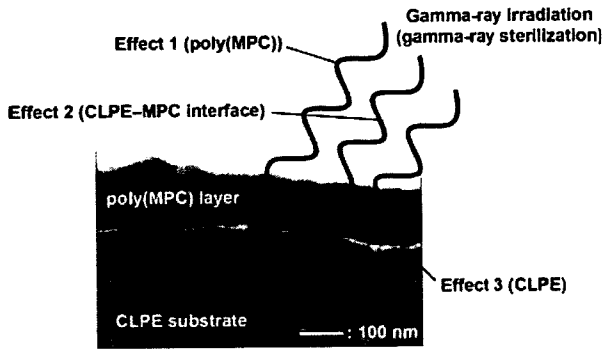

Figure 7. Schematic diagram of the effects of gamma-ray irradiation on CLPE-*g*-MPC.

The dose of gamma-ray sterilization influences the friction response since the dynamic coefficient of friction of CLPE-*g*-MPC slightly increased from 0.007 to 0.021 within the low friction region with an increase in the gamma-ray sterilization dose. It was previously reported that as the polymer concentration (viscosity) increases with the increase in the friction coefficient in the mixed lubrication regime.[33] It was therefore assumed that an ultra-low friction of CLPE-*g*-MPC that appeared during sliding is related to the effective viscosity of poly(MPC) in the mixed lubrication of the intermediate hydrated layer. The viscosity of poly(MPC) reflects the mobility of the free end groups of the MPC polymer or MPC polymer chains themselves; this mobility was limited by the cross-linking of poly(MPC) layer.[34,35] These results seem to suggest that the cross-link corresponds to the viscosity of the poly(MPC) in the bearing interface, the viscosity of the poly(MPC) increases by gamma-ray irradiation, and the poly(MPC) would act as a boundary lubricant in mixed lubrication. These effects are represented as "Effect 1" in Figure 7.

After 5.0×10^6 cycles of the simulator test, the gamma-ray sterilized CLPE-*g*-MPC cups showed low and stable wear (Figure 5). On the contrary, with the nonsterilized CLPE-*g*-MPC cups, the weight change varied in each cup. In the previous study, when a high energy beam was irradiated onto a polymer with a grafted layer, strong bindings were formed between the grafted layer and polymer substrate.[36] Lewis et al. reported that the force required to remove the coating with cross-linking was greater than that without cross-linking.[37] In addition, much more cross-linking and perhaps adhesion to the substrate was induced by the gamma-ray irradiation (gamma-ray sterilization) when compared with the nonsterilized CLPE-*g*-MPC. It is therefore assumed that the higher energy radiation in gamma-ray sterilization induced cross-links not only within the grafting MPC polymer but also between the grafting MPC polymer and CLPE substrate. Then, a much stronger and stable MPC polymer grafted layer was produced on the bearing surface ("Effect 2" in Figure 7).

McKellop et al. reported on the wear performance of UHMWPE in a contemporary hip simulator following gamma-ray irradiation in air as well as in an inert gas and ethylene oxide gas sterilization or gas plasma sterilization.[21] Between 2 and 5×10^6 cycles, the wear rate of the gamma-ray sterilized UHMWPE was significantly lower than that of the UHMWPE sterilized either by gas plasma or ethylene oxide. A similar trend has been reported by Wang et al. who observed more than 50% drop in the hip simulator wear rate after single 25 kGy doses of gamma-ray sterilization.[22] These studies have reported that the wear resistance is better in gamma-ray sterilized UHMWPE than in ethylene oxide sterilized UHMWPE.[21–24] It is therefore assumed that gamma-ray irradiation improved the wear resistance of the CLPE substrate ("Effect 3" in Figure 7).

In the cross-link process of this study, the UHMWPE bar stock was irradiated with a dose of 50 kGy, and then CLPE and CLPE-*g*-MPC were gamma-ray sterilized with a nominal dose of 25 kGy. Thus, the total dosage for the gamma-ray sterilized CLPE and CLPE-*g*-MPC was 75 kGy. The nonsterilized CLPE-*g*-MPC received a total dose of 50 kGy only; this would be a disadvantage for the anti-wear property.[38–40] However, as shown in Figure 6, clear machining marks with regular circles remained on the surfaces of the nonsterilized as well as gamma-ray sterilized CLPE-*g*-MPC cups even after the simulator test. The observed CLPE-*g*-MPC cups were virtually unworn, which is consistent with the relatively low wear in the hip joint simulator tests, as shown in Figure 5. In contrast, the machining marks disappeared from the surface of the gamma-ray sterilized CLPE cups [Figure 6(b)]. In other words, the presence of poly(MPC) on the CLPE surface by MPC grafting would have a greater effect on the wear resistance than the additional cross-links of the CLPE substrate by the gamma-ray irradiation of 25 kGy. The CLPE surface with the poly(MPC) exhibited considerably higher lubricity than that without the poly(MPC) (Figures 2–4). The significant reduction in the coefficient of friction of the grafted poly(MPC) resulted in a substantial improvement in wear resistance. The bearing surface of the artificial hip joint combined with poly(MPC) might exhibit the fluid film lubrication (or mixed lubrication) of the intermediate hydrated layer. This means that artificial hip joints utilizing CLPE-*g*-MPC mimic the natural joint cartilage.[41,42]

The concern about the degradation of polyethylene during shelf aging prompted several orthopedic manufacturers to adopt the sterilization method using gas plasma or ethylene oxide gas for conventional UHMWPE.[43,44] These sterilization methods admittedly generate no free radicals that could be subsequently oxidized during shelf storage. However, UHMWPE sterilized using these methods did not receive the tribological benefit associated with radiation-induced cross-linking. Moreover, the oxidation index of the degraded polyethylene was lower *in vivo* than *in vitro*.[21,45] It has also been reported that the oxygen content might be almost zero in the body.[44,46] Thus, although the oxidation

degradation of polyethylene *in vivo* is related to the surrounding oxygen concentration, that is, that of the body fluid, it is not a main factor of the degradation as a whole. However, recent studies reported that conventional or cross-linked gamma-ray sterilized polyethylene liners undergo *in vivo* oxidation, especially in unworn bearing surface regions and the rim. In contrast, the oxidation of a worn bearing surface was not observed.[47] On the basis of these studies, we assumed that when oxygen is excluded from the package during sterilization, further cross-linking, and additional improvement in the wear performance are attained. However, we must pay attention to the rim fracture in CLPE-*g*-MPC cup by the possible impingements based on the abovementioned studies.[47] In the previous study, for gamma-ray irradiation, the lower molecular weight cross-linked GUR1020 materials had higher mechanical properties (tensile and impact properties) for all doses as compared to the higher molecular weight cross-linked GUR1050 materials.[48] Therefore, we selected a GUR1020 compression-molded bar stock as the CLPE substrate. Nevertheless, the cross-linked GUR1020 materials showed the same wear rate as the cross-linked GUR1050 materials.

