine and retrieval samples in both NWZ and MWZ. The P2p emission at 132 eV could only be observed from the three pristine samples (Samples AR1, AR2, and AR3; cf., Figure 2a–c, respectively). No bands related to phosphorus bonds could be resolved in any retrieval either in their MWZ or NWZ (cf., Figures 2d–k). The twofold N1s emission at 399 eV (N_2) and 402–403 eV ($-N^+[CH_3]_3$), seen in all three as-received samples (Figure 3a–c), became a single band 399 eV in all retrievals (Figure 3d–k). Note that N, unlike P, also stems from contamination by the N-gas atmosphere used during sterilization and. Accordingly, there is a fraction of nitrogen seen as N_2 , which does not belong to the MPC coating. To confirm this statement, we checked and found N contamination also in UHMWPE acetabular cups from different makers, which were gamma-ray-sterilized in nitrogen atmosphere (data not shown here). Note also that the relative intensity of the N_2 band with respect to the ($-N^+[CH_3]_3$) band was quite inhomogeneous among the three pristine samples, thus suggesting a poor control of the graft manufacturing. Nevertheless, the most important finding here was that the two XPS bands P2p at 132 eV and N1s at 402–403 eV ($-N^+[CH_3]_3$), which are the fingerprints of the MPC coating, systematically disappeared from the bearing surface of all the four short-term retrievals investigated, independent of the zone examined.

In the C1s region (Figure 4), the strong C-C singlet at 284 eV remained conspicuously constant among all the investigated samples (with the exception of Sample AR3, in which it was clearly weaker (Figure 4(c)). However, all bands in the triplet at 285.5, 286.5, and 288 eV, which related to C-N, C-O (ether), and C=O (ester) bonds, respectively, experienced a clearly lower intensity relative to the C-C band in the retrievals (Figure 4d–k) as compared to the pristine liners (Figure 4a–c). This observation is emphasized in Figure 5, which shows a comparison between a control as-received nongrafted (labeled as UHMWPE) (a)/(b), an as-received grafted

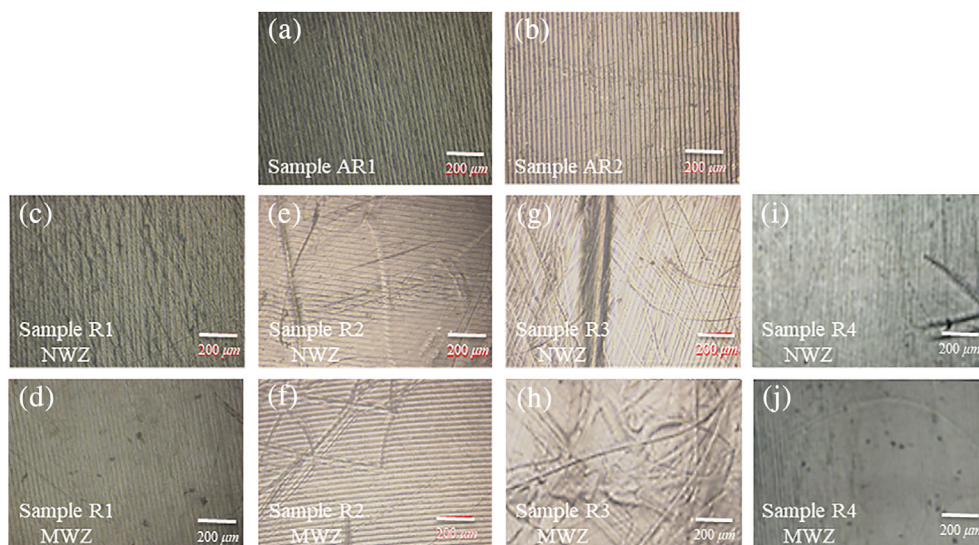


FIGURE 1 Laser micrographs of the surfaces of the as-received and retrieved samples investigated in this study (cf., legends in inset)

FIGURE 2 XPS spectra (P2p) of the MPC-grafted HXLPE as-received (a–c) and retrieved samples in NWZs (d–g), and MWZs (h–k)

