Bull. Inst. Chem. Res., Kyoto Univ., Vol. 72, No. 2, 1994

Chemical Durability of P-Implanted Silica Glass for Radiotherapy

Takeshi YAO*, Yoshio MURASHITA*†, Masakazu KAWASHITA*,
Tadashi KOKUBO*, Gikan H. TAKAOKA** and Isao YAMADA**

Received June 1, 1994

^{31}P can be activated to β-emitter ^{32}P with 14.3 d half-life by neutron bombardment. A chemically durable glass containing a large amount of phosphorus is believed to be useful for *in situ* irradiation of cancers. In the present study, a chemically durable silica glass was ion-implanted with phosphorus at a dose of 2×10^{17} cm^{-2} under 20 keV, and then heat-treated at various temperatures up to 900°C. They were soaked in distilled water at 95°C for 7 d. Phosphorus and silicon leached out from the glasses were analyzed by the inductively coupled plasma atomic emission spectroscopy. The phosphorus ions implanted in the glass were completely dissolved into the water from the as-implanted glass. The dissolution was, however, much suppressed by the heat-treatment at 900°C. The Rutherford backscattering spectrometry showed that an appreciable amount of phosphorus remained in the glass heat-treated at 900°C even after the soak in the hot water. FT-IR spectra showed that the surface structure of the silica glass was damaged by the ion implantation, but healed by the heat-treatment. These results indicate that this type of glass is promising material for the radiotherapy.

KEY WORDS: Ion implantation/ Phosphorus/ β-emitter/ Radiotherapy/ Cancer/ Silica glass/ Chemical durability

1. INTRODUCTION

Radiotherapy is one of the effective treatment of cancers. External irradiations, however, often cause damages to healthy tissues. Recently, Ehrhardt *et al.* showed that glass microsphere 20 to 30 μm in diameter of the composition Y_2O_3 40, Al_2O_3 20, SiO_2 40 wt% was useful for intra-arterial radiotherapy of cancers.[1~3] Subjected to neutron bombardment, ^{89}Y in the glass is activated to β-emitter ^{90}Y with a half-life of 64.1 h. The glass is insoluble in body fluids and non-toxic. Injected to the liver through the hepatic artery, the glass microsphere are entrapped in the capillary bed of liver tumors and give large local radiation dose of the short-ranged, highly ionizing β-ray to the tumors, with little radiation to neighboring organs. For this treatment, β-rays are the best suitable because of its much shorter radiation range than γ-rays and also because of no possibility to activate any nuclides unlike α-rays. The glass microspheres are successfully subjected to clinical trials for liver cancer treatment.[4~10]

However, the short half-life of 64.1 h for ^{90}Y may result in the substantial decay before the

* 八尾 健, 村下良雄, 川下将一, 小久保 正: Division of Materials Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606.
** 高岡義寛, 山田 公: Ion Beam Engineering Experimental Laboratory, Faculty of Engineering, Kyoto University, Kyoto 606.
† On leave from Sumitomo Metal Industries Ltd., Amagasaki, 660.

treatment. ^{31}P with 100% natural abundance can be activated to β-ray only emitting ^{32}P with 14.3 d half-life by neutron bombardment. The biological effectiveness of ^{32}P is about four times as large as that of ^{90}Y. But highly phosphorus-containing glasses prepared by the conventional melting method are usually less chemically durable. To avoid the undesired and dangerous radiation of normal tissues, it is imperative that the ^{32}P stay firmly bound to the glass and that none of ^{32}P dissolved into the blood.

A silica glass has high chemical durability and neither silicon nor oxygen is activated by neutron bombardment. It is expected that phosphorus-containing glasses with high chemical durability could be obtained by phosphorus ion implantation into a silica glass. In the present study, in order to examine potential uses for intra-arterial radiotherapy, a silica glass is ion-implanted with phosphorus followed by heat-treatment at various temperatures. Their chemical durability, the phosphorus distributions and the changes in the surface structure were investigated.

