was gradually diminished. Under such severe rubbing conditions as model B in Fig. 1, the effectiveness of lubricant constituents and the influence of cartilage surface conditions on tribological behaviors were evaluated.

The common features in frictional behaviors of articular cartilage in the reciprocating tests are as follows.

(1) Initial low friction is established by biphasic/hydration and/or mixed lubrication for cartilage surface with sufficient adsorbed films.

(2) Time-dependent gradual increase in friction during rubbing process is controlled by biphasic property of cartilage, interaction of adsorbed molecules and/or slight removal of cartilage surfaces.

(3) Reduction in restarting friction is brought by the recovery of hydration and biphasic property with recovery of deformation accompanied with adsorbed film formation after unloading for 5 min.

As indicated by the Eq. (1) in FE analysis, we can estimate the frictional behaviors of various cartilage surfaces different in adsorbed film formation, i.e., coefficient of friction for solid-to-solid contact μ_{eq}. In Fig. 11, the changes in friction estimated from total traction force in biphasic FE analyses during rubbing process under constant load are shown for μ_{eq} = 0.01 and 0.2. Most cases of frictional behaviors in this study except for addition of a single protein seem to be located between the upper (high friction) and lower (low friction) curves in Fig. 11, although FE analysis was conducted for two dimensional model.

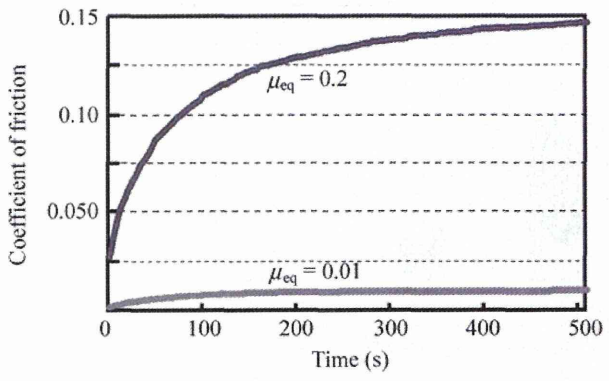

Fig. 11 Influence of μ_{eq} on time-depending frictional behaviors estimated by biphasic theory for cartilage.

In cases of addition of a single constituent into saline solution (Fig. 4), the frictional features as described above are observed, but the friction levels change depending on the properties of lubricant constituents. The addition of protein, i.e., albumin or γ-globulin into saline solution improved the restarting friction but increased the final friction at each 36 m sliding. Particularly, the addition of γ-globulin brought a remarkable lowering in restarting friction but higher final friction than albumin. The reason why two kinds of proteins show different friction levels was considered that γ-globulin has stronger adsorption ability on cartilage than albumin as indicated by fluorescent images [27], and thus γ-globulin showed lower restarting friction with appropriate adsorbed film formation in mild condition immediately after reloading, but exhibited higher friction due to molecular interaction as a bonding effect in very thin film condition after each 36 m sliding.

In the *in situ* observation of the rubbing pair of poly(vinyl-alcohol) (PVA) hydrogel and glass plate by Yarimitsu et al. [28], the fluorescent images for proteins adsorbed on glass plate, protein aggregates between rubbing surfaces and proteins on PVA hydrogel surface were discriminately observed in reciprocating tests for boundary lubrication regime at low sliding speed of 0.2 mm/s and the average contact pressure of 0.104 MPa. This reciprocating apparatus was constructed on the stage of the inverted fluorescent microscope. In saline solution of albumin, the easy peeling of albumin was observed, but in saline solution of γ-globulin, quick adsorption and uniform adsorbed film formation were observed. These phenomena indicate the differences in adsorption abilities for both proteins. In binary protein solutions with coexistence of albumin and γ-globulin, the relative ratio and concentration of proteins had an intense influence on adsorbed film formation [29]. Furthermore, the observation of adsorbed molecules in the evanescent field within about 200 nm from surface by using the total internal reflection fluorescence (TIRF) microscopy indicated in binary protein solutions that the bottom layer of stable protein adsorbed film is mainly composed of γ-globulin and the friction-induced enhancement of forming protein adsorbed film occurs

in lubricant with appropriate protein composition [30, 31]. The competitive adsorption of albumin and γ-globulin appears to affect these behaviors as indicated in study of adsorption and desorption of both proteins with TIRF spectroscopy by Tremsina et al. [32]. Furthermore, the differences in adsorption behaviors of serum proteins depend on the changes in conformation, molecular weight, charge condition, hydrophobic/hydrophilic properties of proteins and solid surfaces, pH of lubricant, and so on. Particularly under rubbing, denatured proteins change their conformations and adsorption properties, and thus affect the tribological behaviors [33–35]. Therefore, overall viewpoints are required to elucidate the actual adsorption behaviors of serum proteins.

The addition of HA with viscous property in lubricants was expected to improve the fluid film thickness, and subsequently improved friction level compared with saline [26]. The addition of DPPC alone is the most effective in reduction of friction but the final coefficient of friction is not so low (about 0.1) in Fig. 4.

