

Figure 1. Chemical reaction on Co-Cr-Mo during polymerization of MPC.

MATERIALS AND METHODS

Chemicals

MPC was synthesized industrially by using the method developed by Ishihara et al.,²² and it was supplied by NOF Corp. (Tokyo, Japan). MPSi was purchased from Shin-Etsu Chemical Co., Ltd. (Tokyo, Japan). Succinic acid and ethanol were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan). 2-Hydroxy-1-[4-(hydroxyethoxy)phenyl]-2-methyl-propanone (DAROCUR[®] 2959; D2959) was purchased from Ciba Specialty Chemicals Holding Inc. (Basel, Switzerland). D2959 is a highly efficient radical photoinitiator for ultraviolet (UV) curing of the systems containing unsaturated monomers and prepolymers, and it is particularly well known as a cytocompatible UV photoinitiator with UV intensities of $<6 \text{ mW/cm}^2$ that can perform polymerization for up to 10 min with a UV light of 365 nm.³⁹

Co-Cr-Mo alloy substrate and pretreatments

The Co-Cr-Mo alloy was supplied by Yoneda Advanced Casting Co., Ltd (Takaoka, Japan). This alloy was manufactured according to the ASTM F75 standard specification for Co-28Cr-6Mo alloy.⁴⁰ The Co-Cr-Mo samples were polished so that the average surface roughness ranged between 0.01 and 0.02 μm .

The polished Co-Cr-Mo samples were washed with acetone and then immersed in 35 vol % nitric acid at room temperature for 35 min according to the ASTM F86-04 standard.^{36,41} This treatment results in passivation by surface oxidation, and it could lead to the dissolution of certain foreign materials that may remain from the previous procedure. Moreover, a previous study reported that the surface of as-polished Co-Cr-Mo alloy might lack the Cr content that the bulk possesses, and that surface etching

by nitric acid treatment would have produced a Cr-rich surface layer.³⁶ We therefore treated the surface with nitric acid with the aim of increasing the Cr concentration by "resurfacing."

After the nitric acid treatment, the Co-Cr-Mo samples were irradiated with O_2 plasma at a 500-W high-frequency output and 150-mL/min O_2 gas flow for 5 min by using an O_2 plasma etcher (PR500, Yamato Scientific Co., Ltd., Tokyo, Japan). The O_2 plasma treatment increased the thickness of the surface oxide layer.⁴²

MPSi silanization and MPC graft polymerization

The synthesis of Co-Cr-Mo-g-MPC is schematically illustrated in Figure 1. The pretreated Co-Cr-Mo samples were immersed in an ethanol solution containing 5 mass % MPSi, 1 mass % succinic acid, and 0.1 mass % D2959 at room temperature for 12 h for silanization of the trimethoxysilane group. In this study, D2959 was used as a photoinitiator for surface-initiated polymerization so as to be included in the MPSi layer. Generally, for surface-initiated polymerization, such an initiator covalently bonded to the substrate to yield a "grafting from" polymerization is usually used. They were then annealed at 70°C for 3 h in air for dehydration. The MPC was dissolved in degassed pure water to attain concentrations ranging from 0.25 to 1.00 mol/L. Subsequently, the MPSi (containing D2959)-coated Co-Cr-Mo samples were immersed in aqueous MPC solutions. Photoinduced graft polymerization on the Co-Cr-Mo surface was performed 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 23–180 min; a filter (Model D-35; Toshiba Corp., Tokyo, Japan) was used restrict the passage of ultraviolet light to wavelengths of $350 \pm 50 \text{ nm}$. After the polymerization, the Co-Cr-Mo-g-MPC samples were removed from the solution, washed with pure water and

ethanol, and dried at room temperature. For purification, washing with pure water and ethanol enables the removal of the free poly(MPC) and/or poly(MPC-co-MPSi) adsorbed on the Co-Cr-Mo surface.⁴³

MPC graft polymerization on crosslinked polyethylene

Compression-molded UHMWPE (GUR1020 resin, Poly Hi Solidur Inc., IN) bar stock was gamma-ray irradiated at 50 kGy in N₂ gas and annealed at 120°C in N₂ gas for crosslinking. After cooling, the crosslinked polyethylene (CLPE) specimens were machined from this bar stock.

MPC grafting onto the CLPE surface was performed as described in previous studies.⁴³⁻⁴⁵ The CLPE 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 the acetone. MPC was dissolved in degassed pure water to a concentration of 0.5 mol/L. The benzophenone-coated CLPE samples were immersed in the aqueous MPC solution. Photoinduced graft polymerization on the CLPE surface was carried out using UV irradiation with an intensity of 5 mW/cm² at 60°C for 90 min. After the polymerization, the CLPE-g-MPC samples were removed from the solution, washed with pure water and ethanol, and dried.

Articular cartilage from porcine ankle joint

Using a surgical hand corer or surgical saw, articular cartilage specimens were harvested from the flat part of the ankle joint of the fresh frozen porcine tibia (ages 6-9 months) for friction test. Pin-type articular cartilage specimens were shaped as cylinders with a height of 5 mm and diameter of 9 mm, and they had ~1 mm of cartilage layer and subcondral bone used for mounting. Throughout the procedure, the articular cartilage surface was hydrated regularly with Dulbecco's phosphate-buffered saline (PBS, pH 7.4, ion strength = 0.15 M; Immuno-Biological Laboratories Co., Ltd., Takasaki, Japan). All the articular cartilage specimens were then stored in Dulbecco's PBS and frozen at -80°C.⁴⁶

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

The functional group vibrations of the Co-Cr-Mo alloy surfaces before and after the MPC grafting were examined by Fourier-transform infrared (FTIR) spectroscopy with attenuated total reflection (ATR) equipment. The FTIR/ATR spectra were obtained using an FTIR analyzer (FT/IR615, JASCO Co. Ltd., Tokyo, Japan) for 32 scans (1.2 s/scan) over the range of 800-2000 cm⁻¹ at a resolution of 4.0 cm⁻¹.

The surface elemental conditions of the Co-Cr-Mo alloy before and after the MPC grafting were analyzed by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS-HSi165, Kratos/Shimadzu Corp., Kyoto, Japan) equipped with a 15-kV MgK α radiation source at the anode. The take-off angle of the photoelectrons was maintained at 90°. Five

scans (~260 to 425 s/scan depending on the atomic signal strength) were taken for each sample.

The static-water contact angles on the Co-Cr-Mo surfaces that were subjected to different types of pretreatments before and after the MPC grafting were measured by the sessile drop method using an optical bench-type contact angle goniometer (Model DM300, Kyowa Interface Science Co., Ltd., Saitama, Japan). Drops of purified water (1 μ L) were deposited on the Co-Cr-Mo-g-MPC surface, and the contact angles were directly measured with a microscope after 60 s of dropping, according to the ISO 15989 standard.⁴⁷ Measurements were repeated six times for each sample, and the average values were considered as the contact angles.

Cross-sectional observation by transmission electron microscopy

A crosssection of the poly(MPC) layer on the Co-Cr-Mo surface was observed using a transmission electron microscope (TEM) and by energy dispersive X-ray (EDX) spectroscopy. The specimens were precoated with an aluminum film using a focused ion beam (FIB) system to prevent charging. After precoating, a thin film of the samples was prepared by the FIB technique using an FB-2000A (Hitachi High-Technologies Co., Tokyo, Japan) FIB system. The samples were thinned to electron transparency by a low gallium ion beam current. The thin film thus prepared was positioned onto a copper TEM mesh grid. TEM observations were then recorded using an HF-2000 electron microscope (Hitachi High-Technologies Co.) at an acceleration voltage of 200 kV. EDX spectra were analyzed on a crosssection of the untreated Co-Cr-Mo sample and the Co-Cr-Mo-g-MPC sample obtained with 0.50 mol/L MPC concentrations and a 90-min photoirradiation time using a Sigma EDX attachment (KeveX Instruments, Inc., Valencia, CA) at an acceleration voltage of 200 kV. The probe size of the electron beam was maintained at 1 nm.

