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Synchrotron radiation at the Photon Factory for non-invasive coronary angiography: Experimental studies

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Summary

Synchrotron radiation available at the Photon Factory, National Laboratory for High Energy Physics, provides a new X-ray source which is highly suitable for K-edge subtraction. This is due to its high intensity, its parallelism and its monochromaticity, available in a monochromator system. Experiments were performed using wiggler synchrotron radiation. Since the beam size is relatively-small for in-vivo imaging, a phantom coupled with a detector was moved horizontally using a scanning table. K-edge subtraction was successfully applied both to the coronary artery phantom filled with barium sulphate, and to rat angiography using iodine contrast material. The potential use and value of energy subtraction was successfully demonstrated.

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Introduction

Digital subtraction angiography (DSA) is a technically advanced, noninvasive means of sequentially imaging the vascular system. However, a major problem relative to temporal subtraction consists of misregistration artifacts caused by blurring due to motion during swallowing, respiration and peristalisis. Coronary angiography employing temporal subtraction has not yet been successfully developed for clinical application.

The K-edge subtraction method, using the K-edge discontinuity in the attenuation coefficient of iodine, may provide a solution to this problem (**Fig. 1**). Some experimental studies using this method have been performed[1,2], but it has not yet been developed for clinical application due mainly to the insufficient intensity of monochromatic X-rays by the conventional filtering method. Synchrotron radiation, due to its high intensity and rapid tunability, facillitates dichromatic absorption radiography for clinical use. This is a report of fundamental studies of K-edge subtraction utilizing the wiggler beam available at the Photon Factory, National Laboratory for High Energy Physics[3,4].

Materials and Methods

Monochromatic X-rays were obtained using a Si crystal with reflection plane (111), during the initial stage of development, and (311) currently. A 4.5 Tesla high field wiggler magnet[5], used as a wave shifter tool, can extend the photon spectrum to the hard X-ray region. This vertical wiggler beam is polarized in the vertical plane and is usefully applied clinically with respect both to the energy and intensity of its radiation (**Fig. 2**). **Fig. 3** shows the radiographic system currently being used.

When white X-rays enter the lattice plane of the crystal at an angle of incidence θ, only X-rays with a wavelength λ, satisfying the following equation are reflected, due to the Bragg condition:

$$2d \sin \theta = \lambda$$

where d: distance between lattice planes
θ: angle between incident X-ray and lattice plane
λ: wavelength of reflected X-ray

The experimental conditions are summarized in **Table 1**.

The Si crystal plane used during the present series of tests was 40 by 140 mm, and the crystal was mounted on top of the goniometer. Rotation of the crystal was controlled by designating the number of pulses, using a pulsemotor controller operated at 10,000 pulses per degree. Such precision was not essential in this study, however. An encoder identified the rotation angles of the

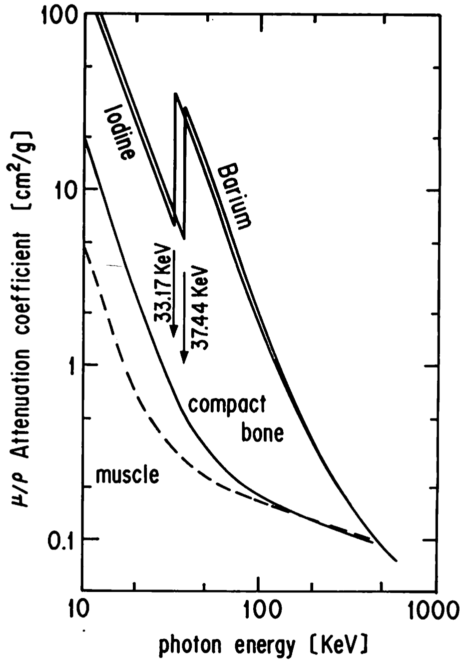

Fig. 1. Discontunity of iodine attenuation curve compared with continuity of bone and soft tissue.

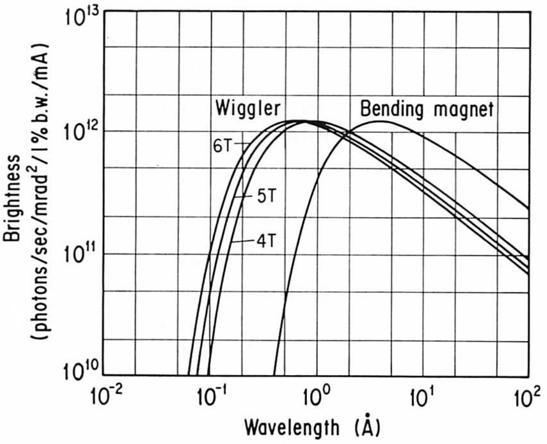

Fig. 2. Brightness of the wiggler radiation.

