

Figure 1. XPS spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC.

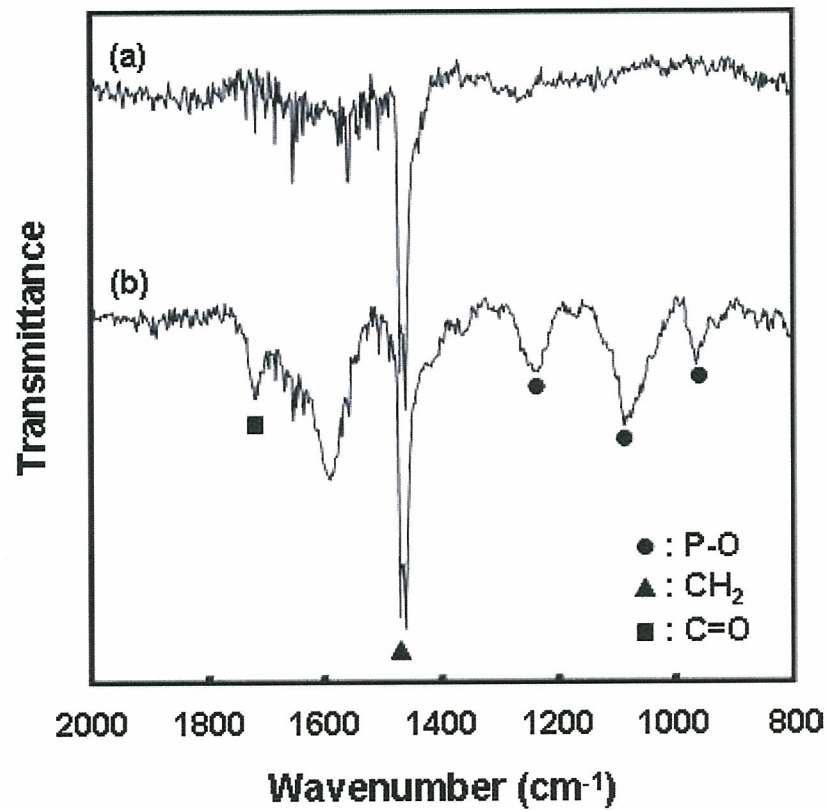


Figure 2. FT-IR/ATR spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC.

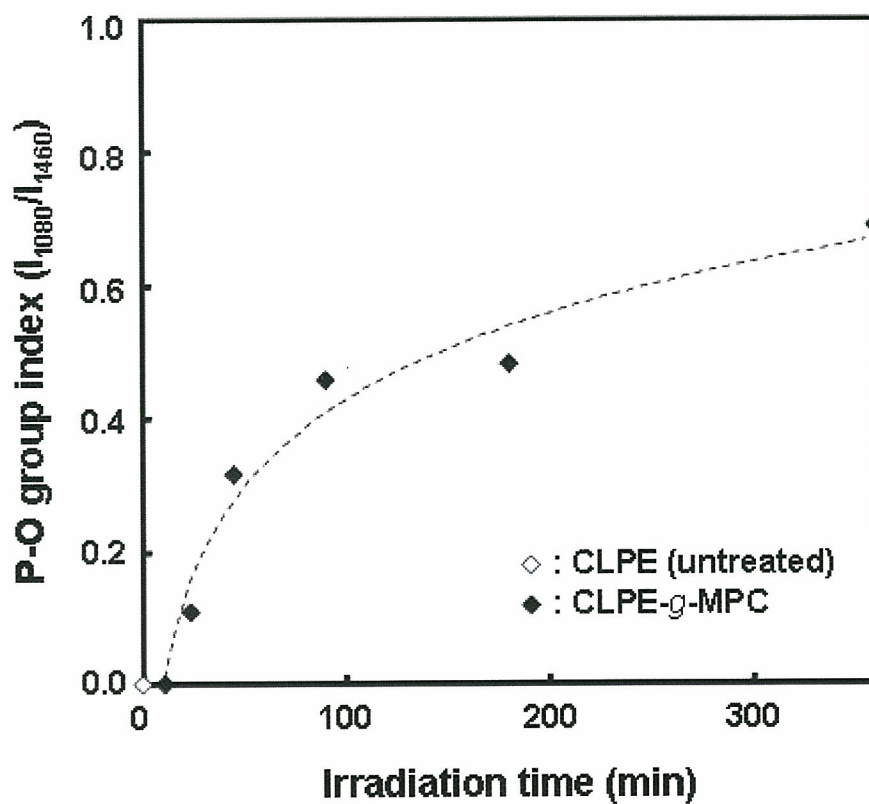


Figure 3. P-O group index as a function of irradiation time for CLPE-g-MPC.

