J Mater Sci: Mater Med (2007) 18:1809–1815
DOI 10.1007/s10856-007-3063-0

Effects of photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on physical properties of cross-linked polyethylene in artificial hip joints

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Received: 15 March 2006 / Accepted: 31 May 2006 / Published online: 5 May 2007

Abstract Osteolysis caused by wear particles from polyethylene in the artificial hip joints is a serious issue. We have used photo-induced radical graft polymerization to graft 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer onto the surface of cross-linked polyethylene (CLPE-*g*-MPC) in order to reduce friction and wear at the bearing surface of the joint. The physical and mechanical properties of CLPE and CLPE-*g*-MPC were not significantly different, expect that the friction coefficient of untreated CLPE cups was 0.0075, compared with 0.0009 for CLPE-*g*-MPC cup, an 88% reduction. After 3.0×10^6 cycles in the hip joint simulator test, we could not observe any wear of CLPE-*g*-MPC cups. We concluded that the advantage of photo-induced radical graft polymerization technique was that the grafted MPC polymer gave a high lubricity only on the surface and has no effect on the bulk properties of the CLPE substrate.

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Introduction

The most widely used bearing couple for artificial joint systems is the combination of an ultra-high molecular weight polyethylene (UHMWPE) acetabular component and a Co–Cr–Mo alloy femoral component. However, osteolysis caused by wear particles of UHMWPE has emerged as a serious issue [1–3]. Decreasing the number of wear particles from UHMWPE is one way to prevent osteolysis, and different combinations of bearing surfaces and improvements in the bearing materials themselves have been focused. Several highly cross-linked polyethylenes (CLPE) irradiated with 50–105 kGy have been launched since 1998, and they have been used extensively [4]. Gamma-ray and electron beam irradiation at various doses are used by many manufacturers to produce CLPE. In published reports, CLPE produced with 50–105 kGy irradiation shows an 80–90% reduction in wear rate compared with conventional polyethylene [5, 6]. Clinical results have confirmed the excellent anti-wear properties of CLPE. While the efficacy of CLPE is attested by many reports [7–11], the in vivo reduction of wear is only a decrease of 40–60%, so further improvement is desired.

We have recently developed a new-concept artificial hip joint system with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted onto the surface of CLPE (CLPE-*g*-MPC), aiming to reduce wear and avoid bone resorption [12]. MPC is a methacrylate monomer which has a phospholipid polar group in a side chain, and which is used to make new concept biomaterials as designed by Ishihara et al. [13], who were inspired by the neutral phospholipids of biomembranes. Many polymers consisting MPC unit are widely used as biomaterials [14, 15]. Various medical devices using MPC polymer have already been developed and clinically used with the approval of the

United States Food and Drug Administration. The efficacy of MPC polymer as a biomaterial is well established [15–17].

Based on the biocompatibility and hydrophilicity of MPC polymer, we have been developing new artificial joints with highly lubricated bearing surfaces produced by photo-induced radical graft polymerization. This technique grafts MPC directly to CLPE, forming C–C covalent bonds between the CLPE substrate and the MPC polymer. In this study, we investigated the effects of this photo-induced radical graft polymerization technique on the physical, mechanical and tribological properties of CLPE-*g*-MPC.

Materials and methods

Chemicals and MPC graft polymerization

Benzophenone and acetone were purchased from Wako Pure Chemical Industries, Ltd (Osaka, Japan). MPC was synthesized industrially using the method of Ishihara, et al. [13] and was supplied by AI Bio-Chips Co., Ltd (Tokyo, Japan).

Compression-molded UHMWPE (GUR1020 resin, Poly Hi Solidur Inc., IN, USA) bar stock was gamma-irradiated with 50 kGy in N_2 gas and annealed at 120°C in N_2 gas for cross-linking. The CLPE specimens were machined from this bar stock after cooling. They were immersed for 30 sec in an acetone solution containing 10 mg/mL benzophenone and then dried in the dark to remove acetone at room temperature [18]. The amount of benzophenone adsorbed on the surface was 3.5×10^{-11} mol/cm^2 by ultraviolet spectroscopy according to the previous study [19]. The MPC was dissolved into degassed pure water to a concentration of 0.5 mol/L. CLPE specimens coated with benzophenone were immersed in the aqueous MPC solution. Photo-induced graft polymerization on the CLPE surface was carried out with ultraviolet irradiation of 5 mW/cm^2 for 10 to 360 min at 60°C using a Toshiba D-35 filter to pass only ultraviolet of 350 ± 50 nm wavelength. After the polymerization, the CLPE-*g*-MPC specimens were removed, washed with pure water and ethanol, and dried.