2. EXPERIMENTAL

2.1 Preparation

Rectangular specimens $10\times10\times1\ mm^3$ in size were cut from highly pure silica glass sheets (metallic impurities$<$0.5 ppm, OH$<$100 ppm) made by the vapor-phase axial deposition (Sumiquartz SK-1300, Sumitomo Metal Industries, Ltd., Tokyo, Japan). Phosphorus ions were implanted on both faces of the specimens at a dose of $2\times10^{17}\ cm^{-2}$ under 20 keV. The samples were then heated up to various temperatures from 400 to 900°C at a rate of 5 deg·cm^{-1} and held at the respective temperature for 1 h.

2.2 Soaking test

The samples thus treated were soaked in 20 ml of distilled water at 95°C for 3 to 7 d in a polypropylene bottle, shaken at 3 cm stroke length and 120 min^{-1} frequency. The amounts of phosphorus and silicon leached out from the samples were measured by an inductively coupled plasma atomic emission spectrometer (SPS1500, Seiko Instruments Inc., Tokyo, Japan).

2.3 Analysis

The distributions of phosphorus in the samples were analyzed by the Rutherford Backscattering spectrometry (RBS) with the ion beam analyzer at Radiation Laboratory of Nuclear Engineering using 2 MeV $^4He^+$ ions with 170° incident angle. Surface structures of the samples were analyzed by Fourier transform infrared (FT-IR) spectrometer (SR-5M, Japan Spectroscopic Co. Ltd., Tokyo, Japan) with the reflection angle of 30°.

3. RESULTS AND DISCUSSION

Figure 1 shows the changes in the concentrations of silicon and phosphorus leached out into the water from the as-implanted sample as a function of the soaking time in comparison with the result for the not-implanted silica glass. The silicon concentration for the as-implanted sample was about 5 times as large as that of the not-implanted sample. The phosphorus concentration for the as-implanted sample also appreciably increased with soaking time. It seems that the surface region of the as-implanted sample was damaged by the ion implantation and became more susceptible to leaching.

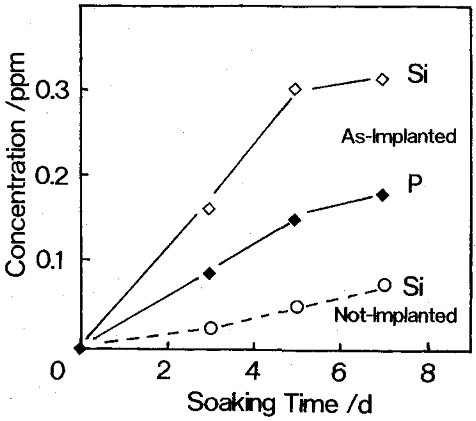

Fig. 1. Change in the concentration of leached silicon and phosphorus as a function of the soaking time. ◇ : silicon and ◆ : phosphorus from the as-implanted sample and ○ : silicon from the not-implanted sample.