Therefore, the effect of combination of different constituents was evaluated. The influences of coexistence of protein with HA on friction were examined in our previous study [26]. The coexistence of γ-globulin and HA showed the lowering of both the restarting and final or steady friction compared with HA solution. However, albumin exhibited higher final friction than HA solution although it showed a little lower restarting friction than HA solution. These facts suggest the synergistic effect of γ-globulin and HA, but indicate the adverse interaction of albumin and HA for intact cartilage. It is reported that albumin and HA show repulsive interaction [36] and the HA-protein complexes in natural synovial fluid contain globulin but almost no albumin at pH 7–8 [37]. These frictional trends for both proteins are similar for damaged cartilage with partially removed surface proteoglycan gel layer. The suppressive action between negatively charged albumin and negatively charged HA molecules was observed in fluorescent images of sparsely distributed adsorbed films, compared with intimate adsorbed films for γ-globulin and HA [26].

In this study, the effect of addition of neutral phospholipid DPPC with and without protein was examined. It should be noted that the coexistence of DPPC with protein is effective for intact cartilage (Fig. 5), but increases friction for damaged cartilage (Fig. 6). This difference appears to be brought about by changes in adsorbed film formation on damaged cartilage surface. For reciprocating tests of PVA hydrogel and glass plate lubricated with saline solution of DPPC alone, the Janus-faced property for high or low friction was affirmed in accord to either irregular adsorbed film or uniform DPPC adsorbed film formation in AFM images [38]. It is pointed out by Hills [10] that even only the oligolamellar phospholipid plays an effective lubricating role in natural synovial joints. By *in situ* fluorescent observation of forming adsorbed films for sliding pair of PVA hydrogel and glass plate in coexistence of DPPC and albumin [38], it was clarified that the formation of albumin-DPPC sheet-like composite film was found and therefore the friction was reduced. It is pointed out that DPPC with a neutral charge is likely to bind to albumin [39].

Next, the influence of addition of DPPC in HA solution with and without proteins was examined. The addition of DPPC alone in HA solution was considerably effective in reduction of friction for intact cartilage compared with coexistence of DPPC and either albumin or γ-globulin in HA solution (Fig. 7). This fact may suggest the formation of lubricating complex materials as membrane-like and roller structures composed of DPPC and HA [40]. Mirea et al. [41] indicated that HA has high affinity to phospholipid bilayer in the force-distance curve in AFM study. The detailed structure of HA-DPPC complex has not yet been clarified but the coexistence of DPPC and HA is likely to act synergistically as lamellar lubrication or related mechanism. Furthermore, for coexistence of DPPC and HA, HA-DPPC composite boundary film was visually confirmed [38] and friction was remarkably lowered, where the lubricating ability by HA-DPPC complex as gel-like film is supposed to become effective with high water retention ability of HA. However, HA solution containing DPPC showed an effective but limited protective property with local scratching as shown in Fig. 10.

On the contrary, albumin-DPPC composite was not

found in coexistence of three constituents, i.e., DPPC, HA and albumin [38], probably due to repulsive interaction between albumin and HA. This fact corresponds to the phenomenon in which the friction for HA solution with DPPC and albumin (Fig. 7) is higher than saline solution with DPPC and albumin (Fig. 5).

However, the supply of both albumin and γ-globulin as definite ratio into HA solution containing DPPC (lubricant No. 13) could remarkably improve the friction at very low level of 0.01 as final coefficient of friction (Fig. 7) and high wear resistance (Fig. 10). For damaged cartilage, the friction level increased in general but No.13 lubricant showed the minimum friction (Fig. 8).

In natural synovial joints, various lubricating constituents such as HA, proteins, glycoproteins and phospholipds different in molecular properties and sizes play different roles. Therefore, the interaction and/or synergistic action between phospholipids and other constituents seem to control the adsorbed film formation and tribological behavior. The influences of lubricants as HA solutions containing DPPC with or without proteins on the friction at restart and at steady state are summarized in Fig. 9 for intact and damaged cartilage specimens. The effectiveness of adsorbed film on reduction in restarting friction and steady friction is clearly demonstrated compared with saline solution. Particularly, it is noticed that the lubricant No.13 (HA solution with 1.4 wt% albumin, 0.7 wt% γ-globulin and 0.01 wt% DPPC) provided very low restarting friction for both intact and damaged cartilage specimens (Fig. 9(a)). This lubricant maintained very low friction until each 36 m sliding for intact cartilage, but the friction gradually increased until 0.05 as coefficient of friction for damaged cartilage (Fig. 9(b)). In the study by Nakashima et al. [29], HA solution with 1.4 wt% albumin and 0.7 wt% γ-globulin (albumin/globulin = A/G ratio of 2:1) or 0.7 wt% albumin and 1.4 wt% γ-globulin (A/G ratio of 1:2) showed very low wear for rubbing of PVA hydrogel against itself. For low wear condition in the latter, the layered adsorbed film formation was observed by the fluorescent method. In these cases, it is suggested that the γ-globulin forms protective adsorbed layer on cartilage surface and albumin plays as low shearing layers. On the contrary, HA solution with 1.4 wt% albumin and 1.4 wt% γ-globulin (A/G ratio of 1:1) formed the heterogeneous adsorbed film and showed higher wear.

