The results obtained in this study show that poly(MPC) grafting markedly reduces the production of wear particles from CLPE liners, without affecting the size of the particles. These results suggest that poly(MPC) grafting is a promising technique for increasing the longevity of artificial hip joints.

1. Introduction

Sir John Charnley introduced the use of polyethylene (PE) components in total hip arthroplasty (THA) in the 1960s, and since then, these components have been extensively used for 50 years (Charnley, 1961). However, aseptic loosening resulting from periprosthetic osteolysis—which is a clinical complication arising from THA—is the prevalent cause of revision surgery (Bozic et al., 2009). Previous studies have revealed that PE particles generated from liners play a major etiological role in periprosthetic osteolysis. Macrophage phagocytosis of the PE particles is followed by the secretion of prostaglandin E2 (PGE2) and cytokines, which induce the receptor activator of the NF-κB ligand (RANKL) expression, consequently resulting in osteoclastogenesis and bone resorption (Harris, 2004; Jacobs et al., 2001). Further, periprosthetic osteolysis is closely related to the rate of PE wear and the characteristics of the wear particles (Catelas and Jacobs, 2010). Hence, various attempts have been made to improve the wear resistance of PE liners, such as enhancing the cross-linking of PE (CLPE) (Callaghan et al., 2008).

In the previous studies, we introduced a nanometer-scaled poly(2-methacryloyloxyethyl phosphorylcholine (MPC)) grafting layer on the surface of CLPE liners. We found that such type of grafting dramatically decreased the wear of the liner surface (Moro et al., 2009, 2006). In the present study, we investigated the effect of poly(MPC) grafting on the production of wear particles, using a hip wear simulator up to 15×10^6 cycles.

2. Materials and methods

2.1. Poly(MPC) grafting

Nanometer-scaled grafting (100–150 nm in thickness) of the poly (MPC) onto the PE liner surface was carried out by a photo-induced polymerization technique. The CLPE liners (K-MAX® CLQC; KYOCERA Medical Corp., Osaka, Japan) were immersed in an acetone solution containing 10 mg/mL of benzophenone for 30 s and then dried at room temperature to remove the acetone. Then, MPC (NOF Corp., Tokyo, Japan) (Ishihara et al., 1990) was dissolved in degassed pure water to obtain a 0.50 mol/L MPC aqueous solution, and the benzophenone-coated CLPE liners were immersed in this solution. Photoinduced graft polymerization was carried out on the CLPE liner surface using ultraviolet irradiation (UVL-400HA ultra-high-pressure mercury lamp; Riko-Kagaku Sangyo Co., Ltd., Funabashi, Japan) with an intensity of 5.0 mW/cm^2 at 60 °C for 90 min; subsequently, a filter (Model D-35; Toshiba Corp., Tokyo, Japan) was used to restrict the passage of ultraviolet light to wavelengths of 350±50 nm. After the poly (MPC)-grafted CLPE (MPC-CLPE) liners were polymerized, they were washed with pure water and ethanol and dried at room temperature. These specimens were then sterilized by 25-kGy gamma rays under N_2 gas (Kyomoto et al., 2008).

2.2. Hip joint simulator

A 12-station hip simulator (MTS Systems Corp., Eden Prairie, MN) with CLPE and MPC-CLPE liners, each with inner and outer diameters of 26 and 52 mm, respectively, was used for the hip simulator wear test performed according to the ISO Standard 14242-3. A Co–Cr alloy femoral head with a diameter of 26 mm (K-MAX® HH-02; KYOCERA Medical Corp.) was used as the femoral component. A biaxial rocking motion was applied to the head/cup interface via an offset bearing assembly with an inclined angle of +23°. Both the loading and motion were synchronized at 1 Hz. According to the double-peaked Paul-type physiologic hip load, the applied peak loads were 1793 and 2744 N (Paul, 1967). Bovine calf serum (25 vol%) diluted in distilled water was used as a lubricant. Sodium azide (10 mg/L) and EDTA (20 mM) were added to prevent microbial contamination and to minimize the formation of calcium phosphate on the implant surface.

The simulator was run up to 15×10^6 cycles. The liners were cleaned and weighed on a microbalance (Sartorius Genius ME215S, Sartorius AG, Goettingen, Germany) at intervals of 0.5×10^6 cycles. The lubricant was collected and stored at −20 °C for further analysis. Wear was determined from the weight loss of each liner and corrected by cyclically loaded soak controls according to the ISO Standard 14242-2. The wear rates were determined by linear regression.

After complete loading, morphological changes in the liner surface were measured using a three-dimensional (3D) coordinate measuring machine (BHN-305, Mitsutoyo Corp., Kawasaki, Japan) and reconstructed using 3D modeling software (Imageware, Siemens PLM Software Inc., TX, USA). The liner surface was analyzed using a confocal scanning laser microscope (OLS1200, Olympus, Tokyo, Japan), as previously reported.

The wear particles were isolated from the bovine serum solution. For isolating the wear particles from the lubricant, the lubricant was incubated with 5.0 mol/L of NaOH solution for 3 h at 65 °C after it was tested, in order to digest adhesive proteins that were degraded and precipitated. To avoid artifacts, contaminating proteins were removed by extraction with sugar solution (1.20 g/cm^3 and 1.05 g/cm^3) and isopropyl alcohol solutions (0.98 and 0.90 g/cm^3). After the lubricant was centrifuged at 25,500 rpm for 3 h at 5 °C, the particles were collected, subjected to sequential filtrations (minimum pore size of 0.1 μm) (Fisher et al., 2004; Tipper et al., 2006), and subsequently dried. The filter was then sputter coated with gold palladium 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) based on the

NIH image software was used to measure the total number, area, and volume of the wear particles per 10^6 cycles (Campbell et al., 1996; Dean et al., 1999). Two size descriptors, namely, the equivalent circle diameter (ECD) and the diameter (D), and two shape descriptors, namely, the aspect ratio (AR) and roundness (R), were used to define each wear particle, according to ASTM F1877-98. Each parameter is defined as follows. ECD is defined as the diameter of a circle with an area that is equivalent to that of one wear particle. Diameter is defined using the maximum dimensions determined by the SEM analysis. Aspect ratio is defined as the ratio of the major diameter to the minor diameter. It should be noted that the major diameter is the longest straight line that can be drawn between any two points on the outline. On the other hand, the minor diameter is the longest line that is perpendicular to the major diameter. Roundness is a measure of how closely a wear particle resembles a circle; its values range from 0 to 1, with a perfect circle having a roundness value of 1.

2.3. *Statistical analysis*

The significance of differences was determined by the student's t-test. All statistical analyses were performed using add-in software (Statcel 2; OMS publishing Inc, Tokorozawa, Japan) on a computerized worksheet (Microsoft Excel® 2003; Microsoft Corp, Redmond, WA).

