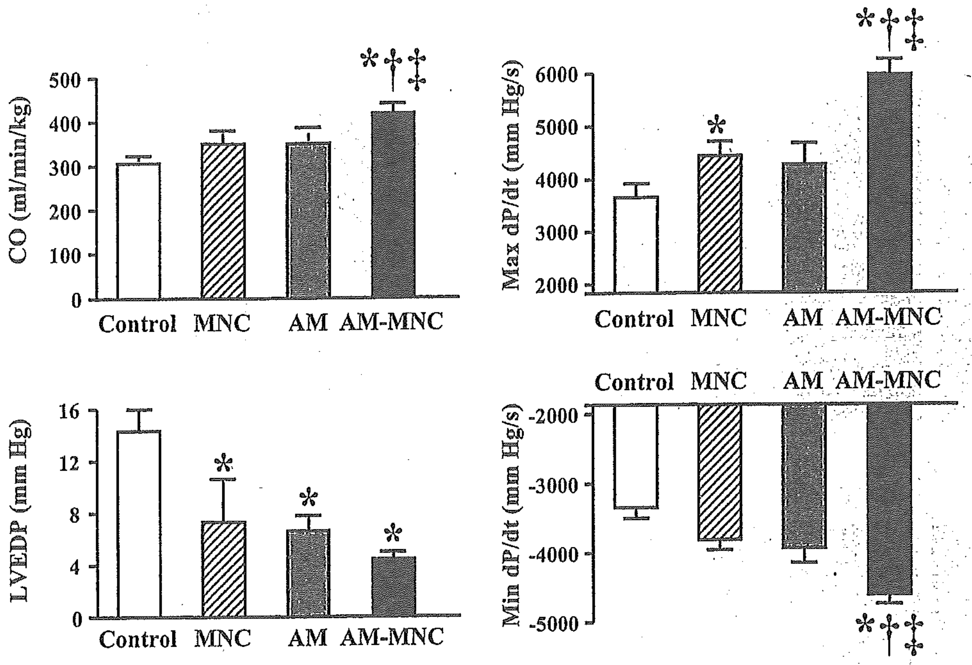

Fig. 2. Effects of AM infusion and MNC transplantation on hemodynamic parameters. CO, cardiac output; LVEDP, LV end-diastolic pressure; Max dP/d*t*, LV maximum change in pressure over time; Min dP/d*t*, LV minimum dP/d*t*. Values are means ± SE. $*P < 0.05$ vs. control; $\dagger P < 0.05$ vs. MNC; $\ddagger P < 0.05$ vs. AM.

were hardly detected in the AM-MNC group. Semiquantitative analysis demonstrated that the number of TUNEL-positive MNC was significantly lower in the AM-MNC group than in the MNC group. Similarly, the number of caspase-3-positive MNC was significantly lower in the AM-MNC group than in the MNC group. These results suggest that infusion of AM inhibits apoptosis of transplanted MNC.

In vitro, serum starvation induced MNC apoptosis. When incubated in the presence of AM (1×10^{-7} M), the percentage of TUNEL-positive cells decreased significantly (19 ± 1 to 9 ± 1%, $P < 0.05$). However, pretreatment with wortmannin, a PI3-kinase inhibitor, diminished the antiapoptotic effect of AM (17 ± 1%).

Differentiation of MNC into endothelial lineage. Four weeks after transplantation, fluorescence-labeled transplanted cells

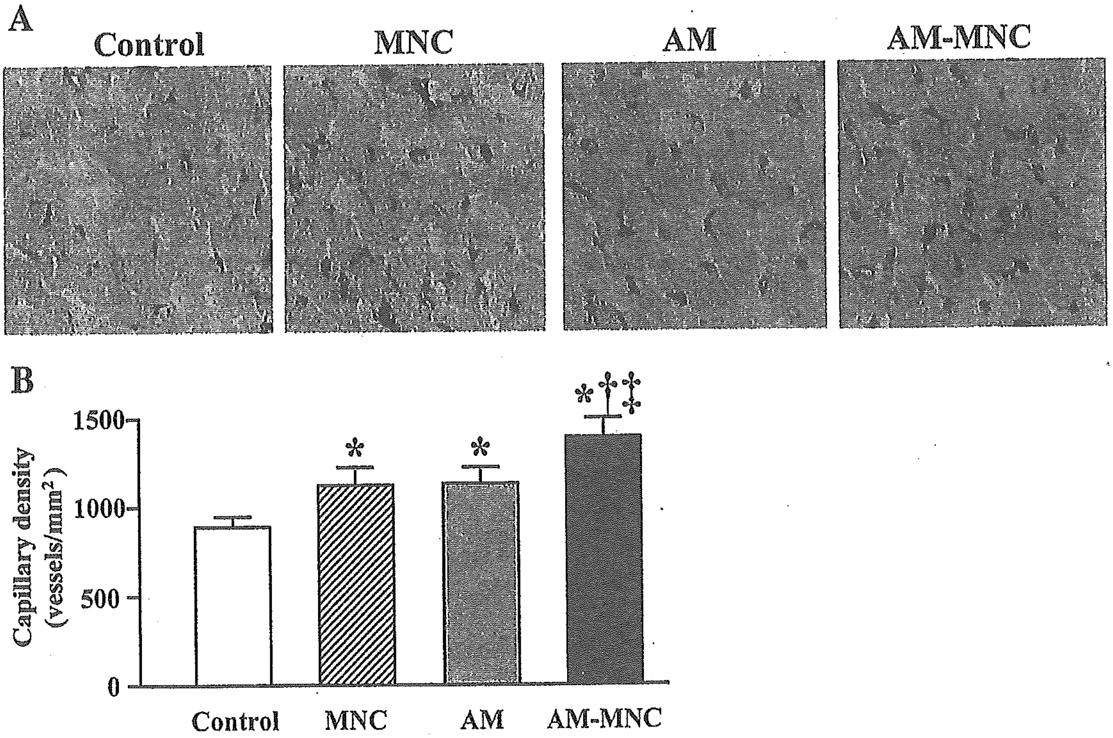

Fig. 3. *A*: representative examples of alkaline phosphatase staining in peri-infarct area. A combination of AM infusion and MNC transplantation markedly induced myocardial neovascularization. Magnification, ×200. *B*: quantitative analysis of capillary density in peri-infarct area. Capillary density in the AM-MNC group was significantly higher than that in the MNC and AM groups. Values are means ± SE. $*P < 0.05$ vs. control; $\dagger P < 0.05$ vs. MNC; $\ddagger P < 0.05$ vs. AM.

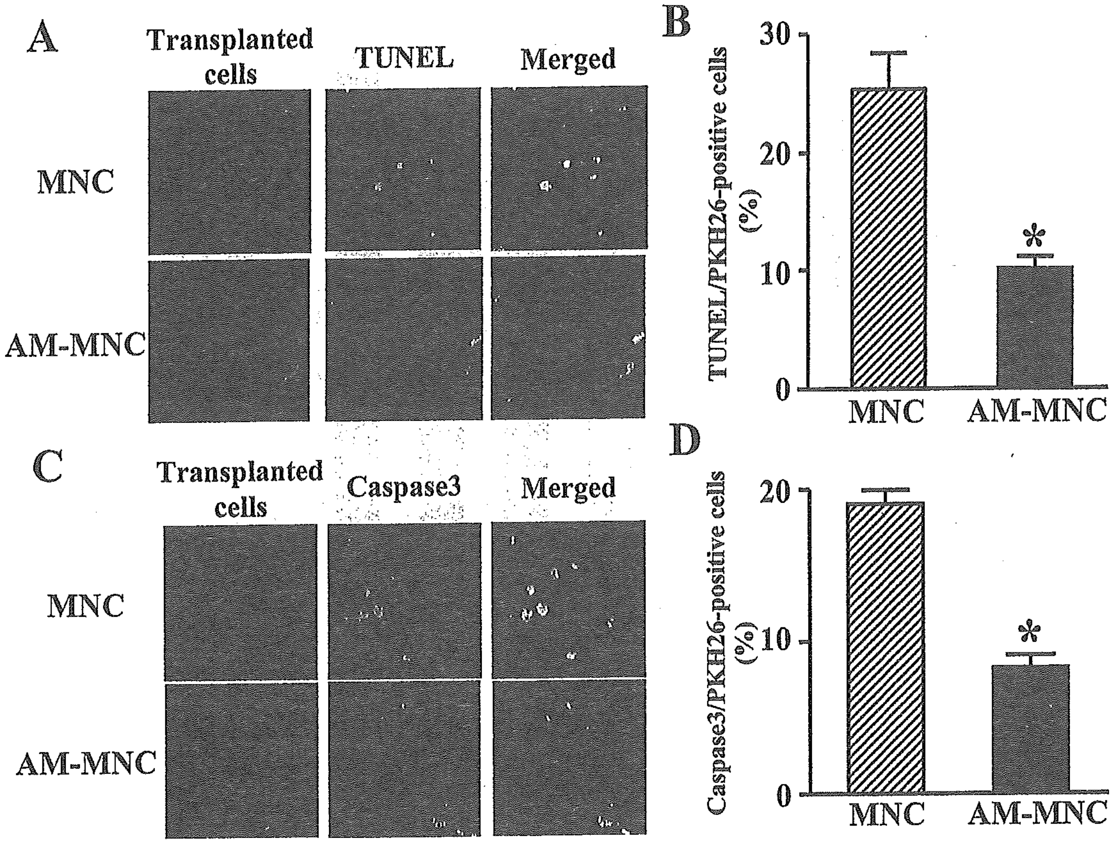

Fig. 4. Detection of transplanted cell apoptosis. *A*: representative photographs of terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) staining. Red fluorescence (PKH26) marks transplanted MNC; green fluorescence indicates TUNEL-positive cells. TUNEL-positive cells were frequently observed in the MNC group, whereas they were hardly detected in the AM-MNC group. Magnification, ×400. *B*: semiquantitative analysis of TUNEL-positive cells in the PKH26-positive (transplanted) cells. *C*: representative photographs of caspase-3 staining. Red fluorescence (PKH26) marks transplanted MNC; green fluorescence indicates caspase-3-positive cells. *D*: semiquantitative analysis of caspase-3-positive cells in the PKH26-positive cells. Values are means ± SE. $^*P < 0.05$ vs. control.

