mechanisms associated with a certain amount of plastic deformation. On the other hand, the worn surface of 100 kGy sample (Fig. 7(c) and Fig. 8(c)) had the distinct machine marks attached with some fine wear debris. Surface cracks related to fatigue mechanisms were also found. However, the fibrillated wear particles and protuberances generated by the adhesive wear process were hardly observed. The increased number of chemical bonds between adjacent molecular chains formed by the increased crosslink density can retard the chain mobility and enhance the molecular resistance against shear rupture. Consequently, increased radiation dose enhanced the resistance to the adhesive wear and had a predominant impact on the wear behavior of UHMWPE.

Although the effects of the crosslink density on the oxidation, mechanical and wear properties of crosslinked UHMWPE were not clear, the wear mechanism seemed to be mainly dependent on the oxidation behavior when the OI is greater than a certain "critical threshold" (Fig. 12). Similar features of masses of fibril formations on the wear surfaces were observed on both crosslinked samples at the center region as shown in Fig. 10. Fractures, cracks, fiber drawing and scratches, which indicated a mixed wear mechanism including abrasive wear and fatigue, are the main wear characteristics observed on the more oxidized subsurface regions for both crosslinked UHMWPEs (Fig. 9). It seems that more severe fractures were founded at the subsurface of 100 kGy sample, which is related to the higher OI and higher wear rate compared with the 50 kGy sample.

A limitation of this study was that the region of each sample for the wear test was not a continuous variable. Only three regions of each sample were analyzed, thus, there was insufficient data to accurately quantify the relationship between the OI, radiation dose and wear rate. In order to clarify the radiation dose and OI effects and determine a "critical threshold", more regions with different oxidation conditions of two shelf-aged gamma-irradiated UHMWPEs should be tested.

5. Conclusions

Oxidation behavior and its effects on the mechanical and wear properties of crosslinked UHMWPE after 7-year shelf-ageing were investigated in this paper. It was shown that the micro-hardness, elastic modulus and crystallinity increased with the increase of the oxidation index, while the wear resistance decreased. The wear analysis may indicate that, when the OI is under a critical threshold, the crosslink density is the main cause of the difference of wear mechanisms; and above the critical threshold, the oxidation will have an important effect on the wear behavior of crosslinked UHMWPE. However, more evidence is needed to confirm this hypothesis.

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Wear Resistance of the Biocompatible Phospholipid Polymer-Grafted Highly Cross-Linked Polyethylene Liner Against Larger Femoral Head

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ABSTRACT: The use of larger femoral heads to prevent the dislocation of artificial hip joints has recently become more common. However, concerns about the subsequent use of thinner polyethylene liners and their effects on wear rate have arisen. Previously, we prepared and evaluated the biological and mechanical effects of a novel highly cross-linked polyethylene (CLPE) liner with a nanometer-scaled graft layer of poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC). Our findings showed that the PMPC-grafted particles were biologically inert and caused no subsequent bone resorptive responses and that the PMPC-grafting markedly decreased wear in a hip joint simulator. However, the metal or ceramic femoral heads used in this previous study had a diameter of 26 mm. Here, we investigated the wear-resistance of the PMPC-grafted CLPE liner with a 40-mm femoral head during 10×10^6 cycles of loading in the hip joint simulator. The results provide preliminary evidence that the grafting markedly decreased gravimetric wear rate and the volume of wear particles, even when coupled with larger femoral heads. Thus, we believe the PMPC-grafting will prolong artificial hip joint longevity both by preventing aseptic loosening and by improving the stability of articular surface. © 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res

Keywords: artificial hip joint; total hip arthroplasty; periprosthetic osteolysis; aseptic loosening

In addition to aseptic loosening, dislocation is one of the most common causes of revision of total hip arthroplasty (THA).[1] The dislocation rates are reported to range from less than 1% to 5% after primary THA[2,3] and up to 5–15% after revision THA.[4] Most dislocations occur in the first 6 weeks after surgery, and about one-third become recurrent and require revision surgery.[5,6]