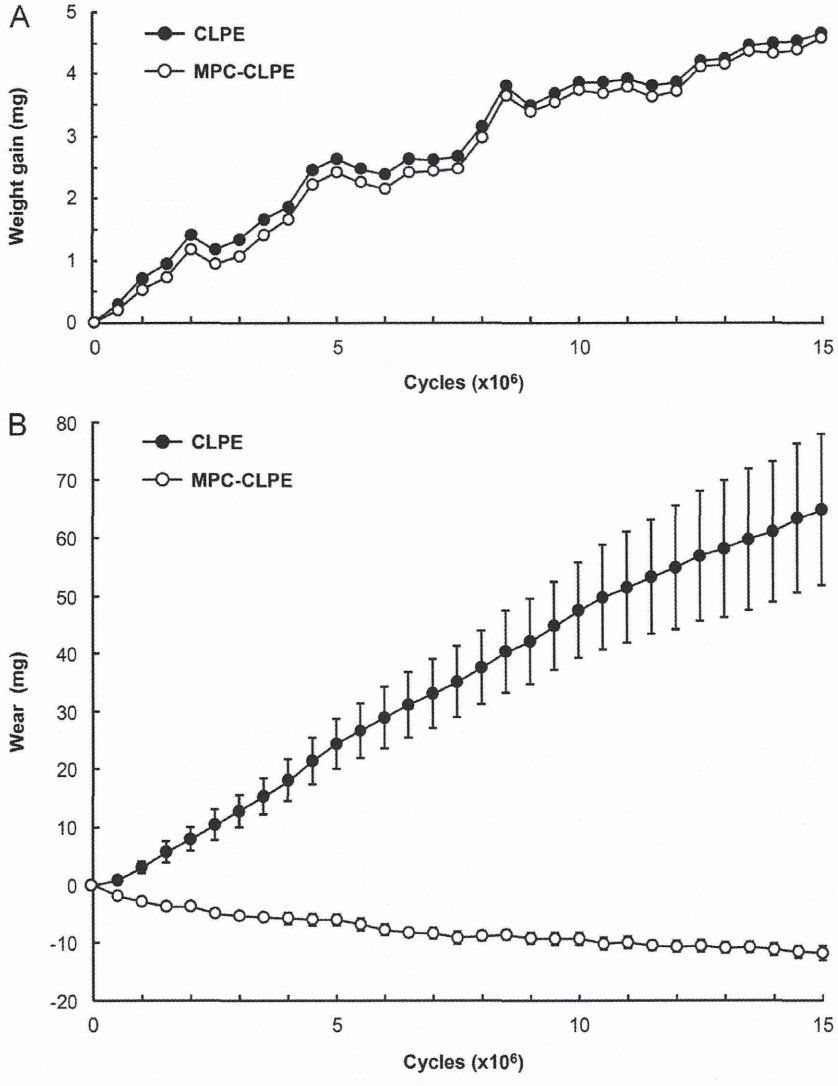

Fig. 1 – Wear amounts of cross-linked PE liners with or without MPC grafting in the THA simulator. (A) Load-soak controls. Fluid absorption of the liners that were axially loaded cyclically to the acetabular liners with the same pressure as the THA simulator, but without rotational motion. Data are expressed as means (symbols) for 2 inserts/group. (B) Time course of wear amount in the THA simulator during 15×10^6 cycles of rotational motion and axial loading against Co–Cr alloy femoral heads. The wear amount was estimated from the weight loss of the inserts after correction by the average weight gain in the respective load-soak controls (weight loss in the THA simulator+average of weight gain in the load-soak control). Data are expressed as means (symbols)±standard deviation (SD) for 4 liners/group.

3. Results

Two types of load-soak control liners, which were only loaded axially to the femoral heads and without any rotational motion in the simulator, showed comparable weight gains during the 15×10^6 cycles, irrespective of whether poly(MPC) grafting (Fig. 1A) was carried out; this observation confirmed that weight gain was caused by the absorption of the fluid by the liner material, and not by the fluid that was retained in the surface poly(MPC) layer (Kyomoto et al., 2011; Moro et al., 2006, 2009). We then evaluated gravimetric wear by assessing the weight loss of the liners after correction by the average weight gain in the respective load-soak controls. The gravimetric analysis performed in the hip simulator study showed that the CLPE liners suffered from a total weight loss of 64.8 ± 11.7 mg (mean ± standard deviation) after 15×10^6 cycles of loading (Fig. 1B). In contrast, it was found that the MPC-CLPE liners continued to gain weight, showing a total weight gain of 13.1 ± 1.2 mg. This weight gain might be at least partially attributed to greater fluid (e.g., water, proteins, and lipids) absorption in the tested liners than in the load-soak controls, suggesting the underestimation of the load-soak control, as reported previously (Dumbleton et al., 2006; Muratoglu et al., 2001; Oral et al., 2006; Shen et al., 2011). When the wear rate was counted at an interval of every 10^6 cycles, poly(MPC) grafting was shown to maintain similar wear resistance in 0–1 ($p=0.0016$), 4–5 ($p=0.0019$), 9–10 ($p=0.0022$), 14–15 ($p=0.0075$), and the total ($p=0.002$) intervals (Table 1).

3D coordinate measurements of the MPC-CLPE liner surface revealed no or very little detectable volumetric wear, while the cross-linked PE liners suffered from substantial wears (Fig. 2A). The confocal scanning laser microscopic analysis of the liner surface showed that the original machine marks that are clearly visible before the loading still remained on the MPC-CLPE liner surface, although they were completely obliterated on the cross-linked PE liner.

Table 1 – Wear rate estimated by the corrected weight loss of CLPE and MPC-CLPE liners.

Test period (10^6 cycles)	Wear rate (mg/10^6 cycles)		p-value
	CLPE	MPC-CLPE	
0–1	2.34 ± 0.99	−3.43 ± 0.42	0.0016
4–5	5.47 ± 1.09	−1.05 ± 0.06	0.0019
9–10	4.85 ± 0.91	−0.47 ± 0.08	0.0022
14–15	3.60 ± 1.22	−0.73 ± 0.23	0.0075
Total	4.01 ± 0.87	−1.09 ± 0.08	0.0020

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

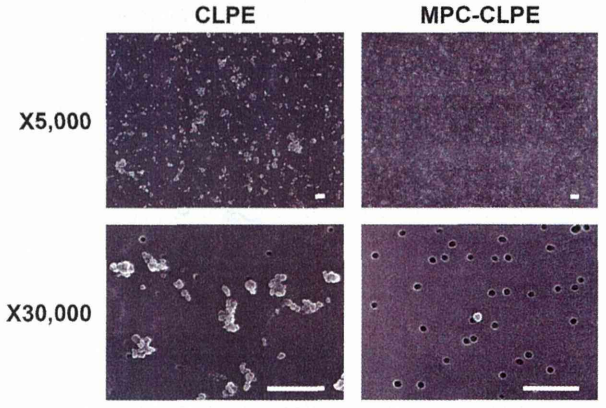

Fig. 3 – Scanning electron microscopic images of the wear particles from CLPE and MPC-CLPE liners. Low (top) and high (bottom) magnifications of the SEM images. Scale bars: 1.0 μm.