Gamma-ray sterilization has had a long history and it has been one of the most popular sterilization methods for various medical products to date. A barrier package has been widely adopted to satisfactorily address the historical problem of the oxidation of gamma-ray sterilized products during shelf storage. In this study, we confirmed that the extra energy supplied by gamma-ray irradiation produced cross-linking in the three regions of the CLPE-*g*-MPC: poly(MPC) layer, CLPE-MPC interface, and CLPE substrate. When the CLPE surface is modified by poly(MPC) grafting, the MPC graft polymer leads to a significant reduction in the sliding friction between the surfaces which are grafted because water thin films formed can act as extremely efficient lubricants. Gamma-ray sterilized CLPE-*g*-MPC showed a slightly higher friction than the nonsterilized one. However, the wear resistance is more stable in the former than in the latter. The cross-links formed by gamma-ray irradiation would give further longevity to CLPE-*g*-MPC cups. Based on the mechanical,[19] biological,[5,49,50] and tribological advantages of MPC polymers, CLPE-*g*-MPC is believed to be promising for use in the next-generation artificial hip joint systems.

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Erratum

Enhanced Wear Resistance of Orthopaedic Bearing Due to the Cross-Linking of Poly(MPC) Graft Chains Induced by Gamma-Ray Irradiation

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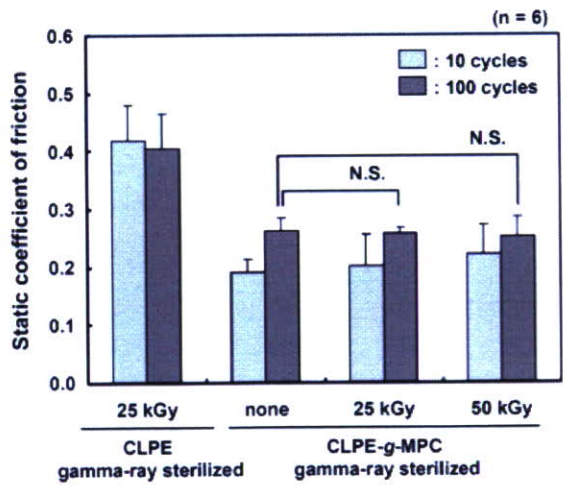

Figure 3. Static coefficients of friction of the gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar, Standard deviations.

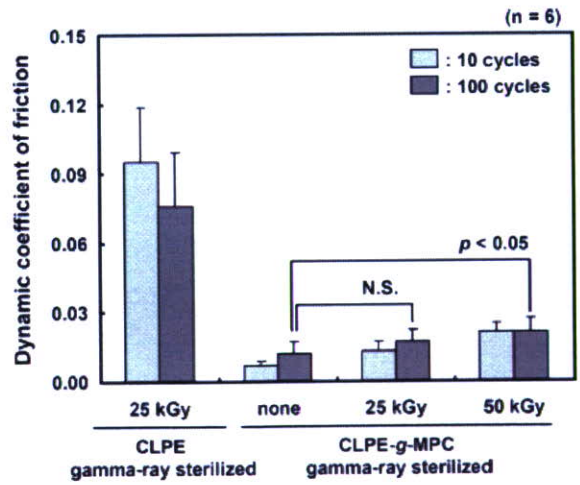

Figure 4. Dynamic coefficients of friction of gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar, Standard deviations.

Effect of 2-methacryloyloxyethyl phosphorylcholine concentration on photo-induced graft polymerization of polyethylene in reducing the wear of orthopaedic bearing surface

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Abstract: Photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine (MPC) on cross-linked polyethylene (CLPE) has been developed as a novel technology for reducing wear of orthopaedic bearings. In this study, the effect of MPC concentration on graft polymerization and the resultant properties of the grafted poly (MPC) layer have been investigated. The grafted poly (MPC) layer thickness increased with the MPC concentration in feed. The hip simulator wear test confirmed that CLPE-*g*-MPC cups exhibited minimal wear compared with untreated CLPE cups. Since MPC is a highly hydrophilic methacrylate, the water-wettability of CLPE-*g*-MPC was greater than that of untreated CLPE due to the formation of a poly(MPC) nanometer-scale layer. The CLPE-*g*-MPC orthopaedic bearing surface exhibited high lubricity, because of the present of the poly(MPC) layer even at a thickness of 10 nm. This layer is considered responsible for the improved wear resistance. Nanometer-scale modification of CLPE with poly(MPC) is expected to significantly increase the durability of the orthopaedic bearings. Poly (MPC) layer thickness can be controlled by changing the MPC concentration in feed. In order to achieve nanometer-scale modification of poly(MPC) in this manner, it is necessary to use a long photo-irradiation time for the MPC graft polymerization system, which contains a high-concentration monomer without its gelation. © 2007 Wiley Periodicals, Inc. J Biomed Mater Res 00A: 000–000, 2007

Key words: joint replacement; polyethylene; phosphorylcholine; graft polymerization; wear mechanism

INTRODUCTION

Polymeric biomaterials are widely used in the biomedical field for manufacturing artificial organs, medical devices, and disposable clinical apparatus.[1,2] The number of artificial hip and knee joints used for primary and revised hip and knee replacement are substantially increasing in the worldwide every year.[3] This indicates that the quality of medical devices such as artificial joints has become increasingly important. The most popular artificial joint system used as a medical device is a bearing couple composed of ultra-high molecular weight polyethylene (UHMWPE) and cobalt–chromium–molybdenum (Co-Cr-Mo) alloy. However, osteolysis caused by the wear particles of UHMWPE in the artificial joint system has emerged as a serious issue.[4,5] Different combinations of bearing surfaces and improvements in bearing materials have been studied with the aim of reducing the number of UHMWPE wear particles inducing osteolysis.[6–9]

Surface modification is important for the improvement of bearing materials. Recently, we developed an artificial hip joint based on a new concept by using 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted onto the surface of cross-linked polyethylene (CLPE; CLPE-*g*-MPC); this device was designed to reduce wear and suppress bone resorp-

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tion.[10–13] MPC, a methacrylate monomer with a phospholipid polar group in the side chain, is a novel biomaterial designed and developed by Ishihara et al., and it mimics the neutral phospholipids of cell membranes.[14] MPC polymers are one of the most common biocompatible and hydrophilic polymers studied thus far, which have potential application in a variety of fields such as biology, biomedical science, and surface chemistry because they possess the unique properties of good biocompatibility, high lubricity and low friction, anti-protein adsorption, and cell membrane-like surface.[15–22]

In general, there are two methods for modifying the polymer surface. The first method involves surface absorption or reaction with small molecules[23–25] and the second, grafting polymeric molecules onto the substrate through covalent bonding.[26] Most frequently, grafting polymerization is performed using either of the following methods: (1) surface-initiated graft polymerization termed as the "grafting from" method in which the monomers are polymerized from initiators or comonomers; and (2) adsorption of the polymer to the substrate termed as the "grafting to" methods (i.e., dipping, cross-linking, and ready-made polymers with reactive end groups reacting with the functional groups of the substrate).[27,28] The "grafting from" method has an advantage over the "grafting to" method in that it synthesizes a high-density polymer brush. The novel artificial joint developed in this study is low-wear bearing with nanometer-scale poly(MPC) surface modification. This surface modification was accomplished by using a photo-induced radical polymerization technique that was similar to that used in the "grafting from" method. However, in this technique, controlling the length and density of the grafted poly(MPC) was difficult.[15] Our previous study confirmed that the density of the grafted poly(MPC) affects wear resistance and that it was controlled by the photo-irradiation time.[12]

In an attempt to resolve another issue in this study, we investigated the effect of MPC concentration variability on photo-induced graft polymerization. The results revealed that it was possible to control the grafted poly(MPC) chains with nanometer scale modification in order to reduce wear of the CLPE-*g*-MPC orthopaedic bearing surface.