The lubricant No.13 has similar composition to that in natural synovial fluid as hyaluronate solution containing lubricating constituents such as 1.25 wt% albumin, 0.75 wt% globulin (including α-, β-, and γ-globulins) as medium values [42], 1.1 wt% albumin and 0.7 wt% globulin [36], or 1.9 wt% albumin, 1.1 wt% globulin and 0.01 wt% DPPC [12]. In this lubricant, the lubricating layered structure in adsorbed film is expected for low friction and minimal wear, but the detailed elucidation of this mechanism is required in the future study. As exhibited in Figs. 7 and 9, lubricant No. 13 showed very low and steady friction in repeated reciprocating test at 20 mm/s. *In situ* fluorescent observation at very slow speed with this lubricant [38] showed the stable mixed adsorbed film containing albumin and γ-globulin but friction is not so low probably due to very thin film condition at 0.2 mm/s condition. Therefore, we plan to observe *in situ* the actual adsorbed film formation and frictional behavior at 20 mm/s or so. In various daily activities, synovia constituents appear to play their appropriate roles depending on the severity of operating conditions. DPPC and albumin are likely to act as low shearing layer, and γ-globulin acts as the protective film as strongly adsorbed on cartilage surface. HA has ability to thicken the lubricating fluid film and form some lubricating gel-like layer. Although some of synergistic mechanisms between lubricating constituents were shown in this study, the overall mechanisms are expected to be clarified from the viewpoint of multiscale level in future. On the role of lubricin as another lubricating constituent, Mirea et al. [41] suggested that it anchors lipid layers on the cartilage. We confirmed that the addition of lubricin in HA solution could reduce friction for intact cartilage in the preliminary test. In future study, we plan to evaluate the effective roles of all influential synovia constituents.

For damaged cartilage specimens with partially removed proteoglycan brush-like layer, the best composition in lubricant for low friction is the same lubricant No. 13 which is the best for intact cartilage, but the second one was changed to the HA solution

containing DPPC with γ-globulin from the HA containing DPPC solution without protein as the second one for intact cartilage. It is suggested for damaged cartilage that the protective role of γ-globulin with strong adsorption ability becomes important.

As discussed above, the effectiveness of lubricant constituents changes depending on rubbing cartilage properties in reciprocating tests of cartilage-on-glass. To evaluate rigorously the influence of synovia constituents on tribological behaviors of articular cartilage in natural synovial joints, the rubbing pair of cartilage-on-cartilage [8, 43] or cartilage-on-meniscus [44] should be used, and therefore the influence of glass plate on tribological behaviors in this study should be discussed. As mentioned in Section 1, the glass plate surface possesses hydrophilic characteristics with negatively charged property similar to proteoglycan on superficial cartilage layer in wet condition, whilst it is hard, smooth and nonporous/impermeable material. The adsorption of synovia constituents on glass plate is expected to be considerably similar to boundary film formation on intact cartilage but the interaction to the smooth, hard and nonporous/impermeable glass surface may be different. HA and albumin (at pH > 4.7) are negatively charged but γ-globulin is positively charged (at pH < 7.5). These electrostatic properties of adsorbed molecules have an influence on adsorption. On the contrary, the ploughing friction may be minimized for smooth surface, but adsorbed proteins on very smooth surface may induce high friction by their intense adhesive effect as hydrophobic bonding in watery system in very thin film condition. However, the effectiveness of lubricant constituents on tribological behaviors of compliant and biphasic articular cartilage appear to be reflected appropriately even in sliding pair of articular cartilage and glass plate. In pendulum friction tests for cartilage-on-cartilage of porcine shoulder joints composed of humerus head and glenoid cavity (cup) [8], the effectiveness in friction reduction by addition of 0.01 wt% DPPC or 1.0 wt% γ-globulin to HA solution for cartilage treated with detergent had been confirmed as similar effect to cartilage-on-glass combination. In contrast, the addition of 1.0 wt% or 3.0 wt% albumin to HA solution did not improve friction of cartilage-on-cartilage, which corresponds to adverse interaction of albumin and HA for cartilage-on-glass [26]. In contrast, the sliding pair of cartilage and clean glass plate showed higher friction in HA solution than that of cartilage and glass plate treated with Langmuir–Blodgett (LB) film as 5 to 10 bilayer of DPPC alone or mixed LB film of DPPC and γ-globulin [12]. As mentioned above, common features and/or some differences seem to occur in frictional behavior for cartilage-glass combination compared with cartilage-cartilage. In the next stage, therefore, further studies for cartilage-on-cartilage or cartilage-on-hydrogel (artificial cartilage) are required to elucidate strictly the influence of synovia constituents on tribological behaviors of articular cartilage in natural synovial joints. The sustaining of the synergistic mechanism of various synovia constituents on matched cartilage surfaces in natural synovial joints is expected to maintain the healthy condition.

5 Conclusions

In this study, at repeated reciprocating tests including restarting after interrupting-unloading process, the changes in friction were observed for intact and damaged articular cartilage specimens against glass plate lubricated with lubricants containing phospholipid, protein and hyaluronic acid as synovia constituents. The optimum composition in lubricants for low friction and minimum wear of both intact and damaged cartilage specimens was exhibited to be similar composition to natural synovial fluid. Furthermore, it was shown that the effectiveness of lubricant constituents changes depending on the surface conditions of articular cartilage.