Although dislocation is a multifactorial complication dependent on various factors (e.g., implant malpositioning),[7] larger femoral heads provide mechanical advantages that can improve stability of the articular surface of THA. The head/neck ratio is increased with the use of larger femoral heads, which can prevent impingement between the trunnion and the acetabular component.[8] Decreased impingement, combined with the increased amount of displacement required before the head dislocates (jump distance), also reduces the dislocation risk.[8] Hence, the use of larger femoral heads for improving the stability of the THA has recently become more common,[2,9] and multiple studies have demonstrated larger femoral heads reduce dislocation rates clinically.[10,11] However, larger femoral heads (e.g., 36 or 40 mm in diameter) have an increased sliding distance and velocity per step between bearing surfaces of the THA, leading to an increased wear rate as compared to smaller femoral heads.[9] Moreover, a larger femoral head requires a thinner polyethylene (PE) liner for retaining acetabular bone, which can produce higher contact stresses, possibly accelerating wear and/or fracture of the liner,[12] and, therefore, may increase the production of wear particles, consequently resulting in osteoclastogenesis, bone resorption, and periprosthetic osteolysis.[13] Thus, larger femoral heads may increase the risk for aseptic loosening, a factor closely related to the rate of PE wear.[14] Therefore, new technologies that decrease not only the dislocation rate but also the production of wear particles are needed.

For preventing periprosthetic osteolysis and aseptic loosening, we developed a novel bearing surface with cartilage-mimicking hydrogel structures. Recent studies have shown the human articular cartilage surface is covered with a nanometer-scaled phospholipid layer that functions to protect the articulating surface from mechanical wear, to provide hydrophilicity, and to act as a boundary lubricant.[15] Thus, we grafted the biocompatible phospholipid polymer, poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC), onto a highly cross-linked PE (CLPE). The nanometer-scale layer of PMPC (100–150 nm in thickness) with the cartilage-mimicking hydrogel structures provides

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hydrophilicity and lubricity mimicking the articular cartilage surface without affecting the CLPE substrate physical or mechanical properties.[16] The PMPC grafting on the CLPE surface was shown to increase the lubrication to levels matching articular cartilage under physiological conditions.[17] Our recent study on the mechanical effects of PMPC grafting revealed that it markedly decreased wear particle production and that the effect of PMPC grafting was maintained through 70 million cycles in a hip joint simulator.[18] The PMPC-grafted particles were also shown to be biologically inert and not to result in bone resorptive responses.[19] Based on multicenter clinical trials of the PMPC-grafted CLPE (PMPC-CLPE) acetabular liners performed from 2007 in Japan (UMIN00003681), the liners were reported as a safe implant option for hip replacement surgery after a 3-year clinical use.[20] In this cohort study of 76 joints, the mean wear rate was 0.002 mm/year, representing about an 80–97% reduction as compared to other CLPE liners.[21–26] At the time this article was written, neither periprosthetic osteolysis nor a requirement for revision surgery had been observed after a minimum of 5 years and a maximum of 7 years of follow-up.

However, metal or ceramic femoral heads with a diameter of 22 or 26 mm were used in our previous studies.[17–19] The present study investigated the wear resistance of the PMPC-grafted CLPE liner with a 40-mm femoral head during 10×10^6 cycles in a hip joint simulator test.

METHODS

Hip Joint Simulator

Acetabular liners were produced from GUR1020 ultra-high molecular weight polyethylene bar stock irradiated at 50-kGy for cross-linking (K-MAX® CLQC, KYOCERA Medical Corporation, Osaka, Japan), and surface modified by using a photoinduced graft polymerization of MPC (NOF Co. Ltd., Tokyo, Japan), as previously reported.[17,19] All liners were subsequently sterilized by 25-kGy gamma-ray irradiation under N_2 gas. Cobalt–chromium–molybdenum (CoCrMo) alloy femoral heads (26 or 40 mm in diameter) (K-MAX® HH-02, KYOCERA Medical Corporation) were used in this study. The thickness of the acetabular liner was 10 and 6 mm in the 26-mm and 40-mm femoral head groups, respectively. Under the conditions recommended by ISO 14242-3, CLPE ($N = 3$) or PMPC-CLPE ($N = 3$) acetabular liners were tested against 26-mm or 40-mm CoCrMo alloy femoral heads on a 12-station hip simulator (MTS Systems Corp., Eden Prairie, MN) at 1 Hz; 700 ml of 25% (v/v) bovine serum was used as the lubricant and was replaced every 0.5×10^6 cycles. Sodium azide (10 mg/L) and ethylenediaminetetraacetic acid (20 mM) were added for preventing microbial contamination and minimizing calcium phosphate formation on the implant surface. A physiological loading curve (Paul-type) with double peaks at 1793- and 2744-N loads with a multidirectional (biaxial and orbital) motion were used as gait cycles.[27] The simulator was run up to 10×10^6 cycles. Wear was determined by gravimetric measurement of the liners at intervals of 0.5×10^6 cycles. Because the liners absorbed fluids (e.g., water, lipids) while soaking in the lubricant, wear measurements were corrected by load-soak controls ($N = 2$), according to ISO 14242-2. Weight loss in the tested liners was corrected by subtracting the weight gain of the load-soak controls. Wear rates were determined by linear regression and were estimated at intervals of 0–10×10^6 cycles.