Surface analysis by FT-IR/ATR and XPS

The functional group vibrations of the CLPE and CLPE-*g*-MPC (90 min irradiation) surfaces were examined by Fourier-transform infrared (FT-IR) spectroscopy with attenuated total reflection (ATR) equipment. CLPE and CLPE-*g*-MPC spectra were obtained in 32 scans over the range of 800 to 2000 cm^{-1} with an FT-IR analyzer (FT/IR615, JASCO Co. Ltd., Tokyo, Japan) at a resolution of 4.0 cm^{-1}.

The surface elemental composition of CLPE was analyzed before and after MPC grafting for 90 min by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained on an AXIS-HSi165 (KRATOS ANALYTICAL Ltd., UK) equipped with Mg–Kα radiation source biased at 15 kV at the anode. The take-off angle of photoelectrons was kept at 90°.

Surface wettability observation by spray method

The spray method is based on the wetting response of the surface of a cup when exposured to a distilled water mist for a short period [20]. The entire bearing surfaces of CLPE and CLPE-*g*-MPC (23 and 90 min irradiation) cups were uniformly exposed to 15 mL of water mist. The appearance of the cup surfaces was evaluated in terms of wettability within 10 sec after spraying. Ratio of surface area covered by water (water-covered ratio) was determined by using the Win-Roof image processing system (Mitani Corporation Inc., Fukui, Japan).

Evaluation of physical and mechanical properties

The density, swelling ratio, network chain density, molecular weight between cross-links and cross-link density of CLPE and CLPE-*g*-MPC with irradiation for 90 min were evaluated according to the methods previously reported [21]. The CLPE and CLPE-*g*-MPC specimens ($23 \times 23 \times 1$ mm^3) were weighed (approximately 0.5 g, V_1), allowed to swell for 72 h in *p*-xylene containing 0.5 wt% 2-*t*-butyl-4-methylphenol at 130 °C, and were then reweighed (V_2). After reweighing, specimens were immersed in acetone, dried at 60 °C under vacuum, and reweighed (V_3). The swelling ratio, q, was determined from the weight gain and densities of the polyethylene and xylene, and the physical properties were calculated as follows.

(a) Swelling ratio, q

$$q = V_2 / V_3 \tag{1}$$

(b) Network chain density, $v*$

$$v* = In\,(1 - q^1) + q^1 + \chi q^2 / V_1\,(q^{-2/3} - 0.5q^{-1})$$
$$V_1 = 136\ mL/mol\ ,\ \chi = 0.37\ (polyethylene) \tag{2}$$

(c) Molecular weight between cross-links, M_c

$$M_c = 1 / \bar{M}c = \mathrm{V}v*$$
$$V = 1 / specimen\ density \tag{3}$$

(d) Cross-link density, *XLD*

$$XLD = M_0/\bar{M}C \qquad M_0 = 14\ (polyethylene) \tag{4}$$

The mechanical properties of CLPE and CLPE-*g*-MPC with irradiation for 90 min were evaluated with tensile, impact, and creep deformation tests, as well as a shore hardness D measurement. Tensile testing was performed according to ASTM standard D638 using a type 4 tensile bar specimen and a crosshead speed of 50 mm/min. A double-notched (notch depth = 4.57 ± 0.08 mm) Izod impact strength test was performed to ASTM standard F648. Ten specimens were used in each tests. Creep deformation was measured by applying a constant load (113 kgf for 24 h) to a specimen, then measuring the height displacement, according to the ASTM D621 test method. Shore hardness D was measured according to the ASTM D2240 test method.

For all the test groups, the results derived from each experiment were expressed as mean values and the standard deviation. The statistical significance ($p < 0.05$) was judged by the Student's *t*-test.

