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Data-Driven Innovations in Joint Replacement: Do Ceramic Femoral Heads Contribute to Polyethylene Oxidation?

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Abstract

Renewed attention is being paid to biomaterials used in total hip arthroplasty (THA) given the continued clinical problems of osteolysis and aseptic loosening which result from the long-term wear of acetabular polyethylene (PE) bearing surfaces. One advantage of using ceramic femoral heads is low PE wear, presumably because of the ceramics' bioinert behavior. However, beyond simple mechanical abrasion, marked differences have been found in the degradation of PE when coupled with different ceramic materials. This study examined the surface characteristics and performance of oxide-based (zirconia-toughened alumina, ZTA) and non-oxide (silicon nitride, Si_3N_4) femoral heads. Under articulation, ZTA femoral heads were found to release detectable amounts of oxygen from their surfaces into the tribolayer, which resulted in enhanced PE oxidation. In contrast, femoral heads made from Si_3N_4 scavenged oxygen from the tribolayer, thereby limiting the degradation of PE. This work is the first to challenge the assumption that ceramic materials are inherently stable *in vivo*, and suggests that the longevity of THA prostheses may depend on the material properties of the ceramic used during surgery. Neglecting these important physical chemistry aspects impedes the scientific development of new materials and favors monopolistic economics in the market, leading to limited choices for surgeons.

Keywords: ZTA, silicon nitride, polyethylene, spectroscopy, hip arthroplasty

I. Introduction

There are crucial physical chemistry characteristics of biomaterial surfaces that directly affect their long-term performance as artificial joints. These features actually provide important insight to biomaterials designers for developing better microstructures. They are important in understanding the actual limits of presently used oxide ceramics and whether, directly or indirectly, their surface chemistry affects the *in vivo* lifetimes of artificial hip joints. In contrast to the multitude of possible reasons for premature implant failure as reported in the literature [1, 2], surface chemistry effects have been neglected. At first glance the surface chemistry of ceramic biomaterials may appear to be of marginal importance. However, while the commonly reported causes of implant failure leading to revision surgery are usually related to design variables that can be corrected, failures associated with intrinsic biomaterial properties are generally inescapable. If the ultimate goal is a prosthetic joint (*e.g.*, THA) that lasts for multiple decades, then an understanding of the chemical interaction between mating and frictional sliding surfaces

are highly relevant. In this study non-oxide bioceramics were identified as possessing favorable surface chemistry that naturally protects the polyethylene-sliding countersurface from oxidation. A key concept in establishing this favorable chemistry is the control of the oxygen activity at the bioceramic surface during tribochemical loading in the otherwise anaerobic body environment.

II. Materials and Methods

Hard-on-soft hip-simulator wear experiments were conducted according to standardized procedures – ASTM F1714 – 96 and ISO 14242:1. Ultra-high molecular weight polyethylene (UHMWPE) acetabular liners (Apex-Link Poly™, OMNI Life Science, East Taunton, MA USA) were tested in a hip simulator against Ø28 mm Si_3N_4 femoral heads (AMEDICA Corporation, Salt Lake City, UT USA) and the structural characteristics of worn femoral heads were then compared to those of pristine specimens. The UHMWPE is a first-generation highly cross-linked and annealed polyethylene. Fabricated from GUR1050 resin, it was gamma-irradiated to 78.5 kGy in inert gas and subsequently annealed in nitrogen at 85 – 90 °C for 24 hours. Final sterilization was

performed in a gaseous ethylene oxide environment. The acetabular liners were artificially aged prior to wear testing according to ASTM F2003 – 02. Using this standard, technologists induced the formation of free radicals in UHMWPE prior to hip simulation testing [3]. The hip simulation study was performed using an AMTI 12-station hip simulator (AMTI, Watertown, MA USA) at a rate of 1 Hz. Tests were carried out to a total of 5 x 10^6 cycles of simulated gait. Test kinematics followed a standard Paul curve as specified by ISO 14242 – 1. For comparison, an oxide bioceramic hard-on-soft couple was also tested under identical conditions. Hip-simulator wear was conducted using six ArCom® UHMWPE liners (Zimmer/Biomet. Inc. Warsaw, IN USA) which articulated against Ø28 mm femoral heads made of zirconia-toughened alumina (ZTA; BIOLOX®*delta*, CeramTec GmbH, Plochingen, Germany). ArCom® polyethylene is a conventional polyethylene fabricated from GUR1050 resin and gamma-irradiated to 33 kGy in Ar gas for its final sterilization.

