
Bioactive glass–mesoporous silica coatings on Ti6Al4V through enameling and triblock-copolymer-templated sol-gel processing

J. M. Gomez-Vega,¹ A. Hozumi,² E. Saiz,³ A. P. Tomsia,³ H. Sugimura,¹ O. Takai¹

¹Department of Materials Processing Engineering, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

²National Industrial Research Institute of Nagoya, 1-1 Hirate-cho, Kita-ku, Nagoya, 462-8510, Japan

³Lawrence Berkeley National Laboratory, Materials Sciences Division, 1 Cyclotron Road, MS 62-203, Berkeley, California 94720

Received 26 September 2000; revised 5 December 2000; accepted 2 March 2001

Abstract: The combination of thick glass coatings that can protect Ti6Al4V from corrosion in the body fluids, and mesoporous silica films able to readily induce the formation of apatite when immersed in a simulated body fluid (SBF), has been investigated in this work as a possible route towards more resistant and long-lasting implants. Glasses in the system Si-Ca-Mg-Na-K-P-O with thermal expansion coefficients close to that of Ti6Al4V were prepared and used to coat this alloy by an enameling technique. However, the glasses apt to coat Ti6Al4V exhibited a very limited capacity to induce apatite formation in SBF. In order to enhance their bioactivity, a thin film of mesoporous silica was applied on the exterior of the specimens by spin coating a sol-gel solu-

tion. When tested in SBF, these coatings induced apatite formation after 7 days. The mesoporosity of the silica film was created through a triblock-copolymer-templating process. The diameters of the mesochannels could be adjusted by changing the size of the directing agent. A preferred alignment of the mesostructure was observed. The removal of the organic templates could be achieved through a photocalcination treatment, which, compared to conventional thermocalcination, offered several advantages. © 2001 John Wiley & Sons, Inc. *J Biomed Mater Res* 56: 382–389, 2001

Key words: glass coating; mesoporous silica; triblock copolymer; apatite; bioactivity

INTRODUCTION

Ti6Al4V is one of the most widely used alloys for the fabrication of implants where body loads are considerable, such as hip prostheses.¹ Nevertheless, Ti6Al4V is a bioinert material the adherence of which to the bone is very low, so the use of coatings has been investigated to improve their adhesion.² Plasma spraying of hydroxyapatite (HA) has been widely investigated, but this method fails to produce reliable and long-lasting coatings mainly because of weak metal/HA interfaces.^{3,4}

Correspondence to: J. M. Gomez-Vega; e-mail: jose@plasma.numse.nagoya-u.ac.jp

Contract grant sponsor: JSPS-RFTF; contract grant number: 99R13101

Contract grant sponsor: NIH/NIDCR; contract grant number: 1R01DE11289

Contract grant sponsor: Spanish Ministry of Education and Culture (MEC)

Coatings of implants should fulfill two main purposes: prevent the metal from being corroded by the body fluids and promote adhesion to the bone. The coatings also may provide an elastic-modulus gradient between metal and bone that reduces the load shielding on bone and allows it to stay healthy. Previous works have indicated that silicate-based glasses can be used successfully to coat Ti6Al4V by an enameling technique.^{5,6} However, when tested *in vitro* (soaked in SBF in physiologic conditions), the ability of these glasses to form apatite on their surfaces was very poor. Therefore different approaches have been explored to improve the bioactivity of these coatings while at the same time maintaining good adhesion to the metal. Some of these methods are (1) embedding particles of Bioglass® (BG) or HA on the exterior of the coating;⁷ (2) preparation of multilayered glass coatings designed to exhibit a more bioactive external surface;^{8,9} and (3) fabrication of graded coatings of glass-HA composites.⁹

In this work, two different methodologies—enameling and sol-gel—are combined to provide pro-

tection and enhanced bioactivity to Ti6Al4V implants. To provide protection, a thick glass layer was applied directly on to the metal by enameling, and bioactivity was enhanced by an application of a mesoporous silica thin film by spin coating of a sol-gel solution. It is well known that gel-silica with regular nanostructures can be synthesized through self assembly of surfactants or amphiphilic block copolymers as structure-directing agents.¹⁰⁻¹³ The mesostructure can exhibit cubic, hexagonal, or lamellae packing, depending on the system and conditions used.¹⁴⁻¹⁶ Once the organic part has fulfilled its roll as template for the formation of the ordered silica frame, it is eliminated in order to hollow the pores, usually by a thermal treatment. Block copolymers comprise two or more blocks of chemically different monomers that can segregate into regular lattices. Compared to conventional low-molecular-weight surfactants, self-assembly of amphiphilic block copolymers can result in mesostructured materials with larger pore sizes (up to 30 nm).¹³ Triblock copolymers were utilized in this work as the structure directing agents, and photocalcination with ultraviolet light was investigated as an alternative to conventional thermocalcination to eliminate the organic templates.

