Spatio-Resolved, Macromolecular Architectural Surface: Highly Branched Graft Polymer via Photochemically Driven Quasiliving Polymerization Technique

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ABSTRACT: We present a new method for highly spatio-resolved graft-copolymerized surface fabrication, in which the stem design (parent graft chain length) and the branch design (daughter graft chain length and degree of branching) are relatively well controlled. This is based on the photochemistry of the benzyl *N,N*-diethyldithiocarbamate (DC) group that acts as an *ini*tiator-trans*fer*-*ter*minator (iniferter) agent. DC-derivatized glass was used as the substrate. Ultraviolet light irradiation of the DC-derivatized glasses in the presence of chloromethylstyrene (CMS) produced polyCMS-graft-polymerized surfaces with different chain lengths (parent graft), depending on the irradiation time. Subsequent dithiocarbamylation of the CMS unit and irradiation in the presence of sodium methacrylate resulted in the formation of a macromolecular architectural surface in which lengths of both parent and daughter chains in graft copolymers were controlled by the irradiation time. The degree of branching was found to be controlled by CMS content in the parent graft chains which were prepared by graft copolymerization of CMS with *N,N*-dimethylacrylamide. These were verified by fluorescence intensity measurements of malachite green-stained samples using a confocal scanning laser microscope.

Introduction

Well-defined synthetic polymers with complex architectures, such as blocks and stars, have been prepared by living anionic,[1−4] cationic,[5,6] or group-transfer polymerization techniques.[7,8] However, the design of architecture by free radical techniques has been a quite difficult task with experimental limitations and has been a synthetic goal for many years because there are a large variety of monomers that polymerize by free radical techniques and not via ionic techniques.

The photochemistry of benzyl *N,N*-diethyldithiocarbamate (DC), which is photolyzed to generate a radical pair (a benzyl radical and an *N,N*-diethyldithiocarbamyl radical), provides quasiliving radical polymerization, which was pioneered by Otsu et al. in 1982.[9,10] This type of compound is called iniferter, which acts as an *ini*tiator, a trans*fer* agent, and a *ter*minator. The reaction involving an *N,N*-diethyldithiocarbamyl radical favors chain termination with a growing polymer chain radical end rather than a reaction with a vinyl monomer, whereas a benzyl radical reacts with a vinyl monomer to reproduce a radical. These reactions proceed only during irradiation and in irradiated regions. The chain length of the growing polymer is controlled by irradiation time, light intensity, and monomer concentration, and the surface graft-polymerized region is easily controlled by using a photomask, resulting in the formation of micropatterned graft-copolymerized, block-graft-copolymerized, and chain-length-gradient graft-copolymerized surfaces.[11−16]

As an extension of our series of studies[11−14] on photochemically driven DC-based surface design, we devised a new method for preparing a highly spatio-resolved, macromolecular architectural surface with controlled graft chains length such as parent (stem) chain length and daughter (branch) chain length and controlled degree of brancing. A parent (stem) graft chain was prepared by photopolymerization of chloromethylstyrene (CMS) on DC-derivatized glass surfaces. The graft chain length was controlled by irradiation time (Figure 1:A). After parent graft chains were derivatized with DC groups, daughter chains were prepared by photopolymerization initiated from the multiply DC-derivatized graft chains. The length of daughter graft chains (branch) was controlled by irradiation time (Figure 1:B1). As for the control of the degree of branching, a parent chain was prepared by graft copolymerization of CMS with *N,N*-dimethylacrylamide (DMAAm) and subsequent dithiocarbamylation, followed by photopolymerization (Figure 1:B3). The control of chain length and the degree of branching were verified by determining the fluorescence intensity of graft-copolymerized surface using a confocal laser scanning microscope.

Experimental Section

Materials. CMS (meta and para mixture) was obtained from Tokyo Chemical Industry Ltd. (Tokyo, Japan). (Chloromethylphenyl)ethylsilane, poly(ethylene glycol) methacrylate (PEGMA; average molecular weight 360), sodium methacrylate (SMA), and bis[*p*-(dimethylamino)phenyl]methylium hydroxide (malachite green carbinol base, Solvent Green 1, C.I. 42000B) were obtained from Aldrich Chemical Co. Inc. (Milwaukee, WI). Sodium *N,N*-diethyldithiocarbamate trihydrate, DMAAm, methacrylic acid (MAA), and solvents were of special reagent

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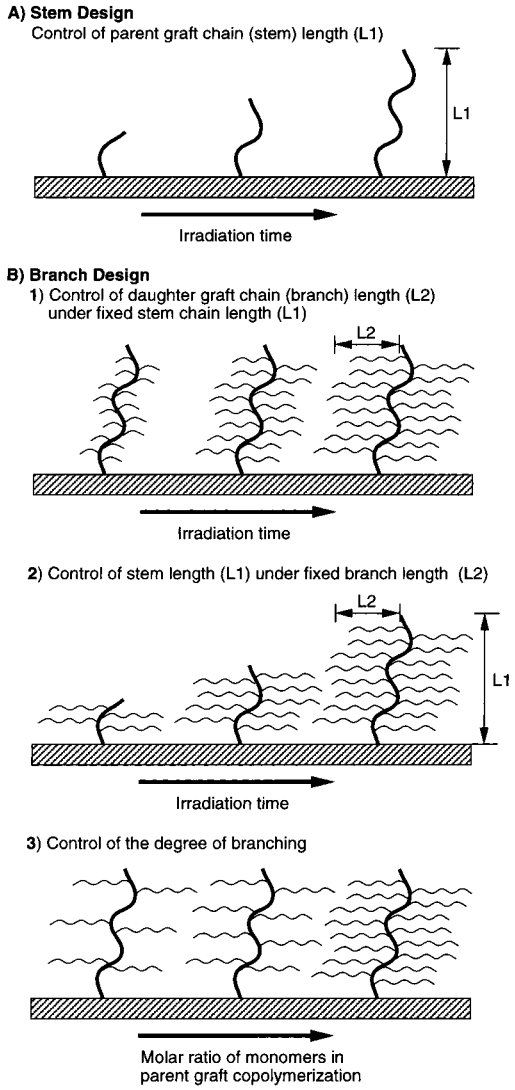