Friction test

The coefficients of dynamic friction between the pins fabricated from various materials (Co-Cr-Mo, CLPE, CLPE-g-MPC, and articular cartilage) and the untreated Co-Cr-Mo or Co-Cr-Mo-g-MPC (obtained with 0.50 mol/L MPC concentrations and a 90-min photoirradiation time) plates were measured using a pin-on-plate machine (Tribostation 32; Shinto Scientific Co., Ltd., Tokyo, Japan) as the preliminary test for tribological properties. Each pin was a cylinder measuring 5 mm in height and 9 mm in diameter and used to prepare five sample pieces. 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.⁴⁸ Pure water was used as a lubricant. The mean coefficients of dynamic friction were determined by averaging five data points from the 100 (96-100) cycle measurements. Standard analysis of variance (ANOVA) was applied to the data of the (at 100 cycles) existed among the eight groups (Co-Cr-Mo, CLPE, CLPE-g-MPC, Cartilage pins against untreated Co-Cr-Mo and Co-Cr-Mo-

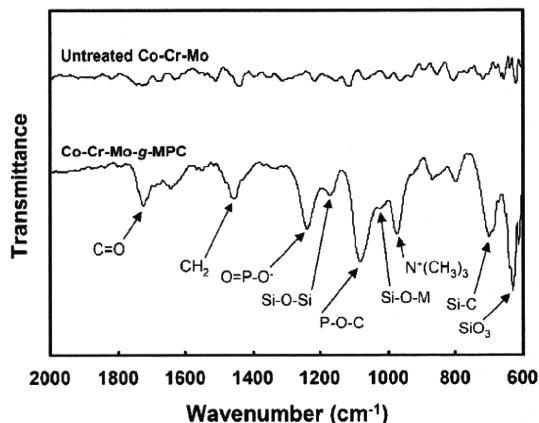


Figure 2. FTIR/ATR spectra of untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC surfaces with a 0.50-mol/L MPC concentration and a 90-min photoirradiation time.

g-MPC plates, respectively), in this study. Two combinations (e.g., Co-Cr-Mo pin against untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC plates, Co-Cr-Mo and CLPE pins against Co-Cr-Mo-g-MPC plate) were especially made with the Student's *t* test ($p < 0.05$).

RESULTS

Figure 2 shows the FTIR/ATR spectra of the Co-Cr-Mo sample and that of photoirradiated grafting of MPC under 0.50-mol/L MPC concentration and 90-min photoirradiation time. Absorption peaks were not observed for the Co-Cr-Mo sample before the MPC graft polymerization in the wavenumber

range of 800–2000 cm^{-1} . In contrast, absorption peaks were newly observed only for the Co-Cr-Mo-g-MPC samples. The peaks at 1720, 1550, and 1460 cm^{-1} are attributed to C=O and $-\text{CH}_2-$ in the MPSi and poly(MPC) graft chains. The peaks at 1180, 1040, 700, and 630 cm^{-1} are attributed to the trimethoxysilane group in the MPSi unit.⁴⁹ The peaks at 1240, 1080, and 970 cm^{-1} are attributed to the $-\text{N}^+(\text{CH}_3)_3$ and phosphate groups in the MPC unit.⁴⁴

In the XPS spectra of the binding energy region of the nitrogen (N_{1s}), phosphorous (P_{2p}), and silicon (Si_{2p}) electrons, peaks appeared in the case of Co-Cr-Mo-g-MPC; however, they were not observed in the case of Co-Cr-Mo (Fig. 3). The peak at 104 eV was attributed to the Si_2O_3 or SiO_2 in the trimethoxysilane group in the MPSi unit. The peaks at 403 and 134 eV were attributed to the $-\text{N}^+(\text{CH}_3)_3$ and phosphate groups, respectively. These peaks reflect the phosphorylcholine present in the MPC units. Figure 4 shows the Si, N, and P concentrations of the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time during polymerization for various MPC concentrations in feeds. Both the N and P concentrations in the Co-Cr-Mo-g-MPC surface increased with the photoirradiation time. In the case of higher MPC concentrations, when the photoirradiation time was greater than 90 min, the N and P concentrations became almost constant above 5.0 atom%. These values were almost equivalent to the theoretical elemental composition (N = 5.3 atom%, P = 5.3 atom%) of poly(MPC). As a trade off, the Si concentration at the Co-Cr-Mo-g-MPC surface decreased with an increase in the photoirradiation time.

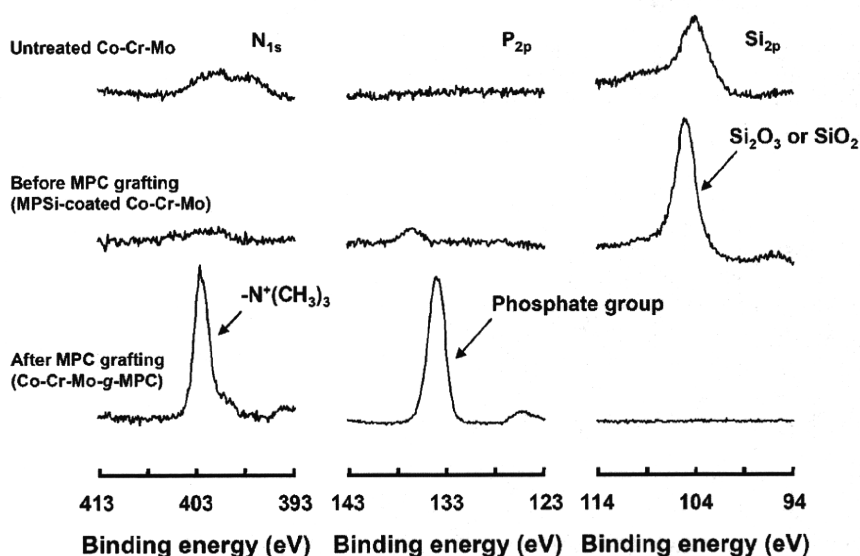


Figure 3. XPS spectra (N_{1s} , P_{2p} and Si_{2p}) of Co-Cr-Mo samples before and after the MPC grafting with a 0.50-mol/L MPC concentration and a 90-min photoirradiation time.

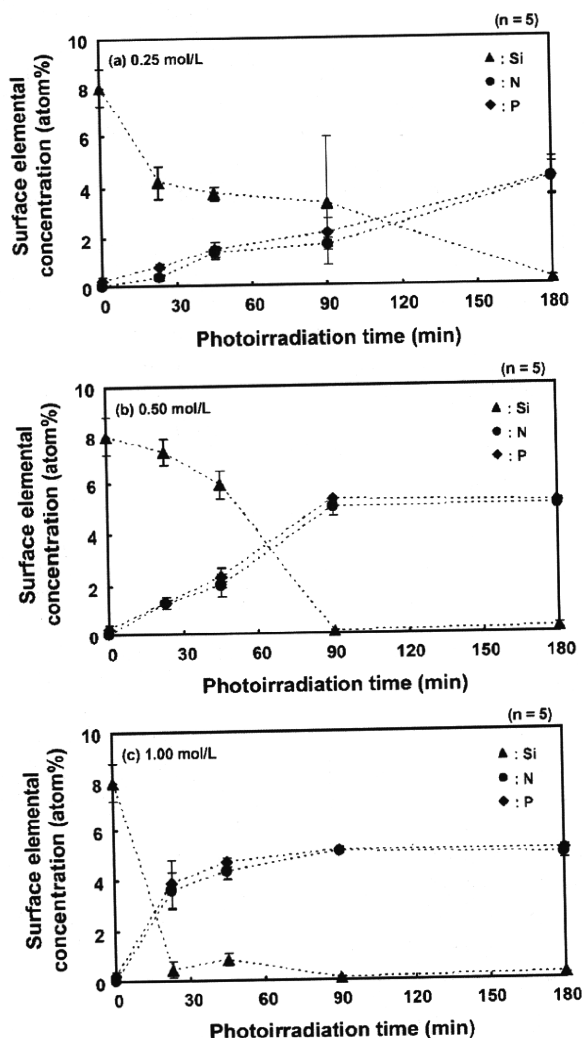


Figure 4. Surface elemental concentrations in the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time for various MPC concentrations in feeds. Bar: standard deviations.

Figure 5 shows the static-water contact angle on the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time during polymerization with various MPC concentrations in feeds. The static-water contact angle on the untreated Co-Cr-Mo surface before the MPC grafting was $\sim 80^\circ$. The static-water contact angle on the Co-Cr-Mo-g-MPC surface decreased markedly with an increase in the photoirradiation time and the MPC concentration. When the photoirradiation time and MPC concentration were greater than 90 min and 0.50 mol/L, respectively, the static-water contact angle became constant at a low value of 20° .

Figure 6 shows the cross-sectional TEM images of Co-Cr-Mo-g-MPC obtained with various MPC con-

centrations and a 90-min photoirradiation time. In the Co-Cr-Mo-g-MPC, a 10 to 360-nm thick poly (MPC) layer was clearly observed on the surface of the Co-Cr-Mo substrate. The thickness of the poly (MPC) layer increased with the MPC concentration during polymerization. At an MPC concentration of 1.00 mol/L, the thickness of the poly(MPC) layer was greatest, that is, 360 nm. These results indicate that the length of the poly(MPC) chain (thickness of the poly(MPC) layer) can be controlled by adjusting the MPC concentration during polymerization. This is explained by the fact that the length of the polymer chains produced in a radical polymerization reaction generally correlates with the MPC concentration.