TEM observation of cross section of CLPE-*g*-MPC

A cross section of the MPC polymer layer on the CLPE-*g*-MPC (90 min irradiation) surface before and after the hip joint simulator test was observed with a transmission electron microscope (TEM). Prior to observation, specimens were embedded in epoxy resin, stained in ruthenium oxide vapor at room temperature, and sliced into ultra-thin films. The specimen after the hip joint simulator test was coated with gold by sputter coater (JFC 1500, JEOL, Ltd., Tokyo, Japan) before embedding in resin. A JEM-1010 (JEOL, Ltd., Tokyo, Japan) was used for the TEM observation at an acceleration voltage of 100 kV.

Hip joint simulator test

The CLPE-*g*-MPC cups (26 mm inner diameter and 52 mm outer diameter) for testing in the hip joint simulator were gamma-ray sterilized under N_2 gas.

Friction torque between the CLPE-*g*-MPC cup and a 26 mm Co–Cr–Mo alloy femoral head (Japan Medical Materials Corp., Japan) was measured using a 2-station hip joint simulator (Kobe Steel, Ltd., Kobe, Japan). Measurements were performed with distilled water as lubricant, a loading of 280 kgf and a swing distance of 80 mm with a period of 1 Hz.

The in vitro wear test was performed using a 12-station hip joint simulator (MTS system Corp., MN, USA). A mixture of 25% bovine serum, 20 mM/L of ethylene diamine tetraacetic acid (EDTA), and 0.1% sodium azide was used as lubricant, according to the ISO 14242-1 standard. A load simulating a physiologic loading curve with double peaks of 183 and 280 kgf load was added with a period of 1 Hz. The wear was measured by a gravimetric method. The cup weights were measured every 0.5×10^6 cycles. The acetabular component was tested with a 26 mm Co–Cr–Mo alloy femoral head (Japan Medical Materials Corp., Japan). Testing then continued until a total of 3.0×10^6 cycles were completed.

Results

Figure 1 shows the FT-IR/ATR spectra of CLPE and CLPE-*g*-MPC. A transmission absorption peak was observed at 1460 cm^{-1} for both CLPE and CLPE-*g*-MPC. This peak is attributed mainly to the methylene chain in the CLPE substrate and MPC graft polymer. However, transmission absorptions at 1240, 1080 and 970 cm^{-1} were observed only for the CLPE-*g*-MPC. These peaks are due to the phosphate group in the MPC unit. Similarly, the transmission absorption at 1720 cm^{-1} observed for CLPE-*g*-MPC can only correspond to the carbonyl in the MPC unit.

Figure 2 shows the XPS spectra (N_{1s} and P_{2p}) of CLPE and CLPE-*g*-MPC. In the N_{1s} and P_{2p} spectra, clear peaks were observed only for CLPE-*g*-MPC. Peaks at 403 and 134 eV were assigned to the $-N^+(CH_3)_3$ and phosphate groups, respectively. These peaks were characteristic of the phosphorylcholine in the MPC unit. Table 1 summarizes the elemental composition of the untreated CLPE and the CLPE-*g*-MPC surfaces with various ultraviolet-ray irradiation times during polymerization. The content of nitrogen and phosphorous in the CLPE-*g*-MPC surface was increased to 5.1 and 5.2, respectively, with polymerization time. The elemental composition of the CLPE-*g*-MPC surface with a polymerization time of 90 min was almost

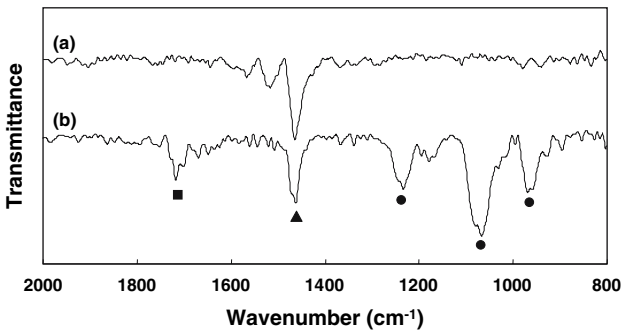

Fig. 1 FT-IR/ATR spectra of CLPE-*g*-MPC. (**a**) CLPE (untreated), (**b**) CLPE-*g*-MPC. •: P–O, ▲: CH_2, ■: C=O

