Longfield et al. [50] and Ikeuchi et al. [51] reported that the lubrication mechanism of joints mainly comprises hydration lubrication. Hydrophilic macromolecules induce low friction by promoting the formation of a fluid film that is retained by the water molecules' attraction forces, indicating that the water molecules' attraction forces are important for realizing low friction. The lubrication of the human joint appears to occur by hydration lubrication because the surface layer of the joint resembles the structure of the gelled material in the human joint. Sasada et al. proposed a new idea for joint lubrication, named "Surface gel hydration lubrication" [49] for a lubrication mechanism peculiar to such hydrophilic macromolecules. A bearing surface with a brush-like structure comprising hydrophilic macromolecules in artificial hip joints was therefore assumed to be similar to that of articular cartilage. The hydration lubrication interface can also be regarded to mimic the natural joint cartilage in vivo. The novel material design with this hydration lubrication should be necessary.

25.2.2.3 Photo-Induced Surface "Grafting from" Polymerization

The grafting of polymers onto various surfaces has been studied for over 50 years and has played an important role in many areas of biomaterial science and technology, e.g., colloidal stabilization, adhesion, lubrication, tribology, and rheology. Recent work has focused on the synthesis of so-called polymer brushes whereby the polymer chains stretch out away from the surface or substrate [52,53]. There are three primary methods for modifying a planar substrate with an organic polymer: (a) physical coating, (b) chemical coating and/or "grafting to," and (c) "grafting from" (Figure 25.12). This includes physical coating such as spin or dip coating; however, the polymer is merely adsorbed onto the substrate and may diffuse away when the substrate is immersed into a solvent in which it is soluble. Chemical coating utilizes the functional group of the polymer to chemically attach onto the substrate via several coating techniques. Robust layers may be created by utilizing a self-assembled monolayer (SAM) in order to immobilize a reactive functionality. Thus, the polymer can be attached to the surface, provided the preformed polymer possesses a functional group that is capable of bonding with the surface (e.g., a polymer containing a primary amine could form an amide bond with a carboxylic acid-terminated SAM). This approach

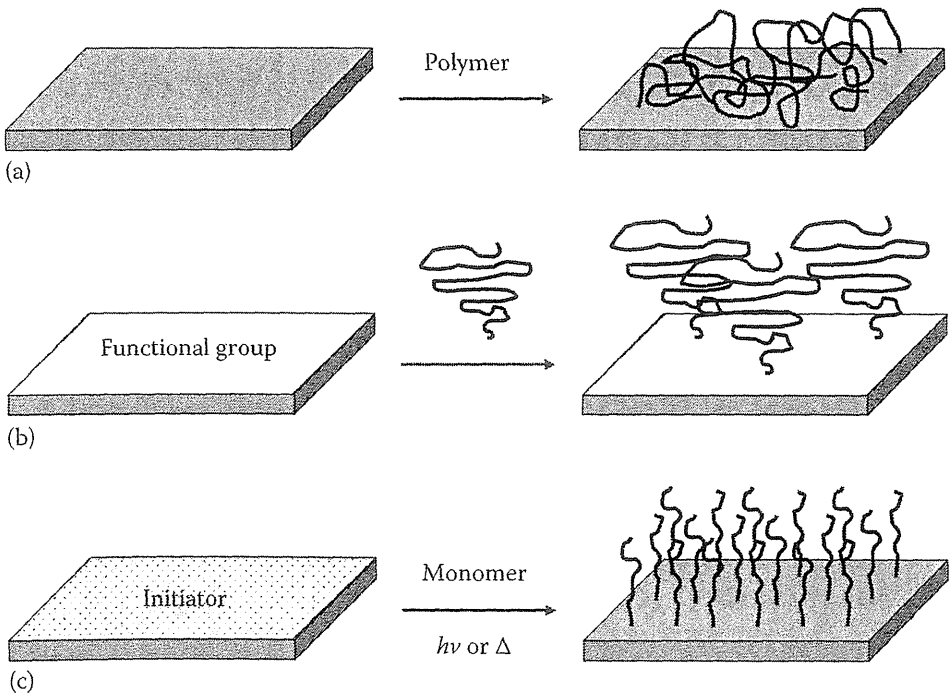

FIGURE 25.12 Approaches for modifying a substrate with a polymer: (a) physical coating (adsorption), (b) chemical coating (immobilization) and/or "grafting to," and (c) "grafting from."

is known as the "grafting to" technique and has been considerably successful at synthesizing robust layers of 1–50 nm in thickness. However, the "grafting to" technique is limited by diffusion barriers that prevent the preformed polymer from intercalating through the tethered polymer to the reactive substrate. Therefore, the "grafting to" method yields a low-density brush. In contrast, the "grafting from" approach has been utilized to synthesize high-density polymer brushes [54]. The conformation of these polymer brushes in a solvent can dramatically change with the graft density. At low-graft density, they will assume a "mushroom" conformation with a coil dimension similar to that of free chains. With increasing graft density, the graft chains will be obliged to stretch away from the substrate, forming a "polymer brush." These high-density brushes can be much thicker and range in size from a nanometer-scale to greater than a micrometer-scale. The great increase in thickness for "grafting from" layers is due to much higher grafting densities compared to those of "grafting to" layers.

Photochemical initiation has several advantages over thermal initiation. First, certain functional groups are not thermally stable; therefore, it is desirable to activate polymerization at room temperature. This also simplifies manufacturing processes. Furthermore, most alkylthiolate SAMs are not stable above 70°C and may begin to degrade at the temperatures required for most thermal initiations. Second, photoinitiation is generally faster than thermal initiation. Third, the initiation process may be activated at almost every temperature; this yields great flexibility when controlling the reactivity and processability of a layer. Surface-initiated polymerization has been carried out with a variety of initiators, and Figure 25.13 describes some of the most common photoinitiators [55]. For surface-initiated polymerization applications, these initiators are typically modified and covalently bonded to the substrate to yield a "grafting from" polymerization. Alternatively, photo-sensitizers can be added to bulk solutions in order to abstract hydrogen atoms from the substrate. For example, benzophenone (BP, Figure 25.13d) is converted to a reactive triplet state after ultraviolet (UV) irradiation; this triplet is capable of abstracting hydrogen atoms from various moieties. Tertiary amines or thiolene systems have been activated with photo-sensitizers, but until recently have not been used for surface-initiated polymerization. Other photoinitiators include peroxides (Figure 25.13a) and benzoin derivatives (Figure 25.13c); of the two, only peroxides have been used for surface-initiated polymerization. The most common free radical photoinitiators are derivatives of 2,2′-azobisisobutyronitrile (AIBN, Figure 25.13b), and these have been used by several research groups for "grafting from" polymerizations from various substrates. Recently, controlled free radical polymerizations have gained much recognition owing to their low polydispersities and "living"-like properties [55]. Indeed, "living" polymerizations have a tremendous advantage for surface-initiated polymerization since it is possible to grow block copolymers and to terminate the polymerization with specific end-groups. However, most living free radical polymerizations utilize thermal initiation; for example, atom transfer radical polymerization may be

