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Table 1. Expression of surface epitopes in MPC-selected cells

Surface epitopes	MPC 0%	MPC 1%	MPC 2%	MPC 5%	MPC 10%
CD29 (Integrin β 1)	++	++	+++	++	++
CD44 (Hyaluronan receptor)	++	++	++	++	++
CD105 (Endoglin)	+	+	+	+	+
CD166 (ALCAM)	+	+	+	+	+
CD34	-	-	-	-	-
CD45 (LCA)	-	-	-	-	-

214x279mm (300 x 300 DPI)

Superlubricious surface mimicking articular cartilage by grafting poly(2-methacryloyloxyethyl phosphorylcholine) on orthopaedic metal bearings

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Abstract: Aseptic loosening of the artificial hip joint with osteolysis due to the wear particles from polyethylene cup has remained as a serious issue. To reduce this wear and develop a novel artificial hip joint system, we produced a superlubricious metal-bearing material: for this, we grafted a 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer onto the surface of a cobalt-chromium-molybdenum (Co-Cr-Mo) alloy. For ensuring long-term benefit retention of poly(MPC) on the Co-Cr-Mo alloy for application as a novel artificial hip joint system, several issues must be considered: strong bonding between poly(MPC) and Co-Cr-Mo surface, high mobility of free end groups of the poly(MPC) layer, and high density of the introduced poly(MPC). Considering these issues, we introduced a 3-methacryloyloxypropyl trimethoxysilane (MPSi) intermediate layer and a photoinduced graft polymerization technique to create a strong covalent bond between the Co-Cr-Mo substrate and the poly(MPC) chain via the MPSi layer. The

thickness and density of the poly(MPC) layer on the surface increased with the MPC concentration and photoirradiation time. The grafted poly(MPC) layer successfully provided super-lubricity to the Co-Cr-Mo surface. The poly(MPC)-grafted crosslinked polyethylene/poly(MPC)-grafted Co-Cr-Mo or cartilage/poly(MPC)-grafted Co-Cr-Mo bearing interface mimicking natural joints showed an extremely low friction coefficient of 0.01, which is as low as that of natural cartilage interface. A superlubricious metal-bearing surface 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 total hip arthroplasty. © 2008 Wiley Periodicals, Inc. *J Biomed Mater Res* 00A: 000-000, 2008

Key words: joint replacement; metal surface treatment; photopolymerization; phosphorylcholine; hydrophilicity

INTRODUCTION

Every year, the number and prevalence of primary and revision hip and knee joint replacements increases substantially worldwide.¹ As a result, the quality of artificial joints is becoming increasingly important. Most patients who receive an artificial joint experience dramatic pain relief and rapid improvement in both their daily activities and qual-

ity of life. The most widely used bearing couple in artificial hip joint systems is a combination of an ultrahigh molecular weight polyethylene (UHMWPE) acetabular component and a metal femoral component. Cobalt-chromium-molybdenum (Co-Cr-Mo) alloy is one of the most widely used metal bearing materials in artificial joint systems. The Co-Cr-Mo alloy has good mechanical properties, castability, corrosion resistance, and wear resistance, whereas stainless steel and titanium alloys have a disadvantage with regard to corrosion resistance and wear resistance, respectively.

In total hip arthroplasty (THA), osteolysis caused by the wear particles from UHMWPE has been recognized as a serious issue.²⁻⁴ Efforts to decrease

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these particles have focused on bearing material improvement and the use of combinations other than metal-on-UHMWPE.⁵⁻⁷ Recently, a metal-on-metal type artificial hip joint system consisting of Co-Cr-Mo acetabular and femoral components has been studied.⁸ The advantages of the Co-Cr-Mo/Co-Cr-Mo bearings are that they do not generate UHMWPE wear debris and they exhibit decreased wear when compared with Co-Cr-Mo/UHMWPE bearings.^{9,10} However, even in Co-Cr-Mo/Co-Cr-Mo bearings, aseptic loosening induced by wear particles and metallosis remains as serious issue in revision surgeries.^{11,12} In addition to metallosis, electrochemical corrosion and carcinogenesis occurring due to the dissemination of wear particles to the other parts of the body have been reported.¹³

On the other hand, improvements in the bearing materials and surface modifications of the Co-Cr-Mo alloy have been attempted, in order to reduce such wear particles.^{14,15} Surface coating may reduce the wear without compromising the bulk mechanical properties of the implant materials. Various "hardening treatments" of metal bearing surfaces, such as diamond-like carbon coating, titanium nitride coating, and ion implantation have also been attempted.^{16,17} Although these surface modifications may improve THA survivorship, the limited THA longevity imposes restrictions for its application to younger patients. Consequently, the possibility of replacing the femoral head alone, whether solid or articular surface replacement, remains an attractive feature of such implants during revision surgeries of THA. However, the Co-Cr-Mo alloy or the hardening-treated Co-Cr-Mo alloy may induce damage to cartilaginous tissue.

In contrast, the previous study reported that highly lubricious hydrogel polymer used as an artificial cartilage did not damage cartilaginous tissue.¹⁸ We have recently developed a highly lubricious artificial hip joint system by a "mild treatment" with soft materials. In this treatment, poly(2-methacryloyloxyethyl phosphorylcholine) (MPC) was grafted onto the surface of CLPE (CLPE-g-MPC).¹⁹⁻²¹ MPC is a methacrylate with a phospholipid polar group in a side chain, and it has both good solubility in polar solvents including water and polymerization ability by conventional radical polymerization.²² Many MPC polymers have been widely investigated as biomaterials.²³⁻²⁷ As a result, various medical devices have already been developed using MPC polymers, and they are being used clinically. The efficacy of MPC polymers as biomaterials has been well verified.²⁸⁻³⁰

In general, there are two methods for modifying the polymer surface. The first method involves surface absorption or reaction with small molecules,^{31,32} and the second is grafting polymeric molecules onto the substrate through covalent bonding.³³ Most fre-

quently, grafting polymerization is performed using either of the following methods: (1) surface-initiated graft polymerization, termed as the "grafting from" method, in which monomers are polymerized from initiators or comonomers and (2) adsorption of the polymer to the substrate, termed as the "grafting to" method (i.e., dipping, crosslinking, and ready-made polymers with reactive end groups reacting with the functional groups of the substrate).^{34,35} In our previous study, the Co-Cr-Mo-g-MPC prepared by the adsorption of the polymer to the Co-Cr-Mo substrate, termed as the "grafting to" method, was not uniform, and the CLPE-g-MPC/Co-Cr-Mo-g-MPC bearing couples showed high friction.³⁶ These results were probably ascribed to a low density of the poly (MPC) on Co-Cr-Mo prepared by the "grafting to" method. To solve the issue in this study, we developed a superlubricious surface with nanometer-scale poly(MPC) modification and was accomplished by using a photo-induced radical polymerization technique that was similar to the one used in the "grafting from" method. The "grafting from" method has an advantage over the "grafting to" method in that it synthesizes a high-density polymer brush.

