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Preparation of phosphorus-containing silica glass for radiotherapy by co-implantation of phosphorus and nitrogen ions

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P-31 can be activated to β-emitter P-32 with 14.3 days 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. When they are subjected to neutron bombardment and injected around the tumor, they can irradiate directly a cancer without giving radiation to normal tissues. In this study, a pure silica glass was implanted with phosphorus and nitrogen ions by a dose of 5×10^{16} cm^{-2} at 30 and 14 keV, respectively, and subjected to two-step heat treatments at 400 °C in H_2 and then at 900 °C in O_2. In the first step, phosphorus colloids were grown in the silica glass. In the second step, the colloids were encapsulated in a SiO_2–P_2O_5 glass film formed at their surfaces and the structural damage produced by ion implantation was healed. It is speculated that the implanted nitrogen forms silicon oxynitride in the glass, strengthening the silica network and suppressing the evaporation of phosphorus during heat treatment. The prepared glass did not dissolve phosphorus or silicon, even after soaking in distilled water at 95 °C for 7 days, and hence is believed to be useful for radiotherapy of cancers.

1. Introduction

Radiotherapy is an effective treatment of cancers. External irradiation, however, often causes damages to healthy tissues. Recently, it has been reported that a glass microsphere 20 to 30 μm in diameter of $40Y_2O_3$–$20Al_2O_3$–$40SiO_2$ (wt %) composition is useful for *in situ* irradiation of cancers [1–3]. Y-89 in the glass can be activated to β-emitter Y-90 with a half-life of 64.1 h by neutron bombardment. The glass is insoluble in body fluids and is non-toxic. Injected into tumours through the hepatic artery, the glass microspheres are trapped in the capillary bed of the tumours and can give a large local radiation dose of short-range highly ionizing β-rays to the tumours with little radiation to neighbouring organs. The glass has been used for clinical trials of the irradiation of diseased kidneys and malignant tumors in the liver, radiation synovectomy of arthritic joints, and so on. [4–11].

The short half-life of 64.1 h for Y-90, however, may result in substantial decay before effective treatment [12]. P-31 with 100% natural abundance similar to Y-89 can be activated to β-emitter P-32 with a half-life of 14.3 days by neutron bombardment. The biological effectiveness of P-32 is about four times as large as that of Y-90. However, phosphorus-containing glass prepared by the conventional melting method is usually less chemically durable.

Phosphorus ion implantation to a silica glass with high chemical durability is one candidate for resolving this problem, since neither silicon nor oxygen is activated by neutron bombardment. Recently, the authors found that a silica glass as-implanted with P^+ ions at 30 keV by 5×10^{16} cm^{-2} dissolved an appreciable amount of phosphorus and silicon in distilled water at 95 °C, but the dissolution of both elements was considerably reduced by two-step heat treatments of the implanted glass; 400 °C in H_2 then 900 °C in O_2 [13, 14]. An appreciable amount of implanted phosphorus, however, evaporated from silica glass during the heat treatments.

It is known that the incorporation of nitrogen into oxide glasses strengthens the glass network [15]. Therefore, nitrogen ion implantation in combination with phosphorus ion implantation is expected to decrease evaporation of phosphorus after implantation. In the present study, a silica glass was implanted with nitrogen ions and phosphorus ions and then subjected to the above two-step heat treatments under different atmospheres. Phosphorus contents and chemical durabilities of the prepared glasses were examined.