Figure 1. Schematic representation of the stem and branch designs.

grade and were obtained from Wako Pure Chemicals Industries Ltd. (Osaka, Japan).

Preparation of a DC-Derivatized Glass. A circular slide glass (diameter 14.5 mm, thickness 0.25 mm, Matsunami Glass Inc., Osaka, Japan) was thoroughly rinsed with aqueous detergent, deionized water, piranha solution (concentrated H_2SO_4/30% H_2O_2, 70:30), and RCA-type ($H_2O/H_2O_2/NH_3$, 5:1:0.5) cleaning protocol. The glass was then thoroughly rinsed sequentially with acetone, acetone/toluene, and toluene. The cleaned glass was immersed into a (chloromethylphenyl)ethylsilane solution (2 mL in 30 mL of freshly distilled toluene) for 36 h at room temperature. The obtained chloromethylated glass was then rinsed carefully with toluene and acetone and then heated at 115 °C for 10 min in air.

The chloromethylated glass was immersed in 30 mL of an ethanolic solution of sodium *N*,*N*-diethyldithiocarbamate trihydrate (5 g, 22 mmol). After the solution was shaken for 24 h at room temperature, the DC-derivatized glass was obtained. The glass was thoroughly washed with ethanol, dried in air, and stored in a dark desiccator.

Surface Photograft Polymerization. The DC-derivatized glass was placed in a glass dish (diameter 30 mm) containing 2.5 mL of methanolic monomer solution (0.5 mol/dm^3). Monomers used were CMS, DMAAm, MAA, SMA, and PEGMA. The DC-derivatized glass was then UV-irradiated in an atmosphere of nitrogen with an ultrahigh-pressure mercury-vapor lamp (250 W, SPOT CURE250, Ushio Inc., Tokyo, Japan). The light intensity, measured with a photometer (UTR-1, Topcon, Tokyo, Japan), was 5 mW/cm^2. The temperature of the polymerized samples was maintained around 20−25 °C. The photograft-copolymerized glass was washed with methanol, toluene, and ethanol and then dried in air.

Preparation of Multiply DC-Derivatized Glass. CMS-graft-copolymerized glass was immersed in 10 mL of an ethanolic solution of sodium *N*,*N*-diethyldithiocarbamate trihydrate (2 g, 9 mmol). After the solution was stirred for 24 h at room temperature, the multiply DC-derivatized glass was obtained. The glass was thoroughly washed with ethanol, dried in air, and stored in a dark desiccator.

Preparation of a Regionally Graft-Copolymerized Surface. The DC-derivatized glass was fitted tightly to a photomask with a slit width of 400 μm and immersed into an aqueous SMA solution and then covered with a sapphire plate. The glass was irradiated through the photomask as described above. The glass was then rinsed with water and alcohols and dried in air. The treated glass was stained with a dilute hydrochloride solution of malachite green carbinol base (1.0 w/v %) for visualization under a confocal laser scanning microscope.

Physical Measurements. All ^{1}H NMR spectra were recorded in $CDCl_3$ solution using tetramethylsilane (0 ppm) as an internal standard with a 270 MHz NMR spectrometer (GX-270, JEOL, Tokyo, Japan) at 30 °C. X-ray photoelectron spectroscopy (XPS) spectra were taken with a Shimadzu ESCA 750 (Kyoto, Japan) using a magnesium anode (Mg Kα radiation) connected to a data processor ESCAPAC-760 at room temperature and 2×10^{-7} Torr (8 kV, 20 mA). The spectra were deconvoluted into subpeaks by computer-aided processing. Static contact angles toward deionized water were measured with a contact angle meter (Kyowa Kaimen Kagaku Co., Ltd., Tokyo, Japan) at 25 °C by the sessile drop method. The image and fluorescence intensity profile of the stained graft surfaces were observed and measured with a confocal laser scanning microscope (Bio-Rad Laboratories, Hercules, CA).

Results

Iniferter-Derivatized Surface. XPS spectra of the glass surface treated with (chloromethylphenyl)ethylsilane revealed the expected features of C_{1s} and Cl_{2p} peaks, indicating that the chloromethyl phenyl group is derivatized on the glass surface (Figure 2:A). When the chloromethylated surface was treated with sodium *N*,*N*-diethyldithiocarbamate, both N_{1s} and S_{2p} peaks in the XPS spectra of the treated surface were newly detected while the Cl_{2p} peak disappeared, and the N/C ratio (determined from the respective peak areas of C_{1s} and N_{1s} signals) increased to 0.045 (theoretical value: 0.071) (Figure 2:B). These indicate that derivatization of iniferter occurred on the outermost layers in quite a high yield.