To ensure *in vivo* long-term retention of this poly(MPC) graft on the Co-Cr-Mo alloy, it is necessary to create strong covalent bonding between the Co-Cr-Mo alloy substrate and the poly(MPC) graft chain. Organosilanes have already been known as surface coupling agents to enhance bonding between a metal or a metal oxide surface and an organic resin such as dental resin, and they can strongly bind metals to resins in dental implants.³⁷ Organic silanes or silane coupling agents comprise at least a hydrolyzable alkoxyethyl or chlorosilyl group and an organofunctional group.³⁸ The agents are effective to introduce organofunctional groups into the siloxane network polymer. The organofunctional group in the silane could be useful to improve bonding with the organic overlayer. 3-Methacryloxypropyl trimethoxysilane (MPSi) is a simple surface coupling agent consisting of three methoxysilane groups, a propyl chain, and a functional methacrylate, and the structure of its main chain is equivalent to that of MPC.

In this study, based on the hypothesis that the "grafting from" method has advantages over the "grafting to" method in that it can synthesize a uniformly and controllable polymer layer, a superlubricious metal bearing material in which the poly(MPC) with biocompatibility and hydrophilicity was grafted onto the surface of the Co-Cr-Mo alloy (Co-Cr-Mo-g-MPC) has been introduced for developing a novel artificial hip joint system, that is, artificial femoral head and metal-on-metal (Co-Cr-Mo/Co-Cr-Mo) type for THA. The surface structure and preliminary tribological properties of Co-Cr-Mo-g-MPC were also investigated.

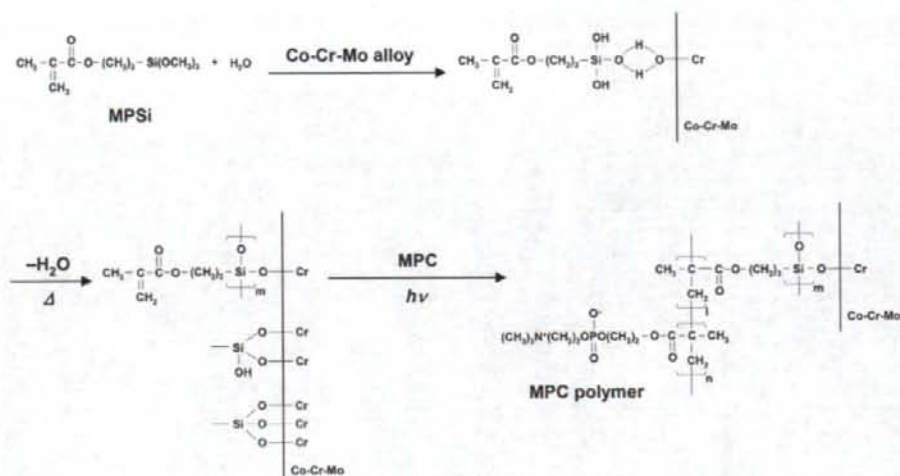


Figure 1. Chemical reaction on Co-Cr-Mo during polymerization of MPC.

MATERIALS AND METHODS

Chemicals

MPC was synthesized industrially by using the method developed by Ishihara et al.,²² and it was supplied by AI Bio-Chips Co., Ltd. (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-methylpropanone (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 mW/cm² 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 O₂ plasma at a 500-W high-frequency output and 150-mL/min O₂ gas flow for 5 min by using an O₂ plasma etcher (PR500, Yamato Scientific Co., Ltd., Tokyo, Japan). The O₂ 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/cm² 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 ± 50 nm. After the polymerization, the Co-Cr-Mo-g-MPC samples were removed from the solution, washed with pure water and

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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 Analytical Ltd., Manchester, UK) 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-

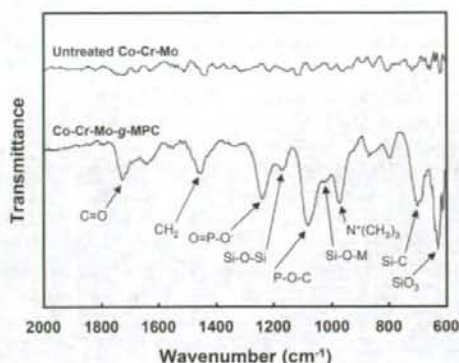


Figure 2. FTIR/ATR spectra of untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC surfaces with a 0.50-mol/L MPC concentration and a 90-min photoirradiation time.

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.

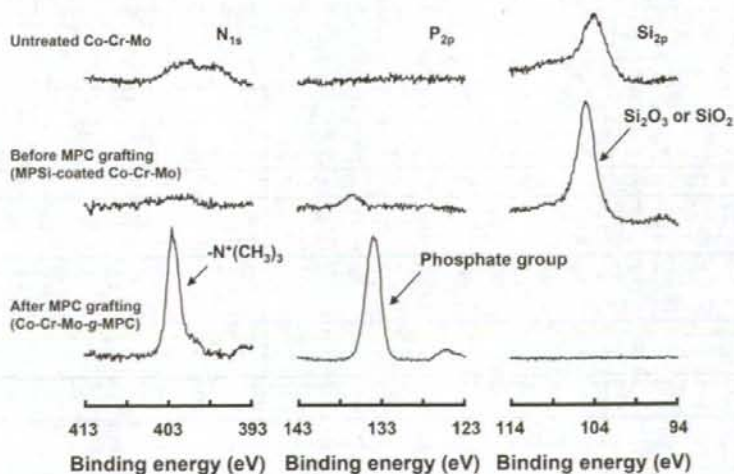


Figure 3. XPS spectra (N_{1s} , P_{2p} , and Si_{2p}) of Co-Cr-Mo samples before and after the MPC grafting with a 0.50-mol/L MPC concentration and a 90-min photoirradiation time.

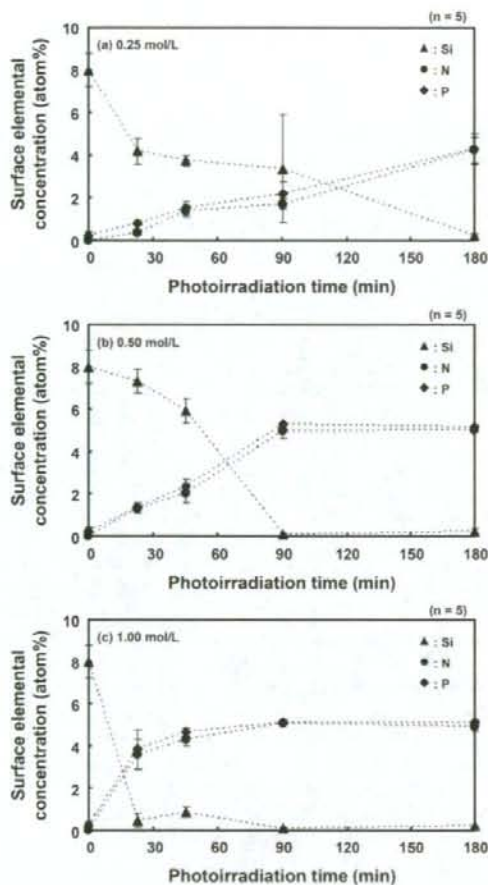


Figure 4. Surface elemental concentrations in the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time for various MPC concentrations in feeds. Bar: standard deviations.

F5 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° .

F6 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

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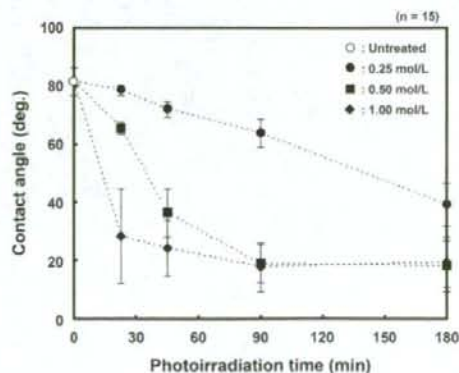


Figure 5. Static-water contact angle of the Co-Cr-Mo-g-MPC surface as a function of the photoirradiation time for various MPC concentrations in feeds. Bar: standard deviations.