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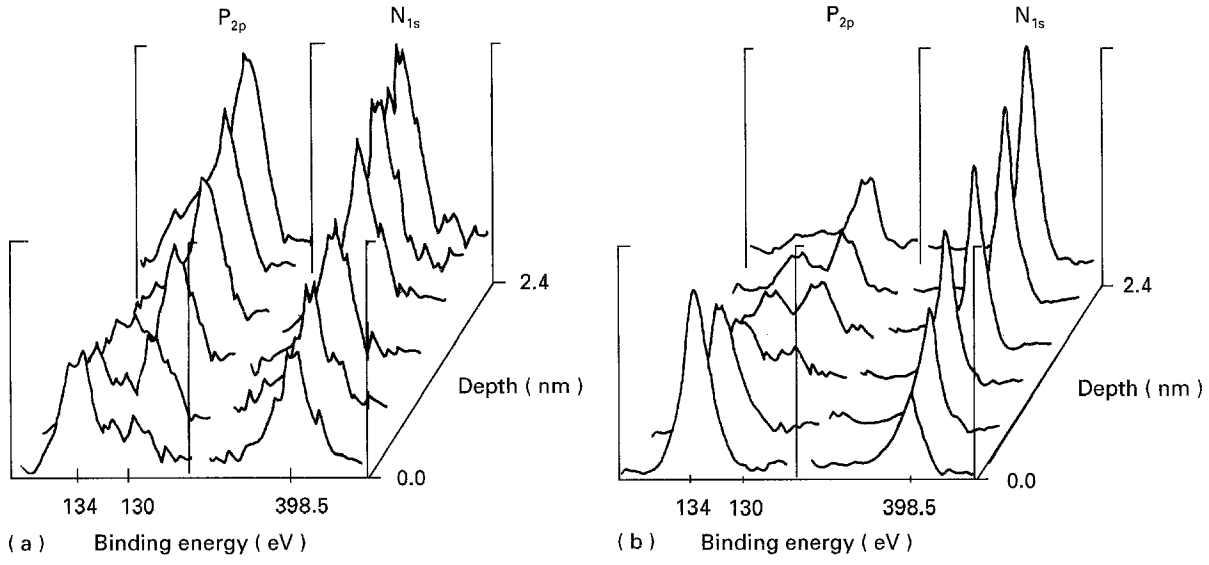

Figure 1 P_{2p} and N_{1s} XPS spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses.

The results are discussed in terms of the surface structure of the glasses.

2. Experimental procedures

2.1. Ion implantation

Highly pure silica glass (metallic impurities < 0.5 ppm, OH < 100 ppm) prepared by vapour-phase axial deposition (SUMIQUARTZ SK-1300, Sumitomo Metal Industries Ltd., Tokyo, Japan) was cut into rectangular specimens 10 mm × 10 mm × 1 mm in size, and annealed at 1100 °C for 1 h in a SiC electric furnace in order to eliminate the strains. The glass was implanted with equal doses of 5×10^{16} cm^{-2} of phosphorus and nitrogen ions at 30 and 14 keV, respectively. It is theoretically estimated that both ions show a Gaussian distribution having maximum concentrations at about 30 nm depth from the surface of the silica glass under these implantation energies [16]. Two kinds of samples were prepared by exchanging the order of implantation; nitrogen followed by phosphorus (N^+, P^+) and phosphorus followed by nitrogen (P^+, N^+). After ion implantation, every sample was preserved in a nitrogen atmosphere in order to prevent surface oxidation of phosphorus.

2.2. Heat treatment

The implanted samples were heated to 400 °C at a rate of 5 °C min^{-1} under an atmosphere of H_2 at 1.0×10^5 Pa and maintained at this temperature for 2 h, then heated to 900 °C at a rate of 5 °C min^{-1} under an atmosphere of O_2 at 1.0×10^5 Pa and kept at this temperature for 2 h.

2.3. Soaking in hot water

The samples thus treated were soaked in 20 ml of distilled water at 95 °C for 7 days in a polypropylene bottle, shaken at 3 cm stroke length and 120 min^{-1} frequency. The amounts of phosphorus and silicon dissolved from the samples were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

