

High lubricious surface of cobalt–chromium–molybdenum alloy prepared by grafting poly(2-methacryloyloxyethyl phosphorylcholine)

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Abstract

Osteolysis caused by wear particles from polyethylene in artificial hip joints is of great concern. Various bearing couple combinations, bearing material improvements, and surface modifications have been attempted to reduce such wear particles. With the aim of reducing the wear and developing a novel artificial hip-joint system, we created a highly lubricious metal-bearing material: A 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer was grafted onto the surface of the cobalt–chromium–molybdenum (Co–Cr–Mo) alloy. For ensuring the long-term retention of poly(MPC) on the Co–Cr–Mo alloy, we used a 4-methacryloyloxyethyl trimellitate anhydride (4-META) intermediate layer and photo-induced graft polymerization technique to create a strong bonding between the Co–Cr–Mo substrate and the poly(MPC) chain via the 4-META layer. The Co–Cr–Mo alloy was pretreated with nitric acid and O₂ plasma to facilitate efficient interaction between the 4-META carboxyl group and the surface hydroxyl group on the Cr oxide passive layer of the Co–Cr–Mo alloy. After MPC grafting, the MPC unit peaks were clearly observed in the Fourier-transform infrared spectroscopy with attenuated total reflection (FT-IR/ATR) and X-ray photoelectron spectroscopy (XPS) spectra of the Co–Cr–Mo surface. Tribological studies with a pin-on-plate machine revealed that surface MPC grafting markedly lowered the friction coefficient. We concluded that the grafted poly(MPC) layer successfully provided high lubricity to the Co–Cr–Mo surface.

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1. Introduction

The number and prevalence of primary and revision hip and knee joint replacements are substantially increasing worldwide every year [1]. This implies that the quality of artificial joints is becoming increasingly important. Most patients who receive an artificial joint experience a dramatic relief from pain and enjoy a rapid improvement in their quality of life. The most widely used bearing couple

in artificial hip-joint systems is the combination of an ultra-high-molecular weight polyethylene (UHMWPE) acetabular component and a metal femoral component. The 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 these particles have focused on bearing material improvement and the use of

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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 [8,9]. The advantages of the Co–Cr–Mo/Co–Cr–Mo bearings are the absence of the generation of UHMWPE wear debris and decreased wear as compared to that in the case of the Co–Cr–Mo/UHMWPE bearings [10,11]. However, even in the Co–Cr–Mo/Co–Cr–Mo bearings, aseptic loosening induced by wear particles and metallosis remain as serious issues in revision surgeries [12,13]. 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 [14].

To reduce such wear particles, improvements in the bearing materials and surface modifications of the Co–Cr–Mo alloy have been attempted [15,16]. Surface coating may reduce the UHMWPE wear without compromising the bulk mechanical properties of the implant materials. Various “hardening treatments” on metal-bearing surfaces, such as diamond-like carbon coating, titanium nitride coating, and ion implantation have been attempted [17–19]. Although these surface modifications may improve the THA survivorship, the limited THA longevity imposes restrictions for its application in younger patients. Consequently, the possibility of replacing the femoral head alone, in either solid or articular surface replacement form, during revision surgeries of metal-on-metal THA remains an attractive feature of such implants. However, the Co–Cr–Mo alloy or the hardening-treated Co–Cr–Mo alloy may induce damage to the cartilaginous tissue.

On the other hand, previous studies reported that highly lubricious hydrogel polymer used as an artificial cartilage did not damage against the cartilaginous tissue [20,21]. 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) [22–24]. MPC is a methacrylate monomer with a phospholipid polar group in a side chain and is used to prepare novel polymer biomaterials, as designed by Ishihara et al. [25] who were inspired by the neutral phospholipids of cell membranes. Many polymers containing the MPC unit are widely used as biomaterials [26–33]. Moreover, various medical devices have already been developed using poly(MPC) and are being used clinically. The efficacy of MPC polymer as a biomaterial has been well verified [34–36]. Based on the biocompatibility and

hydrophilicity of poly(MPC), we have been developing new artificial joints with highly lubricious bearing surfaces that are formed by photo-induced radical graft polymerization.

In this study, we synthesized a highly lubricious metal-bearing material in which the MPC polymer was grafted onto the surface of the Co–Cr–Mo alloy (Co–Cr–Mo-*g*-MPC) for developing a novel artificial hip-joint system—artificial femoral head and metal-on-metal (Co–Cr–Mo/Co–Cr–Mo) type—for THA. We also investigated the surface structure and tribological properties of Co–Cr–Mo-*g*-MPC.

2. Materials and methods

2.1. Co–Cr–Mo alloy substrate and pretreatments

The Co–Cr–Mo alloy was supplied by Yoneda Advanced Casting Co., Ltd (Takaoka, Japan). The chemical composition of the Co–Cr–Mo alloy used in this study is listed in Table 1. This alloy was manufactured according to the ASTM F75 standard specification for Co–28Cr–6Mo alloy [37]. 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 35vol% nitric acid at room temperature for 35 min according to the ASTM F86-04 standard [38]. This treatment provides passivation by surface oxidation and can dissolve certain foreign materials that may remain from the previous procedure. Moreover, a previous study reported that the Cr concentration of dry-polished stainless steel was lower at the surface than in the bulk [39]. We therefore treated the surface with nitric acid with the aim of increasing the Cr concentration by “re-surfacing.”

After the nitric acid treatment, the Co–Cr–Mo samples were irradiated with O₂ plasma at 500-W high-frequency output and 150 mL/min O₂ gas flow for 5 min by using O₂ plasma etcher (PR500, Yamato Scientific Co., Ltd., Tokyo, Japan). The O₂ plasma treatment increased the thickness of the surface oxide layer.

2.2. 4-Methacryloxyethyl trimellitate anhydride coating on Co–Cr–Mo alloy and MPC graft polymerization

4-Methacryloxyethyl trimellitate anhydride (4-META) and acetone were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). The previous studies suggested that 4-META and methacrylates were applicable as photocurable bonding liners that can bind a resin composite to a metal substrate [40–42]. MPC was synthesized industrially by using the method developed by Ishihara et al. [25] and was supplied by AI Bio-Chips Co., Ltd. (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. 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 [43].

The synthesis of Co–Cr–Mo-*g*-MPC is schematically illustrated in Fig. 1. The various pretreated Co–Cr–Mo samples were coated with an

Table 1
Chemical composition (%) of the Co–Cr–Mo alloy

Cr	Mo	C	Ni	Fe	Si	Mn	Al	Co
28.61	5.96	0.03	0.02	0.03	0.54	0.40	0.02	Bal.

acetone solution containing 10mass% 4-META by using a spin coater (K-359 S-1, Kyowariken Inc., Tokyo, Japan) and then dried in the dark at 40 °C for 3 h to remove the acetone. MPC and D2959 were dissolved in degassed ethanol to a concentration of 2mass% and 0.1mass%, respectively. The Co–Cr–Mo samples coated with 4-META after various pretreatments were immersed in the MPC–ethanol solution containing D2959. Photo-induced graft polymerization on the Co–Cr–Mo surface was carried out using UV irradiation (UVL-400HA ultra-high-pressure mercury lamp, Riko-Kagaku Sangyo Co., Ltd., Finabashi, Japan) with an intensity of 5 mW/cm² at 60 °C for 10 min with a Toshiba D-35 filter to allow the passage of UV light of only 350 ± 50 nm wavelength. After the polymerization, the Co–Cr–Mo-*g*-MPC samples were removed from the solution, washed with ethanol, and dried at room temperature.

2.3. MPC graft polymerization on cross-linked polyethylene

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

MPC grafting onto the CLPE surface was performed as described in previous studies [23,24]. They 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. Photo-induced 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.

2.4. 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 (FT-IR) spectroscopy with attenuated total reflection (ATR) equipment. The FT-IR/ATR spectra were obtained using an FT-IR 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 using X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS-HSi165, Kratos Analytical Ltd., UK) equipped with a 15-kV Mg-K α radiation source at the anode. The take-off angle of the photoelectrons was maintained at 90°. Five scans (approximately 260–425 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 using the sessile drop method with 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 [44]. Measurements were repeated six times for each sample, and the average values were considered as the contact angles.

2.5. Surface observation by fluorescence microscopy

We used rhodamine 6G (Wako Pure Chemical Industries, Ltd., Osaka, Japan) that can be applied simply and rapidly to a polymer coating and