were more frequently observed in the AM-MNC group than in the MNC group (6.4 ± 0.4 to 3.1 ± 0.2%, $P < 0.05$). Moreover, some of the transplanted cells were positive for UEA-1 lectin in the AM-MNC group (Fig. 5*A*), suggesting differentiation of MNC into vascular endothelial cells. Semiquantitative analysis demonstrated that the number of DAPI/PKH26 double-positive cells (viable transplanted cells) was significantly higher in the AM-MNC group than in the MNC group (Fig. 5*B*). Moreover, the ratio of lectin-positive cells to DAPI/PKH26 double-positive cells was significantly higher in the AM-MNC group than in the MNC group. The ratio of DAPI/PKH26 double-positive cells to lectin-positive cells was small, but significantly higher in the AM-MNC group than in the MNC group (23.9 ± 0.9 to 17.2 ± 0.6%, $P < 0.01$). Transplanted MNC were negative for troponin T or α-smooth muscle actin-positive cells. Some of the transplanted MNC were positive for ED1, a marker of macrophage (data not shown).

DISCUSSION

In the present study, we demonstrated that *1*) infusion of AM enhanced the angiogenic potency of MNC in a rat model of acute myocardial infarction, resulting in decreased infarct size and improved cardiac function. We also demonstrated that *2*) AM induced angiogenesis and inhibited apoptosis of the transplanted MNC. Thus a combination of AM and MNC may have beneficial effects in rats with myocardial infarction, partly through the angiogenic potency of AM itself and through its antiapoptotic effect on MNC.

Bone marrow-derived MNC include a variety of stem and progenitor cells (1, 15, 19), some of which can differentiate into endothelial cells and secrete numerous cytokines and chemokines (6, 9, 10). Earlier studies (6, 9, 10, 23, 25) have shown that autologous bone marrow transplantation induces angiogenesis and improves LV function in animals and humans. However, some patients are refractory to this cell therapy. Thus an approach to augment the angiogenic potency of MNC transplantation is required.

The present study showed that MNC transplantation or AM infusion alone reduced infarct size. A combination of AM infusion and MNC transplantation resulted in further decreases in infarct size and LV chamber size. MNC transplantation or AM administration modestly improved LV function. On the other hand, a combination of MNC and AM significantly improved cardiac performance compared with MNC or AM alone, as indicated by increases in cardiac output, fractional shortening, and LV maximum dP/d*t*. Earlier studies (6, 9, 10) have reported that MNC transplantation induces therapeutic angiogenesis and preserves LV function through inhibition of cardiomyocyte apoptosis in animal models of myocardial infarction. We have shown that AM infusion during the acute phase of ischemia-reperfusion inhibits apoptosis of cardiomyocytes and produces hemodynamic improvement in an animal

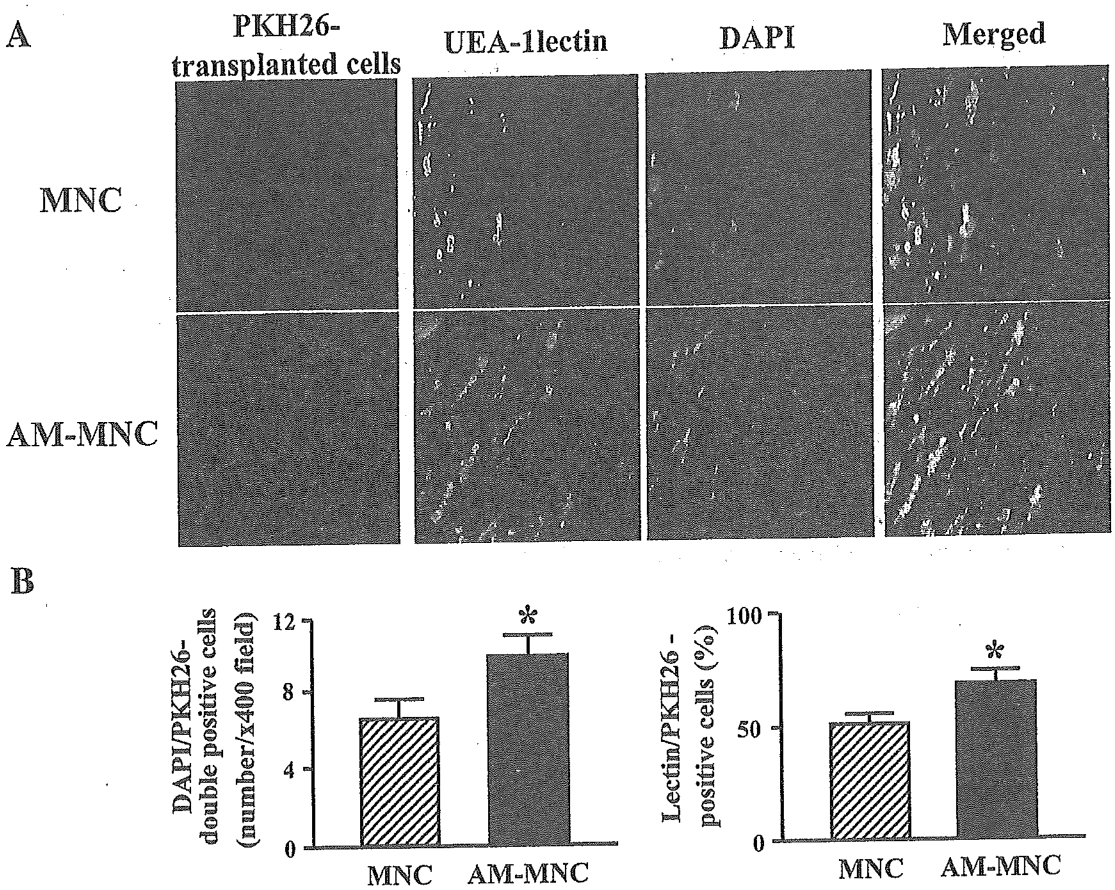

Fig. 5. *A*: representative examples of MNC differentiation into endothelial lineage. Red fluorescence (PKH26) marks transplanted cells; green fluorescence indicates ulex europaeus (UEA)-1 lectin, a marker for vascular endothelial cells. Most of the transplanted cells differentiated into endothelial cells in the AM-MNC group. Magnification, ×400. *B*: quantitative analysis of living transplanted cells and endothelial differentiation. The number of living cells after transplantation was significantly higher in the AM-MNC group than in the MNC group. The ratio of lectin-positive cells to living transplanted cells was significantly higher in the AM-MNC group than in the MNC group. Values are means ± SE. $^*P < 0.05$ vs. control. DAPI, 4′,6′-diamidino-2-phenylindole.

study (18). These findings suggest that the reduction of infarct size induced by this combination therapy may be attributable to additive cardioprotective effects of MNC and AM.

The present study showed that AM infusion significantly increased capillary density in ischemic myocardium. Furthermore, AM infusion plus MNC transplantation demonstrated a further increase in capillary density compared with AM or MNC alone. Contribution of transplanted MNC to neovascularization (the ratio of DAPI/PKH26 double-positive cells to lectin-positive cells) was significantly greater in the AM-MNC group than in the MNC group. A recent study (14) has reported that AM promotes proliferation and migration of human umbilical vein endothelial cells and enhances angiogenesis in a murine gel plug assay through the PI3-kinase/Akt pathway. We have also shown that intramuscular administration of AM DNA induces therapeutic angiogenesis in a rabbit model of chronic hindlimb ischemia via activation of Akt (24). These findings suggest that the beneficial effects of combination therapy using AM and MNC may be attributable, in part, to the angiogenic properties of AM itself. Thus it is possible that AM infusion and MNC transplantation induce additive effects on myocardial damage after myocardial infarction. However, it still remains unknown whether AM infusion plus MNC transplantation induces synergetic effects.

An earlier study has demonstrated that ischemia and mechanical stress induce apoptosis of transplanted cells in the early stage after MNC transplantation (9). These results raise the possibility that the angiogenic potency of MNC transplantation is attenuated by MNC apoptosis. Kim et al. (7) have demonstrated that AM inhibits apoptosis of endothelial cells through the PI3-kinase/Akt pathway in vitro. Activation of the PI3-kinase/Akt pathway has been shown to inhibit apoptosis of endothelial progenitor cells and enhance neovascularization (11). In the present study, AM infusion significantly inhibited MNC apoptosis in ischemic tissue. In vitro, we showed that the antiapoptotic effect of AM on MNC was mediated by activation of the PI3-kinase/Akt pathway. Thus AM may enhance the therapeutic potency of MNC transplantation through a direct action of AM on MNC survival. Moreover, immunohistological examination demonstrated that infusion of AM increased the number of lectin-positive (endothelial) cells in transplanted MNC. These findings raise the possibility that AM may enhance differentiation of MNC into the endothelial lineage. Thus AM may directly act on transplanted MNC, which may result in synergetic effects on the ischemic myocardium.