Crystallinity and oxidation profiles for the pristine liners were collected by means of Raman and infrared spectroscopy, respectively, and compared with data from the tested liners. Raman spectra were recorded in a backscattering configuration using a triple monochromator (T-64000, Horiba/Jobin-Yvon, Kyoto, Japan) equipped with a liquid-nitrogen-cooled charged-coupled device (CCD). The excitation source was a green laser beam (532 nm) Nd:YVO$_4$ diode-pumped solid-state laser (SOC JUNO, Showa Optronics Co. Ltd., Tokyo, Japan). The Raman probe size was on the order of ~ 1 µm in plane and ~ 6 µm and in depth. Crystallinity assessments were performed according to the method introduced by Strobl and Hagerdon which utilizes a set of equations that include the intensities of vibrational bands located at 1296, 1305, and 1418 cm^{-1} from the unpolarized Raman spectra [4]. Fourier-transformed infrared spectroscopy (FT-IR) was conducted using the imaging system Spotlight 200 (Perkin Elmer, Waltham, MA USA). Infrared transmission spectra of polyethylene were acquired at an aperture size of 5 × 5 µm^2. The oxidation index, *OI*, was calculated from FT-IR spectra according to ASTM 2102 as the ratio of the area under the carbonyl peak at around 1720 cm^{-1} to the area under the C-H absorption peak centered around 1370 cm^{-1} [5]. Two-dimensional Raman maps 100 x 100 µm (441 spectral measurements each) were non-destructively collected at different focal depths in the liner's subsurface and average values were extracted for crystallinity fractions. Two-tailed Student's t-tests (95 % confidence level, $p < 0.05$) were used to compare the population means at different depths for the pristine sample, and for both the wear and the non-wear zones of the *in-vitro* tested liners. Crystallinity results were compared with FTIR average data obtained at the same depths after slicing and thinning the samples.

Cathodoluminescence (CL) spectra were acquired using a field-emission gun scanning electron microscope (FEG-SEM, SE-4300, Hitachi Co., Tokyo, Japan). Exactly the same experimental conditions were applied for both the oxide and non-oxide samples. Accelerating voltage and

beam current were fixed for all experiments at 6 kV and 180 pA, respectively. The nominal spatial resolution of the electron beam at the sample surface was 1.5 nm. The microscope was equipped with a CL device consisting of an ellipsoidal mirror and a bundle of optical fibers. These were respectively used to collect and focus the electron-stimulated luminescence emitted by the sample into a high spectrally resolved monochromator (Triax 320, Jobin-Yvon/Horiba Group, Tokyo, Japan). These spectra were subsequently deconvoluted into Gaussian subbands using commercially available software (Origin 9.1, OriginLab Co., Northampton, MA USA).

III. Results

As expected, the volumetric material loss in the hip simulator experiments was low for both ceramic-on-polyethylene couples and consistent with previously reported data [6]. However, the average volume loss for ArCom® vs. BIOLOX®*delta* couples was twofold larger than that of Apex-Link Poly™ vs. AMEDICA Si$_3$N$_4$ (*i.e.* ~ 220 mm^3 vs. ~ 100 mm^3) after 5 million cycles (Mc) principally due to the difference in irradiation cross-linking (*i.e.* 33 kGy vs. 78.5 kGy, respectively). The Raman probe detected an increase in the average fraction of monoclinic phase in the ZTA material after 5 Mc in the hip simulator as compared to the pristine samples (*i.e.* 22 vol% both in the main-wear and non-wear zones vs. 12 % in the pristine samples). No difference in Raman spectra was detected in the Si$_3$N$_4$ femoral heads before and after hip simulation.
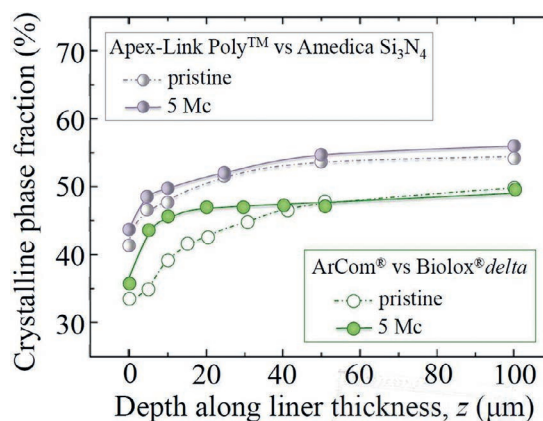

