

Fig. 7. Mass attenuation coefficients of gadolinium and average photon energy of tungsten K α rays. Tungsten K-rays and bremsstrahlung rays with energies beyond the K-edge are absorbed effectively by gadolinium media.

K α rays is 58.9 keV, and gadolinium contrast media with a K-absorption edge of 50.2 keV absorb the rays easily. Therefore, blood vessels are observed with high contrasts.

Magnification angiography was performed using the filter at a voltage of 100 kV, a current of 0.50 mA, a distance of 1.5 m, and a time of 10 s. Figure 8 shows angiograms of a polytetrafluoroethylene (Teflon) tube of 1.0 mm bore diameter in a PMMA case using a contrast medium (Magnevist) that contains 150 mg/mL gadolinium. When the filter was used, the image contrast of the 1.0 mm tube was high.

To carry out fundamental studies on angiography, we usually use animal phantoms utilizing iodine-based microspheres 15 μ m in diameter. In the present study, because there were no ready-made gadolinium microspheres, we used gadolinium oxide microparticles of 1 to 10 μ m in diameter. Figures 9 and 10 show angiograms of two regions in a rabbit head obtained using gadolinium oxide particles. Using the filter, the contrasts of molars substantially decreased, and fine blood vessels were visible (Fig. 9). Next, the contrasts of incisives decreased, and blood vessels were clearly observed using the filter. In addition, spatial resolution was improved utilizing magnification imaging (Fig. 10). In both figures, fine blood vessels of approximately 100 μ m are visible by magnification imaging using the filter.

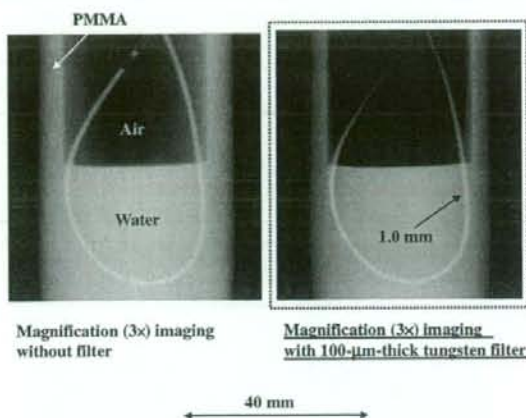


Fig. 8. Magnification angiograms of Teflon tube with bore diameter of 1.0 mm using a contrast medium (Magnevist) that contains approximately 150 mg/mL gadolinium.

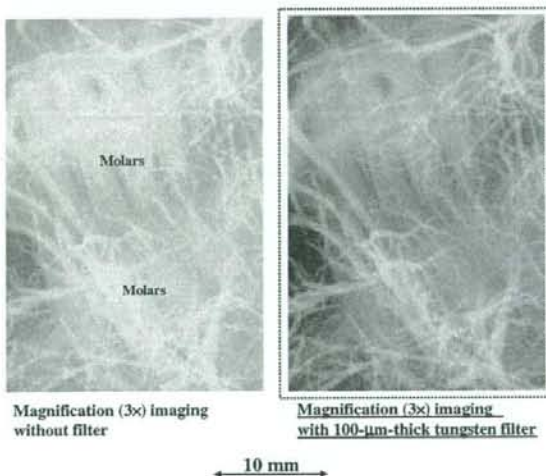


Fig. 9. Magnification angiograms of molar region in rabbit head using gadolinium oxide particles for making phantoms.

4. Conclusions and Outlook

We employed an X-ray generator with a 100- μ m-focus tungsten tube and performed enhanced magnification angiography using K-series characteristic X-rays of tungsten and high-photon-energy bremsstrahlung X-rays with a tube voltage of 100 kV, which can be absorbed easily by gadolinium media. The characteristic X-ray intensity increased with tube voltage, and the tube voltage was determined as 100 kV to increase the image contrast. The contrast of blood vessels was improved by insertion of the 100- μ m-thick tungsten filter for selecting out optimum X-rays. As compared with the dose without filtering, the exposure dose in patients can be reduced to a value below 5% using the filter without lowering image quality.

The spatial resolution of the CR system was approximately 200 μ m, and the resolution was improved to 70 μ m by threefold magnification imaging using a 100- μ m-focus

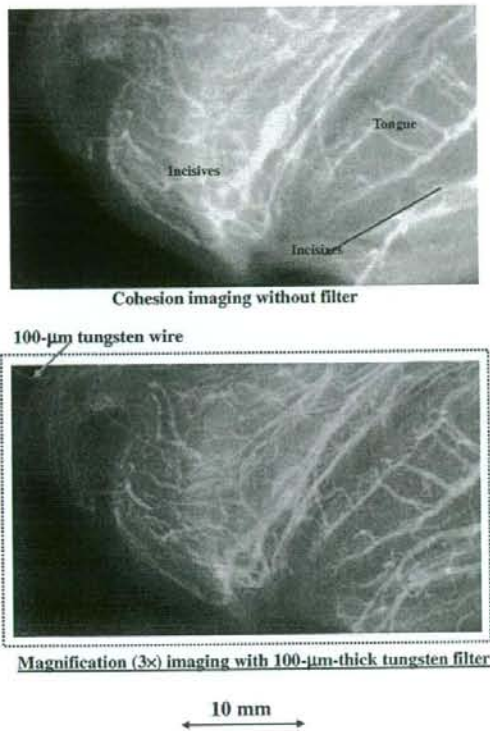


Fig. 10. Magnification angiograms of incisive region in rabbit head using gadolinium oxide particles.

tube. In order to clearly observe fine blood vessels below 100 μm in diameter, the sampling pitch of the CR system should be improved to 43.8 μm (Konica Minolta Regius 190). From experimental results, the maximum magnification rate without blurring was approximately threefold using a 100- μm -focus tube, and the rate increased with decreasing the focus diameter. In addition, the rate should be minimized to decrease the absorbed dose in patients.

Lately, we have developed several different X-ray nanoparticles such as quantum dots by wet dispersion. In particular, gadolinium-oxide nanoparticles can be used as x-ray-fluorescence and magnetic-resonance dots. In novel monochromatic X-ray imaging techniques utilizing drug delivery systems (DDSs), an X-ray fluorescence CT and a K-edge X-ray CT systems have been developed using grants from Japan Science and Technology Agency (JST). Therefore, we are very interested in molecular-level DDS imaging using several different nanoparticles.

At a tube voltage of 100 kV and a current of 0.50 mA, the maximum number of photons after penetrating the filter was approximately 5×10^7 photons $\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$ at 1.0 m from the source, and real time digital magnification radiography can be performed using an image intensifier camera (Hamamatsu C7716) with a frame rate of 30 frames per second (fps). To improve image quality and to increase frame rate using a flat panel detector, we have to increase count rate by increasing

tube current, and photon count rate can be increased to 1×10^9 photons $\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$ at 1.0 m using a kilowatt-range 100- μm -focus tungsten tube with a rotating anode.