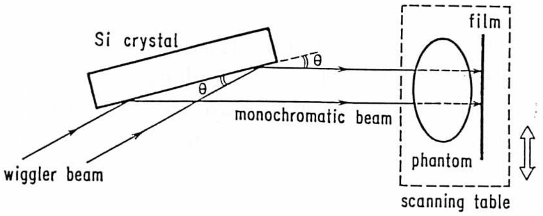

Fig. 3. Experimental setup for the monochromatic beam.

Table 1. Size of beam, monochromator and detector

Monochromator crystal	Si reflection plane (111) Size: 40 mm (vertical) × 140 mm (horizontal)
Incident beam size	40 mm (vertical) × 7 mm (horizontal)
Detector	X-ray film (KODAK-XTL) without intensifying screen for animal experiment Imaging Plate (Fuji Computed Radiography FCR)[6] for coronary artery phantom experiment
Horizontal scanning speed	1 mm/s
Radiation field	40 mm (vertical) × 100 mm (horizontal)

crystal which was surrounded by a set of lead plates 10 mm thick and an iron plate of 6 mm thickness to prevent scatter.

Since the beam available in the currently used optical system was small, the subject was scanned using a scanning table at a speed of 1 mm/sec in a direction perpendicular to the beam to obtain a relatively wide radiation field of approximately 40 × 100 mm.

The following evaluations were performed.

1) monochromaticity;
2) spatial and density resolution; and

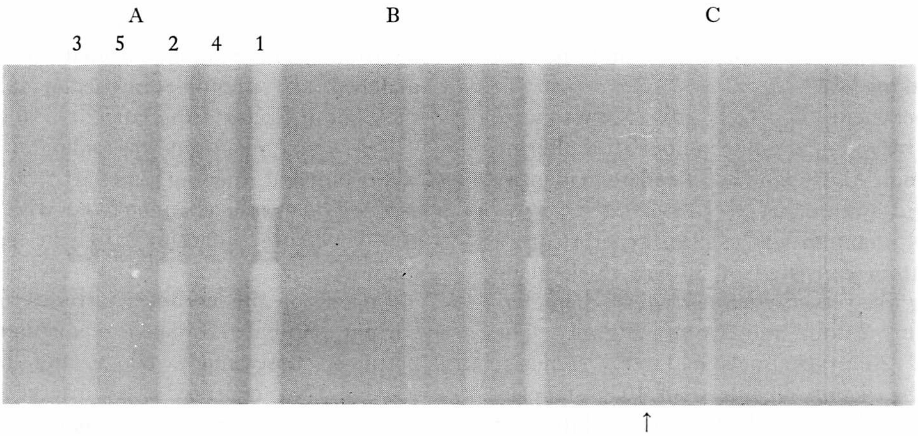

Fig. 4. Vessel phantom: 1 mm channels filled with Conraxin H® 0.5% (arrow).

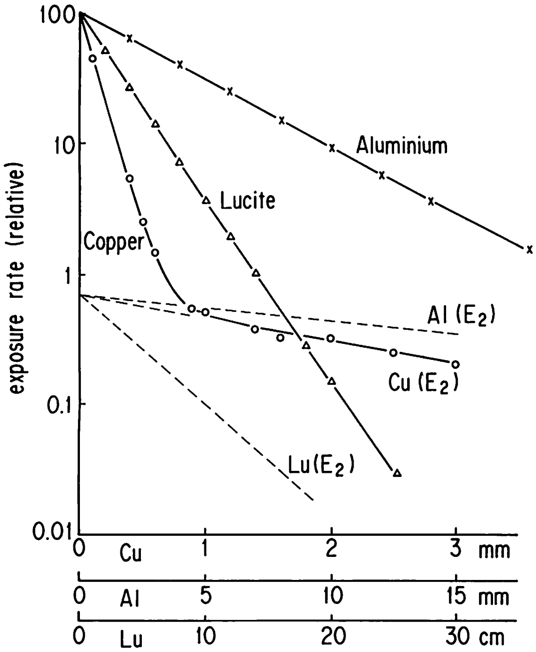

Fig. 5. Relationship between filter thickness and transmitted X-rays (33.17 KeV).