Figure 7 shows the EDX spectra of the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC obtained with a 0.5-mol/L MPC concentration and a 90-min photoirradiation time. In spectra (P1) and (P3) of the substrate of the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC, strong peaks were observed at 0.8, 2.3, 5.4, 6.0, 6.9, and 7.7 keV. These peaks are attributed to the Co, Cr, and Mo atoms in the Co-Cr-Mo substrate. In spectrum (P2) of the surface of the untreated Co-Cr-Mo, a peak was observed at 0.5 keV. This peak is attributed to the O atom in the metal oxide layer of the Co-Cr-Mo. In spectrum (P4) of the intermediate layer of the Co-Cr-Mo-g-MPC, peaks were observed at 0.5 and 1.7 keV. These peaks are attributed to the O and Si atoms in the intermediate layer between the silane of the MPSi and the metal oxide of the Co-Cr-Mo. In spectra (P4) and (P5) of the intermediate layer and the poly(MPC) layer of the Co-Cr-Mo-g-MPC, a significant peak attributed to the P atom was observed at 2.0 keV. This peak is mainly attributed to the MPC units. Several spectra exhibited

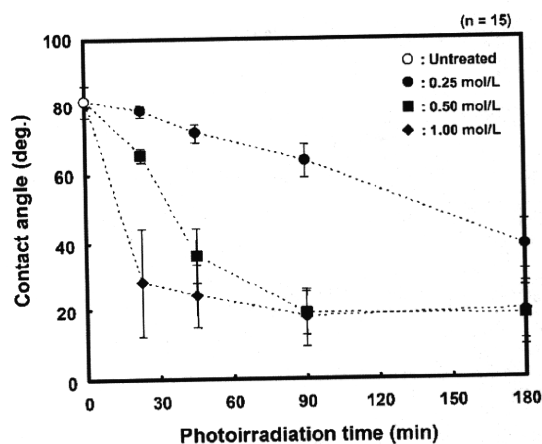


Figure 5. Static-water contact angle of the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time for various MPC concentrations in feeds. Bar: standard deviations.

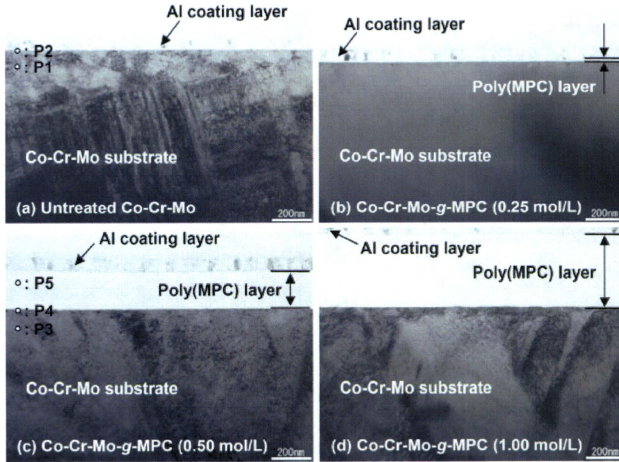


Figure 6. Cross-sectional TEM images of the Co-Cr-Mo-g-MPC surface with various MPC concentration in feeds and a 90-min photoradiation time. Aluminum coating layers (~ 70 nm) for preparation of TEM observation specimen are shown above the poly(MPC) layer of the Co-Cr-Mo-g-MPC surface. In (a) and (c), small open-circles (P1-5) indicate EDX analysis points. Bar: 200 nm.

peaks at 1.5, 8.0, and 8.9 keV. In these cases, the peaks are attributed to the Al and Cu atoms of the Aluminum coating for the preparation of the TEM observation specimen and/or the copper TEM mesh grid.

Figure 8 shows the coefficients of dynamic friction of the sliding couples, namely, untreated Co-Cr-Mo, CLPE, CLPE-g-MPC, and articular cartilage pins sliding against the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC plates. The Co-Cr-Mo/Co-Cr-Mo and CLPE/Co-Cr-Mo couples showed a high friction coefficient of ~ 0.19 and 0.14 in the initial 10 cycles; especially, the value of the Co-Cr-Mo/Co-Cr-Mo couple increased and reached ~ 0.41 in the 100 cycles ($p < 0.005$). After the friction test, some scratches parallel to the sliding direction were clearly observed in the Co-Cr-Mo/Co-Cr-Mo bearing area. The CLPE-g-MPC/Co-Cr-Mo couples showed a low friction coefficient of about 0.05 for both 10 and 100 cycles. This corresponds to $\sim 70\%$ reduction ($p < 0.001$ in both cycles) when compared with the coefficients of untreated CLPE/Co-Cr-Mo couples. The coefficients of dynamic friction of all types of pins sliding against the Co-Cr-Mo-g-MPC couples decreased drastically when compared with those of untreated Co-Cr-Mo couples. The degree of reduction in the coefficient was $\sim 90\%$ (80–99%) for both 10 and 100

cycles ($p < 0.001$ in all types of pins). In particular, in the CLPE-g-MPC/Co-Cr-Mo-g-MPC couple, the poly(MPC) layer sliding against the poly(MPC) layer showed the lowest friction coefficient of ~ 0.005 , and this value was almost steady during the experiment. The friction coefficient of the cartilage/Co-Cr-Mo couple increased gradually and reached ~ 0.09 in the 100 cycles. The friction coefficient of the cartilage/Co-Cr-Mo-g-MPC couple was ~ 0.006 in the 100 cycles, and it remained almost steady. This was much lower than the friction coefficient of the cartilage/Co-Cr-Mo couple ($p < 0.001$).

DISCUSSION

In this study, based on the hypothesis that the “grafting from” method has advantages over the “grafting to” method in that it synthesizes a uniformly and controllable polymer layer, a superlubricious Co-Cr-Mo alloy surface by poly(MPC) grafting was prepared for its application to artificial joints with the aim of reducing wear. Several important issues are involved in the long-term retention of the benefits of poly(MPC) used in artificial joints under variable and multidirectional loads: strong bonding

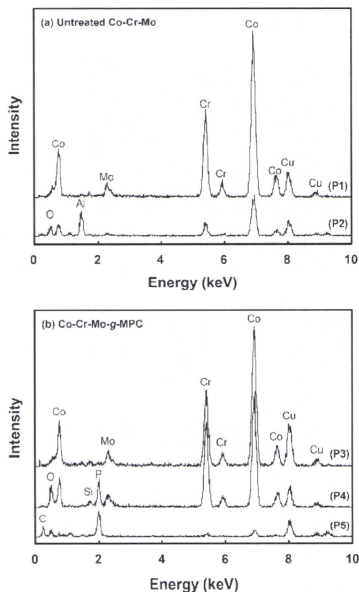


Figure 7. EDX spectra of the Co-Cr-Mo-g-MPC surface with a 0.5-mol/L MPC concentration and a 90-min photoirradiation time. The spectra were analyzed on the cross-section (P1–5) of the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC in Figure 6.

between the poly(MPC) and the Co-Cr-Mo surface, high mobility of the free end groups of the poly(MPC) layer, and a high density of the introduced poly(MPC). Taking these issues into consideration, the photoinduced radical graft polymerization technique and the MPSi intermediate layer were used to obtain covalent bonding between the Co-Cr-Mo substrate and the poly(MPC) chain via the MPSi layer.

Figure 4 shows the N and P concentrations of the Co-Cr-Mo-g-MPC surface obtained with a 0.5-mol/L MPC concentration and a 90-min photoirradiation time; the concentrations became almost constant at high values of 5.0 and 5.3 atom%, respectively. These values were almost equivalent to the theoretical elemental composition of poly(MPC). In addition, the static-water contact angle of the Co-Cr-Mo-g-MPC surface became constant at a low value of 20°, showing a highly hydrophilic nature. The peak attributed to Si atoms was observed in the intermediate layer between the poly(MPC) layer and Co-Cr-

Mo substrate only, as shown in Figure 7. Therefore, it was thought that the poly(MPC) chain was grafted and that it extended from the methacrylate on the MPSi. The hydrophilic layer was formed with the poly(MPC) chain, which attained high mobility, and the poly(MPSi) chain existed as the immobilized end-group of the poly(MPC) graft chains.

