

**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  $10 \times 10^6$  cycles of loading. Data are expressed as mean (symbols)  $\pm$  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.<sup>18</sup>

The wear amount in the hip joint simulator was then estimated. After  $10 \times 10^6$  cycles, the untreated CLPE liners showed a total weight loss of  $40.9 \pm 6.4$  (mean  $\pm$  standard deviation) and  $89.0 \pm 11.4$  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  $-10.0 \pm 1.4$  and  $6.1 \pm 11.8$  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 sub-

jected to load and motion. This underestimation has been previously reported, particularly in several reports on wear-resistant articulating surfaces.<sup>12,30,31</sup>

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  $5 \times 10^6$  cycles (Fig. 1). However, when the wear rate was compared between  $5 \times 10^6$  and  $10 \times 10^6$  cycles, the PMPC-CLPE (40 mm) liners showed a significantly lower wear rate than the untreated CLPE (40 mm) liners ( $1.44 \pm 1.97$  mg/ $10^6$  cycles vs.  $9.82 \pm 0.55$  mg/ $10^6$  cycles,  $p=0.023$ ).

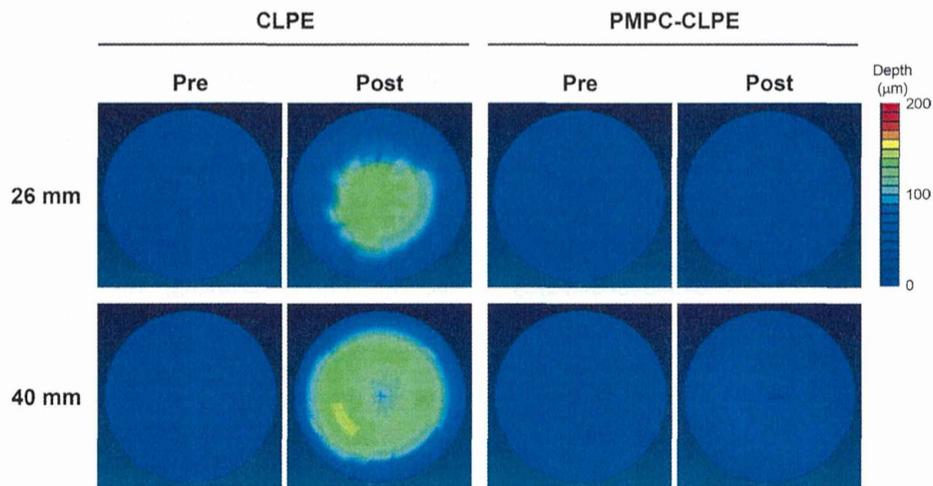
As shown by the 3D morphometric analysis, the surfaces of both PMPC-CLPE (26/40 mm) liners showed little or no detectable volumetric wear. By contrast, the surfaces of both CLPE (26/40 mm) liners suffered from substantial wear (Fig. 2). The confocal scanning laser microscopic analysis revealed the original machine marks were completely absent on both CLPE (26/40 mm) liners after  $10 \times 10^6$  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

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

Data are expressed as mean  $\pm$  standard deviation (SD).



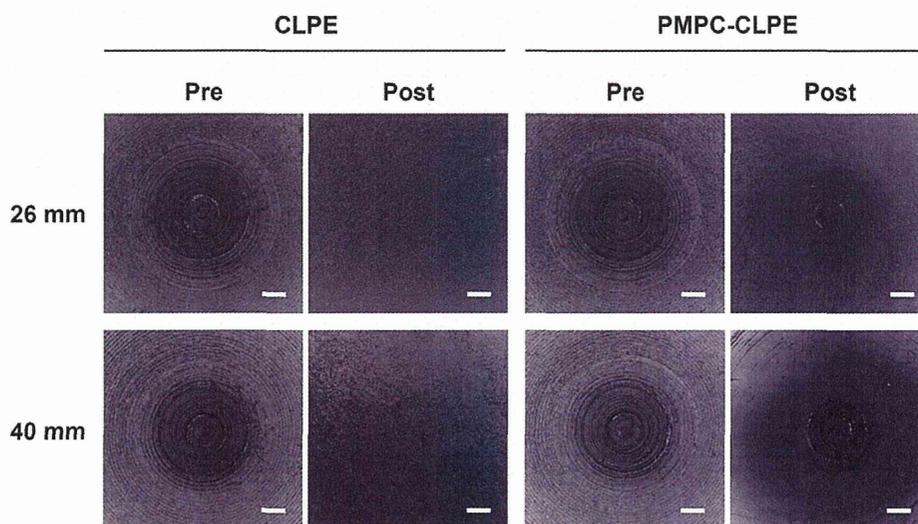
**Figure 2.** 3D morphometric analyses of the surfaces of the CLPE and PMPC-CLPE liners. Surface characteristics of the bearing interfaces with or without PMPC graft layer before (pre) and after (post)  $10 \times 10^6$  cycles of the hip joint simulator test.