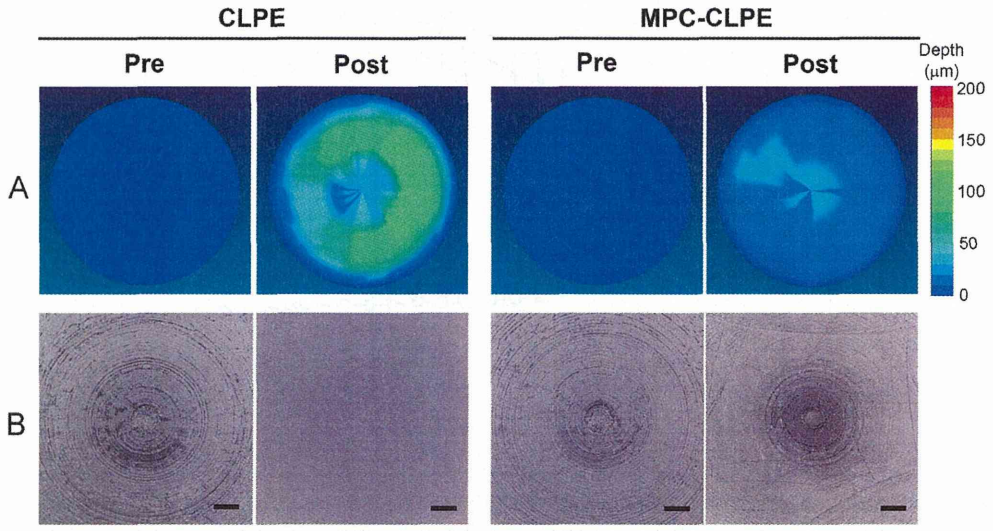

Fig. 2 – Optical findings of the surfaces of the two liners in the THA simulator. (A) Three-dimensional morphometric analyses of surfaces of the CLPE and MPC-CLPE liners before (pre) and after (post) 15×10^6 cycles. (B) Confocal scanning laser microscopic analysis of the contact areas in the two liner surfaces before (pre) and after (post) 15×10^6 cycles. Scale bars: 200 μm.

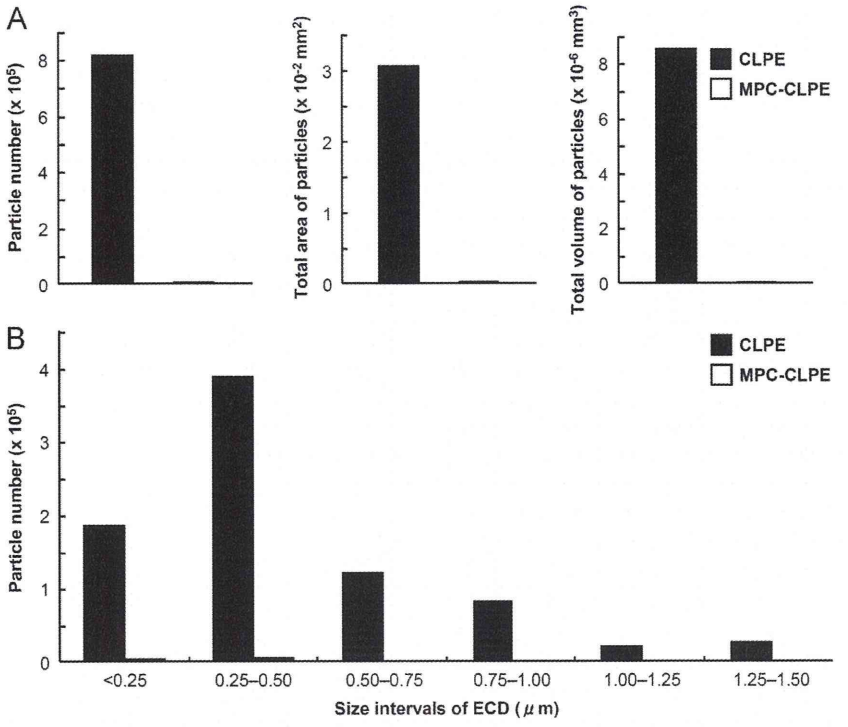

Fig. 4 – Analyses of wear particles isolated from lubricants in the hip simulator. (A) The graphs show the total number, area, and volume of the wear particles per 10^6 cycles. (B) Number of particles per 10^6 cycles in each size range of the equivalent circle diameter from CLPE and MPC-CLPE liners.

Table 2 – Assessments of the particle from CLPE and MPC-CLPE liners using size and shape descriptors.

Particle characterization	CLPE	MPC-CLPE	*p*-value
ECD (μm)	0.18±0.13	0.13±0.06	0.0000
Diameter (μm)	0.28±0.24	0.19±0.11	0.0001
Aspect ratio	2.31±0.79	2.10±0.51	0.0211
Roundness	0.83±0.22	0.92±0.13	0.0000

Two size descriptors, i.e., equivalent circle diameter (ECD) and diameter (*D*), and two shape descriptors, i.e., aspect ratio (AR) and roundness (*R*), were used to define each particle. Data are expressed as mean±standard deviation (SD).

The SEM analysis of the wear particles isolated from the lubricants indicated that poly(MPC) grafting dramatically decreased the total number, area, and volume of the wear particles by 99.3%, 99.9% and 99.9%, respectively (Fig. 3, Fig. 4A). However, there was no significant difference in the particle size distributions expressed by the equivalent circle diameter of each liner, and, in particular, from the SEM image, it was observed that particles with diameters less than 0.50 μm were present in the range of the highest frequency (Fig. 4C). In addition, there were no significant differences in the particle size descriptors, equivalent circle diameter ($p<0.0001$), and diameter ($p=0.0001$), as well as in the particle shape descriptors, aspect ratio ($p=0.0211$), and roundness ($p<0.0001$) (Table 2).

