Si⁺ and N⁺ ion implantation for improving blood compatibility of medical poly(methyl methacrylate)

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Abstract. Si⁺ and N⁺ ion implantation into medical poly(methyl methacrylate) (PMMA) were performed at an energy of 80 keV with fluences ranging from 5×10^{12} to 5×10^{15} ions/cm² at room temperature to improve blood compatibility. The results of the blood contacting measurements *in vitro* showed that the anticoagulability and anticalcific behaviour on the surface morphology were enhanced after ion implantation. No appreciable change in the surface morphology was detected by scanning electron microscopy (SEM). X-ray photoelectron spectroscopy (XPS) analysis indicated that ion implantation broke some original chemical bonds on the surface to form some new Si- and N-containing groups. These results were considered responsible for the enhancement in the blood compatibility of PMMA.

Keywords. Ion implantation; poly(methyl methacrylate); blood compatibility.

1. Introduction

The major clinical problem faced in using biomaterials for implantation in body is their blood compatibility (Courtney *et al* 1994; Ikada 1994). When biomaterials come into contact with internal tissues of body, blood coagulation i.e. thrombosis, may take place. The interaction of a biomaterial surface with blood stimulates platelet activation, coagulation and thrombus formation (Ratnoff and Forbes 1984; Mustard and Packham 1997). Thus while considering biomaterials for applications which are in direct contact with blood, one has to take into account the compatibility of the surface of the biomaterials and blood. Of course the causes affecting this compatibility are complex in a clinical situation due to influence of device components, materials utilization, nature of the application, and status of the patient (Murabayashi and Nose 1986; Courtney *et al* 1993; Forbes and Courtney 1994). However, better anticoagulability and anticalcific behaviour of the biomaterials is a basic prerequisite for research and design of a surface possessing good blood compatibility.

Many studies have shown that ion implantation is a useful method for surface modification of solids. Its applications in semiconductor, metal, and ceramic have achieved great success (Dearnaly *et al* 1973; Iwaki 1989; Nakao *et al* 1992). A great advantage of this technique is that the space localization of the dopant can be precisely controlled. Since thickness of the surface layer affected by ion implantation does not exceed several

micrometers, the bulk properties of exposed materials are practically not changed. In recent years, there have been some reports on the improvement in the blood compatibility (Suzuki *et al* 1991; Li *et al* 1993, 1997; Li and Zhao 1994a, b, 1995; Koh *et al* 1996) and tissue compatibility (Suzuki *et al* 1994; Lhoest *et al* 1995; Nakao *et al* 1996) of biomedical polymers on ion implantation. In previous papers (Li *et al* 1993, 1997; Li and Zhao 1994a, b), we have shown that the coagulation and recalcification time for Si⁺ or O⁺ ion-implanted medical polyurethane were increased dramatically as the fluence increased, the number and deformation of the red cells which adhered on the surface showed a decrease with optimum ion fluence of 2×10^{14} ions/cm².

As an extension of the previous work, we have studied the influence of Si⁺ and N⁺ ion implantation on the anticoagulability and the anticalcific behaviour of medical poly(methyl methacrylate) (PMMA), and to investigate changes in chemical structure, atomic composition, and morphology of the implanted surface by means of X-ray photoelectron spectroscopy (XPS), and scanning electron microscopy (SEM), respectively.

2. Experimental

The samples used were medical grade PMMA (made in Guangdong Medicines and Health Products Imp. and Exp. Corp., Guangdong, China) each with a diameter of 8 mm and a thickness of 3 mm. The samples were cleaned sequentially in an ultrasonic bath of soap solution for 10 min, then in ethyl alcohol and finally in isopropyl alcohol prior to ion implantations.

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Si^+ and N^+ ion implantations were carried out at an energy of 80 keV with the ion fluences ranging from 5×10^{12} to 5×10^{15} ions/cm² at room temperature using a ion implanter (ZLZ-200, China). Under identical conditions the two sides of the samples were implanted with the ions. In order to avoid the decomposition and softness of samples due to PMMA to be softened at 80°C, the beam current density was controlled under 0.2 $\mu\text{A}/\text{cm}^2$ to make the target temperature < 80°C. The pressure in the target chamber was kept at 5×10^{-4} Pa during ion implantations.