MATERIALS AND METHODS

The compositions of the glasses used in this work were tailored to obtain thermal expansion coefficients close to that of Ti6Al4V ($9.6 \times 10^{-6} \text{ }^{\circ}\text{C}^{-1}$) as well as adequate softening points for enameling below the $\alpha \rightarrow \beta$ transformation of Ti in the alloy (~980°C), and were prepared by mixing and firing the necessary reagents in a standard procedure.⁵ The composition and main thermal properties of these glasses (BG included) are listed in Table I. Ti6Al4V (99% purity) plates ($15 \times 10 \times 1 \text{ mm}$) were ground with silicon carbide paper (800 grit) and cleaned ultrasonically with acetone and ethanol before their use. To prepare the coatings, a suspension of glass powder (particle size <20 μm) in ethanol was poured onto the plates placed in a beaker and allowed to sediment for several hours. Afterwards, the clear liquid was removed

with a pipette and the beaker was placed in an oven at 75°C overnight to dry the specimens completely. The green-coatings, prepared as indicated, were fired in air in a Unitek dental furnace (furnace preheated at 600°C, temperature ramp 40°C /min in low vacuum, final temperature 800–840°C, dwell time 30 s, and quenching), as previously determined to be the optimum conditions.⁶ The final thickness of the coating was fixed at ~50 μm .

The silica sol-gel solution was prepared based on conditions reported previously,¹³ and all the chemicals were used as received. A solution of the triblock copolymer (L-121 or P-123) [amphiphilic triblock copolymers poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) type ($\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n (\text{CH}_2\text{CH}(\text{CH}_3)\text{O})_m (\text{CH}_2\text{CH}_2\text{O})_n \text{ H}$) pluronics L-121 (designated EO₄₋₅PO₆₀EO₄₋₅), and P-123 (designated EO₂₀PO₇₀EO₂₀); provided by BASF] was prepared in acid media (pH <1), followed by the addition of the silica precursor tetraethylorthosilicate (TEOS) [tetraethylorthosilicate ($[\text{C}_2\text{H}_5\text{O}]_4\text{Si}$), > 96% purity; purchased from Tokyo Chemical Industry Co.]. The reactant molar ratio was: polymer 0.017:TEOS 1:HCl 6:H₂O 167. In a typical preparation, 0.16 g of polymer L-121 were dissolved at room temperature with the aid of magnetic stirring in 7 mL of Milli Q water containing 1.35 mL of HCl (37 vol %). Thereupon, 0.55 mL of TEOS were added to this solution, and this sol was used immediately in the spin-coating process to minimize the amount of particle formation in bulk solution.

The mesoporous silica films were applied over the glass coatings on Ti6Al4V by spin coating of the sols described above. The rotating speed could be modified according to the desired thickness of the film. In this work, we used two consecutive speeds: 5 s at 1000 rpm plus 5 s at 2000 rpm. In these conditions, thicknesses of ~0.2 μm were obtained. The specimens were allowed to dry overnight at room temperature. Two different methods were investigated to eliminate the organic templates: (1) thermocalcination (firing in air between 300° and 500°C during periods of 1–3 h); and (2) photocalcination [ultraviolet irradiation in air with an excimer lamp ($\lambda = 172 \text{ nm}$) for different periods and pressures].¹⁷

The coating surfaces and cross-sections were examined by optical and scanning electron microscopy with associated energy-dispersive spectroscopy analysis (SEM-EDS). The mesostructure of the coatings was evaluated by low-angle X-ray diffraction (XRD). Fourier transformed-infrared spectroscopy (FT-IR) was used to evaluate the elimination of the

TABLE I
Composition and Main Properties of Glasses

	Composition (Mole %)						α ($10^{-6} \text{ }^{\circ}\text{C}^{-1}$)	T_s (°C)
	SiO ₂	CaO	MgO	Na ₂ O	K ₂ O	P ₂ O ₅		
BG	46.3	26.9	0.0	24.3	0.0	2.5	0.58	15.1
6P50	49.8	16.7	13.3	15.0	2.7	2.5	0.60	12.2
6P53	51.8	19.0	15.1	9.8	1.8	2.5	0.66	11.5
6P55	54.5	16.1	12.7	11.6	2.6	2.5	0.53	11.0
6P57	56.3	16.0	12.7	10.6	1.9	2.5	0.51	10.8
6P61	61.4	13.5	10.8	10.0	1.8	2.5	0.40	10.2
6P68	68.5	10.9	8.6	8.1	1.4	2.5	0.28	8.8

*R = (CaO + MgO)/SiO₂ (data in mole %); α = coefficient of thermal expansion (measured between 200 and 400°C); T_s = softening point.

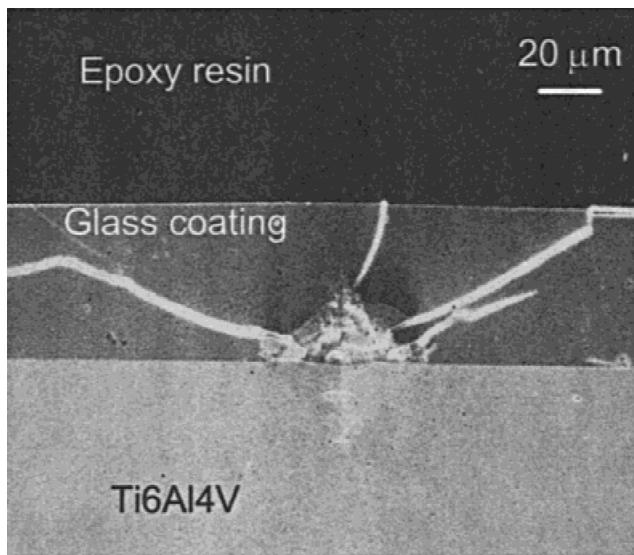


Figure 1. Vickers indentation at the glass 6P61-alloy interface (0.2-Kg load in air). The cracks do not propagate along the interface but tend to be driven into the glass.

organic template. The strength of the coatings was evaluated qualitatively by Vickers indentations on the surface and cross sections in air.