This study includes some study limitations. Although the labeling efficacy of PKH26 has been shown to persist for >8 wk without cell toxicity (3, 4), the used vital marker PKH26 may have some cell toxic effects and cell or membrane fusion can lead to labeling of neighboring cells in the target tissue. Second, the present study demonstrated that AM prolongs MNC survival through the PI3-kinase/Akt pathway and enhances neovascularization in a peri-infarcted area. However, further studies are necessary to examine the effect of AM on MNC differentiation into endothelial cells.

Autologous cell transplantation may be an alternative treatment for ischemic heart disease in the clinical setting. Because their use does not require immunosuppression, the clinical use of MNC for cellular cardiomyoplasty appears to be most advantageous. Administration of AM peptide is simple and relatively noninvasive. We and others (12, 16, 17) have reported the safety of AM infusion in humans. Thus combination therapy using AM infusion and MNC transplantation may be a new therapeutic strategy for the treatment of ischemic heart disease.

In conclusion, infusion of AM enhanced the angiogenic potency of MNC transplantation and improved cardiac function in rats with myocardial infarction. This beneficial effect may be mediated partly by the angiogenic property of AM itself and by its antiapoptotic effect on MNC. Thus combination therapy using AM infusion and MNC transplantation may be a new therapeutic strategy for the treatment of ischemic heart disease.

GRANTS

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Honorable Mention Poster Award

High-speed K-edge angiography achieved with tantalum K-series characteristic x rays

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ABSTRACT

The tantalum plasma flash x-ray generator is useful in order to perform high-speed K-edge angiography using cone beams because Kα rays from the tantalum target are absorbed effectively by gadolinium-based contrast media. In the flash x-ray generator, a 150 nF condenser is charged up to 80 kV by a power supply, and flash x rays are produced by the discharging. The x-ray tube is a demountable diode, and the turbomolecular pump evacuates air from the tube with a pressure of approximately 1 mPa. Since the electric circuit of the high-voltage pulse generator employs a cable transmission line, the high-voltage pulse generator produces twice the potential of the condenser charging voltage. When the charging voltage was increased, the K-series characteristic x-ray intensities of tantalum increased. The K lines were clean and intense, and hardly any bremsstrahlung rays were detected. The x-ray pulse widths were approximately 100 ns, and the time-integrated x-ray intensity had a value of approximately 300 μGy at 1.0 m from the x-ray source with a charging voltage of 80 kV. Angiography was performed using a film-less computed radiography (CR) system and gadolinium-based contrast media. In angiography of non-living animals, we observed fine blood vessels of approximately 100 μm with high contrasts.

Keywords: angiography, gadolinium-based contrast media, characteristic x rays, quasi-monochromatic x rays, tantalum Kα photons

1. INTRODUCTION

The successful uses of monochromatic parallel beams from synchrotron orbital radiation in recent years have greatly increased the demand for phase-contrast radiography[1-3] and enhanced K-edge angiography.[4-6] In particular, the parallel beams with photon energies of approximately 35 keV have been employed to perform angiography, because the beams are absorbed effectively by iodine-based contrast media with a K-absorption edge of 33.2 keV. Without using a synchrotron, we have developed an x-ray generator utilizing a cerium-target tube, and have performed cone-beam K-edge angiography achieved with cerium Kα rays of 34.6 keV.[7] However, the x-ray intensity rate was limited because

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the thermal contact between the target and the anode was not good.

Although various flash x-ray generators have been developed,[8] we have developed flash x-ray generators[9-13] with photon energies of less than 150 keV in order to primarily perform high-speed biomedical radiography. Subsequently, we have developed plasma flash x-ray generators[14-16] to perform a preliminary experiment for producing hard x-ray lasers from weakly ionized linear plasma, and have succeeded in producing intense and clean K-series characteristic x rays using copper and nickel targets. In addition, we have confirmed the weak hard x-ray resonation verified from irradiation of weakly higher harmonic x rays. However, it is difficult to produce high-photon-energy characteristic x rays because the plasma transmits high-photon-energy bremsstrahlung x rays. Therefore, we developed a quasi-monochromatic flash x-ray generator[17,18] with a disk-cathode tube to produce high-energy characteristic x rays utilizing the angle dependence of bremsstrahlung x-ray distribution, because the bremsstrahlung rays are not emitted in the apposite direction to that of electron acceleration. Using this generator, we have succeeded in producing clean characteristic x rays from molybdenum, silver and cerium targets.

Gadolinium-based contrast media with a K-edge of 50.2 keV have been employed to perform angiography in MRI, and the gadolinium density has been increasing. In view of this situation, ytterbium Kα rays (52.0 keV) are useful for enhanced K-edge angiography, because the Kα rays are absorbed effectively by gadolinium media. As compared with angiography using iodine media, the absorbed dose can be decreased considerably utilizing angiography achieved with gadolinium media. However, because ytterbium is a lanthanide series element and has a high reactivity, Kα rays of tantalum and tungsten are also useful to perform angiography.

In this article, we describe an intense quasi-monochromatic plasma flash x-ray generator with a tantalum target tube, and used it to perform a preliminary study on angiography achieved with tantalum K-series characteristic x rays.

2. PRINCIPLE OF K-EDGE ANGIOGRAPHY

Figure 1 shows the mass attenuation coefficients of gadolinium at the selected energies; the coefficient curve is discontinuous at the gadolinium K-edge. The average photon energy of the tantalum Kα lines is shown above the gadolinium K-edge. The average photon energy of tantalum Kα lines is 57.1 keV, and gadolinium contrast media with a K-absorption edge of 50.2 keV absorb the lines easily. Therefore, blood vessels were observed with high contrasts.

3. GENERATOR

3.1 High-voltage circuit

Figure 2 shows a block diagram of a high-intensity plasma flash x-ray generator. The generator consists of the following essential components: a high-voltage power supply, a high-voltage condenser with a capacity of approximately 150 nF, an air gap switch, a turbomolecular pump, a thyratron pulse generator as a trigger device, and a flash x-ray tube. In this generator, a coaxial cable transmission line is employed in order to increase maximum tube voltage using high-voltage reflection (Fig. 3). The high-voltage main condenser is charged up to 80 kV by the power supply, and electric charges in the condenser are discharged to the tube through the four cables after closing the gap switch with the trigger device.

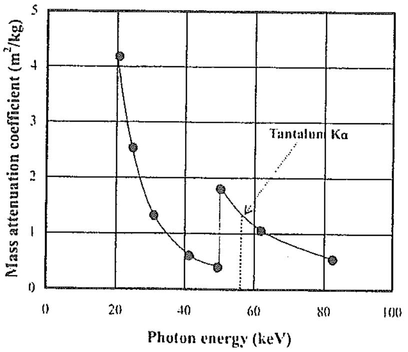

Figure 1: Relation between mass attenuation coefficient of gadolinium and average photon energy of tantalum Kα lines.

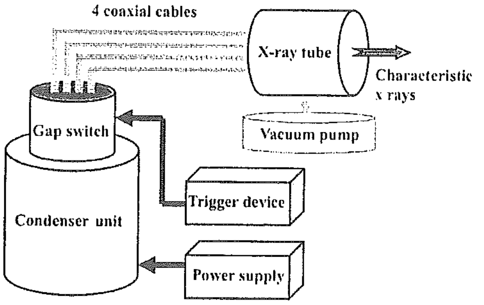

Figure 2: Block diagram of intense quasi-monochromatic flash x-ray generator.

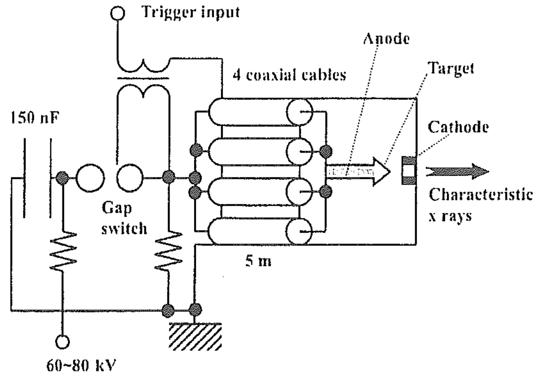

Figure 3: High-voltage circuit of flash x-ray generator.

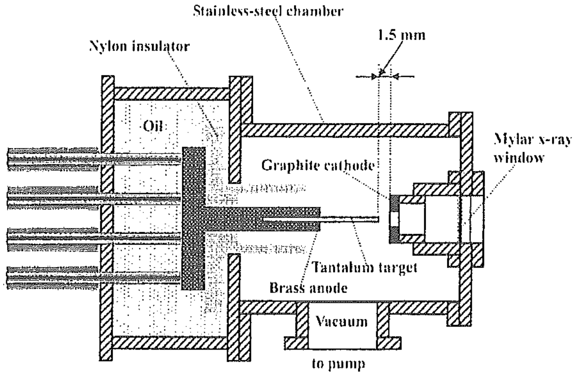

Figure 4: Schematic drawing of flash x-ray tube.

