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Development of a two-dimensional imaging system for clinical applications of intravenous coronary angiography using intense synchrotron radiation produced by a multipole wiggler

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A two-dimensional clinical intravenous coronary angiography system, comprising a large-size view area produced by asymmetrical reflection from a silicon crystal using intense synchrotron radiation from a multipole wiggler and a two-dimensional detector with an image intensifier, has been completed. An advantage of the imaging system is that two-dimensional dynamic imaging of the cardiovascular system can be achieved due to its two-dimensional radiation field. This world-first two-dimensional system has been successfully adapted to clinical applications. Details of the imaging system are described in this paper.

Keywords: coronary angiography; two-dimensional imaging systems; asymmetrical reflections; multipole wigglers; clinical applications.

1. Introduction

The clinical application of monochromatic X-rays from synchrotron radiation, particularly in the diagnosis of the coronary arteries, has been proposed by Rubenstein *et al.* (1981).

The development of a one-dimensional scanning system was first initiated at SSRL (Huges *et al.*, 1983; Thompson *et al.*, 1989) and further developed at NSLS (Thomlinson *et al.*, 1988, 1992), HASYLAB (Dix *et al.*, 1992; Dix, 1995), VEPP IV (Dementyev *et al.*, 1989) and ESRF (Moulin *et al.*, 1993). Rubenstein *et al.* (1987) succeeded in a clinical application of the one-dimensional scanning system for the first time in 1986. Since then, many clinical applications of a one-dimensional scanning system have been established at SSRL, NSLS and DESY.

In Japan, medical doctors have claimed that any system to be developed should be very similar to those that have been and are in daily use at hospitals, meaning that one should be able to observe blood flow in a two-dimensional view area to evaluate the heart motion as well as the morphological information on coronary arteries. In order to obtain an image of the whole heart, however, the small vertical size of the synchrotron radiation beam itself must be magnified by some means. Some of the present authors initiated the development of a two-dimensional dynamic imaging system in 1984 (Akisada *et al.*, 1987; Hyodo *et al.*, 1991). Our system, which is principally based on vertical magnification of the beam by means of asymmetrical reflection from a crystal and visualization by means of an image-intensifier–TV (II–TV) system, has an advantage of producing dynamic two-dimensional images, as does conventional coronary angiography. Since the initial development, the authors have confirmed by animal experiments at ARNE5 (Hyodo *et al.*, 1991, 1994) that the system, which uses a synchrotron radiation beam generated by a bending magnet in the accumulation ring (AR), has potential applications to clinical settings. In particular, the authors have proved that distinction of the coronary artery system can be satisfactorily achieved on dynamic images with monochromatic radiation of the upper *K*-edge, even without performing subtraction between two radiograms taken with X-ray radiation at each upper and lower *K*-edge of iodine. According to this procedure, using a two-dimensional imaging system, the X-ray exposure dose to a patient is expected to be reduced by a factor of two compared with that of a subtraction procedure.

Practical clinical applications have necessitated further development and preparation of some equipment.

The development of a two-dimensional imaging system for human examination is described in this article.

2. Instrumental development

2.1. *Intense synchrotron radiation source*

It has been revealed that the number of photons in the X-ray radiation generated by a bending magnet at the AR is not sufficient to apply this to clinical settings. A multipole wiggler (MPW) for generating circularly polarized synchrotron radiation was installed in the AR for studying magnetic materials at beamline ARNE1 in 1988 (Yamamoto *et al.*, 1989). It also generates dual intense linearly polarized radiation. Consequently, some of the present authors proposed a medical diagnostic system in which MPW-generated linearly polarized radiation is selected, and have been trying to verify its performance using phantoms with a field size of 70 mm × 70 mm (Hyodo *et al.*, 1992, 1994). The intensity of 33 keV of the linearly polarized radiation is approximately 10–20 times as high as that of the bending-magnet radiation, realizing our expectation to obtain monochromatic X-ray radiation with sufficiently high intensity for clinical applications.

2.2. *Beamline technology*

Fig. 1 shows a side view of a vertical section of the system using synchrotron radiation produced by the MPW at ARNE1. The X-ray shutter system for this beamline originally comprised two shutters for radiation safety, *i.e.* a proximally positioned MBS (main beam shutter) and a distally positioned BBS (branch beam shutter) (Kawata *et al.*, 1989). The BBS is operated by the medical doctors in clinical examinations as an X-ray shutter. Furthermore, in our system, an additional high-speed X-ray shutter to decrease the radiation dose received by a patient was positioned immediately in front of the Si monochromator crystal. The crystal was positioned at a distance of 40 m from the source point in order to

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Table 1
Characteristics of the two-dimensional imaging system.