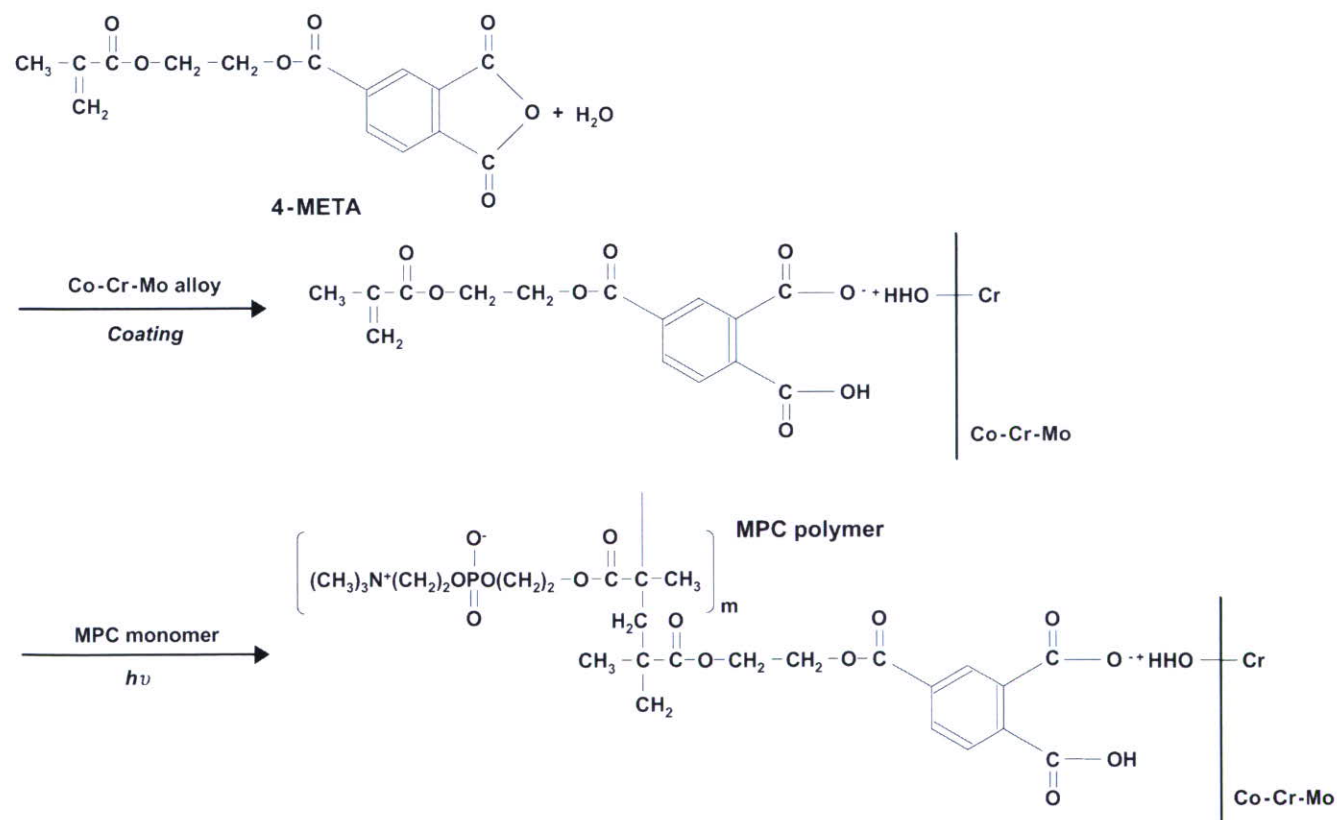


Fig. 1. Scheme for the synthesis of Co–Cr–Mo-*g*-MPC.

imaged using fluorescence microscopy (FM). Wang et al. [45] found that rhodamine 6G effectively stains poly(MPC) that possesses great structural similarity to lipids. This simple staining technique enables the evaluation of the coated area by FM.

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

A fluorescence microscope (Axioskop 2 Plus, Carl Zeiss AG, Oberkochen, Germany) was used for FM imaging and examination of all samples. Pseudo-color images were obtained using a CCD camera (VB-7010, Keyence Co., Osaka, Japan) and imaging software (VH analyzer 2.51, Keyence Co., Osaka, Japan). Lenses with $\times 10$ magnification and appropriate exposure time (approximately 1/10 s) were employed to obtain best image quality of the various samples.

It is known that most fluorescent dyes undergo a process called photobleaching under normal imaging conditions, with subsequent deterioration during fluorescence [45]. In general, the fluorescence intensity decreases with time during imaging [45]. In the present study, the Co–Cr–Mo-*g*-MPC samples were stained with rhodamine 6G, and they were illuminated within 5 min of staining. The time required for appropriate exposure was within 1–2 min. It was therefore assumed that the effect of photobleaching of rhodamine 6G was not very significant under these experimental conditions.

2.6. Friction test

The friction coefficients between the pins fabricated from various materials and the untreated Co–Cr–Mo ($n = 2$) or Co–Cr–Mo-*g*-MPC (pretreated with nitric acid and O₂ plasma, $n = 3$) plates were measured using a custom-made pin-on-plate machine [46]. Each pin was a cylinder measuring 5 mm in height and 9 mm in diameter. Friction tests were carried out at a temperature of 37 °C, a contact stress of 2.4 MPa, and a swing distance of 25 mm with a frequency of 1 Hz [47]. The lubricant used was a mixture of 27 vol% bovine serum, 20 mM/L of ethylene diamine tetraacetic acid (EDTA), and 0.2 mass% sodium azide [48]. The friction tests were performed up to maximum 5.0×10^4 cycles (preliminary test, $n = 1$), and the lubricant was not changed during the tests.

3. Results

Fig. 2 shows the FT-IR/ATR spectra of the untreated Co–Cr–Mo sample and the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC sample. Absorption peaks were not observed for the Co–Cr–Mo sample before the MPC grafting and for either the nitric acid- or O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC samples (data not shown). In contrast, new absorption peaks were observed only for the Co–Cr–Mo-*g*-MPC samples pretreated with both nitric acid and O₂ plasma. The peaks at 1720, 1550, and 1460 cm⁻¹ are attributed to the aromatic ring C=O and -CH₂- in the 4-META and MPC graft polymer. The peaks at 1080 and 970 cm⁻¹ are due to the phosphate group in the MPC unit [25].

Table 2 summarizes the elemental compositions of the Co–Cr–Mo surfaces that were subjected to the different types of pretreatments. After the nitric acid pretreatment, the O₂ and Co compositions decreased and the Cr and Mo compositions increased. After O₂ plasma pretreatment, the O₂ composition increased to approximately 53% due to the formation of the surface oxide layer. After the combined nitric acid and O₂ plasma pretreatment, the compositions

of O₂, Co, and Cr were higher than those before the pretreatment.

The XPS spectra of the binding energy region of the Co_{2p}, Cr_{2p}, and Mo_{3d} electrons obtained from the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo sample before and after the 4-META coating are shown in Fig. 3. Prior to the 4-META coating, the Co oxide (Co²⁺), Cr oxide (Cr³⁺), and Mo oxide (Mo⁴⁺ and Mo⁶⁺) peaks were observed in the Co_{2p}, Cr_{2p}, and Mo_{3d} spectra, respectively. After the 4-META coating, Co_{2p} and Mo_{3d} were depleted but Cr_{2p} was almost unchanged.

Fig. 4 shows the XPS spectra (N_{1s} and P_{2p}) of the untreated Co–Cr–Mo sample and the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC sample. In both N_{1s} and P_{2p} spectra, the peaks appeared only for Co–Cr–Mo-*g*-MPC. The peaks at 403 and 134 eV were assigned to the -N⁺(CH₃)₃ and phosphate groups, respectively. These peaks are the characteristic of the phosphorylcholine present in the MPC units.

Table 3 summarizes the elemental compositions of the Co–Cr–Mo-*g*-MPC surfaces that were subjected to different types of pretreatments. The surface nitrogen (N) and phosphorous (P) compositions in the Co–Cr–Mo-*g*-MPC samples were higher than those in the untreated Co–Cr–Mo samples. It should be noted that in the Co–Cr–Mo-*g*-MPC samples pretreated with both nitric acid and O₂ plasma, the measured N and P compositions increased to 3.0 and 2.9, respectively, and the Co, Cr, and Mo from the Co–Cr–Mo substrate were not detected.

Fig. 5 shows the static water contact angle on the Co–Cr–Mo surfaces subjected to different types of pretreatments before and after the MPC grafting. The

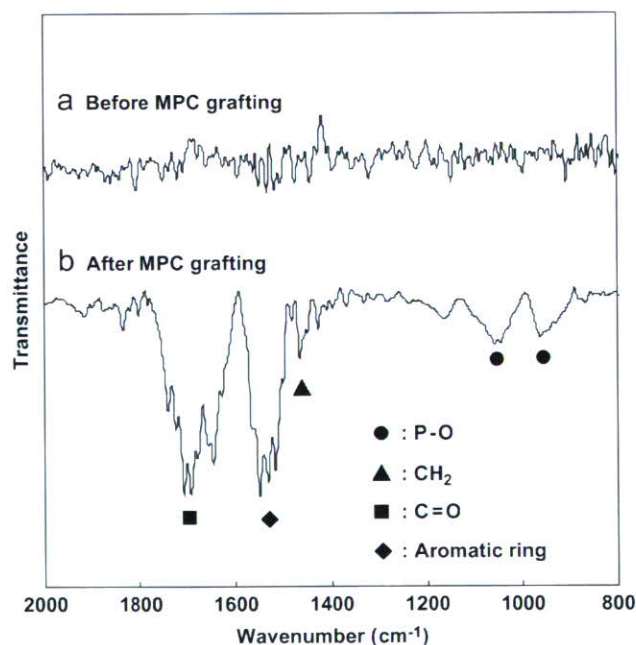


Fig. 2. FT-IR/ATR spectra of the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo sample (a) before and (b) after MPC grafting.

static water contact angle on the Co–Cr–Mo surface before the MPC grafting was approximately 70° – 90° ; however, among the three differently pretreated surfaces, the nitric acid- and O_2 plasma-pretreated Co–Cr–Mo-*g*-MPC surface showed the lowest angle. The static water contact angle on the nitric acid- and O_2 plasma-pretreated Co–Cr–Mo-*g*-MPC surface was as low as 15° . On the other hand, compared to the angle on the untreated Co–Cr–Mo surface, the angle on the only nitric acid-pretreated Co–Cr–Mo-*g*-MPC surface was almost unchanged (approximately 65°) and that on the only O_2 plasma-pretreated Co–Cr–Mo-*g*-MPC surface was slightly decreased to 45° .

Fig. 6 shows the FM images of the untreated Co–Cr–Mo surface and the nitric acid- and O_2 plasma-pretreated Co–Cr–Mo-*g*-MPC surface. On the Co–Cr–Mo-*g*-MPC surface, rhodamine 6G stained poly(MPC) selectively (Fig. 6(b)). This resulted in a large contrast in the fluorescence intensity between the MPC-grafted layer (green–yellow) and the non-grafted substrates (blue) (Fig. 6(d)). The poly(MPC) layer stained with rhodamine 6G was more clearly visible but the staining was not uniform. It therefore indicates that the grafting of the poly(MPC) layer on the Co–Cr–Mo surface is not uniform. On the untreated Co–Cr–Mo surface, such a contrast was not observed (Fig. 6(a) and (c)).