In Figure 4, both the N and P concentrations in the Co-Cr-Mo-g-MPC surface attributed to poly(MPC) increased with the MPC concentration during polymerization. In addition, in the TEM images shown in Figure 6, 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 Co-Cr-Mo-g-MPC are assumed to exhibit a brush-like structure.^{24,50} It is generally well known that the reaction rate of radical polymerization is extremely high.⁵¹ In this study, the length (molecular weight) of the poly(MPC) graft chains was successfully controlled by the MPC concentration used for polymerization as a feed solution. This indicates that the length of the poly(MPC) chain grafted on the Co-Cr-Mo surface increased with the MPC concentration in feed.⁴⁵

The previous study by the authors reported that the density of the poly(MPC) chains on the surface of the CLPE prepared by photoinduced radical polymerization gradually increased with the irradiation

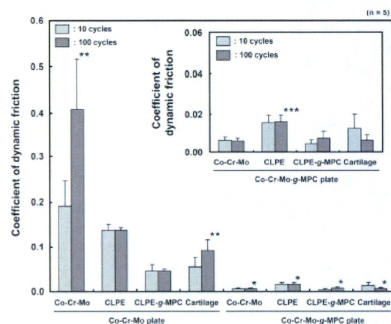


Figure 8. Coefficients of dynamic friction for the various types of pins sliding against the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC plates. Bar: standard deviations. **t* test, significant difference ($p < 0.001$) when compared with the untreated Co-Cr-Mo plate, ***t* test, significant difference ($p < 0.001$) when compared with the coefficients of dynamic friction at 10 cycles, and ****t* test, significant difference ($p < 0.001$) when compared with the Co-Cr-Mo pin against Co-Cr-Mo-g-MPC plate.

time. The study also showed that the entire surface of the CLPE was coated using polymerization times longer than 45 min with almost the same thickness as that of the poly(MPC) layer for longer irradiation times (100–200 nm).⁴⁴ In this study, both the N and P concentrations in the Co-Cr-Mo-g-MPC surface attributed to poly(MPC) increased with the photoradiation time. When the MPC concentration was greater than 0.5 mol/L, the N and P concentrations of the Co-Cr-Mo-g-MPC surface increased to ~5.3 atom%, which was almost equivalent to the theoretical elemental composition of poly(MPC). In addition, the Co-Cr-Mo-g-MPC surface obtained with a 0.5-mol/L MPC concentration and a 90-min photoradiation time retained the uniform poly(MPC) layer with a thickness of 200 nm, as reported in the previous study. These observations indicate that irradiation time control is essential to obtain a high-density poly(MPC) layer.⁴⁴

Several previous studies reported that a silane coating has a low water resistance due to hydrolysis of siloxane bond and to desorption of physisorbed silane. Zhang et al.⁵² and others^{53,54} reported that the limited stability of the Si—O—metal (M) bond against hydrolysis is the main reason for the limited stability in water, and the water stability could be improved by using several factors: (1) an induction of bridged silane coupling agents, when hydrolyzed, contain two or more —Si(OH)₃, (2) the hydrophobic alkyl moieties which limit the contact with water, and (3) a increase of thickness of surface oxide layer. Therefore, we used the MPSi intermediate layer with three methoxysilane groups and a functional methacrylate and the pretreatment (nitric acid treatment and O₂ plasma treatment) for Co-Cr-Mo surface were used.

MPSi binds to the Co-Cr-Mo substrate by a condensation reaction in two steps (Fig. 1). In the first step, the MPSi is hydrolyzed (activated), and in the second step, the hydrolyzed silane molecule binds to the surface by an Si—O—M bond, forming branched hydrophobic siloxane bonds, Si—O—Si.^{38,49} The hydrolyzed silane molecule has three —OH groups that can react with the —OH groups of the surface metallic oxide layer to form siloxane bonds covalently. The peaks at 1180 and 1040 cm⁻¹ in the FTIR/ATR spectrum of the Co-Cr-Mo-g-MPC surface were attributed to Si—O—Si and Si—O—M, respectively (Fig. 2), and these were observed after the MPC grafting. This suggests that the trimethoxysilane group of MPSi binds to the metallic oxides with a stable covalent binding even when the polymerization of MPC was carried out. This MPSi (and/or poly(MPC-co-MPSi)) layer(s) and the Co-Cr-Mo substrate might contribute to the stable polymer/metal interface.⁵⁵

The coefficients of dynamic friction of various bearing couples obtained in previous studies are

TABLE I
Coefficients of Dynamic Friction of Various Bearing Couples in Previous Studies

Bearing Couple		Friction Coefficient	Reference
Pin	Disc or Plate		
Co-Cr-Mo	Co-Cr-Mo	0.19–0.27	36, 56
UHMWPE	Co-Cr-Mo	0.05–0.13	36, 57, 58
CLPE-g-MPC	MPC "grafted to" Co-Cr-Mo	0.07–0.13	36
Cartilage	Stainless steel	0.01–0.05	61
Cartilage	Cartilage	0.02	62

summarized in Table I. In Figure 8, the Co-Cr-Mo/Co-Cr-Mo couple shows a friction coefficient of ~0.19, which is as high as that described in previous studies.^{36,56} The CLPE/Co-Cr-Mo couple also shows a friction coefficient of ~0.14, as high as that described in previous studies.^{36,57,58} In contrast, the Co-Cr-Mo-g-MPC surface with respect to each material shows an extremely low friction coefficient when compared with that of the untreated Co-Cr-Mo surface. As MPC is highly hydrophilic and poly(MPC) is water soluble, the water contact angle of the Co-Cr-Mo-g-MPC surface was lower than that of the untreated Co-Cr-Mo surface, as shown in Figure 5. Consequently, the grafted poly(MPC) layer successfully provided high lubricity in the form of "surface gel hydration lubrication" to the Co-Cr-Mo surface (Fig. 8).⁵⁹

Various factors such as the type of bearing material, surface roughness, homogeneity of the surface, and chemical composition affect the lubricity of artificial joints.⁶⁰ In Figure 8, the friction coefficient of the CLPE/Co-Cr-Mo-g-MPC couple was greater than that of Co-Cr-Mo/Co-Cr-Mo-g-MPC couple ($p < 0.001$ in both 10 and 100 cycles). The significant difference for the friction coefficient of those bearing couples was probably attributed to a surface roughness of bearing pin: although the bearing surface of Co-Cr-Mo pins was polished so that the average surface roughness (R_a) was ~0.01 μm , the bearing surface of CLPE pins was only machine-finished so that the R_a was ~20 μm . These bearing surfaces were actually comparable with those of femoral ball and acetabular cup products, respectively. However, if the bearing surface of CLPE pins was polished or direct molded like that of Co-Cr-Mo pins, the friction coefficient of the CLPE/Co-Cr-Mo-g-MPC couple would be similar to that of Co-Cr-Mo/Co-Cr-Mo-g-MPC couple.

In the case of Co-Cr-Mo-g-MPC, the lubricity changes depending on the ambient *in vitro* and *in vivo* conditions. The previous study reported that the hydrogel cartilage surface is assumed to have a brush-like structure: a part of the proteoglycan ag-

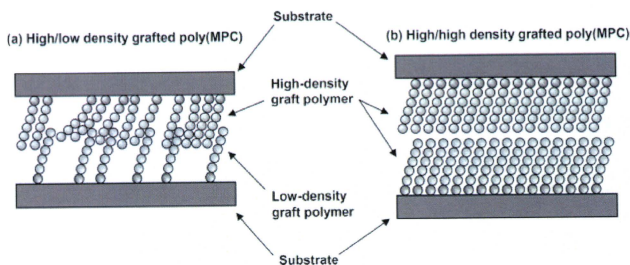


Figure 9. Hypothetical cartoons of high-density grafted poly(MPC)/low-density grafted poly(MPC) and high-density grafted poly(MPC)/high-density grafted poly(MPC) bearing interfaces.

gregate brush is bonded with the collagen network on the cartilage surface.⁵⁹ The bearing surface with poly(MPC) in artificial hip joints is assumed to have a brush-like structure similar to that of articular cartilage. CLPE-g-MPC/Co-Cr-Mo-g-MPC or cartilage/Co-Cr-Mo-g-MPC bearing couples can therefore be regarded to mimic the natural joint cartilage *in vivo*. The friction coefficient of cartilage/stainless steel (SUS) pin-on-plate ranges from 0.01 to 0.05,⁶¹ and that of cartilage/cartilage pin-on-plate is 0.02,⁶² as shown in Table I. In this study, it was found that CLPE-g-MPC/Co-Cr-Mo-g-MPC or cartilage/Co-Cr-Mo-g-MPC bearing couples mimic a natural joint, showed low friction (friction coefficient was ~ 0.01), as low as that of cartilage/SUS or cartilage/cartilage. Hence, it was considered that the Co-Cr-Mo-g-MPC surface is excellent for the femoral head articulating cartilage, because the cartilage/Co-Cr-Mo-g-MPC bearing couples showed a constant low friction coefficient of 0.006. We expect that the hemiarthroplasty with the Co-Cr-Mo-g-MPC femoral head bearing will be promising to preserve acetabular cartilage and extend the duration before THA in young patients.

