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Figure captions

Figure 1 FT-IR/ATR spectra of CLPE-*g*-MPC. (a) CLPE (untreated), (b) CLPE-*g*-MPC. ● : P-O, ▲ : CH₂, ■ : C=O.

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

Figure 3 Optical microscope images of CLPE-*g*-MPC cup surface with various photo-polymerization times. (a) 0 min (untreated CLPE), (b) 12 min, (c) 23 min, (d) 45 min, (e) 90 min. The white rings in (d) and (e) are due to the reflection of the light used in photography.

Figure 4 Cross section of TEM images of CLPE-*g*-MPC. Bar, 200 nm. (a) CLPE (untreated), (b) CLPE-*g*-MPC.

Figure 5 Cross section of TEM images of CLPE-*g*-MPC after a 3×10^6 cycle simulator test. Bar, 200 nm.

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

TABLE II Physical properties of CLPE-g-MPC

TABLE III Mechanical properties of CLPE-g-MPC

TABLE IV Tribological properties of CLPE-g-MPC

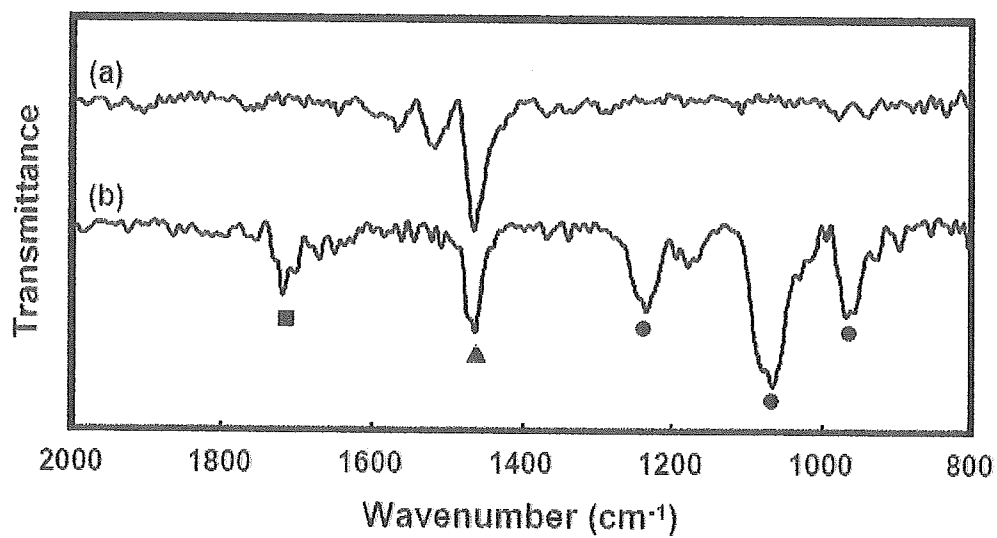


Figure 1

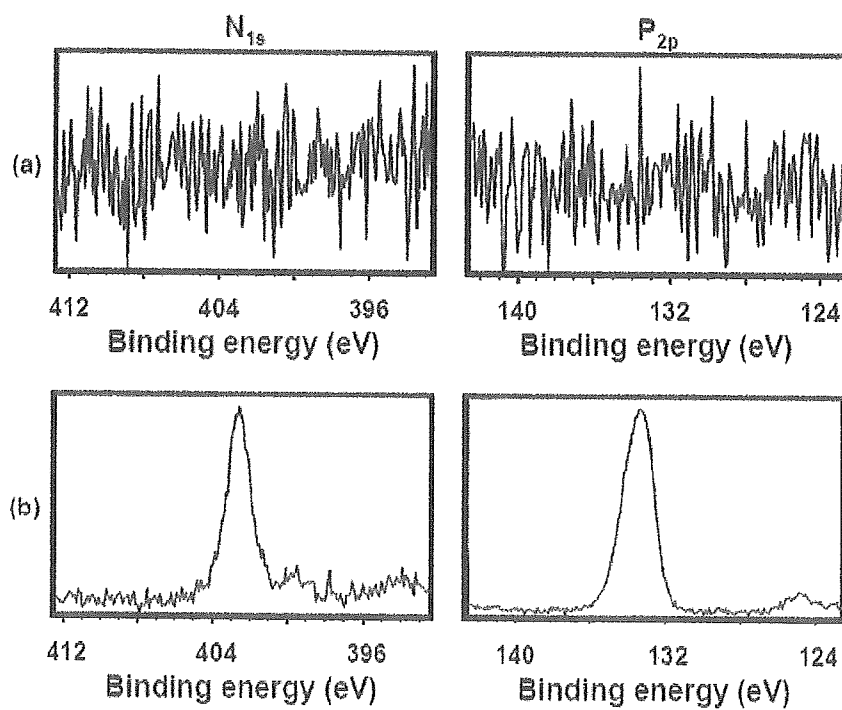


Figure 2

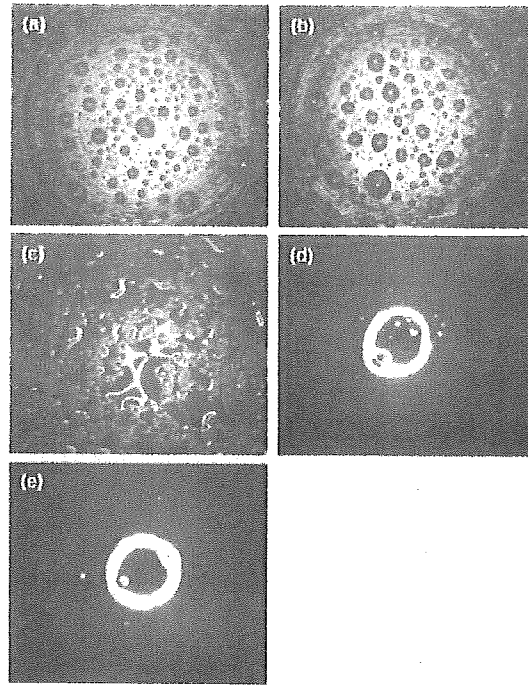


Figure 3

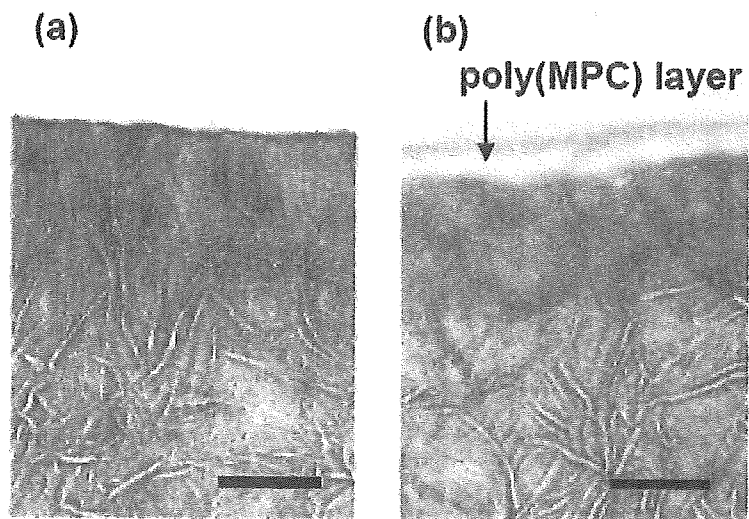


Figure 4

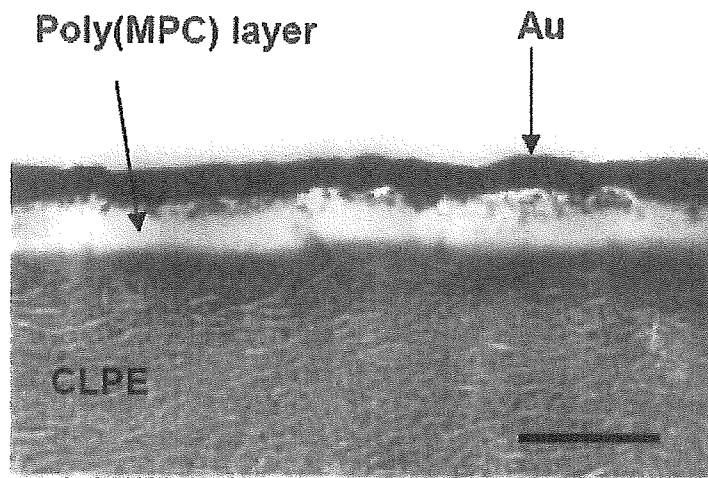


Figure 5

TABLE I 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

TABLE II Physical properties of CLPE-*g*-MPC

Sample	Density (g/cm ³)	Swelling ratio	Network chain density (x 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- <i>g</i> -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 III 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- <i>g</i> -MPC	23.1 (0.5)	77.0 (1.9)	0.63 (0.40)	68.4 (0.5)