Fig. 7 shows the friction coefficients of the sliding couples, namely, Co–Cr–Mo-*g*-MPC, CLPE, CLPE-*g*-MPC, and untreated Co–Cr–Mo pins sliding against the Co–Cr–Mo-*g*-MPC and untreated Co–Cr–Mo plates. The Co–Cr–Mo/Co–Cr–Mo couple showed a high friction coefficient of approximately 0.24 in the initial 10 cycles; the value increased gradually and reached approximately 0.38 after 5.0×10^4 cycles. The CLPE/Co–Cr–Mo-*g*-MPC and Co–Cr–Mo/Co–Cr–Mo-*g*-MPC couples showed a lower friction coefficient than the CLPE/untreated Co–Cr–Mo and Co–Cr–Mo/untreated Co–Cr–Mo couples, respectively. The CLPE/Co–Cr–Mo-*g*-MPC couple showed the lowest friction coefficient of approximately 0.05, and this value was almost steady during the experiment. In both CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC and Co–Cr–Mo-*g*-MPC/Co–Cr–Mo-*g*-MPC couples, the poly(MPC) layer sliding against the MPC polymer layer showed almost the same friction coefficient of approximately 0.12 up to the initial 100 cycles. After 5.0×10^4 cycles, the friction coefficients of the Co–Cr–Mo/Co–Cr–

Mo-*g*-MPC and Co–Cr–Mo-*g*-MPC/Co–Cr–Mo-*g*-MPC couples increased, whereas that of the CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC couple decreased.

4. Discussion

In this study, with the aim of reducing wear, we synthesized a high lubricious Co–Cr–Mo alloy surface by poly(MPC) grafting for its application in artificial joints. To ensure the in vivo long-term retention of this

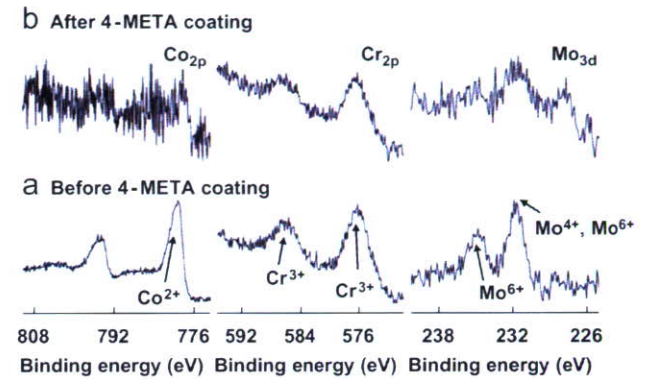


Fig. 3. XPS spectra of the binding energy region of the Co_{2p} , Cr_{2p} , and Mo_{3d} electrons from the nitric acid- and O_2 plasma-pretreated Co–Cr–Mo samples (a) before and (b) after the 4-META coating.

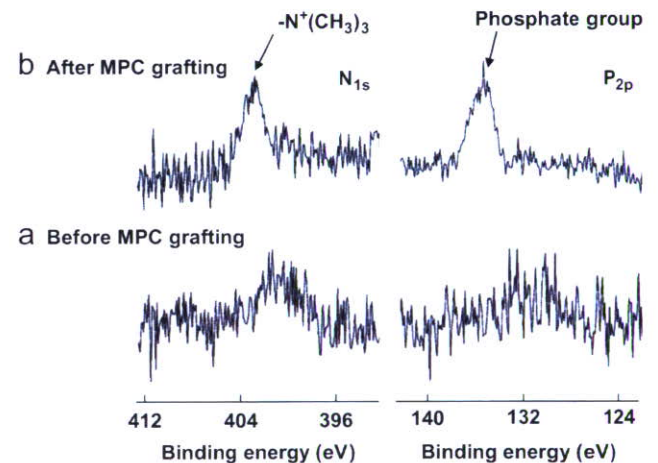


Fig. 4. XPS spectra (N_{1s} and P_{2p}) of the (a) untreated Co–Cr–Mo and (b) nitric acid- and O_2 plasma-pretreated Co–Cr–Mo-*g*-MPC samples.

Table 2
Surface elemental composition (%) of the pretreated Co–Cr–Mo alloy before MPC graft polymerization

Pretreatment	C_{1s}	O_{1s}	N_{1s}	P_{2p}	Co_{2p}	Cr_{2p}	Mo_{3d}
Untreated	44.2 (5.1)	39.3 (2.8)	0.6 (0.2)	0.0 (0.0)	10.5 (2.5)	4.5 (0.5)	1.0 (0.2)
Nitric acid	29.6 (3.8)	37.3 (1.6)	0.4 (0.8)	0.0 (0.0)	9.4 (0.7)	21.3 (2.1)	2.1 (0.2)
O_2 plasma	13.9 (0.5)	53.5 (0.9)	0.0 (0.0)	0.0 (0.0)	30.5 (1.2)	1.8 (0.5)	0.3 (0.1)
Nitric acid + O_2 plasma	14.6 (1.3)	52.9 (2.7)	0.0 (0.0)	0.0 (0.0)	26.7 (1.5)	5.4 (0.2)	0.4 (0.0)

$n = 5$.

The standard deviations are shown in parentheses.

Table 3
Surface elemental composition (%) of the Co–Cr–Mo-*g*-MPC samples that were subjected to different types of pretreatments

Pretreatment	MPC treatment	C _{1s}	O _{1s}	N _{1s}	P _{2p}	Co _{2p}	Cr _{2p}	Mo _{3d}
Nitric acid + O ₂ plasma	Untreated	14.6 (1.3)	52.9 (2.7)	0.0 (0.0)	0.0 (0.0)	26.7 (1.5)	5.4 (0.2)	0.4 (0.0)
Untreated	MPC treatment	52.3 (1.3)	35.3 (0.4)	0.3 (0.2)	0.9 (0.1)	4.8 (0.8)	5.6 (1.1)	0.8 (0.1)
Nitric acid	MPC treatment	52.1 (1.1)	36.2 (0.7)	0.4 (0.2)	1.6 (0.2)	3.4 (0.4)	5.7 (0.7)	0.7 (0.2)
O ₂ plasma	MPC treatment	42.1 (1.1)	45.6 (1.1)	0.2 (0.2)	1.0 (0.1)	10.5 (0.7)	0.4 (0.5)	0.2 (0.1)
Nitric acid + O ₂ plasma	MPC treatment	63.3 (0.6)	30.8 (0.7)	3.0 (0.2)	2.9 (0.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
MPC polymer*	MPC treatment	57.9	31.6	5.3	5.3	—	—	—

n = 5.

*Theoretical elemental composition of MPC polymer. The standard deviations are shown in parentheses.

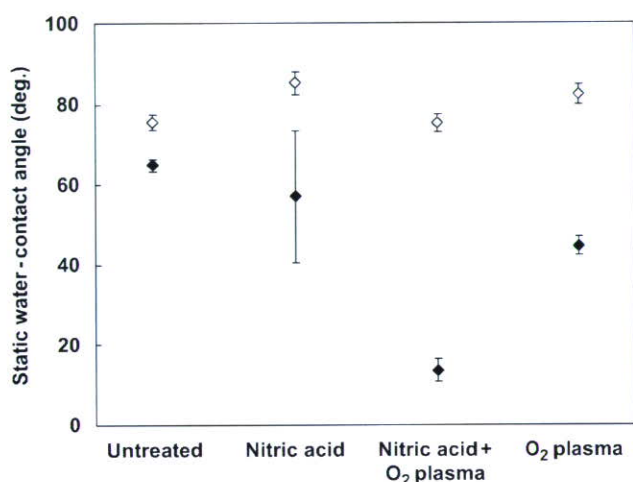


Fig. 5. Static water contact angle on the Co–Cr–Mo surfaces that were subjected to different types of pretreatments before and after the MPC grafting. Open marks, before MPC grafting; closed marks, after MPC grafting.

poly(MPC) graft on the Co–Cr–Mo alloy, we used the 4-META intermediate layer and the photo-induced radical graft polymerization technique to create a strong bonding between the Co–Cr–Mo substrate and the poly(MPC) chain via the 4-META layer. 4-META has already been known as a binder used in dental resin, and it can strongly bind resin to metal in dental implants [41,42]. Suzuki et al. [49] reported a strong evidence that the carboxylate anions were formed due to an ionic interaction between the carboxyl group of poly(carbonic acid) and the surface hydroxyl group on the oxide layer of stainless steel. Yamabe [50] reported that an ionic bond was formed between the carboxyl group and Cr on the surface of stainless steel. The various pretreatments performed in this study aimed at an efficient interaction between the carboxyl group of the 4-META layer and the surface hydroxyl group on the Cr oxide layer of the Co–Cr–Mo alloy.

As presented in Table 2, the surface Cr content in the Co–Cr–Mo alloy after the nitric acid pretreatment was higher than that of the untreated Co–Cr–Mo alloy. Seo and Sato [39] reported that a dry-polished stainless steel lacked in the surface Cr content. Accordingly, the as-polished Co–Cr–Mo alloy in this study may also lack the

surface Cr content, and the surface etching by nitric acid treatment would have produced the Cr-rich surface layer.

Exposure of the Co–Cr–Mo alloy to O₂ plasma formed an oxide layer on the Co–Cr–Mo surface (Table 2 and Fig. 3(a)). The static water contact angle on the nitric acid-pretreated Co–Cr–Mo-*g*-MPC surface was higher than that on the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC surface (Fig. 5). Additionally, the measured compositions of N and P in the only nitric acid-pretreated Co–Cr–Mo-*g*-MPC samples were lower than those in the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC samples (Table 3). It was considered that washing with ethanol removed the 4-META-MPC graft copolymer (4-META-*co*-MPC) from the only nitric acid-pretreated Co–Cr–Mo surface because there was an inadequate ionic bonding between 4-META and the only nitric acid-pretreated Co–Cr–Mo surface without an oxide layer.

The peaks at 780, 236, and 232 eV in the XPS spectra were assigned to Co²⁺, Mo⁴⁺, and Mo⁶⁺, respectively, as shown in Fig. 3. After the 4-META coating, these peaks disappeared from the Co–Cr–Mo surface. The peaks at 586 and 576 eV in the XPS spectra were assigned to Cr³⁺ (Fig. 3), indicating that Cr³⁺ persisted on the Co–Cr–Mo surface even after the 4-META coating. These results suggest that compared to other metallic oxides, Cr³⁺ predominantly binds to the carboxyl group of 4-META with a stronger ionic interaction [50]. This can be explained by the Lewis acid–base interaction model of a previous study [50]. It is assumed that the proton exchange between the carboxyl groups and active electrophilic metallic ions existing in the surface-hydrated oxide resulted in the formation of carboxylate anions; these carboxyl species that diffused into the hydrated oxide layer could easily undergo strong ionic interactions with the polar hydroxyl groups of hydrated Cr³⁺. The binding between 4-META-*co*-MPC and the Co–Cr–Mo substrate might contribute to the stable polymer/metal interface.