Fig. 1: Raman assessments of in-depth profiles of crystallinity fractions for different polyethylene liners coupled with oxide and non-oxide ceramic heads before and after 5 Mc testing in the hip simulator.

Fig. 1 shows the profiles of average crystallinity non-destructively acquired for the in-depth direction, *z*, of the liners used for the Apex-Link Poly™/AMEDICA Si$_3$N$_4$ couples in the main wear zone after 5 Mc of simulator testing in comparison with data collected on the pristine liners. In both plots, the crystalline phase fraction steeply increased within the first few microns of the subsurface, then tended to plateau. This trend is typical for a number of commercially available UHMWPE liners in which an amorphous state of the surface is induced by mechanical machining [7]. It was significantly discovered that crystallinity in the main wear zone of the liners which articulated against Si$_3$N$_4$ femoral heads only increased by

$\leq 3\,\%$ along the subsurface as compared to pristine samples. There were only marginal differences in crystallinity between worn and unworn regions. A comparison is also given in Fig. 1 of the behavior in hip simulation of the ArCom®/BIOLOX®*delta* couples tested for 5 Mc under the same conditions. Unlike the case of non-oxide femoral heads, in-depth Raman scanning in the main wear zone of the ArCom® UHMWPE liners revealed significant crystallization (*i.e.* up to 21 % higher in the first 30 μm of subsurface) when compared to the pristine samples.
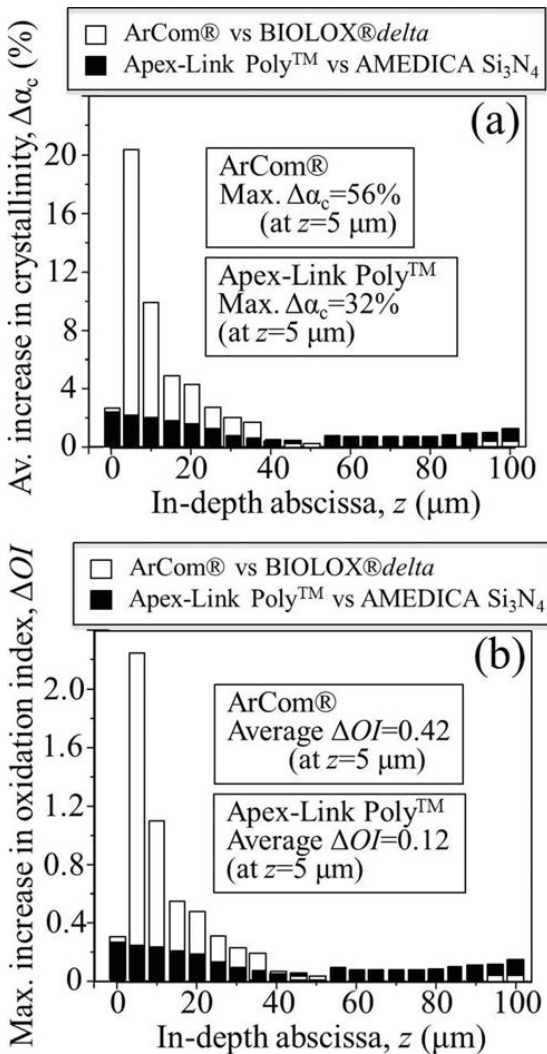

Fig. 2: Increases in (a) average degree of crystallinity, Δa_c, and (b) maximum oxidation index, ΔOI, as a function of in-depth abscissa, z, after 5 Mc testing in the hip simulator. Maximum crystallinity and average oxidation index increases at $z = 5$ μm are shown in the inset.