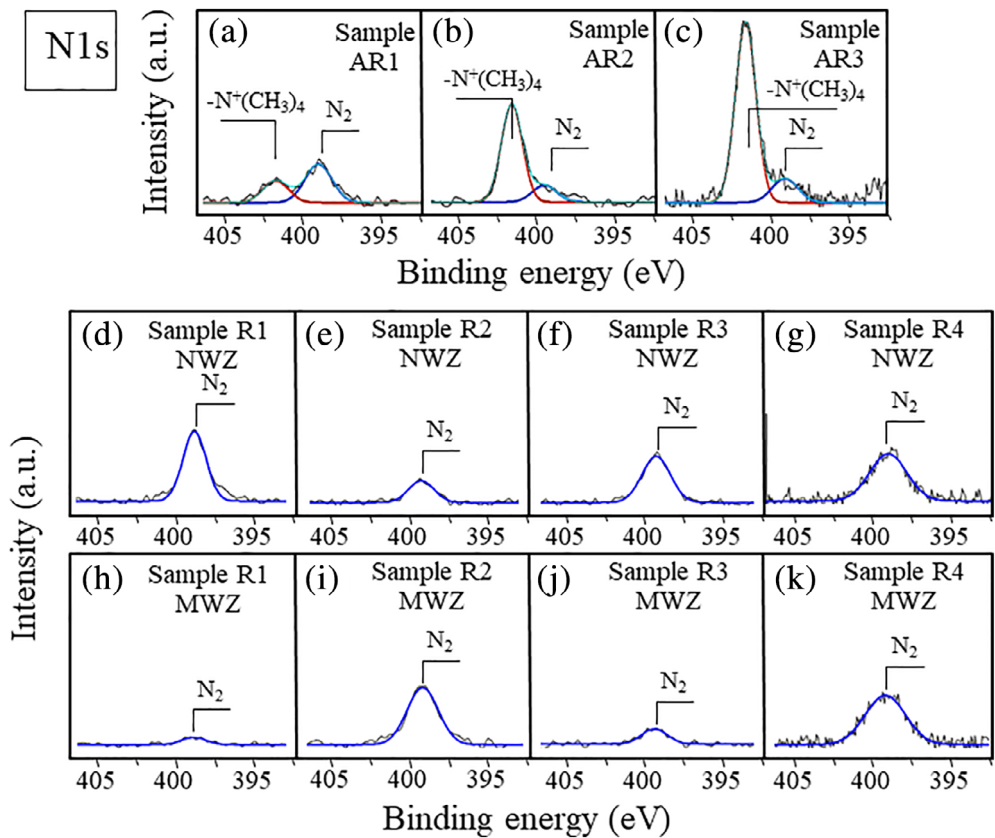
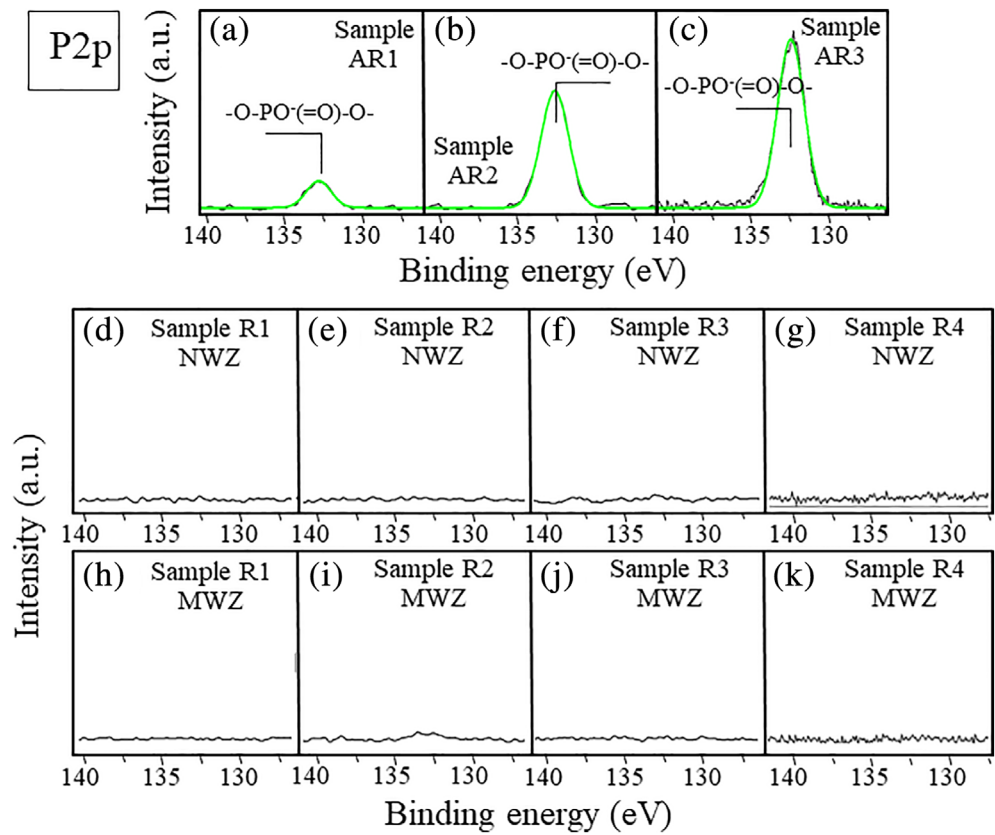


FIGURE 3 XPS spectra (N1s) of the MPC-grafted HXLPE as-received (a–c) and retrieved samples in NWZs (d–g) and MWZs (h–k)