Friction coefficients of various bearing couples in the previous studies are summarized in Table 4. In Fig. 7, the Co–Cr–Mo/Co–Cr–Mo couple showed a friction coefficient of approximately 0.24 as high as the previous studies. The CLPE/Co–Cr–Mo couple also showed a friction coefficient of approximately 0.09 as high as the previous studies. In contrast, it was confirmed that compared to the

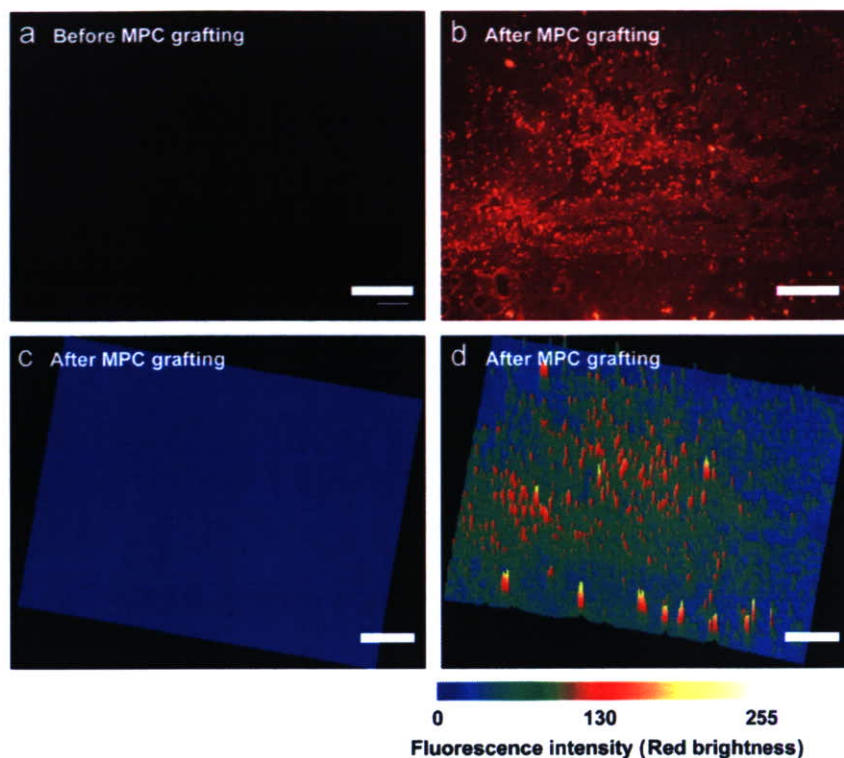


Fig. 6. FM images of (a), (c) the untreated Co–Cr–Mo and (b), (d) the nitric acid- and O₂ plasma-pretreated Co–Cr–Mo-*g*-MPC samples. (a and b) = FM images; (c and d) = color images from fluorescence intensity of the FM images (a and b). Bar = 200 μm. Color scale bar indicates fluorescence intensity (red brightness) for (c and d).

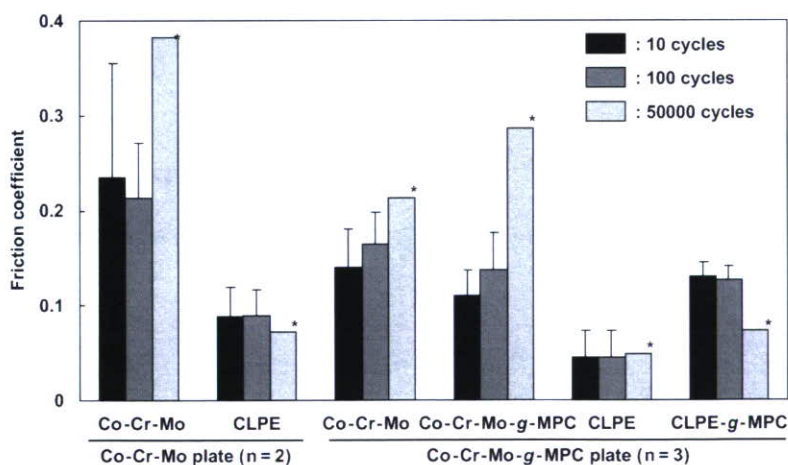


Fig. 7. Friction coefficients as a function of the test duration for the various types of pins sliding against the Co–Cr–Mo-*g*-MPC ($n = 3$) and untreated Co–Cr–Mo ($n = 2$) plates. * $n = 1$. Bars = standard deviations.

untreated Co–Cr–Mo surface, the Co–Cr–Mo-*g*-MPC (excluding the CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC-bearing couple) surface showed an extremely low friction coefficient. Since MPC is highly hydrophilic and poly(MPC) is water soluble, the water wettability of the Co–Cr–Mo-*g*-MPC surface was greater than that of the untreated Co–Cr–Mo surface, as shown in Fig. 5. Consequently, the grafted poly(MPC) layer successfully provided high lubricity to the Co–Cr–Mo surface (Fig. 7). The reduction in the

friction may contribute to the improvement in the anti-wear properties [22]. From the viewpoint of tribological advantage, a highly lubricious metal-bearing material will enable the development of a novel biocompatible artificial hip-joint system.

Various factors such as the type of bearing material, surface roughness, homogeneity of the surface, and chemical composition affect the lubricity of artificial joints [54]. In the case of Co–Cr–Mo-*g*-MPC, the lubricity would

Table 4
Friction coefficients of various bearing couples in the previous studies

Bearing couple		Friction coefficient	References
Pin	Disc or plate		
Co–Cr–Mo	Co–Cr–Mo	0.19–0.27	[51]
UHMWPE	Co–Cr–Mo	0.05–0.09	[52]
UHMWPE	Co–Cr–Mo	0.05–0.09	[53]
Cartilage	Stainless steel	0.01–0.05	[55]
Cartilage	Cartilage	0.02	[56]

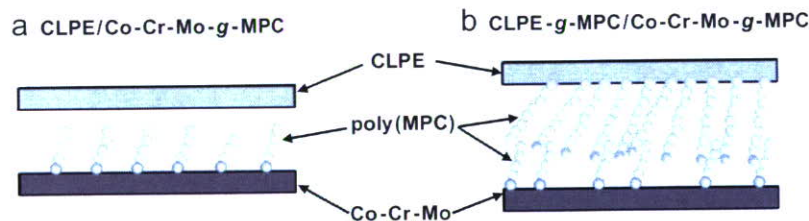


Fig. 8. Images of grafted non-grafted poly(MPC)/grafted poly(MPC) and poly(MPC)/grafted poly(MPC)-bearing interfaces.

change depending on the ambient *in vitro* and *in vivo* conditions. The bearing surface with poly(MPC) in artificial hip joints is assumed to have a structure similar to an artificial cell membrane. The Co–Cr–Mo-*g*-MPC/Co–Cr–Mo-*g*-MPC or CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC-bearing couples therefore mimic the natural joint cartilage *in vivo*. A friction coefficient of cartilage/SUS pin-on-plate was 0.01–0.05 [55], and that of cartilage/cartilage pin-on-plate was 0.02 [56], as shown in Table 4. In contrast, the Co–Cr–Mo-*g*-MPC/Co–Cr–Mo-*g*-MPC or CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC-bearing couples mimicking the natural joint, showed high friction (friction coefficient = 0.12) in this study. Images of grafted non-grafted poly(MPC)/grafted poly(MPC) and poly(MPC)/grafted poly(MPC)-bearing interfaces are shown in Fig. 8. The grafted poly(MPC)/non-grafted poly(MPC)-bearing interface in the CLPE/Co–Cr–Mo-*g*-MPC couple showed a low friction coefficient with the water wettability of poly(MPC) (Fig. 8(a)). The grafted poly(MPC)/grafted poly(MPC)-bearing interface in the CLPE-*g*-MPC/Co–Cr–Mo-*g*-MPC couple showed slightly higher friction than the grafted poly(MPC)/non-grafted poly(MPC)-bearing interface. The MPC graft polymer on Co–Cr–Mo might have low density because the polymerization method used was “grafting to” [57]. Fukuda et al. [58] reported that the friction was higher in a bearing couple with low-density polymer brushes than in a bearing couple with high-density polymer brushes. Therefore, it is assumed that a bearing couple with low-density poly(MPC) brushes may cause high friction with interpenetration as shown in Fig. 8(b) [59]. High-density poly(MPC) by “grafting from” might be possible to resist the interpenetration by its volume effects arising from chain mobility.

5. Conclusions

We created a highly lubricious metal-bearing material for its application as a novel artificial hip-joint system: The MPC polymer was grafted onto the surface of the Co–Cr–Mo alloy by employing the 4-META intermediate layer and using the photo-induced radical graft polymerization technique and the nitric acid and O₂ plasma pretreatments of the Co–Cr–Mo alloy. In conclusion, the grafted poly(MPC) layer successfully provided high lubricity to the Co–Cr–Mo surface. The grafted poly(MPC)/non-grafted poly(MPC)-bearing interface had a lower friction value than that of the grafted poly(MPC)/grafted poly(MPC) bearing interface.

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Prevention of Tissue Adhesion by a Spontaneously Formed Phospholipid Polymer Hydrogel

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Abstract. We investigated phospholipid polymer hydrogels containing Fe³⁺ ions (PMA/PMB/Fe hydrogel) for their use as antiadhesive materials in the healing tissues. These hydrogels were prepared from the aqueous solutions of poly(2-methacryloyloxyethyl phosphorylcholine (MPC)-*co*-methacrylic acid) (PMA) and poly(MPC-*co*-*n*-butyl methacrylate) (PMB). The PMA/PMB hydrogel is formed by the intermolecular interactions between PMA and PMB, and it reversibly dissociates under physiological conditions. The addition of Fe³⁺ ions could control the gelation time and the dissociation time. Mechanical properties such as the gelation time and viscoelastic properties can be controlled by the FeCl₃ concentration. With regard to biocompatibility, no evidence of inflammation was observed *in vivo*. Therefore, the PMA/PMB/Fe hydrogel has a potential to be used as an antiadhesive material.