On the other hand, in the previous study, the CLPE-g-MPC/Co-Cr-Mo-g-MPC prepared by the adsorption of the polymer to the substrate, termed as the "grafting to" method bearing couples showed high friction (friction coefficient was 0.12).³⁶ The poly(MPC) on Co-Cr-Mo used in this study might have a high density because the polymerization method used was surface-initiated graft polymerization, termed as the "grafting from" method, in which the monomers are polymerized from initiators or comonomers, whereas the poly(MPC) on Co-Cr-Mo prepared by the "grafting to" method might have a low density.^{34,35} Figure 9 shows the hypothetical cartoons of high-density grafted poly(MPC)/low-density grafted poly(MPC) and high-density grafted poly(MPC)/high-density grafted poly(MPC) bearing

interfaces. The high-density grafted poly(MPC)/high-density grafted poly(MPC) bearing interface shows a remarkably lower friction than the high-density grafted poly(MPC)/low-density grafted poly(MPC) bearing interface.⁶³ Fukuda and coworkers reported that the friction of the bearing couple was higher in low-density polymer brushes than in high-density ones.⁶⁴ Therefore, it is assumed that a bearing couple with low-density poly(MPC) brushes may cause high friction by stick-slip motion with interpenetration, as shown in Figure 9(a).^{65,65} In contrast, high-density poly(MPC) fabricated by the "grafting from" method may attain low friction, such as that in the case of "superlubricity," owing to resistance to interpenetration by volume effects resulting from chain mobility. The reduction in friction may contribute to the improvement in antiwear properties.¹⁹⁻²¹ Although a hip joint simulator test is necessary to examine tribological advantages in human body environments, a superlubricious metal-bearing material would enable the development of a novel biocompatible artificial hip joint system-artificial femoral head for partial hemiarthroplasty and metal-on-polymer/metal type for THA.

CONCLUSION

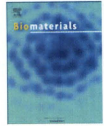
We prepared a superlubricious metal-bearing material for application as a novel artificial hip joint system: poly(MPC) was grafted onto the surface of a Co-Cr-Mo alloy by employing a MPSi intermediate layer and by using the photoinduced radical graft polymerization technique. The thickness and density of the grafted poly(MPC) layer increased with the MPC concentration and photoirradiation time, respectively. In conclusion, the grafted poly(MPC) layer successfully provided superlubricity to the

Co-Cr-Mo surface, and the CLPE-g-MPC/Co-Cr-Mo-g-MPC or cartilage/Co-Cr-Mo-g-MPC bearing interface, which mimicked a natural joint, showed an extremely low friction coefficient of 0.01, a value that is as low as that of a natural cartilage interface.

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Wear resistance of artificial hip joints with poly(2-methacryloyloxyethyl phosphorylcholine) grafted polyethylene: Comparisons with the effect of polyethylene cross-linking and ceramic femoral heads

Toru Moro^a, Hiroshi Kawaguchi^b, Kazuhiko Ishihara^{c,d,*}, Masayuki Kyomoto^{a,c}, Tatsuro Karita^b, Hideya Ito^b, Koza Nakamura^b, Yoshio Takatori^a

^a Division of Science for Joint Reconstruction, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

^b Sensory & Motor System Medicine, Faculty of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

^c Department of Materials Engineering, School of Engineering, The University of Tokyo, Hongo 7-3-1, Bunkyo-ku, Tokyo 113-8656, Japan

^d Center for NanoBio Integration, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

ARTICLE INFO

Article history:

Received 8 November 2008

Accepted 8 February 2009

Available online 9 March 2009

Keywords:

Poly(2-methacryloyloxyethyl

phosphorylcholine)

Polyethylene

Artificial hip joint

Arthroplasty

Cross-linking

Wear

ABSTRACT

Aseptic loosening of artificial hip joints induced by wear particles from the polyethylene (PE) liner remains the ruinous problem limiting their longevity. We reported here that grafting with a polymer, poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC), on the PE liner surface dramatically decreased the wear production under a hip joint simulator condition. We examined that the effect of properties of both PE by cross-linking and femoral head by changing the materials on wearing properties of PE. The PMPC grafting on the liners increased hydrophilicity and decreased friction torque, regardless of the cross-linking of the PE liner or the difference in the femoral head materials. During the hip joint simulator experiments (5×10^6 cycles of loading), cross-linking caused a decrease of wear amount and a reduction of the particle size, while the femoral head materials did not affect it. The PMPC grafting abrogated the wear production, confirmed by almost no wear of the liner surface, independently of the liner cross-linking or the femoral head material. We concluded that the PMPC grafting on the PE liner surpasses the liner cross-linking or the change of femoral head materials for extending longevity of artificial hip joints.

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1. Introduction

Artificial hip joint replacement is one of the most effective treatments for severe arthritis patients whose number has been on the rise due to the growth of the elderly population [1–3]. The Osteoarthritis Research Society (OARS) has given this treatment its highest recommendation and approved its cost-effectiveness [4]. Despite improvements in the implant design and surgical technique, the aseptic loosening secondary to periprosthetic osteolysis remains the most serious problem limiting their survivorship and clinical success. Up to 20% of patients implanted total hip replacement with conventional PE develop aseptic loosening within 10 years, and about half of them become disabled due to pain and loss of function [5,6]. The only therapeutic intervention is revision

surgery, the number of incidents of which has been on the rise and is projected to double by the year 2026, leading to expansion of the social and economic impact [7,8], unless some limiting mechanism can be successfully implemented to prevent the periprosthetic osteolysis.

The most widely used bearing couple for artificial joint systems is the combination of a polyethylene (PE) acetabular liner and a cobalt–chromium (Co–Cr) alloy femoral head. Periprosthetic osteolysis is known to be triggered by the host inflammatory responses to the PE wear particles originating from the interface [9], which induces the phagocytosis by macrophages and the following secretion of bone resorptive cytokines [10]. Hence, aiming at reduction of the PE wear particles, various trials have been performed. Of these, highly cross-linked PE (CLPE) which underwent gamma-ray or electron beam irradiation experimentally exhibited a 42–93% reduction in the wear rate compared with the conventional PE in vivo [11–13]. Clinical results regarding wear resistance of CLPE are now in medium-term follow-up. The percent reductions in the rate of femoral head penetration have ranged

* Corresponding author. Department of Materials Engineering, School of Engineering, The University of Tokyo, Hongo 7-3-1, Bunkyo, Tokyo 113-8656, Japan. Tel.: +81 3 5841 7124; fax: +81 3 5841 8647.

E-mail address: ishihara@mpc.t.u-tokyo.ac.jp (K. Ishihara).

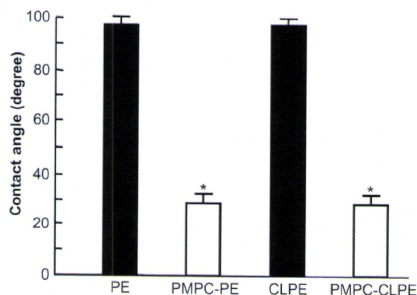


Fig. 1. Contact angles of a water drop on PE plates with or without cross-linking and PMPC grafting. Data are expressed as means (bars) \pm standard errors (error bars) for 10 plates/group. * $p < 0.01$, significant effects of PMPC grafting.

from 23 to 95%, depending on which conventional PE was used as a control [14]. Another strategy for reduction of the wear particles is the change of the femoral head material from metal to ceramics to reduce the friction against the PE liner. Among them, alumina ceramic is prevalent with substantially lower PE wear rates than conventional metal heads [15–17].

Considering that the healthy human joint cartilage surface is covered with a nanometer-scaled phospholipid layer [18], grafting a phospholipid-like layer on the liner surface may realize an ideal lubricity resembling the physiological joint surface. We found that the 2-methacryloyloxyethyl phosphorylcholine (MPC) polymers are biocompatible and hydrophilic due to phospholipid polar groups in the side chain [19,20]. The MPC polymers can suppress biological reactions even when they are in contact with living organisms [21–25]. Medical devices such as intravascular stents, soft contact lenses and the artificial lung are used clinically using the MPC polymers [26–28]. Aiming at the elimination of periprosthetic osteolysis, we have developed a novel hip CLPE liner with poly(MPC) (PMPC) grafting on its surface, and found that the graft dramatically decreased the production of wear particles during 3×10^6 cycles in the hip joint wear simulator using the Co–Cr alloy femoral head [29–31]. We also showed that the polymer particles grafted with PMPC were biologically inert and did not cause the subsequent bone resorptive responses [31]. For clinical

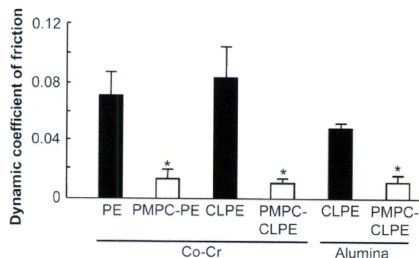


Fig. 2. Dynamic coefficients of friction for the various types of PE plates against Co–Cr alloy and alumina ceramic balls. Data are expressed as means (bars) \pm standard errors (error bars) for 5 plates/group. * $p < 0.01$, significant effects of PMPC grafting.

application, we further confirmed the stability of the PMPC grafting on the liner surface even after the gamma-ray irradiation [32,33]. To compare the effects of the PMPC grafting, liner cross-linking, and the ceramic femoral head, the present study examined the wear resistance by the PMPC grafting on PE and CLPE liners, and against metal and alumina ceramic femoral heads.