with diameters ranging from 0.1 to 0.2  $\mu\text{m}$  occurred at the highest frequency in all groups, and those with diameters of  $<0.5 \mu\text{m}$  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. 6,6 and Figs. 7,7).

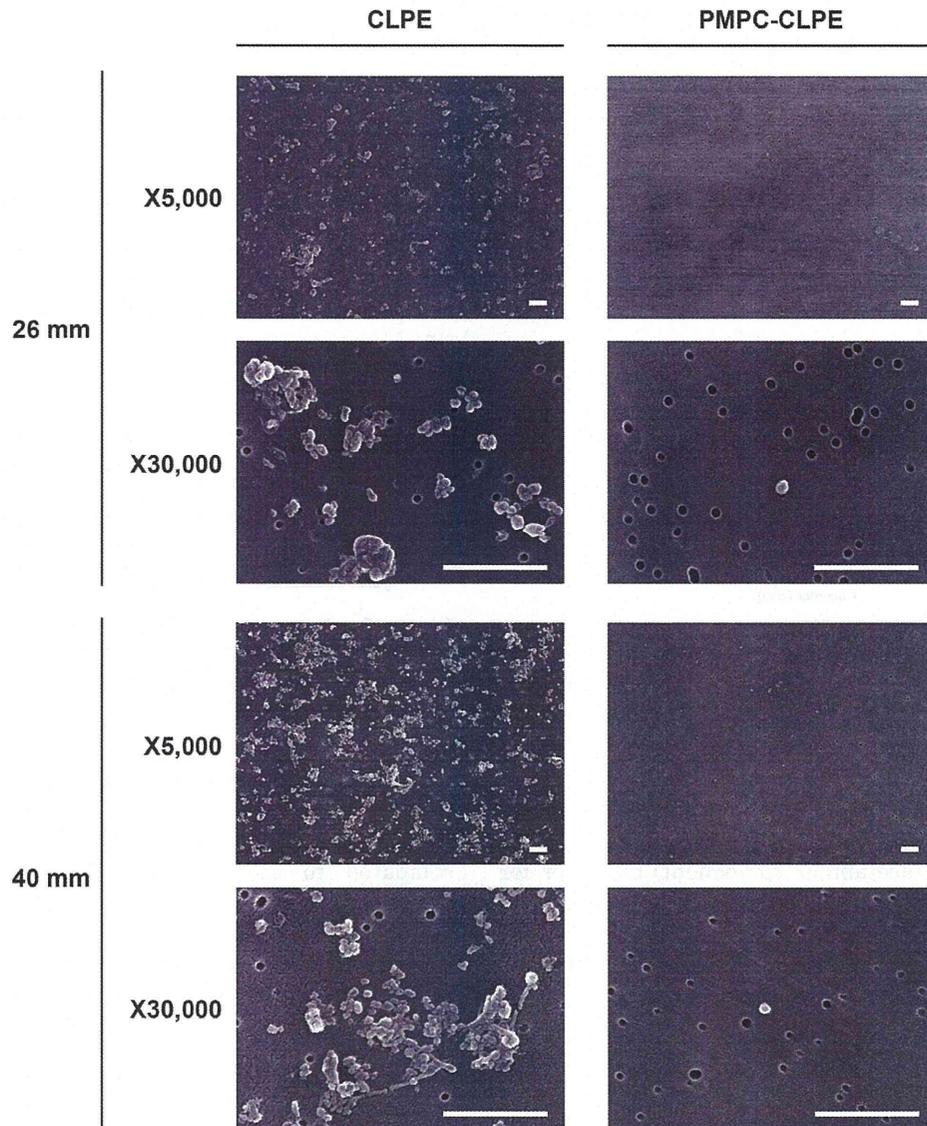
## DISCUSSION

Recent multiple studies demonstrate larger femoral heads clinically reduce dislocation rates. Howie et al.<sup>10</sup> 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.<sup>32</sup> Moreover, the increased contact area and sliding distance of larger heads result in increased volumetric wear. In their retrieval study, Schmalzried et al.<sup>33</sup> reported the volumetric wear increased by 6.3  $\text{mm}^3/\text{year}$  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.<sup>25</sup> 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)  $10 \times 10^6$  cycles of the hip joint simulator test. Scale bar, 200  $\mu\text{m}$ .