2.4. Analysis of structure of glass

The distributions of phosphorus in the glass were measured by Rutherford backscattering spectrometry (RBS) with the ion beam analyser at the Radiation Laboratory of Nuclear Engineering, Kyoto University, using 2 MeV $^4He^+$ ions with 170° incident angle. Surface structures of the samples were analysed by a Fourier transform infrared (FT-IR) reflection spectrometer (SR-5M, Japan, Spectroscopic Co. Ltd., Tokyo, Japan) with 30° reflection angle. The states of the phosphorus and the nitrogen were investigated by measuring P_{2p} and N_{1s} binding energies with an X-ray photoelectron spectroscope (XPS) (MT-5500, ULVAC-phi Co. Ltd., Chigasaki, Japan) using MgK_α (1253.6 eV) X-rays as the excitation source and at 10^{-9} Pa residual pressure. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. Measured binding energies were corrected by reference to the binding energy of carbon 1s of the hydrocarbon (284.6 eV) adsorbed on the sample surfaces.

3. Results and discussion

Fig. 1 shows the P_{2p} and N_{1s} XPS spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses as a function of depth from the surface. Two P_{2p} peaks at 130 and 134 eV were observed at the surface of the N^+, P^+-implanted sample, and only one P_{2p} peak at 134 eV was observed at the surface of the P^+, N^+-implanted sample. The binding energies of 130 and 134 eV coincide with those for elemental red phosphorus and oxidized phosphorus in hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), respectively. With increasing depth, the intensity of the peak ascribed to the elemental phosphorus increased while that ascribed to the oxidized phosphorus decreased for both samples. This indicates that most of the implanted phosphorus exists

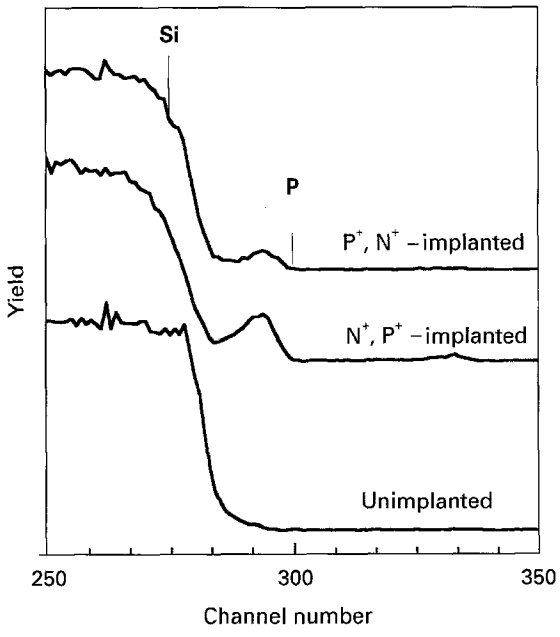

Figure 2 RBS spectra of N^+, P^+- and P^+, N^+-implanted silica glasses, and unimplanted silica glass.

as elemental phosphorus in the glass, but a part of it is oxidized at the surface by the atmospheric oxygen. The implanted samples were coloured brown. This coloration is attributed to the formation of phosphorus colloids [17].

The N_{1s} peak was observed at 398.5 eV for both samples. Carnera *et al.* reported that a N_{1s} peak in silicon oxynitride (SiO_xN_y) was observed at 398.6 eV [18], which is very close to the present value. It is therefore speculated that the implanted nitrogen exists as silicon oxynitride in the glass.

Fig. 2 shows the RBS spectra of N^+, P^+- and P^+, N^+-implanted silica glasses and unimplanted silica glass. The peak area of phosphorus in the P^+, N^+-implanted sample was smaller than that in the N^+, P^+-implanted sample. This indicates that the previously implanted phosphorus was sputtered out during implantation of the nitrogen ion in the case of the P^+, N^+-implanted sample.