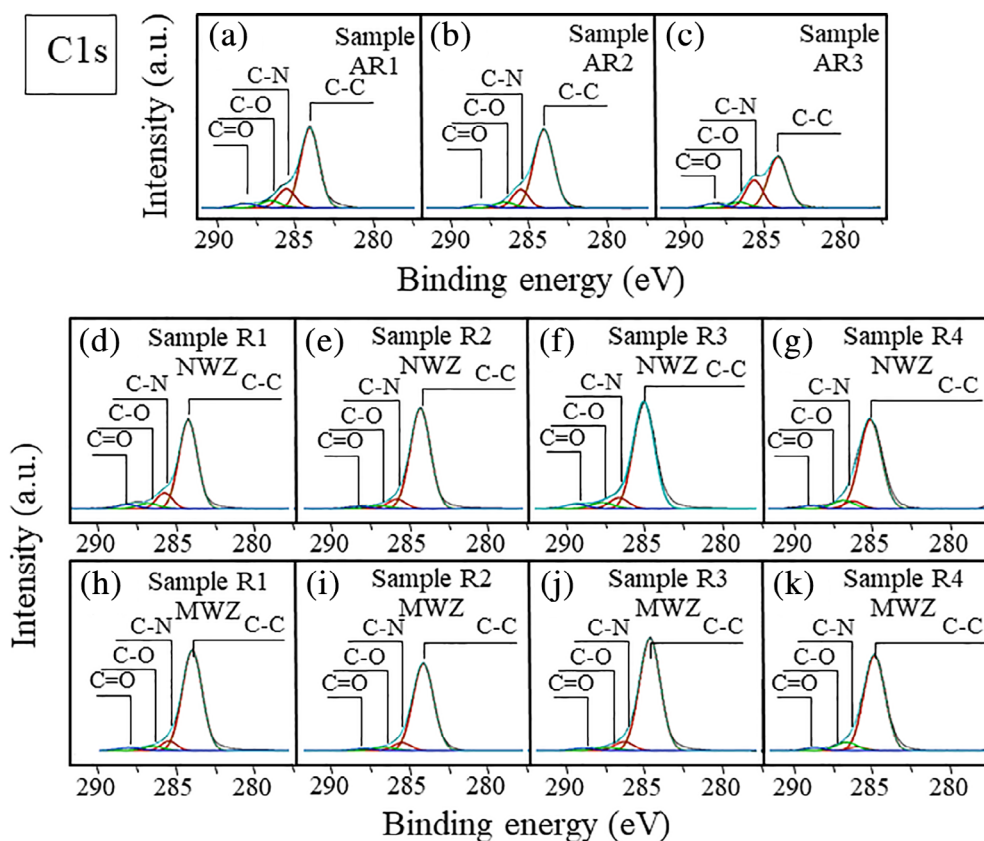


FIGURE 4 XPS spectra (C1s) of the MPC-grafted HXLPE as-received (a–c) and retrieved samples in NWZs (d–g) and MWZs (h–k)

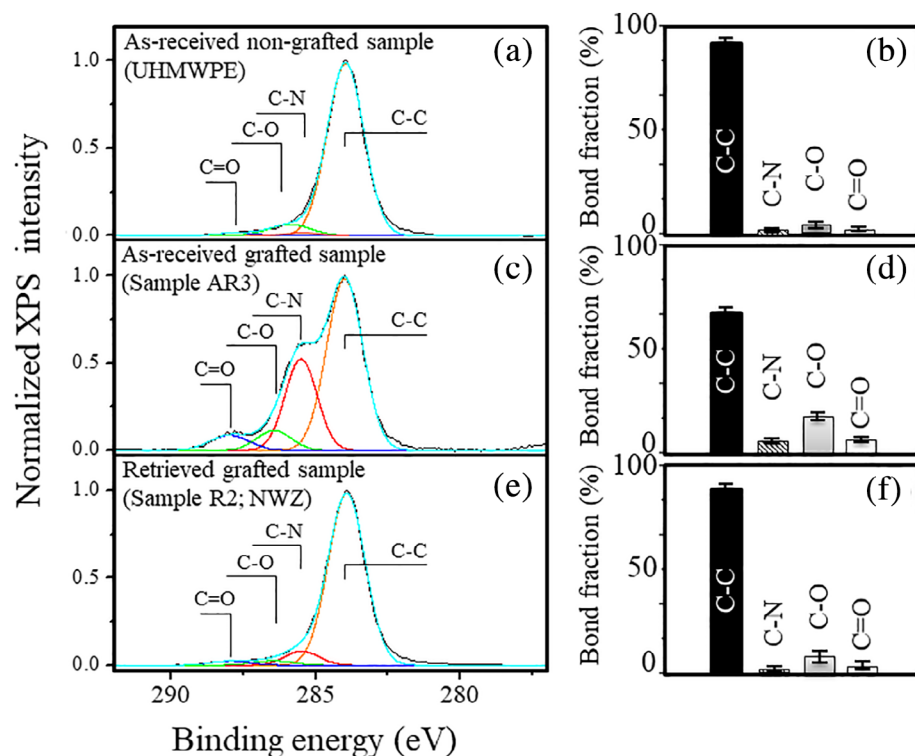


FIGURE 5 Comparison among C1s XPS spectra from (a) as-received nongrafted, (c) as-received grafted, and (e) retrieved (Sample R2); the fractions of different bonds calculated from the spectra are given in (b), (d), and (f), respectively