4. Discussion

An MPC molecule is one of the synthesized phospholipids and mimicks the surface of cellmembranes (Ishihara et al., 1990). Thus, poly(MPC) grafting onto medical devices makes their surface hydrophilic and biocompatible. Further, a thin film of water is formed under physiological conditions (Kitano et al., 2003). At the time of writing, the MPC polymers are applied to the surface of intravascular stents (Kuiper and Nordrehaug, 2000; Palmer et al., 2004), soft contact lenses (Selan et al., 2009), and artificial lungs and hearts (Kihara et al., 2003; Snyder et al., 2007) under the authorization of the U. S. Food and Drug Administration (FDA).

Because the PE liners are subjected to multidirectional heavy loads, we used a photoinduced radical graft polymerization technique for grafting. This technique produces a strong C–C covalent bond between a carbon atom of PE and the end-group of a poly(MPC) main chain. The advantages of this technique are that it not only results in the production of a uniform poly(MPC) layer (100–150 nm in thickness) but also causes a negligible effect on the physical and mechanical properties of the CLPE substrate (Ishihara et al., 2000; Kyomoto et al., 2007). Using this technique, we produced a new MPC-CLPE acetabular liner (Aquala® liner; KYOCERA Medical Corp.,) and the Japanese government (Ministry of Health, Labor, and Welfare) approved its clinical use in artificial hip joints in April 2011.

In addition to wear resistance, the durability of the nanometer-scaled poly(MPC) layer is also of major concern.

When this layer is removed from the liner surface, the steady wear rate of the MPC-CLPE liner increases to almost the same (or slight lower) level as that of the untreated CLPE liner (Kyomoto et al., 2011; Moro et al., 2006, 2010). In the present study, MPC-CLPE liners showed weight gains and a significantly lower wear rate during the 15×10^6 cycles. This finding confirmed that the poly(MPC) layer was maintained even after the test.

In the present study, we showed that poly(MPC) grafting onto the CLPE liner surface decreased the production of wear particles by 99% during 15×10^6 cycles of loading in the hip wear simulator. Moreover, poly(MPC) grafting did not affect the size of the wear particles and their distribution. With regard to the relationship between the number of PE particles in the synovial tissue and periprosthetic osteolysis, the critical number was reported to be around 1.0×10^{10} particles/g tissue (Kadoya et al., 1998). Thus, a marked decrease in the number of particles presumably reduces the incidence of osteolysis. Recently, the size of wear products in relation to the complications arising from metal-on-metal articulation has been the topic of concern (Hosman et al., 2010). In this regard, our results suggest that the influences of the wear products of poly(MPC)-grafted liners are similar to those of the CLPE liners.

There are three limitations of this study, with the first being underestimation in the load-soak test (ISO 14242-2) for determining the cause of weight gain in the liner. When using the gravimetric method, the weight loss in the tested liners is corrected for 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. Fluid absorption in the tested liners is generally slightly higher than that in the load-soak controls. Consequently, the correction for fluid absorption through the use of the load-soak control as the correction factor leads to a slight underestimation of the actual weight loss. This underestimation has previously been reported, particularly in several reports on wear-resistant articulating surfaces (Dumbleton et al., 2006; Muratoglu et al., 2001; Oral et al., 2006; Shen et al., 2011). Because of this underestimation, wear could not be quantified by gravimetric analysis; however, weight change in the MPC-CLPE liners suggests the considerable wear-resistance of them. In the present study, we also analyzed the surface of the liner and the amount of wear particles generated from the liner, as well as confirmed that wear resistance of the acetabular liners was considerably improved by poly(MPC) grafting.

The second limitation of this study is the difference between the in vitro study and clinical settings. This difference was a matter of concern in the case of Hylamer (Graeter and Nevins, 1998; Huddleston et al., 2010). We do, however, believe that this issue is relatively insignificant as compared to that with regard to other materials, because poly(MPC)-grafted particles are biologically inert and do not cause the subsequent bone resorptive responses (Moro et al., 2004). Moreover, to the best of our knowledge, there are no reports on the complications of medical devices using MPC polymers.

The third limitation is that we used only Co–Cr alloy heads with a diameter of 26 mm. In clinical settings, there seems to be a tendency to choose large heads and thin acetabular liners in order to reduce the incidence of dislocation. We believe that this drawback is partially offset by the long duration of simulation. At present, we are conducting additional studies using large heads and thin acetabular liners.

In summary, this study shows that poly(MPC) grafting markedly reduces the production of wear particles from CLPE liners, without affecting the size of the particles. These results suggest that poly(MPC) grafting is a promising technique for increasing the longevity of artificial hip joints.

Acknowledgments

We thank Kozo Nakamura, Tomohiro Konno, Noboru Yamawaki, Fumiaki Miyaji, and Reiko Yamaguchi for their excellent technical assistance.

REFERENCES

Bozic, K.J., Kurtz, S.M., Lau, E., Ong, K., Vail, T.P., Berry, D.J., 2009. The epidemiology of revision total hip arthroplasty in the United States. Journal of Bone & Joint Surgery 91, 128–133.

Callaghan, J.J., Cuckler, J.M., Huddleston, J.I., Galante, J.O., 2008. How have alternative bearings (such as metal-on-metal, highly cross-linked polyethylene, and ceramic-on-ceramic) affected the prevention and treatment of osteolysis? Journal of the American Academy of Orthopaedic Surgeons 16 (Suppl. 1), S33–38.

Campbell, P., Doorn, P., Dorey, F., Amstutz, H.C., 1996. Wear and morphology of ultra-high molecular weight polyethylene wear particles from total hip replacements. Proceedings of the Institution of Mechanical Engineers Part H 210, 167–174.

Catelas, I., Jacobs, J.J., 2010. Biologic activity of wear particles. Instructional Course Lectures 59, 3–16.

Charnley, J., 1961. Arthroplasty of the hip. A new operation. Lancet 1, 1129–1132.

Dean, D.D., Schwartz, Z., Liu, Y., Blanchard, C.R., Agrawal, C.M., Mabrey, J.D., Sylvia, V.L., Lohmann, C.H., Boyan, B.D., 1999. The effect of ultra-high molecular weight polyethylene wear debris on MG63 osteosarcoma cells in vitro. Journal of Bone and Joint Surgery—American Volume 81, 452–461.

Dumbleton, J.H., D'Antonio, J.A., Manley, M.T., Capello, W.N., Wang, A., 2006. The basis for a second-generation highly cross-linked UHMWPE. Clinical Orthopaedics and Related Research 453, 265–271.

Fisher, J., McEwen, H.M., Tipper, J.L., Galvin, A.L., Ingram, J., Kamali, A., Stone, M.H., Ingham, E., 2004. Wear, debris, and biologic activity of cross-linked polyethylene in the knee: benefits and potential concerns. Clinical Orthopaedics and Related Research 428, 114–119.