Table 2. K-edge energy of contrast material and Bragg angle

K-edge energy		Bragg angle for reflection plane (111)
Iodine	33.17 kev	3.41°
Barium	37.41 kev	3.02°

3) coronary artery phantom and in-vivo imaging.

In experiment 1), 33.17 keV X-rays were measured by an ionization chamber after filtering them through Al, Cu, and acrylic plate to identify their output and quality.

A vessel phantom was used in experiment 2). The phantom consisted of 30 mm thick lucite containing five sets of channels whose diameters were 3 mm, 2 mm, and 1 mm (**Fig. 4**). The 3 mm and 2 mm channels had 60% stenosis; whereas the, 1 mm channel had 40% stenosis. These channels were filled with a solution of contrast material, Conraxin H® 80%, providing iodine concentrations of 5%, 3%, 2%, 1% and 0.5%, respectively. The vessel phantom was sandwiched between lucite plates each 60 mm thick and all perpendicular to beam axis. In experiment 3), dichromography of the coronary artery phantom and angiography of the rat were studied.

Superficial coronary arteries were filled with barium sulphate of approximately 5% concentration. The coronary artery phantom was immersed in water 18 cm thick, together with a lung model made of cork, and a portion of a vertebral column.

In the animal experiment, an initial image was obtained above the K-edge after first injecting 6 m*l* Conraxin H® 80% into a tail vein of an anesthetized rat at a rate of 0.1 m*l*/sec. The second image was obtained below the K-edge after a second injection. Subtraction was performed using the two images.

The Bragg angle and the K-edge energy of the contrast materials, barium sulphate and iodine, used in the present studies are shown in **Table 2**. The K-edge energy was changed by ±80 eV, or a total of 160 eV, by rotating the crystal approximately 0.01°.

Results

Fig. 5 shows the relationship between each thickness of the Cu, Al and lucite filters and the relative doses of the transmitted X-rays. A biphasic curve was observed in the case of the Cu filter. The X-ray photon flux density available from a (111) Si monochromator was approximately 2×10^9 photons/mm^2/sec at 33.17 keV at the Photon Factory ring current, 100 mA.

The vessel phantom was radiographed using X-ray film and Imaging Plates (IP)[6] at 33.17 keV +80 eV. A 1 mm channel filled with Conraxin H® 0.5% was identified by the subtraction method.

Images of the coronary arteries filled with barium sulphate revealed a distinct contrast between those made above and below the K-edge. No contrast was observed between each of the two images of the spine, cork or water, above and below the K-edge, respectively, but