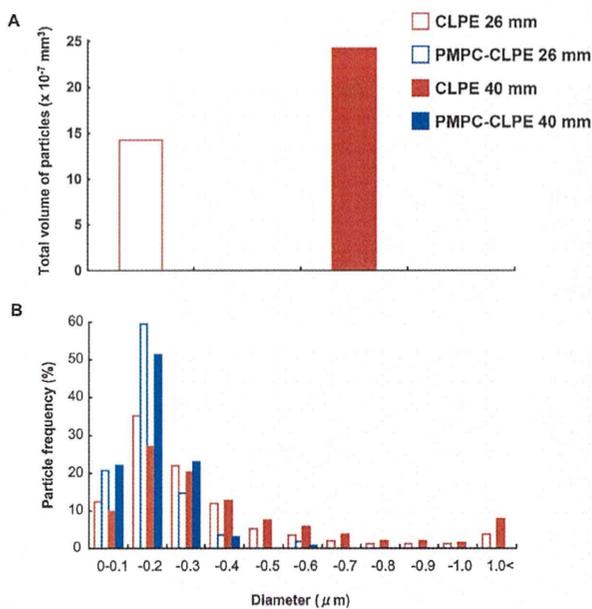


**Figure 4.** SEM images of wear particles from the CLPE and PMPC-CLPE liners. Low (top) and high (bottom) magnification of the SEM images. Scale bar, 1.0  $\mu\text{m}$ .

40 mm) when compared to standard femoral heads (22, 26, and 28 mm) in an evaluation of 146 hips. Hammerberg et al.<sup>8</sup> 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.

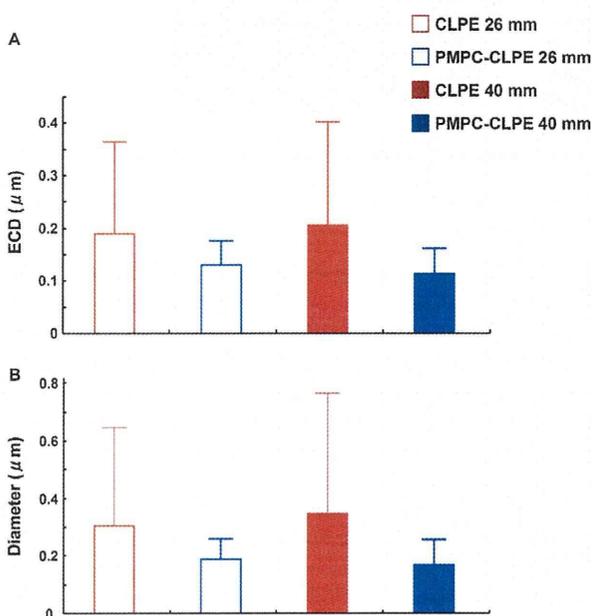
MPC is a methacrylate monomer with a phospholipid polar group in a side chain, resembling the structure of cell membranes.<sup>34</sup> Thus, MPC polymers can suppress biological reactions even when in contact with living organisms, and are now clinically used on

the surfaces of many medical devices.<sup>35</sup> The clinical efficacy and safety of the MPC polymer as a biomaterial are well established.<sup>20</sup> 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  $10 \times 10^6$  cycles. Our previous studies have revealed PMPC grafting on the CLPE surface decreased the friction coefficient/torque by  $\sim 80\text{--}90\%$ ,<sup>17</sup> 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.<sup>18–20</sup>

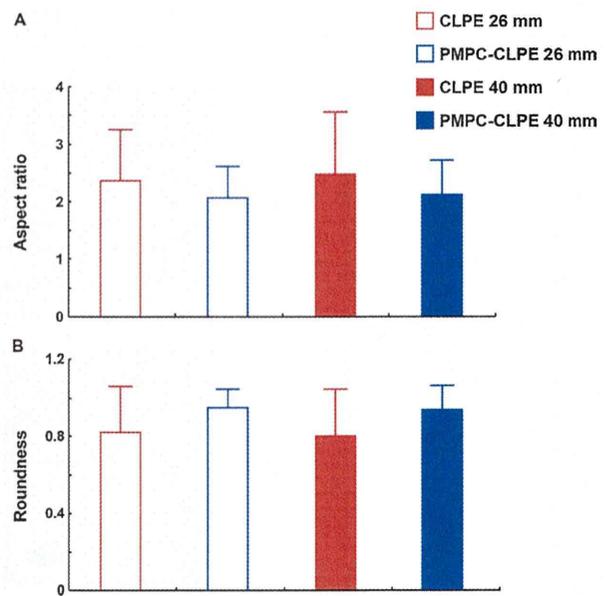


**Figure 5.** Analysis of wear particles isolated from lubricants in the hip joint simulator. (A) Graphs show the total volume of wear particles per  $10^6$  cycles. (B) Size and shape descriptors of each wear particle. Data are expressed as mean  $\pm$  SD.