The standard deviation is in parentheses.

TABLE IV Tribological properties of CLPE-*g*-MPC

Sample	Friction coefficient	Wear rate (mg/10 ⁶ cycles)
CLPE	0.0075	3.12
CLPE- <i>g</i> -MPC	0.0009	-1.43

Biomaterials in contribution

Surface and wear-resistant properties of MPC polymer grafted cross-linked polyethylene

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Abstract

For a serious issue of osteolysis caused by wear particles of polyethylene which is a component of artificial hip joint, the cross-linked polyethylene (CLPE) modified with biocompatible phospholipid polymer has been developed and clinically used for reduction in wear. Our goal is to prevent the aseptic loosening entirely. This could be attained by no formation of CLPE wear particles and the suppressing activation of cell systems due to the wear particles. From this point of view, 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer was grafted on the surface of CLPE (CLPE-g-MPC) have been studied. In this study, the surface and the anti-wear properties of the CLPE-g-MPC were investigated. The relativity density of MPC polymer chains was defined as P-O group index. Generally, the polymerization time corresponds to the number of polymer chains in the radical polymerization. After 5.0×10^6 cycles in hip joint simulator test, while the steady wear rates of the untreated CLPE cups and the CLPE-g-MPC cups with low P-O group index of 0.11 were as high as $4 \text{ mg}/10^6$ cycles, those of the CLPE-g-MPC cups with high P-O group index of 0.46 and 0.48 drastically decreased to -0.29 and -0.44 $\text{mg}/10^6$ cycles, respectively. Therefore, the grafting of MPC polymer with high density is assumed to be prerequisite in order to maintain the stable wear-resistant property of the CLPE-g-MPC as orthopedic bearing materials for long term.

Keywords: Joint replacements; Polyethylene; Phospholipid; Phosphorylcholine; Wear mechanisms

Running title: Surface and wear of CLPE-g-MPC

1. Introduction

As the number of aged persons in the world increases year by year, the increase in patients whose joints have no longer their own functions owing to the external injury or diseases is a serious social problem. In this situation, the artificial joints as joint substitutes become important more and more, and most patients who undergo the artificial joint achieve a dramatic relief of pain and a rapid improvement in quality of life. As a bearing couple for artificial joint systems, the combination of the ultra-high molecular weight polyethylene (UHMWPE) acetabular component and metal (generally Co-Cr-Mo alloy) for the femoral component is most popular and widely used. However, osteolysis caused by wear particles of UHMWPE is a serious and essential problem of the artificial hip joints [1-3]. The reduction of wear particles from UHMWPE is one of the methods to prevent osteolysis. In order to decrease such particles from UHMWPE, the combinations other than metal-on-UHMWPE and improvements of the bearing materials themselves have been attempted so far.

Different highly cross-linked polyethylene (CLPE) irradiated with an energy beam in the range such as 50 to 105 kGy have been launched since 1998, and they have been used extensively [4]. The gamma-ray and electron beam with various doses are used for production of CLPE. There have been a lot of *in vitro* studies on CLPE. In the earlier reports, the CLPE subjected to 50-105 kGy irradiation dose showed 80% to 90% reduction in wear rate compared with conventional polyethylene [5, 6]. In the clinical results, the excellent wear-resistance of the CLPE has also been confirmed. The literature reports linear wear rates of CLPE: 0.008 mm/year by Manning et al. for Zimmer cups (Zimmer Inc. IN) [7]; 0.09 mm/year by Digas, et al. for the Durasul cups (Centerpulse, Switzerland) [8]; 0.02 mm/year by Heichel, et al. for the Marathon cups (DePuy Orthopaedics, Inc. VA) [9]; 0.12 mm/year by Martel, et al. for the Crossfire cups (Stryker Orthopaedic, Inc. NJ) [10]; and 0.12 mm/year by Oonishi, et al. for the Aeonian cups (Kyocera Corp. Japan) [11]. While the efficacy of the CLPE is evidenced by the reports above, *in vivo* reduction of wear is said only as low as 40 to 60%. Therefore, further improvement of the CLPE is desired.