Control of Parent Graft Chain Length. Surface photograft polymerization of the DC-derivatized glass (Scheme 1:I) was carried out in methanolic CMC solution using UV light. Parts C1, C2, and C3 of Figure 2 show the irradiation time-dependent changes of the XPS spectra (irradiation time: 5, 10, and 20 min, respectively). With increasing irradiation time, the intensity of the Cl_{2p} peak increased, whereas the intensities of both N_{1s} and S_{2p} peaks decreased. The S_{2p} peak was still observed even after irradiation for 20 min, although its intensity was reduced to approximately 1/10th of the initial value. Insignificant spectral change was observed after extensive washing with methanol and hexane. This indicates that CMS was polymerized to form a graft chain (parent graft) on the surface. How chain length increases with irradiation time will be described later.

Both advancing and receding water contact angles of the polyCMS-graft surface increased with increasing irradiation time (Table 1). The receding water contact

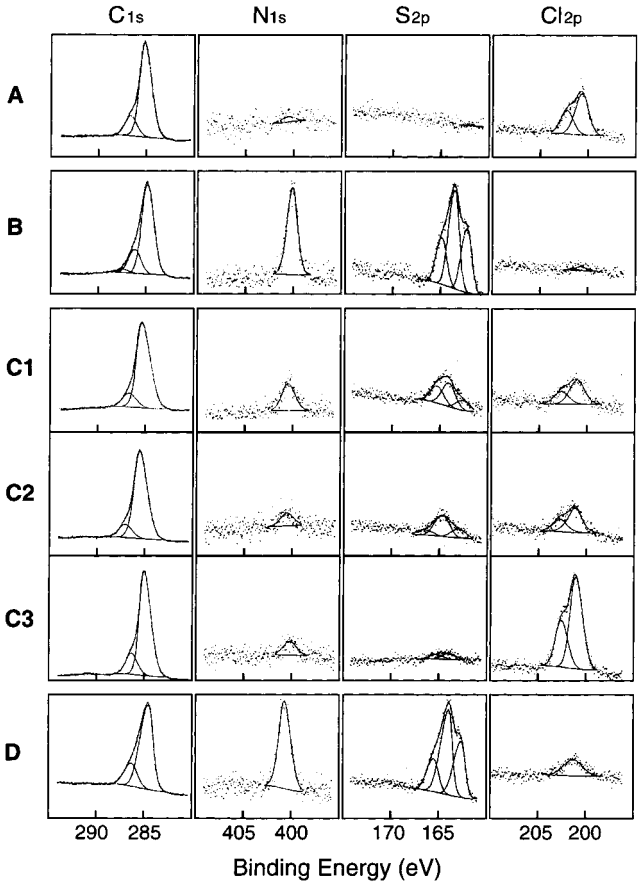

Figure 2. XPS spectra of the chloromethylated glass surface (A), DC-derivatized glass surface (B), the DC-derivatized glass surfaces graft-copolymerized with CMS by UV irradiation for 5 min (C1), 10 min (C2), and 20 min (C3), and multiply DC-derivatized glass surface (D).

angle was approximately 50° for the nonirradiated DC-derivatized glass surface and about 80° for the 20 min irradiated surface, indicating that the polyCMS-graft glass became more hydrophobic with increasing irradiation time. These results suggest that graft polymerization of CMS on the DC-derivatized glass surface proceeded with irradiation time.

Multiply DC-Derivatized Surface. PolyCMS grafted glass surface (Scheme 1:II) prepared by 20 min irradiation of DC-derivatized glass in CMS solution was treated with sodium *N*,*N*-diethyldithiocarbamate. Figure 2:D shows a marked increase in intensities of both N_{1s} and S_{2p} peaks and a significantly decreased intensity of the Cl_{2p} peak, indicating that DC groups were multiply derivatized on the parent graft chains (Scheme 1:III).

Brushlike Daughter Graft Chain. Surface photograft polymerization of the multiply DC-derivatized glass (Scheme 1:III) was carried out under irradiation in methanolic solutions of hydrophilic monomers such as DMAAm, MAA, and PEGMA. Figure 3 shows irradiation time-dependent changes in XPS spectra of these monomer graft-copolymerized surfaces. Irrespective of the monomer used, the elemental ratio of O/C increased but that of S/C decreased with irradiation time (Figure 4:A), indicating that graft copolymerization initiated from the multiply DC-derivatized graft chain proceeded with irradiation time to produce a brushlike graft architecture (Scheme 1:IV). Similarly to graft polymerization of CMS on the DC-derivatized glass, the

Scheme 1. Reaction Scheme for the Preparation of the Design of Stem and Branch Surfaces