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.<sup>36</sup> reported in their hip simulator study using CLPE liners of different thicknesses (1.9, 3.9, 5.9, 7.9 mm), the thinner



**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)  $\pm$  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)  $\pm$  SD.

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.

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.<sup>16</sup> 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.<sup>37</sup> 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.<sup>38</sup> 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.<sup>39</sup> 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  $10 \times 10^6$  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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#### REFERENCES

- Bozic KJ, Kurtz SM, Lau E, et al. 2009. The epidemiology of revision total hip arthroplasty in the United States. *J Bone Joint Surg Am* 91:128–133.
- Jameson SS, Lees D, James P, et al. 2011. Lower rates of dislocation with increased femoral head size after primary total hip replacement: a five-year analysis of NHS patients in England. *J Bone Joint Surg Br* 93:876–880.
- Phillips CB, Barrett JA, Losina E, et al. 2003. Incidence rates of dislocation, pulmonary embolism, and deep infection during the first six months after elective total hip replacement. *J Bone Joint Surg Am* 85:20–26.
- Alberton GM, High WA, Morrey BF. 2002. Dislocation after revision total hip arthroplasty: an analysis of risk factors and treatment options. *J Bone Joint Surg Am* 84:1788–1792.
- Sikes CV, Lai LP, Schreiber M, et al. 2008. Instability after total hip arthroplasty: treatment with large femoral heads vs constrained liners. *J Arthroplasty* 23:59–63.
- Brooks PJ. 2013. Dislocation following total hip replacement: causes and cures. *Bone Joint J* 95-B:67–69.
- Dorr LD, Wan Z. 1998. Causes of and treatment protocol for instability of total hip replacement. *Clin Orthop Relat Res* 355:144–151.
- Hammerberg EM, Wan Z, Dastane M, et al. 2010. Wear and range of motion of different femoral head sizes. *J Arthroplasty* 25:839–843.
- Rodriguez JA, Rathod PA. 2012. Large diameter heads: is bigger always better? *J Bone Joint Surg Br* 94:52–54.
- Howie DW, Holubowycz OT, Middleton R. 2012. Large femoral heads decrease the incidence of dislocation after total hip arthroplasty: a randomized controlled trial. *J Bone Joint Surg Am* 94:1095–1102.
- Lombardi AV Jr., Skeels MD, Berend KR, et al. 2011. Do large heads enhance stability and restore native anatomy in primary total hip arthroplasty? *Clin Orthop Relat Res* 469:1547–1553.
- Shen FW, Lu Z, McKellop HA. 2011. Wear versus thickness and other features of 5-Mrad crosslinked UHMWPE acetabular liners. *Clin Orthop Relat Res* 469:395–404.
- Harris WH. 2004. Conquest of a worldwide human disease: particle-induced periprosthetic osteolysis. *Clin Orthop Relat Res* 429:39–42.
- Catelas I, Jacobs JJ. 2010. Biologic activity of wear particles. *Instr Course Lect* 59:3–16.
- Kirk TB, Wilson AS, Stachowiak GW. 1993. The morphology and composition of the superficial zone of mammalian articular cartilage. *J Orthop Rheumatol* 6:21–28.
- Kyomoto M, Moro T, Konno T, et al. 2007. Effects of photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine on physical properties of cross-linked polyethylene in artificial hip joints. *J Mater Sci Mater Med* 18:1809–1815.
- Moro T, Takatori Y, Ishihara K, et al. 2006. 2006 Frank Stinchfield Award: grafting of biocompatible polymer for longevity of artificial hip joints. *Clin Orthop Relat Res* 453:58–63.
- Moro T, Takatori Y, Kyomoto M, et al. 2014. Long-term hip simulator testing of the artificial hip joint bearing surface grafted with biocompatible phospholipid polymer. *J Orthop Res* 32:369–376.
- Moro T, Takatori Y, Ishihara K, et al. 2004. Surface grafting of artificial joints with a biocompatible polymer for preventing periprosthetic osteolysis. *Nat Mater* 3:829–836.
- Takatori Y, Ishihara MT, Kamogawa K, et al. 2015. Clinical and radiographic outcomes of total hip replacement with poly(2-methacryloyloxyethyl phosphorylcholine)-grafted highly cross-linked polyethylene liners: three-year results of a prospective consecutive series. *Mod Rheumatol* 25:286–291.
- Calvert GT, Devane PA, Fielden J, et al. 2009. A double-blind, prospective, randomized controlled trial comparing highly cross-linked and conventional polyethylene in primary total hip arthroplasty. *J Arthroplasty* 24:505–510.
- Capello WN, D'Antonio JA, Ramakrishnan R, et al. 2011. Continued improved wear with an annealed highly cross-linked polyethylene. *Clin Orthop Relat Res* 469:825–830.
- Engh CA Jr., Stepniewski AS, Ginn SD, et al. 2006. A randomized prospective evaluation of outcomes after total hip arthroplasty using cross-linked marathon and non-cross-linked Enduron polyethylene liners. *J Arthroplasty* 21:17–25.
- Glyn-Jones S, McLardy-Smith P, Gill HS, et al. 2008. The creep and wear of highly cross-linked polyethylene: a three-year randomised, controlled trial using radiostereometric analysis. *J Bone Joint Surg Br* 90:556–561.
- Lachiewicz PF, Heckman DS, Soileau ES, et al. 2009. Femoral head size and wear of highly cross-linked polyethylene at 5 to 8 years. *Clin Orthop Relat Res* 467:3290–3296.