Introduction

Adhesion of tissues such as a tendon and intestines after an injury or surgery is a type of inflammatory reaction. It can cause difficulty in movement or pain, thereby decreasing the quality of life of a patient [1]. Although some efforts have been invested in developing antiadhesive materials for tissues, no effective material has yet been put to practical use. The existing antiadhesive materials serve as a physical barrier to prevent contact of the healing tissue with the surrounding normal tissues. However, these materials have some drawbacks [2]: (1) The permeability of bioactive molecules such as cytokines is so low that healing is delayed. (2) Certain degree of tissue adhesion may occur after an operation for the removal of non-biodegradable materials and during adsorption of biodegradable materials.

Therefore, we propose a spontaneously formed phospholipid polymer hydrogel as a novel anti-adhesive material. This hydrogel can be prepared under physiological conditions simply by mixing the aqueous solutions containing poly(2-methacryloyloxyethyl phosphorylcholine (MPC)-*co*-methacrylic acid) (PMA) and poly(MPC-*co*-*n*-butyl methacrylate) (PMB) (Fig. 1) [3]. The hydrogel is formed by molecular interactions such as hydrogen bonding and hydrophobic interactions, and it demonstrates physical properties that correspond to the polymer structure [4,5]. Thus, it can be dissociated by changing the surrounding conditions, namely, pH, ionic strength, temperature, etc. The *in vivo* injection test did not show toxicity of the constitutive polymers—PMA and PMB. Since the PMA/PMB hydrogel has more than 95 wt% aqueous medium, it is expected to be (1) porous to allow the permeation of humoral factors, (2) biocompatible in order to prevent an inflammatory reaction, and (3) biodegradable so that a special procedure for its removal is not required after the tissues heal. The PMA/PMB hydrogel is dissociated in a large amount of aqueous medium within a few hours, and it is expected to dissociate *in vivo* within a relatively short time. Biodegradability is an advantageous property for its medical use because it can control the release of content as the degradation and eliminate the need of surgery for its removal. However, since the dissociation time of the PMA/PMB hydrogel is short, its long-term application to tissues as an antiadhesive material

is not possible. Thus, we introduced another crosslinking mechanism, that is, ionic crosslinking between counter-cation and carboxylate anion in the PMA/PMB hydrogel for achieving stabilization. Although NaCl and CaCl₂ did not show the expected stabilization effect, FeCl₃ improved the stability of the PMA/PMB hydrogel in a large amount of aqueous medium [3].

In this study, we investigated the PMA/PMB hydrogel containing FeCl₃ for their use as an antiadhesive material in tissues. We examined the stabilization of the PMA/PMB hydrogel by FeCl₃ *in vitro* and *in vivo*. We also evaluated the performance of the PMA/PMB hydrogel as an antiadhesive material *in vivo*.

Materials and Methods

Materials. The phospholipid polymers, PMA (Mn = 2.7 × 10⁵, Mw = 8.4 × 10⁵, and MPC mole fraction = 0.3) and PMB (Mn = 1.1 × 10⁵, Mw = 8.6 × 10⁵, and MPC mole fraction = 0.8), were prepared from the corresponding monomer by radical polymerization [Figure 1][6]. For this study, these polymers were supplied by the NOF Corporation (Tokyo, Japan) as 5 wt% aqueous solutions. Iron (III) hexahydrate (FeCl₃) was purchased from Kanto Chemical Co.

Hydrogel Preparation. Equal volumes of 5 wt% PMA and PMB aqueous solutions were taken in a microtubing and vigorously stirred for 10 s. After 10–20 s, the mixture of these MPC polymer solutions was spontaneously transformed into a hydrogel state. A hydrogel containing FeCl₃ (PMA/PMB/Fe hydrogel) was prepared by using PMB containing FeCl₃. The final concentration of FeCl₃ in a hydrogel is expressed by the number following the PMA/PMB/Fe hydrogel, for example, PMA/PMB/Fe hydrogel-71 implies a PMA/PMB hydrogel containing 71 mM of FeCl₃.

Stability of the PMA/PMB/Fe Hydrogel *in vitro* and *in vivo*. One gram of PMA/PMB/Fe hydrogel was put in a nylon mesh bag and immersed in 100 mL of phosphate buffered saline (PBS; 0.15 M, pH 7.1). The mesh bag was weighed at specific time intervals, and the weight of the remaining hydrogel was determined. For an *in vivo* test, a diffusion chamber (pore size, 0.3 μm) containing the PMA/PMB hydrogel or PMA/PMB/Fe hydrogel-71 was implanted subcutaneously into a mouse. After 3 weeks, the chamber was removed, and the hydrogel was observed by SEM.

Viscoelastic Properties of the Hydrogels. The aqueous solutions of PMA (0.75 mL) and PMB (0.75 mL) were injected slowly into both sides of a vibration blade (1.71 cm²) in a liquid cell. Immediately after the injection, the blade was set in motion (vibrational amplitude, 200 μm; frequency, 20 Hz) to mix these polymer solutions in the cell in order to enable the PMA/PMB hydrogel formation. Changes in the elastic modulus (G') and the viscous modulus (G'') were recorded using a rheometer (Rheograph-Micro, Toyoseiki, Tokyo, Japan). The gelation time is defined as the time when G' becomes greater than G''. The gelation time of the PMA/PMB/Fe hydrogel was also measured by using PMB containing FeCl₃ in the same manner. In addition, the viscoelastic properties of the hydrogel were investigated using the rheometer at a predetermined time after the hydrogel was prepared and kept at room temperature.

Results and Discussion

Fig. 2 shows the effect of FeCl₃ addition on the stability of the PMA/PMB/Fe hydrogel. The relative weight of PMA/PMB/Fe hydrogel-14 gradually decreased, and it completely dissociated within 6 h after its immersion in PBS. PMA/PMB/Fe hydrogel-28 also dissociated completely within 24 h, although PMA/PMB/Fe hydrogel-39 and PMA/PMB/Fe hydrogel-71 retained almost a constant weight after a slight initial decrease. Because a Fe³⁺ ion theoretically interacts with 3 carboxylate anions, the residual carboxylic acid groups exist in PMA/PMB/Fe hydrogel-14 and PMA/PMB/Fe hydrogel-28. The FeCl₃ concentration is adjusted to the theoretical ratio in

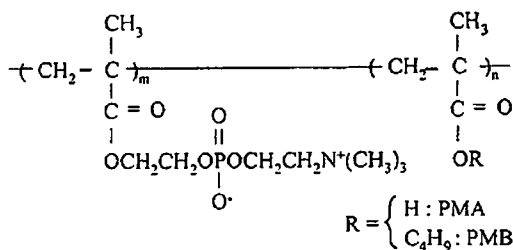


Fig. 1. Structure of PMA and PMB.

PMA/PMB/Fe hydrogel-39. Thus, PMA/PMB/Fe hydrogel-39 and PMA/PMB/Fe hydrogel-71 did not dissociate because of the higher FeCl_3 concentration.

The relative weight of PMA/PMB/Fe hydrogel-28 showed a slight initial increase, and then it steadily decreased. This suggests swelling of the hydrogel immediately after its immersion in PBS, followed by its dissociation. When the PMA/PMB/Fe hydrogel is immersed in PBS, swelling of the hydrogel and diffusion of FeCl_3 starts. Influx of water can cause ionization of the carboxylic acid groups and lead to electrostatic repulsion between the carboxylate anions. As a result, the polymer concentration and the crosslinking density decreases. Subsequently, the polymer networks collapse, i.e., dissociation of the hydrogel occurs. As seen in the yellowish PBS obtained after the immersion of the hydrogel, diffusion of the Fe^{3+} ions and swelling of PMA/PMB/Fe hydrogel-71 and PMA/PMB/Fe hydrogel-39 is possible. However, even during the swelling process, these hydrogels retained the polymer network and attained equilibrium due to a high density of Fe^{3+} crosslinking.

Although PMA/PMB/Fe hydrogel-71 was implanted subcutaneously, stabilization of the PMA/PMB hydrogel containing Fe^{3+} was observed. That is, while the PMA/PMB hydrogel was dissociating, PMA/PMB/Fe hydrogel-71 remained and maintained the hydrogel state even after 3 weeks. A three-dimensional network structure could be observed under SEM, and the results of viscoelastic measurements also indicated the defining characteristic of a hydrogel, that is, $G' > G''$.

Table 1 shows the gelation time of the PMA/PMB hydrogel and the PMA/PMB/Fe hydrogel. The gelation time was longer for the PMA/PMB hydrogel than for the PMA/PMB/Fe hydrogel. Since the FeCl_3 solution has a low pH, ionization of the carboxylic acid groups in PMA can be suppressed by mixing PMA with PMB containing FeCl_3 . Suppression of the carboxylic acid groups leads to hydrogen bond formation, resulting in the shortening of the gelation time of the PMA/PMB/Fe hydrogel when compared with that of the PMA/PMB hydrogel. Increase in the FeCl_3 concentration decreased the gelation time. This is because the pH of PMA/PMB/Fe hydrogel-142 was lower than that of PMA/PMB/Fe hydrogel-71.

Thus, the addition of FeCl_3 significantly reduced the gelation time and the dissociation time of the PMA/PMB/Fe hydrogel; moreover, these parameters can be controlled by the FeCl_3 concentration.