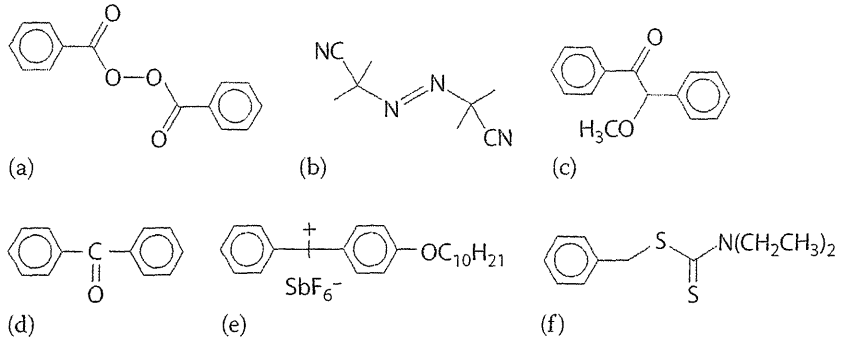

FIGURE 25.13 Various types of photoinitiators: (a) benzoylperoxides, (b) 2,2′-azobisisobutyronitrile compounds based on AIBN, (c) benzoin methylethers, (d) triplet photo-sensitizers, benzophenone (e) onium salts for cationic polymerization, and (f) controlled free radical polymerization with photoiniferters.

used for surface-initiated polymerization, but the rate of initiation and propagation is relatively slow as compared to that of photoinitiation and typically leads to layers that are less than 50 nm thick. Thus, there is a rich variety of photopolymerization strategies that may be utilized in the future, although very few examples of photosurface-initiated polymerization have been reported to date.

25.2.2.4 Poly(MPC)-Grafted Polyethylene

Surface modification is important for improvements in bearing materials. Moro et al. have demonstrated the creation of an artificial hip joint based on the novel concept of "hydration lubrication" by using poly(MPC) (PMPC)-grafted onto the surface of CLPE (PMPC-grafted CLPE); this device is designed to reduce wear and suppress bone resorption [56–58]. A previous study has reported that the hydrogel cartilage surface is assumed to have a brush-like structure: a part of the proteoglycan aggregate brush is bonded with the collagen network on the cartilage surface [49]. Therefore, the bearing surface with PMPC in artificial hip joints is assumed to have a brush-like structure similar to that of articular cartilage (Figure 25.14). The hydration lubrication interface can therefore be regarded to mimic the natural joint cartilage in vivo.

MPC, a methacrylate monomer with a phospholipid polar group in the side chain, is a novel biomaterial designed and developed by Ishihara et al. that mimics the neutral phospholipids of cell membranes [59]. MPC polymers are one of the most common biocompatible and hydrophilic polymers studied thus far, which have potential applications in a variety of fields, such as biology, biomedical science, and surface chemistry, because they possess the unique properties of good biocompatibility, high lubricity and low friction, anti-protein adsorption, and cell membrane-like surface [59–62]. Hence, MPC is hydrophilic and can form a thin film of free water under physiological conditions. Several medical devices have already been developed by utilizing the MPC polymers. These devices have been subjected to clinical use with the approvals of the Ministry of Health, Labour and Welfare (MHLW) of Japan and the Food and Drug Administration (FDA) of the United States; therefore, the efficacy and safety of the MPC polymer as a biomaterial are well established (Table 25.6) [63–82].

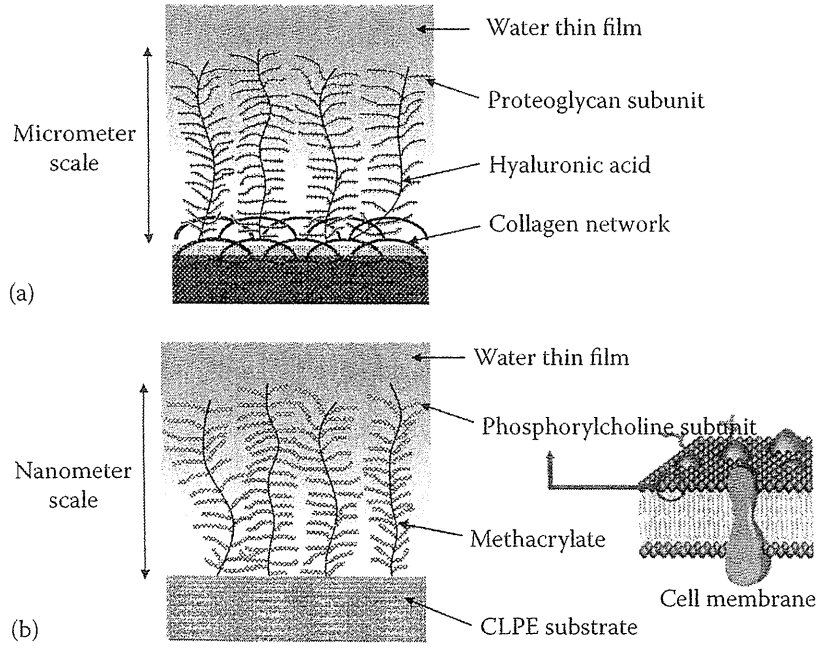

FIGURE 25.14 Schematic model of PMPC-grafted CLPE surface mimicking cartilage. (a) Cartilage. (b) PMPC-grafted CLPE.

TABLE 25.6
Medical Devices with MPC Polymer

Medical Device	Product Name	Manufacturer	Clinical Introduction	Reference
Artificial heart	Evaheart	Sun Medical	Current trial	[63]
Artificial joint	Aquala	Japan Medical Materials	Current trial	[42]
Artificial lung	Mimesys	Sorin Biomedica	2002	[64]
	Synthesis	Sorin Biomedica	2003	[65]
	Physio	Sorin Italia	2005	—
Catheter	Eliminate	Clinical Supply	—	MHLW approval
Contact lens	Proclear	Cooper Vision	1998	FDA approval
Guide wire	Aqua diver	Clinical Supply	—	MHLW approval
	Inter through	Clinical Supply	—	—
	Hunter	Biocompatible	1997	FDA approval
Micro catheter	Londis	Clinical Supply	2005	MHLW approval
Stent	Endeavor	Medtronic	Current trial	[66]
	Endeavor I	Medtronic	Current trial	[67,68]
	Endeavor II	Medtronic	Current trial	[67–69]
	Endeavor II CA	Medtronic	Current trial	[67,68]
	Endeavor III	Medtronic	Current trial	[67,68,70]
	TriMaxx	Abbott Laboratories	2005	[71]
	ZoMaxx	Abbott Laboratories	—	[72]
	Biodiv Ysio	Biocompatible	2000	[73–82]
Tympanostomy tube	—	Gyrus, Grace Medical	2000	FDA approval

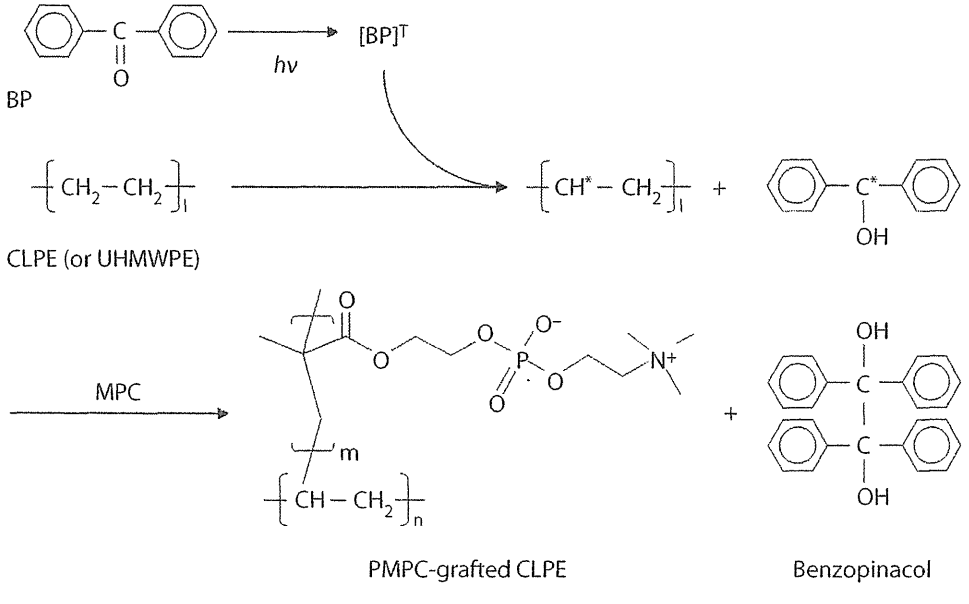

FIGURE 25.15 Schematic illustration of MPC graft polymerization by using the BP system.