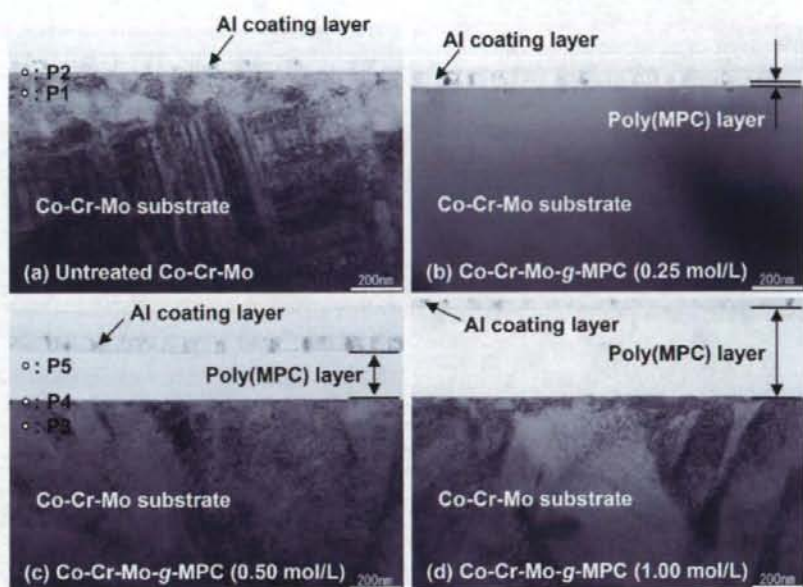


Figure 6. Cross-sectional TEM images of the Co-Cr-Mo-g-MPC surface with various MPC concentration in feeds and a 90-min photoirradiation time. Aluminum coating layers (~ 70 nm) for preparation of TEM observation specimen are shown above the poly(MPC) layer of the Co-Cr-Mo-g-MPC surface. In (a) and (c), 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.

F8 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

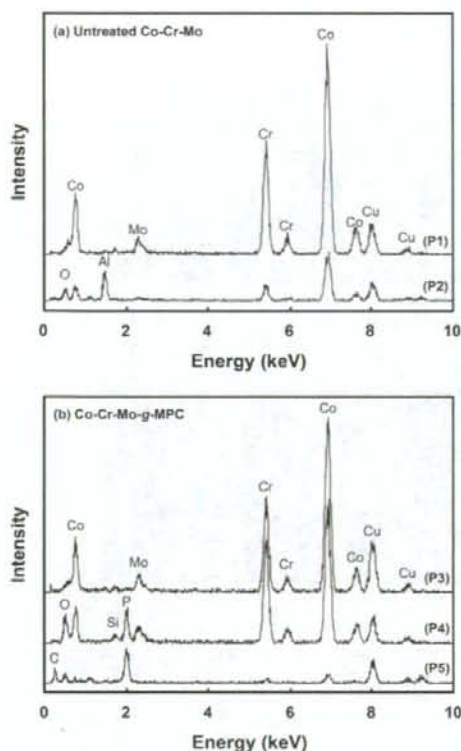


Figure 7. EDX spectra of the Co-Cr-Mo-g-MPC surface with a 0.5-mol/L MPC concentration and a 90-min photoirradiation time. The spectra were analyzed on the cross-section (P1–5) of the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC in Figure 6.

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

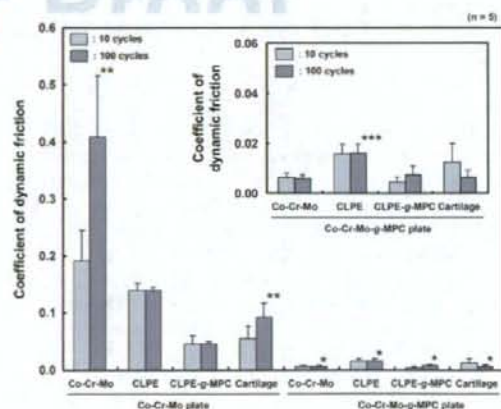


Figure 8. Coefficients of dynamic friction for the various types of pins sliding against the untreated Co-Cr-Mo and Co-Cr-Mo-g-MPC plates. Bar: standard deviations. **t* test, significant difference ($p < 0.001$) when compared with the untreated Co-Cr-Mo plate, ***t* test, significant difference ($p < 0.001$) 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 photoirradiation 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 photoirradiation 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)₂, (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-

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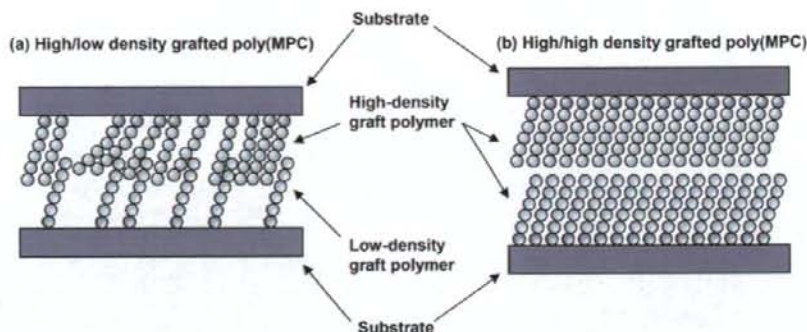


Figure 9. Hypothetical cartoons of high-density grafted poly(MPC)/low-density grafted poly(MPC) and high-density grafted poly(MPC)/high-density grafted poly(MPC) bearing interfaces.

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).^{63,65} 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 bio-compatible 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

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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.