(Sample AR3) (c)/(d), and a retrieved (grafted) (Sample R2; NWZ) (e)/(f) samples. Besides a more intense fraction of C-N bonds, which obviously arises from the presence of the MPC graft, one could note a

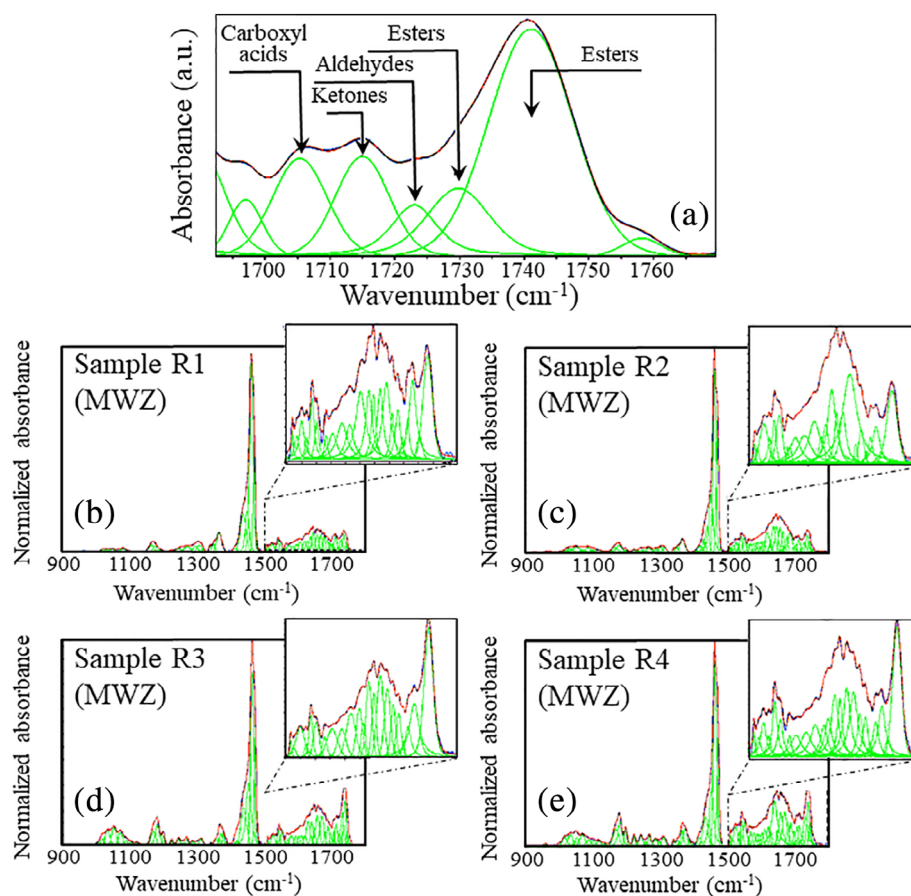
stronger signal from both ether and ester bands in the as-received grafted sample (Figure 5c/d) as compared to the nongrafted pristine one (Figure 5a/b). In the retrieval (Figure 5e/f), the C-N band experienced a

TABLE 2 Atomic percent fractions of different elements at the surface of pristine and retrieval MPC-grafted samples according to XPS analyses in both NWZs and MWZs

Sample	Oxygen (at.%)	Nitrogen (at.%)	Carbon (at.%)	Phosphorus (at.%)
Published data	27.9 [31.6]	5.1 [5.3]	61.8 [57.9]	5.2 [5.3]
UHMWPE (nongrafted)	6.01	1.25	92.35	-
Sample AR1	17.88	1.31	79.73	1.08
Sample AR2	17.29	1.91	76.66	4.14
Sample AR3	22.82	3.24	67.29	6.64
Sample R1 (NWZ)	16.59	1.80	81.38	0.22
Sample R1 (MWZ)	8.85	0.80	90.26	0.09
Sample R2 (NWZ)	7.83	0.67	91.38	0.12
Sample R2 (MWZ)	9.58	1.95	88.15	0.32
Sample R3 (NWZ)	9.87	1.22	88.69	0.22
Sample R3 (MWZ)	5.83	0.44	93.65	0.08
Sample R4 (NWZ)	5.25	1.61	93.00	0.14
Sample R4 (MWZ)	4.17	1.82	93.92	0.09

Note: Comparisons are made with published data (Kyomoto et al., 2007) and with data collected on a nongrafted sample from the same maker.