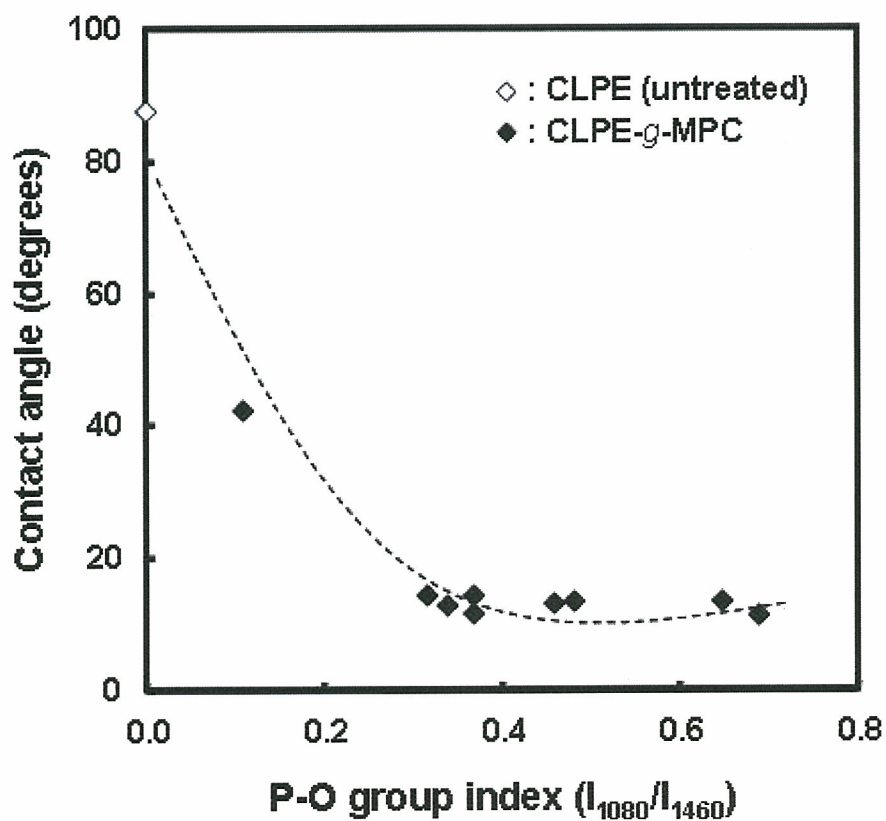


Figure 4. Static water-contact angle as a function of P-O group index for CLPE-g-MPC.