References

- Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005;87:1487-1497.
- Harris WH. The problem is osteolysis. *Clin Orthop* 1995;311:46-53.
- Kobayashi A, Freeman MA, Bonfield W, Kadoya Y, Yamac T, Al-Saffar N, Scott G, Revell PA. Number of polyethylene particles and osteolysis in total joint replacements. A quantitative study using a tissue-digestion method. *J Bone Joint Surg Br* 1997;79:844-848.
- Sochart DH. Relationship of acetabular wear to osteolysis and loosening in total hip arthroplasty. *Clin Orthop* 1999;363:135-150.
- McKellop H, Shen FW, Lu B, Campbell P, Salovey R. Development of an extremely wear-resistant ultra high molecular weight polyethylene for total hip replacements. *J Orthop Res* 1999;17:157-167.
- Muratoglu OK, Bragdon CR, O'Connor DO, Jasty M, Harris WH. A novel method of crosslinking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties: Recipient of the 1999 HAP Paul Award. *J Arthroplasty* 2001;16:149-160.
- Urban JA, Garvin KL, Boese CK, Bryson L, Pedersen DR, Callaghan JJ, Miller RK. Ceramic-on-polyethylene bearing surfaces in total hip arthroplasty. Seventeen to twenty-one-year results. *J Bone Joint Surg Am* 2001;83:1688-1694.
- McMinn DJ, Daniel J, Pynsent PB, Pradhan C. Mini-incision resurfacing arthroplasty of hip through the posterior approach. *Clin Orthop Relat Res* 2005;441:91-98.
- Clarke IC, Good V, Williams P, Schroeder D, Anissian L, Stark A, Oonishi H, Schuldies J, Gustafson G. Ultra-low wear rates for rigid-on-rigid bearings in total hip replacements. *Proc Inst Mech Eng [H]* 2000;214:331-347.
- Fisher J, Hu XQ, Stewart TD, Williams S, Tipper JL, Ingham E, Stone MH, Davies C, Hatto P, Bolton J, Riley M, Hardaker C, Isaac GH, Berry G. Wear of surface engineered metal-on-metal hip prostheses. *J Mater Sci Mater Med* 2004;15:225-235.
- Keel JB, Kuster MS. Massive wear of an incompatible metal-on-metal articulation in total hip arthroplasty. *J Arthroplasty* 2004;19:638-642.
- Korovessis P, Petsinis G, Repanti M, Repantis T. Metallosis after contemporary metal-on-metal total hip arthroplasty. Five to nine-year follow-up. *J Bone Joint Surg Am* 2006;88:1183-1191.
- Savarino L, Granchi D, Ciapetti G, Cenni E, Nardi Pantoli A, Rotini R, et al. Ion release in patients with metal-on-metal hip bearings in total joint replacement: A comparison with metal-on-polyethylene bearings. *J Biomed Mater Res* 2002;63:467-474.
- Dowson D, Hardaker C, Flett M, Isaac GH. A hip joint simulator study of the performance of metal-on-metal joints. I. The role of materials. *J Arthroplasty* 2004;19:118-123.
- Bowsher JG, Nevelos J, Williams PA, Shelton JC. 'Severe' wear challenge to 'as-cast' and 'double heat-treated' large-diameter metal-on-metal hip bearings. *Proc Inst Mech Eng [H]* 2006;220:135-143.
- Brizuela M, Garcia-Luis A, Viviente JL, Braceras I, Onate JL. Tribological study of lubricious DLC biocompatible coatings. *J Mater Sci Mater Med* 2002;13:1129-1133.
- Gutmanas EY, Gotman I. PIRAC Ti nitride coated Ti-6Al-4V head against UHMWPE acetabular cup-hip wear simulator study. *J Mater Sci Mater Med* 2004;15:327-330.
- Oka M, Ushio K, Kumar P, Ikeuchi K, Hyon SH, Nakamura T, Fujita H. Development of artificial articular cartilage. *Proc Inst Mech Eng [H]* 2000;214:59-68.
- Moro T, Takatori Y, Ishihara K, Konno T, Takigawa Y, Matsushita T, Chung UI, Nakamura K, Kawaguchi H. Surface grafting of artificial joints with a biocompatible polymer for preventing periprosthetic osteolysis. *Nat Mater* 2004;3:829-837.
- Moro T, Takatori Y, Ishihara K, Nakamura K, Kawaguchi H. 2006 Frank Stinchfield Award: Grafting of biocompatible polymer for longevity of artificial hip joints. *Clin Orthop Relat Res* 2006;453:58-63.
- Kyomoto M, Moro T, Konno T, Takadama H, Kawaguchi H, Takatori Y, Nakamura K, Yamawaki N, Ishihara K. Effects of photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on physical properties of cross-linked polyethylene in artificial hip joints. *J Mater Sci Mater Med* 2007;18:1809-1815.
- Ishihara K, Ueda T, Nakabayashi N. Preparation of phospholipid polymers and their properties as polymer hydrogel membranes. *Polym J* 1990;22:355-360.
- Ishihara K, Ziats NP, Tierney BP, Nakabayashi N, Anderson JM. Protein adsorption from human plasma is reduced on phospholipids polymers. *J Biomed Mater Res* 1991;25:1397-1407.
- Goda T, Konno T, Takai M, Moro T, Ishihara K. Biomimetic phosphorylcholine polymer grafting from polydimethylsiloxane surface using photo-induced polymerization. *Biomaterials* 2006;27:5151-5160.
- Sibarani J, Takai M, Ishihara K. Surface modification on microfluidic devices with 2-methacryloyloxyethyl phosphorylcholine polymers for reducing unfavorable protein adsorption. *Colloids Surf B Biointerfaces* 2007;54:88-93.
- Ueda H, Watanabe J, Konno T, Takai M, Saito A, Ishihara K. Asymmetrically functional surface properties on biocompatible phospholipid polymer membrane for bioartificial kidney. *J Biomed Mater Res A* 2006;77:19-27.
- Palmer RR, Lewis AL, Kirkwood LC, Rose SF, Lloyd AW, Vick TA, Stratford PW. Biological evaluation and drug delivery application of cationically modified phospholipid polymers. *Biomaterials* 2004;25:4785-4796.
- Snyder TA, Tsukui H, Kihara S, Akimoto T, Litwak KN, Kameneva MV, Yamazaki K, Wagner WR. Preclinical biocompatibility assessment of the EVAHEART ventricular assist device: Coating comparison and platelet activation. *J Biomed Mater Res A* 2007;81:85-92.
- Kuiper KJ, Nordrehaug JE. Early mobilization after protamine reversal of heparin following implantation of phosphorylcholine-coated stents in totally occluded coronary arteries. *Am J Cardiol* 2000;85:698-702.
- Galli M, Sommariva L, Prati F, Zerboni S, Politi A, Bonatti R, Marnetti S, Butti E, Pagano A, Ferraris G. Acute and mid-term results of phosphorylcholine-coated stents in primary coronary stenting for acute myocardial infarction. *Cathet Cardiovasc Intervent* 2001;53:182-187.
- Lewis AL, Hughes PD, Kirkwood LC, Leppard SW, Redman RP, Tolhurst LA, Stratford PW. Synthesis and characterisation of phosphorylcholine-based polymers useful for coating blood filtration devices. *Biomaterials* 2000;21:1847-1859.
- Pavoor PV, Gearing BP, Muratoglu O, Cohen RE, Bellare A. Wear reduction of orthopaedic bearing surfaces using polyelectrolyte multilayer nanocoatings. *Biomaterials* 2006;27:1527-1533.