The viscoelastic properties of the PMA/PMB hydrogel and the PMA/PMB/Fe hydrogel are shown in Fig. 3. With regard to the gelation time, agitation efficiency was so high that it took shorter time compared to the preparation method described in the gelation time measurement section. Vigorous stirring by a vortex mixer for 10 s is sufficient to prepare both PMA/PMB and PMA/PMB/Fe hydrogels. The mechanical strength of the PMA/PMB/Fe hydrogel immediately after its preparation (10 s) was so low that it appeared almost sol. Both G' and G'' of PMA/PMB/Fe hydrogel-142 were lower than those of PMA/PMB/Fe hydrogel-71. G' and G'' of the

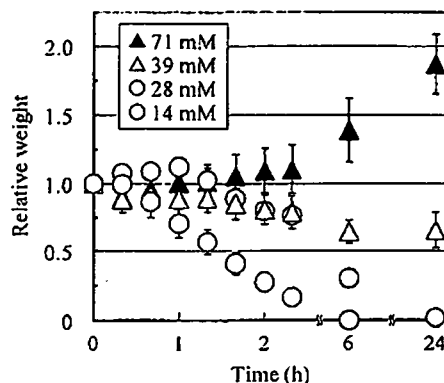


Fig. 2 Change in the weight of PMA/PMB hydrogel containing FeCl_3 immersed in PBS.

Table 1 Gelation time of PMA/PMB hydrogel containing FeCl_3

	Gelation time (s)
PMA/PMB hydrogel	1007 ± 137
PMA/PMB/Fe hydrogel-71	605 ± 101
PMA/PMB/Fe hydrogel-142	468 ± 47

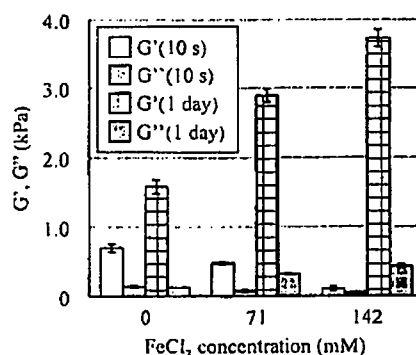


Fig. 3 Change in the elastic modulus (G') and the viscous modulus (G'') of PMA/PMB hydrogel containing FeCl_3 .

PMA/PMB hydrogel were higher than those of the PMA/PMB/Fe hydrogel. One day after the hydrogel preparation, increase in G' and G'' was observed in all the hydrogels; G' of the PMA/PMB hydrogel was more than double its value immediately after the hydrogel preparation, while G'' remained almost constant. It is noteworthy that G' of PMA/PMB/Fe hydrogel-71 increased 6-fold and that of PMA/PMB/Fe hydrogel-142 increased more than 60-fold after 1 day. G'' of PMA/PMB/Fe hydrogel-71 also increased by approximately 4-fold and that of PMA/PMB/Fe hydrogel-142 increased more than 8-fold. Interestingly, among the 3 hydrogels, G' of PMA/PMB/Fe hydrogel-142 was the lowest immediately after the hydrogel preparation, but it was the highest after 1 day; this observation can be explained by the ionic crosslink formation.

During clinical application, the treated tissue will be covered by an antiadhesive agent and then sutured. Thus, the change in the mechanical properties during and after surgery would determine the clinical usefulness of an antiadhesive agent. A point worth noting is that immediately after its preparation, the PMA/PMB/Fe hydrogel is a weak gel; however, it improves its mechanical strength with time. This change in the mechanical properties of the PMA/PMB/Fe hydrogel can enable the hydrogel to attain a specific shape according to the application site and solidify after suturing; these features are a requisite for an antiadhesive material.

Furthermore, implantable antiadhesive materials should also be biocompatible in order to prevent the occurrence of any inflammatory reaction that would result in adhesions. Based on the results of the *in vivo* injection test, we have previously reported that PMA and PMB do not show notable adverse effects [5]. Although $FeCl_3$ is applied to dental materials to facilitate the adhesion of dental prosthesis to the dentin tissue, a report has shown the potential of $FeCl_3$ to cause oxidative stress on cells leading to the development of mutation [7]. The biocompatibility of the PMA/PMB/Fe hydrogel should be closely examined. We have been investigating the antiadhesive property of hydrogels and its effect on healing. No evidence of inflammation was observed in the tissues surrounding the hydrogel. We shall provide detailed reports of the results elsewhere.

Conclusions

A PMA/PMB hydrogel containing $FeCl_3$ (PMA/PMB/Fe hydrogel) shows that the mechanical properties of a hydrogel can be controlled by a combination of hydrogen bonding and ionic crosslinking. Severe inflammatory reaction was not observed in the tissues surrounding the hydrogel. Therefore, it can be concluded that the PMA/PMB/Fe hydrogel satisfies the basic requirements for an antiadhesive material.

Acknowledgement

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

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Abstract Osteolysis caused by wear particles from polyethylene in the artificial hip joints is a serious issue. We have used photo-induced radical graft polymerization to graft 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer onto the surface of cross-linked polyethylene (CLPE-g-MPC) in order to reduce friction and wear at the bearing surface of the joint. The physical and mechanical properties of CLPE and CLPE-g-MPC were not significantly different, except that the friction coefficient of untreated CLPE cups was 0.0075, compared with 0.0009 for CLPE-g-MPC cup, an 88% reduction. After 3.0×10^6 cycles in the hip joint simulator test, we could not observe any wear of CLPE-g-MPC cups. We concluded that the advantage of photo-induced radical graft polymerization technique was that the grafted MPC polymer gave a high lubricity only on the surface and has no effect on the bulk properties of the CLPE substrate.

Introduction

The most widely used bearing couple for artificial joint systems is the combination of an ultra-high molecular weight polyethylene (UHMWPE) acetabular component and a Co–Cr–Mo alloy femoral component. However, osteolysis caused by wear particles of UHMWPE has emerged as a serious issue [1–3]. Decreasing the number of wear particles from UHMWPE is one way to prevent osteolysis, and different combinations of bearing surfaces and improvements in the bearing materials themselves have been focused. Several highly cross-linked polyethylenes (CLPE) irradiated with 50–105 kGy have been launched since 1998, and they have been used extensively [4]. Gamma-ray and electron beam irradiation at various doses are used by many manufacturers to produce CLPE. In published reports, CLPE produced with 50–105 kGy irradiation shows an 80–90% reduction in wear rate compared with conventional polyethylene [5, 6]. Clinical results have confirmed the excellent anti-wear properties of CLPE. While the efficacy of CLPE is attested by many reports [7–11], the *in vivo* reduction of wear is only a decrease of 40–60%, so further improvement is desired.

We have recently developed a new-concept artificial hip joint system with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted onto the surface of CLPE (CLPE-g-MPC), aiming to reduce wear and avoid bone resorption [12]. MPC is a methacrylate monomer which has a phospholipid polar group in a side chain, and which is used to make new concept biomaterials as designed by Ishihara et al. [13], who were inspired by the neutral phospholipids of biomembranes. Many polymers consisting MPC unit are widely used as biomaterials [14, 15]. Various medical devices using MPC polymer have already been developed and clinically used with the approval of the

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United States Food and Drug Administration. The efficacy of MPC polymer as a biomaterial is well established [15–17].

Based on the biocompatibility and hydrophilicity of MPC polymer, we have been developing new artificial joints with highly lubricated bearing surfaces produced by photo-induced radical graft polymerization. This technique grafts MPC directly to CLPE, forming C–C covalent bonds between the CLPE substrate and the MPC polymer. In this study, we investigated the effects of this photo-induced radical graft polymerization technique on the physical, mechanical and tribological properties of CLPE-g-MPC.

Materials and methods

Chemicals and MPC graft polymerization

Benzophenone and acetone were purchased from Wako Pure Chemical Industries, Ltd (Osaka, Japan). MPC was synthesized industrially using the method of Ishihara, et al. [13] and was supplied by AI Bio-Chips Co., Ltd (Tokyo, Japan).

Compression-molded UHMWPE (GUR1020 resin, Poly Hi Solidur Inc., IN, USA) bar stock was gamma-irradiated with 50 kGy in N₂ gas and annealed at 120°C in N₂ gas for cross-linking. The CLPE specimens were machined from this bar stock after cooling. They were immersed for 30 sec in an acetone solution containing 10 mg/mL benzophenone and then dried in the dark to remove acetone at room temperature [18]. The amount of benzophenone adsorbed on the surface was 3.5×10^{-11} mol/cm² by ultraviolet spectroscopy according to the previous study [19]. The MPC was dissolved into degassed pure water to a concentration of 0.5 mol/L. CLPE specimens coated with benzophenone were immersed in the aqueous MPC solution. Photo-induced graft polymerization on the CLPE surface was carried out with ultraviolet irradiation of 5 mW/cm² for 10 to 360 min at 60°C using a Toshiba D-35 filter to pass only ultraviolet of 350 ± 50 nm wavelength. After the polymerization, the CLPE-g-MPC specimens were removed, washed with pure water and ethanol, and dried.

Surface analysis by FT-IR/ATR and XPS

The functional group vibrations of the CLPE and CLPE-g-MPC (90 min irradiation) surfaces were examined by Fourier-transform infrared (FT-IR) spectroscopy with attenuated total reflection (ATR) equipment. CLPE and CLPE-g-MPC spectra were obtained in 32 scans over the range of 800 to 2000 cm⁻¹ with an FT-IR analyzer (FT/IR615, JASCO Co. Ltd., Tokyo, Japan) at a resolution of 4.0 cm⁻¹.

The surface elemental composition of CLPE was analyzed before and after MPC grafting for 90 min by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained on an AXIS-HSi165 (KRATOS ANALYTICAL Ltd., UK) equipped with Mg–K α radiation source biased at 15 kV at the anode. The take-off angle of photoelectrons was kept at 90°.

Surface wettability observation by spray method

The spray method is based on the wetting response of the surface of a cup when exposed to a distilled water mist for a short period [20]. The entire bearing surfaces of CLPE and CLPE-g-MPC (23 and 90 min irradiation) cups were uniformly exposed to 15 mL of water mist. The appearance of the cup surfaces was evaluated in terms of wettability within 10 sec after spraying. Ratio of surface area covered by water (water-covered ratio) was determined by using the Win-Roof image processing system (Mitani Corporation Inc., Fukui, Japan).