Recently, we have developed a new-concept artificial hip joint that 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer is grafted on the surface of CLPE (CLPE-g-MPC), aiming at reduction in wear and suppression of the bone resorption [12]. The MPC is a methacrylate monomer which has a phospholipid polar group in the side chain, which is a novel biomaterial which mimics neutral phospholipids of biomembrane, designed and developed by Ishihara et al [13]. Various polymers containing MPC units are already widely used as biomaterials [14, 15]. The biomembrane-like surface is easily made by treating the substrate materials with MPC polymer. And thus formed artificial biomembrane surface shows excellent biocompatibility where thin film of free water is formed. Several medical devices utilizing MPC polymer already have already been developed, and clinically used under authorization of the Food and Drug Administration of the USA and so on. The efficacy and safety of MPC polymer as a biomaterial therefore have been established [16-18].

We have been developing novel artificial joints with highly lubricant bearing surfaces by combining the biocompatible and hydrophilic MPC polymer with CLPE, performed by a photo-induced radical polymerization technique. This technique makes MPC graft to CLPE directly where C-C covalent bonding is formed between the MPC polymer and the CLPE substrate. The advantage of this technique is that the MPC polymer grafting acts only on the CLPE surface and gives no effect on the bulk properties of the CLPE substrate. In the present study, structure and properties of the MPC polymer layer formed on the CLPE surface by the photo-induced radical graft polymerization were investigated, and wear-resistant properties of the MPC-grafted CLPE were discussed in terms of the characteristics of the MPC polymer layer.

2. Materials and Methods

Chemicals

The benzophenone and acetone were purchased from Wako Pure Chemical Industries, Ltd (Japan). The MPC synthesized industrially using the method reported by Ishihara, et al. [13] was supplied by Ai Bio-Chips Co., Ltd (Japan).

MPC graft polymerization

The compression-molded UHMWPE (GUR1020 resin, Poly Hi Solidur Inc., IN, USA) bar stock was gamma-irradiated with 50 kGy in inert 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 in 10 mg/mL acetone solution containing benzophenone for 30 sec and then dried to remove acetone solution under dark condition at room temperature. The amount of benzophenone adsorbed on the surface was 3.5×10^{-11} mol/cm² [19]. The MPC monomer was dissolved into degassed pure water in order that its concentration was 0.5 mol/L. The CLPE specimens coated with benzophenone were immersed in the MPC aqueous solution. The photo induced graft polymerization on the CLPE surface was carried out with ultraviolet-ray irradiation of 5 mW/cm² for 10 to 360 min at 60°C. Only the ultraviolet-ray with 350±50 nm in wavelength was passed for irradiation using a Toshiba D-35 filter. After the polymerization, the CLPE-g-MPC specimens were picked out, washed with pure water and ethanol and dried.

Surface analysis by using XPS, water-contact angle measurement and FT-IR/ATR

The surface elemental conditions of CLPE before and after the MPC grafting, were analyzed 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 at 15 kV at the anode.

The take-off angle of photoelectron was kept at 90 degree.

The static water-contact angle of the CLPE-g-MPC with various photo polymerization periods, was measured by a sessile drop method using a model DM300 optical bench-type contact angle goniometer (Kyowa interface science Co., Ltd., Japan). The drops of the purified water (1 μ L) were deposited onto the surface of the CLPE-g-MPC and the contact angles were directly measured with a microscope after dropping (60 sec), according to ISO 15989 standard [20].

The functional groups vibration of the CLPE-g-MPC surface with various photo polymerization periods, were examined by Fourier-transform infrared (FT-IR) spectroscopy with the attenuated total reflection (ATR) equipment. The measurements were performed over a range of 800 to 2000 cm⁻¹ by using a FT-IR analyzer (Perkin-Elmer FT-IR 1650, Perkin-Elmer Corp., MA, USA) at a resolution of 4.0 cm⁻¹ for 100 scans.