AQ1

33. Yamamoto M, Kato K, Ikada Y. Ultrastructure of the interface between cultured osteoblasts and surface-modified polymer substrates. *J Biomed Mater Res* 1997;37:29-36.
34. Wang P, Tan KL, Kang ET. Surface modification of poly(tetrafluoroethylene) films via grafting of poly(ethylene glycol) for reduction in protein adsorption. *J Biomater Sci Polym Ed* 2000;11:169-186.
35. Iwata R, Suk-In P, Hoven VP, Takahara A, Akiyoshi K, Iwasaki Y. Control of nanobiointerfaces generated from well-defined biomimetic polymer brushes for protein and cell manipulations. *Biomacromolecules* 2004;5:2308-2314.
36. Kyomoto M, Iwasaki Y, Moro T, Konno T, Miyaji F, Kawaguchi H, Takatori Y, Nakamura K, Ishihara K. High lubricious surface of cobalt-chromium-molybdenum alloy prepared by grafting poly(2-methacryloyloxyethyl phosphorylcholine). *Biomaterials* 2007;28:3121-3130.
37. Yoshida K, Greener EH. Effects of coupling agents on mechanical properties of metal oxide-poly(methacrylate) composites. *J Dent* 1994;22:57-62.
38. Matinlinna JP, Vallittu PK. Bonding of resin composites to etchable ceramic surfaces—An insight review of the chemical aspects on surface conditioning. *J Oral Rehabil* 2007;34:622-630.
39. Bryant SJ, Nuttelman CR, Anseth KS. Cytocompatibility of UV and visible light photoinitiating systems on cultured NIH/3T3 fibroblasts in vitro. *J Biomater Sci Polym Ed* 2000;11:439-457.
40. ASTM. Annual Book of ASTM Standards, vol. 13: Standard specification for cobalt-28 chromium-6 molybdenum alloy casting and casting alloy for surgical implants (UNS R30075). ASTM; 2004. ASTM F75-01.
41. ASTM. Annual Book of ASTM Standards vol. 13: Standard Practice for Surface Preparation and Marking of Metallic Surgical Implants. ASTM; 2004. ASTM F86-04.
42. Seo M, Sato N. Differential composition profiles in depth of thin anodic oxide films on iron-chromium alloy. *Surface Sci* 1979;86:601-609.
43. Ishihara K, Iwasaki Y, Ebihara S, Shindo Y, Nakabayashi N. Photoinduced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on polyethylene membrane surface for obtaining blood cell adhesion resistance. *Colloids Surf B Biointerfaces* 2000;18:325-335.
44. Kyomoto M, Moro T, Konno T, Takadama H, Yamawaki N, Kawaguchi H, Takatori Y, Nakamura K, Ishihara K. Enhanced wear resistance of modified cross-linked polyethylene by grafting with poly(2-methacryloyloxyethyl phosphorylcholine). *J Biomed Mater Res A* 2007;82:10-17.
45. Kyomoto M, Moro T, Miyaji F, Hashimoto M, Kawaguchi H, Takatori Y, Nakamura K, Ishihara K. Effect of 2-methacryloyloxyethyl phosphorylcholine concentration on photo-induced graft polymerization of polyethylene in reducing the wear of orthopaedic bearing surface. *J Biomed Mater Res A* 2008;86:439-447.
46. Northwood E, Fisher J. A multi-directional in vitro investigation into friction, damage and wear of innovative chondroplasty materials against articular cartilage. *Clin Biomech* 2007;22:834-842.
47. ISO. Plastics-film and sheeting-measurement of water-contact angle of corona-treated films. International Organization for Standardization 15989. ISO; 2004.
48. ASTM. Annual Book of ASTM Standards, vol. 13: Standard Test Method for Wear Testing of Polymeric Materials Used in Total Joint Prostheses. ASTM; 2004. ASTM F732-00.
49. Li YS, Tran T, Xu Y, Vecchio NE. Spectroscopic studies of trimethoxypropylsilane and bis(trimethoxysilyl)ethane sol-gel coatings on aluminum and copper. *Spectrochim Acta A: Mol Biomol Spectrosc* 2006;65:779-786.
50. Matsuda T, Kaneko M, Ge S. Quasi-living surface graft polymerization with phosphorylcholine group(s) at the terminal end. *Biomaterials* 2003;24:4507-4515.
51. Braunecker WA, Matyjaszewski K. Controlled/living radical polymerization: Features, developments, and perspectives. *Prog Polym Sci* 2007;32:93-146.
52. Zhang Z, Berns AE, Willbold S, Buitenhuis J. Synthesis of poly(ethylene glycol) (PEG)-grafted colloidal silica particles with improved stability in aqueous solvents. *J Colloid Interface Sci* 2007;310:446-455.
53. Sakamoto H, Doi H, Kobayashi E, Yoneyama T, Suzuki Y, Hanawa T. Structure and strength at the bonding interface of a titanium-segmented polyurethane composite through 3-(trimethoxysilyl) propyl methacrylate for artificial organs. *J Biomed Mater Res A* 2007;82:52-61.
54. Tsukagoshi T, Kondo Y, Yoshino N. Protein adsorption and stability of poly(ethylene oxide)-modified surfaces having hydrophobic layer between substrate and polymer. *Colloids Surf B Biointerfaces* 2007;54:82-87.
55. Puleo DA. Biochemical surface modification of Co-Cr-Mo. *Biomaterials* 1996;17:217-222.
56. Saldívar-García AJ, López HF. Microstructural effects on the wear resistance of wrought and as-cast Co-Cr-Mo-C implant alloys. *J Biomed Mater Res A* 2005;74:269-274.
57. Sheeja D, Tay BK, Nung LN. Tribological characterization of surface modified UHMWPE against DLC-coated Co-Cr-Mo. *Surf Coat Technol* 2005;190:231-237.
58. Saikko V. Wear and friction properties of prosthetic joint materials evaluated on a reciprocating pin-on-flat apparatus. *Wear* 1993;166:169-178.
59. Ishikawa Y, Hiratsuka K, Sasada T. Role of water in the lubrication of hydrogel. *Wear* 2006;261:500-504.
60. Ho SP, Nakabayashi N, Iwasaki Y, Boland T, LaBerge M. Frictional properties of poly(MPC-co-BMA) phospholipid polymer for catheter applications. *Biomaterials* 2003;24:5121-5129.
61. Naka MH, Morita Y, Ikeuchi K. Influence of proteoglycan contents and of tissue hydration on the frictional characteristics of articular cartilage. *Proc Inst Mech Eng [H]* 2005;219:175-182.
62. Bell CJ, Ingham E, Fisher J. Influence of hyaluronic acid on the time-dependent friction response of articular cartilage under different conditions. *Proc Inst Mech Eng [H]* 2006;220:23-31.
63. Kobayashi M, Terayama Y, Hosaka N, Kaido M, Suzuki A, Yamada N, Torikai N, Ishihara K, Takahara A. Friction behavior of high-density poly(2-methacryloyloxyethyl phosphorylcholine) brush in aqueous media. *Soft Matter* 2007;2:740-746.
64. Yamamoto S, Ejaz M, Tsujii Y, Fukuda T. Surface interaction forces of well-defined, high-density polymer brushes studied by atomic force microscopy. 2. Effect of graft density. *Macromolecules* 2000;33:5608-5612.
65. Raviv U, Glasson S, Kampf N, Gohy JF, Jérôme R, Klein J. Lubrication by charged polymers. *Nature* 2003;425:163-165.

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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

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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 (MPC)) (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 (OARSI) 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

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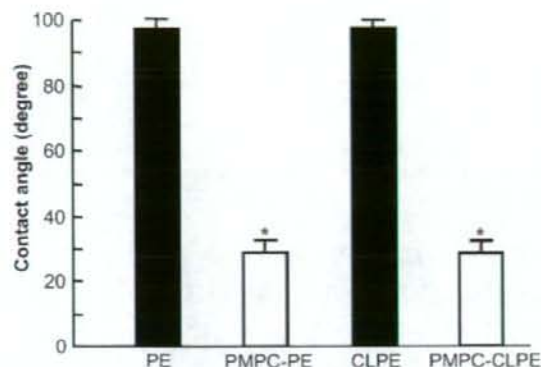


Fig. 1. Contact angles of a water drop on PE plates with or without cross-linking and PMPC grafting. Data are expressed as means (bars) \pm standard errors (error bars) for 10 plates/group. * $p < 0.01$, significant effects of PMPC grafting.