Monochromator	Asymmetrically cut Si(311)
Size	655 mm × 80 mm × 10 mm
Bragg angle	6.5° at 33 keV
Magnification ratio	17.5 at 33 keV
Beam size	
Incident synchrotron radiation beam size	8 mm (V) ×mm (H)
Field size of monochromatic X-ray	120–150 mm (V) × 80 mm (H)
X-ray shutter	
Aperture for transmission of radiation beam	2, 4, 6 ms
X-ray filter	
Thickness of aluminium filter	0–30 mm
ON/OFF speed	<20 ms
Ionization chamber	Applied Engineering Inc. C-178
Detector	
Image intensifier	TOSHIBA RTP9211G
Spatial resolution	150 μm
Image acquisition rate	30 images s^{-1}

convert the synchrotron radiation into monochromatic X-rays, and, simultaneously, to magnify the vertical size of the monochromatic X-rays. The dimensions of the white X-ray radiation are 8 mm vertically by 80 mm horizontally at the point; this is a characteristic feature of the MPW beamline (NE1). The thus-generated monochromatic radiation is led to a newly equipped special station for patients. It is emitted in a direction 13° upwards due to Bragg reflection of 33 keV by the Si(311) plane, and then visualized with an II–TV system, a two-dimensional detector, after passing through the patient's body from the back. An accelerator is operated at an acceleration energy of 5.0 GeV for clinical applications, unlike that of 6.5 GeV for the usual synchrotron radiation experiments (the reason is explained later). The characteristics of the imaging system are summarized in Table 1. A detailed description of each item is given below.

2.2.1. *Monochromator system*. For imaging the heart, it is necessary to magnify the vertical beam size. The magnification ratio, m, of the beam size is given by

$$m = \sin(\theta_B + \alpha)/\sin(\theta_B - \alpha), \qquad (1)$$

where θ_B is the Bragg angle and α is the angle between the diffracting planes and the crystal surface.

The desired length of the crystal, L, is given by

$$L = W/\sin(\theta_B + \alpha), \qquad (2)$$

where W is the width of the incoming beam.

A crystal with a diffraction plane of (311) and an α value from equation (1) of 5.8° was selected for our system. With a crystal having these characteristics, the Bragg angle for 33 keV is 6.5° and the incident angle of the synchrotron radiation beam to the crystal is thus approximately 0.7°. The size of the crystal plate is 655 mm (length) by 80 mm (width) by 10 mm (thickness). Furthermore, the surface of the crystal was ground with No. 1200 mesh silicon carbide in an attempt to achieve as large an integral intensity as possible. By this procedure it could be expected to achieve an integral intensity of the monochromatic X-ray radiation of 33 keV, approximately eight times as large as that obtained with crystals treated by a conventional etching procedure (Akisada *et al.*, 1987). A silicon plate was placed on a copper plate which was located on a goniometer (KOHZE KTG-200) and equipped with a pipe for water cooling.

2.2.2. *High-speed X-ray shutter and high-speed-driven filter*. For the purpose of reducing the X-ray exposure dose to patients as much as possible, a high-speed X-ray shutter and a high-speed-driven aluminium filter were placed before the crystal. The high-speed X-ray shutter chosen is of the stainless-steel rotating-drum type, having an aperture for the transmission of the radiation beam; three kinds of apertures corresponding to 2, 4, 6 ms were prepared (Oku *et al.*, 1998). By employing this type of high-speed X-ray shutter, the generation of pulse-like radiation at a rate of 30 s^{-1} or 15 s^{-1} is feasible.

A high-speed-driven aluminium filter was installed in an attempt to reduce the X-ray exposure dose to patients, *e.g.* at the time of setting the position of a patient, the intensity of 33 keV monochromatic X-ray radiation could be modulated within a range of 1/1–1/1000 by changing the thickness of the aluminium filter within a range 0–30 mm. This filter is driven by an electromagnetic motor, and, thus, ON/OFF switching of the filter at a speed of 20 ms is feasible. The aluminium filter receiving radiation from the incident X-rays was packed in a copper holder equipped with a pipe for water cooling..