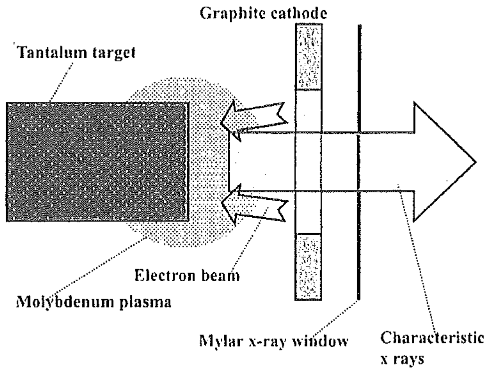

Figure 5: Irradiation of characteristic x rays.

3.2 X-ray tube

The x-ray tube is a demountable cold-cathode diode that is connected to the turbomolecular pump with a pressure of approximately 1 mPa (Fig. 4). This tube consists of the following major parts: a ring-shaped graphite cathode with an bore diameter of 4.5 mm, a stainless-steel vacuum chamber, a nylon insulator, a polyethylene terephthalate (Mylar) x-ray window 0.25 mm in thickness, and a rod-shaped tantalum target 3.0 mm in diameter. The distance between the target and cathode electrodes can be regulated from the outside of the tube, and is set to 1.5 mm. As electron beams from the cathode electrode are roughly converged to the target by the electric field in the tube, evaporation leads to the formation of weakly ionized plasma, consisting of tantalum ions and electrons, around the target. Because bremsstrahlung rays are not emitted in the opposite direction to that of electron acceleration (Fig. 5), tantalum K-series characteristic x rays can be produced without using a filter.

4. CHARACTERISTICS

4.1 Tube voltage and current

In this generator, it was difficult to measure the tube voltage and current since the tube voltages were high, and there was no space to set a current transformer for measuring the tube current. Currently, the voltage and current roughly display damped oscillations. When the charging voltage was increased, both the maximum tube voltage and current increased. At a charging voltage of 80 kV, the estimated maximum values of the tube voltage and current were approximately 160 kV (2 times the charging voltage) and 40 kA, respectively.

4.2 X-ray output

X-ray output pulse was detected using a combination of a plastic scintillator and a photomultiplier (Fig. 6). The x-ray pulse height substantially increased with corresponding increases in the charging voltage. The x-ray pulse widths were approximately 100 ns, and the time-integrated x-ray intensity measured by a thermoluminescence dosimeter (Kyokko TLD Reader 1500 having MSO-S elements without energy compensation) had a value of approximately 300 μGy at 1.0 m from the x-ray source with a charging voltage of 80 kV.

4.3 X-ray source

In order to observe the characteristic x-ray source, we employed a 100-μm-diameter pinhole camera and an x-ray film (Polaroid XR-7) (Fig. 7). When the charging voltage was increased, the plasma x-ray source grew, and both spot dimension and intensity increased. Because the x-ray intensity is the highest at the center of the spot, both the dimension and intensity decreased according to decreases in the pinhole diameter.

4.4 X-ray spectra

X-ray spectra were measured using a transmission-type spectrometer with a lithium fluoride curved crystal 0.5 mm in thickness. The x-ray intensities of the spectra were detected by an imaging plate of a computed radiography (CR) system[19] (Konica Regius 150) with a wide dynamic range, and relative x-ray intensity was calculated from Dicom original digital data corresponding to x-ray intensity; the data was scanned by Dicom viewer in the film-less CR system. Subsequently, the relative x-ray intensity as a function of the data was calibrated using a conventional x-ray generator, and we confirmed that the intensity was proportional to the exposure time. Figure 8 shows measured spectra from the tantalum target. We observed clean K-series lines, while bremsstrahlung rays were hardly detected. The characteristic x-ray intensity substantially increased with increases in the charging voltage.

5. ANGIOGRAPHY

The flash angiography was performed by a computed radiography (CR) system (Konica Regius 150)[19] at 1.2 m from the x-ray source, and the charging voltage was 80 kV.

Firstly, rough measurements of spatial resolution were made using wires. Figure 9 shows radiograms of tungsten wires coiled around a rod made of polymethyl methacrylate. Although the image contrast decreased somewhat with decreases in the wire diameter, due to blurring of the image caused by the sampling pitch of 87.5 μm, a 50 μm-diameter wire could be observed. Because the tungsten wires transmitted the characteristic x rays easily, low contrast radiograms were obtained.

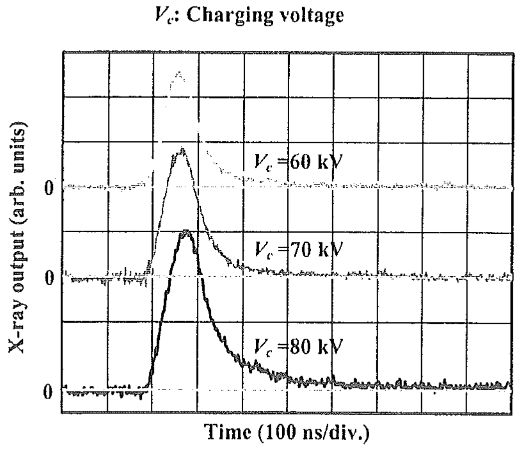

Figure 6: X-ray outputs at indicated conditions.

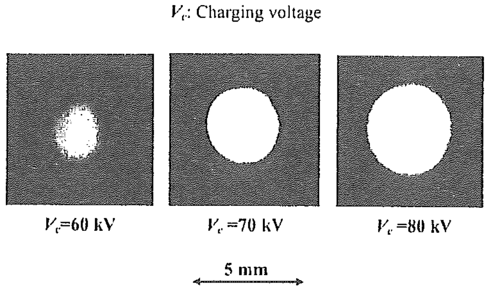

Figure 7: Images of characteristic x-ray source with changes in charging voltage.

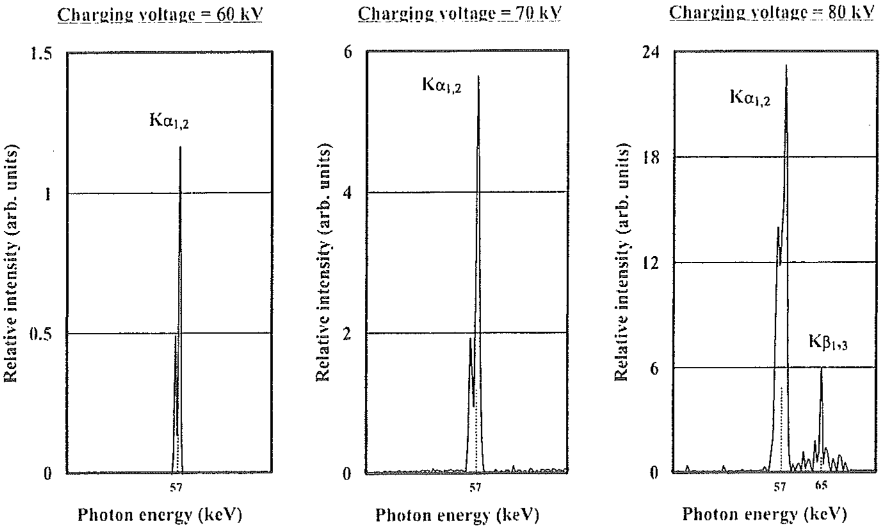

Figure 8: X-ray spectra from tantalum target.

The image of water (gadolinium oxide suspension of 20%) falling into a polypropylene beaker from a plastic test tube is shown in Fig. 10. The diameter of gadolinium oxide powder ranges from 1 to 10 μm. Because the x-ray duration was about 100 ns, the stop-motion image of water could be obtained.

Figure 11 shows an angiogram of a silicone rubber tube in a polymethyl methacrylate (PMMA) case using a contrast medium which contains 32.3% gadodiamidehydrate, and a low contrast tube with a bore diameter of 1.0 mm is observed. In cases where a gadolinium oxide suspension of 50% is employed, high-contrast angiography of the tubes (1.0 mm and 0.5 mm in bore diameter) could be performed (Fig. 12). Figure 13 shows an angiogram of a rabbit head using gadolinium oxide powder, and fine blood vessels of approximately 100 μm were visible.

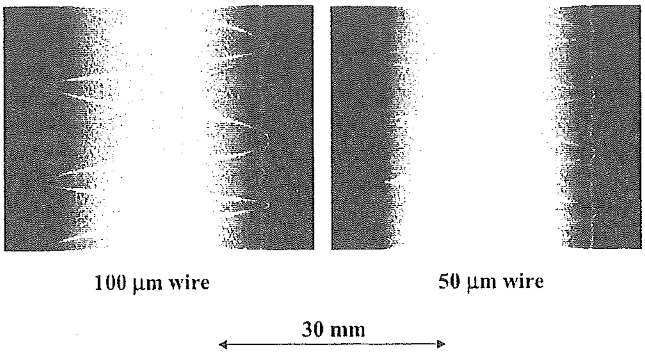

Figure 9: Radiograms of tungsten wires coiled around rod made of polymethyl methacrylate.

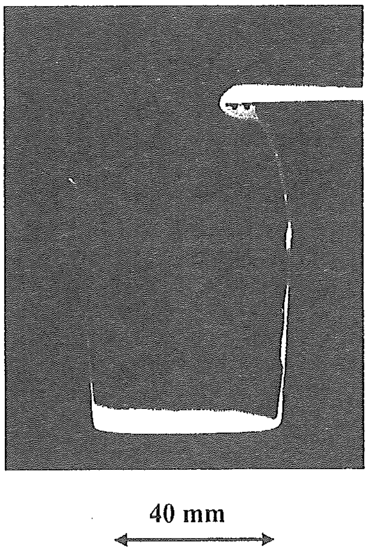

Figure 10: Radiogram of water falling into polypropylene beaker from plastic test tube.