Fig. 3 shows the FT-IR reflection spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses, in comparison with that of the unimplanted original glass. Both the as-implanted samples showed slightly larger reflectance than the unimplanted glass in a region around 1000 cm^{-1}, which is assigned to the vibration between non-bridging oxygen and silicon atoms [19]. This indicates that the silica network near the surface

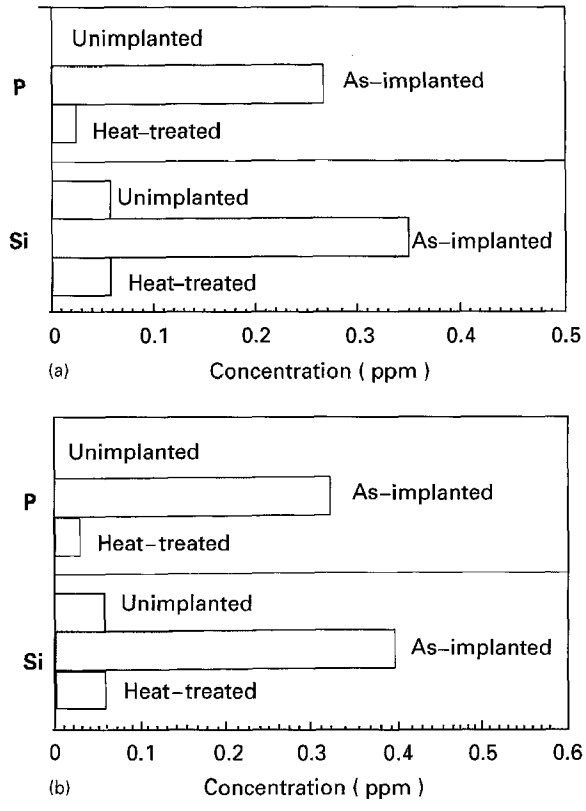

Figure 4 Concentrations of P and Si dissolved from as-implanted samples (□) and their heat-treated samples (■) of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses into water at 95 °C over 7 days, in comparison with those from the unimplanted silica glass (□).

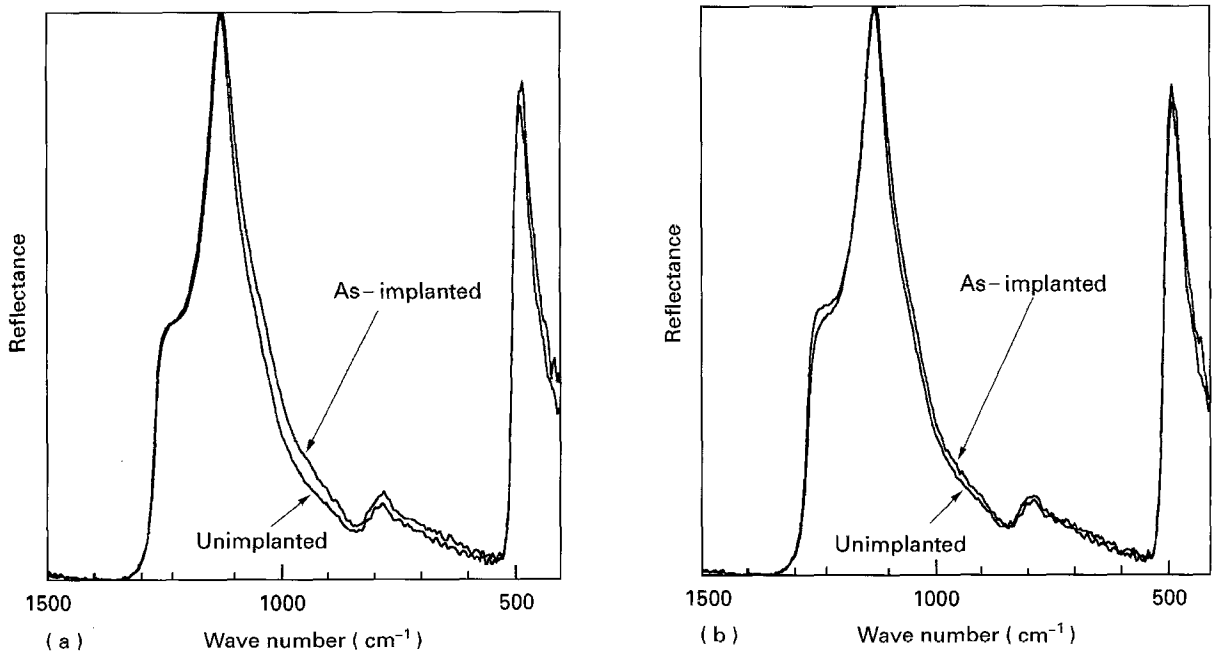

Figure 3 FT-IR reflection spectra (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses, in comparison with that of the unimplanted silica glass.