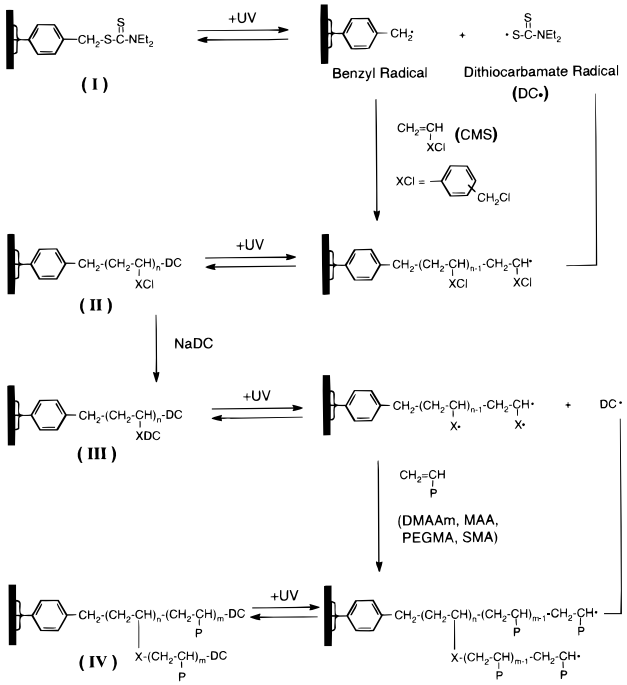

Table 1. Irradiation Time Dependence of Change in Water Contact Angle in Graft Copolymerization with CMS[a]

irradiation time (min)	water contact angle (degree)	
	advancing angle	receding angle
0	62.7 ± 4.6	53.3 ± 2.3
5	78.7 ± 1.2	66.7 ± 2.3
10	79.1 ± 2.2	70.0 ± 3.5
20	88.2 ± 3.1	82.4 ± 2.6

[a] Irradiation (light intensity, 5 mW/cm^2) was carried out on DC-derivatized glass in methanolic CMS solution (0.5 mol/dm^3).

S_{2p} peak was still observed, although its intensity was reduced. This may imply that growing chain ends preferentially recombine with dithiocarbamyl radicals.

Figure 4:B shows irradiation time-dependent changes in water contact angles of surfaces with brushlike graft polymers such as polyDMAAm, polyMAA, and polyPEGMA. Irrespective of polymers grafted, both advancing and receding contact angles decreased with irradiation time. PolyPEGMA-grafted surface exhibited a marked reduction of contact angle upon irradiation and gave the smallest contact angle among three different graft surfaces.

Highly Spatio-Resolved Graft Architecture. More detailed examinations in terms of lengths of parent and branch chains, degree of branching, and regional control were carried out using fluorescence scanning images of grafted and nongrafted regions. Regarding the multiply DC-derivatized glass irradiated in SMA aqueous solution through a slit (Figure 5:A) and then immersed into dilute HCl solution of malachite green carbinol base, which is a cationic dye, only the irradiated regions were stained green, indicating that SMA was graft-copolymerized only in irradiated regions (Figure 5:B). The observed width of the stained lines was approximately 400 μm, which was the same as the slit width of the photomask used.

Upon exposure to light of wavelength 543 nm, the malachite green-stained surface was light red as ob-

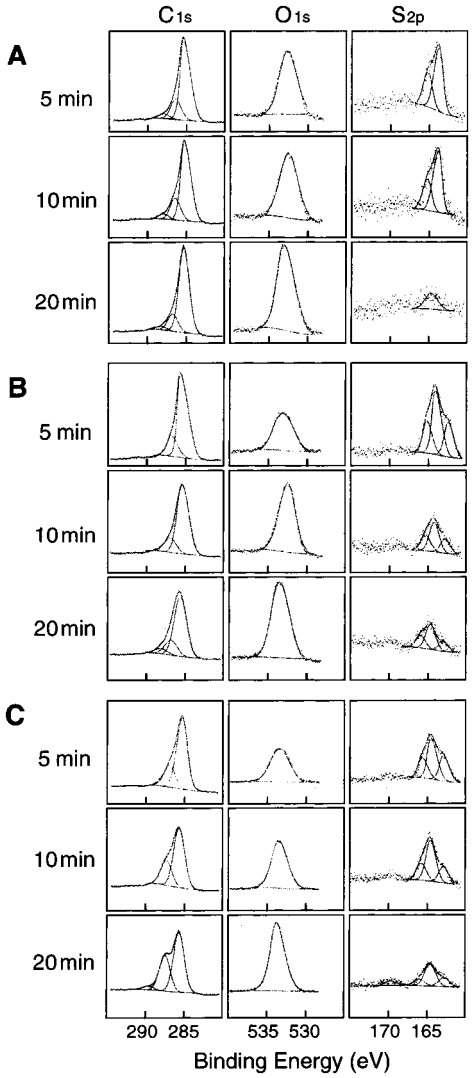

Figure 3. Irradiation time dependence of XPS spectral changes in graft copolymerization with DMAAm (A), MAA (B), and PEGMA (C).

served under a fluorescence microscope. After fluorescence intensity was transversely measured across the stained and nonstained regions with a confocal laser scanning microscope, the differences in fluorescence intensities between the stained and nonstained regions were determined, which are employed as a measure of SMA density in grafted region as follows. Three model surfaces were assessed whether a highly spatio-resolved graft architecture was realized by this photochemically driven quasiliving polymerization technique.