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 peri-prosthetic 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

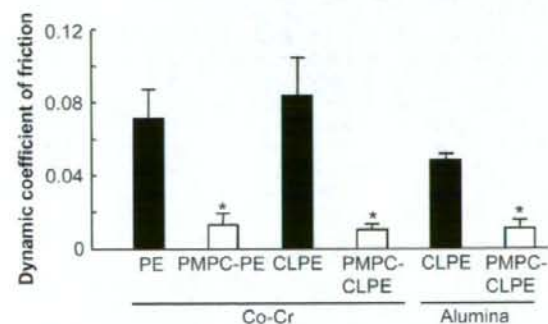


Fig. 2. Dynamic coefficients of friction for the various types of PE plates against Co–Cr alloy and alumina ceramic balls. Data are expressed as means (bars) \pm standard errors (error bars) for 5 plates/group. * $p < 0.01$, significant effects of PMPC grafting.

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 (UVL-400HA, Riko-Kagaku Sangyo, Funabashi, Japan), as previously reported

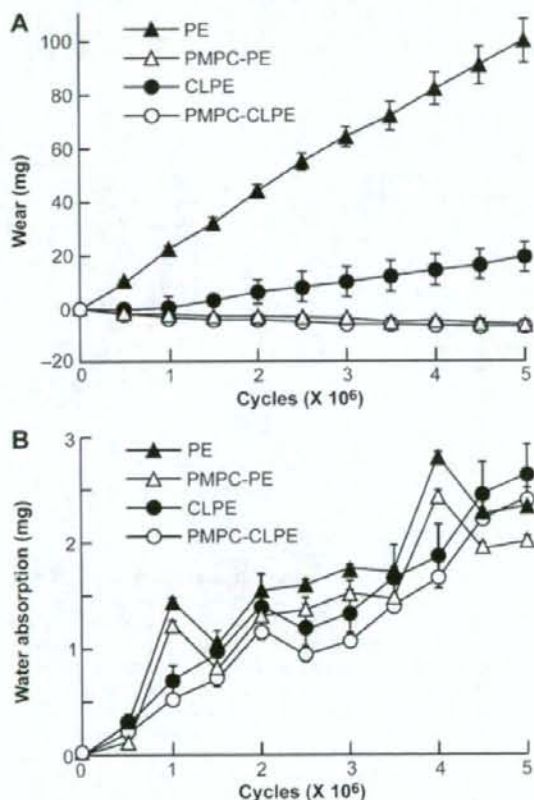


Fig. 3. Wear amount of PE liners with or without cross-linking and PMPC grafting in the hip joint simulator. (A) Time course of wear amount generated from PE, CLPE, PMPC-PE, and PMPC-CLPE liners during 5×10^6 cycles of loading against Co–Cr alloy femoral heads in the hip joint simulator. At intervals 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 (TriboStation 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 μm , 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 (SURFTTEST-501, Mitutoyo, Yokohama, Japan) with a 5 μm 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 μm 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 ($p < 0.05$).

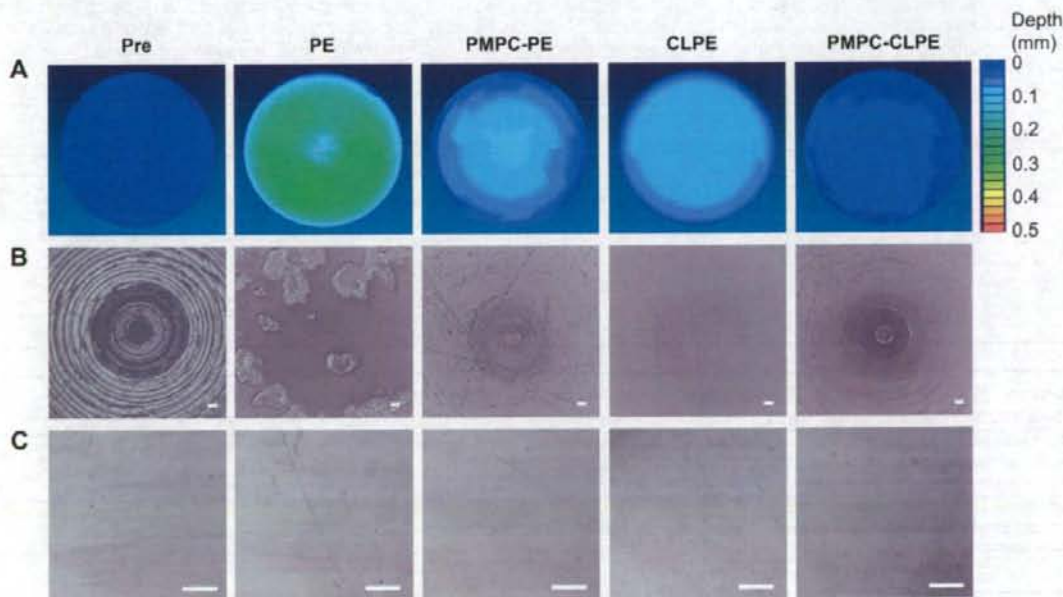


Fig. 4. Optical findings of the surfaces of the four liners and corresponding femoral heads in the hip joint simulator. (A) Three-dimensional morphometric analysis and (B) confocal scanning laser microscopic analysis of PE, PMPC-PE, CLPE, and PMPC-CLPE liners surfaces before (pre) and after 5×10^6 cycles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

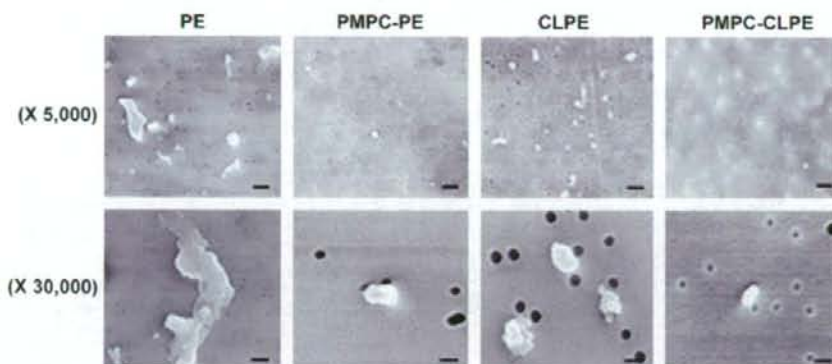


Fig. 5. SEM images of the wear particles isolated from lubricants of the simulators with four kinds of liners. Low (top; $\times 5000$) and high (bottom; $\times 30,000$) magnifications of SEM images of the wear particles isolated from lubricants of the simulators with four kinds of liners. Scale bars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

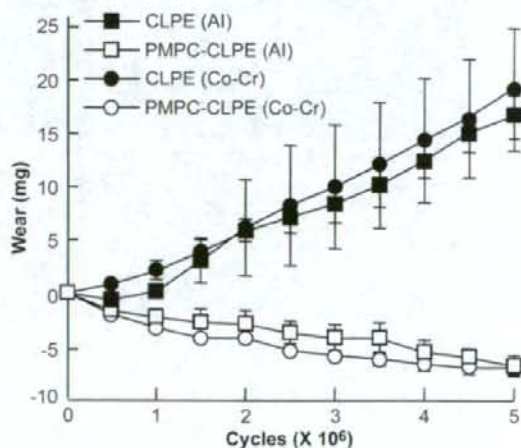


Fig. 6. Wear resistance of CLPE liners with and without PMPC grafting against Co-Cr alloy or alumina ceramic femoral heads in the hip joint simulator. Time course of the wear amount generated from CLPE or PMPC-CLPE liners during 5×10^6 cycles of loading against Co-Cr alloy or alumina ceramic femoral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