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Poly(2-methacryloyloxyethyl phosphorylcholine) grafting and vitamin E blending for high wear resistance and oxidative stability of orthopedic bearings

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ABSTRACT

The ultimate goal in manipulating the surface and substrate of a cross-linked polyethylene (CLPE) liner is to obtain not only high wear resistance but also high oxidative stability and high-mechanical properties for life-long orthopedic bearings. We have demonstrated the fabrication of highly hydrophilic and lubricious poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) grafting layer onto the antioxidant vitamin E-blended CLPE (HD-CLPE(VE)) surface. The PMPC grafting layer with a thickness of 100 nm was successfully fabricated on the vitamin E-blended CLPE surface by using photoinduced-radical graft polymerization. Since PMPC has a highly hydrophilic nature, the water wettability and lubricity of the PMPC-grafted CLPE and HD-CLPE(VE) surfaces were greater than that of the untreated CLPE surface. The PMPC grafting contributed significantly to wear reduction in a hip-joint simulator wear test. Despite high-dose gamma-ray irradiation for cross-linking and further UV irradiation for PMPC grafting, the substrate modified by vitamin E blending maintained high-oxidative stability because vitamin E is an extremely efficient radical scavenger. Furthermore, the mechanical properties of the substrate remained almost unchanged even after PMPC grafting or vitamin E blending, or both PMPC grafting and vitamin E blending. In conclusion, the PMPC-grafted HD-CLPE(VE) provided simultaneously high-wear resistance, oxidative stability, and mechanical properties.

1. Introduction

Over the last half century, total hip arthroplasty (THA) has been one of the most successful joint surgeries for osteoarthritis and rheumatoid arthritis. Most patients experience dramatic pain relief, increased daily activity, and restored quality of life after THA. Owing to the aging global population, the number of primary and revised THAs performed has increased significantly year on year [1]. However, the incidence of osteolysis that leads to aseptic loosening greatly limits the duration and clinical outcome of this type of surgery [2,3]. Osteolysis is triggered by a host inflammatory response to wear particles produced at the bearing interface of the artificial joint. A typical device consists of an ultra-high molecular weight polyethylene (PE; currently cross-linked PE or CLPE) acetabular liner and a cobalt–chromium–molybdenum (Co–Cr–Mo) alloy femoral head, particles of which undergo phagocytosis by macrophages and induce the secretion of bone-resorptive cytokines [4]. Therefore, the reduction of the wear particles has become an important issue and the increasing focus of many studies.

To reduce wear, we have recently developed an articular-cartilage-inspired technology for surface modification with poly (2-methacryloyloxyethyl phosphorylcholine) (PMPC) grafting to develop a life-long acetabular liner in an artificial hip replacement [5–10]. Modification of the bearing surfaces of an artificial joint with a hydrophilic layer should increase lubrication to levels that match articular cartilage under physiological conditions. The synthetic molecule 2-methacryloyloxyethyl phosphorylcholine (MPC) is commonly used to prepare highly hydrophilic and antibiofouling

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polymer biomaterials [11–14]. MPC polymers have great potential for applications in the fields of biomedical science and bioengineering because they possess beneficial properties such as excellent antibiofouling ability and suppression of friction. Thus, a number of medical devices, including intravascular stents [12], soft contact lenses [13], artificial hearts [14], and artificial hip joints [9], have been developed from MPC polymers and applied clinically. The biomedical efficacy and safety of MPC polymers are therefore well established. A nanometer-scale layer of PMPC was formed on a CLPE surface to recreate the ideal hydrophilicity and lubricity of a physiological joint surface [15–17]. In the present study, the PMPC grafting was accomplished using a photoinduced- (i.e., through ultraviolet (UV) irradiation) radical polymerization technique [18–20].

However, lubrication is only one of several important indicators of the clinical performance of acetabular liners. Oxidation degradation of the first generation of CLPE by gamma-ray sterilization has been regarded as a potential limiting factor for the longevity of artificial hip replacements [21,22]. During gamma-ray irradiation, free radicals are formed in the PE molecular structure through cleavage of molecular bonding, and most of these free radicals are recombined in the cross-linking in the amorphous phase of PE. However, the free radicals in the crystalline phase of PE are long-lived and cause embrittlement through a cascading oxidation reaction [21]. Hence, other important indicators of acetabular liner performance include oxidation, which simultaneously preserves the mechanical properties of CLPE. The incorporation of the antioxidant vitamin E (α-tocopherol) has been proposed recently as an alternative to post-irradiation melting treatment after gamma-ray irradiation to avoid oxidation [23]. Vitamin E is a free-radical scavenger and a well-established biological antioxidant. It is a naturally occurring compound whose function as an additive is to react with free radicals in the cell membrane and prevent oxidation-induced degradation of the polyunsaturated fatty acid. Most frequently, vitamin E is incorporated in PE by blending it into PE powder before consolidation to form a molded bar or sheet stock, and subsequent gamma-ray irradiation is carried out for cross-linking. In this process, the vitamin E concentration and irradiation dose are relatively easy to control and can be optimized.