MATERIALS AND METHODS

Chemicals

Benzophenone and acetone were purchased from Wako Pure Chemical Industries, (Osaka, Japan). MPC was industrially synthesized using the method reported by Ishihara et al.[14] and supplied by Ai Bio-Chips, (Tokyo, Japan).

MPC graft polymerization

A compression-molded UHMWPE (GUR1020 resin; Poly Hi Solidur, IN, USA) bar stock was irradiated with gamma-ray of 50 kGy in N_2 gas and annealed at 120°C for 7.5 h in N_2 gas in order to attain cross-linking. The CLPE specimens were machined from this bar stock after cooling. The specimens were immersed in an acetone solution containing 10 mg/mL benzophenone for 30 s and then dried in the dark at room temperature to remove acetone. Using ultraviolet spectroscopy, the amount of benzophenone adsorbed on the surface was reported to be 3.5×10^{-11} mol/cm^2 in previous studies.[15,16] The MPC was dissolved in degassed pure water to attain concentrations ranging from 0.06 to 1.00 mol/L. Subsequently, the CLPE specimens coated with benzophenone were immersed in the aqueous MPC solutions. Photo-induced graft polymerization on the CLPE surface was performed using ultraviolet irradiation (UVL-400HA ultra-high pressure mercury lamp; Riko-Kagaku Sangyo, Funabashi, Japan) with an intensity of 5 mW/cm^2 at 60°C for 12–90 min; a filter (Model D-35; Toshiba, Tokyo, Japan) was used restrict the passage of ultraviolet light to wavelengths of 350 ± 50 nm. After polymerization, the CLPE-*g*-MPC specimens were removed, washed with pure water and ethanol, and dried at room temperature. These specimens were then sterilized by 25 kGy gamma-ray under N_2 gas.

Surface analysis by X-ray photoelectron spectroscopy, water-contact angle measurement, and Fourier-transform infrared spectroscopy

The surface elemental contents of CLPE-*g*-MPC obtained with various photo-irradiation times or MPC concentrations were analyzed using X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS Hsi 165; Kratos Analytical, UK) equipped with an Mg-Kα radiation source by applying a voltage of 15 kV at the anode. The take-off angle of the photoelectrons was maintained at 90°. Each measurement was scanned five times, and five replicate measurements were performed on each sample, and the average values were considered for the surface elemental contents.

The static water-contact angles of CLPE-*g*-MPC obtained at various MPC concentrations were measured with an optical bench-type contact angle goniometer (Model DM300; Kyowa Interface Science, Saitama, Japan) using a sessile drop method. Drops of purified water (1 μL) were deposited on the CLPE-*g*-MPC surfaces, and the contact angles were directly measured after 60 s by using a microscope according to the ISO standard 15989.[29] Subsequently, 15 replicate measurements were performed on each sample, and the average values were taken as the contact angles.

The functional group vibrations of the CLPE-*g*-MPC surface that was polymerized with various MPC concentrations were examined using attenuated total reflection (ATR) by Fourier-transform infrared (FTIR) spectroscopy. FTIR/ATR spectra were obtained in 32 scans over a range of 800–2000 cm^{-1} by using an FTIR analyzer (FT/IR615; Jasco International, Tokyo, Japan) at a resolution of 4.0 cm^{-1}.

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Cross-sectional observation of CLPE-*g*-MPC by transmission electron microscopy

A cross-section of the poly(MPC) layer on the CLPE-*g*-MPC surface produced at various MPC concentrations was observed using a transmission electron microscope (TEM). The specimens were first embedded in epoxy resin, stained with ruthenium oxide vapor at room temperature, and then sliced into ultra-thin films (approximately 100-nm thick) by using a Leica Ultra Cut UC microtome (Leica Microsystems, Wetzlar, Germany). A JEM-1010 electron microscope (JEOL, Tokyo, Japan) was used for the TEM observation at an acceleration voltage of 100 kV.

Surface coated-area observation by fluorescence microscopy

We used rhodamine 6G (Wako Pure Chemical Industries) because it can be easily and rapidly applied to a polymer coating and imaged using fluorescence microscopy (Axioskop 2 Plus; Carl Zeiss AG, Oberkochen, Germany). Wang et al. observed that rhodamine 6G effectively stains the MPC polymer, which shares very high structural similarity to lipids.[30]

An aqueous solution of 200 mass ppm rhodamine 6G was used for all the staining experiments. All the samples were stained using a two-step procedure. (1) The samples were immersed in the rhodamine 6G solution for 30 s and then removed. (2) Subsequently, they were washed twice consecutively in distilled water for 30 s and dried.

All the samples were examined and imaged using fluorescence microscopy. Pseudo-color images were obtained using a charge-coupled-device (CCD) camera (VB-7010; Keyence, Osaka, Japan) and imaging software (VH analyzer 2.51; Keyence). Lenses with a 10× magnification and an appropriate exposure time (approximately 1/10 s) were employed to obtain clear images of the samples.

Friction test

The friction test was performed using a ball-on-plate machine (Tribostation 32; Shinto Scientific, Tokyo, Japan). Each of the CLPE-*g*-MPC surfaces with various MPC concentrations were used to prepare six sample pieces. A Co-Cr-Mo alloy ball with 9 mm in diameter was prepared. The surface roughness of the ball was Ra = 0.01, which was comparable with that of femoral ball products. The friction tests were performed at room temperature with a load of 0.98 N, sliding distance of 25 mm, and frequency of 1 Hz for a maximum of 100 cycles.[31] Pure water was used as a lubricant. The mean static (μ_s) and dynamic (μ_d) coefficients of friction were determined by averaging five data points from the 100 (96–100) cycle measurements.

Hip simulator wear test

A 12-station hip joint simulator (MTS Systems, MN, USA) with CLPE and CLPE-*g*-MPC cups both having an inner and outer diameter of 26 and 52 mm, respectively, was used for the hip simulator wear test. For each MPC concentration [0 (untreated), 0.25, and 0.50 mol/L], two sample pieces were prepared. A Co-Cr-Mo alloy femoral ball component with a size of 26 mm (Japan Medical Materials, Osaka, Japan) was used as the femoral component. A mixture of 25 vol % bovine serum, 20 m*M*/L of ethylene diamine tetraacetic acid (EDTA), and 0.1mass % sodium azide was used as a lubricant, according to the ISO standard 14242-1.[32] The lubricant was replaced every 0.5×10^6 cycles. Walks, which simulated a physiologic loading curve (Paul-type) with double peaks at 1793 and 2744 N loads, with a multidirectional (biaxial and orbital) motion of 1 Hz frequency were applied. Wear was determined by weighing the cups at intervals of 0.5×10^6 cycles. Load-soak controls ($n = 2$) were used to compensate the fluid absorption by the specimens.[33] The testing was continued until a total of 5.0×10^6 cycles were completed.