Acknowledgments

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X-ray fluorescence camera for imaging of iodine media in vivo

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Abstract X-ray fluorescence (XRF) analysis is useful for measuring density distributions of contrast media in vivo. An XRF camera was developed for carrying out mapping for iodine-based contrast media used in medical angiography. Objects are exposed by an X-ray beam from a cerium target. Cerium K-series X-rays are absorbed effectively by iodine media in objects, and iodine fluorescence is produced from the objects. Next,

iodine $K\alpha$ fluorescence is selected out by use of a 58- μm -thick stannum filter and is detected by a cadmium telluride (CdTe) detector. The $K\alpha$ rays are discriminated out by a multichannel analyzer, and the number of photons is counted by a counter card. The objects are moved and scanned by an x-y stage in conjunction with a two-stage controller, and X-ray images obtained by iodine mapping are shown on a personal computer

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monitor. The scan pitch of the x and y axes was 2.5 mm, and the photon counting time per mapping point was 2.0 s. We carried out iodine mapping of non-living animals (phantoms), and iodine K α fluorescence was produced from weakly remaining iodine elements in a rabbit skin cancer.

Keywords X-ray photon counting · Energy discrimination · X-ray camera · X-ray fluorescence · CdTe detector · DDS

1 Introduction

X-ray fluorescence (XRF) analysis [1, 2] is useful for determining the presence of various elements, and monochromatic X-rays are used to produce X-ray fluorescence. We have developed several different monochromatic X-ray generators [3–6] to produce clean K-series characteristic X-rays. In particular, plasma X-ray generators [7, 8] have major capabilities for producing extremely clean K-rays of nickel, copper, and molybdenum from weakly ionized linear plasmas consisting of metal ions and electrons. In addition, high-photon energy K-rays of tantalum and tungsten have been produced from spherical plasma targets [9, 10], and these K-rays have been applied to high-speed gadolinium K-edge angiography [9–11]. However, it is difficult to increase the X-ray duration because these flash K-rays are produced by high-energy spark discharges.

Cerium K-rays are absorbed effectively by iodine-based contrast media and are useful for performing enhanced iodine K-edge angiography. Thus, we have developed a cerium X-ray generator [12, 13], with which fine blood vessels are observed with high contrast with use of iodine media. In addition, these K-rays are usable for producing iodine fluorescence for XRF analysis.

Recently, various drug delivery systems have been developed for cancer therapy and diagnosis; the main elements in drugs are detectable by XRF analysis. In medical angiography, iodine and gadolinium contrast media are employed in computed tomographic angiography (CTA) [14] and magnetic resonance angiography (MRA) [15], respectively. These media are usable for cancer diagnosis via XRF analysis, because neocapillaries in cancers are irregular and imperfect, and weak contrast media remain for a long time in cancer regions.

In this research, we developed an XRF camera utilizing a cadmium telluride (CdTe) detector to perform preliminary experiments for XRF mapping utilizing iodine-based contrast media.

2 Experimental methods

2.1 XRF camera

Figure 1 is a block diagram of a photon-energy discriminating X-ray camera for XRF analysis (Fig. 2). The camera system consists of an x - y stage driven by a two-stage controller, a CdTe detector (Amptek, XR-100T) with an amplifier unit, a multichannel analyzer (MCA) (γ PGT, MCA 4000, 4096 channels), a counter card (CC) (Contec, CNT32-4MT, Card Bus), a personal computer (PC), and a cerium X-ray generator. In this camera, objects are exposed by an X-ray beam formed by use of a 3.0-mm-diameter lead hole. Next, cerium K-series characteristic X-rays are absorbed effectively by iodine-based contrast media in

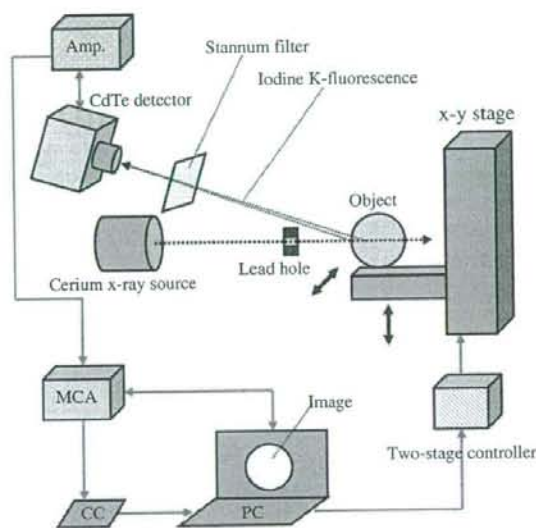


Fig. 1 Block diagram of an XRF camera utilizing a cerium X-ray generator for mapping of iodine media, where MCA is the multichannel analyzer, CC is the counter card, and PC is the personal computer

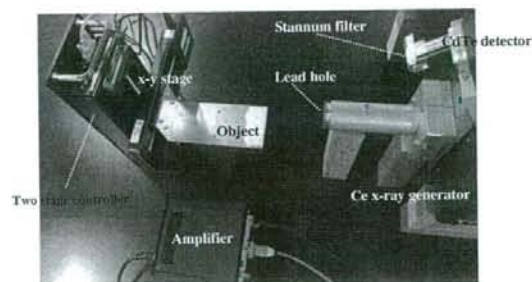


Fig. 2 Experimental setup of the XRF camera

objects, and iodine fluorescence is produced from the objects. Iodine $K\alpha$ rays are selected out with a 58- μm -thick stannum filter and are detected by the CdTe detector. The X-ray photons with energies from 27 to 30 keV ($K\alpha$ rays) are discriminated out by the MCA, and their counting signals from the MCA are sent to the CC. The objects are

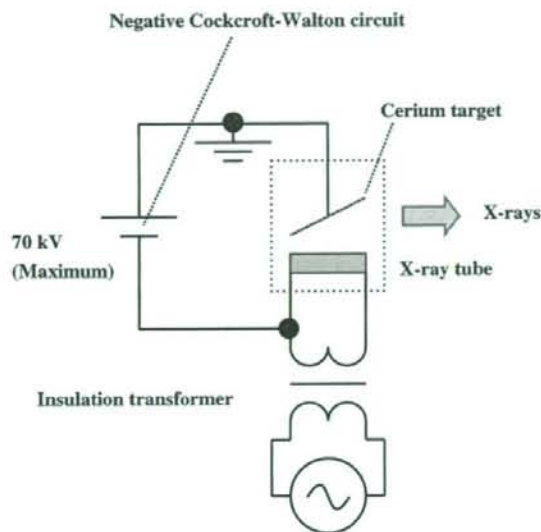


Fig. 3 Main circuit of the cerium X-ray generator

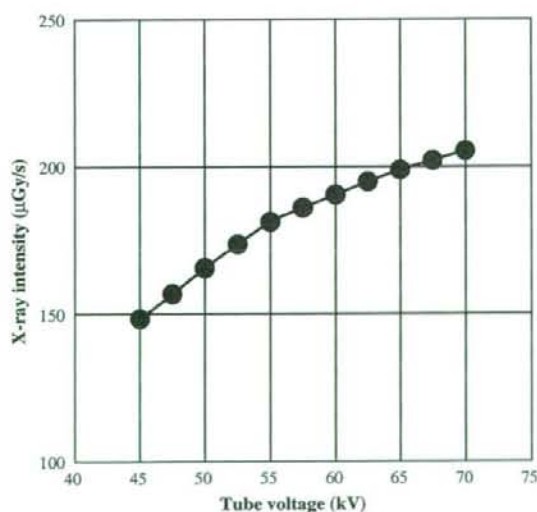


Fig. 4 X-ray intensities without a stannum filter at 1.0 m from the X-ray source according to changes in tube voltage at a tube current of 0.4 mA

moved and scanned by the x-y stage in conjunction with the controller, and X-ray images obtained by iodine mapping are shown on the PC monitor.