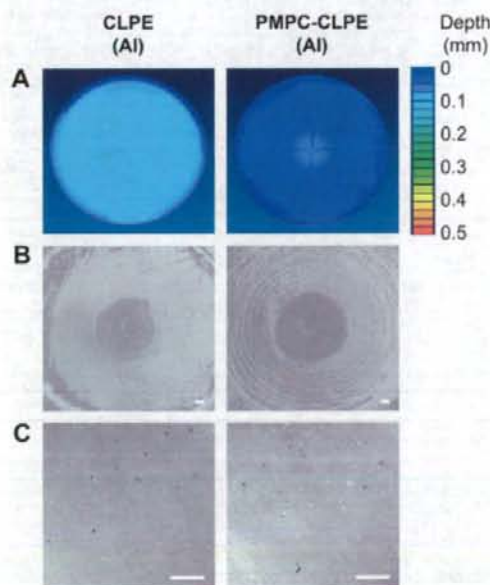


Fig. 7. Optical findings of the surfaces of the CLPE liners with and without PMPC grafting and the alumina ceramic femoral heads in the hip joint simulator. (A) Three-dimensional morphometric analysis and (B) confocal scanning laser microscopic analysis of the liner surfaces after 5×10^6 cycles of loading.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

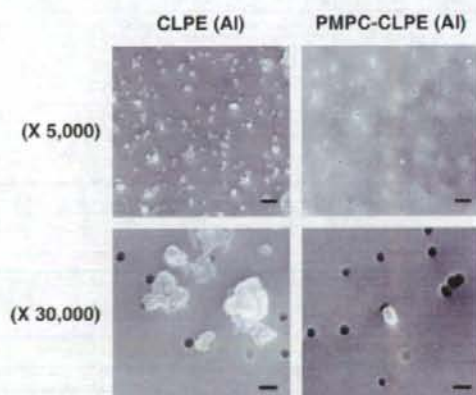


Fig. 8. SEM images of the wear particles isolated from lubricants of the simulators with CLPE liners with and without PMPC grafting against alumina ceramic femoral heads. Low (top; $\times 5000$) and high (bottom; $\times 30,000$) magnifications of SEM images of the wear particles isolated from lubricants 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 factor 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.

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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.

References

- [1] Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005;87:1487–97.
- [2] Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007;89:780–5.
- [3] Merx H, Dreinhöfer K, Schrader P, Stürmer T, Puhl W, Günther KP, et al. International variation in hip replacement rates. *Ann Rheum Dis* 2003;62:222–6.
- [4] Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartil* 2008;16:137–62.
- [5] Dumbleton JH, Manley MT, Eddin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. *J Arthroplasty* 2002;17:649–61.
- [6] Manley MT, D'Antonio JA, Capello WN, Eddin AA. Osteolysis: a disease of access to fixation interfaces. *Clin Orthop* 2002;405:129–37.
- [7] Kim S. Changes in surgical loads and economic burden of hip and knee replacements in the US: 1997–2004. *Arthritis Rheum* 2008;59:481–8.
- [8] Kurtz SM, Ong KL, Schmier J, Mowat F, Saleh K, Dyvik E, et al. Future clinical and economic impact of revision total hip and knee arthroplasty. *J Bone Joint Surg Am* 2007;89:144–51.
- [9] Jacobs JJ, Roebuck KA, Archibeck M, Hallab NJ, Glant TT. Osteolysis: basic science. *Clin Orthop* 2001;393:71–7.
- [10] Glant TT, Jacobs JJ, Molnar G, Shanbhag AS, Valyon M, Galante JO. Bone resorption activity of particulate-stimulated macrophages. *J Bone Miner Res* 1993;8:1071–9.
- [11] Atienza Jr C, Maloney WJ. Highly cross-linked polyethylene bearing surfaces in total hip arthroplasty. *J Surg Orthop Adv* 2008;17:27–33.
- [12] Collier JP, Currier BH, Kennedy FE, Currier JH, Timmins GS, Jackson SK, et al. Comparison of cross-linked polyethylene materials for orthopaedic applications. *Clin Orthop Relat Res* 2003;414:289–304.
- [13] Muratoglu OK, Bragdon CR, O'Connor DO, Jasty M, Harris WH. A novel method of cross-linking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties. Recipient of the 1999 HAP Paul Award. *J Arthroplasty* 2001;16:149–60.
- [14] Jacobs CA, Christensen CP, Greenwald AS, McKellop H. Clinical performance of highly cross-linked polyethylene in total hip arthroplasty. *J Bone Joint Surg Am* 2007;89:2779–86.
- [15] Capello WN, D'Antonio JA, Feinberg JR, Manley MT. Alternative bearing surfaces: alumina ceramic bearings for total hip arthroplasty. *Instr Course Lect* 2005;54:171–6.
- [16] Onishi H, Kim SC, Takao Y, Kyomoto M, Iwamoto M, Ueno M. Wear of highly cross-linked polyethylene acetabular cup in Japan. *J Arthroplasty* 2006;21:944–9.
- [17] Wroblewski BM, Siney PD, Fleming PA. Low-friction arthroplasty of the hip using alumina ceramic and cross-linked polyethylene. A 17-year follow-up report. *J Bone Joint Surg Br* 2005;87:1220–1.
- [18] Kirk TB, Wilson AS, Stachowiak GW. The morphology and composition of the superficial zone of mammalian articular cartilage. *J Orthopaedic Rheumatol* 1993;6:21–8.
- [19] Ishihara K, Ueda T, Nakabayashi N. Preparation of phospholipid polymers and their properties as polymer hydrogel membrane. *Polym J* 1990;22:355–60.
- [20] Ueda T, Oshida H, Kurita K, Ishihara K, Nakabayashi N. Preparation of 2-methacryloyloxyethyl phosphorylcholine copolymers with alkyl methacrylates and their blood compatibility. *Polym J* 1992;24:1259–69.
- [21] Ueda H, Watanabe J, Konno T, Takai M, Saito A, Ishihara K. Asymmetrically functional surface properties on biocompatible phospholipid polymer membrane for bioartificial kidney. *J Biomed Mater Res A* 2006;77:19–27.
- [22] Sawada S, Iwasaki Y, Nakabayashi N, Ishihara K. Stress response of adherent cells on a polymer blend surface composed of a segmented polyurethane and MPC copolymers. *J Biomed Mater Res A* 2006;79:476–84.
- [23] Sibarami J, Takai M, Ishihara K. Surface modification on microfluidic devices with 2-methacryloyloxyethyl phosphorylcholine polymers for reducing unfavorable protein adsorption. *Colloids Surf B Biointerface* 2007;54(1):88–93.
- [24] Snyder TA, Tsukui H, Kihara S, Akimoto T, Litwak KN, Kamenewa MV, et al. Preclinical biocompatibility assessment of the EVAHEART ventricular assist device: coating comparison and platelet activation. *J Biomed Mater Res A* 2007;81:85–92.
- [25] Fujii K, Matsumoto HN, Koyama Y, Iwasaki Y, Ishihara K, Takakuda K. Prevention of biofilm formation with a coating of 2-methacryloyloxyethyl phosphorylcholine polymer. *J Vet Med Sci* 2008;70:167–73.