FIGURE 6 (a) Contributions from different products of oxidation in the ATR-FTIR spectrum of HXLPE; and, ATR-FTIR spectra of four retrievals in their MWZs (Samples R1, R2, R3, and R4 in b, c, d, and e, respectively; cf., labels in inset)



significantly lower intensity, while the decrease in fraction of the oxygen bonds (especially ethers) was proportionally less pronounced than that of C-N bonds. This point will be discussed in the next section. Table 2 summarizes the elemental composition at the surface of all the NWZ and MWZ in the investigated MPC-grafted HXLPE retrievals. Comparisons are carried out with pristine samples, with data previously published by Kyomoto et al. (2007) for a pristine MPC-grafted liner with

nominal values (shown in square brackets), and with a liner of the same type but without MPC grafting (labeled UHMWPE). The most striking feature in the data of Table 2 is the disappearance of the MPC coating at the bearing surface of all the four retrievals both in their NWZs and MWZs.

Figure 6a shows an explanatory figure of the contributions from different products of oxidation in the ATR-FTIR spectrum of HXLPE.

On the other hand, in Figures 6b–e, the ATR-FTIR spectra of the four retrievals are given as collected in their MWZs (Samples R1, R2, R3, and R4 in (b), (c), (d), and (e), respectively; cf., labels in inset). Bands were normalized to the main peak observed at $\sim 1,368\text{ cm}^{-1}$ in all samples, which represents methylene (CH_2) chain wagging in the HXLPE bulk. The intensity of this band was the strongest in all recorded spectra and conspicuously constant among different samples. Absorption peaks in the spectral interval $1,700\text{--}1,760\text{ cm}^{-1}$ were deconvoluted to single out the contributions of different oxidative species at the surface of the respective liners (cf. enlarged zones in inset). The results of such deconvolution are given in Figure 7 in terms of ATR-FTIR intensity ratio to the methylene (CH_2) band. According to this graph, the oxidative species with the most strikingly increasing fraction after in vivo exposure is esters (up to $>300\%$ and statistically significant in three out of four retrievals), followed by ketones (up to $\sim 200\%$ and statistically significant in three out of four retrievals), and carboxyl acids (up to $\sim 200\%$ and statistically significant in three out of four retrievals). On the other hand, the content of aldehydes groups remained conspicuously invariant with respect to the pristine samples. Table 3 summarizes the *OI* values computed for the as-received (average value) and the four retrieved MPC-grafted liners in both NWZs (upper values) and MWZs (lower values), as calculated according to Equation (1).

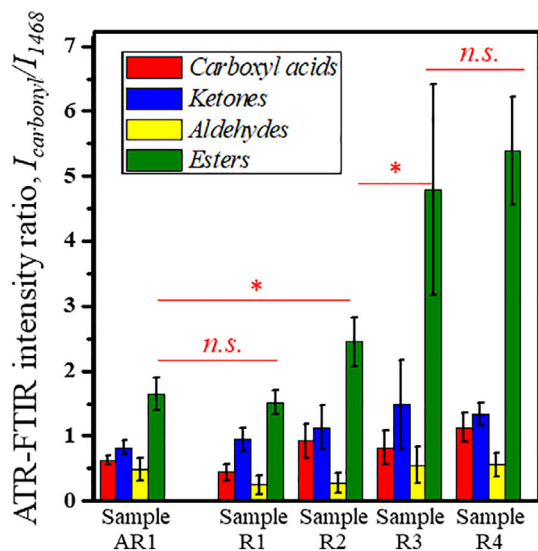


FIGURE 7 Relative intensities of absorption peaks in the spectral interval $1,700\text{--}1,760\text{ cm}^{-1}$ representing the contributions of different oxidative species at the surface of different samples; the ATR-FTIR intensity ratios refer to the methylene (CH_2) band at $1,368\text{ cm}^{-1}$. Results of a statistical elaboration of the data are given in inset

TABLE 3 *OI* values and related standard deviations as calculated from ATR-FTIR measurements according to Equation (1); upper and lower values represent the NWZs and MWZs of the retrievals, respectively