In the study reported here, we prepared a highly hydrophilic and lubricious nanometer-scale surface by grafting a PMPC layer onto the surface of an antioxidative CLPE substrate that was modified by vitamin E blending. Our ultimate goal in manipulating the surface and substrate of the CLPE liner was not just to obtain high wear resistance, but also high oxidative stability and excellent mechanical properties for life-long orthopedic bearings. The presence of vitamin E in the substrate prevented degradation caused by oxidation, but it could also reduce the efficiency of cross-linking and PMPC grafting while the vitamin E itself reacted [24]. Therefore, the modification process for the substrate (i.e., vitamin E blending) and surface (i.e., PMPC grafting) must be optimized to simultaneously obtain wear resistance, oxidative stability, and excellent mechanical properties for life-long orthopedic bearings. We investigated the effects of PMPC grafting and vitamin E blending on these three properties of liners for artificial hip joints; such investigations are of great importance in the design of life-long artificial joints and to better understand how the use of this material can affect the longevity of artificial hip joints.

In the course of the study, we searched for answers to three questions: (1) Is it possible to prepare the PMPC grafting layer on the CLPE surface, regardless of the presence of vitamin E? (2) Will the hydration lubrication characteristics of the PMPC grafting layer affect wear resistance? (3) Will vitamin E provide oxidative stability despite the high-dose gamma-ray irradiation for cross-linking and further UV irradiation for PMPC grafting?

2. Materials and methods

2.1. Chemicals

Benzophenone and acetone were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). Industrially synthesized MPC was supplied by NOF Corp. (Tokyo, Japan) [25]. A compression-molded bar stock of 0.1 mass% vitamin E-blended polyethylene (PE(VE); GUR1020E resin, Orthoplastics Ltd., Lancashire, UK) was irradiated with a high dose (HD; 100 kGy) of gamma-rays in a N_2 gas atmosphere and annealed at 120 °C for 12 h in N_2 gas in order to facilitate cross-linking. Hereafter, this polyethylene material is referred to as HD-CLPE(VE). As the control, a compression-molded bar stock of polyethylene without any additives (GUR1020 resin, Orthoplastics Ltd.) was irradiated with a 50 kGy dose of gamma-rays in a N_2 gas atmosphere, and annealed at 120 °C for 7.5 h in N_2 gas to facilitate cross-linking. Hereafter, this polyethylene material is referred to as CLPE. Samples of CLPE and HD-CLPE(VE) were then machined from the bar stocks after cooling, washed with aqueous polysorbate-surfactant solutions and ethanol, and dried at room temperature.

2.2. PMPC grafting on CLPE

The CLPE and HD-CLPE(VE) samples were immersed for 30 s in acetone containing 10 mg/mL benzophenone, 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 [17]. The benzophenone-coated CLPE and HD-CLPE(VE) samples were then immersed in the aqueous MPC solution. Photoinduced-radical graft polymerization was carried out on the CLPE and HD-CLPE(VE) surfaces using UV irradiation (UVL-400HA ultra-high pressure mercury lamp, Riko-Kagaku Sangyo Co., Ltd., Funabashi, Japan) with an intensity of 5 mW/cm^2 at 60 °C for 90 min; a filter (model D-35, Toshiba Corp., Tokyo, Japan) was used to permit the passage of only UV light with a wavelength of 350 ± 50 nm [8,19,20]. After the polymerization, the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples were removed, washed with pure water and ethanol, and dried at room temperature.

2.3. Surface chemical analysis

The elemental surface conditions of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples were analyzed by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS-HSi165, Kratos/Shimadzu Co., Kyoto, Japan) equipped with a 15 kV Mg-Kα radiation source at the anode. The take-off angle of the photoelectrons was maintained at 90°. The functional group vibrations of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples 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 over the 800–2000 cm^{-1} range at a resolution of 4.0 cm^{-1}.

2.4. Cross-sectional observations by transmission electron microscopy

Cross-sections of the PMPC-grafted CLPE and HD-CLPE(VE) samples were observed using transmission electron microscopy (TEM). The samples were embedded in epoxy resin, stained with ruthenium oxide vapor at room temperature, and then sliced into ultra-thin films (approximately 100 nm-thick) using a Leica Ultra Cut UC microtome (Leica Microsystems, Ltd., Wetzlar, Germany). A JEM-1010 electron microscope (JEOL, Ltd., Tokyo, Japan) was used for the TEM observations at an acceleration voltage of 100 kV.

2.5. Mechanical tests

The mechanical properties of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) substrates were evaluated using a series of tests. Tensile testing was performed according to ASTM D638 using type IV tensile bar specimens that measured 1.5 mm in thickness and a crosshead speed of 50.8 mm/min. Each of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples was divided into ten specimens, and each was evaluated individually. A double-notched (notch depth = 4.57 ± 0.08 mm) Izod impact test was performed according to ASTM F648, with six specimens tested for each PMPC-grafted CLPE samples and each PMPC-grafted HD-CLPE(VE) sample. The shore hardness (*D*) was measured according to ASTM D2240, with five specimens tested for each PMPC-grafted CLPE sample and each PMPC-grafted HD-CLPE(VE) sample. Creep deformation was measured by applying a constant load (1130 kgf for 24 h) to a specimen and then measuring the height displacement, according to ASTM D621, with four specimens tested for each PMPC-grafted CLPE sample and each PMPC-grafted HD-CLPE(VE) sample. Each sample was sterilized by 25 kGy gamma-rays in N_2 gas. The results of each mechanical test were expressed as the mean values ± the standard deviation.

2.6. Wettability and friction tests

Static-water contact angles were measured on each of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples by employing 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 μL) were deposited on the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) surfaces, and

the contact angles were directly measured after 60 s using a microscope. Fifteen areas were evaluated for each sample, and the mean values ± the standard deviation were calculated.