The amount of grafted MPC polymer unit on the CLPE surface was relatively evaluated by quantification of phosphate (P-O) group which was contained in the structure of MPC unit. Thus, the relative amount of the phosphate group was defined as P-O group index, and it was calculated as follows.

$$\text{P-O group index} = (1080 \text{ cm}^{-1} \text{ peak intensity}) / (1460 \text{ cm}^{-1} \text{ peak intensity})$$

Observation of cross section of CLPE-g-MPC with TEM

The cross section of the MPC polymer layer on the CLPE-g-MPC surface with various photo polymerization periods during polymerization was observed by using a transmission electron microscope (TEM). Prior to observation, specimens were embedded in an epoxy resin, stained in ruthenium oxide vapor at room temperature, and sliced to ultra thin films. A JEM-1010 model manufactured by JEOL, Ltd. (Japan) was used for the TEM observation at an acceleration voltage of 100 kV.

Hip simulation wear test

The CLPE-g-MPC cups of 26 mm in inner diameter and 52 mm in outer diameter for hip joint simulator were gamma-sterilized with a dose of 2.5 to 4.0 Mrad under N₂ gas atmosphere. The wear test was performed using a 12-stations hip joint simulator (MTS system Corp., MN, USA). The Co-Cr-Mo alloy femoral head with 26 mm in size (Japan Medical Materials Corp., Japan) was used as an acetabular component. A mixture of 25% bovine serum, 20 mM/L of ethylene di amine tetra acetic acid (EDTA), and 0.1% sodium azide was used as lubrication, according to ISO 14242-1 standard [21]. The loads simulating a physiologic loading curve with double peaks of 183 and 280 kgf loads were applied with a frequency of 1 Hz. The wear was estimated by a gravimetric method. The weights of the cups were measured every 0.5 x 10⁶ cycles. Testing then continued until a total of 5.0 x 10⁶ cycles were completed.

In order to evaluate the net wear corrected with the contribution of plastic deformation, the melt-recovery operation by the previously reported method [22] were performed on selected components from both groups of CLPE and CLPE-g-MPC cups after the hip joint simulator tests (5.0 x 10⁶ cycles). The cups were melted at 150°C in a vacuum and allowed to cool to room temperature. The surface features of the bearing surfaces of the cups were observed by using a confocal laser scanning microscope (OLS1200, Olympus Corp., Japan).

3. Results

Fig. 1 shows the XPS spectra (C_{1s}, O_{1s}, N_{1s} and P_{2p}) of the CLPE and the CLPE-g-MPC. In the C_{1s} spectra of both the CLPE and the CLPE-g-MPC, a strong peak at 285 eV was observed. This is attributed to carbon atoms in the C-C or C-H group. In the O_{1s} spectrum of the CLPE-g-MPC, a considerable peak assigned to the C-O group was observed at 532 eV. This peak is mainly ascribed to the MPC units. Even the untreated CLPE showed a small peak at 532 eV. In this case, the peak is attributed to oxygen atoms and might suggest the oxidation and/or contamination of the CLPE surface. In the case of the N_{1s} and P_{2p} spectra, clear peaks were observed for the CLPE-g-MPC only. The peaks at 403 and 134 eV were assigned to the -N⁺(CH₃)₃ and phosphate groups, respectively, and these peaks were characteristic to the phosphorylcholine in the MPC units.

Fig. 2 shows the FT-IR/ATR spectra of the CLPE and the CLPE-g-MPC. The transmittance absorption peak was observed at 1460 cm⁻¹ for both the CLPE and the CLPE-g-MPC. This peak is attributed mainly to the methylene (CH₂) chain in the CLPE substrate, since the peak intensity is very strong and it is unchanged between the CLPE and the CLPE-g-MPC. On the other hand, the transmittance absorption peaks at 1240, 1080 and 970 cm⁻¹ were observed for the CLPE-g-MPC only. These peaks are ascribed to the phosphate (P-O) group in the MPC unit. Similarly, the transmittance absorption peak at 1720 cm⁻¹ observed for the CLPE-g-MPC only corresponds to the ketone group in the MPC unit.