The anticoagulable behaviour of the samples was investigated by measuring the time taken for blood coagulation when the samples were in contact with blood of rabbit. Venous blood (1.5 ml) of rabbit was injected into a sterile test tube containing the sample, and the test tube was placed immediately in the water bath orbited shaker (Certomat-WK, Germany), at identical frequency and 37°C. The measured interval time from injecting blood into the test tube to its clotting is considered to be the coagulation time. The anticalcific behaviour of the samples was investigated by measuring the recalcification time. 4 ml blood from rabbit heart and 36 ml sodium citrate (3.8%) were placed in a sterile container, and centrifuged at 3000 rev.min⁻¹ for 10 min to obtain plasma. Plasma (0.5 ml) was injected into a sterile test tube containing the sample to which 0.5 ml CaCl_2 solution was injected. The test tube was shaken in shaker at identical frequency. The measured interval time from injecting CaCl_2 solution into the test tube to finding white particles in the plasma is considered to be the recalcification time. Two blood compatibility properties for evaluating blood compatibility were determined immediately after ion implantations.

XPS results were obtained with a multi-technique electron spectrometer (VGESCALAB 5, England) equipped with an Aluminum anode (10 kV, 20 mA). In order to investigate the surface chemical states and atomic composition, a scan of C_{1s} , N_{1s} , O_{1s} , and Si_{2p} lines was performed with a pass energy of 50 eV, a step size of 0.05 eV, and a scan time of 100 s. The pressure in the sample chamber was kept below 10^{-6} Pa. Charging of the samples, due to photoemission, was corrected by setting the energy of main hydrocarbon component of C_{1s} spectra at 284.7 eV. Curve fitting of the spectra was done using a Gaussian and Lorentzian peak shape. The morphology of the surface was observed by SEM (X-650, Japan).

3. Results and discussion

3.1 Coagulation time change

Figure 1 shows effect of the ion fluence on the coagulation time when Si^+ and N^+ ions are implanted into the surface at a fixed energy of 80 keV. Each value in the figure

is an average value of five measurements (± 0.1 min). The open circle (O) line represents the change in the coagulation time with the various fluences of Si^+ ion. The PMMA sample before the ion implantations has a 4.3 min coagulation time, its value gradually increases to 6.7 min as the fluence increases. However, when the fluence is over 5×10^{13} ions/cm², there is gradual decrease in the coagulation time. It is clear from this result that Si^+ ion implantation can result in a longer coagulation time, i.e. enhanced anticoagulability.

The coagulation time change shows a similar result for N^+ -implanted samples with various fluences as shown in figure 1. The coagulation time increases from 4.3 to 5.7 min with increasing ion fluence. When the ion fluence is over 5×10^{14} ions/cm², the coagulation time tends to decrease. When the ion fluence is over 5×10^{13} ions/cm², ion implantation can lead to enhancement in the anticoagulability of PMMA, which is of importance in its clinical applications. The optimum ion fluence for improving surface anticoagulability is about $\sim 10^{14}$ ions/cm².

3.2 Recalcification time change

Figure 2 shows the relation between the recalcification time, measured immediately after ion implantation, and the ion fluence at a energy of 80 keV. Each value is an average of five measurements (± 0.1 min). From the figure it is apparent that the change in the recalcification time for the ion-implanted samples depends on the ion fluence and the species of the implanted ions. While the recalcification time of pristine sample is 0.4 min, N^+ ion implantation results in a slight increase in the recalcification time with increasing fluence, reaching a

Figure 1. Coagulation time vs ion fluence at 80 keV.

value of 0.9 min. However, its value reveals a tendency to decrease when the fluence is over 5×10^{13} ions/cm².

Compared with N⁺ ion implantation, Si⁺ ion implantation causes the recalcification time to increase with increasing fluence, the value gradually increases from 0.4 to 1.6 min as the fluence increases, reaching more than 4 times that of pristine sample. A slight decrease in the recalcification time, however, is observed when the fluence is over 5×10^{13} ions/cm². The above result shows that ion implantation with the fluence of 5×10^{13} ions/cm² can lead to a longer recalcification time, i.e. enhanced anticalcific behaviour. On the whole, Si⁺ ion implantation can result in a more effective improvement in the anticalcific behaviour than N⁺ ion implantation.