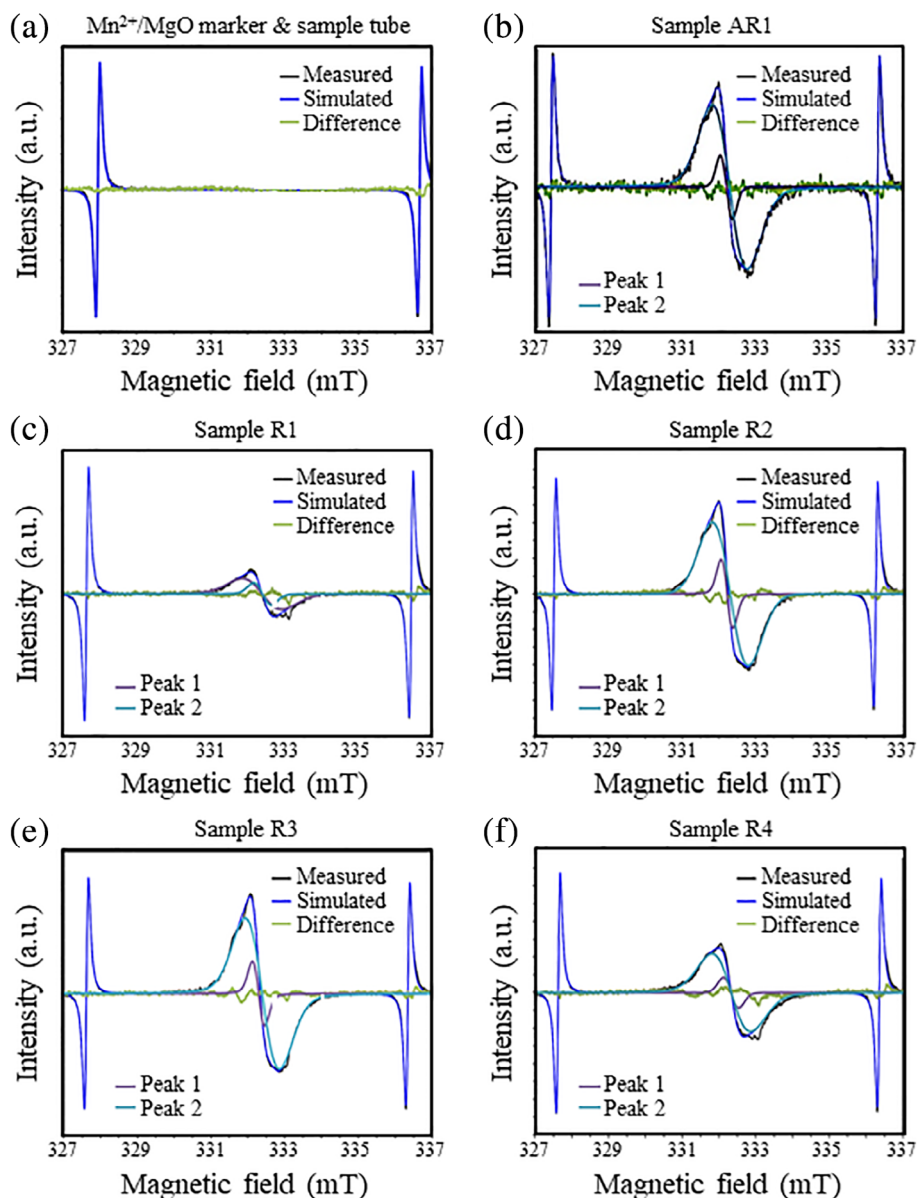
Sample	Samples AR (average)	Sample R1	Sample R2	Sample R3	Sample R4
<i>OI</i>	4.58 ± 0.55	11.21 ± 0.27 3.60 ± 0.38	5.98 ± 0.31 6.27 ± 0.69	7.54 ± 0.41 8.73 ± 1.48	9.22 ± 0.88 10.07 ± 0.77

Figure 8 shows the ESR spectra of: (a) $\text{Mn}^{2+}/\text{MgO}$ marker and the sample tube used in the present experiments; (b) Sample AR1; and, (c)–(f) Sample R1–R4. As seen, all the ESR spectra of as-received and retrieved liners were well resolved and composed of two hyperfine lines. The hyperfine splitting of the radical signal depends on the geometric angle between the magnetic field and the radical bond direction. The radical concentration was the lowest in Sample R1, which also showed the lowest *OI* value (cf., Table 3). Figure 9a shows the *g* values calculated from the spectra recorded in Figure 8 for the two detected signals g_1 and g_2 . The presence of two hyperfine lines was interpreted as a consequence of alkoxy radicals associated with the bonding with two different carbon atoms (methine and unprotonated carbon, denoted as 1 and 2, respectively) in the polyethylene chain (see discussion section). The results indicate that CO^* alkoxy radicals were produced predominantly during manufacturing of the MPC-grafted HXLPE liners. The amounts of radicals per unit weight, R_a , are plotted in Figure 9b for the four retrieved samples in comparison with that of the pristine one. These values were calculated according to Equation (2). As seen, all retrievals experienced a lesser amount of free radicals as compared with the pristine sample, with the retrieval Sample R1 containing the lowest amount among all the investigated samples.