RESULTS

Figure 1 shows the phosphorous (P) concentration of the CLPE-*g*-MPC surface as a function of the photo-irradiation time during polymerization. The P concentration increased proportionally with the photo-irradiation time. When the photo-irradiation time was greater than 45 min, the P concentration of the CLPE-*g*-MPC surface with 0.17, 0.25, and 0.50 mol/L MPC concentration became almost constant at high values of 2.9, 3.8, and 4.6 atom %, respectively. F1

Figure 2 shows the nitrogen (N) and P content in the CLPE-*g*-MPC surface polymerized with various MPC concentrations and a 90-min photo-irradiation time. Both the N and P content in the CLPE-*g*-MPC surface increased to 5.2 up to an MPC concentration of 0.50 mol/L; it then gradually decreased with an F2

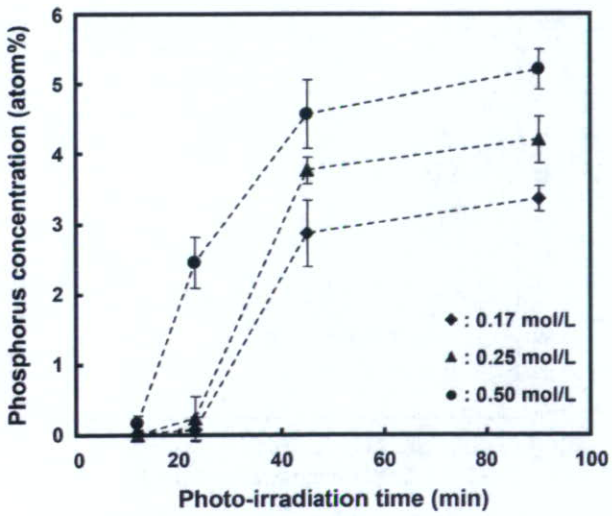

Figure 1. Phosphorus concentration in the CLPE-*g*-MPC surface as a function of the photo-irradiation time.

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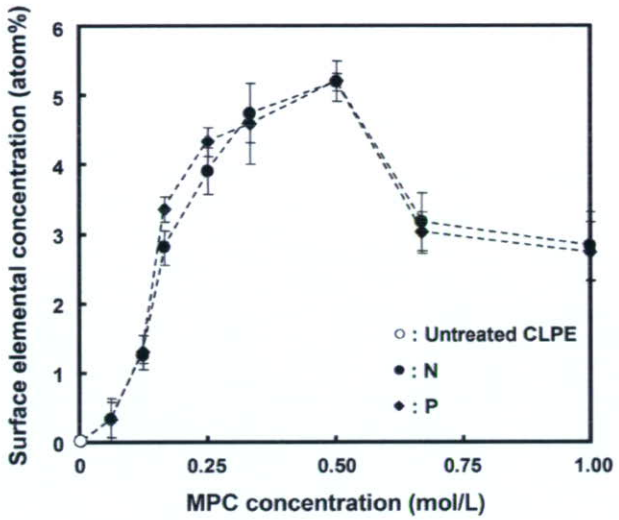

Figure 2. Surface elemental concentration of CLPE-*g*-MPC as a function of the MPC concentration with a 90-min photo-irradiation time.

increase in the MPC concentration. The N and P content at 0.50 mol/L MPC concentration was almost equivalent to the theoretical elemental composition (N = 5.3, P = 5.3) of poly(MPC).

F3 Figure 3 shows the static water-contact angle of CLPE-*g*-MPC as a function of the MPC concentration used for polymerization (90-min photo-irradiation time). The static water-contact angle of untreated CLPE was 90° and decreased markedly with an increase in the MPC concentration during polymerization. When the MPC concentration was between 0.25 and 0.50 mol/L, the static water-contact angle was constant; the lowest value was recorded at 15°.

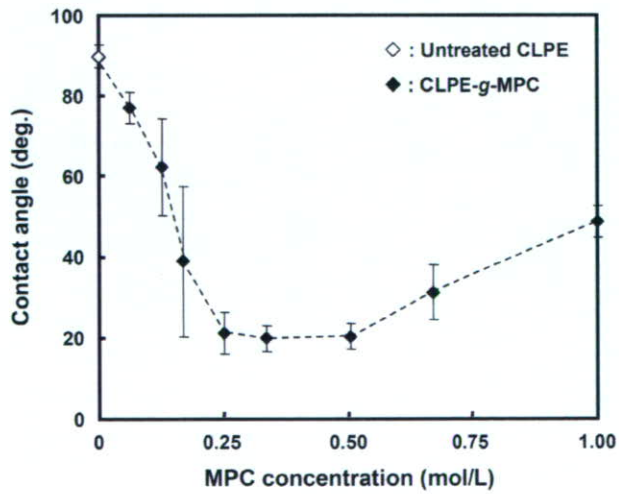

Figure 3. Static water-contact angle of CLPE-*g*-MPC as a function of the MPC concentration with a 90-min photo-irradiation time.

Figure 4 shows the FTIR/ATR spectra of untreated CLPE and CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time. An absorption peak was observed at 1460 cm^{-1} for both CLPE and CLPE-*g*-MPC. This peak is chiefly attributed to the methylene (CH_2) chain in the CLPE substrate and the poly(MPC) chain. However, transmission absorption peaks at 1240, 1080, and 970 cm^{-1} were observed only for CLPE-*g*-MPC. These peaks corresponded to the phosphate group (P—O) in the MPC unit. Similarly, an absorption peak at 1720 cm^{-1} observed in CLPE-*g*-MPC corresponded only to the carbonyl group (C=O) in the MPC unit. The absorption peak intensity of the P—O group increased with the MPC concentration used for polymerization and reached its maximum at a concentration of 0.5 mol/L. F4

Figure 5 shows the cross-sectional TEM images of CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time. At MPC concentrations greater than 0.25 mol/L, a 10–250-nm thick grafted poly(MPC) layer was clearly observed on the surface of the CLPE substrate. At an MPC concentration of 1.00 mol/L, the MPC-covered region coexisted with the uncovered regions, although the thickness of the poly(MPC) layer was greatest in the cover region, that is, 200–250 nm. At MPC concentrations below 0.06 mol/L, no poly(MPC) layer was observed on the CLPE surface (data not shown). These results indicate that the length of the grafted F5

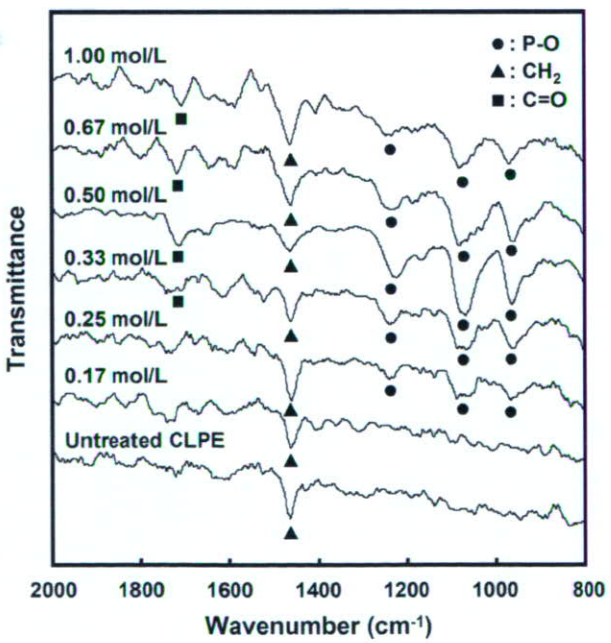

Figure 4. FT-IR/ATR spectra of CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time.