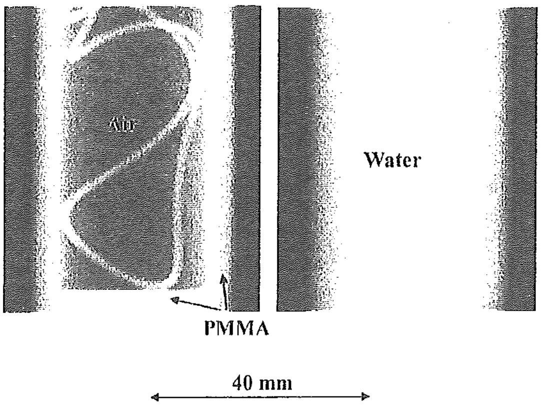

Figure 11: Angiograms of silicon tube using contrast medium of 32.3% gadodiamidehydrate.

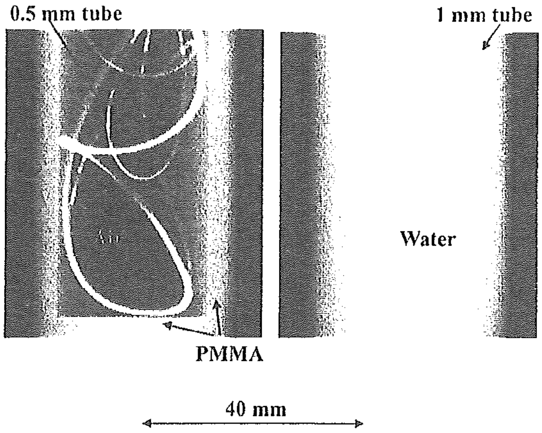

Figure 12: Angiography of silicon tube using gadolinium oxide suspension of 50%.

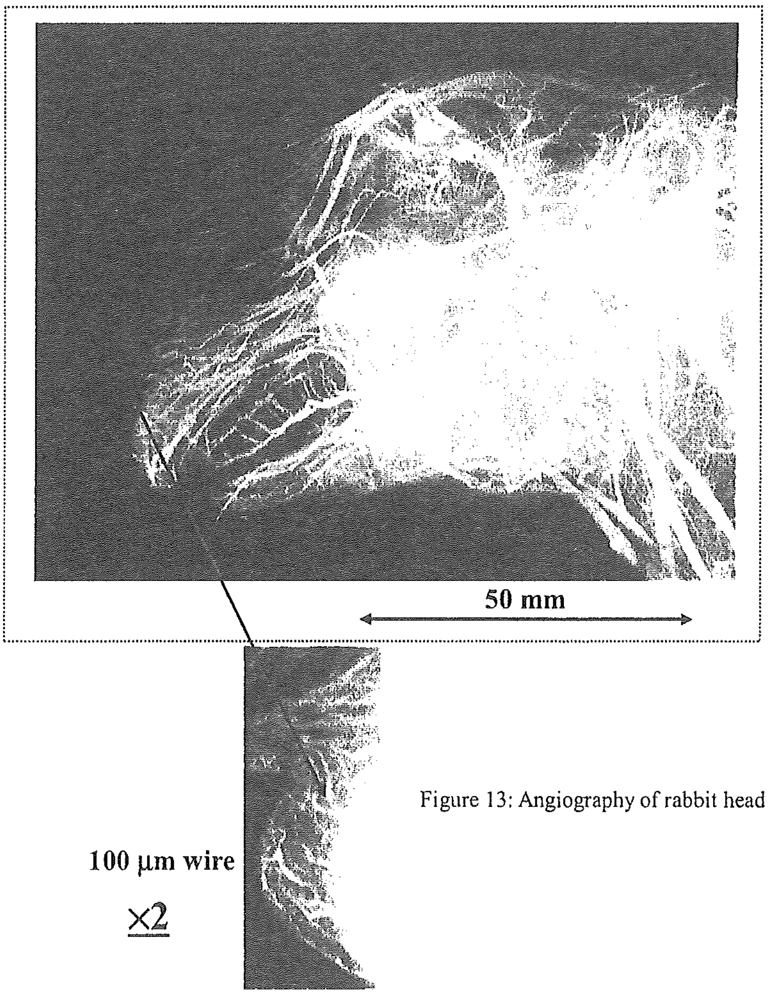

Figure 13: Angiography of rabbit head using gadolinium oxide powder.

6. DISCUSSION AND CONCLUSIONS

In summary, we succeeded in producing K-series characteristic x rays of tantalum and in performing K-edge angiography using gadolinium contrast media with a K-edge of 50.2 keV, and this K-edge angiography could be a useful technique to decrease the dose absorbed by patients. Although we employed tantalum Kα (57.1 keV) and Kβ (approximately 65 keV) rays, Kβ rays should be absorbed using an ytterbium oxide filter with an ytterbium K edge of 61.3 keV in order to increase the image contrast of blood vessels.

To perform K-edge angiography using gadolinium media, although an ytterbium target with a Kα energy of 52.0 keV is useful, the ytterbium has a high reactivity. If we assume that the ytterbium is employed, an alloy target should be developed. In this research, we obtained sufficient x-ray intensity per pulse for angiography, and the intensity can be increased by increasing the electrostatic energies in the high-voltage condenser. At a condenser capacity of 150 nF, the generator produced instantaneous number of K photons was approximately 1×10^9 photons/cm^2 per pulse at 1.0 m from the source.

In the flash x-ray tube, bremsstrahlung x rays with energies higher than the K-edge are absorbed effectively by the weakly ionized plasma and are converted into fluorescent (characteristic) x rays. In conjunction with this property, because the bremsstrahlung x rays are not emitted in the opposite direction to that of electron acceleration, clean characteristic x rays are produced. Using this flash x-ray generator, with which the photon energy of characteristic x rays can be selected, quasi-monochromatic imaging such as enhanced K-edge angiography using iodine contrast media and mammography can be performed.

ACKNOWLEDGMENT

This work was supported by Grants-in-Aid for Scientific Research (13470154, 13877114, 16591181, and 16591222) and Advanced Medical Scientific Research from MECSST, Health and Labor Sciences Research Grants(RAMT-nano-001, RHGTEFB-genome-005 and RHGTEFB-saisei-003), Grants from Keiryo Research Foundation, The Promotion and Mutual Aid Corporation for Private Schools of Japan, Japan Science and Technology Agency (JST), and New Energy and Industrial Technology Development Organization (NEDO, Industrial Technology Research Grant Program in '03).

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High-speed enhanced K-edge angiography utilizing cerium plasma x-ray generator

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Abstract. The cerium target plasma flash x-ray generator is useful to perform high-speed enhanced K-edge angiography using cone beams, because K-series characteristic x-rays from the cerium target are absorbed effectively by iodine-based contrast mediums. In the plasma generator, a 200-nF condenser is charged up to 60 kV by a power supply, and flash x-rays are produced by the discharging. The x-ray tube is a demountable triode with a trigger electrode, and the turbomolecular pump evacuates air from the tube with a pressure of approximately 1 mPa. Target evaporation leads to the formation of weakly ionized linear plasma, consisting of cerium ions and electrons, around the target, and intense flash x-rays are produced. At a charging voltage of 55 kV, the maximum tube voltage is almost equal to the charging voltage of the main condenser, and the maximum current is approximately 20 kA. When the charging voltage is increased, weakly ionized cerium plasma forms, and the K-series characteristic x-ray intensities increase. The x-ray pulse widths are about 500 ns, and the time-integrated x-ray intensity has a value of about 40 μC/kg at 1.0 m from the x-ray source with a charging voltage of 55 kV. In the angiography, we employ a filmless computed radiography (CR) system and iodine-based microspheres.
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Subject terms: plasma x-ray; cerium target; weakly ionized cerium plasma; characteristic x-ray; K-edge angiography.

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1 Introduction

Flash x-rays are useful to perform high-speed radiography, and various generators have been developed to correspond to specific radiographic objectives.[1–5] In the cases of multishot and cine radiographies, we have developed several different repetitive-flash[6–10] and stroboscopic x-ray generators.[11–17] Although most flash x-ray generators have cold-cathode tubes, the stroboscopic generators utilize hot-cathode tubes.

In conjunction with single crystals, synchrotrons generate monochromatic x-rays. These rays play important roles in parallel radiography and have been employed to perform high-contrast K-edge angiography[18] and x-ray phase imaging.[19,20] However, it is difficult to obtain sufficient machine times for various research projects, including medical applications.

As for angiography using iodine-based contrast mediums, K-series characteristic x-rays of cerium are extremely useful, since the rays are absorbed easily by iodine. In particular, since fairly intense and sharp characteristic x-rays have been produced from weakly ionized linear plasmas[21–24] of nickel, copper, and molybdenum, the development of a cerium-target x-ray tube for angiography is highly desirable.

In this research, we developed a single flash x-ray generator with a cerium-target plasma tube and performed a preliminary study on weakly ionized cerium plasma angiography.

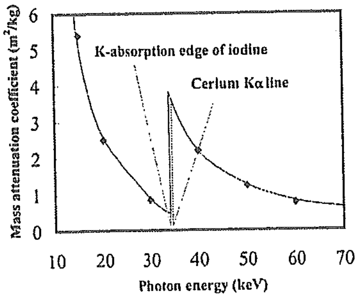

Fig. 1 Relation between mass attenuation coefficient of iodine and average photon energy of cerium Kα lines.