Unidirectional friction tests were performed using a ball-on-plate machine (Tribostation 32, Shinto Scientific Co., Ltd., Tokyo, Japan). Six specimens of each of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples were evaluated. Each specimen was sterilized by 25-kGy gamma-rays in N_2 gas. A 9-mm-diameter pin made of a Co–Cr–Mo alloy was also prepared. The surface roughness (R_a) of the pin was <0.01 μm, which was comparable to that of currently used femoral head products. The friction test was performed for each specimen at room temperature using a load of 0.98 or 4.9 N (the contact stress roughly calculated by Hertzian theory was approximately 29 or 49 MPa, respectively), a sliding distance of 25 mm, and a frequency of 1 Hz. A maximum of 100 cycles were carried out, and pure water was used for lubrication. The mean dynamic coefficients of friction were determined by averaging the values of five data points taken from the 96–100 cycles.

2.7. Hip-simulator wear test

A 12-station hip simulator (MTS Systems Corp., Eden Prairie, MN, USA) using the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) liners with an inner and outer diameter of 26 and 52 mm, respectively, was used for the wear test according to ISO 14242-3. Four specimens of each of the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) liners were prepared. Each liner was sterilized by 25 kGy gamma-rays in N_2 gas. A Co–Cr–Mo alloy ball measuring 26 mm in diameter (K-MAX® HH-02; KYOCERA Medical Corp., Osaka, Japan) was used as the femoral head. A mixture of 25 vol% bovine serum, 20 mmol/L ethylene diamine-*N, N, N', N'*-tetraacetic acid (EDTA), and 0.1 mass% sodium azide was used as the lubricant. The lubricant was replaced every 5.0×10^5 cycles. Gait cycles were applied to simulate a physiological loading curve (Paul-type) with double peaks at 1793 and 2744 N, and multidirectional (biaxial and orbital) motion with a frequency of 1 Hz. Gravimetric wear was determined by weighing the liners at intervals of each 5.0×10^5 cycles. Load-soak controls ($n = 2$) were used to compensate for fluid absorption by the specimens, according to ISO 14242-2. Testing was continued for a total of 1.0×10^7 cycles. Because the gravimetric method was used, the weight loss of each of the tested liners was corrected by subtracting the weight gain resulting from the load-soak control. However, this correction was not considered to be perfect because only the tested liners were continuously moved and subjected to the load.

After 1.0×10^7 cycles of the hip-simulator wear test, the volumetric wear of the liners was evaluated using a three-dimensional (3D) coordinate-measurement machine (BHN-305, Mitutoyo Corp., Kawasaki, Japan). The structures were then reconstructed using 3D modeling software (Imageware, Siemens PLM Software Inc., Plano, TX, USA).

The wear particles were isolated from the bovine serum solution, which was then used as a lubricant in the hip-simulator wear test. To isolate the wear particles, the lubricant was incubated in a 5 mol/L sodium hydroxide solution for 3 h at 65 °C to digest adhesive proteins that degraded and precipitated. In order to avoid artifacts, the contaminating proteins were removed by extraction with solutions of several densities: sugar solution, 1.20 g/cm^3 and 1.05 g/cm^3; isopropyl alcohol solution, 0.98 g/cm^3 and 0.90 g/cm^3. This was followed by centrifugation at 2.55×10^4 rpm for 3 h at 5 °C (himac CP 70MX; Hitachi Koki Co., Ltd., Tokyo, Japan). The collected solution was sequentially filtered through a 0.1-μm membrane filter, and the membrane was observed under a field-emission scanning electron microscope (FE-SEM; JSM-633OF, JEOL DATUM Co., Ltd., Tokyo, Japan) at an acceleration voltage of 20 kV after gold deposition.

2.8. Oxidative stability tests

The residual free radicals of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples, obtained before and after gamma-ray sterilization at 25 kGy in N_2, were analyzed by electron spin resonance (ESR). The ESR spectra of PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) were obtained using an ESR spectrometer (JES-FA300, JEOL RESONANCE Inc., Akishima, Japan) in a cylindrical TE011 resonant cavity at 9.1 GHz and 25 °C. The external magnetic field was modulated at 100 kHz to detect the first-order derivative of the absorption line. The relative concentration of defects in each grain was calculated by double numerical integration of the observed absorption-derivative peaks relative to the signal of 4-hydroxy-2,2,6,6-tetramethyl-4-piperidinol-1-oxyl (Sigma–Aldrich Corp., Saint Louis, MO, USA) as a control sample. Six specimens were evaluated for each PMPC-grafted CLPE sample and each PMPC-grafted HD-CLPE(VE) sample, and the results were expressed as the mean values ± the standard deviation.

The oxidative stability (oxidative-induction time) of PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) sterilized by 25-kGy gamma-rays in N_2 gas was evaluated by differential scanning calorimetry (DSC) with a DSC-Q100 differential scanning calorimeter (TA Instruments Inc., New Castle, DE, USA) according to ASTM D3895. Samples weighing approximately 5 mg were placed in an aluminum pan. The samples were kept at 30 °C for 5 min under a nitrogen flow of 50 mL/min, heated to 200 °C at a rate of 20 °C/min, and then held for 5 min for equilibration while the nitrogen flow was maintained. After that, the purge gas was switched to oxygen with a flow rate of 50 mL/min. The oxidative-induction time was obtained as the time between the oxygen switch and the sharp increase in heat flow resulting from the exothermic nature of the oxidation reaction. Six specimens were evaluated for each PMPC-grafted CLPE sample and each PMPC-grafted HD-CLPE(VE) sample, and the results were expressed as the mean values ± the standard deviation.