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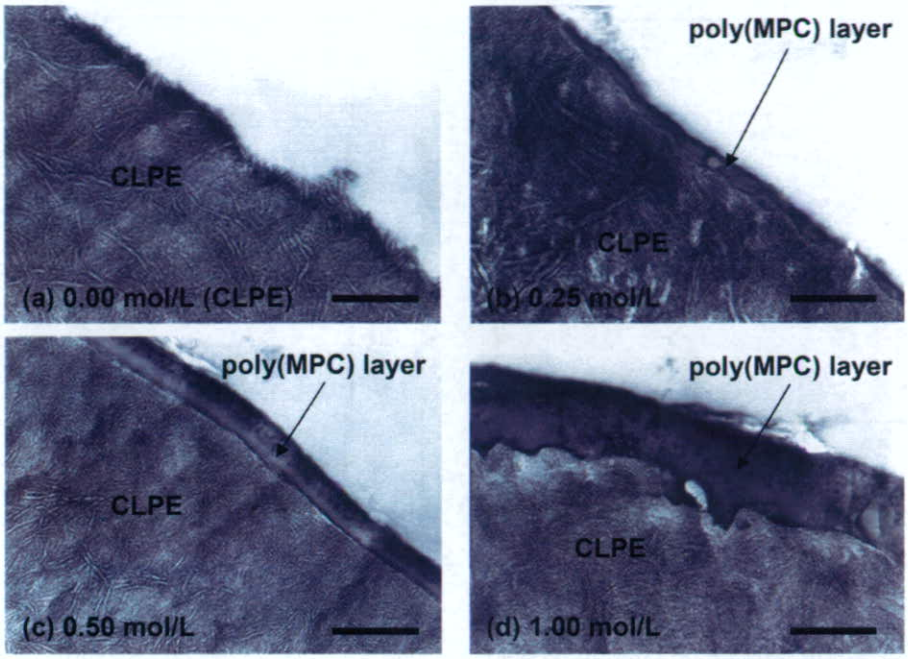

Figure 5. Cross-sectional TEM images of CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time. Bar; 200 nm.

poly(MPC) chain (thickness of the poly(MPC) layer) can be controlled by adjusting the MPC concentration during polymerization. This is attributable to the fact that the length of the polymer chains produced in a radical polymerization reaction generally correlates with the MPC concentration.

F6 Figure 6 shows the FM images of the CLPE-*g*-MPC surface with 0.50 and 1.00 mol/L MPC concentrations and a 90-min photo-irradiation time. The multiple lines observed on the FM images are machining marks. On the CLPE-*g*-MPC surface with an MPC concentration of 0.50 mol/L, the poly(MPC) layer stained with rhodamine 6G was clearly visible and showed uniform staining. On the CLPE-*g*-MPC surface with an MPC concentration of 1.00 mol/L, an ungrafted (unstained) region was observed, indicating nonuniform grafting of the poly(MPC) layer on the CLPE surface.

Figure 7 shows the static and dynamic coefficients F7 of friction of CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time. For CLPE-*g*-MPC, These coefficients of friction decreased markedly with an increase in MPC concentration and were the lowest at 0.5 and 0.25–0.5 mol/L, respectively; however, they increased at MPC concentrations above 0.67 mol/L. The CLPE-*g*-MPC specimens obtained with MPC concentrations of 0.25 and 0.50 mol/L exhibited ~80% reduction (i.e., 75–80%) in their dynamic coefficients of friction when compared with the untreated CLPE specimens.

Figure 8 shows the relationship between the F8 dynamic coefficient of friction and the contact angle.

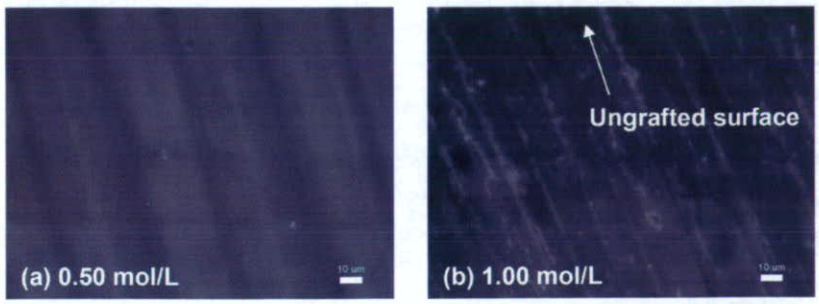

Figure 6. FM images of CLPE-*g*-MPC obtained with various MPC concentrations and a 90-min photo-irradiation time. Bar; 10 μm. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.] AQ2

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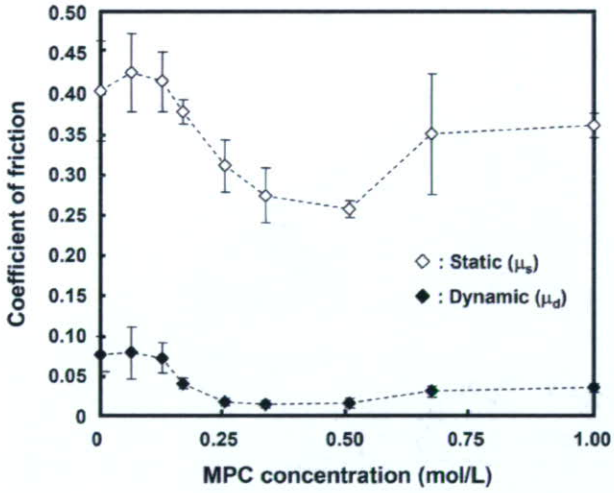

Figure 7. Coefficients of friction of the CLPE-*g*-MPC surface as a function of MPC concentration with a 90-min photo-irradiation time.

The dynamic coefficient of friction tended to increase with the contact angle. This increase was linear to a degree of accuracy, and the correlation coefficient was 0.920.