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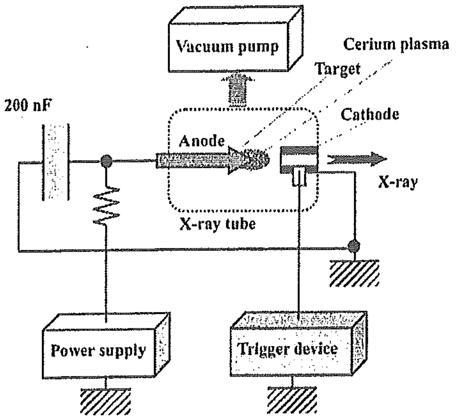

Fig. 2 Block diagram of high intensity plasma flash x-ray generator.

2 Principle of K-Edge Angiography

Figure 1 shows the mass attenuation coefficients of iodine at the selected energies; the coefficient curve is discontinuous at the iodine K-edge. The average photon energy of the cerium Kα lines is shown just above the iodine K-edge. Cerium is a rare earth element and has a high reactivity; however, the average photon energy of Kα lines is 34.566 keV, and iodine contrast mediums with a K-absorption edge of 33.155 keV absorb the lines easily. Therefore, blood vessels were observed with high contrasts.

3 Generator

3.1 *High-Voltage Circuit*

Figure 2 shows a block diagram of a high-intensity plasma flash x-ray generator. This generator consists of the following essential components: a high-voltage power supply, a high-voltage condenser with a capacity of about 200 nF, a turbomolecular pump, a krytron pulse generator as a trigger device, and a flash x-ray tube. The high-voltage main condenser is charged up to 60 kV by the power supply, and electric charges in the condenser are discharged to the tube after triggering the cathode electrode by the trigger device. The plasma flash x-rays are then produced.

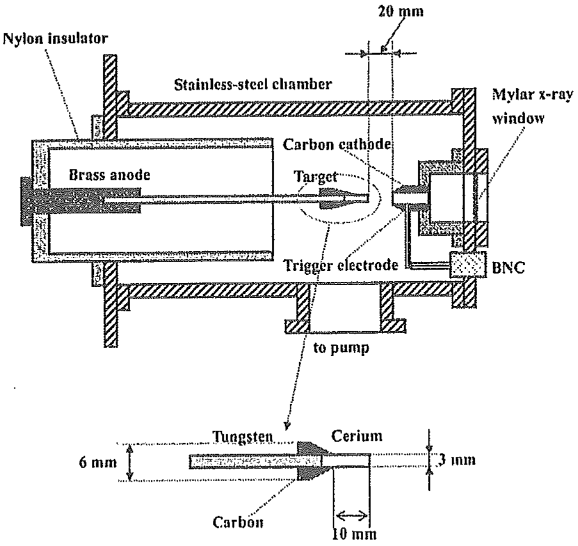

Fig. 3 Schematic drawing of flash x-ray tube.

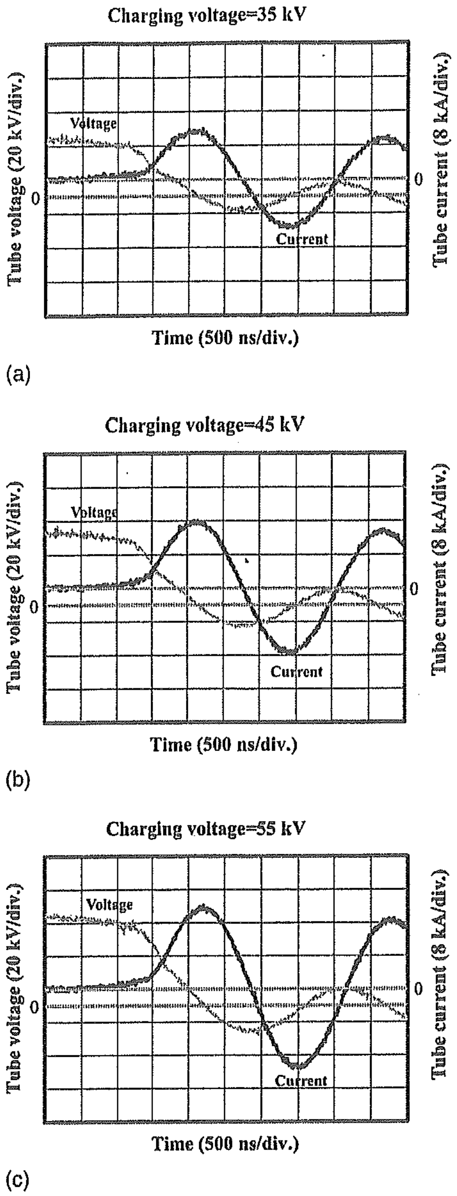

Fig. 4 Tube voltages and currents with charging voltage of (a) 35, (b) 45, and (c) 55 kV.

3.2 *X-Ray Tube*

The x-ray tube is a demountable cold-cathode triode that is connected to the turbomolecular pump with a pressure of approximately 1 mPa (Fig. 3). This tube consists of the following major parts: a hollow cylindrical carbon cathode with a bore diameter of 10.0 mm, a trigger electrode made from a copper wire, a stainless-steel vacuum chamber, a nylon insulator, a polyethylene terephthalate (Mylar) x-ray window of 0.25 mm, and a rod-shaped cerium target of 3.0 mm in diameter. The target tip is embedded in the carbon rod to absorb the characteristic x-rays of carbon by the window. The distance between the target and cathode electrodes is approximately 20 mm, and the trigger electrode is

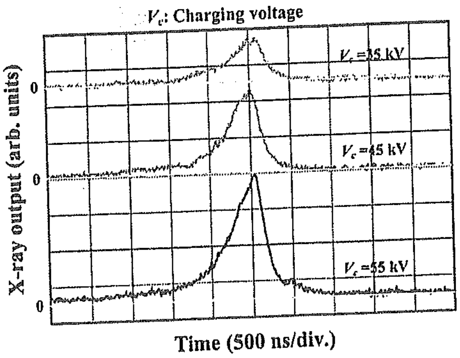

Fig. 5 X-ray outputs at indicated conditions.

set in the cathode electrode. As electron beams from the cathode electrode are roughly converged to the target by an electric field in the tube, the weakly ionized plasma, which consists of cerium ions and electrons, forms around the target by evaporating.

4 Characteristics

4.1 *Tube Voltage and Current*

Tube voltage and current were measured by a high-voltage divider with an input impedance of 1 GΩ and a current transformer, respectively. Figure 4 shows the time relation between the tube voltage and current. At the indicated charging voltages, they roughly displayed damped oscillations. When the charging voltage was increased, both the maximum tube voltage and current increased. At a charging voltage of 55 kV, the maximum tube voltage was almost equal to the charging voltage of the main condenser, and the maximum tube current was about 20 kA.

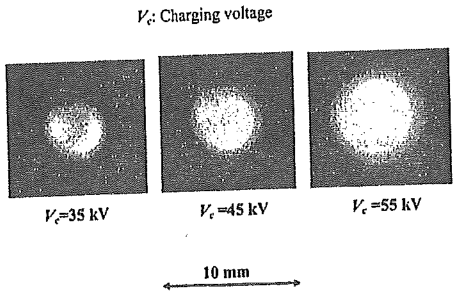

Fig. 6 Images of plasma x-ray source.

4.2 *X-Ray Output*

An x-ray output pulse was detected using a combination of a plastic scintillator and a photomultiplier. The x-ray pulse height substantially increased with corresponding increases in the charging voltage (Fig. 5). The x-ray pulse widths were about 500 ns, and the time-integrated x-ray intensity measured by a thermoluminescence dosimeter (Kyokko TLD Reader 1500 utilizing MSO-S elements without energy compensation) had a value of about 40 μC/kg at 1.0 m from the x-ray source with a charging voltage of 55 kV.

4.3 *X-Ray Source*

To measure images of the plasma x-ray source, we employed a pinhole camera with a hole diameter of 100 μm (Fig. 6). When the charging voltage was increased, the plasma x-ray source grew, and both spot dimension and intensity increased. Because the x-ray intensity is the highest at the center of the spot, both the dimension and intensity decreased according to both increases in the thickness of a filter for absorbing x-rays and decreases in the pinhole diameter.

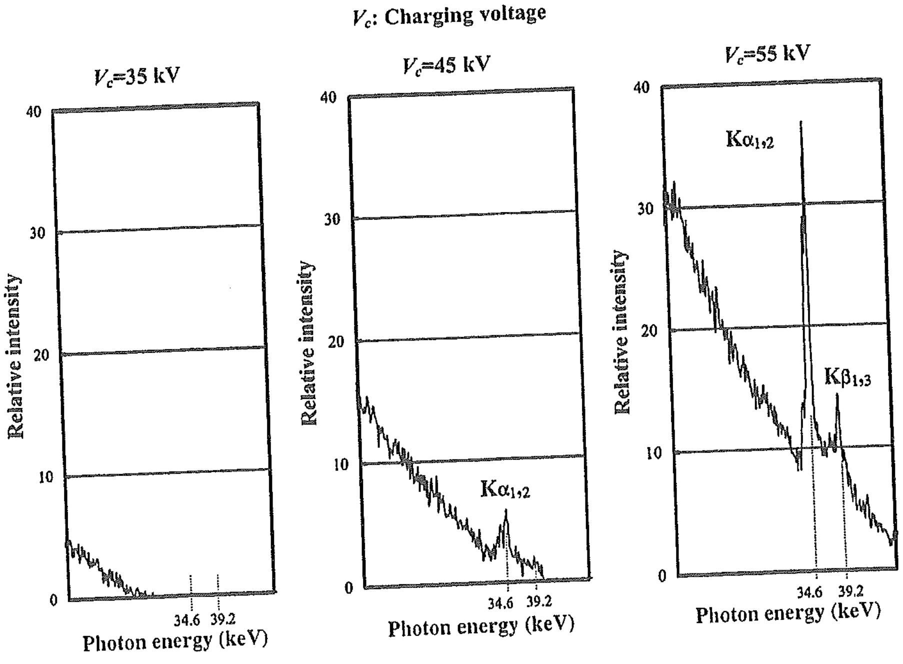

Fig. 7 X-ray spectra from weakly ionized cerium plasma.