Model A: Variable Daughter Chain Lengths but Fixed Parent Chain Length. Irradiation time to control the branch architecture (Figure 1:B1) with SMA as a monomer was varied (5, 10, and 20 min) on the fixed stem architecture (multiply DC-derivatized surface prepared by 20 min irradiation of the DC-derivatized glass in CMS solution and subsequent dithiocarbamylation) (Scheme 1:III). Figure 6:A shows the irradiation time-dependent changes in the fluorescence intensity profiles obtained from the fluorescence images of the regionally grafted surfaces prepared by copolymerization with the photomask and subsequent staining with malachite green, as described above. The average intensities of the stained regions (difference in fluorescence intensities between the stained and nonstained

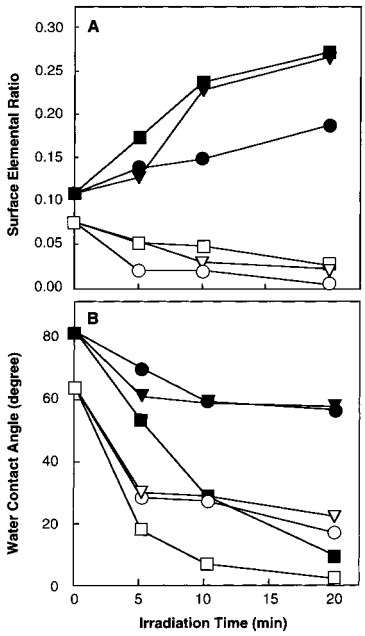

Figure 4. XPS elemental ratio changes (A): O/C ratios after graft copolymerization with PEGMA (■), DMAAm (●), MAA (▼), and S/C ratios with PEGMA (□), DMAAm (○), MAA (▽). Water contact angle changes (B): advancing angle after graft copolymerization with DMAAm (●), MAA (▼), PEGMA (■) and receding angles with DMAAm (○), MAA (▽), PEGMA (□).

regions) increased proportionally with irradiation time (Figure 6:B), indicating that the length of daughter graft chains on the fixed length of parent graft chain of the stem design increased with irradiation time (Figure 1:B1).

Model B: Variable Parent Chain Lengths but Fixed Branch Chain Length. Irradiation time to control stem design with CMS as a monomer was varied (5, 10, and 20 min), but the irradiation time to control branch design with SMA was fixed (20 min). Figure 7:A shows the fluorescence intensity profiles of malachite green-stained, regionally grafted surfaces. The average fluorescence intensities exhibited a linear dependence on irradiation time of the stem design (Figure 7:B), indicating that the parent graft chain length with fixed daughter graft chain length increased with irradiation time (Figure 1:B2).

Model C: Variable Degrees of Branching but Fixed Parent and Daughter Chain Lengths. DC-derivatized surface was graft-copolymerized with CMS and DMAAm at different feed ratios under 20 min irradiation. Then, the resultant surfaces were treated with sodium *N*,*N*-diethyldithiocarbamate to derivatize multiply on grafted chains. Subsequent photopolymerization using SMA was carried out. The fluorescence intensity profiles are shown in Figure 8:A. The average intensity of the irradiated portion increased with an increase in relative content of CMS in the mixed solution in the parent graft chain. This strongly indicates that the degree of branching is controlled by the content of CMS in the parent graft chain (Figure 1:B3). The compositions of CMS unit in the parent chains were estimated from those of copolymers produced in solutions containing CMS and DMAAm in different mixed ratios using benzyl *N*,*N*-diethylcarbamate as an iniferter under 20 min irradiation. The CMS content of the stem architecture, estimated from solution photopolymerization, was plotted against the fluorescence intensity

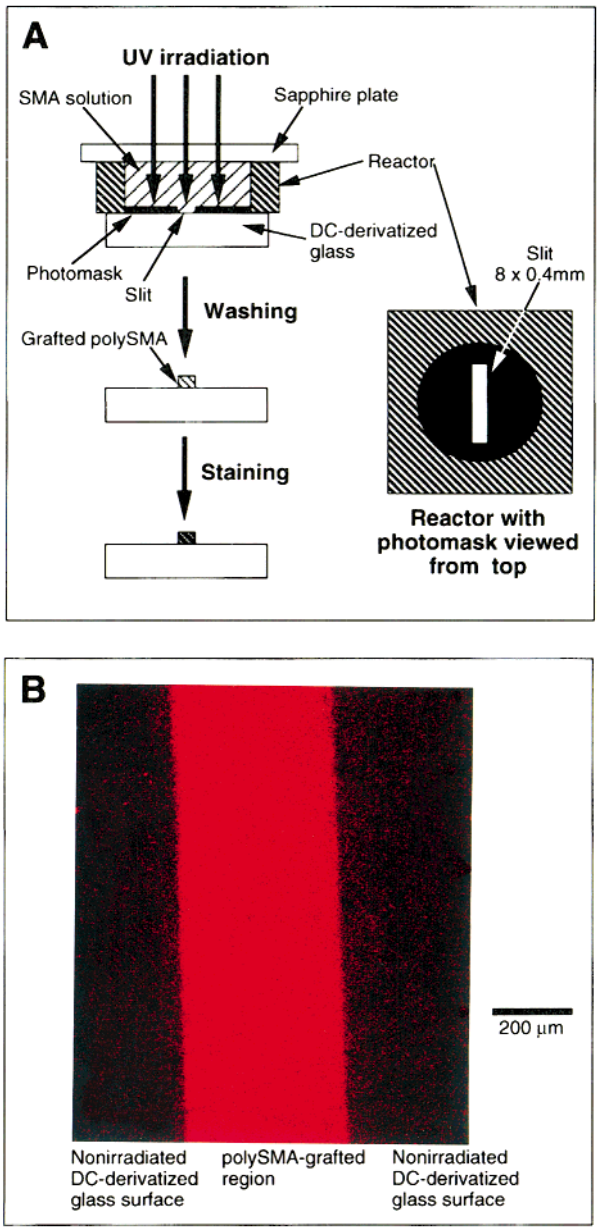

Figure 5. (A) Schematic diagram of the line-patterned graft copolymerization method using a photomask with a slit and its visualization by confocal scanning laser microscopy. (B) Fluorescence micrograph of the obtained line-patterned grafted surface.