2.2.3. *Clinical hutch*. The distance between the front of the new hutch and the crystal is approximately 4 m, and the monochromatic X-ray radiation is transmitted to the hutch through a pipe surrounded by a 2 mm-thick lead sheet in a direction 13° upwards from the crystal. At the entrance of the hutch, a calibrated 20 ml ionization chamber of the free-air type (Applied Engineering Inc. C-178) was arranged for measuring the X-ray exposure dose to patients. The hutch has three entrances, each for the patients, doctors and experimental equipment. Inside the hutch a vertically and horizontally driven chair for the patients, which is controllable from outside of the hutch, a small X-ray generator (TOSHIBA SXT-650A) for use during the insertion of catheters into the veins, a bed for the patient, an auto-injector (Nemoto Kyorindo M800)

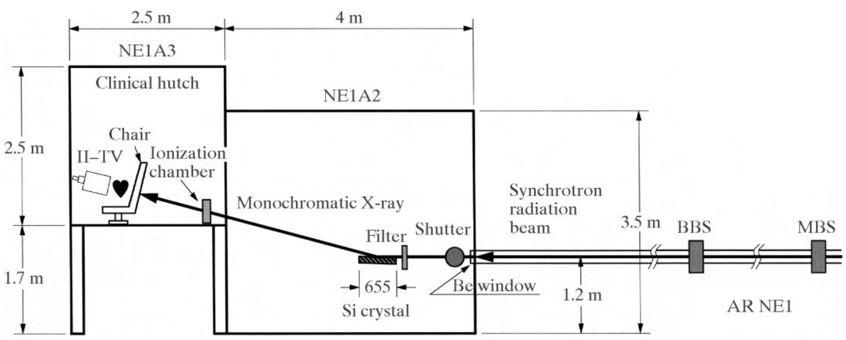

Figure 1
Clinical imaging system using intense synchrotron radiation from the MPW at BLNE1A, Accumulation Ring (AR). A monochromatic X-ray beam was introduced to the new clinical hutch after enlarging the vertical beam size by asymmetrical reflection from an Si crystal. Images were taken by an II–TV system. The radiation field was 130–150 mm in the vertical and 80 mm in the horizontal at the position of the detector.

for contrast media, and two TV cameras (SONY XC-77) for monitoring the patient, were arranged. The projection angle for a patient is set by rotating the chair by manual operation. The wall and floor of the hutch were covered with 6 mm lead sheets for shielding scattered X-rays. An audio system (Victor PA-604, XL-M61) was introduced to allow conversation between the patient and doctors across the hutch; furthermore, music flow was made available to maintain the patient's tranquil psychologically during the procedure. An inside view of the hutch is presented in Fig. 2. The arrangement of a circular X-ray exposure-dose counter on the left-hand side, a special chair for the patient and a two-dimensional X-ray imaging system (II–TV) on the right-hand side can be seen.

2.2.4. *Special interlock system for clinical use*. The hutch has a special interlock system, which is not usually installed for use in synchrotron radiation experiments for the following reasons. (*a*) A special console linked to the beam shutter, BBS, has been installed for use only by medical doctors. (*b*) The beam shutter is in an open status in the condition that all doors are closed; in an emergency, the beam shutter is closed when any one of the doors is opened. Thus, the operation of an emergency opening of either one of the doors for the patient and for the doctor is feasible without the use of an interlock key, which are used in synchrotron radiation experiments. During the imaging procedure, the doctor can monitor the patient's condition either through a lead-glass window of the hutch or on TV monitors. (*c*) The beam shutter is automatically closed when the skin dose to a patient exceeds the upper limit set by the medical doctor.

2.2.5. *Detector and data-processing system*. For the present two-dimensional imaging system, an II–TV system of the conventional type (TOSHIBA RTP9211G-10) for clinical applications is employed. The spatial resolution of the detector system is about 150 µm. Image signals from a TV can be processed in various ways using image processors (TOSHIBA DFP-2000A) after A/D conversion at $1024 \times 1024 \times 10$ bits. The image transmission is 30 images s^{-1}.

3. Phantom experiment

Imaging of a vessel phantom was performed using the system described in §2. The phantom was prepared by cutting holes of 1, 2, 5 and 8 mm diameter in an acrylic plate, and by sealing a contrast medium of 5% concentration by weight, which corresponds to the concentration of the contrast medium in the heart after being infused through the artery in the case of intravenous injection, in each hole. Imaging of the vessel phantom with a bone phantom was performed on piled acrylic plates having a total thickness of 200 mm for the purpose of simulating the size of the human body. The conditions of the AR during the procedure were 5.0 GeV for the energy of acceleration and 28 mA for the stored current. The rate of radiation was 4 ms image^{-1}. These conditions resulted in a phantom-incoming radiation dose of approximately 1 mGy image^{-1}.

Fig. 3 shows the result of a phantom experiment. The image was taken above the *K*-edge of iodine (33.17 keV + 160 eV). The vertical size, having a view area of 140 mm or above, was large enough to see a heart. Its uniformity, as measured by the contrast difference between the centre and edge, was within 25% vertically and 3% horizontally. The front face of the image intensifier was placed 500 mm distant from the patient position in an attempt to reduce the incoming scattered beams generated by the patient into the imaging system. In other words, precaution was taken not to lose the resolving power of the imaging system caused by the longer distance between the patient and the image intensifier, which most likely takes place when a surface grinding-processed monochromator crystal is used. The spatial resolution of the II–TV system measured by an MTF chart, which was set at the patient position, was 200 µm.