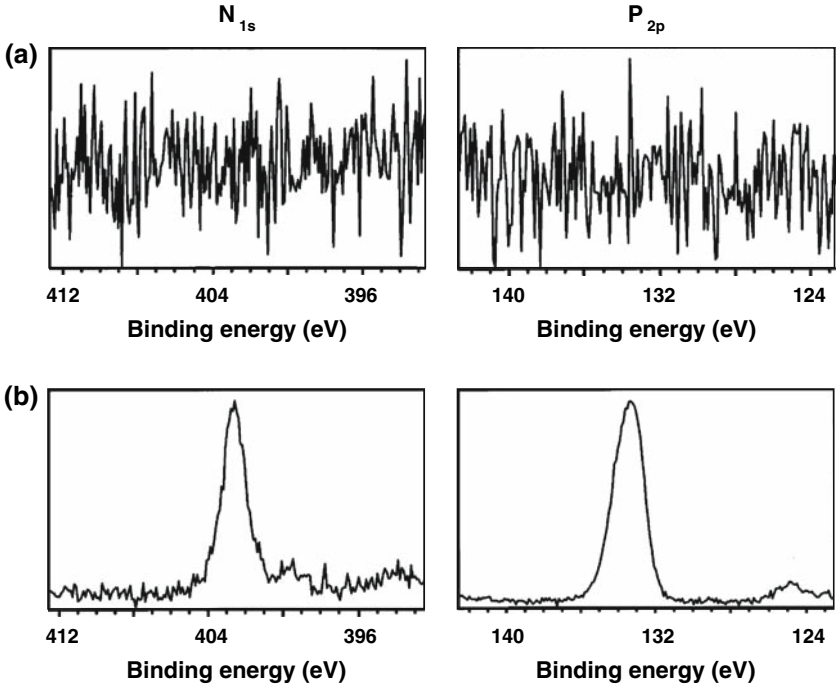

Fig. 2 XPS spectra of CLPE-*g*-MPC. (**a**) CLPE (untreated), (**b**) CLPE-*g*-MPC

Table 1 Surface elemental composition (%) of CLPE-*g*-MPC with various photo-polymerization times

Polymerization time (min)	C	O	N	P
0 (untreated CLPE)	99.6	0.4	0.0	0.0
12	96.6	3.4	0.0	0.0
23	78.5	17.0	1.9	2.7
45	60.4	30.2	4.1	5.3
90	61.8	27.9	5.1	5.2
MPC polymer*	57.9	31.6	5.3	5.3

*: Theoretical elemental composition of MPC polymer

equivalent to the theoretical elemental composition (N = 5.3, P = 5.3) of MPC polymer.

Figure 3 shows optical microscope images of moistened CLPE-*g*-MPC surfaces that were produced by various photo-irradiation times during polymerization. The surface image progressively alters from a hydrophobic surface to a hydrophilic one as polymerization time increases. On an untreated CLPE surface after spraying with water mist, typical hydrophobic behavior was observed, including the formation of many water droplets (Fig. 3a). In contrast, on the CLPE-*g*-MPC surface hydrophilic behavior was observed, characterized by a thin film of water (Fig. 3c).

The physical properties of CLPE and CLPE-*g*-MPC including density and swelling ratio are summarized in Table 2. It is generally said that energy irradiation to polyethylene causes a decrease in the swelling ratio. However, all of the bulk physical properties of CLPE and CLPE-*g*-MPC that were examined in this study differed little ($p < 0.05$) between the two materials.

The tensile yield strength, impact strength, creep deformation and shore hardness D of CLPE and CLPE-*g*-MPC are shown in Table 3. Tensile yield strength, impact strength and shore hardness D did not differ significantly ($p \leq 0.05$) between CLPE and CLPE-*g*-MPC, and both CLPE and CLPE-*g*-MPC met ASTM requirements (F648).

Figure 4 shows a TEM image of a cross section of CLPE-*g*-MPC. A grafted MPC polymer layer about 100 nm thick was observed on the CLPE substrate (Fig. 4b). Lamellae on the order of 100–400 nm long and 10–20 nm thick were observed in the CLPE substrate regardless of irradiation, and the lamellae were especially thin near the surface.