F9 Figure 9 shows the gravimetric wear of the untreated CLPE and CLPE-*g*-MPC cups in the hip simulator wear test obtained with 0.50 and 1.00 mol/L MPC concentrations and a 90-min photo-irradiation time. It was observed that wear was significantly lower in the CLPE-*g*-MPC cups than in the untreated CLPE cups. There was no significant difference in wear of the CLPE-*g*-MPC cups obtained with 0.25 and 0.50 mol/L MPC concentrations. The CLPE-*g*-MPC cups exhibited a slight increase in weight. This was partially attributable to enhanced fluid absorption in the tested cups than in the load-soak controls. When using the gravimetric method, the weight loss in the tested cups is corrected by subtracting the weight gain in the load-soak controls; however, this correction can not be perfectly achieved because only the tested cups are continuously subjected to motion and load. Fluid absorption in the tested cups is generally slightly higher than that in the load-soak controls. Consequently, the correction for fluid absorption by using the load-soak data as the correction factor leads to a slight underestimation of the actual weight loss.[12,33] In this study, a steady wear rate was calculated using data from 4.0×10^6 to 5.0×10^6 cycles; this value was 5.11 mg/10^6 cycles in the untreated CLPE cups. In contrast, the wear rates of the CLPE-*g*-MPC cups with 0.25 and 0.50 mol/L MPC concentrations were markedly lower, that is, 0.12 and 0.32 mg/10^6 cycles, respectively.

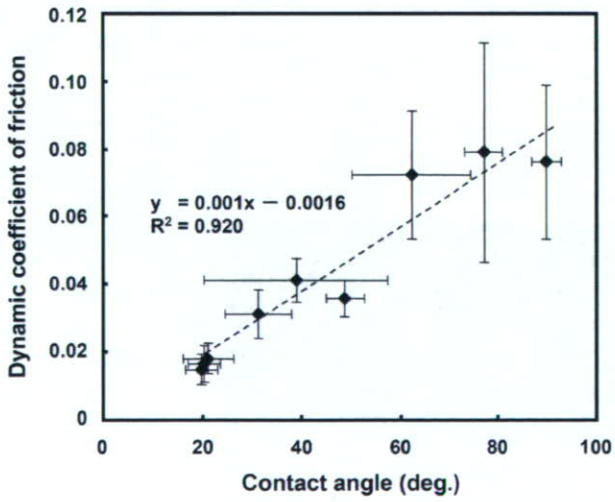

Figure 8. Relationship between dynamic coefficient of friction and contact angle in the CLPE-*g*-MPC surface. Bar; Standard deviations.

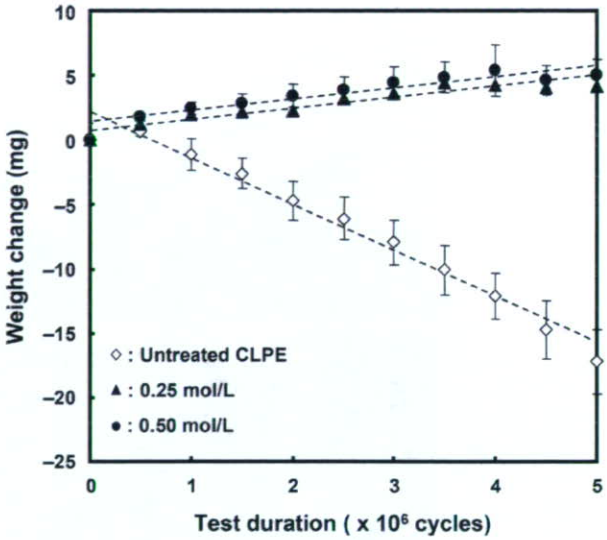

Figure 9. Weight change of the CLPE-*g*-MPC cups obtained with various MPC concentrations and a 90-min photo-irradiation in the hip joint simulator wear test. Bar; Standard deviations.

DISCUSSION

In this study, we investigated the properties of the poly(MPC) layer formed on the CLPE surface with various MPC concentrations by using photo-induced radical graft polymerization. The wear resistant properties of CLPE-*g*-MPC in terms of the characteristics of the nanometer-scale layer of poly(MPC) will be discussed hereafter.

In Figure 2, both the N and P content in the CLPE-*g*-MPC surface attributed to poly(MPC) increased to

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5.2 with an increase in the MPC concentration during polymerization. In addition, in the TEM images shown in Figure 5, the thickness of the poly(MPC) layer increased with the MPC concentration. When the poly(MPC) layer has a brush-like structure, the layer thickness may correlate with the molecular weight of the grafted poly(MPC). The high-density poly(MPC) graft chains in the CLPE-*g*-MPC, are assumed to exhibit a brush-like structure.[34,35] It is generally well known that the reaction rate of radical polymerization is extremely high.[36] In this study, the length (molecular weight) of the poly(MPC) graft chains was assumed to be successfully controlled by the MPC concentration used for polymerization. This indicates that the length of the poly(MPC) chain grafted on the CLPE surface increased with the MPC concentration during polymerization.[37] The molecular weight of the grafted poly(MPC) chain on the CLPE-*g*-MPC surface could not be determined due to the difficulty in separating the grafted poly(MPC) chain from the CLPE substrate. Additional efforts are needed in this aspect.

In the TEM observation, the thickest poly(MPC) layer (200–250 nm) was observed on the CLPE-*g*-MPC surface with a 1.00 mol/L MPC concentration [Fig. 5(d)]. However, the N and P content in the CLPE-*g*-MPC surface decreased at MPC concentrations above 0.67 mol/L (Fig. 2). On the CLPE-*g*-MPC surface with a 1.00 mol/L MPC concentration, an ungrafted (unstained) CLPE region was observed in the FM image [Fig. 6(b)]. The present graft polymerization reaction with free radicals is photo-induced by ultraviolet-ray irradiation using benzophenone as a radical initiator. On the contrary, a certain amount of ultraviolet-ray irradiation energy can directly produce free radicals form the methacryl acid group of the MPC unit in the monomer solution. When the MPC concentration in a feed is high, graft polymerization between the radicals on the CLPE surface and the MPC monomer and homopolymerization of MPC occurs simultaneously in the reaction system. The free radicals not only facilitate direct grafting of MPC to CLPE, thereby forming C—C covalent bonds between the MPC polymer and the CLPE substrate, but also induce homopolymerization of MPC as a free polymer in the solution. Moreover, the diffusion of the monomer might be interfered in the polymer solution with high concentration because of high viscosity. When the monomer and initiator attached to the CLPE surface were subjected to ultraviolet-ray irradiation, radicals were freely formed on the CLPE surface in the early stage but not in the late stage of polymerization, probably because the increased polymer radicals and/or grown grafted polymer chains blocked the diffusion of the radicals to the CLPE surface.[38] Therefore, it is supposed that the ungrafted bare CLPE surface appeared due to a decrease in the MPC concentration during graft polymerization and homopolymerization.

When the photo-irradiation time was fixed (90 min in the present study), the grafting efficiency (N and P content) of the CLPE-*g*-MPC surface increased with the MPC concentration up to 0.50 mol/L and then decreased at concentration above 0.67 mol/L. It is assumed that when the monomer concentrations in a feed is low (0–0.50 mol/L), the rate of MPC homopolymerization is higher than that of MPC graft polymerization. In contrast, when the monomer concentrations in a feed is high (>0.67 mol/L), the rate of MPC graft polymerization might be higher than that of MPC homopolymerization. Moreover, while the rate of MPC graft polymerization increases with the MPC concentration, the entire polymerization system begins to show gelation at MPC concentrations above 0.67 mol/L and the grafting efficiency might drastically decrease. In Figure 1, when the photo-irradiation time was greater than 45 min, the P concentration in CLPE-*g*-MPC became constant at high values for all the MPC concentrations. It has been reported that the photo-irradiation time must be controlled to obtain a high-density poly(MPC) layer.[12] The density of the poly(MPC) chains on the CLPE surface gradually increased with the photo-irradiation time and the entire CLPE surface was grafted with a photo-irradiation time greater than 45 min (approximately 90 min in the present study). From the above results, it is clear that to achieve high grafting efficiency for CLPE-*g*-MPC, it is essential to use a long photo-irradiation time in the polymerization system, which contains a high-concentration monomer without gelation.