Previous to the *in vitro* test, the uncoated surface of the specimens (edges and back side), where metallic surface is exposed, was polished with silicon carbide paper (600 grit) in order to remove the metallic oxide layer produced during the enameling process. The surface then was cleansed in ethanol and dried with hot air. Some studies have shown that cation impurities with 3+, 4+, 5+ charges, such as Al^{3+} , can inhibit formation of hydroxy-carbonate apatite layer on a glass and destroy bioactivity;¹⁸ therefore the metallic oxide scales formed during the firing treatment on the uncoated areas were removed to prevent the possibility of some metallic cations dissolving in the simulated body fluid and interfering with the formation of apatite. The coated surface is effectively sealed by the coating.⁶ Afterwards, the coatings were put in polyethylene containers with 20 mL of simulated body fluid (SBF) and placed in a water bath with constant temperature at 37°C. The SBF was prepared by dissolving reagent chemicals of NaCl , KCl , CaCl_2 , $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$, NaH_3CO_3 , K_2HPO_4 , and $(\text{CH}_2\text{OH})_3\text{CNH}_2$ in deionized water and buffering it with HCl at pH = 7.25.⁵ After having been soaked, the coatings were rinsed with distilled water and dried in air at room temperature.

RESULTS

The glasses that could be applied on Ti6Al4V and resulted in crack-free coatings were 6P57, 6P61, and 6P68. The thermal-induced stress generated during the enameling process was not enough to crack the coatings because the thermal expansion coefficients of these glasses are very similar to that of Ti6Al4V ($\alpha_{\text{Ti6Al4V}} \approx 9.6 \cdot 10^{-6} \text{ }^{\circ}\text{C}^{-1}$; Table I). To the contrary,

glasses with <57 mol % silica content, and therefore higher values of α , always resulted in flawed coatings due to the high thermal expansion mismatch with the substrate.⁶ The qualitative evaluation of adhesion using Vickers indentation implied that the interfaces of glasses 6P57, 6P61, and 6P68 with Ti6Al4V were strong since the produced cracks never propagated along the interface but were driven into the glass (Fig. 1). Likewise, the silica film did not delaminate after indentations on the surface.

Mesoscopic ordering of the spin-cast silica-copolymer films was characterized by low-angle XRD. Diffractograms of as-deposited silica films using the triblock copolymer P-123 as the directing agent are shown in Figure 2. Three well-resolved peaks indexable as (100) reflections associated with hexagonal symmetry can be observed. The absence of (110) reflections indicates that the mesochannels of the film run parallel to the substrate.¹⁹ The intensity of the peaks depends highly on the orientation of the sample. There is a narrow sector where peaks were most intense, but moving the sample azimuthally away from this orientation resulted in a decrease of the peak's intensity, as shown in Figure 2. The coat-

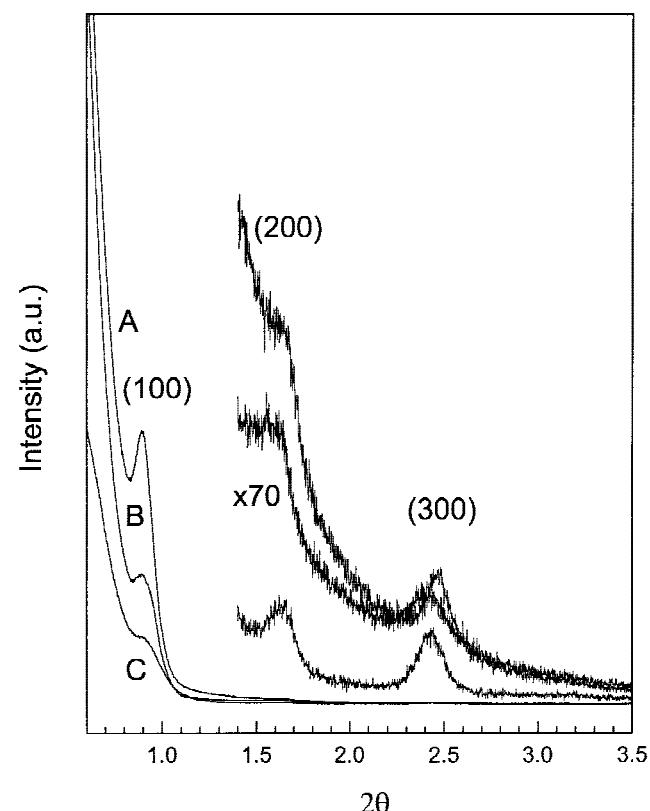


Figure 2. Low-angle X-ray diffraction patterns of as-deposited silica films on glass 6P61 coatings using the tri-block copolymer P-123 as directing agent. The diffractograms correspond to the sample orientation (A) where peaks were most intense, and after rotating the sample azimuthally (B) 30° and (C) 60°.