4 | DISCUSSION

This study confirmed previous findings on retrievals (Nakasone et al., 2015; Sugano et al., 2016; Tone et al., 2018) that no traces of MPC polymer remained on the bearing surfaces in any samples, not even in nonloaded areas, after short-term service in the human body. Despite the optimistic expectations for their in vivo performance and the positive data collected by in vitro simulation according to the ISO standard protocol 14242 (Kyomoto et al., 2007, 2017; Moro et al., 2004; Moro et al., 2014; Takatori et al., 2015), the MPC-graft disappeared from the bearing surface due to frictional forces or environmental conditions (i.e., even in NWZs). This output confirmed that the in vivo environment represents a much more severe testing workbench as compared to in vitro predictions (Zietz et al., 2015). Despite the low amount of wear damage found in all the short-term retrievals investigated (cf., Figure 1), XPS and ATR-FTIR analyses consistently showed significant differences in oxygen contents between pristine and in vivo exposed liners (cf., Tables 2 and 3). Note that the amount of oxygen belonging to the MPC polymer is negligible in the retrievals because the grafted layer was almost completely peeled off in both NWZs and MWZs, as confirmed by P- and N-bonding signals. However, it is worth noting that not all XPS peaks have the same relative

FIGURE 8 ESR spectra and their decomposition into two hyperfine lines for: (a) $\text{Mn}^{2+}/\text{MgO}$ marker and the sample tube; (b) Sample AR1; and, (c–f) Sample R1–R4 (cf., legends in inset)



intensity. That is clear in particular for carbon, which has a really strong signal when compared to Nitrogen. It is not surprising that a bonding that can be barely observed on the Carbon side is not visible from the Nitrogen side. N binding to 3C ($\text{N}-\text{C}_3$ or $-\text{N}^+-\text{C}_3$) shows a higher binding energy than $\text{H}-\text{N}(\text{H})-\text{C}$ or $\text{C}-\text{N}(\text{H})-\text{C}$, which generally has a binding energy at around 399–400 eV. So there is a high possibility that $\text{N}-\text{C}$ exists (due to the generation of Carbon radicals) cannot be fully excluded if we cannot confirm the presence of N_2 . Despite that, as mentioned above, because of the difference in the sensitivity factor between C and N, it is possible that the $\text{N}-\text{C}$ binding may be invisible. Moreover, the relatively high *OI* value found in the as-received samples (cf., Table 3) might arise from free radicals induced by the thermal treatment procedure (annealing) applied during manufacturing and remained trapped within the polyethylene structure. This was confirmed by the relatively high amount of free radicals measured by ESR in the as-received samples (cf., Figure 9b).

Regarding the nature of the detected free radicals, they essentially hop along the polymer chains since manufacturing, and the fraction of them not generating crosslinks becomes the source of potential oxidation through a complex cascade of reactions (usually referred to as Bolland cycle). ATR-FTIR data (Figure 7) revealed that the most abundant oxidation products in retrievals were esters, ketones, and carboxyl acids. The formation of alkoxy radicals could be considered as the last stage of a chain reaction involving the reactions with oxygen of alkyl and allyl radicals. Frictional peeling off of the MPC graft is seen here as a trigger of chain scission leading to exposure of the radicals formed in polyethylene liner during manufacturing to the biological environment, so it reduced the radical amount in the retrievals (cf., Figure 9b) and enhanced surface oxidation (Figure 10). In substance, the great amount of proclaimed innovation associated to MPC grafting of polyethylene liners was confirmed to have no foundation since the grafted polymer disappeared very quickly after joint

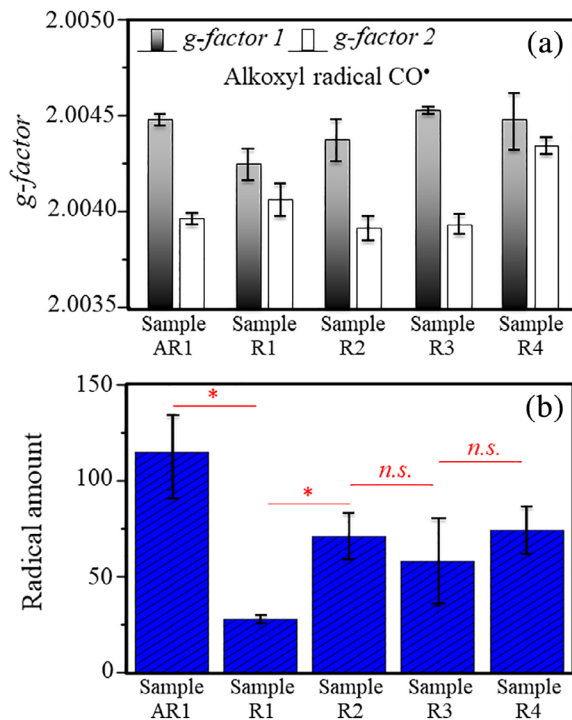


FIGURE 9 (a) g values calculated from the spectra recorded in Figure 8 for the two detected signals g_1 and g_2 ; and, (b) the amounts of radicals per unit weight, R_a , for the four retrieved samples in comparison with that of the pristine one according to Equation (2)