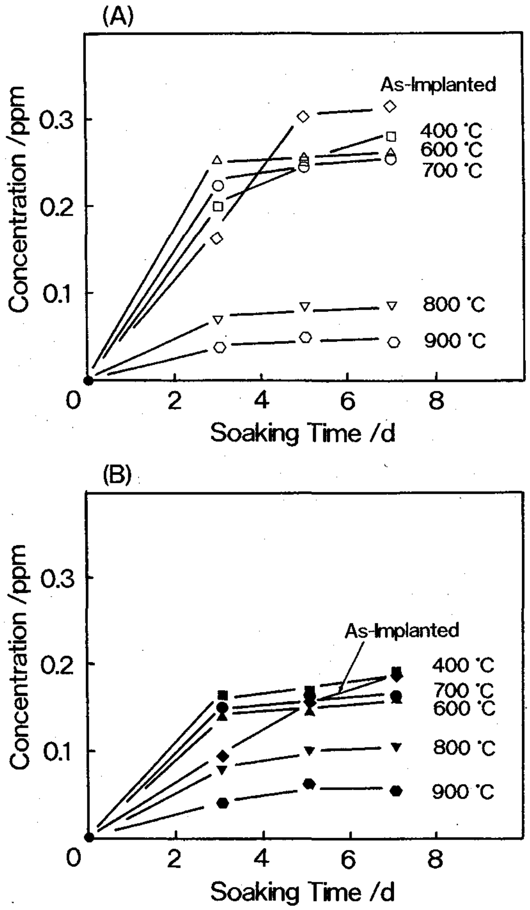

Fig. 2. Change in the concentration of leached (A) silicon and (B) phosphorus from ◇◆ : the as-implanted sample and the sample implanted and heat-treated □■ : at 400°C, △▲ : at 600°C, ○● : at 700°C, ▽▼ : at 800°C, and ⬡⬢ : at 900°C.

Figure 2 shows the effect of the heat-treatment on the concentrations of silicon and phosphorus leached out into the water. Both the silicon and the phosphorus concentrations decreased after the heat-treatment at above 800°C. Especially by the heat-treatment at 900°C, both were reduced to about one-fifth for silicon and about a quarter for phosphorus to that of the as-implanted sample, respectively. This small amount of the leached phosphorus should assure the safe use for the intra-arterial radiotherapy.

Figure 3 shows RBS spectra of the as-implanted sample, the sample implanted and soaked in water for 7 d, and the sample implanted, heat-treated at 900°C and soaked in water for 7 d. The peak of phosphorus was observed in the surface region for the as-implanted sample as shown in figure 3(A), but not observed for the sample implanted and soaked for 7 d as shown in figure 3(B). This indicates that implanted phosphorus in the surface region was released completely into water by the soaking, being consistent with the results of the soaking test. In figure 3(C),

