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A phospholipid polymer graft layer affords high resistance for wear and oxidation under load bearing conditions

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ABSTRACT

Manipulating the surface and substrate of cross-linked polyethylene (CLPE) is an essential approach for obtaining life-long orthopedic bearings. We therefore proposed a bearing material comprised of an antioxidative substrate generated by vitamin E blending (HD-CLPE[VE]) with a poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC)-grafted surface, and investigated its wear resistance and oxidative stability under accelerated aging and load bearing conditions. Neither the hydration nor friction kinetics of the molecular network structure of the PMPC-grafted surface or the HD-CLPE(VE) substrate were influenced by accelerated aging but rather exhibited high stability even under high oxidation conditions. The characteristics of the PMPC-grafted surface improved the wear and impact fatigue resistance of the HD-CLPE(VE) liner regardless of accelerated aging. Notably, the PMPC-grafted surface was found to affect the potential oxidative stability at the rim part of the acetabular liner. PMPC chains serve several important functions on the surface regardless of load bearing, such as high lubricity or low lipophilicity attributed to phosphorylcholine groups and/or surrounding water-fluid film, and suppression of lipid diffusion attributed to methacrylate main chains on the surface. Together, these results provide preliminary evidence that the PMPC graft layer and vitamin E-blended substrate might positively affect the extent of orthopedic implant durability.

1. Introduction

The number of annual revision surgeries with primary total hip arthroplasty (THA) procedures has increased significantly owing to the aging global population, despite advances in surgical techniques and implant designs (Bozic et al., 2015). In particular, one of the major complications of THA, aseptic loosening caused by periprosthetic osteolysis limits the duration and clinical outcomes following revision surgery (Bozic et al., 2009). For example, the national joint replacement registry of Australia reported that the number of revision surgeries increased annually and the revision rate was 5.6% at 15 years post operatively, even for current primary THA using a highly cross-linked polyethylene (CLPE) liner (Graves and Turner, 2016). Furthermore, 26.4% of the revision surgeries for young active patients aged less than 55 years were caused by aseptic loosening as well. Specifically, periprosthetic osteolysis is triggered by a host inflammatory response to wear particles produced at the bearing interface of the artificial joint. Therefore, we developed an articular cartilage-inspired technology that allows surface modification of the acetabular liners used in artificial hip joints by grafting water-soluble poly(2-methacryloyloxyethyl phosphorylcholine [MPC]) (PMPC) on CLPE for obtaining high wear resistance (Moro et al., 2004, 2014, 2017). Notably, the surface modification of CLPE bearings with a hydrophilic layer has been reported to increase lubrication to a degree similar to that obtained for articular cartilage under physiological conditions. Our previous study on the function and efficacy of PMPC revealed that such grafting greatly improves the wear resistance of the CLPE bearing surface (Moro et al., 2014).

However, wear resistance constitutes only one of several important indicators of the clinical performance of acetabular liners; oxidation stability is also an important indicator. Generally, oxidation of polyethylene (PE) comprises a free radical-initiated chemical reaction and is expected to result in molecular chain scission (Bracco et al., 2005). A sequential decrease in the molecular weight and cross-link density or

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increase in crystallinity would be facilitated following oxidative degradation of the PE or CLPE; such changes in the chemical and physical structures have been shown to compromise their mechanical properties and might ultimately lead to implant failures such as rim fracture or delamination (Kurtz et al., 2015; Hara et al., 2013; Laska et al., 2016). In particular, two potential triggers have been recently considered to play a role in inducing the changes *in vivo* that lead to the oxidation of CLPE. One trigger constitutes the residual free radicals in the CLPE substrate as mentioned above, whereas the other is the absorbed lipids from the synovial fluid that can initiate and accelerate an oxidation cascade. Oral et al. (2012) suggested that the oxidative degradation caused by the lipid (*e.g.,* squalene) absorption of PE or CLPE served as an additional oxidation cascade, based on the results from a previous retrieval study reported by Costa et al. Costa et al. (2001). Accordingly, the incorporation of the antioxidant vitamin E (α-tocopherol) as a free-radical scavenger has begun to be utilized in the orthopedic field to avoid oxidation owing to its well-established biological safety (Bracco and Oral, 2011). Therefore, we previously proposed a bearing material with a highly lubricious surface afforded by PMPC grafting and an antioxidative CLPE substrate modified by vitamin E blending (Kyomoto et al., 2014a, 2015a, 2015b, 2017). We found that the PMPC-grafted surface was resistant to lipid absorption and diffusion as well as subsequent lipid-related oxidative degradation, likely because of the presence of the hydrated PMPC graft layer (Kyomoto et al., 2017). Results from the previous study provided preliminary evidence that the resistance against lipid absorption and diffusion afforded by a hydrated PMPC graft layer in turn might positively affect the extent of resistance of orthopedic implants to *in vivo* oxidation. However, the lipid adsorption and diffusion measured in the previous study were restricted under the static condition and were not measured under dynamic conditions such as load bearing or repeated load cycling conditions as commonly occur during orthopedic bearing failure. In particular, the lipid diffusion would likely become accelerated owing to the molecular chains gaining increased mobility.

The purpose of this study was therefore to investigate the effects of a PMPC-grafted surface and vitamin E-blended CLPE substrate on wear and oxidation resistance even under severe conditions such as accelerated aging and load bearing states. The ultimate goal in manipulating the surface and substrate of a CLPE liner is not just to obtain high wear resistance but also to achieve high oxidative stability for lifelong orthopedic bearings. We thus addressed whether: (1) the (accelerated) aging might affect the hydration lubrication characteristics of the PMPC graft layer and the fatigue resistance of HD-CLPE(VE) substrate, and (2) the PMPC-grafted HD-CLPE(VE) liner could provide wear and oxidation resistance despite the accelerated aging under the controlled load bearing condition.