2. Materials and methods

2.1. Materials

The MPC was obtained from NOF Co. Ltd. (Tokyo, Japan), which is synthesized by the same procedure as previously reported by Ishihara [19]. PE liners with and without cross-linking (CLPE and PE, respectively) (K-MAX[®] CLQC and K-MAX[®] QPIC), and Co–Cr and alumina ceramic femoral heads (K-MAX[®] HH-02 and K-MAX[®] HHA) were obtained from Japan Medical Materials Co. (Osaka, Japan). For PMPC grafting, PE and CLPE liners after coating with benzophenone as photosensitizer were placed in the MPC aqueous solution (0.5 mol/L) and photoinduced polymerization on the liner surface was carried out using an ultra-high pressure mercury lamp (UVI-400HA, Riko-Kagaku Sangyo, Funabashi, Japan), as previously reported

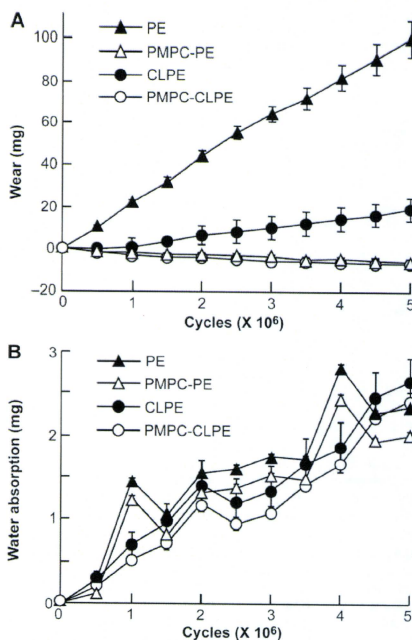


Fig. 3. Wear amount of PE liners with or without cross-linking and PMPC grafting in the hip joint simulator. (A) Time course of wear amount generated from PE, CLPE, PMPC-PE, and PMPC-CLPE liners during 5×10^6 cycles of loading against Co–Cr alloy femoral heads in the hip joint simulator. At intervals of 5×10^5 cycles the liners were removed from the simulator, and the weight loss was determined as the wear amount. (B) Water absorption of the liners which was only loaded axially to the femoral heads without rotational motion to determine the water weight absorbed by the liners during soak in the lubricant. Data are expressed as means (symbols) \pm standard errors (error bars) for 8, 10, 5 and 10 liners for PE, CLPE, PMPC-PE, and PMPC-CLPE liners, respectively.

[30,31,34,35]. The wavelength of photopolymerization was selected by a glass color filter as 350 ± 50 nm.

2.2. Surface analyses

The surface elemental conditions of the PE and CLPE liners or plates with and without PMPC grafting were analyzed using highly sensitive X-ray photoelectron spectroscopy (XPS AXIS-HSI165, Kratos/Shimadzu, Kyoto, Japan) equipped with a 15-kV Mg-K α radiation source at the anode. The functional group vibrations of the surfaces were examined by Fourier-transform infrared (FT-IR) spectroscopy with attenuated total reflection (ATR) equipment. The FT-IR/ATR spectra were obtained using an FT-IR analyzer (FT/IR615, JASCO, Tokyo, Japan) for 32 scans (1.2 s/scans) over the range of 800–2000 cm^{-1} at a resolution of 4.0 cm^{-1} . Hydrophilicity was evaluated by the static water contact angles on the surfaces using the sessile drop method with an optical bench-type contact angle goniometer (Model DM300, Kyowa Interface Science, Saitama, Japan). Drops of purified water (1.0 mL) were deposited on the liner surface, and the contact angles were directly measured with a microscope 60 s after dropping, according to the International Organization for Standardization (ISO) 15989 standard. At least ten contact angles were measured and averaged.

2.3. Dynamic coefficient of friction

The dynamic coefficients of friction between the plates and the Co-Cr alloy and alumina ceramic balls were measured using a ball-on-plate machine (Tri-bostation 32; Shinto Scientific, Tokyo, Japan) as a preliminary test for tribological properties [36]. A Co-Cr alloy and alumina ceramic ball with a diameter of 9.0 mm was prepared. The surface roughness of the ball was about $0.010 \mu\text{m}$, which was comparable to that of the femoral head products. Each of the untreated CLPE and PMPC grafted CLPE surfaces were used to prepare five sample pieces. 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. Pure water was used as the lubricant medium.

2.4. Hip joint simulator

A hip joint wear simulator test was performed under the conditions recommended by the ISO standard [37]. A 12-station hip simulator apparatus (MTS, MTS Systems, Minneapolis, MN, USA) with PE and CLPE liners with or without PMPC grafting in 46 mm acetabular cups that were coupled to 26 mm Co-Cr alloy or

alumina ceramic femoral head were mounted on the rotating blocks to produce a biaxial or orbital motion. A Paul-type loading profile which is a physiological walking simulation with continuous cyclic motion and loading was applied (maximum force: 2744 N, frequency: 1 Hz) [38]. A diluted bovine calf serum (25 vol%) in distilled water was used as the lubricant. Sodium azide (10 mg/L) and EDTA (20 mM) were added to prevent microbial contamination and minimize calcium phosphate formation on the implant surface. The simulator was run up to 5×10^6 cycles for 3 months. At intervals of 5×10^5 cycles the liners were removed from the simulator and weighed on a microbalance (Sartorius GENIUS ME215S, Sartorius AG, Gottingen, Germany) to determine the wear amount. The lubricant was collected and stored at -20°C for further analysis. Since the liners are known to absorb water during their soak in the lubricant, therefore we also measured the weight gain of the liners which were cyclically axial-loaded to the femoral heads without rotational motion (i.e., load-soak control) every 5×10^5 cycles to determine the amount of wear sustained.

After the total loading, morphological change of the liner surface was measured by a 3-dimensional coordinate measuring machine (XYZAX G5800B, Tokyo Seimitsu, Tokyo, Japan). To evaluate the actual removal of material caused by wear, melt-recovery experiments were performed and the liner surface was analyzed with a confocal scanning laser microscope (OLS1200, Olympus, Tokyo, Japan) as previously reported [39]. For the femoral head surface, in addition to field emission scanning electron microscopy (SEM, JSM-6330F, JEOL DATUM, Tokyo, Japan) evaluation, the surface roughness value R_a was measured using a roughness measuring instrument (SURFTEST-501, Mitutoyo, Yokohama, Japan) with a $5 \mu\text{m}$ diameter contact probe.

For isolation of wear particles, the lubricant after the loading was incubated with 5.0 N NaOH solution in order to digest adhesive proteins that were degraded and precipitated; the particles were then collected and underwent sequential filtrations ($0.1 \mu\text{m}$ of minimum pore size), as previously reported [40]. Particle size was defined using the maximum dimensions determined by the SEM analysis.

2.5. Statistical analysis

The results derived from each measurement in the static water contact angle measurement and friction test were expressed as mean values and standard deviation. Standard analysis of variance (ANOVA) was applied to the data of the existed among those groups, in this study. Two combinations (e.g., PE and PMPC-PE in the static water contact angle measurement) were especially made with Student's *t*-test ($p < 0.05$).

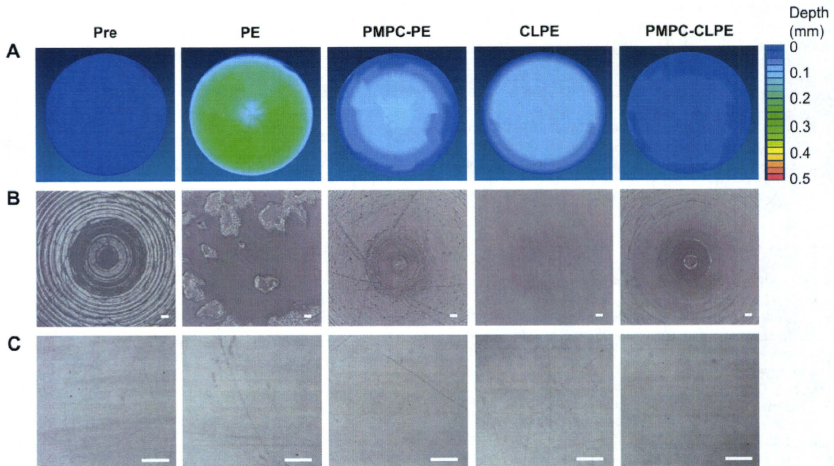


Fig. 4. Optical findings of the surfaces of the four liners and corresponding femoral heads in the hip joint simulator. (A) Three-dimensional morphometric analysis and (B) confocal scanning laser microscopic analysis of PE, PMPC-PE, CLPE, and PMPC-CLPE liners surfaces before (pre) and after 5×10^6 cycles of loading in the hip joint simulator. Scale bars 200 μm . (C) SEM images of the Co-Cr femoral head surfaces before (pre) and after 5×10^6 cycles of loading. Scale bars 5 μm .