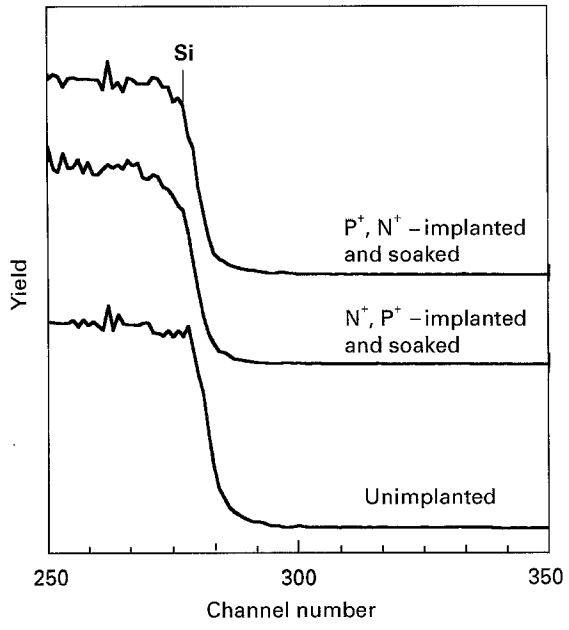

Figure 5 RBS spectra of N^+, P^+- and P^+, N^+-implanted silica glasses soaked in water at 95 °C for 7 days, in comparison with that of the unimplanted silica glass.

of the glass was considerably broken by the ion implantation. The degree of increase in reflectance is smaller in the P^+, N^+-implanted sample than in the N^+, P^+-implanted sample. This suggests that surface structural damage or strain was decreased by the partial sputtering of the surface layer of the glass during nitrogen ion implantation.

Fig. 4 shows the concentrations of phosphorus and silicon dissolved from (a) N^+, P^+- and (b) P^+, N^+-implanted silica glass into water at 95 °C over 7 days, in comparison with those from unimplanted original glass. It can be seen that for the original silica glass only a small amount of silicon and no phosphorus was dissolved, but that for N^+, P^+- and P^+, N^+-implanted glasses appreciable amounts of phosphorus as well as silicon, were dissolved.

Fig. 5 shows the RBS spectra of N^+, P^+- and P^+, N^+-implanted samples soaked in distilled water at 95 °C for 7 days. As can be seen, no peak of phosphorus are observed for both samples, indicating that the implanted phosphorus completely dissolved into the water during soaking. This might be attributed to the formation of a chemically less-durable oxidized phosphorus at the glass surface and to surface structural damage of the glass caused by the ion implantation.

Concentrations of phosphorus and silicon dissolved from (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses subjected to two-step heat treatments at 400 °C in H_2 then 900 °C in O_2 are also shown in Fig. 4. Dissolution of phosphorus and silicon was significantly decreased by the two-step heat treatments for both samples.

Fig. 6 shows the RBS spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses which were heat-treated and soaked in distilled water at 95 °C for 7 days. It can be seen that most of the implanted phosphorus remained in both the heat-treated samples, even after the soaking.