3.3 Surface chemical states, radicals, and morphology analysis

The above observations show that Si⁺ and N⁺ ion implantations can result in the improvement of blood compatibility, such as the anticoagulability and the anticalcific behaviour of PMMA. The production of some new Si-containing and N-containing groups on the surface may be responsible for the observed improvement. In order to confirm this hypothesis, XPS study on surface chemical states was performed, because of its great potential and capability to reveal a large quantity of information on the structure and chemical states on the surface of polymers. Figures 3–7 present characteristic C_{1s}, O_{1s}, N_{1s}, and Si_{2p} XPS signals for the samples used for the blood compatibility studies.

As reference, we present in figure 3, together with a representation of the chemical structure of PMMA, C_{1s}

and O_{1s} core-level photoemission spectra of pristine sample. The observed peaks in the spectra correspond to the carbon and oxygen atoms having different bonding states in chemical structure. To analyze the chemical bonding of C and O atoms, C_{1s} and O_{1s} spectra are fitted using a combination of Gaussian and Lorentzian peak shapes. The binding energy and the relative peak area of the fitted peaks are given in table 1. In C_{1s} spectra of figure 3a, the peak at the binding energy of 284.7 eV represents ¹C which is surrounded by neighbouring carbon atoms, the peak at 286.5 eV corresponds to ²C which is bonded to O², and the peak at 289.1 eV corresponds to ³C which is bonded to O¹ and O². From the chemical structure of PMMA we can see that there are three carbons of C–C (including C–H) type, 1 carbon of C–O type, and 1 carbon of C=O type. The result of C–C (C–H):C–O:C=O ratio equals to 60:20:20 and is in agreement with the calculated values of peak area in table 1 (61:22:17). In O_{1s} spectra of figure 3b, the peak at 532 eV is associated with C=O bond, and the peak at 533.6 eV represents C–O bond. The C–O:C=O ratio of 50:50 is consistent with the structure of PMMA.

In the following, the effects of Si⁺ and N⁺ ion

Figure 2. Recalcification time vs ion fluence at 80 keV.

Figure 3. The chemical structure (a) C_{1s} and (b) N_{1s} XPS spectra obtained from pristine.

implantation at a fixed energy of 80 keV with the ion fluence of 5×10^{14} ions/cm² on the surface chemical states and composition are analysed. The calculated atomic composition (%) are given in table 2. It can be seen from figure 4 and table 2 that as the relative intensity of O_{1s} peak is decreased, the atomic composition of oxygen is decreased from 26.2% to 18.3% for Si⁺ ion-implanted sample, and 16.6% for N⁺ ion-implanted sample. Si and N element contents are increased after ion implantation (table 2). These big differences reveal strong changes of surface chemical states. The decrease of oxygen content indicates the decomposition of O-C=O group. In figures 5 and 6, C_{1s} and O_{1s} spectra show detailed chemical modification after ion implantation. The C_{1s} spectra of figure 5a reveals that Si⁺ ion implantation decreases the intensity of two peaks at 286.5 and 289.1 eV, compared to the corresponding peaks obtained from pristine sample (figure 3a). Further, the peak at 289.1 eV decreases much more than the peak at 286.5 eV. This result indicates that Si⁺ ion implantation broke some C=O and C-O bonds on the surface. The reason why C=O bond peak decreases more than C-O bond is because the implanted ion is easier to interact with C=O bond than C-O bond due to higher polarity of C=O bond. According to the principle of ion-dipole

interaction (Israelachvili 1991), the implanted ion can recombine with one electron of C=O group easily and induce the decomposition of C=O bond. Another evidence supporting the decomposition of O-C=O group after Si⁺ ion implantation is obtained by measuring O_{1s} signal. In figure 6a, the big differences observed in the intensity and line shape of O_{1s} spectra also reveal strong changes of O-containing groups. Compared to the corresponding peaks obtained from pristine sample (figure 3b), the intensity of two peaks at 532 and 533.6 eV corresponding to C-O and C=O bonds is decreased after Si⁺ ion implantation, whereas the peak assigned to C=O bond decreases much more. This result is in excellent agreement with that of C_{1s} analysis. Of course, the cleavage of some pendant groups after ion implantation has also occurred, which also contributes to the decomposition of O-C=O group.

Similar results can be observed for N⁺ ion-implanted sample. The difference is that N⁺ ion implantation can

Figure 4. XPS survey spectra obtained from (a) pristine, (b) Si⁺ implanted and (c) N⁺ implanted samples with the fluence of 5×10^{14} ions/cm².