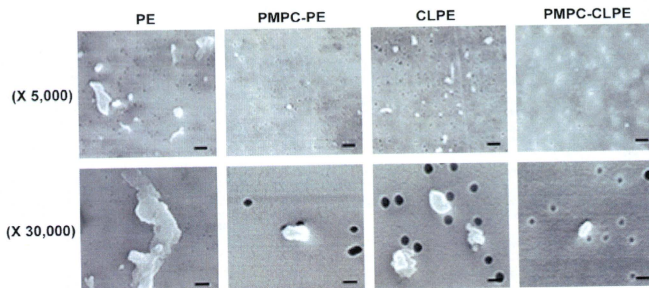


Fig. 5. SEM images of the wear particles isolated from lubricants of the simulators with four kinds of liners. Low (top; $\times 5000$) and high (bottom; $\times 30,000$) magnifications of SEM images of the wear particles isolated from lubricants of the simulators with four kinds of liners. Scale bars 1.0 and 0.1 μm , respectively.

3. Results

3.1. Surface analyses of PE plates with or without cross-linking and PMPC grafting

Successful photoinduced graft polymerization of tMPC on both PE and CLPE plates was confirmed by XPS and FT-IR/ATR spectroscopy. The XPS for nitrogen (N_{1s}) and phosphorus (P_{2p}) atoms showed the respective peaks at 403 eV and 133 eV only on the plates with PMPC grafting (PMPC-PE & PMPC-CLPE), but not on those without it (PE & CLPE). These peaks were characteristic of the phosphorylcholine present in the MPC units, since they were assigned to the $-\text{N}^+(\text{CH}_3)_3$ and phosphate groups, respectively. The FT-IR/ATR spectra representing phosphate group (P=O) at 1240, 1080 and 970 cm^{-1} , and ketone group (C=O) at 1720 cm^{-1} were also confirmed to be detected only on the plates with PMPC grafting. The contact angles of a water drop on the plates after PMPC grafting were 1/3–1/4 those of the original plates (Fig. 1), indicating that PMPC grafting increased hydrophilicity on the hydrophobic PE and CLPE surfaces. We then measured the dynamic coefficients of friction of the plates against Co-Cr alloy and alumina ceramic balls. The friction coefficient was about 80–90% lower in the liners with PMPC grafting than in those without it, regardless of the ball materials (Fig. 2). Cross-linking by itself did not alter both the water-drop contact angles and the friction coefficient (Figs. 1 and 2).

3.2. Effects of cross-linking and PMPC grafting on wear of the liners in a hip joint simulator

We then compared the wear of the liners with or without cross-linking and PMPC grafting using a hip joint simulator during 5×10^6 cycles of loading against Co-Cr alloy femoral heads. In the absence of the grafting, wear amount from the PE liner determined by the weight loss was increased in a cycle-dependent manner (Fig. 3A). This was suppressed in the CLPE liner by 80%, clearly demonstrating that the cross-linking provided wear resistance. The PMPC grafting dramatically decreased the wear amount not only in the CLPE liner, but also to a similar level in the PE liner. Interestingly, both PMPC-PE and PMPC-CLPE showed no weight loss, but rather continued to gain weight. This might be at least partly due to water absorption into the liners during the load-soak test. When using the gravimetric method, the weight loss in the tested liners is corrected by subtracting the weight gain in the load-soak controls; however, this correction cannot be perfectly achieved because only the tested

liners are continuously subjected to load and motion. Water absorption in the tested liners is generally slightly higher than that in the load-soak controls. Consequently, the correction for water absorption by using the load-soak control as the correction factor leads to a slight underestimation of the actual weight loss. In fact, all four kinds of liners, which were only cyclically axial-loaded to the femoral heads without rotational motion in the simulator, gained weight, regardless of the presence or absence of cross-linking and PMPC grafting (Fig. 3B).

Three-dimensional morphometric analyses confirmed the wear resistance by the cross-linking and PMPC grafting (Fig. 4A). Although the CLPE liner showed less surface wear than the PE liner after 5×10^6 cycles of loading, both PMPC-PE and PMPC-CLPE liners exhibited almost no wear. Confocal scanning laser microscopic analyses of the liner surfaces revealed that the original machine marks that were clearly visible before the loading still remained on the PMPC-PE and PMPC-CLPE surfaces, while they were completely

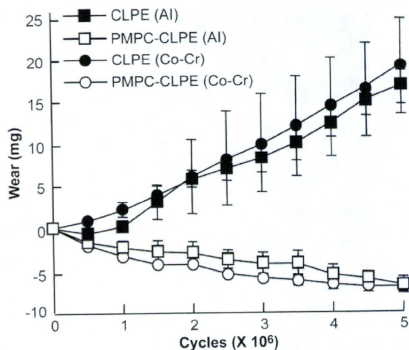


Fig. 6. Wear resistance of CLPE liners with and without PMPC grafting against Co-Cr alloy or alumina ceramic femoral heads in the hip joint simulator. Time course of the wear amount generated from CLPE or PMPC-CLPE liners during 5×10^6 cycles of loading against Co-Cr alloy or alumina ceramic femoral heads in the hip joint simulator. At intervals of 5×10^5 cycles the liners were removed from the simulator, and the weight loss was determined as the wear amount.

obliterated not only on the PE, but also on the CLPE surfaces (Fig. 4B). The XPS analysis also confirmed the remainder of the specific spectra of N_{1s} and P_{2p} at 403 eV and 133 eV, respectively, on the PMPC-PE and PMPC-CLPE surfaces, indicating that PMPC grafting remains even after 5×10^6 cycles of loading. The Co-Cr alloy femoral heads were free of visible scratches, and the surface roughness expressed by the R_a values was not different between before and after the loading in all groups ($R_a = 0.01\text{--}0.02 \mu\text{m}$), suggesting that there was no abrasive contamination with metal particles from the heads in the simulator (Fig. 4C).

PMPC grafting on both PE and CLPE liners decreased the amount of wear particles isolated from the lubricants (Fig. 5, top). Since the wear particles from PMPC-PE and PMPC-CLPE surfaces were hardly observed due to the extremely small amount, the wear particles could not be classified according to their size. In contrast, there was a substantial difference in the particle size between PE and CLPE: the majority of the particle length was 1.0–10 μm in PE while 0.1–1.0 μm in CLPE (Fig. 5).

3.3. Effects of femoral head materials on wear of the liners in a hip joint simulator

Next, we compared the wear of CLPE and PMPC-CLPE liners that underwent 5×10^6 cycles of loading against Co-Cr alloy and alumina ceramic femoral heads in the hip joint simulator. The wear from the CLPE liner increased in a cycle-dependent manner, and was little affected whether the material was Co-Cr alloy or alumina ceramic (Fig. 6). The PMPC grafting on the CLPE liner abrogated the wear production by femoral heads of both materials similarly. Three-dimensional morphometric analyses (Fig. 7A) and the confocal scanning laser microscopic analyses (Fig. 7B) confirmed a marked

enhancement of wear resistance by PMPC grafting, regardless of the femoral head materials. The femoral heads of both materials were free of visible scratches (Fig. 7C), and the surface roughness expressed by the R_a values was not different between before and after the loading in all groups ($R_a = 0.01\text{--}0.02 \mu\text{m}$). SEM analyses showed that the number of wear particles of identical shape and size in both materials was decreased by PMPC grafting (Fig. 8).

4. Discussion

The present study demonstrated that surface grafting of MPC on the PE liner diminished the wear production during 5×10^6 cycles of loading in the hip joint simulator. This effect was independent of the presence or absence of cross-linking of PE, as well as the material of the femoral heads.

As a mechanism underlying the wear resistance by the PMPC grafting, we should consider an increase of lubrication between the liner and femoral head. Although phospholipids work as effective boundary lubricants, a study of natural synovial joints showed that fluid film lubrication by the intermediate hydrated layer is the predominant mechanism under physiologic walking conditions [41,42]. Because the present study showed that the PMPC grafting increased hydrophilicity and decreased the friction (Figs. 1 and 2) and our previous study showed that the free water fraction on the MPC polymer surface is kept at a higher level [43–45], the enhancement of wear resistance is likely attributable to the hydrated lubricating layer formed by the PMPC grafting. Contrarily, although cross-linking also suppressed the wear in the simulator, it affected neither the surface hydrophilicity nor the friction (Figs. 1 and 2). This means that cross-linking of PE did not alter the surface lubricity, but increases the hardness of the liner material, so that this procedure may not be essential once the liner surface was grafted with MPC, explaining the similar wear resistance between PMPC-PE and PMPC-CLPE liners (Fig. 3A).