Crystallization occurring during frictional interaction between head and liner is ascribed to the formation of oxidized species within the polymer's microstructure. Residual free radicals are generated in the amorphous phase; and they easily react with oxygen to form hydroperoxides (*i.e.* the first product of oxidation). Evolution to ketones, carboxyl acids, and other oxidized species containing carbonyl groups is then responsible for breakage of polyethylene chains, increased molecular mobility, and subsequent crystallization [8,9]. This is the phenomenon observed in this study. Indeed, this mechanism was confirmed after slicing the polyethylene liners and measuring

the oxidation index, *OI*, as a function of sample depth. Figs. 2(a) and (b) compare average increases in crystalline fraction, Δa_c, and maximum increases in oxidation index, ΔOI, respectively, for the different liners as a function of in-depth z-axis. Maximum crystallinity values and average oxidation indices in the immediate sub-surface of the tested liners are given in the insets. These data were collected for both groups of the tested liners and compared with their corresponding pristine samples. The results suggest that there is an apparent link between crystallization of UHMWPE and the ceramic counterface. Significantly higher crystallization and oxidation were observed in the liners which articulated against the oxide femoral heads, while the amount of chemical and phase changes detected due to articulation against the non-oxide ceramics was negligible.

In gamma-irradiated polyethylene, ageing before wear testing (*i.e.* a conservative condition purposely superimposed by the ASTM standard) favors oxidation and crystallization during hip simulation [3]. This is especially true in deeper regions since gamma rays are known to induce a concentration gradient of free-radicals with their maxima along the in-depth axis [10]. This negative effect systematically appeared in the oxidation trends for the UHMWPE/ZTA couples, but it was absent in UHMWPE/Si$_3$N$_4$ couples. Therefore, for a similar amount of free radicals formed by preliminary gamma-irradiation, oxygen was promptly available to the UHMWPE structure during testing of the oxide couples, while it was unavailable to the non-oxide pairs.

Confirmation of this tribochemical-induced difference between Si$_3$N$_4$ and ZTA femoral heads and their respective UHMWPE liners was determined using cathodoluminescence spectroscopy. Figs. 3(a) and (b) show laser micrographs of the bearing surface of a Si$_3$N$_4$ femoral head before and after hip simulation, respectively. The surface of the pristine head contained a small fraction of open porosity from the manufacturing process (Fig. 3(a)). Note that this porosity was almost completely filled after simulation testing (Fig. 3(b) and inset). Comparative cathodoluminescence analyses of the pristine and tested Si$_3$N$_4$ heads indicated that the porosity had been filled with silica (SiO$_2$) glass (*cf.* average spectra of the main wear zone in Fig. 3(c), (d), and (e)). While these spectra display complex features which have been addressed previously [10], the spectral area at around 630 nm is relevant to this discussion. The pronounced shoulder recorded in this spectral area for the Si$_3$N$_4$ samples points to the presence of an oxidized layer of silica-rich glass. The main emission band for silica located at around 630 nm in Fig. 3(e) coincides with the location of the shoulder recorded in Fig. 3(d) for the tested Si$_3$N$_4$ sample. This band represents oxygen-rich sites (non-bridging oxygen hole centers, NBO-HC) [11]. These spectroscopic data unequivocally demonstrate the transfer of oxygen molecules onto the surface of Si$_3$N$_4$ during simulation testing.
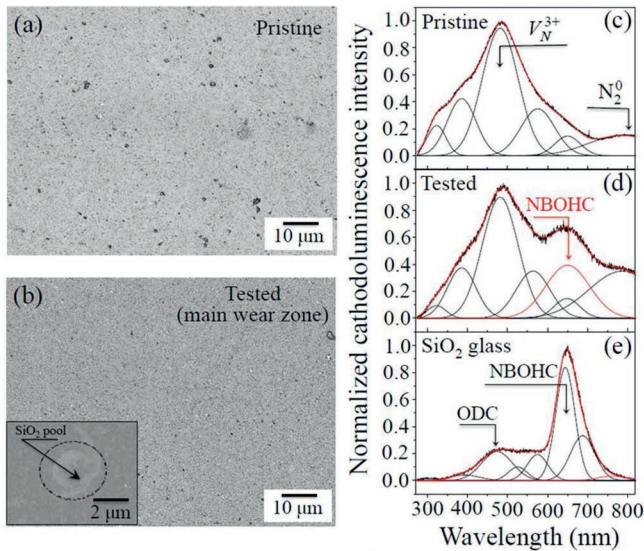
Fig. 3: Laser micrograph of the surface of the Si_3N_4 femoral head before (a) and after (b) testing in the hip simulator (see also enlarged area in the inset). The outputs of cathodoluminescence analyses on pristine and tested Si_3N_4 head samples are reported in (c) and (d), respectively, in comparison with the cathodoluminescence spectrum of pure silica (SiO_2) glass (e). Labels are explained in the text.