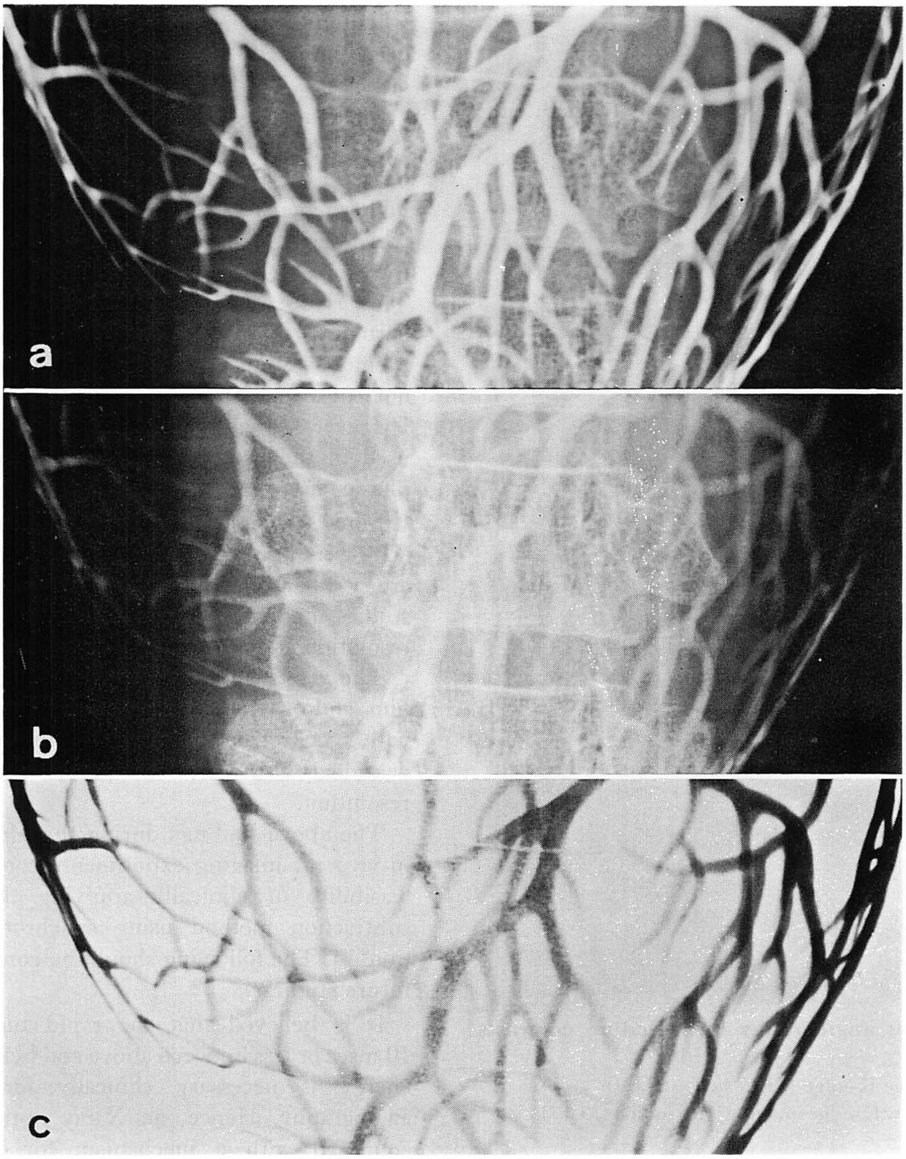

Fig. 6. Imaging of coronary arteries filled with barium sulphate.
(a) Above K-edge (37.41 keV+80 eV).
(b) Below K-edge (37.41 keV−80 eV).
(c) Subtracted image.

subtracted barium-filled coronary arteries were clearly shown (**Fig. 6**). The inferior vena cava, both kidneys and the ureters were well identified in the animal experiment. Peristalsis of the bowel caused misregistration artifacts during a five minute time lag between the above and below K-edge exposures (**Fig. 7**).

Discussion

Patients with coronary heart disease would

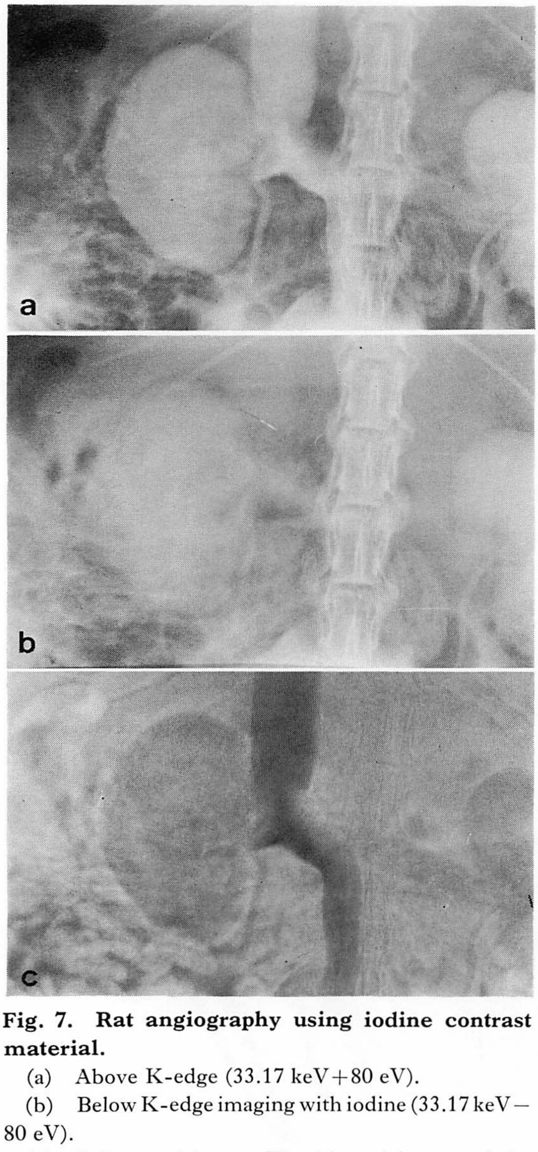

Fig. 7. Rat angiography using iodine contrast material.