26. Whittaker JP, Charron KD, McCalden RW, et al. Comparison of steady state femoral head penetration rates between two highly cross-linked polyethylenes in total hip arthroplasty. *J Arthroplasty* 25:680–686.
27. Paul JP. 1967. Forces transmitted by joints in the human body. *Proc Inst Mech Eng* 181:8–15.
28. Tipper JL, Galvin AL, Williams S, et al. 2006. Isolation and characterization of UHMWPE wear particles down to ten nanometers in size from in vitro hip and knee joint simulators. *J Biomed Mater Res A* 78:473–480.
29. Campbell P, Doorn P, Dorey F, et al. 1996. Wear and morphology of ultra-high molecular weight polyethylene wear particles from total hip replacements. *Proc Inst Mech Eng H* 210:167–174.
30. Dumbleton JH, D'Antonio JA, Manley MT, et al. 2006. The basis for a second-generation highly cross-linked UHMWPE. *Clin Orthop Relat Res* 453:265–271.
31. Oral E, Christensen SD, Malhi AS, et al. 2006. Wear resistance and mechanical properties of highly cross-linked, ultrahigh-molecular weight polyethylene doped with vitamin E. *J Arthroplasty* 21:580–591.
32. Rathi P, Pereira GC, Giordani M, et al. 2013. The pros and cons of using larger femoral heads in total hip arthroplasty. *Am J Orthop* 42:E53–E59.
33. Schmalzried TP, Callaghan JJ. 1999. Wear in total hip and knee replacements. *J Bone Joint Surg Am* 81:115–136.
34. Ishihara K, Ueda T, Nakabayashi N. 1990. Preparation of phospholipid polymers and their properties as polymer hydrogel membranes. *Polym J* 22:355–360.
35. Kuiper KK, Nordrehaug JE. 2000. Early mobilization after protamine reversal of heparin following implantation of phosphorylcholine-coated stents in totally occluded coronary arteries. *Am J Cardiol* 85:698–702.
36. Johnson AJ, Loving L, Herrera L, et al. 2014. Short-term wear evaluation of thin acetabular liners on 36-mm femoral heads. *Clin Orthop Relat Res* 472:624–629.
37. Kyomoto M, Moro T, Takatori Y, et al. 2011. Cartilage-mimicking, high-density brush structure improves wear resistance of crosslinked polyethylene: a pilot study. *Clin Orthop Relat Res* 469:2327–2336.
38. Kelly NH, Rajadhyaksha AD, Wright TM, et al. 2010. High stress conditions do not increase wear of thin highly cross-linked UHMWPE. *Clin Orthop Relat Res* 468:418–423.
39. Tower SS, Currier JH, Currier BH, et al. 2007. Rim cracking of the cross-linked longevity polyethylene acetabular liner after total hip arthroplasty. *J Bone Joint Surg Am* 89:2212–2217.