The X-ray mapping was carried out by repetition of the static counting and the moving of an object. The moving velocity was 5.0 mm/s. With this camera, the total scanning time T is equal to the X-ray exposure time for mapping, and T is given by

$$T = (t_c + t_m)xy/S_x S_y, \quad (1)$$

where t_c is the photon counting time per mapping point, t_m is the moving time between two points, x is the horizontal dimension of the scanning field, y is the vertical dimension, and s_x and s_y are moving steps in the horizontal and vertical directions, respectively. Although the maximum scan-field dimensions are 100 mm \times 100 mm, the dimensions were reduced to 50 mm \times 50 mm for decreasing T . In this experiment, x , y , s_x , s_y , t_c , and t_m are 50 mm, 50 mm, 2.5 mm, 2.5 mm, 2.0 s, and 0.5 s, respectively, and T is calculated as 1,000 s.

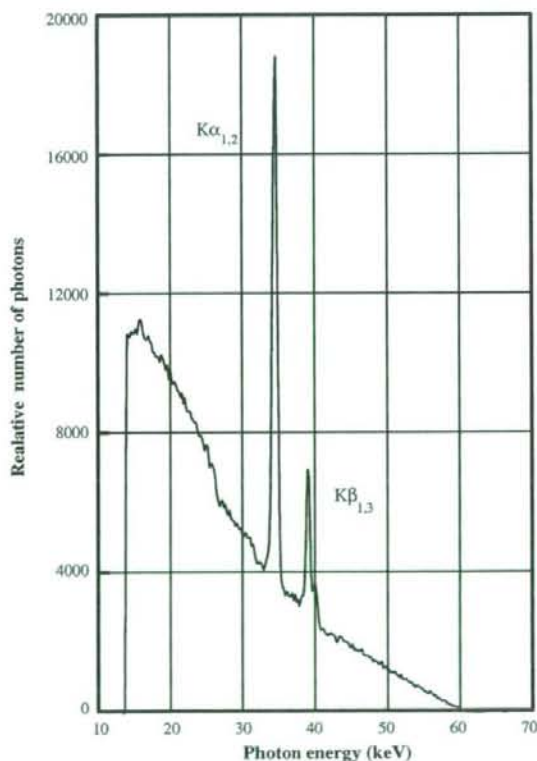
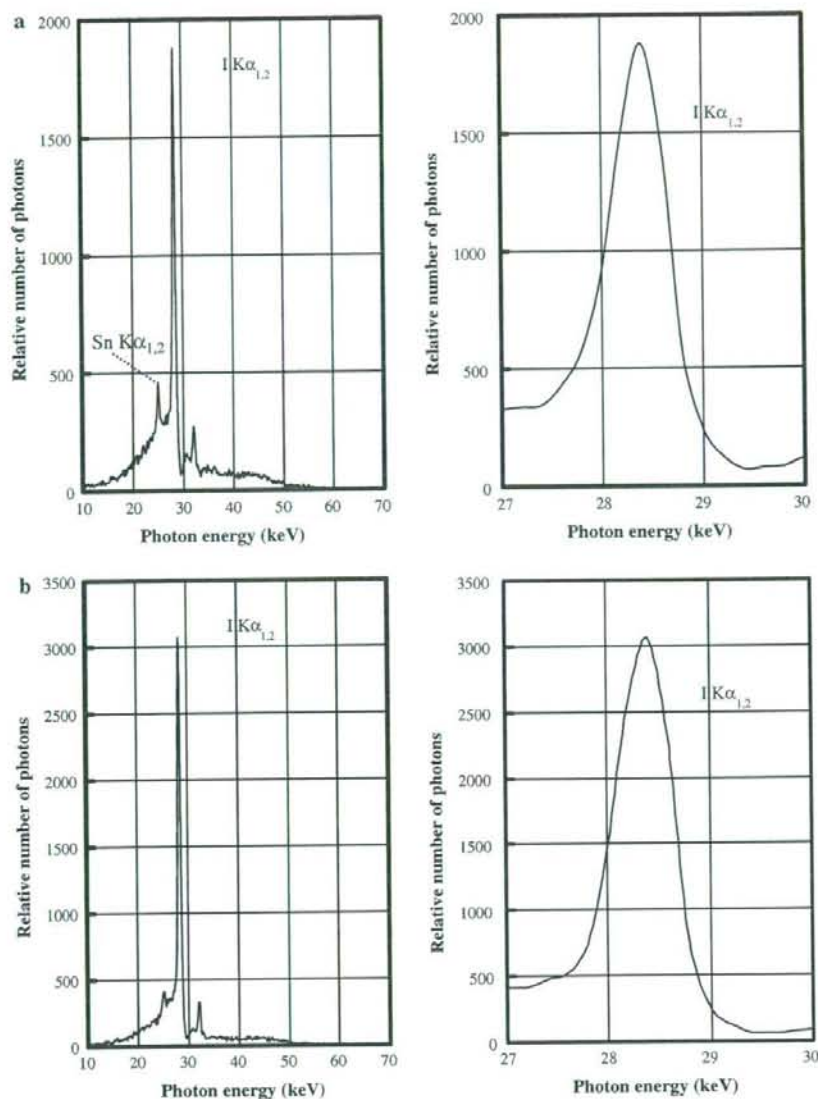


Fig. 5 X-ray spectra without a stannum filter from a cerium target at a tube voltage of 60 kV

Fig. 6 X-ray spectra with a 58- μm -thick stannum filter from glass vials filled with two iodine media with densities of **a** 15 mg/ml and **b** 30 mg/ml (right side selected iodine $\text{K}\alpha_{1,2}$ rays)



2.2 Cerium X-ray generator

The cerium X-ray generator consists of a main controller and an X-ray tube unit with a Cockcroft-Walton circuit and a cerium target tube (Hitachi Medical, Ce-sp70 k) for enhanced K-edge angiography. The tube voltage, current, and exposure time can be set by the controller. The high-voltage line employs a negative Cockcroft-Walton circuit to decrease the dimensions of the tube unit. The X-ray tube is a fixed anode diode with a cerium target with an anode angle of 22° . In the X-ray tube, negative high voltages are applied to the cathode, and the anode (target) is connected

to the tube unit case (ground potential) to cool the anode and the target effectively (Fig. 3). In this experiment, the tube voltage ranged from 45 to 65 kV, and the tube current was 0.40 mA (maximum current).

3 Results

3.1 X-ray intensity and spectra

The X-ray intensity without a stannum filter was measured using an ionization chamber (Victoreen, 660) with a 400-

cm^3 -volume probe (660-5) at 1.0 m from the X-ray source and a tube current of 0.40 mA (Fig. 4). When the tube voltage was increased, the X-ray intensity increased. At a tube voltage of 60 kV, the X-ray intensity was 190 $\mu\text{Gy/s}$.