Cathodoluminescence emissions from the surface of BIOLOX®*delta* femoral heads before and after testing revealed an opposite trend with respect to oxygen interactions at the bearing surface. Fig. 4 shows average spectra for the cathodoluminescence emission at around 335 nm before and after simulation testing. This band indicates the presence of oxygen vacancies in the alumina (Al_2O_3) lattice. Given that the emissions are proportional to the number of vacancy sites on the surface of the Al_2O_3 phase, the higher intensity of the emission band after testing as compared with the pristine sample verifies the release of oxygen from the ZTA femoral head during tribological loading.
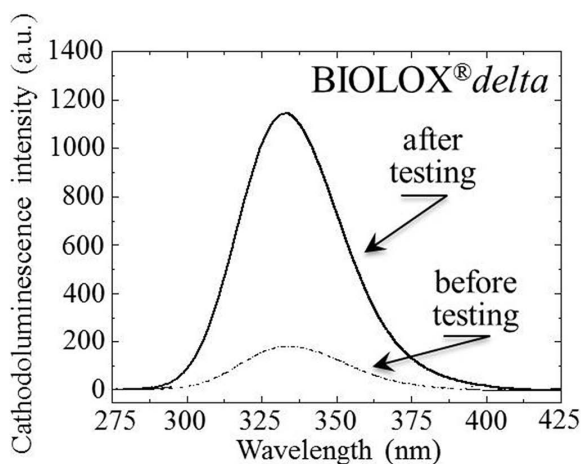
Fig. 4: Increase in cathodoluminescence emission from oxygen vacancy sites at the surface of the Al_2O_3 phase in BIOLOX®*delta* heads before and after *in vitro* testing.

IV. Discussion

By examining retrieved UHMWPE liners, it was demonstrated that free radicals unavoidably form within the polymer during *in vivo* use [12]. Even highly cross-linked and annealed liners (with no detectable free radicals at

the time of their implantation) showed significant oxidation after as little as three years of *in vivo* service [13]. Remarkably, some of these explants continued to oxidize even after their removal [14]. The *in vivo* chemical origin of free-radical formation in fully stabilized polyethylene resides in the action of lipids (*e.g.* squalene) absorbed from the synovial fluid [15]. The unsaturated C=C bonds, a peculiarity of the lipid molecules, quickly oxidize and subsequently form hydroperoxides at the oxidized sites. The hydrogen ions needed for this process are extracted from the polyethylene chains resulting in the formation of new free radicals. The process of lipid-driven free-radical formation in biomedical polyethylene is schematically shown in Fig. 5(a). Note that the attack by lipids preferentially starts in the amorphous phase of the polyethylene. The high mobility of free radicals in this phase accelerates oxidation. Enhanced crystallinity and oxidation generally occur concurrently, (which is exactly what was observed in Figs. 1 and 2). Oxidation generates chain scission and the formation of polyethylene domains having lower molecular weight. These domains undergo recrystallization more readily than the pristine UHMWPE structure. It is important to note that oxidation of lipids will unavoidably start as soon as oxygen molecules become available. Therefore, degradation of the host polymer is just a matter of time once it is exposed to the *in vivo* environment. As discussed by Oral *et al.*, this phenomenon is independent of the efforts of polyethylene manufacturers to provide surgeons with pristine acetabular liners that are absent of free radicals [16]. As soon as lipids interact with the polyethylene structure and oxygen becomes available, the cascade of events leading to free-radical formation will inescapably begin.