The grafting of biocompatible and hydrophilic PMPC with CLPE has been accomplished by using a photo-initiated "grafting-from" polymerization. The photo-initiated "grafting-from" polymerization reaction by using a typical BP photoinitiator is shown in Figure 25.15. First, the physically coated BP on CLPE is excited by UV irradiation. The BP excited to the triplet state extracts a hydrogen atom from the $-CH_2-$ group and then generates a radical that is capable of initiating the graft polymerization of MPC.

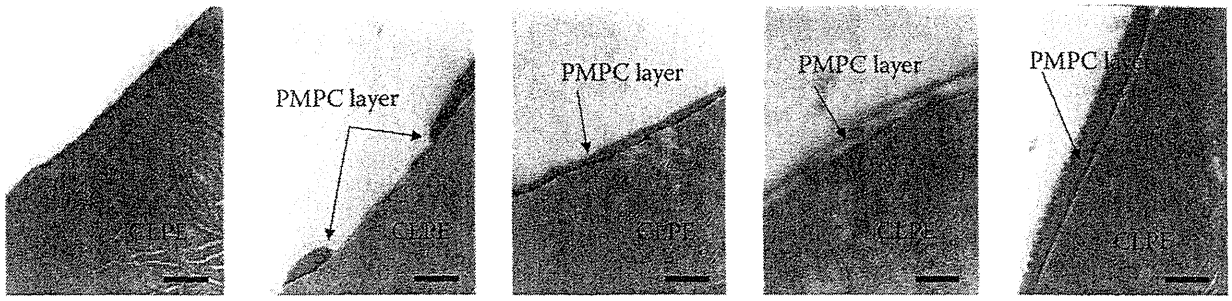

FIGURE 25.16 Cross-sectional TEM images of PMPC-grafted CLPE obtained with a 0.5 mol/L MPC concentration and various photo-irradiation times. Bar: 200 nm. (a) 11 min. (b) 23 min. (c) 45 min. (d) 90 min. (e) 180 min.

This technique has several important benefits as follows: direct grafting of PMPC to CLPE—thereby forming C–C covalent bonding between the PMPC and CLPE substrate, high mobility of the chains of the PMPC, a high density, and controlling the length of the introduced PMPC.

Figure 25.16 shows cross-sectional transmission electron microscope (TEM) images of PMPC-grafted CLPE produced with various photo-irradiation times during polymerization [83]. With photo-irradiation times longer than 45 min, a 100- to 200-nm-thick PMPC-grafted layer was clearly observed on the surface of the CLPE substrate. The MPC-covered region was coexistent with uncovered regions after a photo-irradiation time of 23 min, although the thickness of the covered region on the PMPC layer remained the same (100–200 nm). With photo-irradiation for 11 min, no PMPC layer was observed on the surface of the CLPE. These results indicate that the density of the grafted PMPC can be controlled by the polymerization time. This is attributable to the fact that the number of polymer chains produced in a radical polymerization reaction is generally correlated with the photo-irradiation time.

Figure 25.17 shows the static water-contact angle of PMPC-grafted CLPE as a function of the photo-irradiation time used for polymerization (0.50 mol/L MPC concentration) [83]. The static water-contact angle of untreated CLPE was 90° and decreased markedly with a decrease in the photo-irradiation time. The static water-contact angle decreased as the irradiation time was increased.

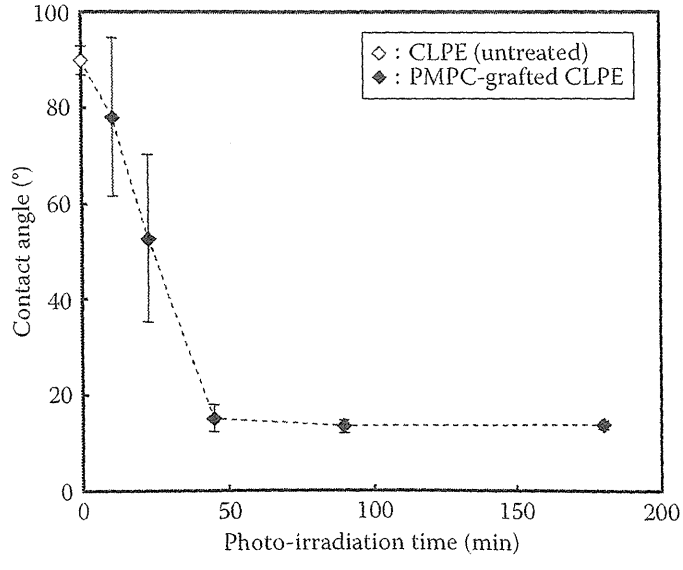

FIGURE 25.17 Static water-contact angle of PMPC-grafted CLPE as a function of the photo-irradiation time with a 0.5 mol/L MPC concentration. Bar: Standard deviations.

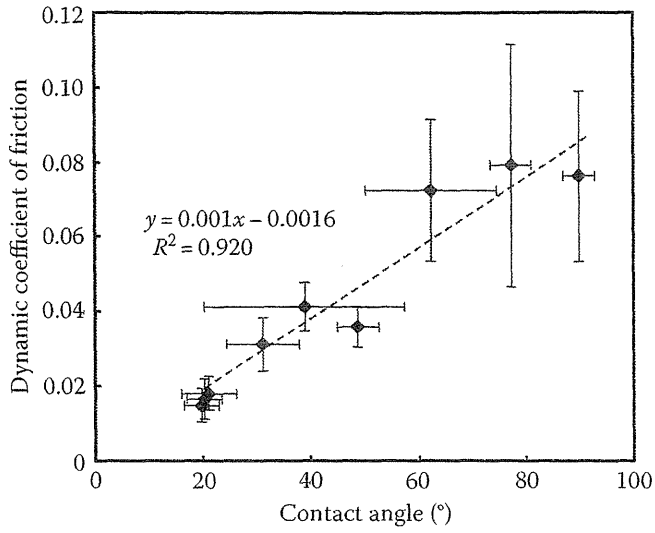

FIGURE 25.18 Relationship between dynamic coefficient of friction and contact angle in the PMPC-grafted CLPE surface. Bar: Standard deviations.