To measure X-ray spectra without a stannum filter at photon energies ranging from 14 to 70 keV, we employed a

CdTe detector (Fig. 5). At a tube voltage of 60 kV, cerium K-series X-rays were detected, and the bremsstrahlung X-ray intensity increased with decreasing photon energy. Figure 6 shows spectra from glass vials filled with iodine media with densities of 15 and 30 mg/ml. The iodine $K\alpha$ intensity increased with increasing iodine density, and

Fig. 7 X-ray spectra with a 58- μm -thick stannum filter from a glass vial filled with water at a tube voltage of 60 kV (right side background X-ray spectra)

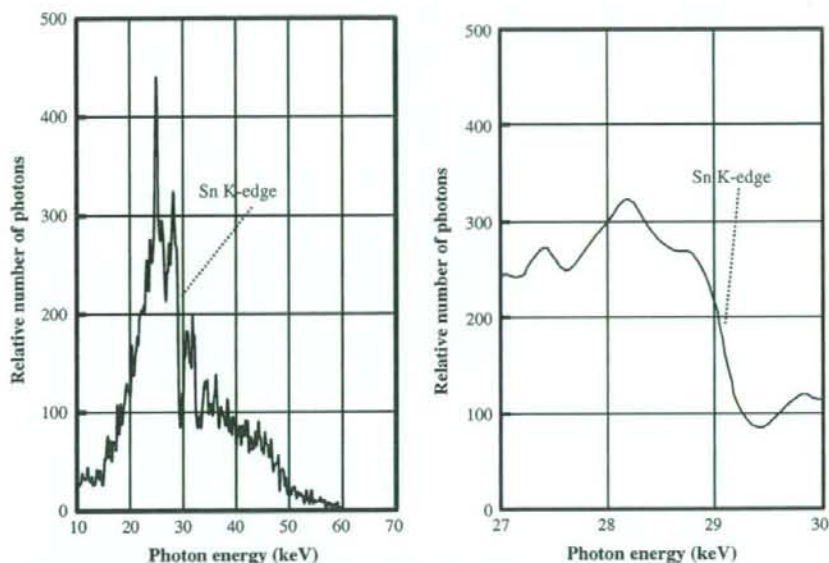
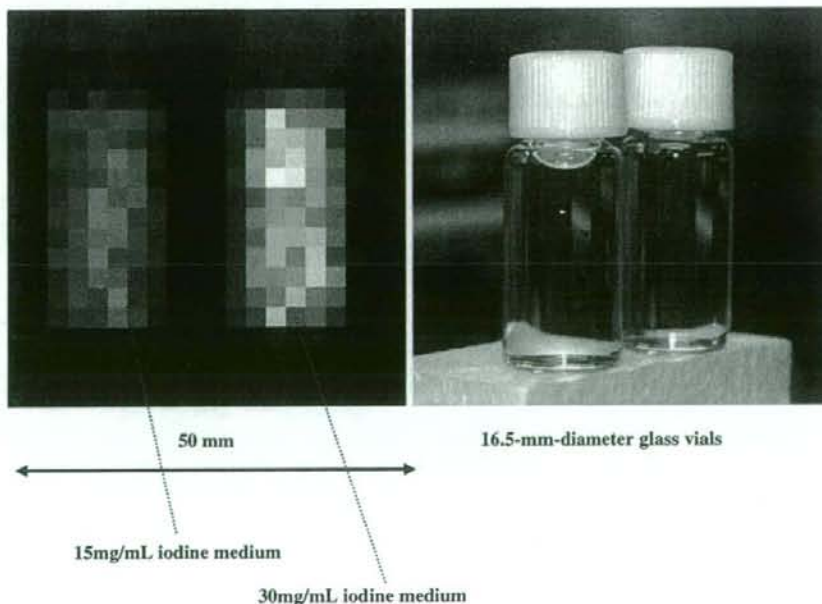


Fig. 8 X-ray image of two 16.5-mm-diameter glass vials filled with iodine media with densities of 15 and 30 mg/ml



stannum $K\alpha$ fluorescence from the filter was observed. As compared with background intensities, the iodine $K\alpha$ intensities were high, and we observed stannum K-edges (Fig. 7).

3.2 XRF mapping

In the XRF mapping, the maximum and minimum counts correspond to the maximum and minimum image densities,

Fig. 9 X-ray image of a PMMA phantom with two 8.0-mm-diameter holes filled with iodine media with densities of 15 and 30 mg/ml

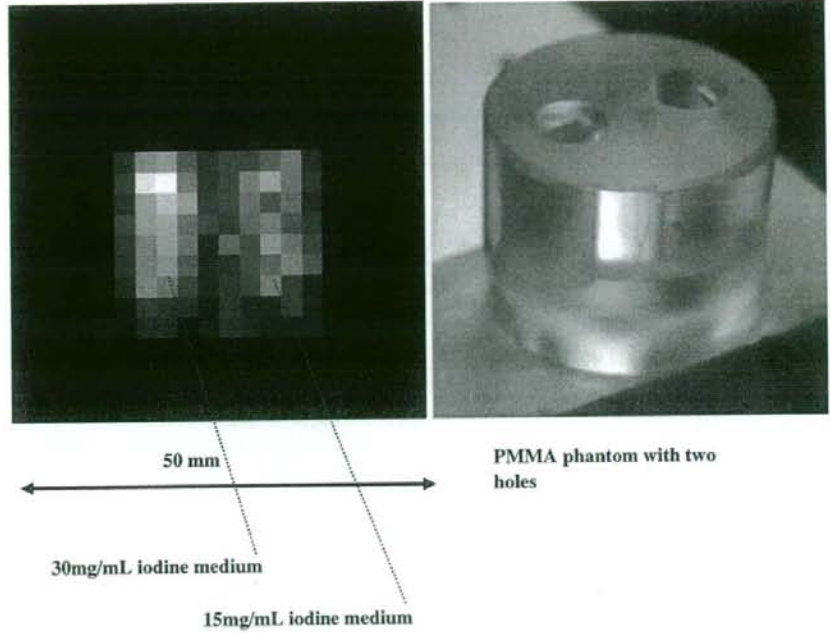


Fig. 10 X-ray image of a PMMA phantom with a 8.0-mm-diameter hole filled with iodine medium with a density of 30 mg/ml

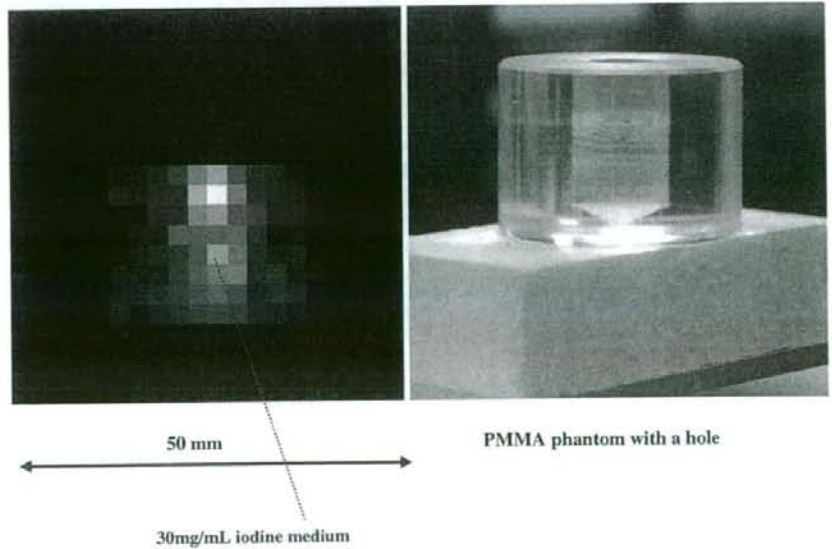


Fig. 11 X-ray image of a rabbit heart for angiography. Coronary arteries are filled with iodine microspheres