ings were analyzed by XRD after the treatments to eliminate the organic components in the same orientation where diffraction intensities were at their maximum level. The retention of the mesoporosity over the treatments was proved by the presence of the (100) peaks (Fig. 3). A contraction of the d spacing and a decrease in the diffraction intensity can be observed in the diffractograms of treated coatings. FT-IR spectra of coatings using the triblock copolymer L-121, before and after thermo- and photocalcination treatments, are shown in Figure 4. Under these conditions, both calcined films were totally free of organics (disappearing of C-H stretching peaks around $2900\text{--}3000\text{ cm}^{-1}$), and abundant hydroxyl groups (O-H stretching broad band around 3300 cm^{-1}) can be detected in the photocalcined coatings.

Coatings of glasses 6P57 and 6P61 with an external film of mesoporous silica photooxidized at 100 Pa for 2 h were tested *in vitro* by immersion in SBF. The analysis of the samples by SEM-EDS showed the presence of apatite crystals precipitating on the surface after 7 days of immersion in SBF (Fig. 5). The hemi-

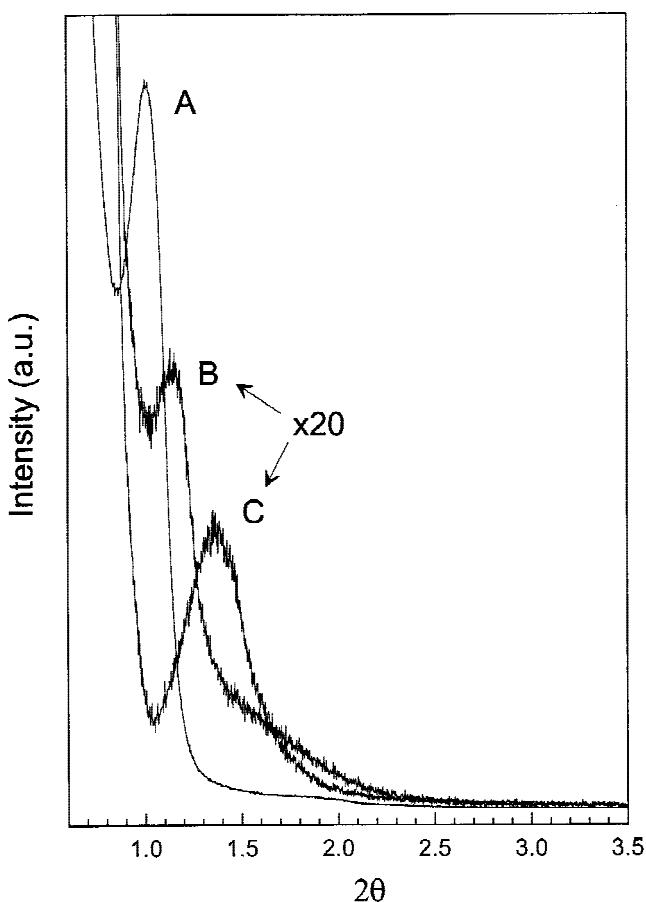


Figure 3. Low-angle X-ray diffraction spectra of as-deposited silica films on glass 6P61 coatings using the tri-block copolymer L-121 as directing agent. A: as-prepared; B: photocalcined ($10\text{ Pa}/3\text{ h}$); C: thermocalcined ($300^\circ\text{C}/1^\circ\text{C min}^{-1}/3\text{ h}$).

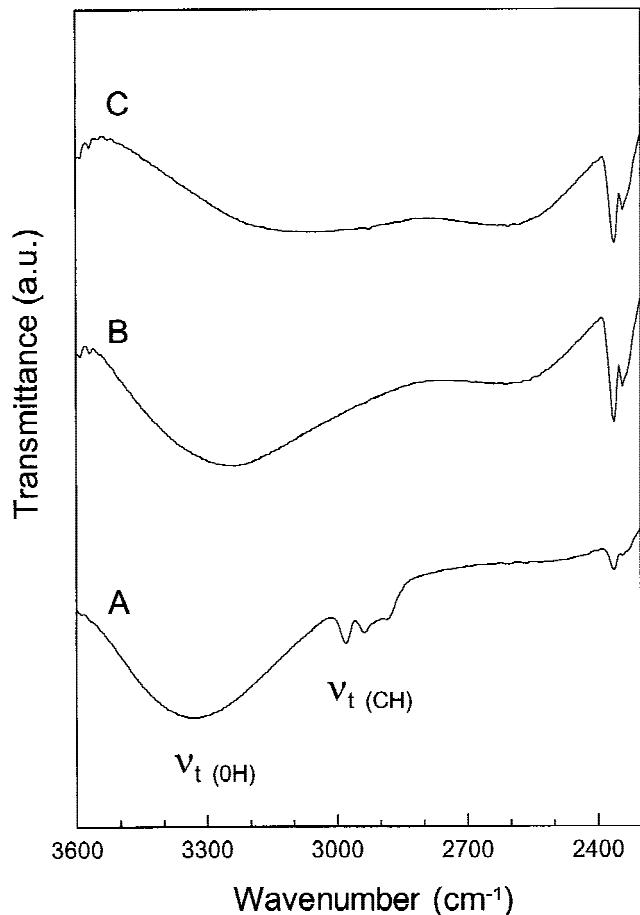


Figure 4. FT-IR spectra of silica films on glass 6P61 coatings using the tri-block copolymer L-121 as directing agent. A: as-prepared; B: photocalcined ($1000\text{ Pa}/1\text{ h}$); C: thermocalcined ($500^\circ\text{C}/5^\circ\text{C min}^{-1}/1\text{ h}$).