To counteract the above inexorable process, biomaterials scientists have successfully introduced the use of antioxidants in biomedical polyethylene [17]. Vitamin E, whose anti-oxidant properties arise from the presence of an alcoholic hydroxyl group attached to the chroman ring of the vitamin structure, has garnered the most attention. The alcoholic hydroxyl possesses a "sacrificial" tendency and gives away its hydrogen to become a stabilized phenoxy radical. The free hydrogen can therefore quickly annihilate an *in vivo* formed free radical in the UHMWPE according to a "peroxyl radical trapping" mechanism. The chemical mechanism of vitamin E-activated free-radical annihilation in biomedical polyethylene is schematically shown in Fig. 5(b).

This *in vitro* study suggests another powerful method to delay polyethylene oxidation *in vivo*: oxygen scavenging by a Si_3N_4 femoral head. It is both compatible and synergistic with anti-oxidant doping of polyethylene, and may provide the same efficacy with potentially longer-term effectiveness. This mechanism is schematically depicted in Fig. 5(c). It occurs due to the thermodynamic driving force behind the conversion of silicon nitride to silica in accordance with the following reaction:

$$Si_3N_4 + 6H_2O \rightarrow 3SiO_2 + 4\ NH_3;\ \Delta G = -439\ kJ/mol \qquad (1)$$
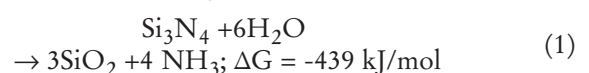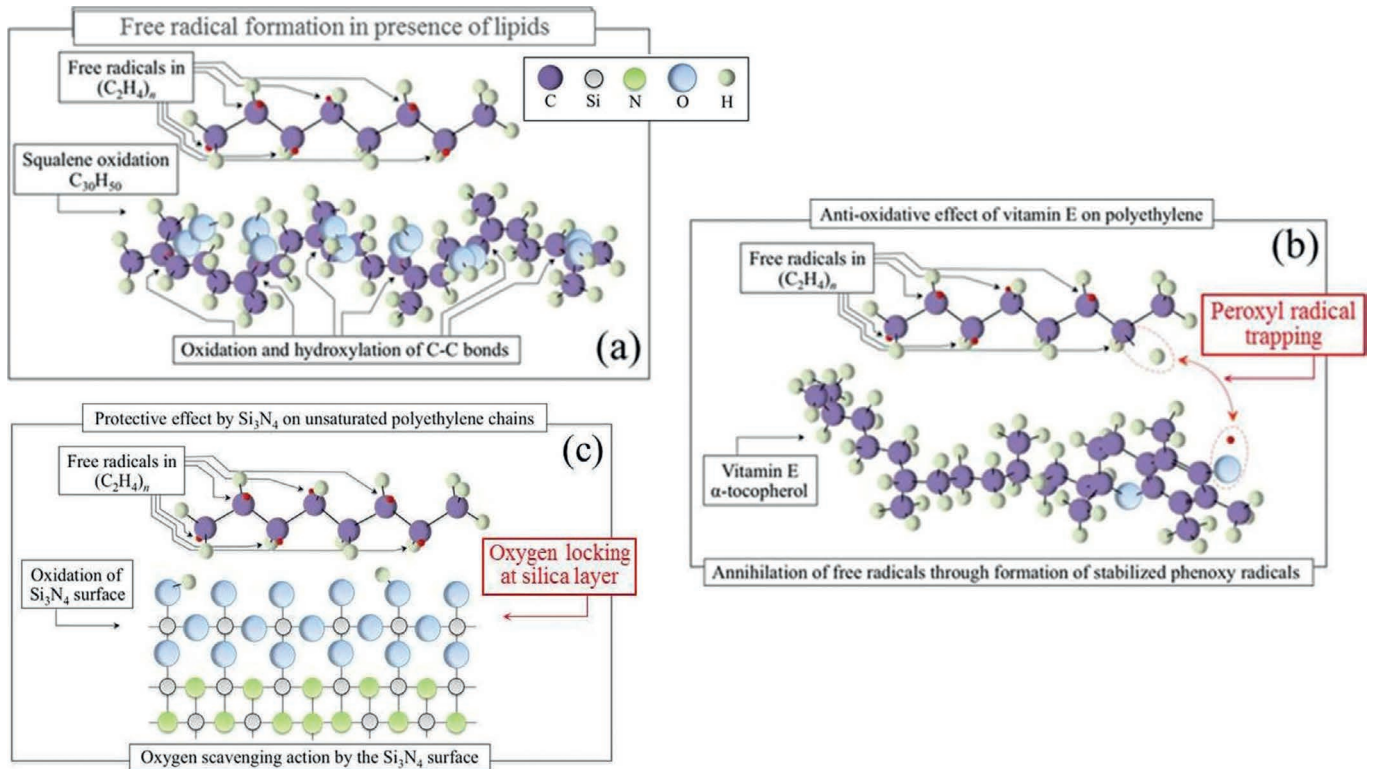
Fig. 5: (a) Mechanism of free-radical formation in saturated polyethylene chains in the presence of lipids; (b) beneficial effect of anti-oxidant vitamin E on the annihilation of free radicals in polyethylene; and, (c) beneficial effect by oxygen scavenging at the Si_3N_4 surface in preventing oxidation at free radical sites in polyethylene.