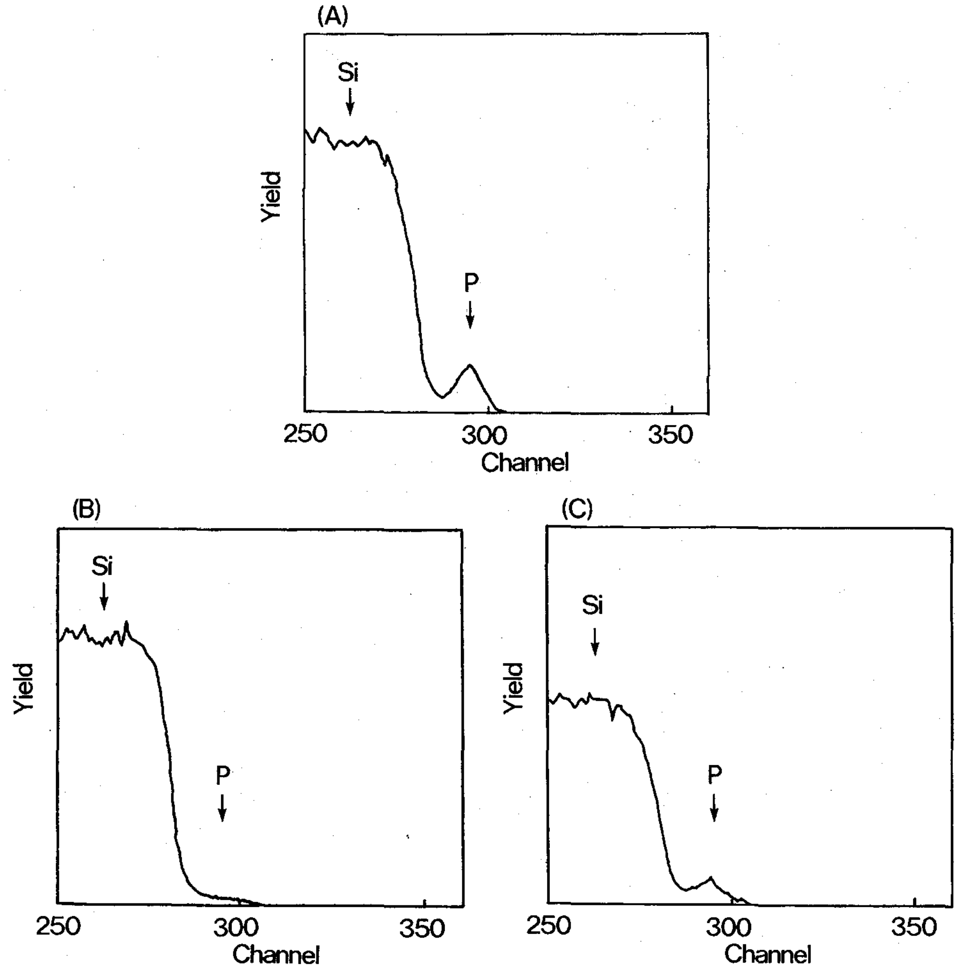

Fig. 3. Rutherford backscattering spectra of (A) the as.implanted sample, (B) the sample implanted and soaked in water for 7 d, and (C) the sample implanted, heat-treated at 900°C and soaked in water for 7 d.

for the sample implanted, heat-treated at 900°C and soaked in water for 7 d, the peak of phosphorus is still observed. It was somewhat broader and weaker than that of the as-implanted sample, probably because part of the phosphorus diffused and/or evaporated during the heat-treatment. It is emphasized, however, that this sample still holds the implanted phosphorus even after the soaking.

Figure 4 shows the FT-IR spectra of the as-implanted sample and the sample implanted and soaked in water for 7 d in comparison with that of the not-implanted original sample. The as-implanted sample showed slightly larger reflectance in a region around 1,000 cm^{-1} assigned to non-bridging oxygen bonded to silicon atom.[11] This indicates that silica network in the surface layer was broken by the ion implantation. This structural damage of the surface layer due to the ion-implantation might be responsible for the decrease in the chemical durability of the silica glass. For the sample implanted and soaked for 7 d, this reflectance disappeared and the profile of the spectrum became nearly the same as that of the not-implanted sample. This suggests that

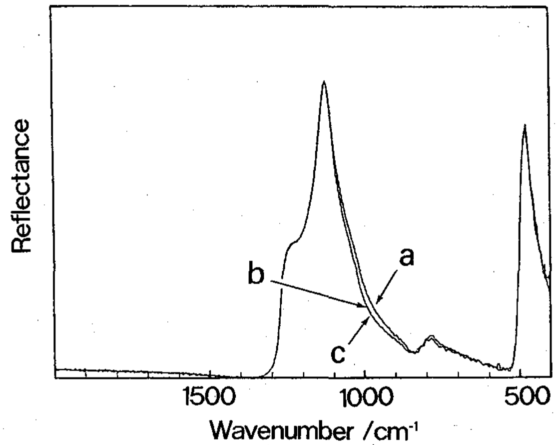

Fig. 4. FT-IR reflection spectra of the as-implanted sample (a→) and the sample implanted and soaked in water for 7 d (b→), compared with that of the not-implanted sample (c→).

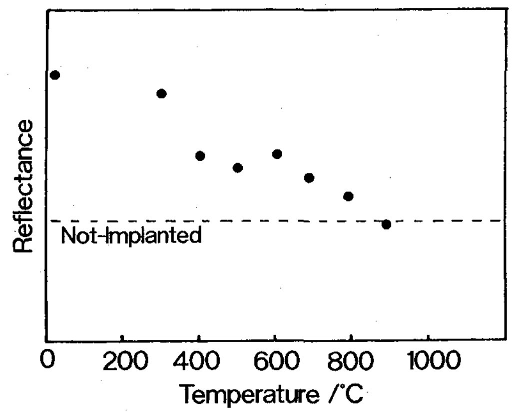

Fig. 5. Change in intensities of FT-IR reflections at 1,000 cm^{-1} as a function of the heat-treatment temperature.