Table 4 shows the friction coefficient and the wear rate of the MPC polymer grafted CLPE cup in the hip joint simulator test. The friction coefficients of the untreated CLPE cups and the CLPE-*g*-MPC cups were 0.0075 and 0.0009, respectively. The CLPE-*g*-MPC cups reduced 88% in the friction coefficient compared with untreated CLPE cups, showed a high lubricity. We calculated the wear rate between 2.5×10^6 and 3.0×10^6 cycles. The wear rate of CLPE cups showed 3.12 mg/10^6 cycles. In contrast, the CLPE-*g*-MPC cups showed the reduction in wear to an essentially zero of –1.43 mg/10^6 cycles. The volumetric change was then calculated from the weight loss over time. In this study, the weight loss was calculated without considering the effect of water absorption.

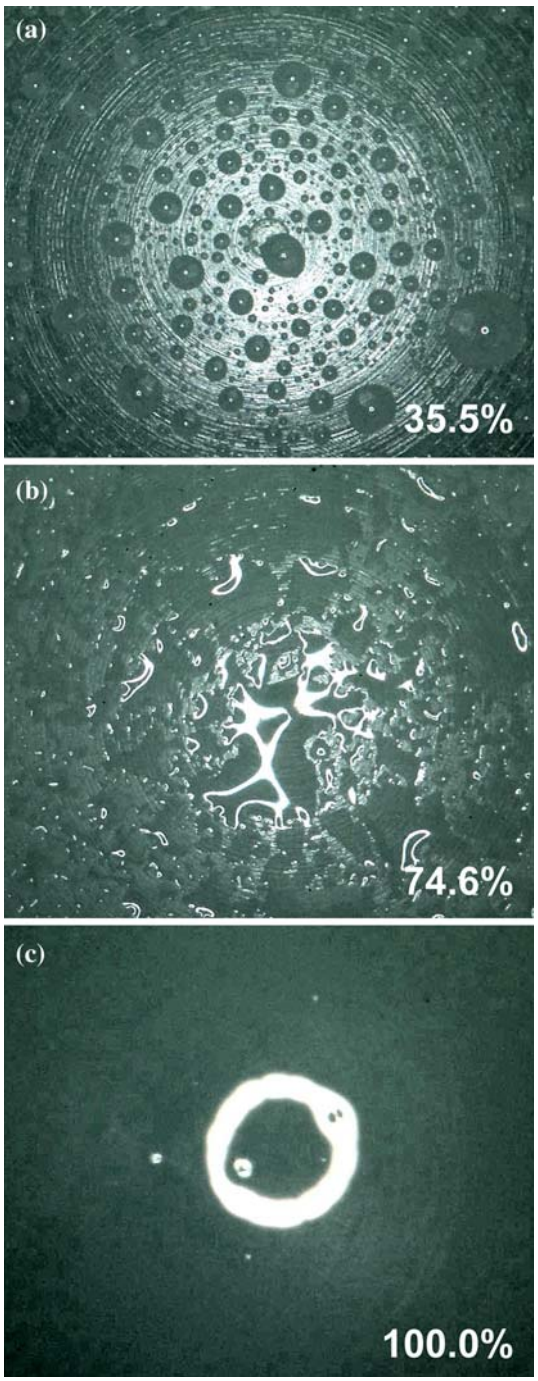

Fig. 3 Optical microscope images of CLPE-*g*-MPC cup surface with various photo-polymerization times. (**a**) 0 min (untreated CLPE), (**b**) 23 min and (**c**) 90 min. The water-covered ratio (%) is also shown. The white ring in (**c**) is due to the reflection of the light used in photography

Discussion

We have developed an artificial hip joint that uses CLPE-*g*-MPC on the bearing surface, with the goal of reducing wear and avoiding bone resorption. In this study, we investigated the effects of photo-induced radical graft polymerization technique on properties of the CLPE-*g*-MPC, and this report discusses the characteristics of the MPC polymer layer and the properties of the CLPE substrate.