In addition to enhancement of wear resistance of the liner, reduction of bone resorptive responses to wear particles generated is important for the prevention of periprosthetic osteolysis. The responses are dependent not only on the total amount of particles, but also on their proportion which are within the most biologically active size range [46]. The present SEM analysis of

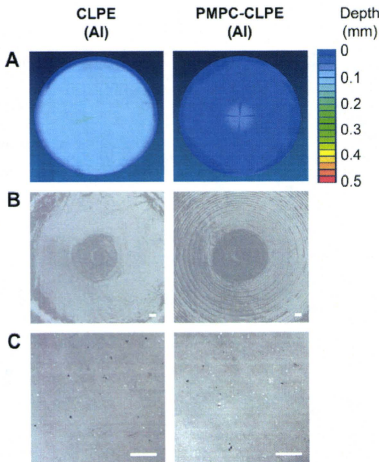


Fig. 7. Optical findings of the surfaces of the CLPE liners with and without PMPC grafting and the alumina ceramic femoral heads in the hip joint simulator. (A) Three-dimensional morphometric analysis and (B) confocal scanning laser microscopic analysis of the liner surfaces after 5×10^6 cycles of loading. Scale bars 200 μm . (C) SEM images of the alumina ceramic femoral head surfaces after 5×10^6 cycles of loading. Scale bars 5 μm .

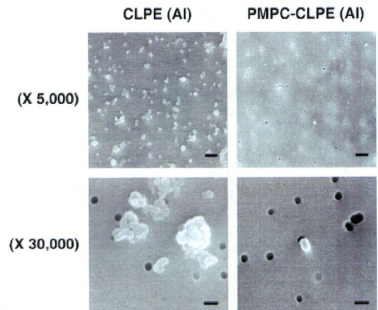


Fig. 8. SEM images of the wear particles isolated from lubricants of the simulators with CLPE liners with and without PMPC grafting against alumina ceramic femoral heads. Low (top; $\times 5000$) and high (bottom; $\times 30000$) magnifications of SEM images of the wear particles isolated from lubricants of the simulators. Scale bars 1.0 and 0.1 μm , respectively.

the wear particles in the lubricants revealed substantial difference of the particle size distribution between CLPE and PE liners, as previously reported [47,48]. The CLPE liner releases a high number of submicrometer and nanometer-sized particles which are known to induce a greater inflammatory response than larger particles [46]. Hence, although cross-linking of PE indeed causes a reduction in the total amount of particles, it might not necessarily lead to the prevention of periprosthetic osteolysis. Another problem raised with the cross-linking of PE is that it may possibly deteriorate the mechanical properties of the liner causing fatigue cracking [12,49,50]. Clinical evidence regarding the longevity of artificial joints with CLPE is anticipated in the future.

Our previous report has shown that polymer particles covered with the PMPC are biologically inert with respect to phagocytosis by macrophages and subsequent bone resorptive actions [31]. An increasing number of studies address the potential pharmacologic modification of the adverse host response to wear particles [51–53] including cytokine antagonists, cyclooxygenase-2 inhibitors, and osteoprotegerin, or anti-RANKL (receptor activator of nuclear κ B ligand) antibody; however, they may cause serious side effects because the agents must be taken for a long period after surgery and because they are not currently targeted to the site of the problem. Because the lack of side effects of the MPC polymer has already been confirmed clinically by several biomedical devices [26–28], this grafting exceeds the developing pharmacologic treatments.

A limitation of this study is the confined period of loading. Although the 5×10^6 cycles in the hip simulator is generally comparable to 5–10 years of physical walking, this may not be long enough for young active patients who show 2×10^6 daily steps/year by the previous study [54]. We are now running the hip simulator with longer loading up to three and a half years, and so far have confirmed almost no wear on the PMPC–CLPE liner after 7×10^7 cycles. Although the results of this study are promising, the third-body wear is a matter of concern. Additional testing needs to be done to determine the effects of third substance on the beneficial influence of PMPC grafting. Another limitation of the hip simulator experiment is that it does not entirely capture the range of loading conditions of a hip, in terms of either the variety of positions or the magnitude of loading, although we believe the simulator experiment can provide some indication of trends.

5. Conclusions

From the advantages shown in this study, we believe that the PMPC grafting for obtaining super-lubrication on the PE liner is more efficient than the cross-linking of the PE liner and the change of the femoral head materials for extending longevity of artificial hip joints. The development of this nanotechnology in the biomaterials science would improve the quality of care of patients having joint replacement and have a substantial public health impact. A large-scale clinical trial is now underway.

Acknowledgements

This study was supported by Health and Welfare Research Grant for Translational Research (H17-005), Research on Medical Devices for Improving Impaired QOL (H20-004) from the Japanese Ministry of Health, Labour and Welfare. We thank Dr. T. Konno, Ms. R. Yamaguchi, The University of Tokyo, and Mr. N. Yamawaki, Mr. T. Miyashita, Japan Medical Materials Co., and Dr. M. Hashimoto, Japan Fine Ceramics Center for their excellent technical assistance.

Appendix

Figures with essential colour discrimination. Parts of Figs. 4 and 7 in this article are difficult to interpret in black and white. The full colour images can be found in the on-line version, at doi:10.1016/j.biomaterials.2009.02.020.

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

Masayuki Kyomoto,^{1,2} Toru Moro,³ Fumiaki Miyaji,¹ Masami Hashimoto,⁴ Hiroshi Kawaguchi,³ Yoshio Takatori,³ Koza Nakamura,³ Kazuhiko Ishihara^{2,5}

¹Research Department, Japan Medical Materials Corporation, Osaka, Japan

²Department of Materials Engineering, School of Engineering, The University of Tokyo, Tokyo, Japan

³Department of Orthopaedic Surgery, School of Medicine, The University of Tokyo, Tokyo, Japan

⁴Materials Research and Development Laboratory, Japan Fine Ceramics Center, Nagoya, Japan

⁵Center for NanoBio Integration, The University of Tokyo, Tokyo, Japan

Received 11 December 2007; revised 29 February 2008; accepted 27 March 2008

Published online 2 June 2008 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jbm.a.32092

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, and so forth, 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. © 2008 Wiley Periodicals, Inc. *J Biomed Mater Res* 90A: 362–371, 2009

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. Multicompo-

nent 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

Correspondence to: M. Kyomoto, Uemura Nissei Bldg. 9F, 3-3-31 Miyahara, Yodogawa-ku, Osaka 532-0003, Japan; e-mail: kyomotom@jmcc.jp

Contract grant sponsor: Japanese Ministry of Education, Culture, Sports, Science and Technology; contract grant number: 15390449

Contract grant sponsor: Japanese Ministry of Health, Labor and Welfare

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, antiprotein 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 poly-

mer, 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, and so forth, 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 orthopedic 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, IN) sheet stock was irradiated with 50 kGy γ -rays in N₂ gas and annealed at 120°C for 7.5 h in N₂ 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 Figure 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 placed 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 O₂ plasma at a 200 W high-frequency output and 150 mL/min O₂ gas flow for 2 min by using an O₂ plasma etcher (PR500,

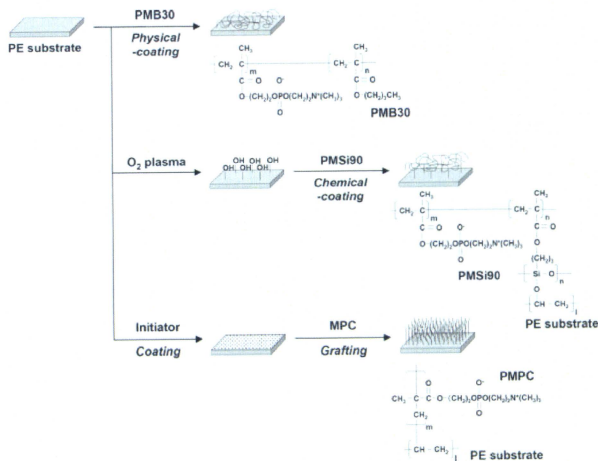


Figure 1. Scheme for the preparation of MPC polymer-coated CLPE and PMPC-grafted CLPE.

Yamato Scientific Co., Tokyo, Japan). The O₂ 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., Tokyo, Japan) for 10 s for the silanization of trimethoxysilane group of PMSi90 and placed 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 γ -rays in N₂ gas.

MPC graft polymerization

The preparation of the PMPC-grafted CLPE is schematically illustrated in Figure 1. The CLPE specimens were immersed in acetone (Wako Pure Chemical Industries, Osaka, Japan) solution containing 10 mg/mL benzophenone (Wako Pure Chemical Industries) 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/cm².³ 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., Funabashi, Japan) with an intensity of 5 mW/cm² 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 γ -rays in N₂ 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 (FTIR) spectroscopy. The 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 Co., Tokyo, Japan) at a resolution of 4.0 cm⁻¹.

The surface elemental contents of the untreated CLPE, PMB30-coated CLPE, PMSi90-coated CLPE, and PMPC-grafted CLPE were analyzed using X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS Hsi 165; Kratos Analytical Ltd., Manchester, UK) equipped with an Mg-K α 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; five replicate measurements were performed for each sample, and the average values were considered for the surface elemental contents.

The static water-contact angles of the untreated CLPE, PMB30-coated CLPE, PMSi90-coated CLPE, and PMPC-grafted CLPE were measured using an optical bench-type contact angle goniometer (model DM300; Kyowa Interface