Graeter, J.H., Nevins, R., 1998. Early osteolysis with Hylamer acetabular liners. Journal of Arthroplasty 13, 464–466.

Harris, W.H., 2004. Conquest of a worldwide human disease: particle-induced periprosthetic osteolysis. Clinical Orthopaedics and Related Research 429, 39–42.

Hosman, A.H., van der Mei, H.C., Bulstra, S.K., Busscher, H.J., Neut, D., 2010. Effects of metal-on-metal wear on the host immune system and infection in hip arthroplasty. Acta Orthopaedica 81, 526–534.

Huddleston, J.I., Harris, A.H., Atienza, C.A., Woolson, S.T., 2010. Hylamer vs conventional polyethylene in primary total hip arthroplasty: a long-term case-control study of wear rates and osteolysis. Journal of Arthroplasty 25, 203–207.

Ishihara, K., Iwasaki, Y., Ebihara, S., Shindo, Y., Nakabayashi, N., 2000. Photoinduced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on polyethylene membrane surface for obtaining blood cell adhesion resistance. Colloids and Surfaces B: Biointerfaces 18, 325–335.

Ishihara, K., Ueda, T., Nakabayashi, N., 1990. Preparation of phospholipid polymers and their properties as polymer hydrogel membrane. Polymer Journal 22, 355–360.

Jacobs, J.J., Roebuck, K.A., Archibeck, M., Hallab, N.J., Glant, T.T., 2001. Osteolysis: basic science. Clinical Orthopaedics and Related Research 393, 71–77.

Kadoya, Y., Kobayashi, A., Ohashi, H., 1998. Wear and osteolysis in total joint replacements. Acta Orthopaedica Scandinavica 278, 1–16.

Kihara, S., Yamazaki, K., Litwak, K., Litwak, P., Kameneva, M., Ushiyama, H., Tokuno, T., Borzelleca, D., Umezu, M., Tomioka, J., Tagusari, O., Akimoto, T., Koyanagi, H., Kurosawa, H., Kormos, R., Griffith, B., 2003. In vivo evaluation of a MPC polymer coated continuous flow left ventricular assist system. Artificial Organs 27, 188–192.

Kitano, H., Imai, M., Mori, T., Gemmei-Ide, M., Yokoyama, Y., Ishihara, K., 2003. Structure of water in the vicinity of phospholipid analogue copolymers as studied by vibrational spectroscopy. Langmuir 19, 10260–10266.

Kuiper, K.K., Nordrehaug, J.E., 2000. Early mobilization after protamine reversal of heparin following implantation of phosphorylcholine-coated stents in totally occluded coronary arteries. American Journal of Cardiology 85, 698–702.

Kyomoto, M., Moro, T., Konno, T., Takadama, H., Kawaguchi, H., Takatori, Y., Nakamura, K., Yamawaki, N., Ishihara, K., 2007. Effects of photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on physical properties of cross-linked polyethylene in artificial hip joints. Journal of Materials Science: Materials in Medicine 18, 1809–1815.

Kyomoto, M., Moro, T., Miyaji, F., Konno, T., Hashimoto, M., Kawaguchi, H., Takatori, Y., Nakamura, K., Ishihara, K., 2008. Enhanced wear resistance of orthopaedic bearing due to the cross-linking of poly(MPC) graft chains induced by gamma-ray irradiation. Journal of Biomedical Materials Research Part B: Applied Biomaterials 84, 320–327.

Kyomoto, M., Moro, T., Takatori, Y., Kawaguchi, H., Ishihara, K., 2011. Cartilage-mimicking, high-density brush structure improves wear resistance of crosslinked polyethylene: a pilot study. Clinical Orthopaedics and Related Research 469, 2327–2336.

Moro, T., Kawaguchi, H., Ishihara, K., Kyomoto, M., Karita, T., Ito, H., Nakamura, K., Takatori, Y., 2009. Wear resistance of artificial hip joints with poly(2-methacryloyloxyethyl phosphorylcholine) grafted polyethylene: comparisons with the effect of polyethylene cross-linking and ceramic femoral heads. Biomaterials 30, 2995–3001.

Moro, T., Takatori, Y., Ishihara, K., Konno, T., Takigawa, Y., Matsushita, T., Chung, U.I., Nakamura, K., Kawaguchi, H., 2004. Surface grafting of artificial joints with a biocompatible polymer for preventing periprosthetic osteolysis. Nature Materials 3, 829–836.

Moro, T., Takatori, Y., Ishihara, K., Nakamura, K., Kawaguchi, H., 2006. 2006 Frank Stinchfield Award: grafting of biocompatible polymer for longevity of artificial hip joints. Clinical Orthopaedics and Related Research 453, 58–63.

Moro, T., Takatori, Y., Kyomoto, M., Ishihara, K., Saiga, K., Nakamura, K., Kawaguchi, H., 2010. Surface grafting of biocompatible phospholipid polymer MPC provides wear resistance of tibial polyethylene insert in artificial knee joints. Osteoarthritis Cartilage 18, 1174–1182.

Muratoglu, O.K., Bragdon, C.R., O'Connor, D.O., Jasty, M., Harris, W.H., 2001. A novel method of cross-linking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties. Recipient of the 1999 HAP Paul Award. Journal of Arthroplasty 16, 149–160.

Oral, E., Christensen, S.D., Malhi, A.S., Wannomae, K.K., Muratoglu, O.K., 2006. Wear resistance and mechanical properties of highly cross-linked, ultrahigh-molecular weight polyethylene doped with vitamin E. Journal of Arthroplasty 21, 580–591.

Palmer, R.R., Lewis, A.L., Kirkwood, L.C., Rose, S.F., Lloyd, A.W., Vick, T.A., Stratford, P.W., 2004. Biological evaluation and drug delivery application of cationically modified phospholipid polymers. Biomaterials 25, 4785–4796.

Paul, J.P., 1967. Forces transmitted by joints in the human body. Proceedings of the Institution of Mechanical Engineers 181, 8–15.

Selan, L., Palma, S., Scoarughi, G.L., Papa, R., Veeh, R., Di Clemente, D., Artini, M., 2009. Phosphorylcholine impairs susceptibility to biofilm formation of hydrogel contact lenses. American Journal of Ophthalmology 147, 134–139.

Shen, F.W., Lu, Z., McKellop, H.A., 2011. Wear versus thickness and other features of 5-Mrad crosslinked UHMWPE acetabular liners. Clinical Orthopaedics and Related Research 469, 395–404.

Snyder, T.A., Tsukui, H., Kihara, S., Akimoto, T., Litwak, K.N., Kameneva, M.V., Yamazaki, K., Wagner, W.R., 2007. Preclinical biocompatibility assessment of the EVAHEART ventricular assist device: coating comparison and platelet activation. Journal of Biomedical Materials Research Part A 81, 85–92.