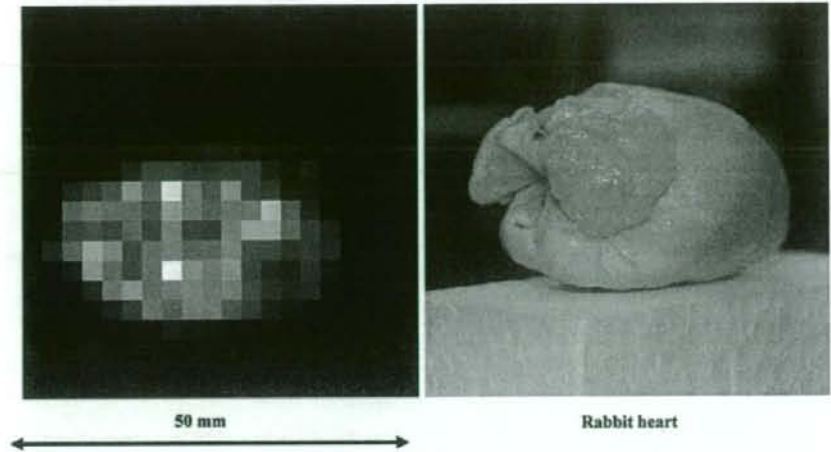
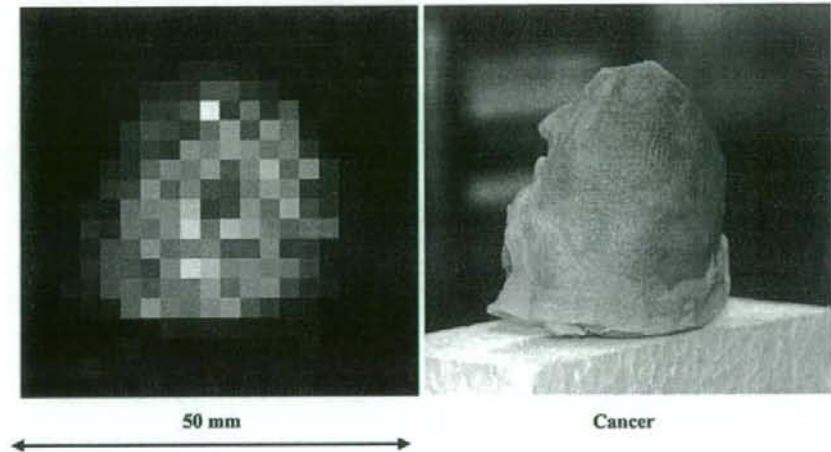


Fig. 12 X-ray image of a rabbit skin cancer. Weakly remaining iodine elements in a cancer region were detected



respectively, and the pixel sizes are equal to the steps on the x and y axes of 2.5 mm \times 2.5 mm. The mapping image was constructed as a Bitmap file with the maximum and minimum densities of 255 (white) and 0 (black), respectively. Figure 8 shows an X-ray image of two 16.5-mm-diameter glass vials filled with two different-density contrast media of 15 and 30 mg/ml. The image density decreases with decreasing iodine density. When we used a polymethyl methacrylate (PMMA) phantom with two holes of 8.0 mm in diameter, two different-density media were observed (Fig. 9). Figure 10 shows an image of a PMMA phantom with an 8.0-mm-diameter hole filled with iodine medium at a density of 30 mg/ml. In both PMMA phantoms, scattering X-rays with energies beyond the iodine K-edge produce iodine fluorescence in the iodine medium, and the fluorescence is detected by the CdTe detector.

Thus, the hole dimensions increased slightly by approximately 1 pixel (2.5 mm).

An image of an extracted rabbit heart for angiography is shown in Fig. 11. Coronary arteries were filled with iodine microspheres 15 μ m in diameter, and iodine elements in blood vessels were detected by mapping. In mapping of a rabbit skin cancer, iodine elements that remained in the cancer were detected (Fig. 12).

4 Discussion

We developed an XRF camera utilizing a cerium X-ray generator and detected iodine K α rays from objects with a photon energy resolution of 1.5 keV. The count rate of the K α rays increased with increasing iodine density, and

iodine fluorescence was detected from a cancerous region in a rabbit ear. With PMMA phantoms, because $K\alpha$ fluorescence is produced by the scattering beam from the PMMA regions, these photons should be subtracted from the mapping counts.

The spatial resolution improved with decreasing sampling pitches on the x and y axes and with decreasing beam diameter for scanning. At a constant tube voltage of 60 kV, the sampling time decreased with increasing count rate of iodine $K\alpha$ rays by increasing the iodine density at a maximum tube current of 0.4 mA.

Recently, an energy-discriminating 64-channel CdTe linear detector, developed by Hamamatsu Photonics, has been useful for constructing an X-ray camera with a stage. As compared with the single detector described in this paper, the X-ray exposure time can be decreased when the linear detector is used. However, it is not easy to determine the photon energy just beyond the iodine K-edge of 33.2 keV and to control the energy width.

For increasing the count rate of a CdTe detector setup, the time constants in the amplifier circuits should be minimized so that pileups of event signals without a decrease in energy resolution are prevented. In conjunction with a multipixel photon counter, a high-light-yield scintillator with a short decay time (below 1 ns) is usable for discriminating photon energy, and a high-speed X-ray photon-discriminating system for decreasing the total scanning time for imaging will become possible.

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Embossed radiography utilizing energy subtraction

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Abstract Currently, it is difficult to carry out refraction-contrast radiography by using a conventional X-ray generator. Thus, we developed an embossed radiography system utilizing dual-energy subtraction for decreasing the absorption contrast in unnecessary regions, and the contrast resolution of a target region was increased by use of image-shifting subtraction and a linear-contrast system in a flat panel detector (FPD). The X-ray generator had a 100- μ m-focus tube. Energy subtraction was performed at tube

voltages of 45 and 65 kV, a tube current of 0.50 mA, and an X-ray exposure time of 5.0 s. A 1.0-mm-thick aluminum filter was used for absorbing low-photon-energy bremsstrahlung X-rays. Embossed radiography was achieved with cohesion imaging by use of the FPD with pixel sizes of $48 \times 48 \mu\text{m}$, and the shifting dimension of an object in the horizontal direction ranged from 100 to 200 μm . At a shifting distance of 100 μm , the spatial resolutions in the horizontal and vertical directions measured with a lead test chart were both 83 μm . In embossed radiography of non-living animals, we obtained high-contrast embossed images

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of fine bones, gadolinium oxide particles in the kidney, and coronary arteries approximately 100 μm in diameter.

Keywords Embossed radiography · Digital subtraction · Energy subtraction · Contrast resolution · Polychromatic X-rays

1 Introduction

Extremely clean monochromatic parallel X-ray beams have been formed by use of synchrotrons and single silicon crystals, and these beams have been applied to carrying out enhanced iodine K-edge angiography [1–3], phase-contrast radiography [4–6], and topography [7, 8]. For performing K-edge angiography, monochromatic X-rays with energies just beyond the iodine K-edge of 33.2 keV have been used, because these rays are absorbed effectively by iodine-based contrast media. Currently, phase-contrast radiography is based primarily on X-ray refraction in objects, and soft tissues, such as breast cancers [6], can be imaged with high contrast. However, it is difficult to carry out phase-contrast imaging of contrast media for medical angiography, delivered nano-particles, and hard tissues. Two-dimensional X-ray topography also is a method for imaging defects in crystals by utilizing X-ray diffraction.