Analyses of Joint Surfaces

After 10×10^6 cycles, morphological changes in the liner surface were measured using a 3-dimensional (3D) coordinate measuring instrument (BHN-305, Mitsutoyo Corp., Kawasaki, Japan) and reconstructed using 3D modeling software (Imageware, Siemens PLM Software, Inc., Plano, TX). For evaluating wear-induced alterations in surface morphology, the liner surface was analyzed using a confocal scanning laser microscope (OLS1200, Olympus, Tokyo, Japan).

Analyses of Wear Particles

After isolation from the bovine serum solution,[28] wear particles were analyzed according to the ASTM F1877-05 standard and digitally imaged on a field emission scanning electron microscope (JSM-633OF, JEOL Datum Co. Ltd., Tokyo, Japan). An image-processing program (Scion Image, Scion Corp., Frederick, MD) was used to determine the volume of wear particles per 10^6 cycles.[29] Two size descriptors (equivalent circle diameter [ECD], diameter) and two shape descriptors (aspect ratio, roundness) were used to define each wear particle, according to ASTM F1877-98.[18] Each parameter was defined as follows: ECD was defined as the diameter of a circle with an area equivalent to that of one wear particle. The diameter was defined using the maximum dimensions as determined by the SEM analysis. The aspect ratio was defined as the ratio of the major diameter to the minor diameter. It should be noted that the major diameter represented the longest straight line that could be drawn between any two points on the outline. On the other hand, the minor diameter represented the longest line perpendicular to the major diameter. Roundness was a measure of how closely a wear particle resembled a circle; its values ranged from 0 to 1, with a perfect circle having a roundness value of 1.

Statistical Analysis

Differences between wear rates and between the size and shape descriptors of particles were accessed for significance by the Student's *t*-test. All statistical analyses were conducted using add-in software (Statcel 2; OMS Publishing, Inc., Tokorozawa, Japan) on Microsoft Excel.

RESULTS

We initially estimated the weight gain of the load-soak control liners. The mean weight gain in the load-soak controls of the untreated CLPE liners was 3.87 and 4.20 mg for the 26- and 40-mm CoCrMo alloy femoral heads, respectively. Similarly, the mean weight gain in the load-soak controls of the PMPC-CLPE liners was 3.74 and 3.28 mg for the 26- and 40-mm CoCrMo alloy femoral heads, respectively. For the 26-mm CoCrMo alloy femoral heads, the load-soak control liners showed comparable weight gains during 10×10^6 cycles, irrespective of the PMPC grafting. For the 40-mm CoCrMo alloy femoral heads, the

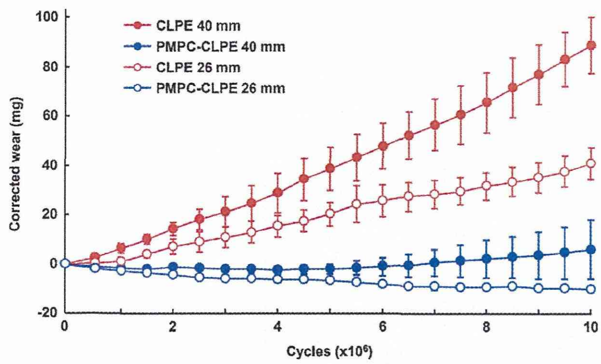

Figure 1. Wear amount of CLPE and PMPC-CLPE liners in the hip joint simulator. Time course of corrected wear amount of CLPE liners with or without PMPC grafting against 26- or 40-mm CoCr heads in the hip joint simulator during 10×10^6 cycles of loading. Data are expressed as mean (symbols) ± standard deviation (SD) for three liners/group.

load-soak controls of the PMPC-CLPE liners absorbed less than the untreated CLPE liners. Because both PMPC-CLPE (26/40 mm) liners had no greater weight gains than the untreated CLPE (26/40 mm) liners, these observations confirmed that weight gain was attributable to the absorption of the fluid by the liner material and not to its retention on the surface PMPC layer, as previously reported.[18]