Tipper, J.L., Galvin, A.L., Williams, S., McEwen, H.M., Stone, M.H., Ingham, E., Fisher, J., 2006. Isolation and characterization of UHMWPE wear particles down to ten nanometers in size from in vitro hip and knee joint simulators. Journal of Biomedical Materials Research Part A 78, 473–480.

Clin Orthop Relat Res (2015) 473:942–951
DOI 10.1007/s11999-014-3995-x

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SYMPOSIUM: ADVANCES IN UHMWPE BIOMATERIALS

Multidirectional Wear and Impact-to-wear Tests of Phospholipid-polymer-grafted and Vitamin E-blended Crosslinked Polyethylene: A Pilot Study

Masayuki Kyomoto PhD, Toru Moro MD, Yoshio Takatori MD, Sakae Tanaka MD, Kazuhiko Ishihara PhD

Published online: 24 October 2014

Abstract

Background Modifying the surface and substrate of a crosslinked polyethylene (CLPE) liner may be beneficial for high wear resistance as well as high oxidative stability and excellent mechanical properties, which would be useful in contributing to the long-term performance of orthopaedic bearings. A grafted poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) layer on a vitamin E-blended crosslinked PE (HD-CLPE[VE]) surface may provide hydrophilicity and lubricity without compromising the oxidative stability or mechanical properties.

Questions/purposes (1) Will the modifications (PMPC grafting and vitamin E blending) affect the lubrication characteristics of the CLPE surface? (2) Will the modifications affect wear resistance? (3) Will the modifications affect fatigue resistance?

Methods We investigated the effects of surface and substrate modifications (PMPC grafting and vitamin E blending) on the wear and fatigue fracture of thin CLPE samples. For each of the untreated and PMPC-grafted CLPE surfaces with and without vitamin E blended (four groups), wettability and lubricity surface analyses were conducted as well as multidirectional wear and impact-to-wear tests using a pin-on-disk testing machine.

Results The water wettability and lubricity (CLPE [mean ± 95% confidence interval]: 23.2° ± 1.8°, 0.005 ± 0.001; HD-CLPE[VE]: 26.0° ± 2.3°, 0.009 ± 0.003) of the PMPC-grafted surfaces were greater ($p < 0.001$) than that (CLPE: 90.3° ± 1.2°, 0.067 ± 0.015; HD-CLPE[VE]: 90.8° ± 2.0°, 0.063 ± 0.008) of the untreated surface regardless of vitamin E additives. It was observed that the PMPC grafting (CLPE: 0.23 ± 0.06 mg; HD-CLPE[VE]: 0.05 ± 0.10 mg) was associated with reduced gravimetric wear (CLPE: 0.53 ± 0.08 mg, $p = 0.004$ HD-CLPE[VE]: 0.23 ± 0.07 mg, $p = 0.038$) in the multidirectional wear test. The PMPC-grafted surface characteristics did not appear to affect the impact fatigue resistance regardless of vitamin E blending.

Conclusions PMPC grafting improved the surface hydrophilicity and lubricity, and it reduced the gravimetric wear in terms of multidirectional sliding. It did not result in differences in terms of the impact-to-unidirectional sliding regardless of vitamin E blending. Further research is needed to evaluate the wear resistance of PMPC-grafted HD-CLPE(VE) in long-term hip simulator tests under normal

One or more of the authors (YT) received funding from a Health and Welfare Research Grant for Research on Medical Devices for Improving Impaired QOL (H20-004) and Research on Measures for Intractable Diseases (H24-001) from the Japanese Ministry of Health, Labour and Welfare.
All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research*® editors and board members are on file with the publication and can be viewed on request.
Clinical Orthopaedics and Related Research® neither advocates nor endorses the use of any treatment, drug, or device. Readers are encouraged to always seek additional information, including FDA-approval status, of any drug or device prior to clinical use.
This work was performed at The University of Tokyo, Tokyo, Japan.

M. Kyomoto, K. Ishihara
Department of Materials Engineering, The University of Tokyo, Tokyo, Japan

M. Kyomoto, T. Moro, Y. Takatori
Division of Science for Joint Reconstruction, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

M. Kyomoto (✉)
Research Department, KYOCERA Medical Corporation, 3-3-31, Miyahara, Yodogawa-ku, Osaka 532-0003, Japan
e-mail: masayuki.kyomoto@kyocera-md.jp

T. Moro, Y. Takatori, S. Tanaka
Sensory & Motor System Medicine, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

and severe conditions, which may offer useful clues to the possible performance of these materials in vivo.

Clinical Relevance Our preliminary in vitro findings suggest that some improvement in the wear performance of crosslinked polyethylene acetabular liners in total hip arthroplasty could be obtained using PMPC grafting. Further research is needed to evaluate the wear resistance of PMPC-grafted HD-CLPE(VE) in long-term hip simulator tests under normal and severe conditions, which may offer useful clues to the possible performance of these materials in vivo.

Introduction

Wear and oxidative degradation are two important indicators of the clinical performance of polyethylene (PE) acetabular liners. PE wear particles from the acetabular liner are responsible for osteolysis, which may lead to aseptic loosening [10]. Many different strategies or techniques have been introduced to reduce the number of PE wear particles and extend the longevity of THA [5, 16, 25, 26, 29, 34].

To reduce wear and thus suppress bone loss, we recently developed a new articular cartilage-inspired technology for surface modification with synthetic phospholipid polymer grafting using poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) for PE acetabular liners in THAs [18–24, 29, 30, 35, 36]. Modification of the bearing surfaces of an artificial joint with a hydrophilic layer should increase lubrication to levels comparable to that provided by articular cartilage under physiological conditions [17, 20, 21, 23]. 2-Methacryloyloxyethyl phosphorylcholine (MPC) polymers are one of the most common biocompatible and hydrophilic polymers that have been clinically applied [13, 35, 36]. It has been demonstrated that a nanometer-scale layer of PMPC can be formed on a crosslinked PE (CLPE) surface to better reproduce the ideal hydrophilicity and lubricity of the physiological joint surface [18, 20–24].

However, wear is only one of several important indicators of the clinical performance of acetabular liners. Oxidative degradation of some of the first generation of CLPE formulations has been considered a potential limiting factor for the long-term performance of THA [7, 28]. During gamma irradiation (for crosslinking or for sterilization), free radicals formed in the PE molecular structure cause embrittlement through a cascading oxidation reaction [7]. Hence, the incorporation of the antioxidant vitamin E (α-tocopherol) has been proposed to prevent oxidation and has been introduced into clinical use [5, 15, 34]. Vitamin E is a free radical scavenger and is well established as a biological antioxidant.