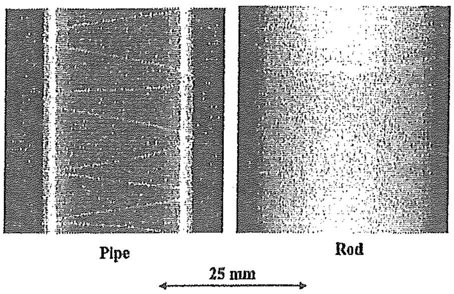

Fig. 8 Radiograms of tungsten wires of 50 μm in diameter coiled around pipe and rod made of PMMA.

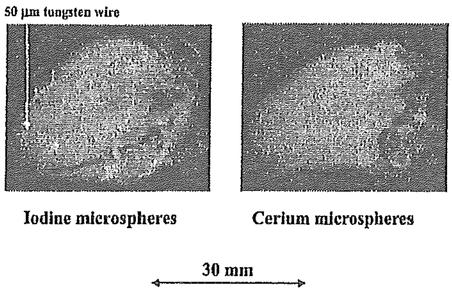

Fig. 10 Angiograms of rabbit hearts using iodine and cerium microspheres.

4.4 *X-Ray Spectra*

X-ray spectra from the plasma source were measured by a transmission-type spectrometer with a lithium fluoride curved crystal of 0.5 mm in thickness. The spectra were taken by a computed radiography (CR) system[25] (Konica Regius 150) having a wide dynamic range, and relative x-ray intensity was calculated from Dicom digital data. Figure 7 shows measured spectra from the cerium target. In this experiment, although we observed both the bremsstrahlung and characteristic x-rays, we could not observe characteristic x-rays with a charging voltage of 35 kV, because the critical excitation energy is 40.3 keV. Both intensities increased substantially with increases in the charging voltage.

5 Angiography

The plasma angiography was performed by the CR system without using a monochromatic filter, and the distance between the x-ray source and the imaging plate was 1.2 m. Subsequently, in angiography testing, we usually employ nonliving animal phantoms using microspheres.

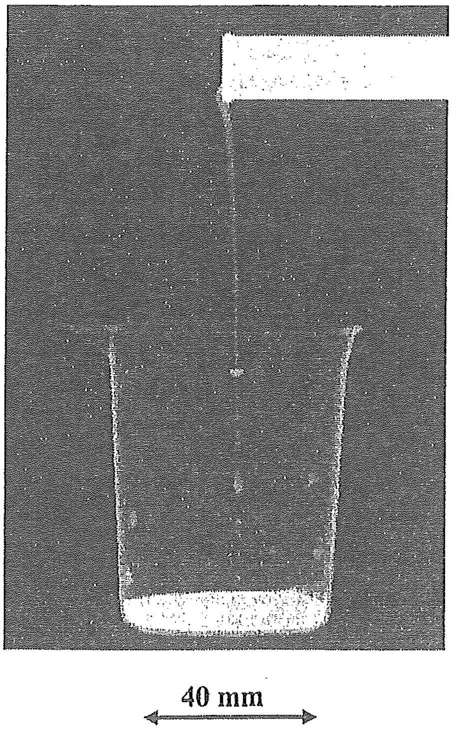

Fig. 9 Radiogram of water falling into a polypropylene beaker from a glass test tube.

First, rough measurements of image resolution were made using wires. Figure 8 shows radiograms of 50-μm-diam tungsten wires coiled around a pipe, and a rod made of polymethyl methacrylate (PMMA) with a charging voltage of 55 kV. Although the image contrast increased using the pipe, 50-μm-diam wires could be observed.

The image of water falling into a polypropylene beaker from a glass test tube is shown in Fig. 9. This image was taken with a charging voltage of 55 kV, with the slight addition of an iodine-based contrast medium. Because the x-ray duration was about 1 μs, the stop-motion image of water could be obtained.

Angiograms of rabbit hearts are shown in Fig. 10. These two images were obtained using iodine and cerium microspheres of 15 μm, respectively, with a charging voltage of 55 kV. In cases where the cerium spheres were employed, the coronary arteries were barely visible. Figure 11 shows an angiogram of the external ear of a rabbit using iodine spheres with a charging voltage of 55 kV, and fine blood vessels of about 50 μm are visible. In angiography of a larger heart extracted from a dog, using iodine spheres, a PMMA plate was set in front of a heart facing x-ray source, and image contrast of coronary arteries improved with increases in the plate thickness (Fig. 12).

6 Discussion

In an earlier experiment using a copper target,[24] bremsstrahlung x-rays were hardly observed at all, and we confirmed the irradiation of fairly clean K-series characteristic x-rays such as lasers. In the present work, although we confirmed intense characteristic x-rays with a higher charging voltage, bremsstrahlung x-rays were detected, since the bremsstrahlung intensity is proportional to the atomic num-

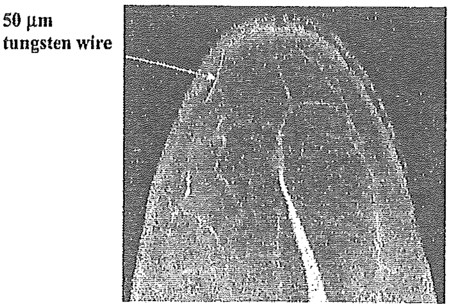

Fig. 11 Angiograms of external ear of rabbit.

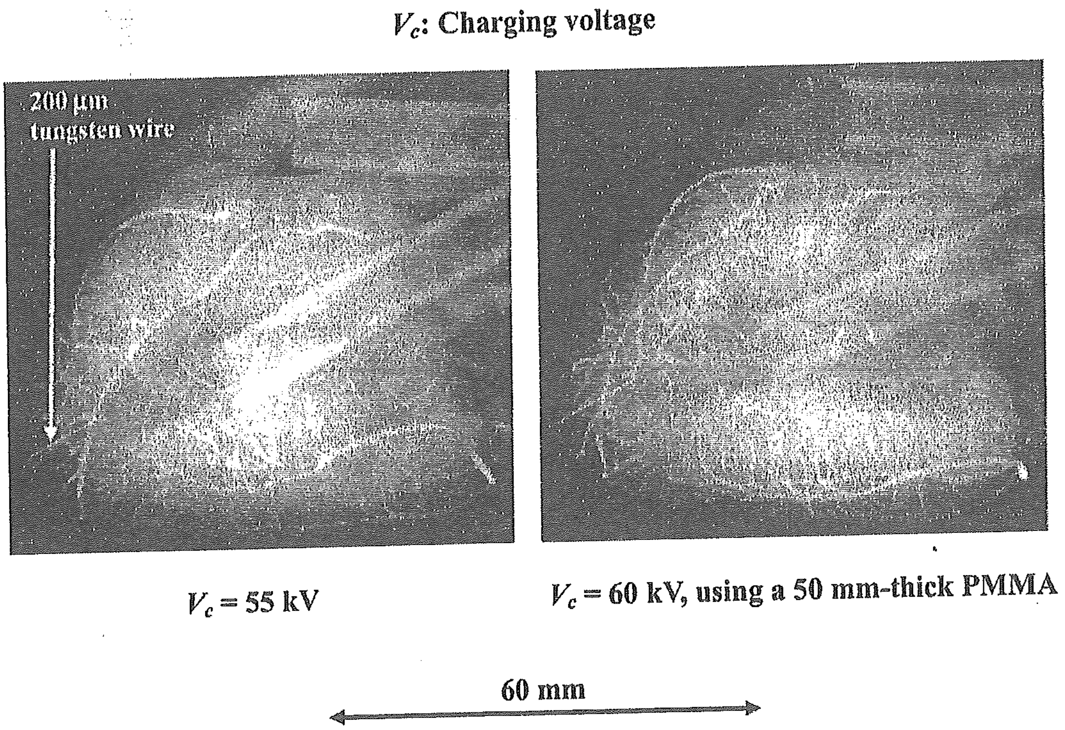

Fig. 12 Angiograms of extracted heart of dog.

ber of the target element, and high-photon-energy bremsstrahlung x-rays are not absorbed effectively in the plasma. Therefore, the condenser charging voltage should be raised as high as possible to increase the characteristic x-ray intensity. To decrease emission of bremsstrahlung x-rays from the carbon target holder, the target length should also be set as long as possible. Next, since the spheres easily transmit bremsstrahlung x-rays with energies lower than the edge, it is important that the rays be absorbed as much as possible before angiography to increase the image contrast.

In this research, we obtained sufficient x-ray intensity per pulse for CR radiography, and the generator produced high-dose-rate plasma x-rays of approximately 80 C/kg·s at 1.0 m with a charging voltage of 55 kV. In addition, because the x-ray intensity increases with increases in the electrostatic energy in the main discharge condenser, the flash x-rays from weakly ionized linear cerium plasma can be employed to perform high-speed angiography for cardiovascular disease.