spheric formations observed are very similar to the apatite formed on the surface of bioactive glasses and glass-ceramics.^{6,20} The coatings fabricated with glasses 6P61 or 6P68, with high silica content and therefore highly packed lattice networks, were observed to be highly resistant to dissolution in SBF, and no corrosion or variation in the coating composition could be observed even after immersions up to 4 months, which indicates a good protection of the glass/metal interface from the aqueous environment.

Using optical microscopy, the crack growth of well-defined cracks generated by Vickers indentation (1.2 kg load) on the coatings immersed in SBF or in dehydrated mineral oil at 36.5°C was monitored after selected periods up to 8 days. Also, the relative crack resistance of the glass/metal interface after immersion in SBF was evaluated qualitatively by indentation on polished cross sections with loads ranging from 0.05 to 1.2 Kg in air and in SBF. In this case, the cracks did not propagate along the interface but rather tended to be driven into the glass, as it had occurred with the original coatings before the *in vitro* tests, and therefore im-

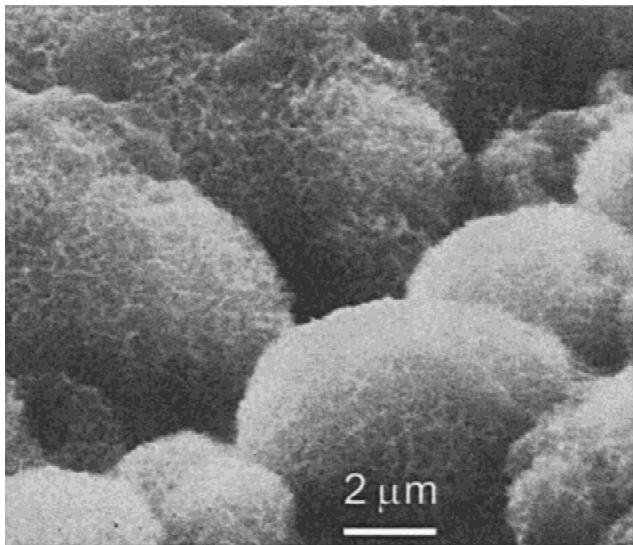


Figure 5. SEM photograph of the formed apatite on silica films applied on glass 6P61 coatings soaked in SBF for 7 days. A leaf-like hemispheric morphology can be observed.

merseion in SBF did not affect the adhesion of the glass/metal interfaces that were not exposed to the fluid.

When tested *in vitro*, cracks perpendicular to the substrate formed spontaneously on the 6P57 coatings, and after reaching the interface they initiated delamination, whereas no cracks were observed on 6P61 and 6P68 coatings. The cracks induced on 6P57 coatings grew during immersion in SBF at velocities $\leq 10^{-10}$ m/s, up to lengths of ~ 200 μm . The coating tensile stress estimation (for 50 μm in thickness) is 50, 25, and -25 (compressive) MPa for 6P57, 6P61, and 6P68, respectively. Therefore, cracks do not grow in the 6P61 and 6P68 coatings due to low stresses and high resistance to corrosion whereas the stress in 6P57 coating can drive the slow growth of cracks. The formed apatite *in vitro* did not shield the crack.²¹ Moreover, in the case of 6P68 coatings, the compressive residual stresses effectively arrested the growth of indentation cracks.

DISCUSSION

Among the glasses apt to be used to coat Ti6Al4V, only glass 6P57 was able to induce the formation of apatite after long periods of immersion in SBF (>1 month), and 6P61 and 6P68, which have silica contents above 60 mol %, could not form apatite at all. The bioactivity of $\text{Na}_2\text{O}-\text{CaO}-\text{P}_2\text{O}_5-\text{SiO}_2$ glasses prepared by calcination of mixed reagents at elevated temperatures (usually 1200°–1500°C)⁵ depends on their composition. The greatest bioactivity is exhibited by Bioglass® 45S5 (BG; 46 mol % silica; Table I), and its bio-

activity decreases as the composition moves away from that of this glass. Compositions with lower silica content tend to create more unstable glasses (problems of crystallization) whereas higher silica contents result in bioinert behavior.¹ When the silica content in the glass is increased, the network becomes more compact and closed due to an increase in bridging bonds (Si-O-Si) that hold the network together. In contrast, when the silica is reduced, the disruption of the network grows due to an increase in nonbridging oxygen between Si and the modifier atoms (e.g., Na, K, Ca, Mg, etc.). Therefore, an increase in the CaO/SiO_2 mole ratio of the glasses results in a more open structure because of the presence of more nonbridging oxygen and, consequently, in a more bioactive behavior by virtue of the easier diffusion of ions through the glass.