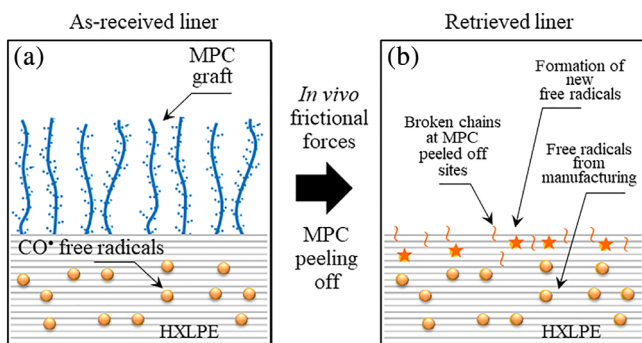


FIGURE 10 Schematic draft of (a) the pristine MPC-grafted liner and (b) the in vivo alterations at its surface after peeling off of the polymeric grafted layer

implantation in vivo. Conversely, the studied liners appeared to have serious problems of surface oxidation due to a relatively large amount of free radicals created both during manufacturing and as a consequence of MPC peeling off. A more recent follow-up study which was co-authored by a representative of Kyocera Medical Corp., performed on 80 patients which received such implants, reported no adverse reactions and lower wear rates when compared to not-grafted liners, but the study did not include controls and the outstandingly low average wear rate measured (0.002 mm/year) resulted to be one order of magnitude lower than the data dispersion (0.023 mm/year), which suggests the presence of (unrealistic) negative wear rate values or a

few exceptionally damaged liners which were not mentioned anywhere else in the document (Moro et al., 2017). Negative average wear rates and abnormal dispersions were indeed reported on the paper (table 6; Moro et al., 2017), rising concerns on the significance and objectivity of the study itself.

<https://www.businesswire.com/news/home/20180625005394/en/> states the reasons for awarding the MPC grafting of a prestigious award from the Minister of Economy, Trade and Industry of Japan; reviewing such motivations in light of the present data, we shall notice the following

- 1 The development of artificial joints that reduce or eliminate the cycle of wear, peripheral inflammation, loosening of the implant and premature failure caused by microscopic “wear debris” through a “hydrophilic nano-surface treatment on a biocompatible polymer as the bearing surface of the hip joint” should be questioned considering that we observed its failure over times in vivo as short as months;
- 2 The statement that the MPC-grafting “technology is expected to contribute to a longer service life for the hip implant as compared to conventional implants with extremely low wear even after long-term testing equivalent to 70 years in vivo” (Moro et al., 2014) appears to be overly optimistic in light of the preliminary retrievals’ data published in this paper and in Nakasone et al. (2015), Sugano et al. (2016) and Tone et al. (2018) and, in particular, occasional short-term delamination.

Finally, it should be stressed that the main limitation of our study resides in the fact that it deals with the limited number of four retrieved MPC-grafted liners, although such limited number adds to a comparable number of retrievals of the same type analyzed in each of references Nakasone et al. (2015), Sugano et al. (2016), and Tone et al. (2018).

5 | CONCLUSION

Four HXLPE MPC-grafted retrieval liners were analyzed on their bearing surfaces in comparison with three as-received samples of the same type. The two main purposes of this investigation were, as follows:

- 1 To evaluate whether the MPC layer had any role in reducing wear or, at least, if it remained on the surface after short-term in vivo exposure;
- 2 To detect whether or not oxidation or other structural modifications occurred during service.

In all the short-term retrieval samples, we observed that the MPC layer was completely peeled off from the bearing surface in both NWZs and MWZs. Furthermore, we observed oxidative degradation not only in the MWZ, but also in the NWZ of the samples. A general trend of increase above the as-received samples could be found for different kinds of oxidative species, but such increases were statistically significant only for ester, carboxyl acid and ketone species according to ATR-FTIR measurements.

In conclusion, the present results represent additional evidence on short-term MPC-grafted retrieved liners, which sums up to those of our previous study of three short-term retrievals (Jay & Waller, 2014) and to a number of additional short-term retrievals presented by other researchers (Stewart, 2010; Zhu et al., 2017). Given this body of independent evidences, we now believe that MPC grafting produces insignificant benefits in terms of wear and oxidation as compared to conventional (i.e., nongrafted) HXLPE liners.

We thus recommend that the commercial presentation of the MPC-grafted liners be updated into a more factual report of the actual performance of this product for the sake of transparency toward both patients and surgeons.

INSTITUTIONAL REVIEW BOARD STATEMENT

This study has been approved by the Institutional Review Board (IRB) of Mie University.

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