Figure 5. C_{1s} XPS spectra obtained from (a) Si⁺ implanted and (b) N⁺ implanted samples with the fluence of 5×10^{14} ions/cm².

lead to decomposition of C=O bond on the surface than Si⁺ ion implantation (figures 5b and 6b). This result means that the surface chemical states change is related to species of the implanted ion.

We have to analyze the surface chemical states of Si_{2p} and N_{1s}, because the implanted ion is reactive one. Figures 7a and b show Si_{2p} and N_{1s} spectra of Si⁺ and N⁺ ion-implanted samples with the fluence of 5×10^{14} ions/cm² at a fixed energy of 80 keV. Si atoms are absent on the surface of the pristine sample. The increase of Si atomic composition (table 2) is a evidence supporting Si⁺ ion-implanted into the surface. A new peak at 103.6 eV attributed to Si-O bond, although its intensity is weak, is most likely due to the implanted Si incorporation with O of the broken C=O bond. Simi-

larly, reactive N⁺ ion implantation induces the formation of C-N bond on the surface, which is indicated by new peak at 399.9 eV (figure 7b), and increased atomic composition of N (table 2). From the above results, we therefore conclude that Si⁺ and N⁺ ion implantation break some C=O and C-O bonds, and form some new Si-containing and N-containing groups on the surface.

No appreciable change in the surface morphology is observed for the pristine and Si⁺, N⁺ ion-implanted samples with the fluence of 5×10^{14} ions/cm² in SEM analysis. From this observation it can be inferred that

Figure 6. O_{1s} XPS spectra obtained from (a) Si⁺ implanted and (b) N⁺ implanted samples with the fluence of 5×10^{14} ions/cm².

Figure 7. (a) Si_{2p} XPS spectra obtained from Si⁺ implanted samples with the fluence of 5×10^{14} ions/cm² and (b) N_{1s} XPS spectra obtained from N⁺ implanted samples with the fluence of 5×10^{14} ions/cm².

Table 1. Binding energy and relative peak area of the fitted C_{1s} and O_{1s} peaks of pristine.

Peak no.	C _{1s}			O _{1s}	
	¹ C	² C	³ C	O ¹	O ²
Binding energy (eV)	284.5	286.3	288.9	532	533.6
Peak area (%)	61	22	17	50	50

Table 2. Atomic composition for pristine and implanted samples with the fluence of 5×10^{14} ions/cm².

Sample	Atomic composition			
	%C	%O	%N	%Si
Pristine	73.8	26.2	—	—
Si ⁺ implantation	76	18.3	—	4.1
N ⁺ implantation	78.2	16.6	5.2	—

surface roughness is not the main reason for the surface modification. Thus in this work, the reason why the anticoagulability and the anticalcific behaviour are improved after Si⁺, N⁺ ion implantation can be explained using the above results of XPS analysis. It is well known that high adhesion of the platelets to the surface is related to the low anticoagulability of the surface. Further, it will accelerate the deposition of Ca⁺ on the surface. Our studies have shown that Si⁺ and N⁺ ion implantation lead to decomposed O-containing groups such as C=O, C–O bonds and form some new Si–O, C–N bonds on the surface. These changes may be responsible for inhibiting the adhesion of the platelets, and then reducing the deposition of Ca⁺. Other factors, such as the presence of long-lived radicals and implanted Si⁺, N⁺ charged, can also influence the adhesion of the platelets. However, we are not able to ascertain as to which is the main factor. Further experiment is needed to determine the relationship between the adhesion of the platelets to the surface and the ion fluence and the surface chemical states.

4. Conclusion

A study of the surface blood compatibility has been made for Si⁺ and N⁺ ion-implanted PMMA. Ion implantation resulted in some improvement in the anticoagulability and the anticalcific behaviour of the biomaterial. The improved properties of it are related to the fluence and species of the implanted ion. Si⁺ ion implantation led to a more obvious improvement compared with Si⁺ ion implantation. The optimum ion fluence for improving

the blood compatibility is about $\sim 10^{14}$ ions/cm². XPS analysis indicated that ion implantation broke some C=O, C–O bonds and formed some functional groups such as Si–O, C–N bonds. At the same time, the number of Si and N atoms was increased. These changes are believed to be responsible for the enhanced blood compatibility of PMMA.

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