The wear amount in the hip joint simulator was then estimated. After 10×10^6 cycles, the untreated CLPE liners showed a total weight loss of 40.9 ± 6.4 (mean ± standard deviation) and 89.0 ± 11.4 mg for the 26- and 40-mm CoCrMo alloy femoral heads, respectively (Fig. 1). In contrast, the PMPC-CLPE liners showed a total weight loss of -10.0 ± 1.4 and 6.1 ± 11.8 mg for the 26- and 40-mm CoCrMo alloy femoral heads, respectively. For both femoral head sizes, the PMPC grafting decreased the total weight loss of the liners. The weight gain in the 26- and 40-mm PMPC-CLPE liners might be due at least in part to the absorption of fluid by the liners during soaking in the lubricant, suggesting underestimation of the load-soak control. When using the gravimetric method, the weight loss in the tested liners is corrected by subtracting the weight gain in the load-soak controls; however, this correction cannot be precisely achieved because only the tested liners are continuously subjected to load and motion. This underestimation has been previously reported, particularly in several reports on wear-resistant articulating surfaces.[12,30,31]

For both femoral head diameters, the wear rates for the PMPC-CLPE liners were significantly lower than those of the untreated CLPE liners ($p = 0.007$ and 0.002, respectively) (Table 1). When compared to the CLPE (40 mm) liners, the PMPC-CLPE (40 mm) liners showed a decreased wear rate of 93%. In the absence of the PMPC grafting, the CLPE (40 mm) liners showed an approximately twofold higher wear rate than the CLPE (26 mm) liners ($p = 0.013$). However, the wear rates were not significantly different between the PMPC grafting for the 26-mm and 40-mm femoral heads ($p = 0.193$). These results confirmed that PMPC grafting was unaffected by the increased femoral head diameter. In the time course for the gravimetric wear, the PMPC-CLPE (40 mm) liners shifted from slightly gaining weight to losing it after 5×10^6 cycles (Fig. 1). However, when the wear rate was compared between 5×10^6 and 10×10^6 cycles, the PMPC-CLPE (40 mm) liners showed a significantly lower wear rate than the untreated CLPE (40 mm) liners (1.44 ± 1.97 mg/10^6 cycles vs. 9.82 ± 0.55 mg/10^6 cycles, $p = 0.023$).

As shown by the 3D morphometric analysis, the surfaces of both PMPC-CLPE (26/40 mm) liners showed little or no detectable volumetric wear. By contrast, the surfaces of both CLPE (26/40 mm) liners suffered from substantial wear (Fig. 2). The confocal scanning laser microscopic analysis revealed the original machine marks were completely absent on both CLPE (26/40 mm) liners after 10×10^6 cycles (Fig. 3, left). However, these markings were still present on both PMPC-CLPE (26/40 mm) liner surfaces (Fig. 3, right), suggesting very little or no detectable volumetric wear.

Based on the SEM analysis, the wear particles from the CLPE and PMPC-CLPE liners in all groups were predominantly submicrometer-sized granules (Fig. 4). However, substantially fewer wear particles were found for both PMPC-CLPE (26/40 mm) liners than the CLPE (26/40 mm) liners. Moreover, PMPC grafting decreased the total volume of the wear particles by 93% and 99% in the 26-mm and 40-mm femoral head groups, respectively (Fig. 5A). The particle size distribution among the four liners revealed the particles

Table 1. Wear Rate Estimated by the Corrected Weight Loss of CLPE and PMPC-CLPE Liners

		p-Value			
	Wear Rate (mg/10^6 Cycles)	vs CLPE 26 mm	vs CLPE 40 mm	vs MPC-CLPE 26 mm	vs MPC-CLPE 40 mm
CLPE 26 mm	4.09 ± 0.64		0.013	0.007	0.034
CLPE 40 mm	8.90 ± 1.14	0.013		0.006	0.002
MPC-CLPE 26 mm	-1.00 ± 0.14	0.007	0.006		0.193
MPC-CLPE 40 mm	0.61 ± 1.18	0.034	0.002	0.193	

Data are expressed as mean ± standard deviation (SD).