Evaluation of physical and mechanical properties

The density, swelling ratio, network chain density, molecular weight between cross-links and cross-link density of CLPE and CLPE-g-MPC with irradiation for 90 min were evaluated according to the methods previously reported [21]. The CLPE and CLPE-g-MPC specimens ($23 \times 23 \times 1$ mm³) were weighed (approximately 0.5 g, V_1), allowed to swell for 72 h in *p*-xylene containing 0.5 wt% 2-*t*-butyl-4-methylphenol at 130 °C, and were then reweighed (V_2). After reweighing, specimens were immersed in acetone, dried at 60 °C under vacuum, and reweighed (V_3). The swelling ratio, q , was determined from the weight gain and densities of the polyethylene and xylene, and the physical properties were calculated as follows.

(a) Swelling ratio, q

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

(b) Network chain density, v^*

$$v^* = \ln(1 - q^1) + q^1 + \chi q^2 / V_1 (q^{-2/3} - 0.5q^{-1})$$

$$V_1 = 136 \text{ mL/mol}, \chi = 0.37 \text{ (polyethylene)} \quad (2)$$

(c) Molecular weight between cross-links, M_c

$$M_c = 1 / \bar{M}c = Vv^*$$

$$V = 1 / \text{specimen density} \quad (3)$$

(d) Cross-link density, *XLD*

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

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

The mechanical properties of CLPE and CLPE-g-MPC with irradiation for 90 min were evaluated with tensile, impact, and creep deformation tests, as well as a shore hardness D measurement. Tensile testing was performed according to ASTM standard D638 using a type 4 tensile bar specimen and a crosshead speed of 50 mm/min. A double-notched (notch depth = 4.57 ± 0.08 mm) Izod impact strength test was performed to ASTM standard F648. Ten specimens were used in each tests. Creep deformation was measured by applying a constant load (113 kgf for 24 h) to a specimen, then measuring the height displacement, according to the ASTM D621 test method. Shore hardness D was measured according to the ASTM D2240 test method.

For all the test groups, the results derived from each experiment were expressed as mean values and the standard deviation. The statistical significance ($p < 0.05$) was judged by the Student's *t*-test.

TEM observation of cross section of CLPE-g-MPC

A cross section of the MPC polymer layer on the CLPE-g-MPC (90 min irradiation) surface before and after the hip joint simulator test was observed with a transmission electron microscope (TEM). Prior to observation, specimens were embedded in epoxy resin, stained in ruthenium oxide vapor at room temperature, and sliced into ultra-thin films. The specimen after the hip joint simulator test was coated with gold by sputter coater (JFC 1500, JEOL, Ltd., Tokyo, Japan) before embedding in resin. A JEM-1010 (JEOL, Ltd., Tokyo, Japan) was used for the TEM observation at an acceleration voltage of 100 kV.

Hip joint simulator test

The CLPE-g-MPC cups (26 mm inner diameter and 52 mm outer diameter) for testing in the hip joint simulator were gamma-ray sterilized under N_2 gas.

Friction torque between the CLPE-g-MPC cup and a 26 mm Co–Cr–Mo alloy femoral head (Japan Medical Materials Corp., Japan) was measured using a 2-station hip joint simulator (Kobe Steel, Ltd., Kobe, Japan). Measurements were performed with distilled water as lubricant, a loading of 280 kgf and a swing distance of 80 mm with a period of 1 Hz.

The in vitro wear test was performed using a 12-station hip joint simulator (MTS system Corp., MN, USA). A

mixture of 25% bovine serum, 20 mM/L of ethylene diamine tetraacetic acid (EDTA), and 0.1% sodium azide was used as lubricant, according to the ISO 14242-1 standard. A load simulating a physiologic loading curve with double peaks of 183 and 280 kgf load was added with a period of 1 Hz. The wear was measured by a gravimetric method. The cup weights were measured every 0.5×10^6 cycles. The acetabular component was tested with a 26 mm Co–Cr–Mo alloy femoral head (Japan Medical Materials Corp., Japan). Testing then continued until a total of 3.0×10^6 cycles were completed.

Results

Figure 1 shows the FT-IR/ATR spectra of CLPE and CLPE-g-MPC. A transmission absorption peak was observed at 1460 cm^{-1} for both CLPE and CLPE-g-MPC. This peak is attributed mainly to the methylene chain in the CLPE substrate and MPC graft polymer. However, transmission absorptions at 1240, 1080 and 970 cm^{-1} were observed only for the CLPE-g-MPC. These peaks are due to the phosphate group in the MPC unit. Similarly, the transmission absorption at 1720 cm^{-1} observed for CLPE-g-MPC can only correspond to the carbonyl in the MPC unit.

Figure 2 shows the XPS spectra (N_{1s} and P_{2p}) of CLPE and CLPE-g-MPC. In the N_{1s} and P_{2p} spectra, clear peaks were observed only for CLPE-g-MPC. Peaks at 403 and 134 eV were assigned to the $-N^+(\text{CH}_3)_3$ and phosphate groups, respectively. These peaks were characteristic of the phosphorylcholine in the MPC unit. Table 1 summarizes the elemental composition of the untreated CLPE and the CLPE-g-MPC surfaces with various ultraviolet-ray irradiation times during polymerization. The content of nitrogen and phosphorous in the CLPE-g-MPC surface was increased to 5.1 and 5.2, respectively, with polymerization time. The elemental composition of the CLPE-g-MPC surface with a polymerization time of 90 min was almost

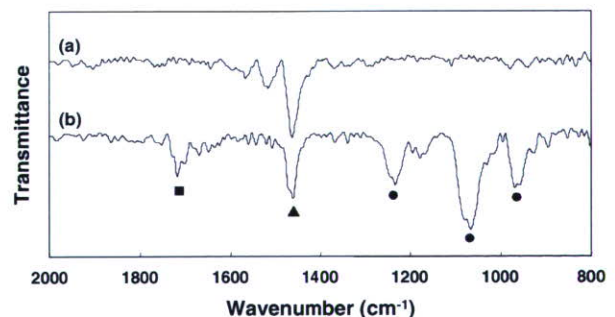


Fig. 1 FT-IR/ATR spectra of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC. ●: P–O, ▲: CH_2 , ■: C=O

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

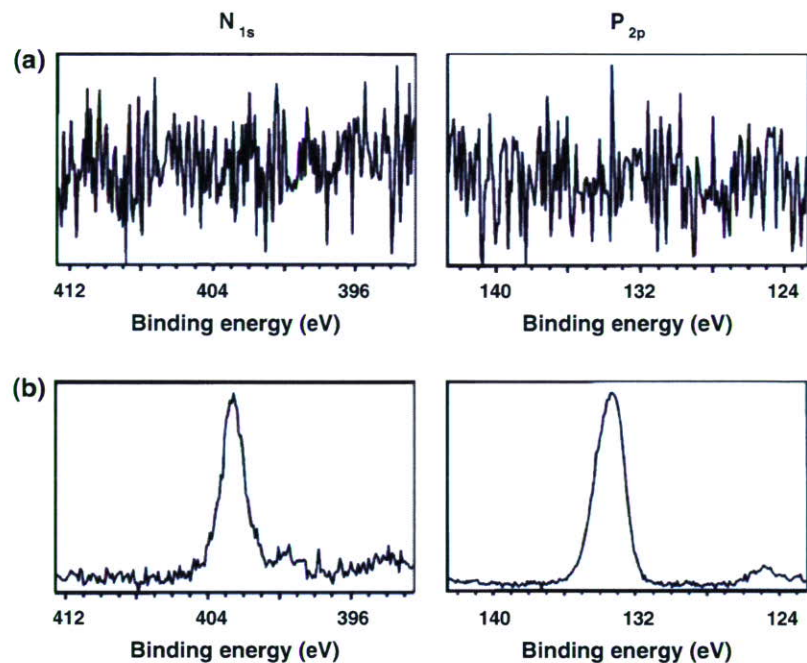


Table 1 Surface elemental composition (%) of CLPE-g-MPC with various photo-polymerization times

Polymerization time (min)	C	O	N	P
0 (untreated CLPE)	99.6	0.4	0.0	0.0
12	96.6	3.4	0.0	0.0
23	78.5	17.0	1.9	2.7
45	60.4	30.2	4.1	5.3
90	61.8	27.9	5.1	5.2
MPC polymer*	57.9	31.6	5.3	5.3

*: Theoretical elemental composition of MPC polymer

equivalent to the theoretical elemental composition (N = 5.3, P = 5.3) of MPC polymer.

Figure 3 shows optical microscope images of moistened CLPE-g-MPC surfaces that were produced by various photo-irradiation times during polymerization. The surface image progressively alters from a hydrophobic surface to a hydrophilic one as polymerization time increases. On an untreated CLPE surface after spraying with water mist, typical hydrophobic behavior was observed, including the formation of many water droplets (Fig. 3a). In contrast, on the CLPE-g-MPC surface hydrophilic behavior was observed, characterized by a thin film of water (Fig. 3c).

The physical properties of CLPE and CLPE-g-MPC including density and swelling ratio are summarized in Table 2. It is generally said that energy irradiation to polyethylene causes a decrease in the swelling ratio. However, all of the bulk physical properties of CLPE and

CLPE-g-MPC that were examined in this study differed little ($p < 0.05$) between the two materials.

The tensile yield strength, impact strength, creep deformation and shore hardness D of CLPE and CLPE-g-MPC are shown in Table 3. Tensile yield strength, impact strength and shore hardness D did not differ significantly ($p \leq 0.05$) between CLPE and CLPE-g-MPC, and both CLPE and CLPE-g-MPC met ASTM requirements (F648).

Figure 4 shows a TEM image of a cross section of CLPE-g-MPC. A grafted MPC polymer layer about 100 nm thick was observed on the CLPE substrate (Fig. 4b). Lamellae on the order of 100–400 nm long and 10–20 nm thick were observed in the CLPE substrate regardless of irradiation, and the lamellae were especially thin near the surface.

Table 4 shows the friction coefficient and the wear rate of the MPC polymer grafted CLPE cup in the hip joint simulator test. The friction coefficients of the untreated CLPE cups and the CLPE-g-MPC cups were 0.0075 and 0.0009, respectively. The CLPE-g-MPC cups reduced 88% in the friction coefficient compared with untreated CLPE cups, showed a high lubricity. We calculated the wear rate between 2.5×10^6 and 3.0×10^6 cycles. The wear rate of CLPE cups showed $3.12 \text{ mg}/10^6$ cycles. In contrast, the CLPE-g-MPC cups showed the reduction in wear to an essentially zero of $-1.43 \text{ mg}/10^6$ cycles. The volumetric change was then calculated from the weight loss over time. In this study, the weight loss was calculated without considering the effect of water absorption.