Acknowledgments

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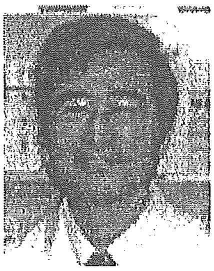

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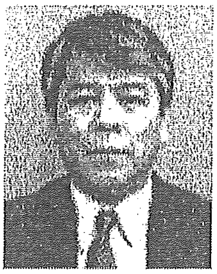

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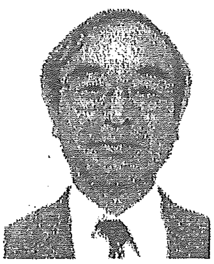

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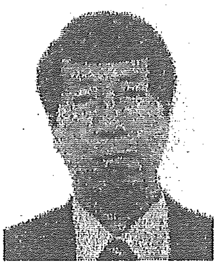

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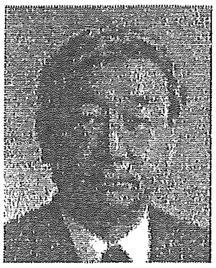

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Clean monochromatic x-ray irradiation from weakly ionized linear copper plasma

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Abstract. In the plasma flash x-ray generator, a 200-nF condenser is charged up to 50 kV by a power supply, and flash x-rays are produced by the discharging. The x-ray tube is a demountable triode with a trigger electrode, and the turbomolecular pump evacuates air from the tube with a pressure of approximately 1 mPa. Target evaporation leads to the formation of weakly ionized linear plasma, consisting of copper ions and electrons, around the fine target, and intense Kα rays are produced using a 10-μm-thick nickel filter. At a charging voltage of 50 kV, the maximum tube voltage is almost equal to the charging voltage of the main condenser, and the peak current is about 15 kA. When the charging voltage is increased, the linear plasma forms, and the copper Kα intensities substantially increase. The Kα lines are quite clean and intense, and hardly any bremsstrahlung rays are detected at all. The x-ray pulse widths are approximately 700 ns, and the time-integrated x-ray intensity has a value of approximately 20 μC/kg at 1.0 m from the x-ray source with a charging voltage of 50 kV. © *2005 Society of Photo-Optical Instrumentation Engineers.* [DOI: 10.1117/1.1882373]

Subject terms: flash x-ray; weakly ionized linear plasma; copper target; Kα characteristic x-rays; monochromatic x-rays.

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1 Introduction

Flash x-rays have been produced by several different methods, and various generators have been developed corresponding to specific radiographic objectives.[1–3] Currently, maximum photon energy has been increased to approximately 1 MeV using multistage Marx pulse generators[1,2] to produce hard x-rays for military studies. In soft x-ray generators,[4–7] high-intensity single generators with large capacity condensers were originally developed. Subsequently, repetitive generators[8–12] have been developed, and the repetition rate has been increased to subkilohertz using a cold-cathode triode.

Recently, soft x-ray lasers have been produced by a gas-discharge capillary,[13–16] and the laser pulse energy substantially increased in proportion to the capillary length. These kinds of fast discharges can generate hot and dense plasma columns with aspect ratios approaching 1000:1. However, it is difficult to increase the laser photon energy to 10 keV or beyond. Because there are no x-ray resonators in the high photon energy region, new methods for increasing coherence will be desired in the future.

We have developed several different plasma flash x-ray generators corresponding to specific radiographic objectives, and a major goal in our research is the development of an intense and clean monochromatic x-ray generator that can impact applications with biomedical radiography. By forming weakly ionized linear plasma,[17–20] because we have succeeded in producing fairly intense and clean quasi-monochromatic x-rays from the plasma axial direction, monochromatic x-rays should be produced using a K-edge filter.

We describe a plasma flash x-ray generator utilizing a new plasma x-ray tube, and used it to perform a preliminary experiment for generating clean monochromatic x-rays by forming a linear copper plasma cloud around a fine target.

2 Generator

2.1 *High-Voltage Circuit*

Figure 1 shows a block diagram of the high-intensity plasma flash x-ray generator. This generator consists of the following essential components: a high-voltage power supply, a high-voltage condenser with a capacity of approximately 200 nF, a turbomolecular pump, a krytron pulse

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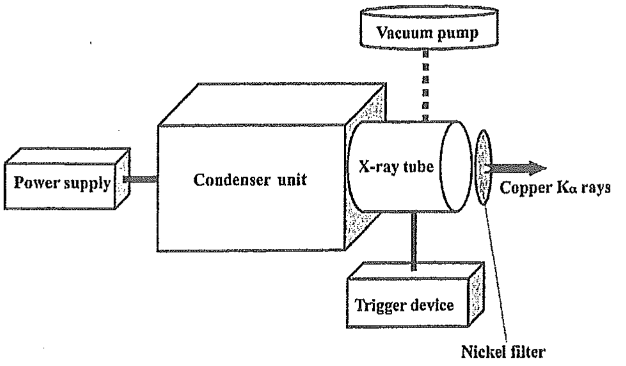

Fig. 1 Block diagram of high-intensity plasma flash x-ray generator.

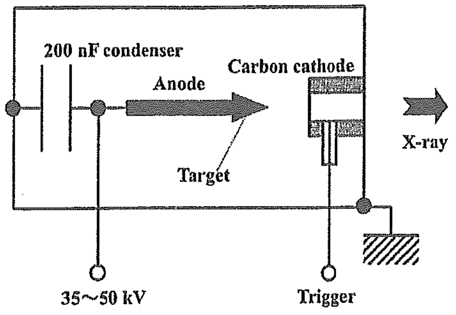

Fig. 2 Circuit diagram of generator.

generator as a trigger device, and a flash x-ray tube. In this generator, a low-impedance transmission line (Fig. 2) is employed to increase maximum tube current. The high-voltage main condenser is charged to 50 kV by the power supply, and electric charges in the condenser are discharged to the tube after triggering the cathode electrode with the trigger device. The plasma flash x-rays are then produced.

2.2 *X-Ray Tube*

The x-ray tube is a demountable cold cathode triode that is connected to the turbomolecular pump with a pressure of approximately 1 mPa (Fig. 3). This tube consists of the following major parts: a hollow cylindrical carbon cathode with a bore diameter of 10.0 mm, a brass focusing electrode, a trigger electrode made from copper wire, a stainless-steel vacuum chamber, a nylon insulator, a polyethylene terephthalate (Mylar) x-ray window 0.25 mm thick, and a rod-shaped copper target 3.0 mm in diameter with a tip angle of 60 deg. The distance between the target and cathode electrodes is approximately 20 mm, and the trigger electrode is set in the cathode electrode. As electron beams from the cathode electrode are roughly converged to the target by the focusing electrode, evaporation leads to the formation of a weakly ionized linear plasma, consisting of copper ions and electrons, around the fine target.

2.3 *Principle of Clean Kα-Ray Irradiation*

In the linear plasma, bremsstrahlung photons with energies higher than the K-absorption edge are effectively absorbed and are converted into fluorescent x-rays (Fig. 4). The plasma then transmits the fluorescent rays easily, and bremsstrahlung rays with energies lower than the K edge are also absorbed by the plasma. In addition, because bremsstrahlung rays are not emitted in the opposite direction to that of electron acceleration, intense characteristic x-rays are generated from the plasma-axial direction. Sub-

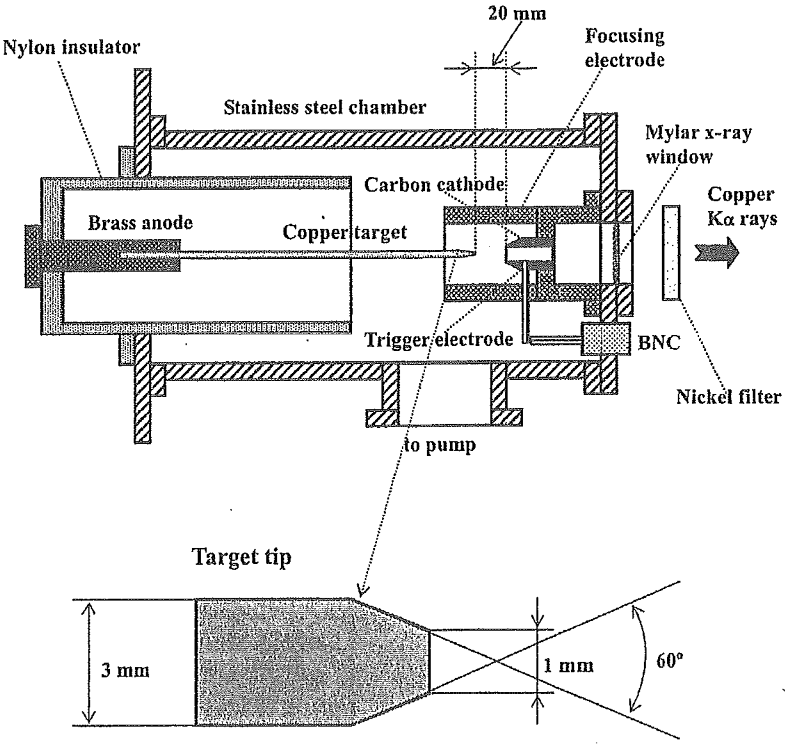

Fig. 3 Schematic drawing of flash x-ray tube with rod target.