(Figure 8:B). The linear relationship observed indicates that the SMA content in the daughter chain is proportional to CMS content in the parent chain.

Discussion

The fabrication of surfaces that exhibit minimal protein adsorption, noncell adhesion, or nonfouling characteristics has been the ultimate goal of surface engineering in industries such as medical device manufacturing.[17−19] Nonionic polymer surface grafting has been applied to short-term blood-contacting devices.[20−22] The operation mechanism has been well discussed from physicochemical aspects, such as entropic repulsion, hydration, and segmental mobility.[23−28] If segmental density in the graft layer is low, low-molecular-weight protein or lipids may be absorbed and accumulated in the graft layer with time, resulting in the loss of nonadsorptive or nonadhesive character after

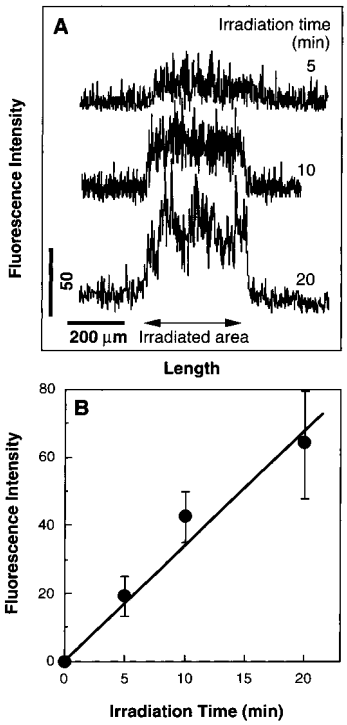

Figure 6. (A) Fluorescence intensities of model A surface (Figure 1.B1). (B) Relationship between the mean fluorescence intensities and irradiation time.

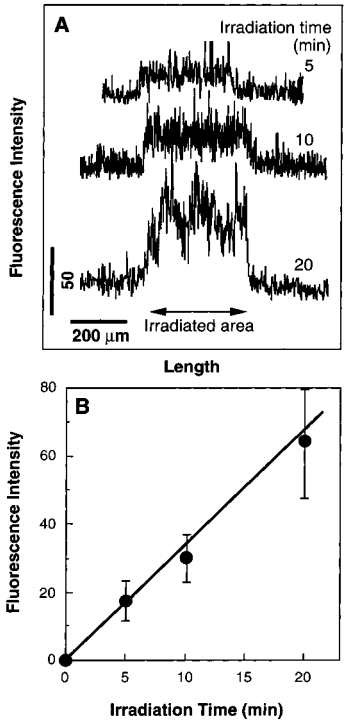

Figure 7. (A) Fluorescence intensities of model B surface (Figure 1.B2). (B) Relationship between the mean fluorescence intensities and irradiation time.

prolonged period of implantation.[29,30] Therefore, the precise design of a graft layer for a highly dense and topologically well-controlled graft architecture, which may prevent deposition of biocolloids in a graft layer, has been long awaited.

Existing surface graft polymerization methods include the formation of radical precursors or derivatization of radical initiators on the surfaces and subsequent ther-

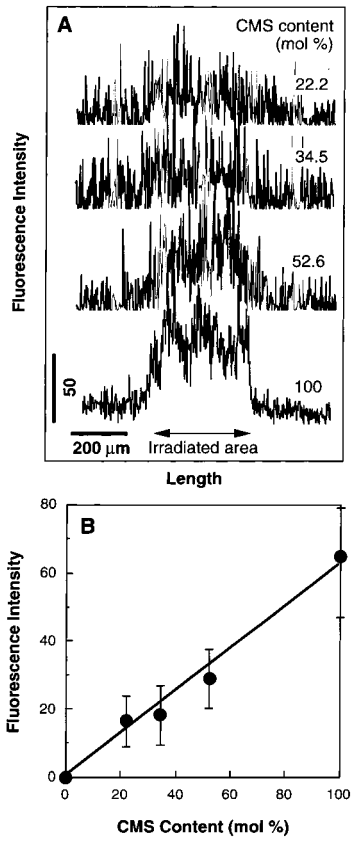

Figure 8. (A) Fluorescence intensities of model C surface (Figure 1.B3). (B) Relationship between the mean fluorescence intensities and CMS content in copolymer.

mal polymerization. That is, corona discharge, γ-ray irradiation, or UV irradiation, by which precursors of radicals were generated, and subsequent thermal radical polymerization[31−36] resulted in the formation of graft polymers on treated surfaces. However, by these techniques, control of graft architectures including graft chain length, graft branching, and segmental spatiodensity is impossible since a free radical is highly reactive.