According to Hench et al.,²² and in agreement with our results, compositions >60 mol % silica are not bioactive, and the silicate array is mainly a three-dimensional one where the indispensable ion exchange that eventually leads to bone adhesion is highly impaired. Following this reasoning, the use of pure silica to induce apatite formation may look contradictory.

Nonetheless, Li et al.^{23–27} have proved that pure silica fabricated by a sol-gel method can precipitate apatite when tested in SBF. The rate of apatite formation was shown to depend on pH, concentration of ions in solution, and sintering temperature of the gel silica, and it was suggested that the silanol groups present on the surface might be responsible for the apatite formation. Additionally, Karlsson et al.²⁸ suggested that, in contrast to dense silica and durable silicate glasses, gel–silica is flexible enough to provide the oxide–oxide spatial requirement to match the bone apatite lattice, thereby providing epitaxial sites for bone growth. Pereira et al.²⁹ found a great effect of texture (pore size and volume) on the rate of apatite formation on gel–silica surfaces. Peltola et al.³⁰ also have indicated that a great mesopore volume and a wide mesopore size distribution favor hydroxycarbonate nucleation.

Through the use of different mesostructure directing agents, the pore diameter of the silica films prepared in this work could be modified. As expected, the *d*-spacing of the X-ray d_{100} peak correlated with the molecular weight of the used polymer. Thus the values of the unit cell parameter of the hexagonally arranged lattice were 100 and 126 Å when L-121 (MW = 3850 g mol⁻¹) or P-123 (MW = 5800 g mol⁻¹) were used, respectively. These values are within the range reported in the literature.¹³ A combination of electrostatic, hydrogen bonding and preferential silica interactions with one of the blocks of the copolymer are presumed to be responsible for mesoscopic silica–triblock copolymer assembly into hexagonal arrays of mesochannels.³¹

Variation of the diffraction peak intensities when a sample is rotated (Fig. 2) can be attributed to a preferential alignment of the mesostructure.³² In the case of crystalline substrates such as graphite,³³ mica,³⁴ or silicon,³² the micelle rods of the directing agent can be accommodated in a preferred direction according to the atomic surface of the substrate, followed by an epitaxial-like growth of the mesoporous silica film. However, a mechanism that explains oriented mesoporous silica films on amorphous substrates such as glass is not evident. In this work, the precursor solution in its state of sol was utilized in the spin-coating process just after TEOS was added and before any appreciable gel formation took place. Under these conditions of restrained reactivity (hydrolysis and condensation) of the inorganic precursor, the rheology of the sol is governed mainly by the block copolymers since their motion is not impeded by the incipient silica network.³⁵ Block copolymers are recognized for their tendency to form well-ordered periodic microstructures, often with exceptionally intricate geometries, especially under the effect of shear.^{36,37} As a consequence, the spinning process and/or the formation of regular, dissipative structures, caused by convection during the evaporation of the solvent,³⁸ may be responsible for inducing a preferred orientation in the nucleation and growth of the mesochannels. The entire silica network is formed around the organic template replicating its preferred orientation.

The contraction of the *d* spacing and the decrease in the diffraction intensity of the coatings treated to remove the organic material (Fig. 3) implies that the structures underwent further condensation of residual hydroxyl groups that resulted in disordering of the mesostructure. This contraction depended on the type of treatment, and photocalcination was less aggressive than thermocalcination. Nevertheless, it was found that the capacity to eliminate the organic component and its effect on the mesostructure depended highly on the conditions of the treatments. For example, neither thermocalcination at 300°C for 3 h nor photocalcination at 10 Pa for 3 h was able to eliminate completely the organic template whereas it could be achieved at 500°C for 1 h or at 1000 Pa for 1 h, respectively (Fig. 4). However, the ordered channel structure could not be preserved over these more aggressive treatments, so a compromise needs to be found between mesoporosity and the conditions used to remove the organic part, particularly temperature of thermocalcination and air pressure at photocalcination.

A great disadvantage of thermocalcination in the type of specimens studied in this work is that it ruined the coatings by causing overreaction at the glass/Ti6Al4V interface.⁶ In contrast, since the ultraviolet excimer lamp does not generate infrared rays, photocalcination occurs at room temperature and therefore

does not affect the glass/metal interface. Hozumi et al.¹⁷ also proved that effective elimination of cetyltrimethyl ammonium chloride from mesostructured silica films can be achieved using the photocalcination approach. Photocalcination can eliminate any organic molecules (including bacteria) because it depends on the photo-induced cleavage of C-C bonds. Therefore the specimens are perfectly sterilized after its application, which is worth mentioning since they have been proposed for use as implants. In addition, this technique produced silanol groups on the surface of the coatings (Fig. 4) that could result in enhanced bioactivity.