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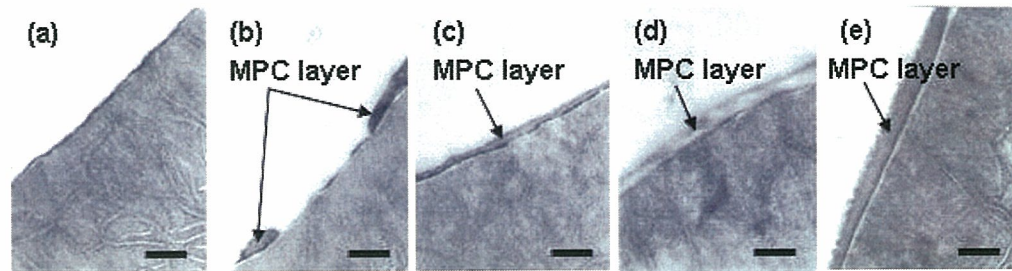
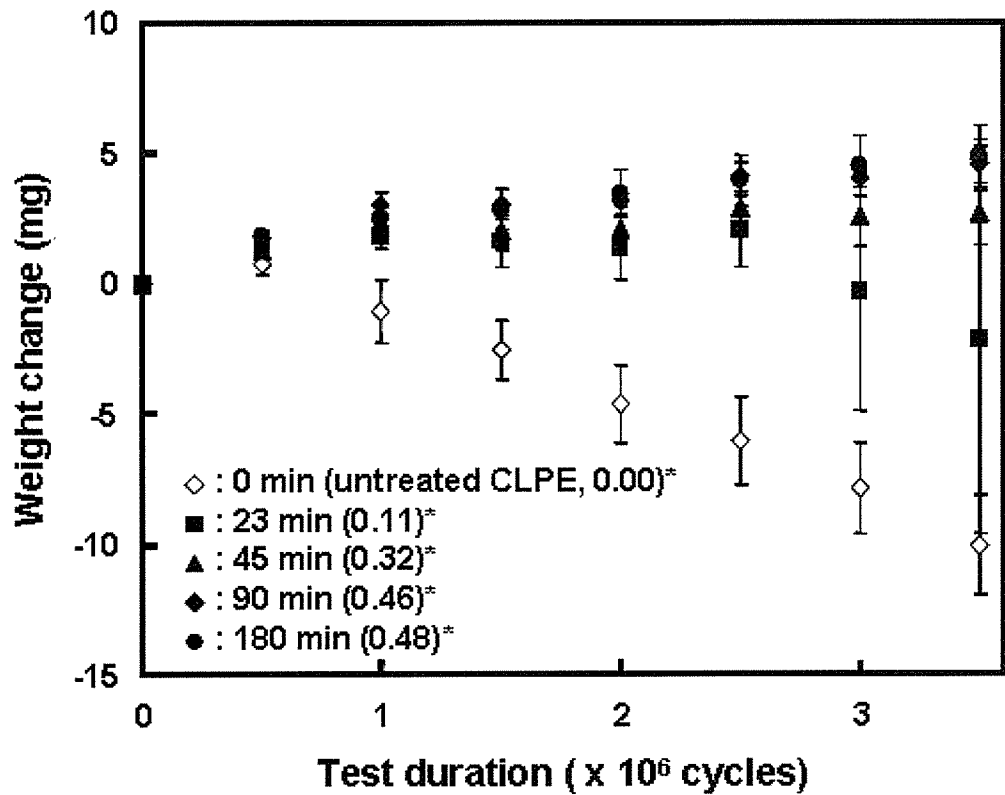


Figure 5. Cross-section TEM images of CLPE-*g*-MPC with various photo-polymerization times. Bar = 200 nm. (a) 11 min, (b) 23 min, (c) 45 min, (d) 90 min, and (e) 180 min.



Weight change of CLPE-g-MPC cups with various irradiation times during polymerization in the hip joint simulation test. Bars = Standard deviations. *P-O group indexes are in parentheses.