The relativity P-O group index was calculated from FT-IR peak intensities ratio at 1080 and 1460 cm⁻¹, as measure of amount of the MPC unit graft-binded on the CLPE surface because 1460 cm⁻¹-peak intensity is unchanged. Fig. 3 shows the static water-contact angle as a function of the calculated P-O group index for the CLPE-g-MPC specimens. The static water-contact angle on the untreated CLPE was 88°, and drastically decreased with increasing the P-O group index. When the P-O group index was higher than 0.3, the static water-contact angle became constant as low as 15°.

Fig. 4 shows the cross-section TEM images of the CLPE-g-MPC with various ultraviolet-ray irradiation time during polymerization. The lamellae were on the order of 100 to 400 nm in length and 10 to 20 nm in thickness, were observed in the CLPE substrate regardless of irradiation time, and the lamellae thickness were quite thin near surface. On the surface of CLPE structure for irradiation time longer than 45 min, the grafted MPC polymer layer of 100 to 200 nm in thickness was clearly observed. The MPC-covered region was coexistent with uncovered one for irradiation time of 23 min, although the thickness of the MPC polymer layer of the covered region was same

(100 to 200 nm). With irradiation for 11 min, the MPC graft layer was not observed on surface of CLPE. These results indicate that the density of the grafted MPC polymer can be controlled by the polymerization time, since the number of polymer chains produced in the radical polymerization is generally parallel to the photo irradiation time. The grafted MPC polymer layer on the CLPE was less stained with ruthenium oxide as irradiation time increased.

Table 1 shows the change in wear rate of the CLPE-g-MPC cups with the various P-O group index in the hip joint simulation test. We defined the initial wear rate as that from start to 1.0×10^6 cycles and did the steady wear rate as that from 4.0×10^6 to 5.0×10^6 cycles. All of the untreated CLPE and CLPE-g-MPC cups showed the low initial wear rate of -0.54 to -3.84 mg/ 10^6 cycles. The steady wear rate of the untreated CLPE cups and the CLPE-g-MPC cups with low P-O group index of 0.11 showed the increase to 3.65 and 4.61 mg/ 10^6 cycles. In contrast, those of the CLPE-g-MPC cups with high P-O group index of 0.46 and 0.48 drastically decreased to -0.29 and -0.44 mg/ 10^6 cycles.

Fig. 5 shows the confocal laser scanning microscope images the bearing surface of the untreated CLPE and CLPE-g-MPC cups with the melt-recovery after 5.0×10^6 cycles simulator test. The clear machining marks of the regular circular were observed on the surface of the CLPE-g-MPC, although no marks were observed on that of the untreated CLPE, indicating that the former was hardly worn.

4. Discussion

We have developed the artificial hip joint that CLPE-g-MPC, aiming at reduction in wear and suppression of the bone resorption. Our previous study reported the effects of graft polymerization of MPC onto the CLPE surface. The MPC grafting markedly decreased the function and amount of wear. In the present study, structure and properties of the MPC polymer layer formed on the CLPE surface by the photo-induced radical graft polymerization were investigated, and wear-resistant properties of the CLPE-g-MPC were discussed in terms of the characteristics of the MPC polymer layer.

After 5.0×10^6 cycles of the hip joint simulator test, we confirmed that the CLPE-g-MPC cups with P-O group index of 0.32 to 0.48 showed the quite low steady wear rate (-0.44 to 0.26 mg/ 10^6 cycles). This indicates that the CLPE-g-MPC cups with P-O group index higher than 0.32 achieves >90% reduction in the steady wear rate compared with the untreated CLPE, and the CLPE-g-MPC with low P-O group index (0.11) cups with low density of grafted MPC polymer chains. Since the MPC is a highly hydrophilic compound, and the poly (MPC) is water-soluble. In fact, the water-wettability of the CLPE-g-MPC surface was much larger than that of the untreated CLPE surface as enhanced in Fig. 3. Therefore, the artificial hip joint bearing with the grafted MPC polymer surface showed much higher lubricity compared with that without the MPC polymer. Because the more lubricant surface with the grafted MPC polymer gave significant reduction in friction coefficient [12], the great improvement of wear-resistant properties was achieved. The bearing surface of artificial hip joint combined with the MPC polymer is assumed to be the artificial cell membrane structure. In this meaning, the function of this novel artificial hip joint mimics that of the natural joint cartilage.