The oxidative degradation (oxidation index) of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples that underwent accelerated aging was evaluated by microscopic FT-IR according to ASTM F2102. The PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) samples sterilized by 25-kGy gamma-rays in N_2 gas were subjected to the conditions of accelerated aging, i.e., exposure to 80 °C in air for 21 days [26]. A thin film (thickness of 100–200 μm) of the cross-section was sliced from each of the aged samples. The FT-IR spectra were obtained using a microscopic FT-IR analyzer (Spectrum BX, Perkin–Elmer Corp., MA, USA) for 100 scans over the range of 800–2000 cm^{-1} at a resolution of 4.0 cm^{-1}. The oxidation index was defined as the ratio of the carbonyl peak area at 1720 cm^{-1} to the methylene peak area at 1360 cm^{-1}. Four films were evaluated for each sample, and the mean values ± the standard deviation were calculated.

2.9. Statistical analyses

The mean values of the three groups (untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE)) were compared by one-factor analysis of variance (ANOVA), and the significant differences of the all comparable properties were determined by post-hoc testing using the Bonferroni method. The dynamic coefficients of friction (unidirectional friction test) of each group under loadings of 0.98 and 4.9 N were compared by using a Student's *t*-test. All the statistical analyses were performed using an add-on (Statcel 2, OMS Publishing Inc., Tokorozawa, Japan) to Microsoft Excel® 2003 (Microsoft Corp., Redmond, WA, USA).

3. Results

Vitamin E blending was found to have no effect on the extent of PMPC grafting. Fig. 1 shows the XPS and FT-IR/ATR spectra of the untreated CLPE, and PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE). The XPS spectra of the binding energy region of the nitrogen (N) and phosphorous (P) electrons showed peaks for PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE), while these peaks were not observed in the case of untreated CLPE (Fig. 1A). The peaks at 403 and 134 eV are attributed to the trimethylammonium group and phosphate group, respectively, which indicate the presence of phosphorylcholine in the MPC units. A transmission absorption peak was observed at 1460 cm^{-1} for all samples (Fig. 1B). This peak is chiefly attributed to the methylene (CH_2) chain in the CLPE or HD-CLPE(VE) substrate, the blended vitamin E, and the grafted PMPC. However, absorption peaks at 1720, 1240, 1080, and 970 cm^{-1} were observed only in the spectra for PMPC-grafted surfaces. These peaks correspond to the carbonyl group (C=O) and the phosphate group (P–O) in the MPC unit, respectively. After PMPC grafting, peaks attributed to the MPC unit were clearly observed in both XPS and FT-IR/ATR spectra of PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE). As shown in the cross-sectional TEM images in Fig. 2, the PMPC-grafting process afforded a uniform grafted PMPC layer with an almost constant thickness of 100–150 nm on the surface of both CLPE and HD-CLPE(VE). In addition, neither cracking nor delamination was observed at the substrates and the interface between the grafted PMPC layer and the CLPE or HD-CLPE(VE) substrate. These results indicate that PMPC was successfully grafted on the CLPE and HD-CLPE(VE) surfaces [15–20].

Some mechanical properties of the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) are summarized in Table 1. The tensile ultimate strength, hardness, and creep deformation properties did not differ significantly between all groups examined in this study. In contrast, the tensile yield strength differed slightly among all three groups. The elongation and impact strength in the PMPC-grafted HD-CLPE(VE) were also slightly decreased compared to those in the untreated CLPE and PMPC-grafted CLPE. However, all mechanical properties of the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) met the requirements of ASTM F648 and F2695.

The PMPC grafting affected the hydration and friction kinetics of the CLPE surface, regardless of vitamin E blending. Fig. 3 shows the