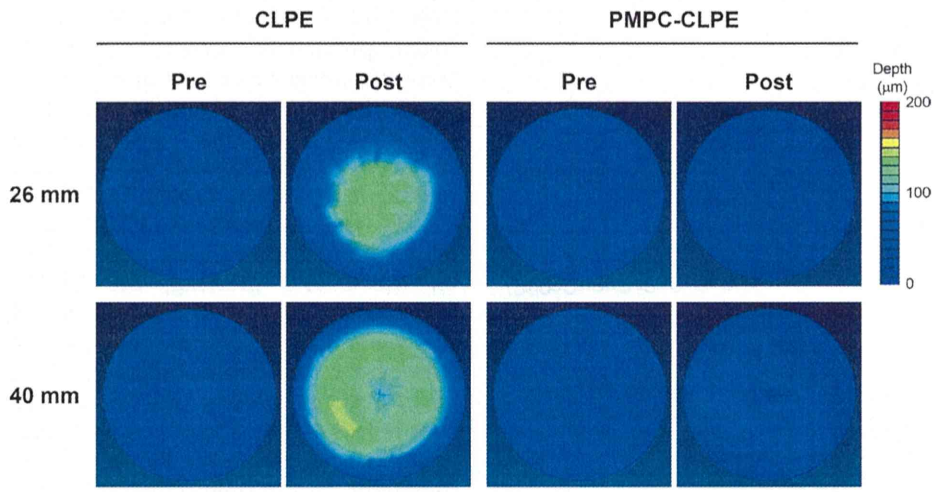

Figure 2. 3D morphometric analyses of the surfaces of the CLPE and PMPC-CLPE liners. Surface characteristics of the bearing interfaces with or without PMPC graft layer before (pre) and after (post) 10×10^6 cycles of the hip joint simulator test.

with diameters ranging from 0.1 to 0.2 μm occurred at the highest frequency in all groups, and those with diameters of <0.5 μm represented over 75% of the particles in all groups (Fig. 5B). No significant differences in the particle size and shape descriptors were found among the four liners (Figs. Figs. 6,6 and Figs. 7,7).

DISCUSSION

Recent multiple studies demonstrate larger femoral heads clinically reduce dislocation rates. Howie et al.[10] reported that the early dislocation rate of primary/revision THAs was 4.4/12.2% and 0.8/4.9% for 28- and 40-mm femoral head, respectively. Hence, the use of larger femoral heads can be expected to continue to increase for preventing dislocations of the artificial hip joint. However, the femoral head size can affect the wear of CLPE acetabular liners. Based on a simple formula for the volume of a sphere, volumetric wear is proportional to the cube of the radius (femoral head diameter); that is, it increases exponentially with increasing femoral head diameter for any given amount of linear wear.[32] Moreover, the increased contact area and sliding distance of larger heads result in increased volumetric wear. In their retrieval study, Schmalzried et al.[33] reported the volumetric wear increased by 6.3 mm^3/year for each millimeter increase in head diameter.Indeed, in the present study, CLPE (40 mm) liners showed a greater wear rate and volume of wear particles than CLPE (26 mm) liners. Clinically, Lachiewicz et al.[25] reported the volumetric wear of CLPE was greater with larger femoral heads (36 and

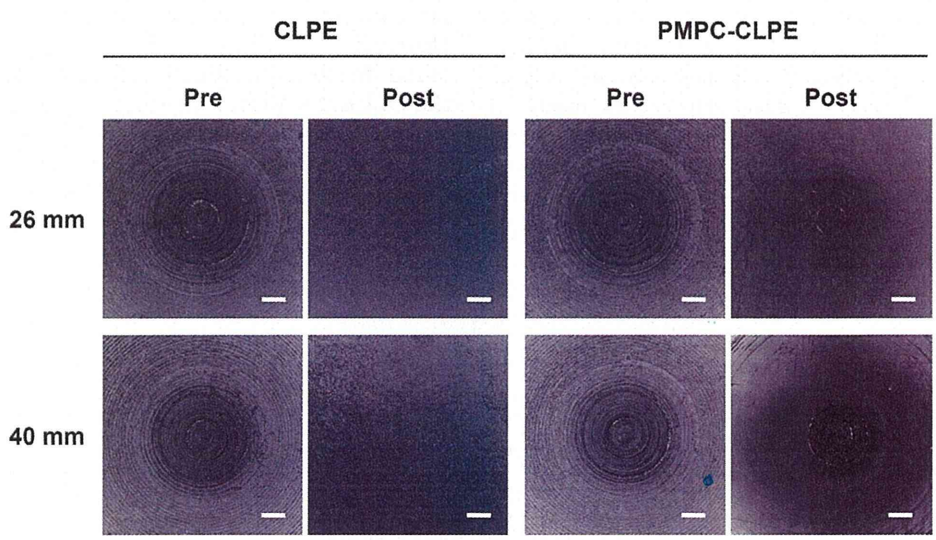

Figure 3. Confocal scanning laser microscopic analysis of the contact areas in the liner surfaces. Surface characteristics of the bearing interfaces with or without PMPC graft layer before (pre) and after (post) 10×10^6 cycles of the hip joint simulator test. Scale bar, 200 μm.