Recent topics on radical polymerization methods focus on the control of the growing chain ends, which involves radical recombination using relatively stable counter radicals. One method is thermally driven, while the other is photochemically driven. Irrespective of the method used, a radical pair is produced upon treatment. The radical pair tends to recombine to form a covalent bond which can reproduce a radical pair. For example, the thermal method utilizes stable radicals such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) radical which can react with a growing radical end to produce a covalent bond which is thermally decomposed at high temperatures to produce a radical pair (over 100 °C).[37−42] The requirement of such high temperatures is disadvantageous for the surface modification of fabricated devices made of polymers. On the other hand, the iniferter-based photochemical quasiliving polymerization technique produces a radical pair upon UV irradiation at room temperature.[8,9,16,43,44] The method pioneered by Otsu et al. allowed us to utilize unique features of photochemical polymerization of iniferters for surface modification of fabricated devices since the polymerization proceeds at room temperature. The other advantage is the very high regional and dimensional control since the reaction proceeds only at the irradiated portion. Our previous studies have shown that macromolecular architectures, such as well-controlled graft chain length,[11,12] well-defined block graft,[12,14] and gradient graft chain length control[11−13] and regional as well as dimensional control,[11−13] were easily realized by this photopolymerization initiated from iniferter-derivatized surfaces.

In this study, our interest was extended to the preparation of a highly spatio-resolved graft architectural surface using iniferter-based photopolymerization in order to attempt the fabrication of surfaces exhibiting minimal biocolloidal adsorption and adhesion. There are a few methods that can achieve high segmental density in a graft layer or be used to prepare hyperbranched graft chains. The first method increses the surface density of the immobilized iniferter, the second one increases the graft chain length, and the third one increases the degree of branching as well as branch chain length. Since the chain length of the iniferter-based surface subjected to photopolymerization increased with irradiation time, as verified quantitatively by the quartz crystal microbalance technique and qualitatively by atomic force microscopy in our previous studies,[11,13,45] the graft or branch chain length should be easily manipulated. We selected CMS as the major component monomer for the stem or parent chain design since polyCMS is easily derivatized with sodium diethyldithiocarbamate to generate a multiply iniferter-derivatized stem. Our first attempt was to produce a brushlike graft architecture which is hyperbranched with hydrophilic polymers such as polyDMAAm, polyMAA, and polyPEGMA. If all the iniferters, each of which is immobilized on each monomer unit of the stem chain, initiate photopolymerization, highly brushlike graft copolymers are expected to be formed on the multiply iniferter-derivatized surface. Our XPS and wettability measurements suggest that a longer period of photoirradiation resulted in the formation of a thicker graft layer (Figures 3 and 4). Especially, polyPEGMA graft chains, which have the smallest advancing and receding contact angles toward water among three hydrophilic polymers grafted, should have a high density of poly(ethylene glycol) segments in the graft layer since PEGMA is a macromer.

More precisely controlled graft architectures were demonstrated in three models (Figure 1:B): (1) variable length of daughter chain length (L2) but fixed length of parent chain (L1), (2) variable L1 at a fixed L2, and (3) variable degree of branching. The precision of chain length control was assessed from the fluorescence intensity of a dye-stained carboxylate group of SMA of the daughter chain. The difference in intensity (ΔI) between the photografted and nongrafted regions, which is a measure of the density of carboxyl groups, clearly provided quantitative information on the chain architecture. That is, at fixed L1 (photoirradiation time for stem design is fixed), there was a linear relationship between ΔI and photoirradiation time on the branch design, indicating that L2 increases proportionally with photoirradiation time. Second, at fixed L2 (photoirradiation time for daughter chain design is fixed), there was a linear relationship between ΔI and photoirradiation for preparation of the parent chain, indicating that L1 is well controlled by photoirradiation time. Last, the degree of branching was found to be well controlled by the composition of the parent chain. The higher the CMS content is, the denser the branching is. This was

confirmed by the linear relationship between ΔI and the content of CMS in the parent chain. Thus, a very finely structured graft architecture was achieved by the iniferter-based polymerization technique. It is of primary important to define the nature of the structured graft architecture, that is, molecular weight and its distribution, branch length, and so on. To assess this problem, the confocal scanning laser microscopic technique was applied for fluorescent-stained grafted chains. The results appear to promise that our design strategy does operate well semi-qualitatively. However, such determination give us only the overall graft architecture of graft chains. The characterization of fine structure of graft architecture remains still unsolved. The authors' future study will direct toward the quantitative assessment of graft architecture.

In conclusion, we demonstrated that a highly dense graft surface architecture can be prepared by a two-step photoiniferter-based polymerization in which the first step of polymerization determines the parent or stem architecture and the second step of polymerization determines the daughter or branch architecture. The chain lengths of both parent and daughter chains and the degree of branching were easily manipulated under appropriate reaction conditions. This highly spatioresolved surface architectural design, which has been realized for the first time via the photoinduced quasiliving copolymerization technique, may help in designing nonprotein adsorbing and nonfouling surfaces.