Previous studies on surface structural change of glasses and glass-ceramics *in vivo* as well as *in vitro* have shown that the essential condition for a material to bond with living bone is the formation of hydroxyapatite on its surface in the body environment.^{19,37} Both the mesoporous structure and a surface rich in silanol groups can explain the formation of apatite on the silica films after immersion in SBF (Fig. 5). A mechanism that assumes pores as nucleation sites for hydroxyapatite was proposed by Pereira et al.²⁷ According to these authors, the nucleation of apatite occurs likely inside the pores through the establishment of an electrical double layer with higher ionic concentration. This does not exclude the role of hydroxyl coverage because rehydration and establishment of the electrical double layer depend on this parameter.

Ongoing research is focused on investigating in more detail the effect of the mesostructure in the early stages of the formation of apatite. Pore size and alignment may be critical parameters in adhesion to the bone of these coatings. An appropriate range of pore size and a preferred alignment of the mesochannels could induce the formation of anisotropic ordered hydroxyapatite and collagen structures that may result in more resistant implants.

CONCLUSIONS

Silicate-based glasses with a composition tailored to match the thermal expansion of Ti6Al4V can be applied successfully on the substrate by enameling. A thick coating (50 µm) of these glasses can be prepared to protect the metal from corrosion by body fluids. In order to improve the bioactivity of these implants, a thin film of mesoporous silica was applied to the glass coating by spinning a sol-gel solution. The use of different triblock copolymers permitted modification of the pore sizes of the mesochannels. In addition, the mesostructure of the silica film appeared to be partially oriented, which could have been a consequence of the restrained reactivity of the inorganic precursor (TEOS) and the orientational order of the block co-

polymers in response to dynamic processes, such as spin-induced shear and/or evaporation.

Photocalcination offered several advantages over conventional thermocalcination to remove the organic part in that it did not ruin the glass/Ti6Al4V interface, it caused less disorder of the mesostructures, and it generated silanols on the surface. The mesoporous structure and the presence of abundant silanol groups may be responsible for the capacity of these pure silica coatings to form apatite when soaked in SBF. The possibility of designing at a nanoscale level the structure of the silica films through self-assembling methods opens a wide panorama for engineering new implant coatings that, by virtue of preferred hydroxyapatite precipitation, may exhibit enhanced osseointegration.