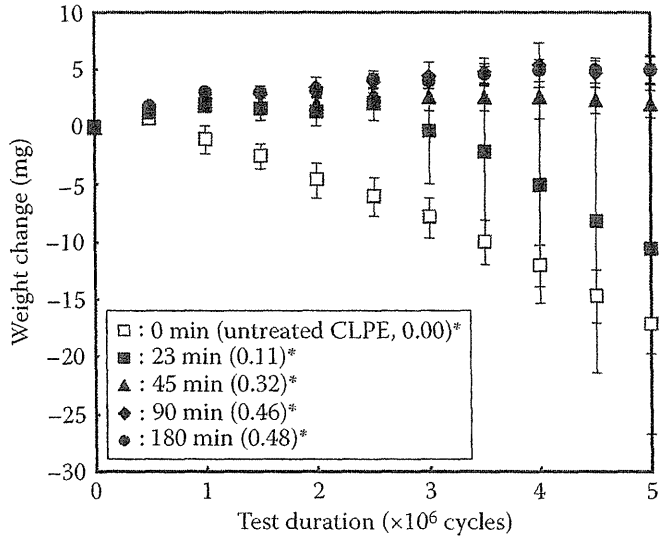

FIGURE 25.19 Weight change (gravimetric wear) of the PMPC-grafted CLPE cups obtained with a 0.5 mol/L MPC concentration and various photo-irradiation times in the hip joint simulator wear test. Bar: Standard deviations. *P–O group indexes are in parentheses.

Figure 25.18 shows the relationship between the dynamic coefficient of friction and the contact angle [84]. The dynamic coefficient of friction tended to increase with the contact angle. This increase was linear to a degree of accuracy, and the correlation coefficient was 0.920.

Figure 25.19 shows the gravimetric wear of PMPC-grafted CLPE with various photo-irradiation times during the hip joint simulation test. The PMPC-grafted CLPE cups were found to wear significantly less than the untreated CLPE cups. The wear of the PMPC-grafted CLPE cups subjected to 23-min photo-irradiation time started to increase after 2.5×10^6 cycles. The PMPC-grafted CLPE cups exhibited a slight increase in weight. This was partially attributable to enhanced fluid absorption in the tested cups than in the load-soak controls. When using the gravimetric method, the weight loss in the tested cups is corrected by subtracting the weight gain in the load-soak controls; however, this correction cannot be perfectly achieved because only the tested cups are continuously subjected to motion and load. Fluid absorption in the tested cups is generally slightly higher than that in the load-soak controls. Consequently, the

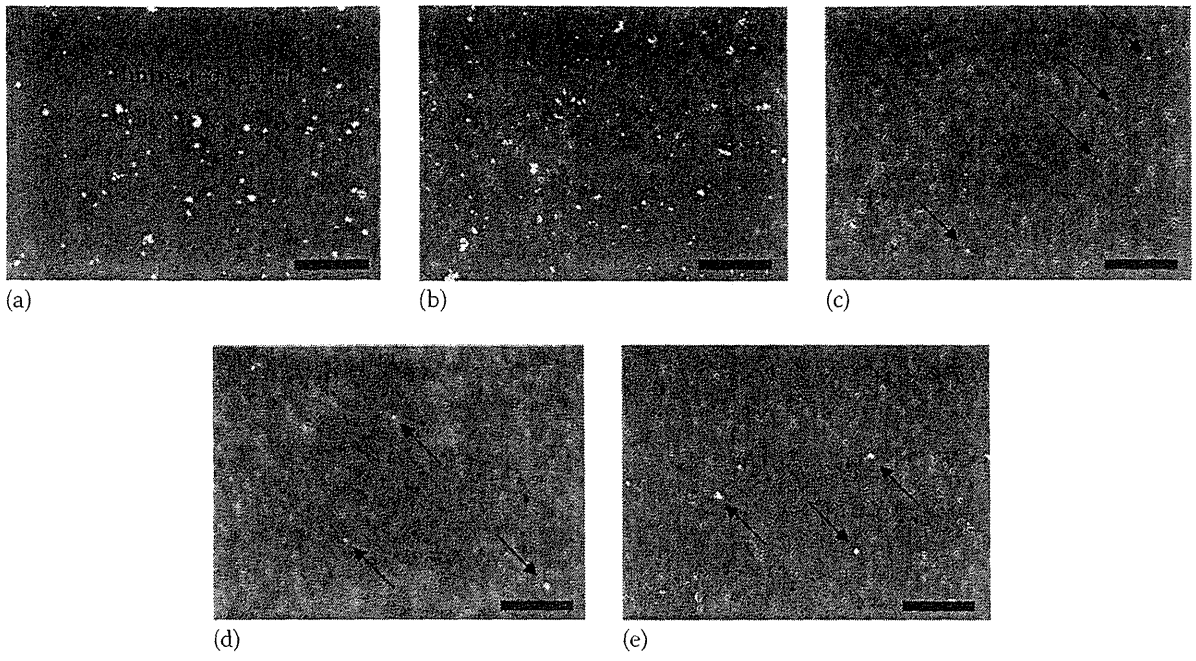

FIGURE 25.20 FE-SEM images of wear particles of the untreated CLPE and PMPC-grafted CLPE with various photo-irradiation times during the 4.5×10^6–5.0×10^6 cycles of the hip joint simulation test. Arrows: wear particles. Bar: 5 μm. (a) 0 min. (b) 23 min. (c) 45 min. (d) 90 min. (e) 180 min.

correction for fluid absorption by using the load-soak data as the correction factor leads to a slight underestimation of the actual weight loss. The initial wear rate is defined as that from the start to 0.5×10^6 cycles, and the steady wear rate is considered as that from 4.0×10^6 to 5.0×10^6 cycles. All the untreated CLPE and PMPC-grafted CLPE cups showed low initial wear rates of −1.42 to −3.74 mg/10^6 cycles. The steady wear rate of the untreated CLPE cups and the PMPC-grafted CLPE cups with a low P–O group index of 0.11 (23-min photo-irradiation time) increased to 5.11 and 5.48 mg/10^6 cycles, respectively. In contrast, the wear rates of the PMPC-grafted CLPE cups with high P–O group indexes, i.e., 0.46 (90-min photo-irradiation time) and 0.48 (180-min photo-irradiation time), were markedly lower at 0.32 and −0.02 mg/10^6 cycles, respectively.

Figure 25.20 shows field emission scanning electron microscope (FE-SEM) images of wear particles of the untreated CLPE and PMPC-grafted CLPE with various photo-irradiation times during the 4.5×10^6–5.0×10^6 cycles of the hip joint simulation test. The wear particles of the untreated CLPE and PMPC-grafted CLPE cups, as characterized by FE-SEM, were predominantly submicrometer-sized granules. The wear particles of the PMPC-grafted CLPE cups with 45-, 90-, and 180-min photo-irradiation times were found to be significantly lesser than those for the untreated CLPE cups and the PMPC-grafted CLPE cups with 23-min photo-irradiation time.

In summary, an artificial hip joint based on the novel concept of "hydration lubrication" was created by using PMPC grafted onto the surface of CLPE for reducing the wear debris of UHMWPE. The approach using "hydration lubrication" is surely novel in the field of orthopedic biomaterials science, and joint replacement with hydration lubrication can pioneer the "next generation" artificial joint. Furthermore, these joint replacements have the potential to be applied in the orthopedic field in the near future [85]. The clinical trial for such joint replacements with hydration lubrication (i.e., PMPC-grafted CLPE acetabular cup) has been started at the University of Tokyo and other hospitals in Japan since 2007. For this novel PMPC-grafted CLPE material, close monitoring of clinical performance and accurate quantification of wear rates would be essential for the early recognition of unforeseen problems.