The effects of the two-step heat treatment after ion-implantation are speculated to be as follows [13, 14]. When the N^+, P^+- and P^+, N^+-implanted silica glasses are first heat-treated at 400 °C (below the sublimation point of red phosphorus) in H_2 atmosphere, the phosphorus colloids grow larger without oxidation, and then when they are heat-treated at

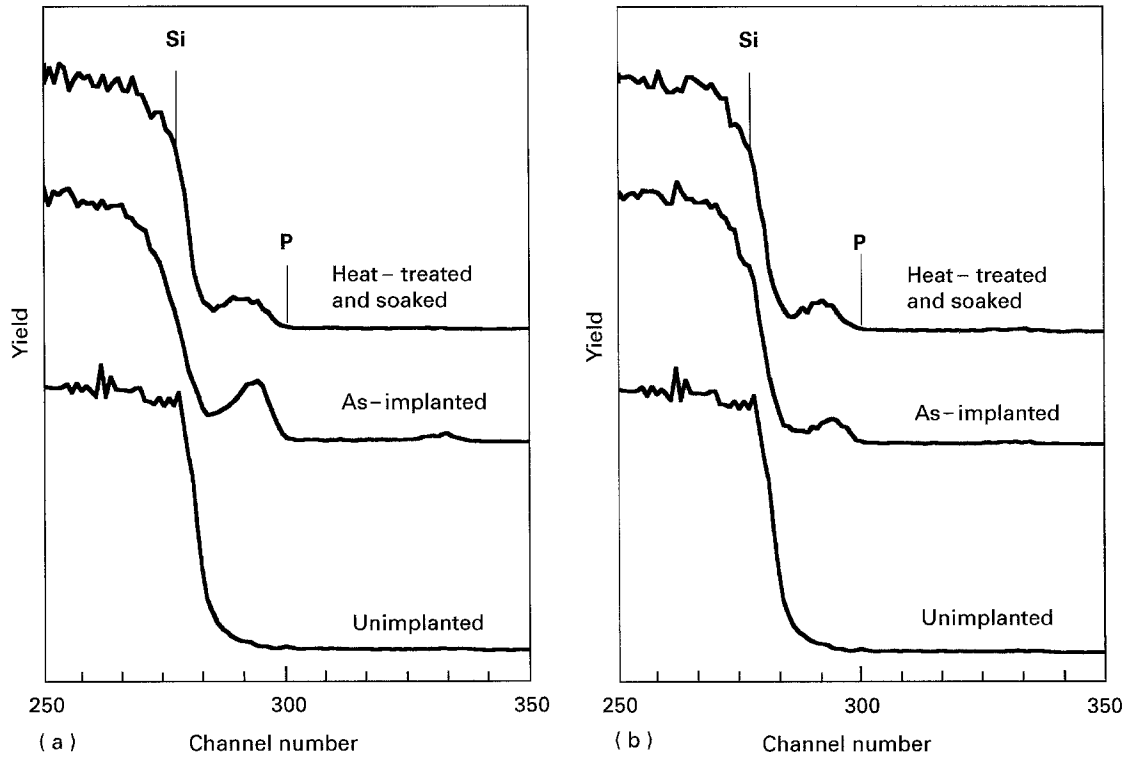

Figure 6 RBS spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses which were heat-treated and soaked in water at 95°C for 7 days, in comparison with that of the unimplanted silica glass.