Without the use of synchrotrons, several different monochromatic X-ray sources [9–12] have been developed, and K-edge angiography, phase radiography, and topography have been carried out. In particular, a cerium X-ray generator [13, 14] has been developed and has been applied to carrying out cone-beam K-edge angiography because cerium K α rays (34.6 keV) are absorbed effectively by iodine media. Next, phase radiography for edge enhancement of objects has been performed by magnification radiography with a microfocus X-ray generator and polychromatic X-rays [15]. However, this conventional phase radiography is usable for imaging only of soft tissues, and a microfocus X-ray tube is necessary. Therefore, we are very interested in the development of a novel radiography system instead of the phase imaging by use of a generalized digital X-ray image sensor and a conventional large-focus tungsten tube that produces polychromatic X-rays.

Energy subtraction radiography [16, 17] is an important technique for imaging target regions in vivo by removing muscle and bone regions from radiograms. Currently, two different energy radiograms are obtained with two different tube voltages, and dual-energy subtraction radiography is carried out by digital subtraction between the high- and low-energy images. Furthermore, embossed radiography (ER) [18] is a novel technique for constructing concavo-convex radiography, such as phase-differential imaging,

and is realizable with digital image subtraction after image shifting with an optimal dimension between two images. The image shifting is carried out by moving an X-ray source [18], by moving an object precisely, and by shifting image pixels in a flat panel detector (FPD) with use of a computer program before subtraction. By use of this radiography, the target region in various objects can be imaged with embossing, and the maximum contrast resolution is achieved without a drop in spatial resolution. In addition, our ultimate goal of embossing is the development of a novel computed tomography (CT) system with a high contrast resolution for cancer diagnosis that utilizes a drug delivery system.

In our research, major objectives are as follows: construction of edge enhancement radiography such as phase-differential imaging utilizing embossing, an increase in the contrast resolution of the target region, and energy subtractions of contrast media and nano-particles. Therefore, we carried out preliminary experiments for ER utilizing two-shot dual-energy subtraction by shifting objects.

2 Experimental methods

2.1 Experimental setup for ER

Figure 1 shows an experimental setup for performing ER utilizing an FPD (1024EV, Rad-Icon Imaging, Santa Clara, CA). This experiment is carried out for a fundamental study on single-dimensional ER, although two-dimensional shifting is realizable with a pixel-shifting computer program. ER was performed by digital subtraction, cohesion radiography, and shifting of an object with a dimension ranging from 100 to 200 μm and with a traveling microscope (NRM-2XZ, Shimadzu Rika, Tokyo, Japan) that had a length resolution of 10 μm . The computer program names for observing raw-file images and for carrying out

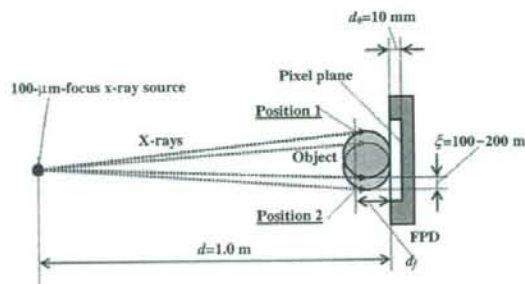


Fig. 1 Experimental setup for performing embossed radiography (ER) utilizing energy subtraction, where ζ is the image-shifting dimension in the FPD, d_f is the distance from the FPD to the position in the object, d_0 is the distance between the FPD face and the pixel plane, and d is the distance between the source and the FPD face

subtraction radiography were ShadoCam (Rad-Icon Imaging, Santa Clara, CA) and EnergyCalc Composition 1.0 (AD Science, Funabashi, Japan), respectively.

For carrying out ER such as phase-differential imaging, the minimum shifting dimension is two times the pixel size of 48 μm , and the maximum shifting dimension is almost equal to an allowable spatial resolution. Absorption contrast of unnecessary regions is decreased by energy subtraction. An object is exposed by an X-ray generator with a 100- μm -focus X-ray tube, and the first radiogram is obtained at position 1 in Fig. 1. The second radiogram is taken at position 2 in Fig. 1 after shifting of the object. Two radiograms are taken using two different photon energy spectra with maximum photon energies of 45 and 65 keV, and are recorded as raw files. In this setup, the image shifting dimension ξ in the FPD is given by

$$\xi = \sigma(d + d_0)/(d - d_f) \cong \sigma, \quad (1)$$

where σ is the shifting dimension of the object, d_f is the distance from the FPD to the position in the object, d_0 (=10 mm) is the distance between the FPD face and the pixel plane, and d is the distance between the source and the FPD face. In our research, σ and d were determined to be 100–200 μm and 1.0 m, respectively. In dual-energy subtraction for embossing, an embossed raw-file $R_e(x, y)$ as a function of horizontal x and vertical y distances in the FPD is calculated by

$$R_e(x, y) = R_1(x, y) - KR_2(x - \xi, y), \quad (2)$$

where $R_1(x, y)$ is the first raw-file image at position 1, $R_2(x - \xi, y)$ is the second raw-file image with different energy spectra at position 2 after shifting of the object, K ($0 < K \leq 1.0$) is a constant for subtraction, and K varies by 0.1 increments.

Typical one-dimensional projection curves for ER are shown in Fig. 2. $R_1(x)$ is the first projection curve from the FPD, $KR_2(x - \xi)$ is the shifted curve for subtraction, and $R_e(x)$ is the embossed projection curve in the raw file system. In this experiment, an embossed projection curve $T(x)$ and its inverted curve $T_i(x)$ in the TIFF file system are written as

$$T(x) = \{R_1(x) - KR_2(x - \xi) - R_{\min}\} \times D_m / (R_{\max} - R_{\min}), \quad (3)$$

$$T_i(x) = D_m - T(x), \quad (4)$$

where D_m (= 255) is the maximum density, and R_{\max} and R_{\min} are the maximum and minimum densities of $R_e(x)$, respectively. In the FPD, the densities of 0 and D_m correspond to black and white, respectively. Therefore, the contrast resolution increases to 1 after subtraction by a linear-contrast system. The matrix size is about 1 M (1,048 \times 1,048) pixels, and the pixel sizes are

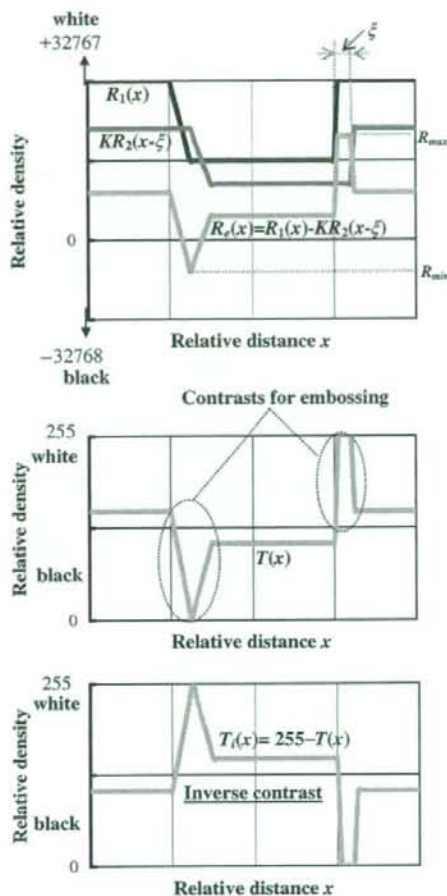


Fig. 2 One-dimensional projection curves for performing ER utilizing subtraction, where ξ the image shifting dimension in the FPD, $R_e(x)$ is the embossed projection curve in the raw file system, $R_1(x)$ is the first projection curve from the FPD, $KR_2(x - \xi)$ is the shifted curve for subtraction, K is a constant, $T(x)$ is an embossed projection curve in the TIFF file system, $T_i(x)$ is its inverted curve, and R_{\max} and R_{\min} are the maximum and minimum densities of $R_e(x)$, respectively

48 $\mu\text{m} \times 48 \mu\text{m}$. The gray scale ranges from 0 to 255, and the relation between the X-ray intensity and the gray level is linear.