2. Materials and methods

2.1. Chemicals, surface modification by PMPC grafting, and accelerated aging

Benzophenone (BP) and acetone were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). Industrially synthesized MPC (purity ≥ 98.0%) was purchased from NOF Corp. (Tokyo, Japan). A compression-molded bar stock of 0.1 mass% vitamin E-blended polyethylene (PE[VE]; GUR1020E resin, Orthoplastics Ltd, Lancashire, UK) was irradiated with a high dose (HD; 100 kGy) of gamma-rays in a N_2 gas atmosphere and annealed at 120 °C for 12 h in N_2 gas in order to facilitate cross-linking; this PE(VE) material is hereafter referred to as HD-CLPE(VE). HD-CLPE(VE) samples were then machined from the bar stocks after cooling, washed with aqueous polysorbate-surfactant solutions and ethanol, and dried at room temperature for 1 h in a vacuum.

The HD-CLPE(VE) samples were immersed for 30 s in acetone containing 10 mg/mL BP, and then dried in the dark at room temperature to remove the acetone. MPC was dissolved in degassed pure water to a concentration of 0.5 mol/L (Kyomoto et al., 2008a). The BP-coated HD-CLPE(VE) samples were then immersed in the aqueous MPC solution. Photoinduced-radical graft polymerization was carried out on the HD-CLPE(VE) surfaces using ultraviolet (UV) irradiation (UVL-400HA ultra-high pressure mercury lamp; Riko-Kagaku Sangyo Co., Ltd., Funabashi, Japan) with an intensity of 5 mW/cm^2 at 60 °C for 90 min (Kyomoto et al., 2014a); a filter (model D-35; Toshiba Corp., Tokyo, Japan) was used to permit the sole passage of UV light with a wavelength of 350 ± 50 nm. After polymerization, the PMPC-grafted HD-CLPE(VE) samples were removed, washed with pure water and ethanol, and dried at room temperature for 1 h in a vacuum.

The untreated HD-CLPE(VE) and PMPC-grafted HD-CLPE(VE) samples were sterilized with a 25-kGy dose of gamma-ray irradiation under N_2 gas, and then were subjected to conditions of accelerated aging, *i.e.,* exposure to 80 °C in air for 21 days (Kurtz et al., 2001).

2.2. Wettability and friction tests

Static-water contact angles were measured on the obtained samples of the 4 groups: HD-CLPE(VE), PMPC-grafted HD-CLPE(VE), aged HD-CLPE(VE), and aged PMPC-grafted HD-CLPE(VE), by employing the sessile-drop method using an optical-bench-type contact-angle goniometer (Model DM300, Kyowa Interface Science Co., Ltd., Saitama, Japan). Drops of purified water (1 μL) were deposited on the surface of each sample and the contact angles were directly measured after 60 s using a microscope. For each sample, 15 areas were evaluated with the mean values reported for the static contact angles of water.

Unidirectional friction tests were performed using a ball-on-plate machine (Tribostation 32, Shinto Scientific Co., Ltd., Tokyo, Japan). A total of 12 specimens of each of the HD-CLPE(VE), PMPC-grafted HD-CLPE(VE), aged HD-CLPE(VE), and aged PMPC-grafted HD-CLPE(VE) samples were evaluated. A 9-mm-diameter pin made of a Co–Cr–Mo alloy was also prepared. The surface roughness (R_a) of the pin was < 0.01 μm, which was comparable to that of currently used femoral head products. The friction test was performed for each specimen at room temperature using a load of 0.98 N (the contact stress roughly calculated by Hertzian theory was approximately 25 MPa; the Young's modulus of the Co–Cr–Mo alloy and HD-CLPE(VE) was assumed to be 242 and 1.12 GPa, respectively, whereas their Poisson's ratios were assumed to be 0.30 and 0.38, respectively), a sliding distance of 25 mm, and a frequency of 1 Hz. A maximum of 100 cycles were carried out, with pure water used for lubrication. The mean dynamic coefficients of friction were determined by averaging the values of five data points taken from the 96–100th cycles.

2.3. Swelling tests

The swelling ratio and cross-link density of the HD-CLPE(VE) and PMPC-grafted HD-CLPE(VE) substrates that underwent accelerated aging were evaluated according to previously reported methods (Kyomoto et al., 2014b). We divided three sample pieces (23 × 23 × 1 mm^3) from the surface (0–1 mm in depth) and sub-surface (3–4 mm in depth) of each the HD-CLPE(VE), PMPC-grafted HD-CLPE(VE), aged HD-CLPE(VE), and aged PMPC-grafted HD-CLPE(VE) substrates. The sample pieces were allowed to swell for 72 h in *p*-xylene containing 0.5 mass% 2-*t*-butyl-4-methylphenol at 130 °C, and then immersed in acetone and dried at 60 °C under vacuum. The swelling ratio (w/w) was determined from the increase in the weights of the samples before and after swelling. The network chain density was calculated using the Flory-Rehner equation, and the cross-link density was defined as the mole fraction of the cross-linked units (Shen et al., 1996).

2.4. Impact-to-wear tests

Impact-to-wear tests were conducted using a pin-on-disk testing machine (Ortho POD; AMTI, Watertown, MA, USA), according to ASTM