4. Discussion

The usefulness of the clinical settings was confirmed by the trial imaging on phantoms. In clinical applications the AR must be

Figure 2
Inside the clinical hutch. A circular X-ray exposure-dose counter on the left-hand side, a special chair for the patient, an X-ray imaging system (II–TV), and an auto-injector for contrast media on the right-hand side can be seen.

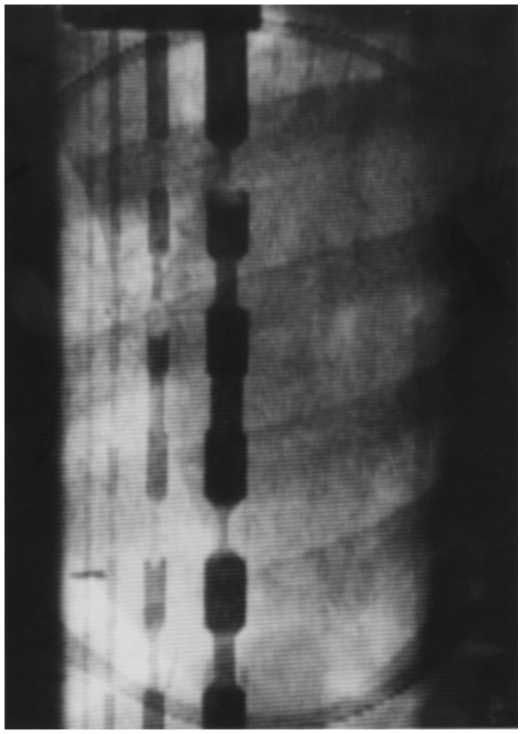

Figure 3
Result of the vessel phantom experiment. This image was taken above the *K*-edge energy of iodine (33.17 keV + 160 eV) with a field size of 140 mm in the vertical and 80 mm in the horizontal. Vessels filled with a 5% concentration by weight of iodine, overlapping the bone phantom, can be clearly distinguished.

Table 2
Estimated skin dose onto patient per injection for synchrotron radiation angiography and conventional digital subtraction angiography (DSA).

Imaging method	Skin dose/injection	Imaging sequence
Synchrotron radiation angiography	195 mGy	4 ms image^{-1} (exposure time) 1 mGy image^{-1} (skin dose) 30 images s^{-1} 15 s (450 images) with Al filter 5 s (150 images) without filter
Conventional DSA	450 mGy	5 ms image^{-1} (exposure time) 1 mGy image^{-1} (skin dose) 30 images s^{-1} 15 s

operated at 5.0 GeV in order to minimize contamination by the third higher harmonics (99 keV); thus, the critical energy of the synchrotron radiation spectrum from the MPW in the ring for this purpose is 17 keV. Furthermore, contamination by the third higher harmonics could be reduced relatively by modulating the gap (minimum gap 30 mm) and hence the intensity of the magnetic field (1.0 T at minimum gap) of the MPW. The estimated skin doses received by a patient per injection for synchrotron radiation angiography and conventional digital subtraction angiography (DSA) are given in Table 2. Imaging will be performed while keeping the aluminium filter inserted until the contrast media has reached the desired region in the case of synchrotron radiation angiography.

The first human examinations of intravenous coronary angiography using the two-dimensional imaging system were performed at the AR on 23 and 29 May 1996. Four patients (from 60 to 75 years old) were examined using the system. The AR was operated at 5.0 GeV and the average stored current was about 20 mA. Images were taken above the *K*-edge energy (33.34 or 37 keV). Three or four injections were performed for each patient to detect left and right coronary arteries at LAO (left anterior position) and RAO (right anterior position). Images were recorded in about 5 s at a rate of 30 images s^{-1}. The exposure time for each image was 4 ms. The maximum surface dose onto a patient was limited to up to 1 Gy for each patient by medical doctors. The photon intensity in front of a patient was approximately 5×10^{10} photons mm^{-2} s^{-1}. Contrast material, total amount 40 ml, was injected into the carotid vein or arm vein for each examination. The advantage of the two-dimensional imaging system for coronary angiography was confirmed by the examinations. Furthermore, the possibility of quantitative diagnostic imaging has been substantiated, because quantification of the coronary artery blood flow could be accomplished on dynamic images. The details concerning the patient examinations will be reported (Ohtsuka *et al.*, 1998).

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