25.2.3 Poly(Ether-Ether Ketone) Bearing Materials

25.2.3.1 Structure and Properties

Poly(aryl-ether-ketone) (PAEK), including poly(ether-ether-ketone) (PEEK), is a new family of high-performance thermoplastic polymers, consisting of an aromatic backbone molecular chain interconnected by ketone and ether functional groups, i.e., a BP unit is included in its molecular structure. Polyaromatic ketones exhibit enhanced mechanical properties, and their chemical structure is stable, resistant to chemical and radiation damage, and compatible with several reinforcing agents (such as glass and carbon fibers; carbon fiber-reinforced PEEK [CFR-PEEK], Figure 25.21). Therefore, they are considered to be promising materials for not only industrial applications but also biomedical applications.

In the 1980s, the in vivo stability of various PAEK materials and the tissue response to the same were investigated [86]. Recently, PEEK has emerged as the leading high-performance super-engineering plastic candidate for replacing metal implant components, especially in the field of orthopedics and spinal surgery (Table 25.7) [87]. In recent studies, the tribological and bioactive properties of PEEK, which is used as a bearing material and flexible implant in orthopedic and spinal surgeries, has been investigated [88–90]. However, conventional single-component PEEK cannot satisfy these requirements (e.g., antibiofouling, wear resistance, and fixation to a bone) for use as an artificial joint or intervertebral body fusion cage [87]. For further improving the capabilities of PEEK as an implant biomaterial, various studies have focused upon the lubricity and antibiofouling of the polymer, either via reinforcing agents or surface modifications [91,92]. Therefore, multicomponent polymer systems have been designed in order to synthesize new multifunctional

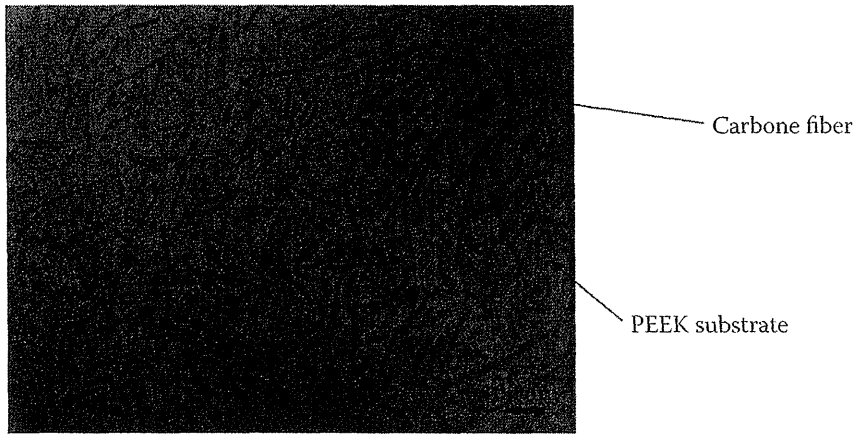

FIGURE 25.21 Fluorescence microscopic images of CFR-PEEK. Bar: 100 μm.

TABLE 25.7
Typical Physical and Chemical Properties of PEEK and CFR-PEEK

Property	PEEK	30% CFR-PEEK	60% CFR-PEEK
Molecular weight (10^6 g/mol)	0.08–0.12	0.08–0.12	0.08–0.12
Melting temperature (°C)	343	343	—
Poisson's ratio	0.36–0.40	0.40–0.44	0.38–0.44
Specific gravity	1.3	1.4	1.6
Flexural modulus (GPa)	4	20	135
Tensile ultimate strength (MPa)	93–97	170–228	>2000
Elongation (%)	30–40	1–2	1
Crystallinity (%)	30–35	30–35	30–35

biomaterials. In order to use PEEK and related composites in the implant applications, they can be engineered to have a wide range of physical, mechanical, and surface properties.

25.2.3.2 Tribological Properties

In the 1990s, CFR-PEEK was evaluated as a bearing material for hip and knee joint replacement [88]. Wang et al. carried out a more comprehensive tribological investigation of PEEK composites for both hip and knee joint replacements. CFR-PEEK formulations were blended with 20%–30% mass discontinuous polyacrylonitrile (PAN) or pitch fibers. Under higher stress, cylinder-on-flat loading conditions, the PEEK composites exhibited higher wear rates than conventional UHMWPE. In contrast, under the lower stress hip simulator test conditions, all the PEEK composites had substantially lower wear rates than conventional UHMWPE, with the lowest wear observed between 30% pitch CFR-PEEK against ceramics. In contrast, unreinforced PEEK wore at six times the rate of UHMWPE. The results of this study underscored the importance of fiber reinforcement in lowering stress and conforming contact applications and provided a further basis for exploring PEEK composites for hip joint replacements, especially in combination with ceramics as opposed to Co-Cr heads. Therefore, alumina became the femoral head material of choice for THA applications with CFR-PEEK. Co-Cr heads, when used in conjunction with CFR-PEEK liners, exhibited substantially higher wear, with observations of scratching of the metallic surface by the carbon fibers. On the other hand, this study also suggested that PEEK composites were unsuitable for knee applications, regardless of the fiber content of the composite or the type of the counter surface. The authors recommended that the composite materials should not be used as a tibial insert for knee joint replacement.

To validate the in vivo wear behavior and compatibility of CFR-PEEK wear debris, a clinical study was initiated in Italy starting in 2001 using the ABG II total hip system (Stryker SA, Montreux, Switzerland). The CFR-PEEK liners were fabricated from injection-molded PEEK blended with 30% pitch fibers, and the bearing surfaces were machined to achieve the desired final tolerance. After a mean follow-up period of 3 years, none of the liners needed to be revised due to aseptic loosening. This clinical trial is still ongoing, and the detailed results have not yet been published. Overall, the available preliminary clinical data support the short-term effectiveness of CFR-PEEK as a bearing material for hip joint replacement. However, in a conventional hip joint replacement design, the current data do not yet demonstrate a long-term clinical advantage of CFR-PEEK over other well-established bearing alternatives, such as CLPE.

25.2.3.3 Surface Modification

On the other hand, surface modification is one of the most important technologies for the preparation of new multifunctional biomaterials for satisfying several requirements. Surface modifications used today include coating, blending, and grafting.

It is well known that when BP is exposed to photo-irradiation such as ultraviolet-ray (UV)-irradiation, a pinacolization reaction is induced; this results in the formation of semi-benzopinacol radicals (i.e., ketyl radicals) that act as photo-initiators. Therefore, in this study, we have focused upon a BP unit in PEEK and formulated a novel self-initiated surface-graft polymerization method that utilizes the BP unit in "graft from" polymerization (Figure 25.22) [93,94]. This polymerization reaction involving free radicals is photoinduced by UV-irradiation. Under UV-irradiation, a BP unit in PEEK can undergo the following reactions in monomeric aqueous solutions [95–101] as follows: the pinacolization reaction (photoreduction by H-abstraction of a BP unit in PEEK) results in the formation of a semi-benzopinacol radical, which can initiate the graft-from polymerization of the feed monomer as the main reaction, and the graft-to polymerization (the radical chain end of the active-polymer couples with the semi-benzopinacol radical of the PEEK surface) as a subreaction. In addition, a photoscission reaction occurs as a subreaction, which may not need a hydrogen (H) donor. The cleavage reaction induces recombination and graft-from polymerization. When water polymerization is performed in the presence of an H-donor, a phenol unit may be subsequentially formed due to H-abstraction. This technique enables the direct grafting of the functional polymer