2.2 X-ray generator

Figure 3 shows the circuit diagram of an X-ray generator that was designed for regulating the focal size of an X-ray tube (Toshiba, 1-311) by controlling the negative bias voltage of the focusing electrode. In this experiment, the size was regulated as 100 μm at a bias voltage of -20 V because the size decreased with increasing negative bias

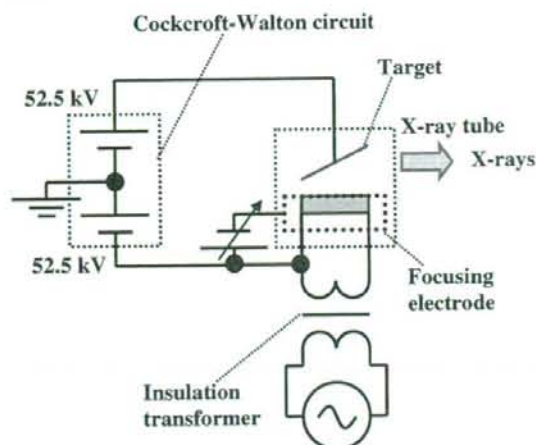


Fig. 3 Circuit diagram of a 100- μm -focus X-ray generator

voltage, and tube voltage, current, and exposure time could be controlled by a main controller. The high-voltage line employs the Cockcroft-Walton circuit, and positive and negative high voltages are applied to the anode and cathode electrodes, respectively. The filament heating current is supplied by an AC power supply with an insulation transformer that is used for isolation from the high voltage from the Cockcroft-Walton circuit. For measurement of X-ray intensity, the tube voltage ranged from 40 to 70 kV, and the tube current was regulated to be 0.50 mA. Because the maximum exposure time of the FPD was 6.0 s, the time was set as 5.0 s, which increased the X-ray intensity for radiography.

2.3 Measurement of X-ray intensity

The measurement of X-ray intensity for ER is important because the intensity is decreased by the subtraction. The X-ray intensity was measured with an ionization chamber (660, Victoreen, Solon, OH) with a 400-cm³ volume probe (660-5, Victoreen, Solon, OH) with a tube current of 0.50 mA at 1.0 m from the X-ray source. For performing ER utilizing dual-energy subtraction, the total X-ray intensity of the two shots is equal to the exposed dose I_{ex} for patients. Thus, I_{ex} and the X-ray intensity after the subtraction I_s are given by

$$I_{\text{ex}} = I_1 + I_2, \quad (5)$$

$$I_s = I_1 - KI_2, \quad (6)$$

where I_1 and I_2 are the X-ray intensities at positions 1 and 2, respectively. Roughly speaking, the absorption contrast decreases when I_s decreases. Moreover, the image contrast reverses in a case where I_s is a negative value.

2.4 Measurement of X-ray spectra

The image contrast varies corresponding to the X-ray spectra for radiography, and we have to measure the spectral distributions before energy subtraction. In order to measure X-ray spectra, we employed a cadmium telluride (CdTe) detector (XR-100T, Amptek, Bedford, MA) and measured spectra at 1.0 m from the X-ray source. The cooled detector unit with a charge amplifier was set at 1.0 m from the X-ray source, and event signals from the detector unit were amplified again by a shaping amplifier unit. A 0.1-mm-diameter lead pinhole was set in front of the detector facing the X-ray source to decrease the photon count rate. The photon energy was discriminated by a multichannel analyzer (MCA-8000A, Amptek, Bedford, MA), and the X-ray spectra were observed on a personal computer monitor. Measurement results for the X-ray spectra are important for carrying out dual-energy subtraction because the spectral distribution is the X-ray intensity as a function of the photon energy. In particular, when we perform K-edge subtraction, we have to confirm the spectra with energies below and beyond the K-edge energy, and the spectra should be controlled to optimal distributions by selection of the tube voltage, the element of the filter, and its filter thickness.

2.5 Method for ER utilizing single-energy subtraction

Although unnecessary regions are not deleted by single-energy subtraction, we carried out single-energy ER to observe the effect of embossing. Two radiograms were taken at positions 1 and 2 at a tube voltage of 45 kV by use of the filter, and the embossing was performed by image shifting. The embossed raw-file radiogram $R_e(x, y)$ was calculated by

$$R_e(x, y) = R_{45}(x, y) - KR_{45}(x - \xi, y), \quad (7)$$

where $R_{45}(x, y)$ is a radiogram obtained with a tube voltage of 45 kV and $R_{45}(x - \xi, y)$ is a radiogram at a voltage of 45 kV after shifting of the object.

The X-ray exposure time was 5.0 s, and two embossed radiograms were obtained with K values of 1.0 and 0.7. At a K of 1.0, the absorption contrast is removed, and the embossed effect is confirmed easily. When K is decreased, the absorption contrast increases, and the embossed effect decreases. Because the absorption contrast seldom varied in a K range from 0.5 to 0.7, K was determined as 0.7 for performance of single-energy ER with absorption contrast.

2.6 Method for ER utilizing dual-energy subtraction

As compared with single-energy ER, the target regions are imaged effectively by dual-energy ER. Because the K

edges of iodine and gadolinium are 33.2 and 50.3 keV, respectively, a high-energy radiogram should be taken at an energy region beyond 50.3 keV. The minimum difference between the high and low tube voltages was approximately 20 kV. Therefore, two different energy radiograms were obtained with tube voltages of 45 and 65 kV with use of the filter, and dual-energy ER was performed by image shifting. Utilizing energy subtraction, $R_e(x, y)$ was written as

$$R_e(x, y) = R_{45}(x, y) - KR_{65}(x - \xi, y), \quad (8)$$

where $R_{65}(x - \xi, y)$ is a radiogram with a voltage of 65 kV after shifting of the object. For an increase in the embossed effect with high contrast, K is determined to be within a range from 0.7 to 1.0.

2.7 Measurement of spatial resolution

The spatial resolution of the horizontal and vertical directions was measured with a conical lead test chart. The resolution was measured for line pairs L per 1.0 mm. Therefore, the spatial resolution S (μm) is given by

$$S = 1,000/2L. \quad (9)$$

Thus, when five line pairs (LP) are seen, the spatial resolution is determined as 100 μm .

2.8 Making of gadolinium oxide particles

A gadolinium oxide suspension for injection was made in a high-pressure machine (Starburst Mini, Sugino Machine, Namerikawa, Japan) for dispersing micro-particles. The high-pressure dispersing was carried out five times with use of physical saline, and the average particle diameter and the density of gadolinium oxide were 700 nm and 20%, respectively.