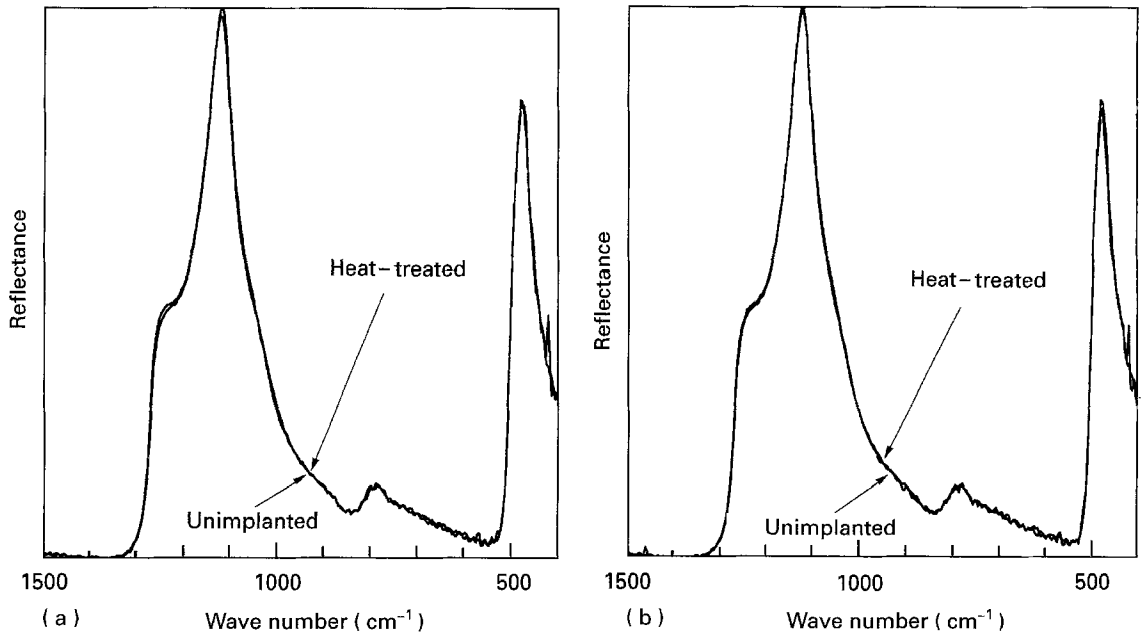

Figure 7 FT-IR reflection spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses which were heat-treated, in comparison with that of the unimplanted silica glass.

900 °C in O_2 atmosphere, the phosphorus colloids are oxidized at their surfaces to be encapsulated by the resulting thin SiO_2–P_2O_5 layer, and simultaneously the structural damage at the surface was healed. In fact, both the N^+, P^+- and P^+, N^+-implanted silica glasses remained coloured brown, showing the presence of phosphorus colloids even after heat treatment.

Fig. 7 shows the FT-IR reflection spectra of (a) N^+, P^+- and (b) P^+, N^+-implanted silica glasses subjected to the two-step heat treatments, in comparison with that of unimplanted original glass. The spectra of the two-step heat-treated samples were identical to that of the original silica glass. This proves the speculation that the structural damage at the surface of the glass caused by ion implantation was healed by the heat treatment.

The amount of the phosphorus remaining in the N^+, P^+- and P^+, N^+-implanted silica glasses after heat treatment and soaking was almost equal to that present in the as-implanted samples, as can be seen from Fig. 6, whereas the amount of phosphorus remaining in the silica glass implanted with P^+ ion alone after the same heat treatment and soaking was lower than that in the as-implanted samples [13, 14]. This is interpreted as follows. Evaporation of the phosphorus during heat treatment was suppressed by strengthening of the silica network due to formation of silicon oxynitride in the former glasses, whereas evaporation was prominent in the latter glasses.

In conclusion, silica glass implanted with phosphorus ions in combination with nitrogen ions and then subjected to two-step heat treatment is a promising material for radiotherapy because of its high phosphorus content and chemical durability.

4. Conclusions

Nitrogen and phosphorus ions implanted into a silica glass at 30 and 14 keV, respectively, formed mainly elemental phosphorus colloids and silicon oxynitride, respectively. As-implanted glass was chemically less durable, since part of the implanted phosphorus was oxidized at the surface, and the surface structure of the glass was damaged by ion implantation. Phosphorus colloids were grown by a heat treatment at 400 °C in H_2 atmosphere, and then the colloids were oxidized at their surfaces to be encapsulated in a thin SiO_2–P_2O_5 glass layer and the surface structural damage was healed by subsequent heat treatment at 900 °C in O_2 atmosphere. Evaporation of phosphorus during the heat treatment was suppressed by the silicon oxynitride structure. Consequently, thus heat-treated glass kept most of the implanted phosphorus and little phosphorus or silicon dissolved into water at 95°C. The resultant glass is believed to be useful for direct radiotherapy of deep cancers.

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