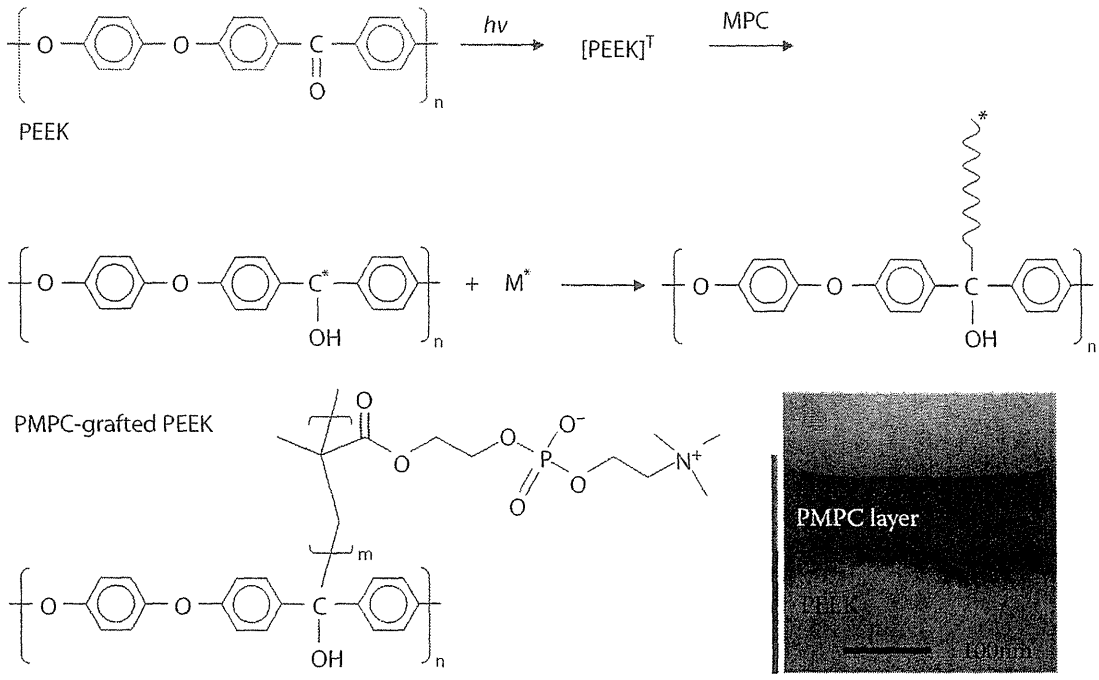

FIGURE 25.22 Schematic illustration for the preparation and cross-sectional TEM image of PMPC-grafted PEEK.

onto the PEEK surface in the absence of a photoinitiator, thereby resulting in the formation of a C–C covalent bond between the functional polymer and PEEK substrate.

Kyomoto et al. demonstrated the fabrication of a biocompatible and highly hydrophilic nanometer-scale-modified surface by PMPC-grafting onto the self-initiated PEEK surface using a photo-induced pinacolization reaction (Figure 25.22) [93,94].

This novel and simple self-initiated surface-graft polymerization on the PEEK surface induces unique properties such as lubricity and anti-protein adsorption by PMPC grafting, which are novel phenomena in the field of orthopedic and spinal surgery (Figure 25.23). Moreover, the fabrications of the PMPC-grafted PEEK and CFR-PEEK can result in next-generation orthopedic and spinal applications.

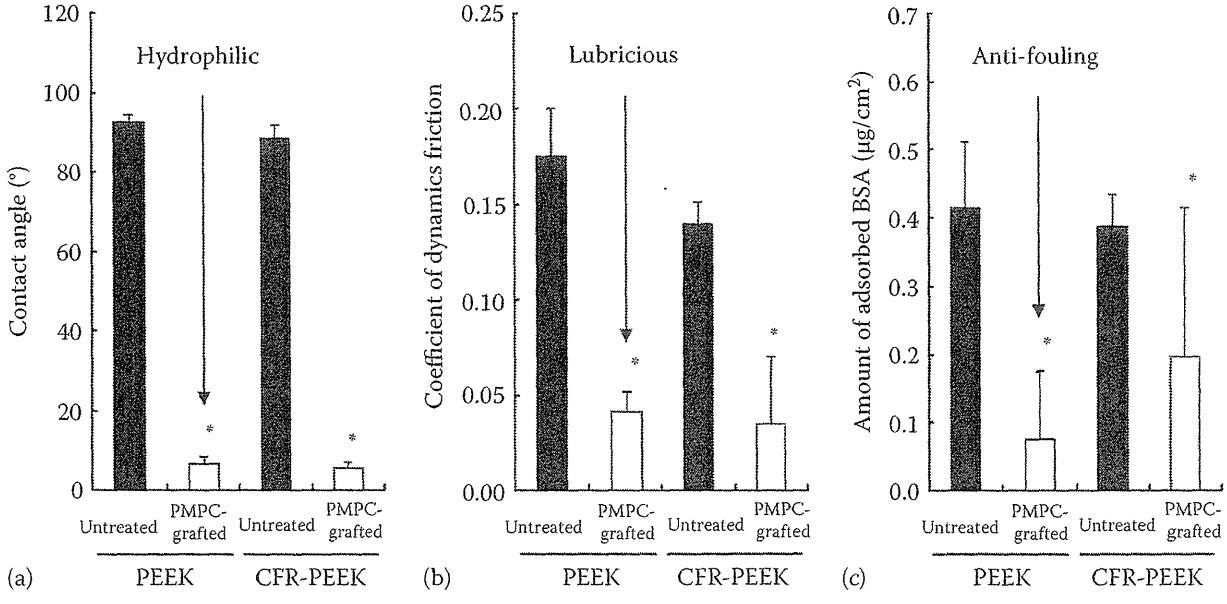

FIGURE 25.23 (a) Static water-contact angle, (b) coefficient of dynamic friction, and (c) amount of adsorbed BSA of PMPC-grafted PEEK and CFR-PEEK. *t-test, significant difference ($p < 0.05$) as compared to the untreated PEEK and CFR-PEEK, respectively.

25.3 FIXATION MATERIALS FOR JOINT REPLACEMENTS

25.3.1 Poly(Methyl Methacrylate) Bone Cement

Bone cements based on poly(methyl methacrylate) (PMMA) are important polymer materials in joint replacement surgery: PMMA bone cements are primarily used for the fixation of joint replacement. In the fixation of joint replacement, the self-curing bone cement fills the free space between the joint replacement and bone and constitutes a very important interface.

The PMMA bone cements are two-component systems, comprising a polymer powder and a liquid methyl methacrylate (MMA) monomer. The polymer powder component is composed of PMMA and/or methacrylate copolymer. The polymer powder contains benzoyl peroxide (BPO), which acts as an initiator for radical polymerization. The polymer powder also contains an X-ray contrast agent. In the liquid monomer, MMA is the main constituent; however, at times, other methacrylates—such as butyl methacrylate—are used. In order for the MMA to be used in bone cements, it must be polymerizable, i.e., it must contain a carbon double bond that can be broken. Furthermore, the liquid monomer contains an aromatic amine, such as *N,N*-dimethyl-*p*-toluidine (DMT), as an activator of radical formation. Additionally, it contains an inhibitor (e.g., hydroquinone) to avoid premature polymerization in storage aging.