- [26] Bakhal A, Booth J, Delahunty N, Nugara F, Clayton T, McNeill J, et al. The SV stent study: a prospective, multicentre, angiographic evaluation of the Bio-divySio phosphorylcholine coated small vessel stent in small coronary vessels. *Int J Cardiol* 2005;102:95–102.
- [27] Goda T, Ishihara K. Soft contact lens biomaterials from bioinspired phospholipid polymers. *Expert Rev Med Devices* 2006;3:167–74.
- [28] Myers GJ, Johnstone DR, Swyer WJ, McFeer S, Maxwell SL, Squires C, et al. Evaluation of Mimesys phosphorylcholine (PC)-coated oxygenators during cardiopulmonary bypass in adults. *J Extra Corp Technol* 2003;35:6–12.
- [29] Kyomoto M, Moro T, Konno T, Takadama H, Kawaguchi H, Takatori Y, et al. Effects of photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on physical properties of cross-linked polyethylene in artificial hip joints. *J Mater Sci Mater Med* 2007;18:1809–15.
- [30] Kyomoto M, Moro T, Konno T, Takadama H, Yamawaki N, Kawaguchi H, et al. Enhanced wear resistance of modified cross-linked polyethylene by grafting with poly(2-methacryloyloxyethyl phosphorylcholine). *J Biomed Mater Res A* 2007;82:10–7.
- [31] Moro T, Takatori Y, Ishihara K, Konno T, Takigawa Y, Matsushita T, et al. Surface grafting of artificial joints with a biocompatible polymer for preventing periprosthetic osteolysis. *Nat Mater* 2004;3:829–36.
- [32] Kyomoto M, Moro T, Miyaji F, Konno T, Hashimoto M, Kawaguchi H, et al. Enhanced wear resistance of orthopaedic bearing due to the cross-linking of poly(MPC) graft chains induced by gamma-ray irradiation. *J Biomed Mater Res B Appl Biomater* 2008;84:320–7.
- [33] Moro T, Takatori Y, Ishihara K, Nakamura K, Kawaguchi H. 2006 Frank Stinchfield Award: grafting of biocompatible polymer for longevity of artificial hip joints. *Clin Orthop Relat Res* 2006;453:58–63.
- [34] Kyomoto M, Moro T, Miyaji F, Hashimoto M, Kawaguchi H, Takatori Y, et al. Effect of 2-methacryloyloxyethyl phosphorylcholine concentration on photo-induced graft polymerization of polyethylene in reducing the wear of orthopaedic bearing surface. *J Biomed Mater Res A* 2008;86:439–47.
- [35] Ishihara K, Iwasaki Y, Ebihara S, Shindo Y, Nakabayashi N. Photoinduced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on polyethylene membrane surface for obtaining blood cell adhesion resistance. *Colloids Surf B Biointerface* 2000;18:325–35.
- [36] Kumar P, Oka M, Ikeuchi K, Shimizu K, Yamamoto T, Okumura H, et al. Low wear rate of UHMWPE against zirconia ceramic (Y-PSZ) in comparison to alumina ceramic and SUS 316L alloy. *J Biomed Mater Res* 1991;25:813–28.
- [37] Jono K, Takigawa Y, Takadama H, Mizuno M, Nakamura T. A multi-station hip joint simulator study and wear characterization of commercial hip endoprostheses. *Ceram Eng Sci Proc* 2003;24:255–60.
- [38] Paul JP. Forces transmitted by joints in the human body. *Proc Inst Mech Eng* 1967;181:8–15.
- [39] Muratoglu OK, Greenbaum ES, Bragdon CR, Jasty M, Freiberg AA, Harris WH. Surface analysis of early retrieved acetabular polyethylene liners: a comparison of conventional and highly crosslinked polyethylenes. *J Arthroplasty* 2004;19:68–77.
- [40] Tipper JL, Galvin AL, Williams S, McEwen HM, Stone MH, Ingham E, et al. Isolation and characterization of UHMWPE wear particles down to ten nanometers in size from in vitro hip and knee joint simulators. *J Biomed Mater Res A* 2006;78:473–80.
- [41] Dowson D, Jin ZM. Micro-elastohydrodynamic lubrication of synovial joints. *Eng Med* 1986;15:63–5.
- [42] Hills BA. Boundary lubrication in vivo. *Proc Inst Mech Eng [H]* 2000;214:83–94.
- [43] Ishihara K, Nomura H, Mihara T, Kurita K, Iwasaki Y, Nakabayashi N. Why do phospholipid polymers reduce protein adsorption? *J Biomed Mater Res* 1998;39:323–30.
- [44] Matsuda Y, Kobayashi M, Annaka M, Ishihara K, Takahara A. Dimensions of a free linear polymer and polymer immobilized on silica nanoparticles of a zwitterionic polymer in aqueous solutions with various ionic strengths. *Langmuir* 2008;24:8772–8.
- [45] Kobayashi M, Terayama Y, Hosaka N, Kaido M, Suzuki A, Yamada N, et al. Friction behavior of high-density poly(2-methacryloyloxyethyl phosphorylcholine) brush in aqueous media. *Soft Mater* 2007;2:740–6.
- [46] Green TR, Fisher J, Stone M, Wroblewski BM, Ingham E. Polyethylene particles of a 'critical size' are necessary for the induction of cytokines by macrophages in vitro. *Biomaterials* 1998;19:2297–302.
- [47] Galvin AL, Tipper JL, Ingham E, Fisher J. Nanometre size wear debris generated from crosslinked and non-crosslinked ultra high molecular weight polyethylene in artificial joints. *Wear* 2005;259:977–83.
- [48] Ingram JH, Stone M, Fisher J, Ingham E. The influence of molecular weight, crosslinking and counterface roughness on TNF-alpha production by macrophages in response to ultra high molecular weight polyethylene particles. *Biomaterials* 2004;25:3511–22.
- [49] Bradford L, Baker DA, Graham J, Chawan A, Ries MD, Pruitt LA. Wear and surface cracking in early retrieved highly cross-linked polyethylene acetabular liners. *J Bone Joint Surg Am* 2004;86:1271–82.
- [50] Pruitt LA. Deformation, yielding, fracture and fatigue behavior of conventional and highly cross-linked ultra high molecular weight polyethylene. *Biomaterials* 2005;26:905–15.
- [51] Childs LM, Goater JJ, O'Keefe RJ, Schwarz EM. Efficacy of etanercept for wear debris-induced osteolysis. *J Bone Miner Res* 2001;16:338–47.
- [52] Childs LM, Paschalis EP, Xing L, Dougall WC, Anderson D, Boskey AL, et al. In vivo RANK signaling blockade using the receptor activator of NF-kappa B:Fc effectively prevents and ameliorates wear debris-induced osteolysis via osteoclast depletion without inhibiting osteogenesis. *J Bone Miner Res* 2002;17:192–9.
- [53] Goater JJ, O'Keefe RJ, Rosier RN, Puzas JE, Schwarz EM. Efficacy of ex vivo OPG gene therapy in preventing wear debris induced osteolysis. *J Orthop Res* 2002;20:169–73.
- [54] Heisel C, Streich N, Krachler M, Jakubowitz E, Kretzer JP. Characterization of the running-in period in total hip resurfacing arthroplasty: an in vivo and in vitro metal ion analysis. *J Bone Joint Surg Am* 2008;90(Suppl. 3):125–33.