In our previous studies, the mechanism of wear reduction has been reported.[10–13] Since MPC is a highly hydrophilic compound, poly(MPC) is water-soluble. The water-wettability of the CLPE-*g*-MPC surface is considerably greater than that of the untreated CLPE surface. Kobayashi et al. reported that the water molecules adsorbed on the surface of the highly hydrophilic poly(MPC) brushes act as a lubricants and reduce the interaction between the brushes and the counter-bearing face.[39] Therefore, the artificial hip joint bearing with the grafted poly(MPC) surface exhibits considerably greater lubricity than that without the poly(MPC) surface. In Figure 8, we observed that water-wettability (static water-contact angle) corresponded with the dynamic coefficient of friction. The significant reduction in the coefficient of friction of the grafted poly(MPC) surface resulted in a substantial improvement in wear resistance.[10,40] Fluid-film lubrication (or mixed lubrication) of the artificial hip joint bearing with the grafted poly(MPC) surface was achieved by the intermediate hydrated layer. It can be affirmed that this novel artificial hip joint utilizing poly(MPC) mimics the natural joint cartilage. The fluid (water)-film forming ability of a

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10-nm-thick poly(MPC) layer is equivalent to that of a micrometer-order-thick poly(MPC) layer because the outermost poly(MPC) layer determines this ability. The hip joint simulator wear test confirmed that the wear rate was much lower in the CLPE-*g*-MPC cups than in the untreated CLPE cups (Fig. 9). The water-wettability of the CLPE-*g*-MPC surface was greater than that of the untreated CLPE surface because of the presence of a poly(MPC) nanometer-scale layer. At an MPC concentration of 0.25 mol/L, the orthopaedic bearing with the CLPE-*g*-MPC surface exhibited high lubricity because the poly(MPC) layer supported a thin film of water on its surface even at a thickness of 10 nm. Consequently, the 10-nm-thick poly(MPC) layer was responsible for the improved wear resistance, which is independent of its thickness. When the CLPE surface is modified by poly(MPC) grafting, the MPC graft polymer causes a significant reduction in sliding friction between the graft surfaces because the water thin films that are formed act as extremely efficient lubricants. The water-lubrication systems utilizing poly(MPC) suppress direct contact of the counter-bearing face with the CLPE substrate in order to reduce the frictional force.[39,41] Thus nanometer-scale modifications of CLPE with poly(MPC) is expected to significantly increase the durability of the orthopaedic bearings. Poly(MPC) grafting obtained with an MPC concentration of 0.50 mol/L is particularly effective in maintaining the wear resistance of CLPE-g-MPC for use as an orthopedic bearing material over a long time periods.[11]

CONCLUSION

The effect of MPC concentration on photo-induced radical graft polymerization was examined, and the resultant properties of CLPE-*g*-MPC were discussed with respect to the characteristics of the poly(MPC) nanometer-scale layer. The thickness of the grafted poly(MPC) layer increased with the MPC concentration in the feed. The hip joint simulator wear test confirmed that the wear rate of the CLPE-*g*-MPC cups was considerably lower than that of the untreated CLPE cups. Since MPC is a highly hydrophilic compound, the water-wettability of the CLPE-*g*-MPC surface was greater than that of the untreated CLPE surface due to the formation of a poly(MPC) nanometer-scale layer. The CLPE-*g*-MPC orthopaedic bearing surface exhibited high lubricity by poly(MPC) layer even 10-nm thick. This layer is considered responsible for the improved wear resistance. Nanometer-scale modification of CLPE with poly(MPC) is expected to significantly increase the durability of the orthopaedic bearings. It is necessary to use a long photo-irradiation time in the polymerization system, which contains a high-concentration monomer without gelation, to attain such a nanometer scale modification with poly(MPC).

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Effects of mobility/immobility of surface modification by 2-methacryloyloxyethyl phosphorylcholine polymer on the durability of polyethylene for artificial joints

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Effects of mobility/immobility of surface modification by 2-methacryloyloxyethyl phosphorylcholine polymer on the durability of polyethylene for artificial joints

Running title: Effects of structure of MPC polymer on durability of PE

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ABSTRACT

Surface modification is important for the improvement in medical device materials. 2-Methacryloyloxyethyl phosphorylcholine (MPC) polymers have attracted considerable attention as surface modifiable polymers for several medical devices. In this study, we hypothesize that the structure of the surface modification layers might affect the long-term stability, hydration kinetics, wear resistance, etc., of medical devices such as artificial joints, and the poly(MPC) (PMPC) grafted surface might assure the long-term performance of such devices. Therefore, we investigate the surface properties of various surface modifications by using dip coatings of MPC-*co*-*n*-butyl methacrylate (PMB30) and MPC-*co*-3-methacryloxypropyl trimethoxysilane (PMSi90) polymers, or photoinduced radical grafting of PMPC and also the effects of the surface properties on the durability of cross-linked polyethylene (CLPE) for artificial joints. The PMPC grafted CLPE has an extremely low and stable coefficient of dynamic friction and volumetric wear as compared to the untreated CLPE, PMB30 coated CLPE, and PMSi90 coated CLPE. It is concluded that the photoinduced radical graft polymerization of MPC is the best method to retain the benefits of the MPC polymer used in artificial joints under variable and multidirectional loads for long periods with strong bonding between the MPC polymer and the CLPE surface and also to retain the high mobility of the MPC polymer.

Key words: joint replacement; polyethylene; phosphorylcholine; surface modification; wear mechanism

INTRODUCTION

Polymeric biomaterials are widely used in the biomedical field for manufacturing artificial organs, medical devices, and disposable clinical apparatus.[1,2] Advancements in the biomedical field also demand substantial improvements in polymeric biomaterials. Conventional single-component polymer biomaterials cannot satisfy these requirements. Multicomponent polymer systems have therefore been designed and prepared for new multifunctional biomaterials.