It is assumed that there are several important points to maintain the effects of MPC polymer stably in the artificial joint under the multi-directions and loads for long term; strong bonding between the MPC polymer and the CLPE surface, high mobility of the free end-group of MPC polymer and the high density of the introduced MPC polymer. From these points of view, we chose the photo-induced radical graft polymerization technique in order to produce a C-C covalent bonding between the carbon atom of CLPE and the end-group of MPC polymer chain. As shown in Fig. 4, the crystalline structure of CLPE substrate is unchanged even after the grafting of MPC regardless of irradiation time (polymerization time). This indicates that the photo-induced radical graft polymerization technique with ultraviolet-ray irradiation gives no influence on the structure of the CLPE substrate. The unchanged structure of the CLPE substrate itself is very important, because

the CLPE cup acts not only as a bearing material but also as a structural material in the artificial hip joint.

In order to obtain the MPC polymer layer with high density, the irradiation time of the ultraviolet-ray must be controlled [18]. The density of MPC polymer chains gradually increased on the surface of CLPE with increasing ultraviolet-ray irradiation time, and whole the surface of CLPE was coated at polymerization time longer 45 min. In this case, the thickness of the MPC polymer layer was same (100 to 200 nm) as shown in Fig. 4. On the other hand, Fig. 3 implies that the density of the MPC polymer chains on the surface of CLPE was the different even if the water-wettability of the CLPE-g-MPC is same (as low as 15°), because the P-O group index remarkably changed in the range between 0.3 and 0.7.

As mentioned above, the steady wear rate of the CLPE-g-MPC cups with high P-O group index was quite low even after the 5.0×10^6 cycles simulator test. Although the volumetric change was calculated from the weight loss, the weight loss was not corrected concerning the effect of water absorption in this study. As shown in Fig. 5, the clear machining marks with regular circles are remained on the surfaces of CLPE-g-MPC cups even after the 5.0×10^6 cycles simulator test. In other words, the CLPE-g-MPC cups were hardly worn, supporting the quite low wear in the hip joint simulator tests.

The excellent functions of the CLPE-g-MPC could suppress activation of cell systems due to the wear particles, and then prevent the periprosthetic osteolysis and the subsequent aseptic loosening entirely [12]. Because of the excellent mechanical and biological advantages, the CLPE-g-MPC is strongly expected as a next-generation bearing material for artificial hip joints, and is now under arrangements of clinical trials.

5. Conclusions

We investigated the surface and wear-resistant properties of CLPE-g-MPC. After the hip joint simulator test, we confirmed that the CLPE-g-MPC cups with high density of MPC graft chain showed the quite low steady wear rate. These CLPE-g-MPC cups showed 90% reduction in the steady wear rate, compared with the untreated CLPE, and the CLPE-g-MPC with low P-O group index cups with low density of grafted MPC polymer chain. Thus, it was appeared that the CLPE-g-MPC drastically reduces the generation of the wear particles. However, the grafting of MPC polymer with high density is prerequisite in order to maintain the stable wear-resistant property of the CLPE-g-MPC as orthopedic bearing materials for long period. We concluded that the grafting of MPC on CLPE is significantly useful method to maintain lubrication of artificial hip joint for long period.

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 further express special thank to Dr. Fumiaki Miyaji and Mr. Yoshiki Ando (Japan Medical Materials Corp., Japan) for their excellent technical assistance.

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Figure captions

- Fig. 1. XPS spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC.
- Fig. 2. FT-IR/ATR spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC. ● : P-O, ▲ : CH₂, ■ : C=O.
- Fig. 3. Static water-contact angle as a function of P-O group index for CLPE-g-MPC. ◇: CLPE (untreated), ◆: CLPE-g-MPC.
- Fig. 4. Cross-section of TEM images of CLPE-g-MPC with various photo polymerization time. Bar; 200 nm. (a) 11 min, (b) 23 min, (c) 45 min, (d) 90 min, (e) 360 min.
- Fig. 5. Confocal laser scanning microscope images of the bearing surfaces of the cups with the melt-recovery after 5×10^6 cycles simulator test. Bar; 400 μm . (a) CLPE (untreated), (b) CLPE-g-MPC.