Amphoteric silicon oxide forms on the surface of silicon nitride upon its exposure to atmospheric oxygen [18]; the initial O_2 chemisorption rate is rapid and saturation occurs quickly. The amphoteric silica acts as an Arrhenius acid with the fluid in the tribolayer being the corresponding Arrhenius base. The surface charge depends on the pH of the synovial fluid which in turn alters the interactive solid/liquid equilibrium. A silicon oxide and oxynitride layered structure ensues at the surface of Si_3N_4. It is this chemical structure that traps oxygen and protects the polyethylene from oxidation. Under frictional sliding, resorbable orthosilicic acid (H_4SiO_4) and ammonia (NH_3) are released [19]. However, the CL experiments from these *in vitro* studies confirmed the reformation of silica at the surface of the Si_3N_4 during tribological loading. Consequently, silicon nitride acts as a sacrificial scavenger of oxygen analogous to that of vitamin E scavenging free radicals. Additionally, the formation of silicic acid at the ceramic polymer interface may potentially lead to a reduction in friction due to the build-up of a coherent tribochemical lubricating film (as has been demonstrated for other silicon nitride/polymer sliding couples) [20]. Note also that the peculiar sequence of surface structures involved with oxidation reactions of Si_3N_4 lead to the unique possibility of tailoring its surface chemistry in order to minimize friction and wear. This provides important flexibility in engineering the material's microstructure to optimize its tribological efficiency in artificial hip joints.

Finally, it could be argued that metallic femoral heads also have a tendency to scavenge oxygen from the tribolayer by sacrificially oxidizing their surface. However, unlike the biocompatible and resorbable release of silica and nitrogen from Si_3N_4, metal femoral heads generate discrete debris whose solubility is known to be toxic to local tissues [21]. From this standpoint, Si_3N_4 femoral heads offer the same advantage of metallic heads in terms of oxygen affinity while minimizing abrasive interactions and associated lysis within the joint capsule and surrounding soft tissues.

V. Conclusions

Because of its unique capability of scavenging oxygen rather than releasing it into the tribolayer, this study demonstrated that Si_3N_4 is an oxygen-*cleansing* biomaterial, and therefore a polyethylene-friendly counterpart. Conversely, oxide ceramics (*e.g.* alumina and ZTA) are *oxygen polluters* since they tend to release oxygen from their surface into the tribolayer. Independent of the quality of the polyethylene liner, the use of Si_3N_4 may delay the *in vivo* crystallization/oxidation of UHMWPE by the same microscopic mechanisms demonstrated in these *in vitro* hip simulation tests. While no synthetic biomaterial can be fully bioinert, Si_3N_4 appears to offer considerable promise in "down-regulating" some of the deleterious free oxygen interactions associated with oxide bioceramics in joint arthroplasty. The surface of this non-oxide material naturally drifts towards a protective action with respect to oxidation of UHMWPE. Its peculiar surface chemistry, coupled with advances in anti-oxidative doping, might lead to improved articulation couples which will collectively contribute to achieving the desired second-to-third decade extension in the lifetime of artificial orthopaedic joints.

Conflicts of Interest

Bryan J. McEntire and B. Sonny Bal are employees of Amedica Corporation, a silicon nitride orthopaedic device manufacturer. G. Pezzotti is a consultant to Amedica Corporation.

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