Surface modification is one of the important means of preparing new multifunctional biomaterials. 2-methacryloyloxyethyl phosphorylcholine (MPC) polymers have attracted considerable attention as surface modifiable polymers for several medical devices.[3–11] MPC, a methacrylate with a phospholipid polar group in the side chain, is a monomer for preparing novel polymer biomaterials. An excellent synthetic route for MPC has been developed by Ishihara *et al.*[12] MPC can undergo conventional radical copolymerization with other methacrylate and styrene derivatives such as *n*-butyl methacrylate (BMA), *n*-dodecyl methacrylate (DMA), and 3-methacryloxypropyl trimethoxysilane (MPSi) to form poly(MPC-*co*-BMA), poly(MPC-*co*-DMA), and poly(MPC-*co*-MPSi), respectively.[5–11] These MPC polymers are some of the most common biocompatible and hydrophilic polymers studied thus far. They have potential applications in a variety of fields such as biology, biomedical science, and surface chemistry because they possess unique properties such as good biocompatibility, high lubricity and low friction, anti-protein adsorption, and cell membrane-like surfaces. Several medical devices have already been developed by utilizing the MPC polymers and used clinically; therefore, the efficacy and safety of the MPC polymers as biomaterials are well established.[9–11]

When a natural joint in the human body ceases to function, for example, due to disease, trauma, or overuse, an artificial joint replacement often becomes necessary. There is a substantial increase in the number of artificial hip and knee joints used worldwide each year for primary and revised hip and knee joint replacements.[13] This indicates that a higher quality and longer lifetime have been increasingly desired for artificial joint replacements. Normally, artificial joints allow the body to regain mechanical

and biological functions. Medical implants must be adapted to the dynamic loads experienced during use, and they must have the desired long-term biological interaction with the surrounding tissue. A typical artificial joint replacement system used as a medical device comprises a metallic surface made of a cobalt-chromium-molybdenum (Co-Cr-Mo) alloy that articulates against an ultra-high molecular weight polyethylene (UHMWPE) polymeric component. However, the artificial joint replacements are subjected to adhesive and abrasive wear and both metallic and polymeric debris. These are known to produce a variety of cytokines and tumor necrosis factors that progressively resorb the bone by osteolysis, leading to aseptic loosening of the artificial joint after a number of years, which is recognized as a serious problem.[14,15] Different combinations of bearing surfaces and improvements in bearing materials have been studied with the aim of reducing the number of UHMWPE wear debris that induce osteolysis.[16–18]

Recently, we have developed an artificial hip joint by using poly(MPC) (PMPC) grafted onto the surface of cross-linked polyethylene (CLPE; PMPC grafted CLPE); this device is designed to reduce wear and suppress bone resorption.[19–24] MPC has also been directly grafted from biomaterial surfaces through photoinduced radical polymerization.[25,26] This photoinduced radical polymerization facilitates the direct grafting of MPC onto biomaterial surfaces. The following are the expected advantages of this technique: (1) controllable graft polymer density and length and grafting site,[21,24] (2) covalent bonding between the graft polymer and biomaterial surfaces (as high immobility), which assures the long-term stability of graft chains, (3) high mobility of the graft polymer chain and/or free end groups of the polymer, and (4) occurrence of grafting only on the surface, and no effect of grafting on the bulk properties.[22] In particular, strong bonding between the surface modification and the surface is an important issue, which is associated with the long-term retention of the benefits of the surface modification used in artificial joints under variable and multidirectional loads, for a promising long-term performance of artificial joints.

In this study, we hypothesize that the structure of surface modification layers might affect the surface density of the phosphorylcholine group, long-term stability and mobility of the polymer chain, hydration kinetics, etc., and the PMPC grafted surface might assure the long-term performance of artificial joints.

Therefore, we investigate the surface properties of various surface modification layers with the MPC polymer and the effects of the surface properties on the durability of the CLPE for artificial joints. The results reveal that the structure of the PMPC grafted layer on the CLPE surface plays an important role in reducing the wear of the orthopaedic bearing surface in the long term.

MATERIALS AND METHODS

Materials

MPC was industrially synthesized using a previously reported method.[12] Poly(MPC-*co*-BMA) (PMB30; MPC:BMA unit mole fraction = 0.3:0.7)[12] and poly(MPC-*co*-MPSi) (PMSi90; MPC:MPSi unit mole fraction = 0.9:0.1)[8] were synthesized in ethanol using 2,2'-azobisisobutyronitrile as initiator by a conventional radical copolymerization method. A compression-molded UHMWPE (GUR1020 resin; Poly Hi Solidur Inc., IN, USA) sheet stock was irradiated with 50 kGy gamma-rays in N_2 gas and annealed at 120°C for 7.5 h in N_2 gas in order to achieve cross-linking. The CLPE specimens were machined from this sheet stock after cooling.

MPC polymer coating

The preparation of the MPC polymer coated CLPE is schematically illustrated in Fig. 1. The physical coating of PMB30 was carried out by the solvent evaporation method, where the CLPE specimens were dipped into ethanol solution containing 0.2 mass% PMB30 for 10 s for coating and then placed in an ethanol vapor atmosphere at room temperature for 1 h. The coated CLPE specimens were again dipped for 10 s and place in the ethanol vapor atmosphere at room temperature for 1 h (PMB30 coated CLPE).

The chemical coating of PMSi90 was also carried out by the solvent evaporation method. Before the PMSi90 coating, the CLPE specimens were irradiated with O_2 plasma at a 200 W high-frequency output and 150 mL/min O_2 gas flow for 2 min by using an O_2 plasma etcher (PR500, Yamato Scientific Co., Ltd., Tokyo, Japan). The O_2 plasma irradiation formed the surface hydroxide layer. The CLPE specimens

were dipped into ethanol solution containing 0.5 mass% PMSi90 and 0.063 mg/mL succinic acid (Kanto Chemical Co., Inc., Tokyo, Japan) for 10 s for the silanization of trimethoxysilane group of PMSi90 and place in the ethanol vapor atmosphere at room temperature for 1 h. The coated CLPE specimens were annealed in air at 70°C for 3 h for dehydration (PMSi90 coated CLPE). These PMB30 and PMSi90 coated CLPE specimens were then sterilized by 25 kGy gamma-rays in N_2 gas.

MPC graft polymerization

The preparation of the PMPC grafted CLPE is schematically illustrated in Fig. 1. The CLPE specimens were immersed in acetone (Wako Pure Chemical Industries, Ltd., Osaka, Japan) solution containing 10 mg/mL benzophenone (Wako Pure Chemical Industries, Ltd.) for 30 s and then dried in the dark at room temperature in order to remove the acetone. In previous studies, using ultraviolet spectroscopy, the amount of benzophenone adsorbed on the surface was reported to be 3.5×10^{-11} mol/cm^2.[3] MPC was dissolved in degassed pure water to obtain a concentration of 0.5 mol/L. Subsequently, the benzophenone coated CLPE specimens were immersed in the aqueous MPC solutions. Photoinduced graft polymerization was carried out on the CLPE surface using ultraviolet irradiation (UVL-400HA ultra-high pressure mercury lamp; Riko-Kagaku Sangyo Co., Ltd., Funabashi, Japan) with an intensity of 5 mW/cm^2 at 60°C for 90 min; a filter (model D-35; Toshiba Corp., Tokyo, Japan) was used to restrict the passage of ultraviolet light to wavelengths of 350 ± 50 nm. After the polymerization, the PMPC grafted CLPE specimens were removed, washed with pure water and ethanol, and dried at room temperature. These specimens were then sterilized by 25 kGy gamma-rays in N_2 gas.

Surface analysis

The functional group vibrations of the untreated CLPE, PMB30 coated CLPE, PMSi90 coated CLPE, and PMPC grafted CLPE surfaces were examined using attenuated total reflection (ATR) by Fourier transform infrared (FT-IR) spectroscopy. The FT-IR/ATR spectra were obtained in 32 scans over a range