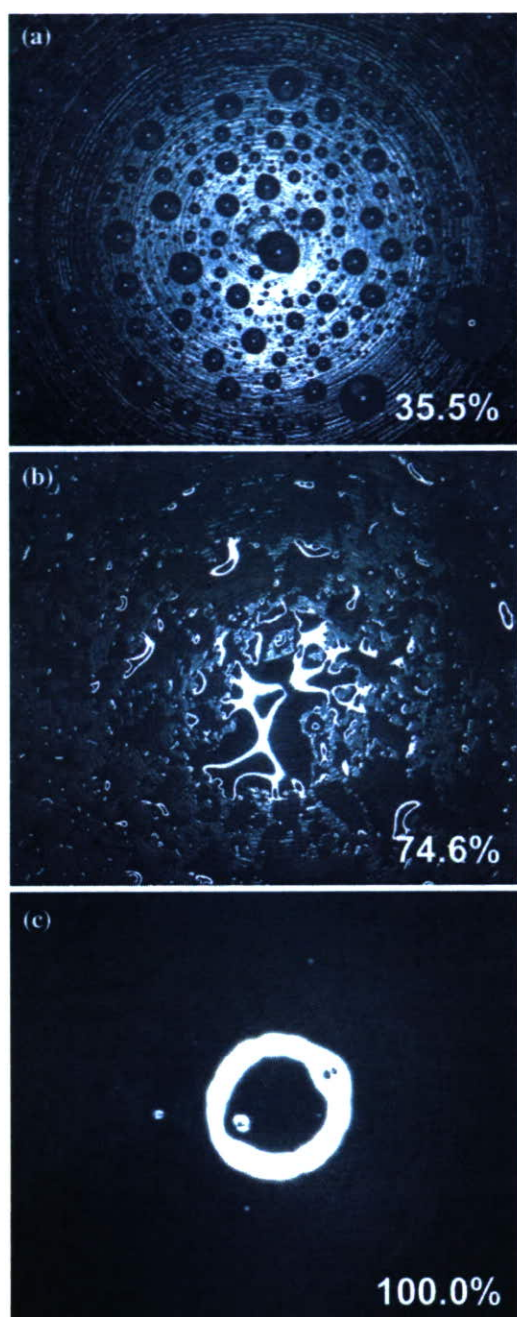


Fig. 3 Optical microscope images of CLPE-g-MPC cup surface with various photo-polymerization times. **(a)** 0 min (untreated CLPE), **(b)** 23 min and **(c)** 90 min. The water-covered ratio (%) is also shown. The white ring in **(c)** is due to the reflection of the light used in photography

Discussion

We have developed an artificial hip joint that uses CLPE-g-MPC on the bearing surface, with the goal of reducing wear and avoiding bone resorption. In this study, we investigated

the effects of photo-induced radical graft polymerization technique on properties of the CLPE-g-MPC, and this report discusses the characteristics of the MPC polymer layer and the properties of the CLPE substrate.

After 3.0×10^6 cycles of the hip joint simulator test, we confirmed that the CLPE-g-MPC cups showed a quite low wear rate compared with untreated CLPE. Since MPC is a highly hydrophilic compound, and poly(MPC) is water-soluble, the water-wettability of the CLPE-g-MPC surface was greater than that of a CLPE surface due to the poly(MPC) chains, as shown in Fig. 3. It was observed that the CLPE-g-MPC surface supported a thin film of water. Consequently, the artificial hip joint bearing with an CLPE-g-MPC surface had high lubricity. The reduction in friction is assumed to have contributed to the improvement of anti-wear properties that was observed [22]. However, different processes such as migration of low molecular weight compounds, rotation of flexible polymer chains, inter- and intra-molecular rearrangements, and adhesion of contaminant particles, may take place at different rates depending on materials and ambient conditions [23]. Various factors such as type of bearing material, surface roughness, homogeneity of the surface and chemical composition affect the lubricity of the artificial joint [24]. In CLPE-g-MPC, the lubricity can change depending on the ambient conditions *in vitro* and *in vivo*. The bearing surface of the artificial hip joint with MPC polymer is assumed to have a structure similar to an artificial cell membrane, meaning this new concept artificial hip joint mimics the natural joint cartilage *in vivo*. To ensure the long-term retention of the benefits of this MPC polymer, we used photo-induced radical graft polymerization technique, to produce C–C covalent bonding between a carbon atom of the CLPE and the end-group of an MPC polymer chain. The results clearly show that the crystalline structure, physical and mechanical properties of the CLPE substrate were minimally changed, if at all, even after MPC grafting [25]. This indicates that photo-induced radical graft polymerization does not affect the properties of the CLPE substrate [18]. Retaining the properties of the CLPE substrate unchanged is very important in clinical use, because the CLPE cup acts not only as a bearing material but also as a structural material in the artificial hip joint system. Generally, increased cross-linking in the CLPE degrades its mechanical properties, producing a trade-off between wear-resistance and mechanical properties [5, 26]. It is desirable to reduce wear while maintaining the mechanical properties necessary for proper *in vivo* function. The advantage of photo-induced radical graft polymerization comes from the fact that the grafted MPC polymer gave a high lubricity only on the surface, and had no effect on the bulk properties of the CLPE substrate.

Table 2 Physical properties of CLPE-g-MPC

Sample	Density (g/cm ³)	Swelling ratio	Network chain density (×10 ³ mol/ml)	M.W. between Cross-links (g/mol)	Cross-link density (mol%)
CLPE	0.944 (0.002)	2.99 (0.11)	0.437 (0.043)	2165 (214)	0.65 (0.06)
CLPE-g-MPC	0.943 (0.001)	2.94 (0.10)	0.459 (0.044)	2069 (186)	0.68 (0.07)

The standard deviation is in parentheses

Table 3 Mechanical properties of CLPE-g-MPC

Sample	Yield strength (MPa)	Impact strength (kJ/m ²)	Creep deformation (%)	Hardness (shore D)
CLPE	23.2 (0.4)	75.0 (1.4)	0.89 (0.17)	68.2 (0.9)
CLPE-g-MPC	23.1 (0.5)	77.0 (1.9)	0.63 (0.40)	68.4 (0.5)

The standard deviation is in parentheses

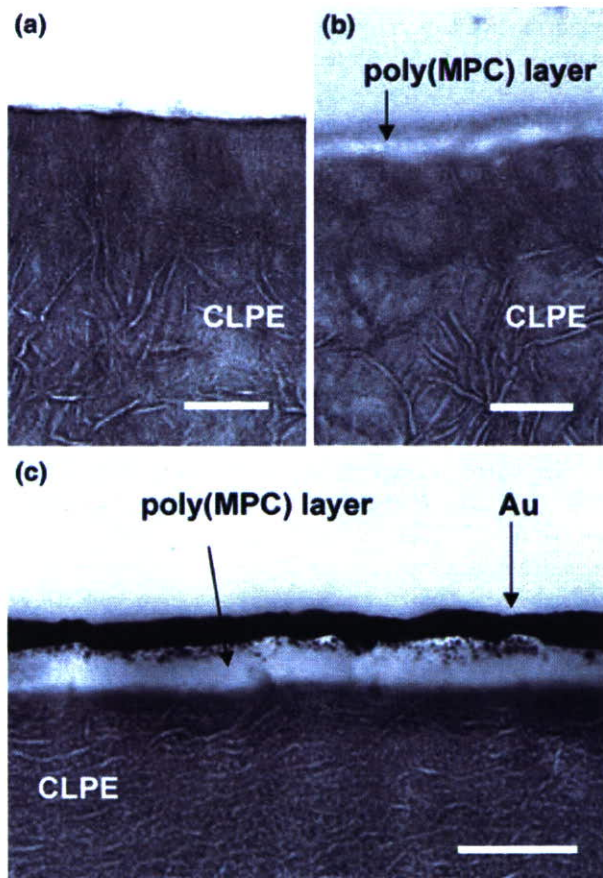


Fig. 4 Cross-sectional TEM images of CLPE-g-MPC. (a) CLPE (untreated), (b) CLPE-g-MPC before simulator test and (c) CLPE-g-MPC after a 3×10^6 cycle simulator test. Bar; 200 nm

After 3.0×10^6 cycles in the hip joint simulator test, the wear rate of CLPE-g-MPC cups remained low. The cross-sectional TEM image of the CLPE-g-MPC bearing surface after 3.0×10^6 cycles of the hip simulator test (Fig. 4c)

Table 4 Tribological properties of CLPE-g-MPC

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

showed that most of the bearing surface was covered by the MPC polymer layer even after the hip simulator test. In other words, the CLPE-g-MPC cups showed little wear on inspection, supporting the quite low wear observed in the hip joint simulator test.

On the CLPE-g-MPC surface, the nitrogen and phosphorus attributed to the phosphorylcholine in the MPC units increased with increasing polymerization time. This indicates that the density of the grafted MPC polymer can be controlled by the polymerization time, since the number of polymer chains produced in a radical polymerization is generally proportional to the photo-irradiation time. The elemental composition obtained by XPS (N = 5.1, P = 5.2) of the CLPE-g-MPC surface with a polymerization time of 90 min was almost equivalent to the theoretical elemental composition of MPC polymer. Therefore, the entire surface of the CLPE was assumed to be coated with an MPC polymer layer.

However, the area observed by the X-ray spot (approximately $400 \times 800 \mu\text{m}^2$) in XPS was quite limited. As a supplementary probe to examine the MPC polymer layer, wettability measurement of cups should be performed on many separate areas on the cups. The wettability measurement of a surface is readily performed in the laboratory on well defined, homogeneous, smooth and planar surfaces of prepared specimens. In the case of artificial hip joint cups, for which non-destructive measurements are usually required (and where excision of material samples is usually undesirable), these conditions do not exist and measurement with high precision is a difficult task. Hence,