Table 1 P-O group index and wear rate in hip joint simulator tests

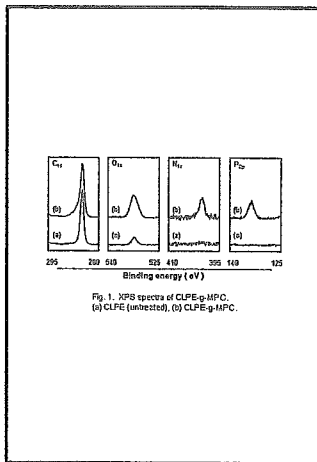


Fig. 1. XPS spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC.

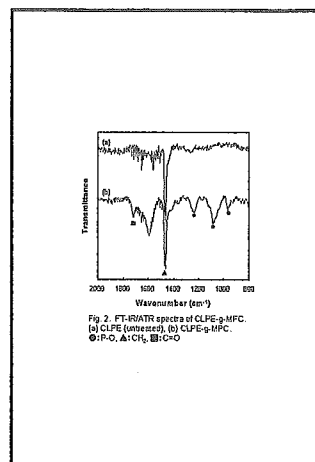


Fig. 2. FT-IR spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC. \odot : P-O, \triangle : C-H, \square : C=O

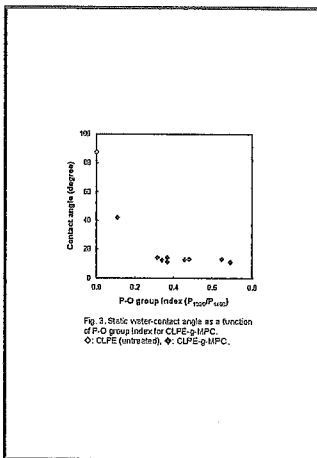


Fig. 3. Static water contact angle as a function of P-O group index for CLPE-g-MPC. \diamond : CLPE (untreated), \circ : CLPE-g-MPC.

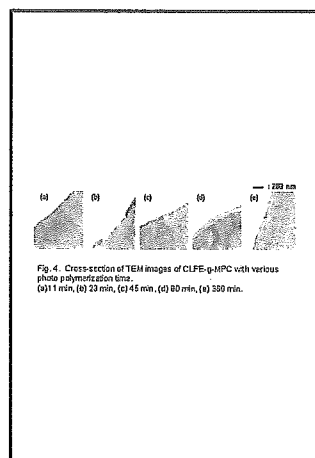


Fig. 4. Cross-section of TEM images of CLPE-g-MPC with various photo polymerization time. (a) 1 min, (b) 23 min, (c) 45 min, (d) 80 min, (e) 330 min.

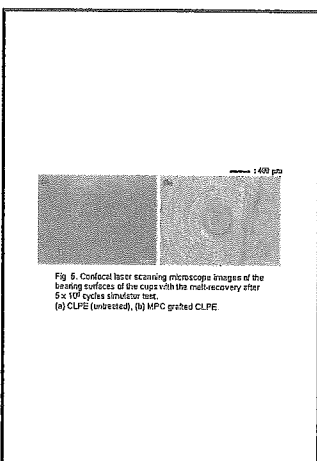


Fig. 5. Confocal laser scanning microscope images of the bearing surfaces of the cups with the malrecovery after 5×10^5 cycles simulator test. (a) CLPE (untreated), (b) MPC grafted CLPE.

Table 1 P-O group index and wear rate in hip joint simulator tests

P-O group index (P_{ox}/P_{tot})	Total wear rate (mg/MP cycles)	Steady wear rate (mg/MP cycles)
0 (untreated CLPE)	0.64	3.65
0.11	2.42	4.61
0.33	3.14	0.26
0.46	3.64	4.29
0.49	3.03	0.44

ポリエチレンライナー表面の MPC 処理は
人工股関節の弛みを抑制する

——ナノ表面制御による長寿命型人工股関節の開発——

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