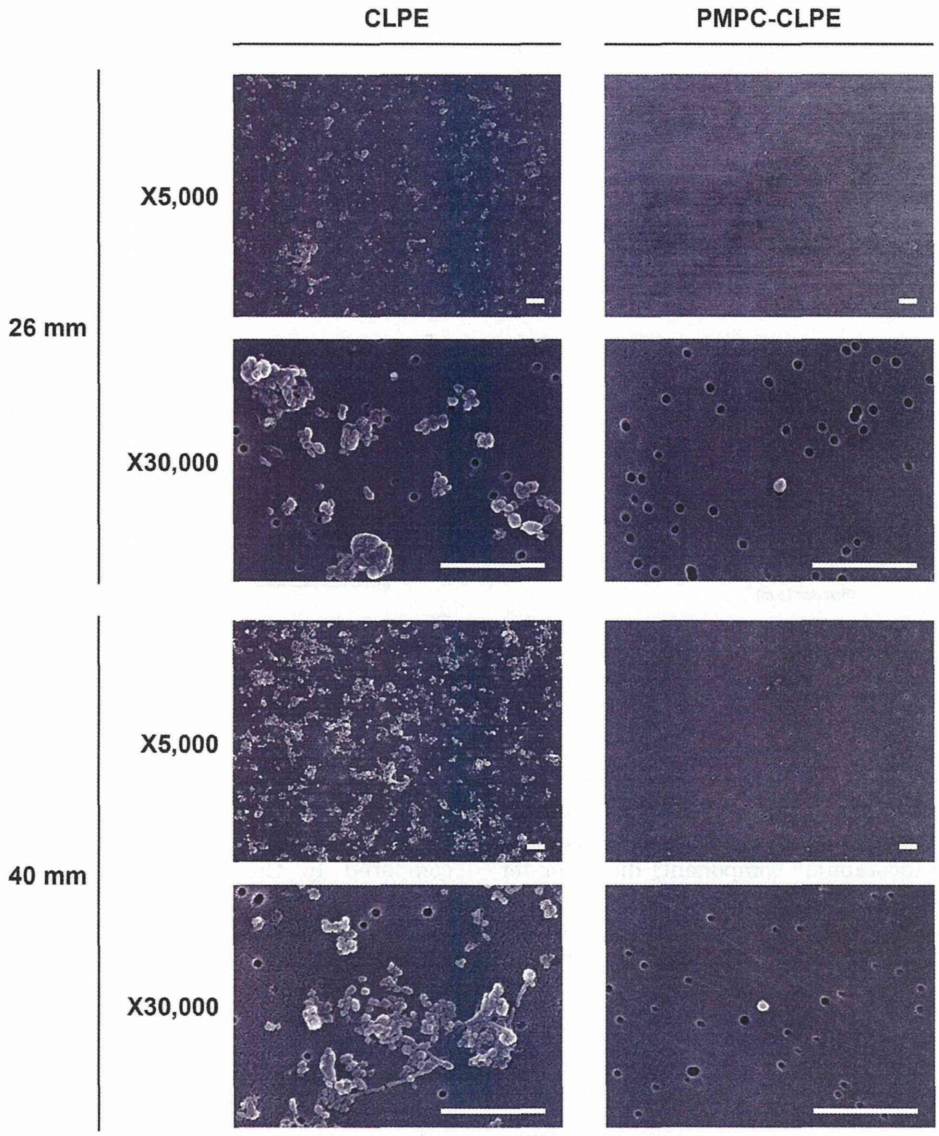

Figure 4. SEM images of wear particles from the CLPE and PMPC-CLPE liners. Low (top) and high (bottom) magnification of the SEM images. Scale bar, 1.0 μm.