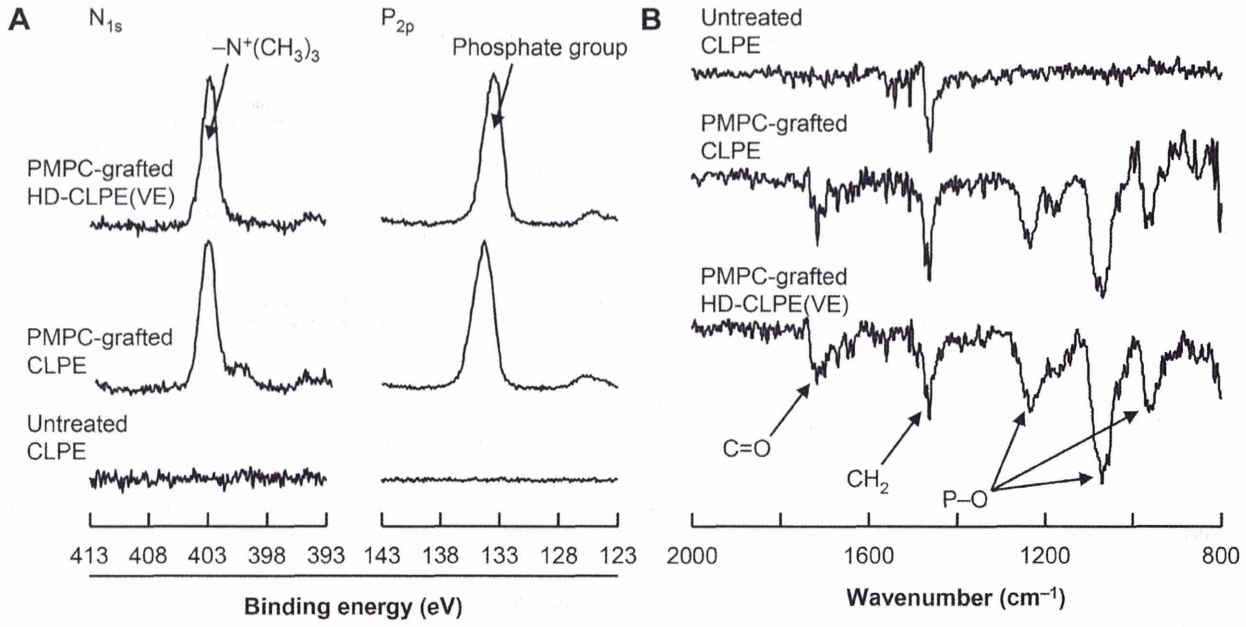

Fig. 1. (A) XPS and (B) FT-IR/ATR spectra of untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) samples.

static-water contact angles on the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) surfaces, as well as the dynamic coefficient of friction between water and all three surfaces. The static-water contact angle on untreated CLPE was 96°, and it decreased markedly to 27° and 30°, respectively, after PMPC grafting was carried out on the CLPE and HD-CLPE(VE) surfaces (Fig. 3A). The dynamic coefficients of friction between water and PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) decreased markedly, with the surfaces exhibiting an approximately 80–90% reduction in the coefficient compared with the untreated CLPE surface (Fig. 3B). Interestingly, the dynamic coefficients of friction of the PMPC-grafted CLPE under a 4.9 N loading decreased significantly compared to those under a 0.98 N loading, regardless of vitamin E blending.

In the hip-simulator wear test with 1.0×10^7 cycles, the characteristics of the PMPC-grafted surface affected the durability of the CLPE or HD-CLPE(VE) liner. In the absence of vitamin E blending or PMPC grafting, fluid (e.g., water, proteins, and lipids) absorption in the load-soak control liners, determined by the weight gain, was increased in a cycle-dependent manner (Fig. 4A). During the hip-simulator wear test, the PMPC grafting drastically decreased the gravimetric wear not only in the CLPE liner, but also to a similar level in the HD-CLPE(VE) liner (Fig. 4B). Furthermore, there was a slight and gradual increase in weight of the untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) liners during the testing period, which is partially attributed to greater fluid absorption by the tested liners than was allowed for by the load-soak controls. As noted earlier, correction using the load-soak control was not a perfect approach because only the tested liners were continuously moved and loaded. Three-dimensional coordinate measurements of the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) liners revealed barely detectable volumetric wear, in contrast to the substantial wear detected for the untreated CLPE liners (Fig. 5A). The volumetric wear images in Fig. 5A are in agreement with the gravimetric wear data shown in Fig. 4B. Remarkably, extremely small and barely observable wear particles were produced by the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) liners during the hip-simulator wear test (Fig. 5B). The wear particles of the untreated CLPE liners, and the small quantity of wear particles produced by the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) liners, consisted of only sub-micrometer-sized granules. The vitamin E blending and PMPC grafting did not affect the morphologies of the wear particles.

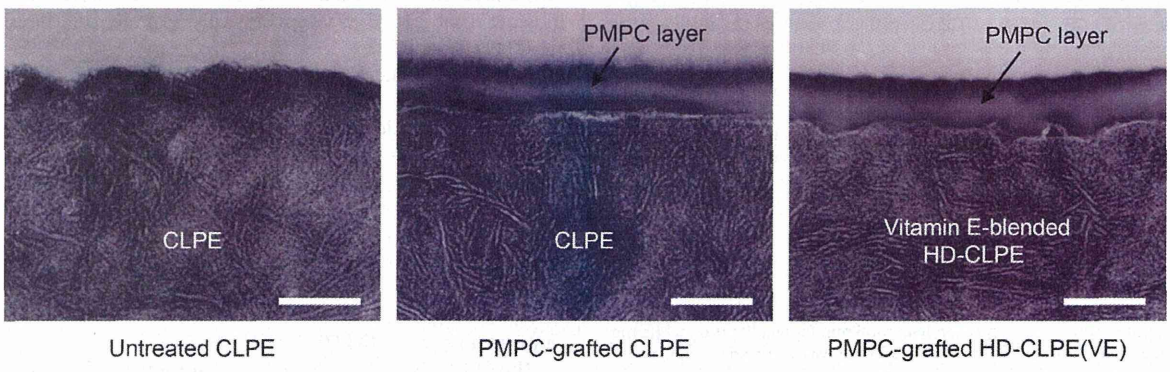

Fig. 2. Cross-sectional TEM images of untreated CLPE, PMPC-grafted CLPE, and PMPC-grafted HD-CLPE(VE) samples. The scale bar corresponds to 200 nm.