Moreover, dislocation has been reported to be a major reason for revision in THA [4]. In artificial hips, dislocation is almost always caused by the impingement of the femoral stem neck on the acetabular liner. The impaction between the femoral stem neck and the acetabular cup can be potentially avoided by using a large-diameter femoral head to treat the condition [33]. However, a large-diameter femoral head must be used in conjunction with a thin PE liner owing to the limited volume along the acetabulum, and a thin PE liner poses a risk in terms of wear and fatigue fracture when subjected to severe physiological conditions.

We investigated the effects of surface and substrate modifications (PMPC grafting and vitamin E blending) on the wear and fatigue fracture of thin CLPE samples by conducting a multidirectional wear test and an impact-to-wear test in this pilot study. We sought answers to three questions: (1) Will the modifications (ie, PMPC grafting and vitamin E blending) affect the lubrication characteristics of the CLPE surface? (2) Will the modifications affect wear resistance? (3) Will the modifications affect impact fatigue resistance?

Materials and Methods

Four treatment groups were considered: untreated and PMPC-grafted CLPE with and without vitamin E blending. For each treatment group, 27 sample pieces were prepared for surface lubrication analysis and 12 disks were prepared for specific durability analysis (Fig. 1). To answer the first question regarding the dependent variables of hydration kinetics and stability of the grafted PMPC layer, the hydrophilicity and lubricity of the PMPC layers on the substrates with and without vitamin E were evaluated using the contact angle of a water drop and a ball-on-plate friction test. The dependent variable in our second research question (the wear resistance of the PMPC-grafted substrates with and without vitamin E) was examined using a pin-on-disk (POD) testing machine under a multidirectional sliding condition. Finally, to answer our third question, the fatigue resistance of the PMPC-grafted substrates with and without vitamin E was examined using a POD testing machine under an impact-to-unidirectional sliding condition.

A compression-molded bar stock of 0.1 mass% vitamin E-blended PE (PE[VE]; GUR1020E resin; Orthoplastics Ltd, Lancashire, UK) was gamma-irradiated with a high dose (HD; 100 kGy) in a N_2 gas atmosphere and annealed at 120 °C for 12 hours in N_2 gas to facilitate crosslinking. Hereafter, this PE material is referred to as HD-CLPE(VE). As the control, a compression-molded bar stock of PE without any additives (GUR1020 resin; Orthoplastics Ltd) was gamma-irradiated with a 50-kGy dose in a N_2 gas atmosphere. It was then annealed at 120 °C for 7.5 hours in

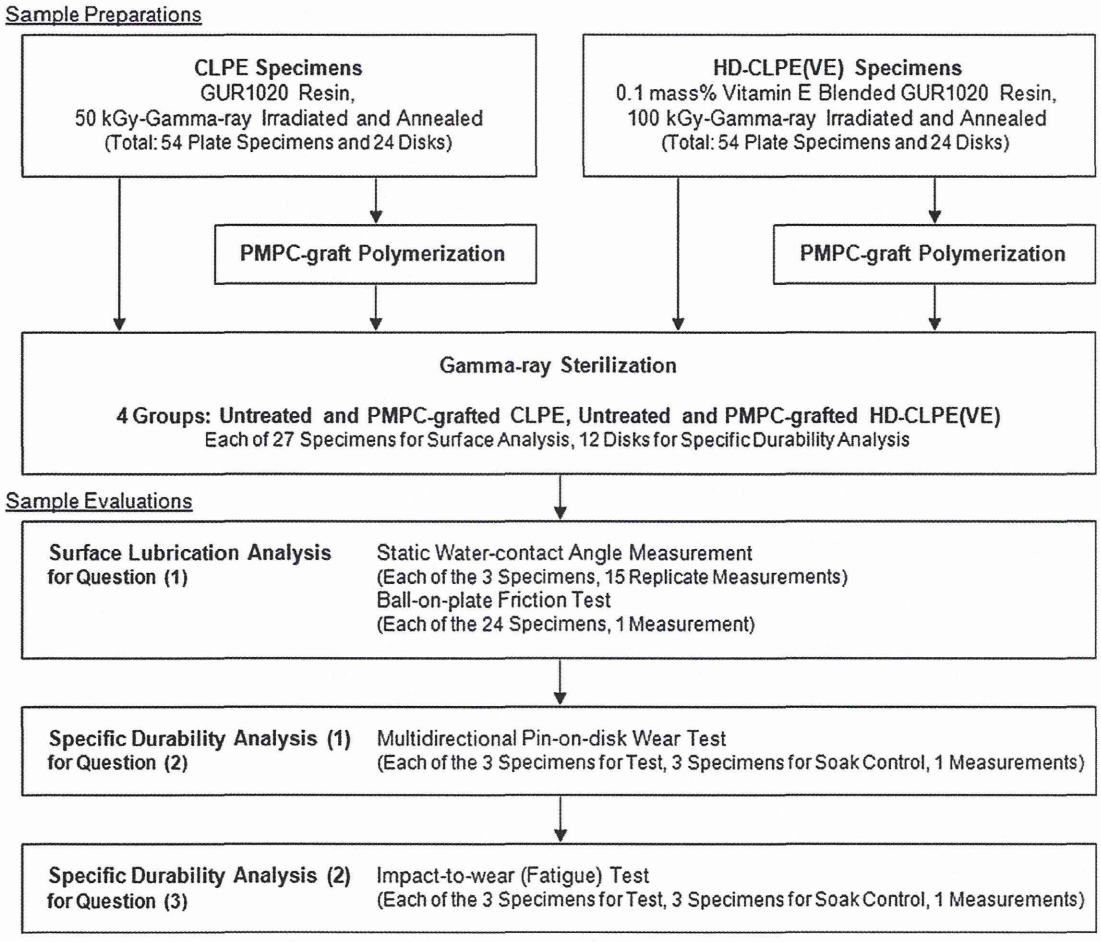

Fig. 1 The flow chart provides an overview of the study.

N_2 gas to facilitate crosslinking. Hereafter, this PE material is referred to as CLPE. Samples of CLPE and HD-CLPE(VE) were machined from the bar stocks and then washed. Surface cleanliness without fouling that involved an antioxidant (radical scavenger) was critical for the polymerization. In particular, the vitamin E surface was fully washed with an aqueous polysorbate-surfactant solution and ethanol to remove vitamin E from the surface. PMPC grafting of the surfaces of the CLPE and HD-CLPE(VE) was performed using a photoinduced polymerization technique as previously reported [17–22, 25, 28, 29]. Photoinduced graft polymerization was carried out on the CLPE and HD-CLPE(VE) surfaces using ultraviolet irradiation with an intensity of 5 mW/cm^2 at 60 °C for 90 minutes and an aqueous 0.5 M MPC (NOF Corp, Tokyo, Japan) solution. The resulting samples were then gamma-radiation-sterilized at 25 kGy under a N_2 gas atmosphere.