PMMA bone cements are polymeric materials produced by the radical polymerization of MMA (Figure 25.24). The polymerization process starts when the polymer powder and liquid monomer are mixed, resulting in a reaction between the BPO initiator and DMT activator, forming radicals. Consequently, the DMT causes a breakdown of the BPO in the reaction process by electron transfer, resulting in the formation of benzoyl radicals. The C=C of the MMA monomer has a pair of electrons that is attacked by the free radical to form a new chemical bond between the initiator fragment and one of the C=C bond of the monomer molecule. The other electron of the C=C bond stays on the C atom that is not bonded to the initiator fragment, creating a new free radical. This unpaired electron is capable of attacking the C=C bond of a new monomer unit. This process, with the breakdown of the initiator molecule to form radicals, is called the "initiation reaction" of the radicals' polymerization. The new radical reacts with another MMA molecule in the same way as the initiator fragment reaction. Another radical is always formed when this reaction takes place, over and over again. This process of the growing polymer chain is called a "propagation reaction." As the polymerization continues, the rate of termination (termination reaction) is decreased,

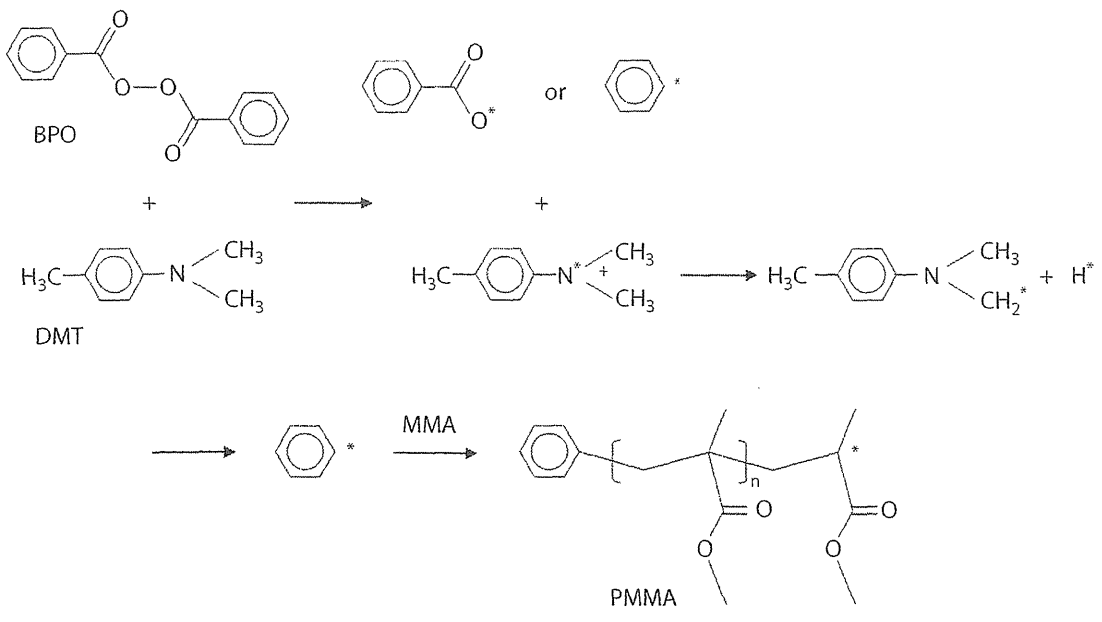

FIGURE 25.24 Schematic illustration of formation of radical polymerization chains in PMMA bone cement.

because the diffusion of chain growth and the combination of chain ends is reduced. The system becomes depleted of free radicals by recombination of the two radical chains and the polymerization ceases.

25.3.2 Bone Cement History

In 1936, Heraeus Kulzer GmbH & Co. KG (Wehrheim, Germany) found that dough material could be produced by mixing PMMA powder and a liquid MMA monomer, which was cured when BPO was added and the blend was heated to 100°C [102]. In 1958, Charnley et al. successfully fixed a femoral stem prosthesis by using PMMA as bone cement [103]. Since the introduction of PMMA bone cement by Charnley et al., many people have had their lives dramatically and remarkably improved by this innovation. At the beginning of the 1970s, in an effort to alleviate periprosthetic infection—the most feared complication after joint replacement—Buchholz et al. advocated the addition of antibiotics to bone cement [104]. Their idea was to add antibiotics to the bone cement in order to reduce the incidence of infection. The PMMA bone cement with a gentamicin powder was demonstrated to be stable and offered suitable antibiotic activity.

25.3.3 Problems with PMMA Bone Cement

Since the introduction of PMMA bone cement in the orthopedic field, bone cement is considered to have become one of the effective polymer materials for fixation in joint replacement. However, aseptic loosening remains a serious issue on a multifactorial basis as follows. Aseptic loosening is suggested to be a result of monomer-mediated bone damage; during end-polymerization, there is volumetric shrinkage of the cement, potentially compromising the bone–cement interface. Using a fluid displacement model, Charnley observed that the volume of cement increases to a maximum during polymerization, before shrinking slightly, although not to its initial volume. This may be a largely theoretical concern, but there is a conflict between the stiffness of cement and the adjacent bone. The Young's modulus is 0.5–1.0 GPa for cancellous bone; 15–20 GPa, for cortical bone; 2 GPa, for bone cement; 1 GPa, for titanium alloy; and 220 GPa, for cobalt–chromium–molybdenum alloy. The bone cement may provide a shock-absorbing layer between elastic bone and a stiff implant. The conflict between degrees of stiffness is therefore much greater for cementless implants, and in some instances, the cement mantle and its interfaces may be the weak link in the construct. The bone–cement interface is the key to the survival of a THR. The combination of matte-surfaced collared femoral stems and poor cementing technique are intrinsic to the failure of some implants. Polished collarless tapered stems generally give better fixation, while cement particles were once considered a biological cause of aseptic loosening. However, wear particles of polyethylene are now seen as primary initiators of the biological reactions in aseptic osteolysis.

25.3.4 Solutions for the Problems of PMMA Bone Cement

25.3.4.1 Antibiotic-Loaded Acrylic Cement

In 1969, Buchholz et al. incorporated gentamicin in PMMA bone cement for the treatment of infection in prosthetic joints [104]. Initially, the antibiotic was added during the operation, and subsequently during manufacture, making antibiotic-loaded PMMA bone cement widely available as part of antimicrobial prophylaxis in primary arthroplasty. There is valid evidence to support the prophylactic use of antibiotic-loaded PMMA bone cement, which remains a standard practice in Europe, and is in transition in the United States. In 2003, the Food and Drug Administration accepted the use of three commercial antibiotic-loaded PMMA bone cements in the second stage of revision surgery for prosthetic joint infection. Their use in primary THA has not been authorized. The use of antibiotic-loaded PMMA bone cement in joint replacement provides short- to

medium-term protection against prosthetic infection. It aims to overlap with, and then replace, the prophylaxis provided by perioperative intravenous antibiotics. To achieve this, the antibiotic must be released from cement in adequately high concentrations that exceed the minimum inhibitory concentration of potential colonizing bacteria. Gentamicin is the most common additive because it has, among other features, a good spectrum of concentration-dependent bactericidal activity, thermal stability, and high water solubility. In 1980, Wahlig et al. gave robust evidence of gentamicin release from PMMA bone cement for up to 5.5 years in patients who had undergone hip joint replacement [105]. Others have also confirmed the reliable release of gentamicin from PMMA bone cement. However, concerns regarding antibiotics in cement still persist, including concerns regarding the induction of antibiotic resistance. In 1989, Hope et al. found that 90% of Staphylococcal strains isolated from infected hip joint replacements were resistant to gentamicin, but if plain cement had been used at the initial operation, the resistance rate was only 16% [106]. Other studies have confirmed that antibiotic-loaded PMMA bone cement reduces infection in total joint replacement at the price of increasing bacterial resistance. These problems have not been demonstrated clinically, although they have been postulated. Despite the aim of achieving early and total release, all in vitro studies show that only 5%–8% of the added antibiotic is ever freed. Clinical studies have shown a low concentration of the release of gentamicin in failing hip joint replacements up to 25 years after the primary operation, a potent stimulus for antibiotic resistance. In summary, we need to design guidelines regarding the use of antibiotic-loaded PMMA bone cement and advise its use only in cases where the patient has significant risk factors for infection.