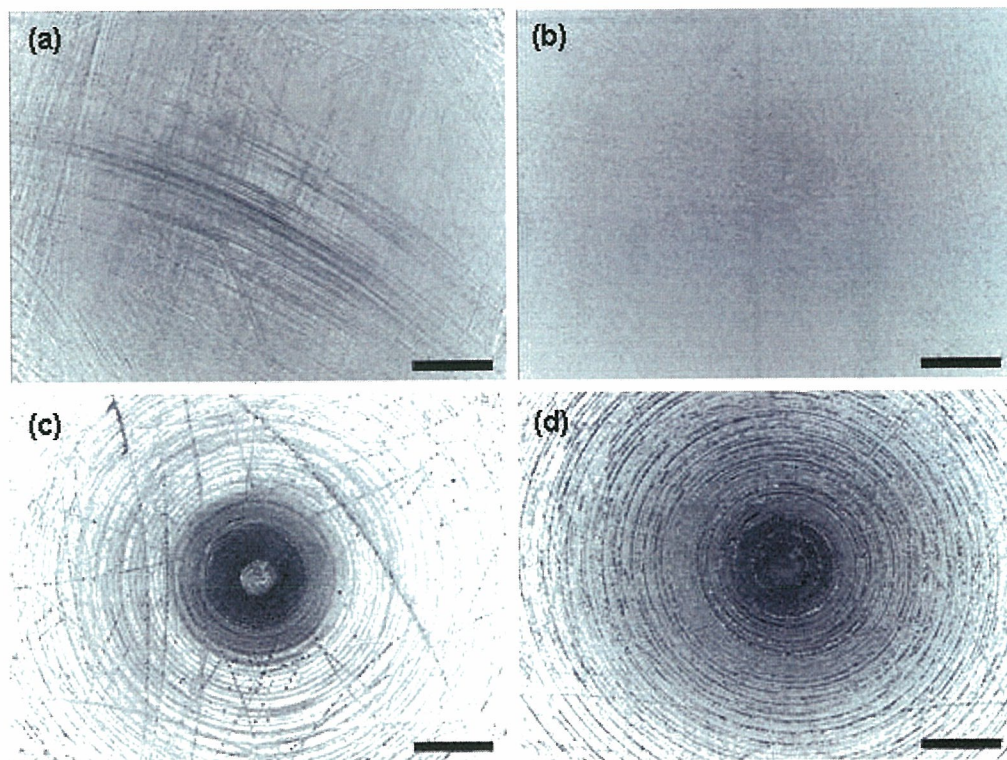


Figure 7. Confocal laser scanning microscope images of the bearing surfaces of the cups before and after a melt-recovery test that was performed after the simulator test. (a) CLPE before melt-recovery test, (b) CLPE after melt-recovery test, (c) CLPE-*g*-MPC before melt-recovery test, and (d) CLPE-*g*-MPC after melt-recovery test. Bar = 400 μ m.

Editorial Manager(tm) for Journal of Materials Science: Materials in Medicine
Manuscript Draft

Manuscript Number: JMSM461R1

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

Article Type: Manuscript

Section/Category:

Keywords: Joint replacement; CLPE; Phosphorylcholine; Mechanical properties; Photo-inducing

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Manuscript Region of Origin:

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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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, except 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.

Keywords: Joint replacements; CLPE; Phosphorylcholine; Photo-inducing

Running title: Effects of photo-induce technique on CLPE-g-MPC

1. 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 to 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 to 105 kGy irradiation shows an 80% to 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 to 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., who were inspired by the neutral phospholipids of biomembranes [13]. 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.

2. Materials and Methods

2.1. 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 N₂ gas and annealed at 120°C in N₂ 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 x

10^{-11} mol/cm² 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/cm² 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.

2.2. 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-K α radiation source biased at 15 kV at the anode. The take-off angle of photoelectrons was kept at 90 degrees.

2.3. Surface wettability observation by spray method

The spray method is based on the wetting response of the surface of a cup when exposed 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).

2.4. 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 x 23 x 1 mm³) were weighed (approximately 0.5 g, V_1), allowed to swell for 72 hours in *p*-xylene containing 0.5wt% 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

$$q = V_2 / V_3 \quad (1)$$

(b) Network chain density, v^*

$$v^* = \ln(1 - q^l) + q^l + \chi q^2 / V_l (q^{-2/3} - 0.5q^{-l}) \quad (2)$$

$$V_l = 136 \text{ mL/mol}, \chi = 0.37 \text{ (polyethylene)}$$

(c) Molecular weight between cross-links, M_c

$$M_c = 1 / \bar{M}_c = Vv^* \quad (3)$$

$$V = 1 / \text{specimen density}$$

(d) Cross-link density, XLD

$$XLD = M_0 / \bar{M}_c \quad (4)$$

$$M_0 = 14 \text{ (polyethylene)}$$

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 hours) 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.

2.5. 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.

2.6. 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 N₂ 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.

3. Results

Fig. 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.

Fig. 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 $-\text{N}^+(\text{CH}_3)_3$ 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 equivalent to the theoretical elemental composition (N = 5.3, P = 5.3) of MPC polymer.

Fig. 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. 3(a)). In contrast, on the CLPE-g-MPC surface hydrophilic behavior was observed, characterized by a thin film of water (Fig. 3(c)).

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 ($p < 0.05$) between CLPE and CLPE-g-MPC, and both CLPE and CLPE-g-MPC met ASTM requirements (F648).

Fig. 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. 4 (b)). Lamellae on the order of 100

to 400 nm long and 10 to 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 $3.12 \text{ mg}/10^6$ cycles. In contrast, the CLPE-g-MPC cups showed the reduction in wear to an essentially zero of $-1.43 \text{ mg}/10^6$ 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.

4. 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