The static contact angles of water on PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) were measured with an optical bench-type contact angle goniometer (Model DM300; Kyowa Interface Science Co, Ltd, Saitama, Japan) using the sessile-drop (1 μL) method according to ISO 15989 [11]. Subsequently, 15 measurements were repeated on each of the three samples, and the mean values ± SD were calculated.

The friction test was performed using a ball-on-plate machine (Tribostation 32; Shinto Scientific Co, Ltd, Tokyo, Japan). Six samples of PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) were evaluated. A cobalt-chromium-molybdenum (Co-Cr-Mo) alloy ball with a diameter of 9 mm was prepared. The surface roughness (R_a) of the ball was < 0.01 μm, which is comparable to that of femoral head products. The friction test was performed at 37 °C with a load of 0.49 to 9.8 N (the contact pressure roughly calculated using Hertzian theory is approximately 22–62 MPa), sliding distance of 25 mm, frequency of 1 Hz for a maximum of 100 cycles, and pure water as the lubricant. The mean coefficients of dynamic friction were determined by averaging five data points from the 96 to 100 cycle measurements.

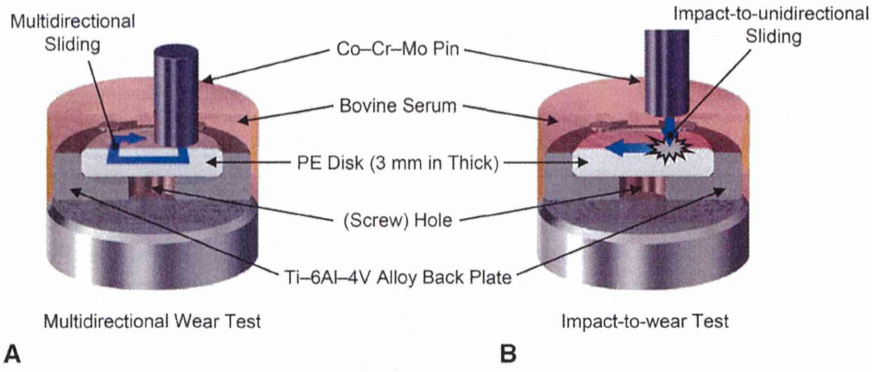

Fig. 2A–B The schematic illustrates the pin-on-disk wear test: (**A**) multidirectional wear test; (**B**) impact-to-wear test.

Multidirectional wear and impact-to-wear tests were conducted using a POD testing machine (Ortho POD; AMTI, Watertown, MA, USA). PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) disks were used for the wear tests and control soak tests to correct the water absorption increments ($n = 3$). The disks were attached to the POD testing machine with a Ti-6Al-4V alloy fixation component that had an 8-mm-diameter hole to simulate an acetabular shell with a screw hole (Fig. 2). The Co-Cr-Mo alloy pins had a 30-mm surface curvature radius and surface roughness of $R_a < 0.01$. A mixture of 27 vol% fetal bovine serum (Biowest, Nuaillé, France), 20 mM ethylene diamine-N, N, N′, N′-tetraacetic acid, and 0.1 mass% sodium azide was used at 37 °C as the lubricant. The multidirectional wear test was conducted on a rectangular sliding surface. The test conditions were specified to be a static load of 213 N, sliding distance of 30 mm, and frequency of 1 Hz for a maximum of 1.0×10^6 cycles. Impact-to-wear testing was performed on a unidirectional sliding surface with a maximum impact load of 150 N, sliding distance of 10 mm, and frequency of 1 Hz for a maximum of 2.0×10^6 cycles. These sliding conditions were implemented according to ASTM F732 [2]. Gravimetric wear was determined by weighing the disks. Soak controls were used to compensate for fluid absorption by the specimens. Because the gravimetric method was used, the weight loss of each of the tested disks was corrected by subtracting the weight gain resulting from the soak control. After the multidirectional wear and impact-to-wear tests, the volumetric wear of the disks was evaluated using a noncontact optical three-dimensional profiler (Talysurf CCI Lite; Taylor Hobson Ltd, Leicester, UK).

The mean values of the three comparative groups (untreated CLPE versus PMPC-grafted CLPE, untreated HD-CLPE[VE] versus PMPC-grafted HD-CLPE[VE], and PMPC-grafted CLPE versus PMPC-grafted HD-CLPE[VE]) were evaluated using a Student's t-test (statistical significance, $p < 0.05$). The mean values of the coefficient of dynamic friction obtained for each treatment group under four loadings (0.49, 0.98, 4.9, and 9.8 N) in the friction test were compared by one-factor analysis of variance (ANOVA), and the significance of differences was determined by post hoc testing using Bonferroni's method ($p < 0.05$). All statistical analyses were performed using an add-on (Statcel 2; OMS Publishing Inc, Tokorozawa, Japan) to Microsoft Excel® 2003 (Microsoft Corp, Redmond, WA, USA).

Results

The PMPC grafting improved the hydration and friction kinetics of the surfaces, regardless of vitamin E blending. The static water contact angles on the PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) surfaces as well as the coefficients of dynamic friction between water and the surfaces changed as a result of the modification (Fig. 3). The static water contact angles on untreated CLPE and HD-CLPE(VE) were 90.3° (SD = ± 2.3, 95% confidence interval [CI], ± 1.2) and 90.8° (SD = ±3.9, 95% CI, ± 2.0), and they decreased markedly to 23.2° (SD = ± 3.5, 95% CI, ± 1.8, $p < 0.001$) and 26.0° (SD = ± 4.5, 95% CI, ± 2.3, $p < 0.001$), respectively, after PMPC grafting (Fig. 3A). The coefficients of dynamic friction of PMPC-grafted CLPE (mean = 0.005, SD = ± 0.001, 95% CI, ± 0.001) and PMPC-grafted HD-CLPE(VE) (mean = 0.009, SD = ± 0.003, 95% CI, ± 0.002) also decreased markedly with the surfaces exhibiting an approximately 85% to 90% reduction ($p < 0.001$ and $p < 0.001$, respectively) in the coefficient compared with the untreated CLPE (mean = 0.067, SD = ± 0.015, 95% CI, ± 0.008) and untreated HD-CLPE(VE) (mean = 0.063, SD = ± 0.008, 95% CI, ± 0.007) surfaces under 9.8-N loadings (Fig. 3B). Interestingly, the coefficient of dynamic friction of both PMPC-grafted CLPE and PMPC-grafted HD-CLPE(VE) decreased gradually with an increase in loading.