25.3.4.2 Bone Bioactive Organic–Inorganic Hybrid Bone Cement

Recently, Ishihara et al. reported that PMMA bone cement containing hydroxyapatite as a bone bioactive-filler was developed using 4-methacryloyloxyethyl trimellitate anhydride (4-META) to promote adhesion to both bone and hydroxyapatite [107]. The mechanical properties of this PMMA cement with 4-META and hydroxyapatite did not decrease significantly with increasing hydroxyapatite filler content in the cement. In contrast, the mechanical properties decreased with increasing hydroxyapatite filler content in the absence of 4-META. The fracture surface of the cement clearly showed that there are no gaps between hydroxyapatite filler and PMMA matrix resin; this means that the hydroxyapatite filler adhered to the PMMA matrix resin by addition of 4-META [108]. The hydroxyapatite filler along the surface increased with increased hydroxyapatite filler content in the cement. The PMMA cement with 4-META and hydroxyapatite adhered also to bone with a tensile bond strength of higher than 10 MPa [109–111].

The sol–gel process is popular for the preparation of nanometer-scaled composites of organic–inorganic components. It has been reported that organically modified silicates can be synthesized through hydrolysis and polycondensation of tetraethoxysilane and poly(dimethylsiloxane). The nanometer-scaled organic–inorganic composite has the potential to show the properties of both organic and inorganic components. Based on the finding that a $CaO–SiO_2$ glass is effective in producing bone bioactivity, Ohtsuki et al. applied organic modification with Si–OH and Ca^{2+} to PMMA bone cement in order to induce the bone bioactivity in the bone cement (Figure 25.25) [112,113]. This bone bioactive PMMA cement has the potential to demonstrate bone-bonding properties in the bone–cement interface (Figure 25.25d).

25.4 FUTURE PERSPECTIVES

Every year, the number and prevalence of primary and revision hip, knee, and other joint replacements are increasing substantially worldwide. As a result, the quality of all artificial joints is becoming increasingly important. Therefore, we can see that functional, durable, and natural joint-like artificial joint replacements will be necessary for all artificial joints. We consider that the important research goal for the future is the creation of the ultimate artificial joint interface that mimics the

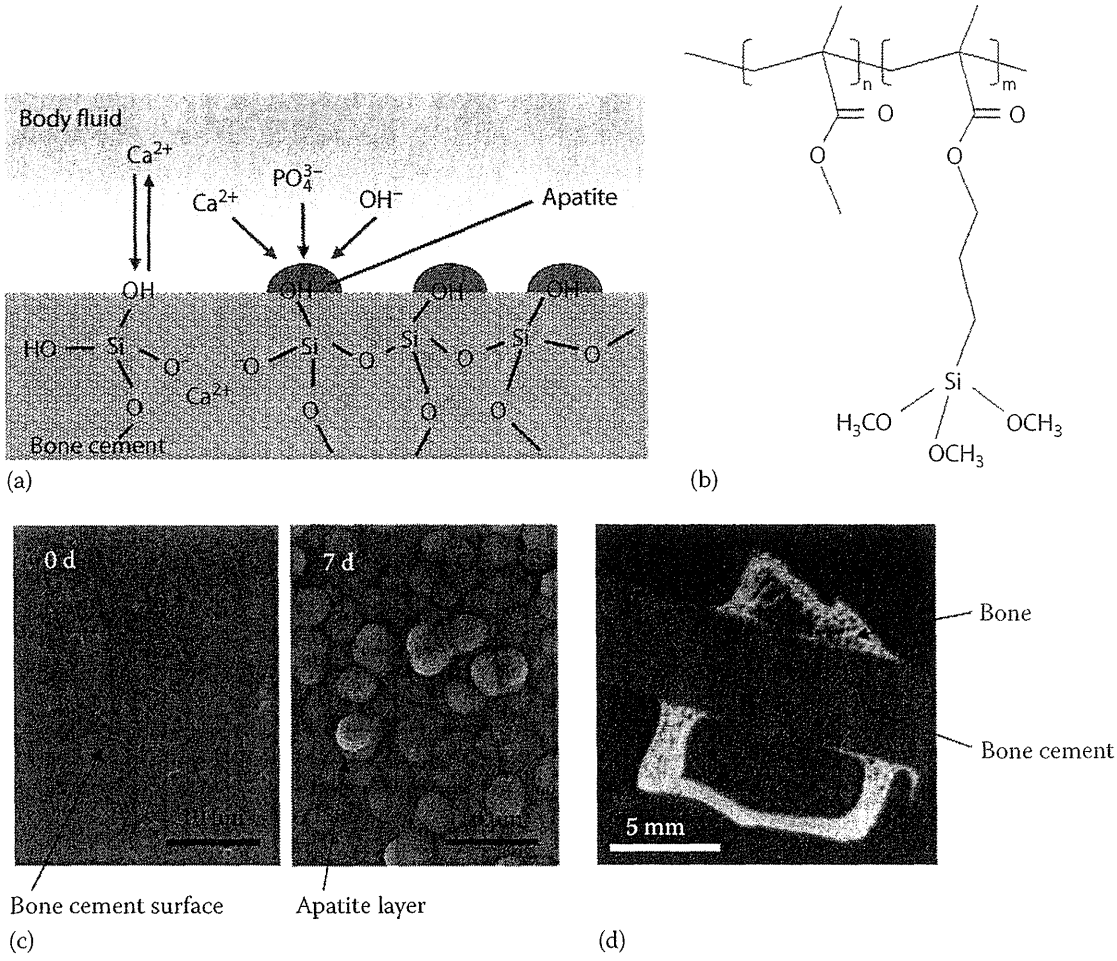

FIGURE 25.25 Schematic illustration of bone bioactive PMMA bone cement: (a) concept of bone bioactive cement, (b) chemical structure, (c) apatite formation in simulated body soaking fluid by SEM observation, and (d) pQCT image after 9 weeks implantation, Animal experiment.

natural joint cartilage. Additionally, a functional, durable, and natural surface not only would be of great service to applications as medical devices such as artificial joints but also would be important to biomaterial and bioengineering sciences. For example, it is well known that the composition elements of the articular cartilage surface consist of the collagen network, hyaluronic acid, and proteoglycan subunits. However, the functions of the articular cartilage surface have not been well explained. We consider that a bioengineering surface with new polymeric biomaterial would help in clarifying these phenomena; further, researches in biotribological science can elucidate the functions of articular cartilage surface. We believe that the designs of polymeric biomaterials and bioengineering surfaces will act as key technologies for further evolving biomaterial and bioengineering sciences, and we hope that this issue will be addressed by future scientists in polymeric biomaterial and bioengineering sciences.

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