(a) Above K-edge (33.17 keV+80 eV).

(b) Below K-edge imaging with iodine (33.17 keV−80 eV).

(c) Subtracted image. The blurred images of the bowel region are shown at the left lower corner.

benefit greatly if their coronary arteries could be visualized by intravenous digital subtraction angiography (IVDSA) rather than by Judkins' or Sones' method. Theoretically, the K-edge subtraction method using synchrotron radiation is most suitable for IVDSA of the coronary arteries.

Experimental studies of this method have been initiated at the Stanford Synchrotron Laboratory[7,8], but no clinical application has yet been reported.

Our Cu filter experiment showing a biphasic curve (**Fig. 5**) may indicate a contribution by higher energy X-rays in the 99 KeV region which are three times higher in energy than the 33.17 KeV X-rays of the K-edge of iodine. This is due to Si reflection (333) as a higher harmonic of (111). The existence of higher harmonic X-rays 1% or less in intensity does not pose problems in K-edge subtraction. However, Al and lucite filters of thicknesses used in the present study did not exhibit biphasic curves.

Film systems, including an Imaging Plate (IP), were used for the vessel phantom, coronary artery phantom and in-vivo imaging in these studies, because film systems have high spatial resolution and are suitable for scanning images.

The vessel phantom experiment showed that film and/or Imaging Plate (IP) systems used with synchrotron radiation are superior to conventional DSA in both spatial and contrast resolution.

The above findings during the phantom and in-vivo rat imaging experiments confirmed the feasibility of clinically applying the K-edge subtraction method using synchrotron radiation[9,10]. The following should be considered for future studies.

It is believed that the rapid tunability of 10 msec or less between above and below K-edge energy is necessary clinically for coronary angiography. Hence, an X-ray optical system equipped with a mechanism for high-speed energy conversion, coupled with a large radiation field, is required. During clinical application, when the contrast medium is injected intravenously, distinguishing the opacified coronary arteries from the superimposed opacified cardiac chambers, especially the left ventricle, becomes a problem. This could be resolved using the K-edge subtraction system with a wide dynamic range associated with the full range of digital image-processing techniques, although the signal due to the coronary arteries is not stronger than that due to quantum noise11). Moreover, development of an imaging system capable of a high-speed image pick up and processing is necessary.

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要　　約

非侵襲的冠状動脈造影に関する実験的研究

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高エネルギー研放射光実験施設(Photon Factory)から得られる放射光(synchroton radiation)を縦型ウィグラーに通し，Si 111面(あとの実験ではSi 311面)で分光することにより，十分な量の2つのエネルギーの単色光が得られる．ヨウ素はK吸収端(33.17 KeV)で吸収係数が非連続性を示し，一方，骨，軟部は連続性であるため，33.17 KeV+80 eVおよび33.17 KeV−80 eVの2つのエネルギー間の差分を行えば，骨，軟部を消去し得て，冠状動脈の微量のヨウ素を検出しうることになる．結晶の回転はパルスモータコントローラーによった．33.17 KeV±80 eVの2つエネルギーはSi結晶を0.01°回転させて得た．

分光ビーム強度は33 KeV付近で約2×10^9 photons/mm^2/secで，アルミ，ルサイト透過実験では，その単色性は完全なものであった．

イメージングプレートによる血管ファントム実験では，33.17 KeV+80 eVで40%狭窄のある直径1 mm，ヨウ素濃度0.5%が識別し得た．

ヒト心臓ファントムの冠状動脈にバリウムを封入し，バリウムのK吸収端上下，37.14 KeV±80 eVのエネルギー差分で，骨，軟部が見事に消去でき，冠状動脈像のみが得られた．

ラットの尾静脈からヨウ素造影剤を注射し，下大静脈，尿管，腎静脈の差分画像が得られた．ただしこの場合，エネルギー差分の間隔は5分間あり，動物は麻酔下で体動がなかった．

ヨウ素K吸収端を用いた放射光によるエネルギー差分は，従来の造影剤注入前後の差分法(時間差分法)に比べ明らかに優れ，後者では不可能とされた静注法による冠状動脈造影法の可能性を示すが，十分な線量，ヒト胸部をカバーする照射野，超高速エネルギー変換，超高速画像取り込み，およびその画像処理など，多くの解決を必要とする問題点があり，その研究が進行中である．

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