References

- Hench LL. Bioceramics: From concept to clinic. *J Am Ceram Soc* 1991;74:1487–1510.
- Kitsugi T, Nakamura T, Oka M, Senaha Y, Goto T, Shibuya T. Bone-bonding behavior of plasma-sprayed coatings of bio-glass(R), AW-glass ceramic, and tricalcium phosphate on titanium alloy. *J Biomed Mater Res* 1996;30:261–269.
- Lacefield WR. Hydroxylapatite coating. In: Hench LL, Wilson J, editors. An introduction to bioceramics. Singapore: World Scientific; 1993. p 223–238.
- Suchanek W, Yoshimura M. Processing, properties of hydroxyapatite-based biomaterials for use as hard tissue replacement implants. *J Mater Res* 1998;13:94–117.
- Pazo A, Saiz E, Tomsia AP. Silicate glass coatings on Ti-based implants. *Acta Mater* 1998;46:2551–2558.
- Gomez-Vega JM, Saiz E, Tomsia AP. Glass-based coatings for titanium implant alloys. *J Biomed Mater Res* 1999;46:549–559.
- Gomez-Vega JM, Saiz E, Tomsia AP, Marshall SJ, Marshall GW. Bioactive glass coatings with hydroxyapatite and Bio-glass® particles on Ti-based implants. I. Processing. *Biomaterials* 2000;21:105–111.
- Gomez-Vega JM, Saiz E, Tomsia AP, Marshall SJ, Marshall GW. A multilayer approach to bioactive glass coatings on Ti alloys. In: Neenan T, Marcolongo M, Valentini RF, editors. Biomedical materials—drug delivery, implants and tissue engineering. *Mater Res Soc Proc* 1999;550:349–354.
- Gomez-Vega JM, Saiz E, Tomsia AP, Oku T, Suganuma K, Marshall GW, Marshall SJ. Novel bioactive functionally graded coatings on Ti6Al4V. *Adv Mater* 2000;12:894–898.
- Beck JS, Vartuli JC, Roth WJ, Leonowicz ME, Kresge CT, Schmitt KD, Chu CT-W, Olson DH, Sheppard EW, McCullen SB, Higgins JB, Schlenker JL. A new family of mesoporous molecular sieves prepared with liquid crystal templates. *J Am Chem Soc* 1992;114:10834–10843.
- Monnier A, Schuth F, Huo Q, Kumar D, Margolese D, Maxwell RS, Stucky GD, Krishnamurti M, Petroff P, Firouzi A, Janicke M, Chmelka BF. Cooperative formation of inorganic–organic interfaces in the synthesis of silicate mesostructures. *Science* 1993;261:1299–1302.
- Aksay IA, Trau M, Manne S, Honma I, Yao N, Zhou L, Fenter P, Eisenberger PM, Gruner SM. Biomimetic pathways for assembling inorganic thin films. *Science* 1996;273:892–898.
- Zhao D, Feng J, Huo Q, Melosh N, Fredrickson GH, Chmelka BF, Stucky GD. Triblock copolymer syntheses of mesoporous silica with periodic 50 to 300 angstrom pores. *Science* 1998;279:548–552.
- Ciesla U, Schuth F. Ordered mesoporous materials. *Micropor Mesopor Mater* 1999;27:131–149.
- Huo Q, Margolese DI, Stucky GD. Surfactant control of phases in the synthesis of mesoporous silica-based materials. *Chem Mater* 1996;8:1147–1160.
- Lee YS, Surjadi D, Rathman JF. Compositional effect and hydrothermal reorganization of mesoporous silicates synthesized in surfactant solutions. *Langmuir* 2000;16:195–202.
- Hozumi A, Yokogawa Y, Kameyama T, Hiraku K, Sugimura H, Takai O, Okido M. Photocalcination of mesoporous silica films using vacuum ultraviolet light. *Adv Mater* 2000;12:985–987.
- Hench LL. In: Hench LL, Wilson J, editors. An introduction to bioceramics. Singapore: World Scientific; 1992. p 322.
- Ogawa M. Formation of novel oriented transparent films of layered silica–surfactant nanocomposites. *J Am Chem Soc* 1994;116:7941–7942.
- Kokubo T, Ito S, Huang ZT, Hayashi T, Sakka S, Kitsugi T, Yamamuro T. Ca/P-rich layer formed on high strength bioactive glass–ceramic A-W. *J Biomed Mater Res* 1990;24:331–343.
- Bloyer DR, Gomez-Vega JM, Saiz E, McNaney JM, Cannon RM, Tomsia AP. Fabrication and characterization of a bioactive glass coating on titanium implant alloys. *Acta Mater* 1999;47:4221–4224.
- Hench LL, LaTorre GP. In: Yamamuro T, Kokubo T, Nakamura T, editors. *Bioceramics 5*. Kyoto: Kobonshi Kankokai Inc.; 1992. p 67.
- Li P, Kangasniemi I, de Groot K, Kokubo T. Bone-like hydroxyapatite induction by a gel-derived titania on a titanium substrate. *J Am Ceram Soc* 1994;77:1307–1312.
- Li P, Kangasniemi I, de Groot K, Kokubo T, Yli-Urpo AU. Apatite crystallization from metastable calcium phosphate solution on sol-gel-prepared silica. *J Noncryst Solids* 1994;168:281–286.
- Li P, Kangasniemi I, de Groot K, Kokubo T. Induction and morphology of hydroxyapatite, precipitated from metastable simulated body fluids on sol-gel prepared silica. *Biomaterials* 1993;14:963–968.
- Li P, Ohtsuki C, Kokubo T, Nakanishi K, Soga N, de Groot K. Role of hydrated silica, titania, alumina in inducing apatite on implants. *J Biomed Mater Res* 1994;28:7–15.
- Klein CPAT, Li P, de Blieck-Hogervorst JMA, de Groot K. Effect of sintering temperature on silica gels and their bone bonding ability. *Biomaterials* 1995;16:715–719.
- Karlsson KH, Froberg K, Ringbom TJ. A structural approach to bone adhering of bioactive glasses. *J Noncryst Solids* 1989;112:69–72.
- Pereira MM, Clark AE, Hench LL. Effect of texture on the rate of hydroxyapatite formation on gel–silica surface. *J Am Ceram Soc* 1995;78:2463–2468.
- Peltola T, Jokinen M, Rahiala H, Levanen E, Rosenholm JB, Kangasniemi I, Yli-Urpo A. Calcium phosphate formation on porous sol-gel-derived SiO₂ and CaO-P₂O₅-SiO₂ substrates *in vitro*. *J Biomed Mater Res* 1998;44:12–21.
- Yang P, Zhao D, Margolese DI, Chmelka BF, Stucky GD. Block copolymer templating syntheses of mesoporous metal oxides with large ordering lengths and semicrystalline framework. *Chem Mater* 1999;11:2813–2826.
- Miyata H, Kuroda K. Preferred alignment of mesochannels in a mesoporous silica film grown on a silicon (110) surface. *J Am Ceram Soc* 1999;121:7618–7624.
- Yang H, Coombs N, Sokolov I, Ozin GA. Registered growth of

- mesoporous silica films on graphite. *J Mater Chem* 1997;7:1285–1290.
- 34. Yang H, Kuperman A, Coombs N, Mamiche-Afara S, Ozin GA. Synthesis of oriented films of mesoporous silica on mica. *Nature* 1996;379:703–705.
 - 35. Colby RH. Block copolymer dynamics. *Curr Opin Colloid Interface Sci* 1996;1:454–465.
 - 36. Matsen MW. Self-assembly of block copolymers in thin films. *Curr Opin Colloid Interface Sci* 1998;3:40–47.
 - 37. Chen Z-R, Kornfield JA, Smith SD, Grothaus JT, Satkowski MM. Pathways to macroscale order in nanostructured block copolymers. *Science* 1997; 277:1248–1253.
 - 38. Karthaus O, Grasjo L, Maruyama N, Shimomura M. Formation of ordered mesoscopic patterns in polymer cast films by dewetting. *Thin Solid Films* 1998;829:327–329.
 - 39. Li R, Clark AE, Hench LL. Effects of structure and surface area on bioactive powders by sol-gel process. In: Hench LL, West JK, editors. *Chemical processing of advanced materials*. New York: Wiley; 1992. p 627–633.