40 mm) when compared to standard femoral heads (22, 26, and 28 mm) in an evaluation of 146 hips. Hammerberg et al.[8] also reported the volumetric wear of CLPE with larger femoral heads (38 and 44 mm) was nearly twofold when compared to standard femoral heads (28 and 32 mm). Hence, concerns have arisen that increases in volumetric wear will lead to aseptic loosening secondary to periprosthetic osteolysis. Therefore, we employed PMPC grafting onto the surface of the acetabular liner to decrease the amount of volumetric wear and increase the femoral head size.

MPC is a methacrylate monomer with a phospholipid polar group in a side chain, resembling the structure of cell membranes.[34] Thus, MPC polymers can suppress biological reactions even when in contact with living organisms, and are now clinically used on the surfaces of many medical devices.[35] The clinical efficacy and safety of the MPC polymer as a biomaterial are well established.[20] In the present study, PMPC grafting onto the surface of the CLPE liner resulted in high wear resistance, irrespective of the femoral head size. Moreover, the PMPC-grafted CLPE showed a significantly lower wear rate during 10×10^6 cycles. Our previous studies have revealed PMPC grafting on the CLPE surface decreased the friction coefficient/torque by ~80–90%,[17] that is, to levels matching those of articular cartilage under physiological conditions. In the present study, PMPC grafting decreased the gravimetric wear rate by 93% and the volume of wear particles by 99% even when coupled with 40-mm femoral heads, in agreement with our previous in vitro/vivo studies.[18–20]

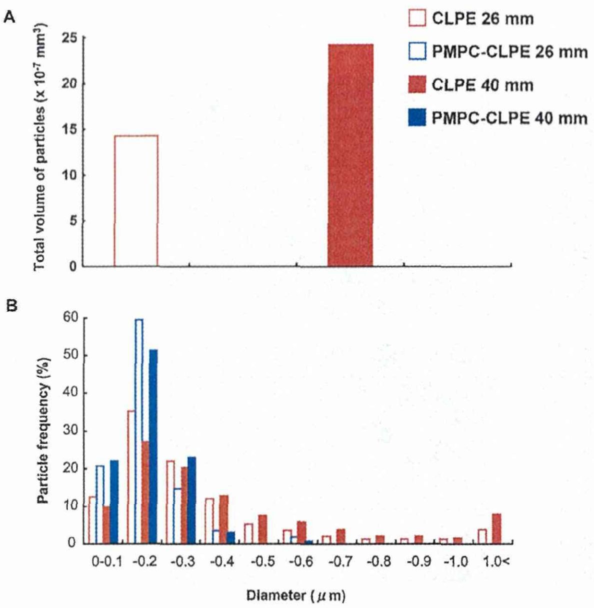

Figure 5. Analysis of wear particles isolated from lubricants in the hip joint simulator. (A) Graphs show the total volume of wear particles per 10^6 cycles. (B) Size and shape descriptors of each wear particle. Data are expressed as mean ± SD.

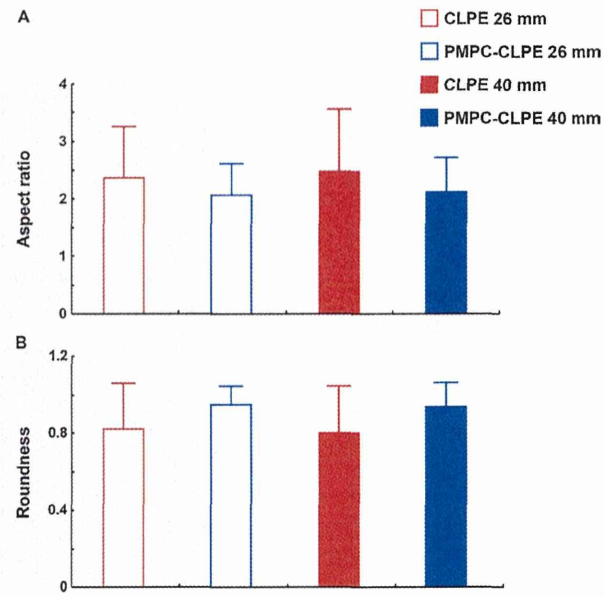

Figure 7. Assessments of the particle from CLPE and PMPC-CLPE liners using shape descriptors. Two shape descriptors, i.e., aspect ratio and roundness, were used to define each particle. Data are expressed as mean (symbols) ± SD.