After 3.0×10^6 cycles of the hip joint simulator test, we confirmed that the CLPE-*g*-MPC cups showed a quite low wear rate compared with untreated CLPE. Since MPC is a highly hydrophilic compound, and poly(MPC) is water-soluble, the water-wettability of the CLPE-*g*-MPC surface was greater than that of a CLPE surface due to the poly(MPC) chains, as shown in Fig. 3. It was observed that the CLPE-*g*-MPC surface supported a thin film of water. Consequently, the artificial hip joint bearing with an CLPE-*g*-MPC surface had high lubricity. The reduction in friction is assumed to have contributed to the improvement of anti-wear properties that was observed [22]. However, different processes such as migration of low molecular weight compounds, rotation of flexible polymer chains, inter- and intra-molecular rearrangements, and adhesion of contaminant particles, may take place at different rates depending on materials and ambient conditions [23]. Various factors such as type of bearing material, surface roughness, homogeneity of the surface and chemical composition affect the lubricity of the artificial joint [24]. In CLPE-*g*-MPC, the lubricity can change depending on the ambient conditions in vitro and in vivo. The bearing surface of the artificial hip joint with MPC polymer is assumed to have a structure similar to an artificial cell membrane, meaning this new concept artificial hip joint mimics the natural joint cartilage in vivo. To ensure the long-term retention of the benefits of this MPC polymer, we used photo-induced radical graft polymerization technique, to produce C–C covalent bonding between a carbon atom of the CLPE and the end-group of an MPC polymer chain. The results clearly show that the crystalline structure, physical and mechanical properties of the CLPE substrate were minimally changed, if at all, even after MPC grafting [25]. This indicates that photo-induced radical graft polymerization does not affect the properties of the CLPE substrate [18]. Retaining the properties of the CLPE substrate unchanged is very important in clinical use, because the CLPE cup acts not only as a bearing material but also as a structural material in the artificial hip joint system. Generally, increased cross-linking in the CLPE degrades its mechanical properties, producing a trade-off between wear-resistance and mechanical properties [5, 26]. It is desirable to reduce wear while maintaining the mechanical properties necessary for proper in vivo function. The advantage of photo-induced radical graft polymerization comes from the fact that the grafted MPC polymer gave a high lubricity only on the surface, and had no effect on the bulk properties of the CLPE substrate.

Table 2 Physical properties of CLPE-*g*-MPC

Sample	Density (g/cm^3)	Swelling ratio	Network chain density ($\times 10^3$ mol/ml)	M.W. between Cross-links (g/mol)	Cross-link density (mol%)
CLPE	0.944 (0.002)	2.99 (0.11)	0.437 (0.043)	2165 (214)	0.65 (0.06)
CLPE-*g*-MPC	0.943 (0.001)	2.94 (0.10)	0.459 (0.044)	2069 (186)	0.68 (0.07)

The standard deviation is in parentheses

Table 3 Mechanical properties of CLPE-*g*-MPC

Sample	Yield strength (MPa)	Impact strength (kJ/m^2)	Creep deformation (%)	Hardness (shore D)
CLPE	23.2 (0.4)	75.0 (1.4)	0.89 (0.17)	68.2 (0.9)
CLPE-*g*-MPC	23.1 (0.5)	77.0 (1.9)	0.63 (0.40)	68.4 (0.5)