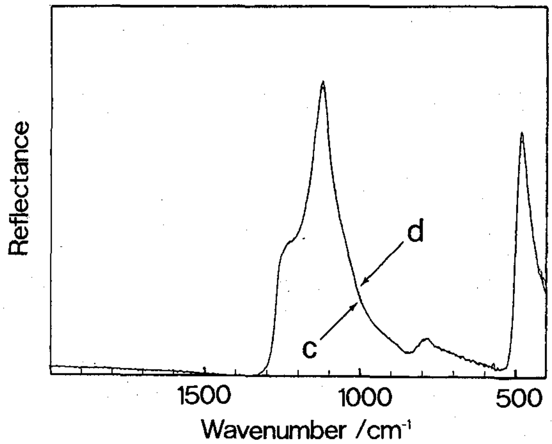

Fig. 6. FT-IR reflection spectra of the sample implanted and heat-treated at 900°C for 1 h (d→) compared with that of the not-implanted sample (c→).

the surface layer structurally damaged by the ion implantation was dissolved by the soaking. Figure 5 shows the change in the intensities of the FT-IR reflection spectra at 1,000 cm^{-1} with the heat-treatment temperature. The reflectance decreased towards the value for the not-implanted sample with increasing temperature of the heat-treatment. The reflectance increase around 1,000 cm^{-1} completely disappeared for the sample heat-treated at 900°C. As shown in figure 6, the FT-IR profile of the sample implanted and heat-treated at 900°C was nearly the same as that of the not-implanted sample. It is considered that the structural damage caused by the ion-implantation at the surface of the glass was healed by the heat-treatment at 900°C and results in the suppression of phosphorus leaching. These results promise the actual use of the phosphorus implanted silica glass for the intra-arterial radiotherapy.

4. CONCLUSION

A silica glass was ion-implanted with phosphorus and subsequently heat-treated at various temperatures up to 900°C. The surface layer of the silica glass was damaged by the ion beam bombardment and became soluble in water. After the heat-treatment at 900°C, the surface damage was healed nearly to that before ion implantation and a phosphorus rich layer was retained just beneath even after the soaking in hot water for 7 d. This process may be successfully applied to provide phosphorus containing and chemically durable microspheres for the intra-arterial radiotherapy.

ACKNOWLEDGMENT

This work was supported by a Grant-in-Aid for Scientific Research, the Ministry of Education, Science and Culture, Japan.

REFERENCES

(1) G.J. Ehrhardt and D.E. Day, *Nucl. Med. Biol.*, **14**, 233 (1987).
(2) M.J. Hyatt and D.E. Day, *J. Am. Ceram. Soc.*, **70**, 283 (1987).

(3) E.M. Erbe and D.E. Day, *J. Biomed. Mat. Res.*, **27**, 1301 (1993).
(4) J.H. Anderson, J.A. Goldberg, R.G. Bessent, D.J. Kerr, J.H. Mckillop, I. Stewart, T.G. Cooke and C.S. Mcardle, *Radiotherapy and Oncology*, **25**, 137 (1992).
(5) R.V.P. Mantravadi, D.G. Spigos, W.S. Tan and E.L. Felix, *Radiology*, **142**,783 (1982).
(6) F.A. Shepherd, L.E. Rotstein, S.Houle, T.K. Yip, K.Paul and K.W. Sniderman, *Cancer*, **70**, 2250 (1992).
(7) S. Houle, T.K. Yip, F.A. Shepherd, L.E. Rotstein, K.W. Sniderman, E. Theis, R.H. Cawthorn and K. Richmond-Cox, *Radiology*, **172**, 857 (1989).
(8) M.A. Burton, B.N. Gray, C. Jones and A. Coletti, *Nucl. Med. Biol.*, **16**, 495 (1989).
(9) I. Wollner, C. Knutsen, P. Smith, D. Prieskorn, C. Chrisp, J. Andrews, J. Juni, S. Warber, J. Klevering, J. Crudup and W. Ensminger, *Cancer*, **61**, 1336 (1988).
(10) M.J. Herba, F.F. Illescas, G.J. Bones, L. Rosenthall, M. Atri and P.M. Bret, *Radiology*, **169**, 311 (1988).
(11) M.R. Filgueiras, L.T. Torre and L.L. Hench, *J. Biomed. Mat. Res.*, **27**, 445 (1993).