Our study has several limitations. First, the thickness of the acetabular liner was different between the 26- and 40-mm femoral heads because of the specified metal outer cup (acetabular component) diameter for the hip simulator study. Johnson et al.[36] reported in their hip simulator study using CLPE liners of different thicknesses (1.9, 3.9, 5.9, 7.9 mm), the thinner CLPE liners had higher wear rates. Hence, in the present study, it is possible the nearly twofold higher wear rate in the untreated CLPE (40 mm) liners as compared to the untreated CLPE liners (26 mm) resulted from the differences in liner thickness and not the femoral head diameter. However, the PMPC grafting similarly decreased the wear rate for the 26- and 40-mm femoral heads, suggesting it suppressed the effect of the femoral head diameter and acetabular liner thickness.

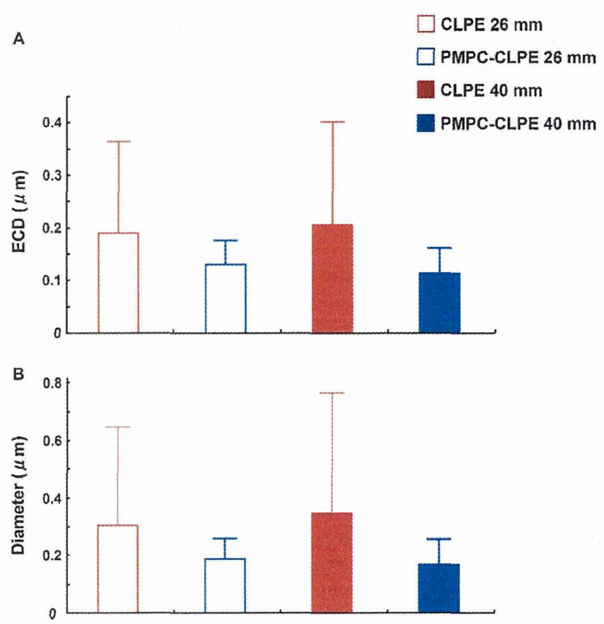

Figure 6. Assessments of the particle from CLPE and PMPC-CLPE liners using size descriptors. Two size descriptors, i.e., equivalent circle diameter (ECD) and diameter, were used to define each particle. Data are expressed as mean (symbols) ± SD.

Second, although the present hip joint simulator test was performed in accordance with ISO14242-3, we did not entirely capture the range of loading and motion conditions of the in vivo environment with respect to the variety of positions, the loading magnitude, or daily routine. Further, because PMPC grafting is nanometer-scaled, there is a concern how well the PMPC-CLPE liner will resist abrasion by a femoral head damaged by third-body abrasion in vivo. However, in our previous study, we found PMPC grafting causes a negligible effect on the physical and mechanical properties of the CLPE substrate.[16] Clinically, lack of effect on bulk properties provides an advantage because when the PMPC graft layer is removed from the surface of the liner, only the surface of the CLPE substrate is exposed. Hence, in such cases, the steady wear rate of the PMPC-CLPE increases to nearly the same (or slightly lower) level as that of the untreated CLPE liner.[37] To extend our findings, we are now running the hip simulator tests with more severe conditions (e.g., the use of several types of roughened femoral heads) to simulate more completely physiological loading.

Third, damage to the thin acetabular liners is an important issue with larger femoral heads. In the trade-off between wear resistance, a disadvantage of CLPE is the decrease in the mechanical properties that accompany some of the cross-linking/thermal processing, including yield strength, ultimate tensile strength, and resistance to fatigue.[38] This disadvantage may play an important role in the fracture of liner rims and locking mechanisms occurring under conditions such as impingement and microseparation. Tower et al.[39] reported rim fractures in their retrieval study of CLPE acetabular liners. Hence, the mechanical properties of PMPC-grafted thin acetabular liner against higher stresses by larger femoral heads remain a major concern. Because modification of bearing surfaces with PMPC increases the hydration of the surfaces and decreases the wear of the substrates, a PMPC layer can potentially cushion the impact and improve the resistance to fracture and fatigue of CLPE. We are now running the pin-on-disk test under impact-to wear and multidirectional sliding conditions according to ASTM F732-00.

In conclusion, the different results obtained in this study clearly demonstrate that PMPC-grafting onto a CLPE liner surface markedly decreased the production of wear particles during 10×10^6 cycles in the hip joint simulator even when coupled with larger femoral heads. This suggests that the PMPC-CLPE liner may be a promising approach to extending the longevity of artificial hip joints not only by preventing aseptic loosening but also by preventing dislocation.

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