The standard deviation is in parentheses

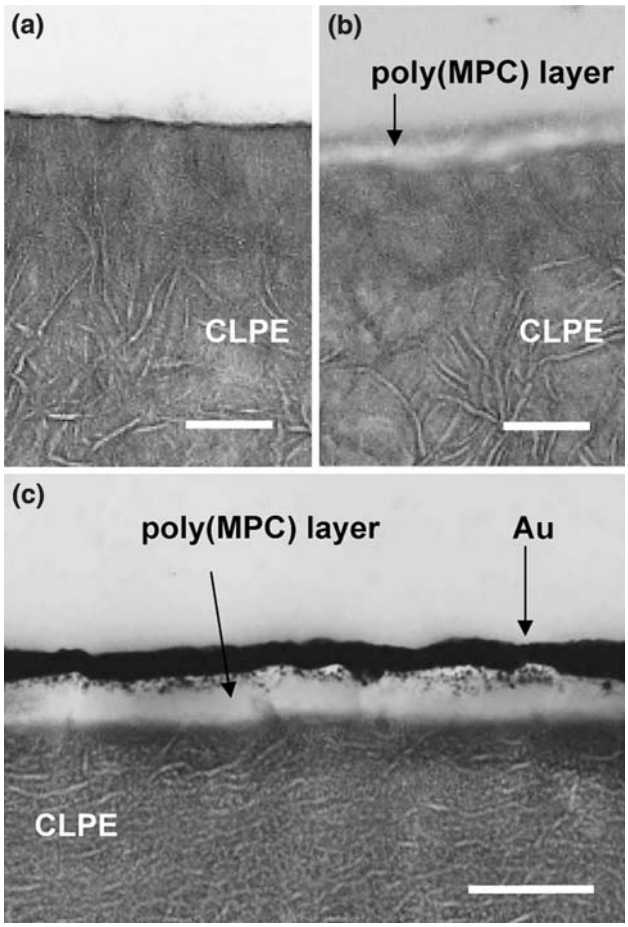

Fig. 4 Cross-sectional TEM images of CLPE-*g*-MPC. (**a**) CLPE (untreated), (**b**) CLPE-*g*-MPC before simulator test and (**c**) CLPE-*g*-MPC after a 3×10^6 cycle simulator test. Bar; 200 nm

After 3.0×10^6 cycles in the hip joint simulator test, the wear rate of CLPE-*g*-MPC cups remained low. The cross-sectional TEM image of the CLPE-*g*-MPC bearing surface after 3.0×10^6 cycles of the hip simulator test (Fig. 4c) showed that most of the bearing surface was covered by the MPC polymer layer even after the hip simulator test. In other words, the CLPE-*g*-MPC cups showed little wear on inspection, supporting the quite low wear observed in the hip joint simulator test.

Table 4 Tribological properties of CLPE-*g*-MPC

Sample	Friction coefficient	Wear rate ($mg/10^6$ cycles)
CLPE	0.0075	3.12
CLPE-*g*-MPC	0.0009	–1.43

On the CLPE-*g*-MPC surface, the nitrogen and phosphorus attributed to the phosphorylcholine in the MPC units increased with increasing polymerization time. This indicates that the density of the grafted MPC polymer can be controlled by the polymerization time, since the number of polymer chains produced in a radical polymerization is generally proportional to the photo-irradiation time. The elemental composition obtained by XPS (N = 5.1, P = 5.2) of the CLPE-*g*-MPC surface with a polymerization time of 90 min was almost equivalent to the theoretical elemental composition of MPC polymer. Therefore, the entire surface of the CLPE was assumed to be coated with an MPC polymer layer.

However, the area observed by the X-ray spot (approximately 400×800 μm^2) in XPS was quite limited. As a supplementary probe to examine the MPC polymer layer, wettability measurement of cups should be performed on many separate areas on the cups. The wettability measurement of a surface is readily performed in the laboratory on well defined, homogeneous, smooth and planar surfaces of prepared specimens. In the case of artificial hip joint cups, for which non-destructive measurements are usually required (and where excision of material samples is usually undesirable), these conditions do not exist and measurement with high precision is a difficult task. Hence,

we evaluated wettability of CLPE-*g*-MPC cup by the spray method, because this method can be used non-destructively on large areas.

Since CLPE-*g*-MPC reduces the production of wear particles and bone-resorptive responses, periprosthetic osteolysis could be eliminated [12]. Based on the mechanical, tribological and biological advantages, we confidently expect CLPE-*g*-MPC be used in the next-generation of artificial hip joint systems.

Conclusions

In this study, effects of a photo-induced radical graft polymerization technique on physical, mechanical and tribological properties of CLPE-*g*-MPC were investigated. The crystalline structure, physical and mechanical properties of the CLPE substrate were unchanged after the addition of a layer of MPC polymer by photo-polymerization. However, CLPE-*g*-MPC cups reduced 88% in the friction coefficient compared with untreated CLPE cups. After 3.0×10^6 cycles in the hip joint simulator test, the wear rate of CLPE-*g*-MPC cups remained low. We concluded that the advantage of this photo-induced radical graft polymerization technique was that the grafted MPC polymer layer produces high lubricity while only affecting the surface, and has no effect on the properties of the CLPE substrate.

Acknowledgements This work was supported by a Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Culture, Sports, Science and Technology (#15390449), and a Health and Welfare Research Grant for Translational Research from the Japanese Ministry of Health, Labour and Welfare. The authors also express special thank to Dr. Fumiaki Miyaji, Mr. Yoshiki Ando and Mr. Takatoshi Miyashita (Japan Medical Materials Corp., Japan) for their excellent technical assistance.

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