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References and Notes

(1) Szwarc, M. *Nature* **1956**, *178*, 1169.
(2) Hsieh, H. L.; Quirk, R. P. *Anionic Polymerization. Principles and Practical Applications*; Marcel Dekker: New York, 1996; pp 279−291.
(3) Heiz, T.; Hocker, H. *Macromol. Chem*. **1999**, *32*, 48.
(4) Hirao, A.; Haraguchi, N.; Sugiyama, K. *Macromolecules* **1999**, *32*, 48.
(5) Szwarc, M. *Carbonions, Living Polymers, and Electron-Transfer Process*; Interscience: New York, 1968.
(6) Sawamoto, M.; Higashimura, T. *Encyclopedia of Polymer Science and Engineering*, 2nd ed., 1989; Suppl. Vol., p 399.
(7) Webster, O. W.; Hertler, W. R.; Sogah, D. Y.; Farmham, W. B.; Babu, T. V. R. *J. Am. Chem. Soc.* **1983**, *105*, 5706.
(8) Lowe, A. B.; Billingham, N. C.; Armes, S. P. *Macromolecules* **1998**, *31*, 5991.
(9) Otsu, T.; Yoshida, M. *Makromol. Chem., Rapid Commun.* **1982**, *3*, 127.
(10) Otsu, T.; Yoshida, M.; Tazaki, T. *Makromol. Chem., Rapid Commum*. **1982**, *3*, 133.
(11) Nakayama, Y.; Matsuda, T. *Macromolecules* **1996**, *29*, 8622.
(12) Nakayama, Y.; Matsuda, T. *Advances in Polymeric Biomaterial Science*; Akaike, T., Okano, T., Akashi, M., Terano, M., Yui, N., CMC: Tokyo, 1997; p 411.
(13) Higashi, J.; Nakayama, Y.; Marchant, R. E.; Matsuda, T. *Langmuir* **1999**, *15*, 2080.
(14) Nakayama, Y.; Matsuda, T. *Langmiur* **1999**, *15*, 5560.
(15) Inoue, H.; Kohama, S. *J. Appl. Polym. Sci.* **1984**, *29*, 877.
(16) Otsu, T.; Ogawa, T.; Yamamoto, T. *Macromolecules* **1986**, *19*, 2089.
(17) Szycher, M. In *Biocompatible Polymers, Metals and Composites*; Technomic Publ., Co., Inc.: Lancaster, 1983.
(18) Park, J. B. In *Biomaterials Science and Bioengineering*; Plenum Press: New York, 1984.
(19) Andrade, J. D. In *Surface and Interfacial Aspects of Biomedical Polymers*; Andrade, J. D., Ed.; Plenum Press: New York, 1985; Vol. 1, p 1.
(20) Nagaoka, S. *Proc. MRS Int. Manuf. Adv. Mater.* **1989**, *1*, 151.
(21) Seeger, J. M.; Ingegno, M. D.; Bigatan, E.; Klingman, N.; Amery, D.; Widenhouse, C.; Goldberg, E. P. *J. Vasc. Surg.* **1995**, *22*, 335.
(22) Inoue, H.; Fujimoto, K.; Uyama, Y.; Ikada, Y. *J. Biomed. Mater. Res*. **1997**, *35*, 255.
(23) Mori, Y.; Nagaoka, S.; Takiuchi, H.; Kikuchi, T.; Noguchi, N.; Tanzawa, H.; Noishiki, Y. *Trans. Am. Soc. Artif. Intern. Organs* **1982**, *28*, 459.
(24) Epand, R. M.; Hui, A. W. *FEBS Lett*. **1986**, *15*, 257.
(25) Martz, H.; Beaudoin, G.; Payter, R.; King, M.; Marcean, D.; Guidon, R. *J. Biomed. Mater. Res.* **1987**, *21*, 399.
(26) Hari, P. R.; Sharma, C. P. *J. Biomater. Appl*. **1991**, *6*, 170.
(27) Amiji, M. M. *Biomaterials* **1995**, *16*, 593.
(28) Lee, J. H.; Ju, Y. M.; Lee, W. K.; Park, K. D.; Kim, Y. M. *J. Biomed. Mater. Res*. **1995**, *16*, 593.
(29) Lee, J. H.; Jeong, B. J.; Lee, H. B. *J. Biomed. Mater. Res.* **1997**, *34*, 105.
(30) Ueda, T. Y.; Matsuda, T. *Langmuir* **1995**, *11*, 4135.
(31) Tazuke, S.; Kimura, H. *J. Polym. Sci., Polym. Lett. Ed*. **1978**, *16*, 497.
(32) Ogiwara, Y.; Kanda, M.; Takumi, M.; Kubota, H. *J. Polym. Sci., Polym. Lett. Ed.* **1981**, *19*, 457.
(33) Uchida, E.; Uyama, Y.; Ikada, Y. *J. Polym. Sci., Polym. Chem. Ed.* **1989**, *27*, 527.
(34) Chapiro, A. *Eur. Polym. J*. **1983**, *19*, 859.
(35) Suzuki, M.; Kishida, A.; Iwata, H.; Ikada, Y. *Macromolecules* **1986**, *19*, 1804.
(36) Kim, M.; Kojima, J.; Saito, K.; Furusaki, S.; Sugo, T. *Biotechnol. Proc.* **1994**, *10*, 114.
(37) Georges, M. K.; Veregin, R. P. N.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 2987.
(38) Veregin, R. P. N.; Georges, M. K.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 5316.
(39) Veregin, R. P. N.; Georges, M. K.; Hamer, G. K.; Kazmair, P. M. *Macromolecules* **1995**, *28*, 4391.
(40) Matyjaszewski, K.; Shigemoto, T.; Frechet, J. M. J.; Leduc, M. *Macromolecules* **1996**, *29*, 4167.
(41) Moad, G.; Rizzarodo, E. *Macromolecules* **1995**, *28*, 8722.
(42) Hawker, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 11185.
(43) Otus, T.; Matsunaga, T.; Doi, T.; Matsumoto, A. *Eur. Polym. J*. **1995**, *31*, 67.
(44) Otsu, T.; Matsumoto, A. *Adv. Polym. Sci*. **1998**, *136*, 75.
(45) Nakayama, Y.; Matsuda, T. *Macromolecules* **1999**, *32*, 5405.

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