2.9 Objects for ER

For performing ER, we used five objects as follows: a nonliving nude mouse with a weight of 15 g, a lead test chart (PTW, L659035), an extracted rabbit kidney (8 g), an extracted rabbit heart (11 g), and a dried pig vertebra (22 g). The mouse, kidney, and heart were preserved in 10% formalin solution. The kidney and heart were extracted from two different rabbits with weights of approximately 2 kg after anesthetic (5% Nembutal) injection of 1.8 ml in an ear. A renal pelvis in the kidney was filled with gadolinium oxide suspension of 0.3 ml as described above by injection, and coronary arteries were filled with iodine-based microspheres. When a 20%-microsphere suspension by use of physical saline was injected into the arteries, the saline penetrated capillaries

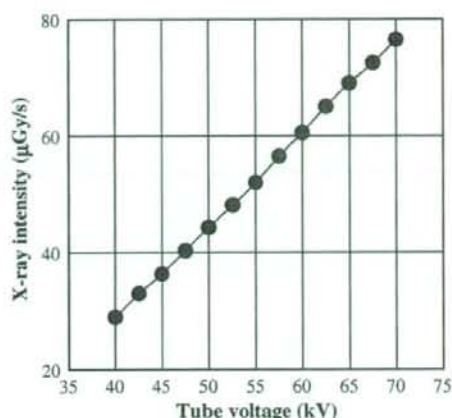


Fig. 4 X-ray intensities with a 1.0-mm-thick aluminum filter at 1.0 m from the X-ray source and a tube current of 0.5 mA

with diameters below 10 μm and reached the veins. Thus, the 37%-iodine microspheres 15 μm in diameter remained in the arteries.

3 Results

3.1 X-ray intensity

When the tube voltage was increased, the X-ray intensity after penetrating a 1.0-mm-thick aluminum filter increased (Fig. 4). At a tube voltage 65 kV, the X-ray intensity was 69.0 $\mu\text{Gy/s}$, with errors of less than 0.2%. For carrying out dual-energy ER, the exposure time was 5.0 s, and the low and high tube voltages were 45 and 65 kV, respectively. Thus, the total exposed dose for patients was approximately 0.5 mGy. In our experimental results for chest radiography with a computed radiography (CR) system, because the exposure dose ranged from 0.2 to 1.0 mGy, these values were almost equal to the dose in dual-energy ER.

3.2 X-ray spectra

When the tube voltage was increased, both the maximum photon energy and the spectral peak energy increased (Fig. 5). When the filter was used for absorbing soft bremsstrahlung rays, the peak energies at tube voltages of 45 and 65 kV were 23 and 27 keV, respectively, where the K-edge absorption of the CdTe detector was considered.

3.3 ER utilizing single-energy subtraction

Figure 6 shows ER of a nude mouse according to changes in K . As compared with normal radiography (Fig. 6a), the

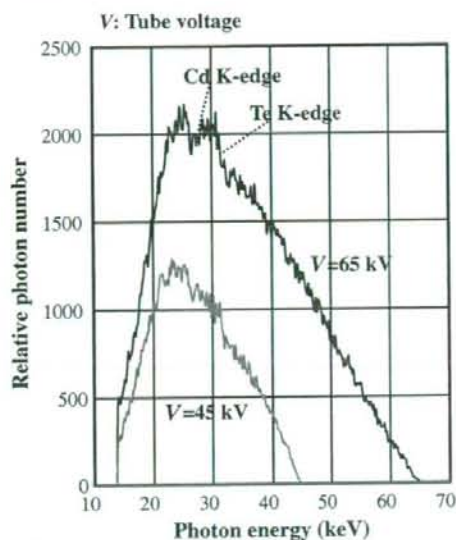


Fig. 5 X-ray spectra measured with a cadmium telluride detector and the filter at tube voltages of 45 and 65 kV

absorption contrast was removed at a K of 1.0 (Fig. 6b), and the contrast increased with decreasing K (Fig. 6c). With embossing, edge enhancement images of a mouse skull were obtained. In this single-energy ER, because the object was shifted horizontally, the vertical edges were effectively enhanced.

3.4 ER utilizing dual-energy subtraction

The spatial resolution of the horizontal and vertical directions was measured with a lead test chart (Fig. 7). In cohesion radiography, the spatial resolution of the horizontal and vertical directions was approximately $80 \mu\text{m}$. ER was performed at a K of 0.7, and the spatial resolution fell with increasing shifting dimension in the horizontal direction. The horizontal spatial resolutions were 83 and $143 \mu\text{m}$ at the shifting dimensions of 100 and $200 \mu\text{m}$, respectively (Fig. 7a). However, the resolution seldom varied with increasing shifting dimension, and $83\text{-}\mu\text{m}$ lines were visible in the vertical direction (Fig. 7b). Therefore, the shifting dimension should be controlled corresponding to the allowable spatial resolution, and two-dimensional image shifting is useful for enhancing of the target region.

Figure 8 shows a radiogram and an embossed radiogram of a region of the mouse abdomen. The embossed radiogram was calculated by a formula (8) with changing K . In radiography with a tube voltage of 45 kV , a mouse dung was barely visible. When K was increased in dual-energy ER, the absorption contrast of the muscle decreased

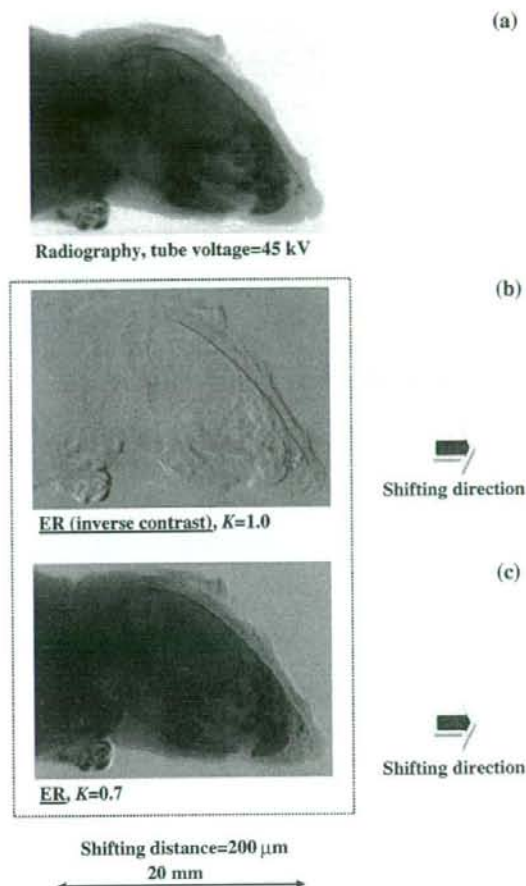


Fig. 6 Radiography of a nude-mouse head at a tube voltage of 45 kV . a Normal radiography, b embossed radiography (ER) at a K of 1.0, and c ER at a K of 0.7. Edge enhancement images of a skull were obtained in ER with use of single-energy subtraction

slightly, and both the dung and the dorsal were observed clearly with embossing.

Radiography of a rabbit kidney is shown in Fig. 9, and gadolinium oxide particles 700 nm in average diameter were used for observing a renal pelvis in the kidney. As compared with a normal radiogram, the image contrast of the renal pelvis was improved by use of embossing. With increasing K , the absorption contrast of the muscle decreased too, and the contrast of the renal pelvis was improved. For imaging of the pelvis, an iodine-based contrast medium used in medical angiography and a cerium oxide suspension are also usable.

Angiograms of an extracted rabbit heart with iodine-based microspheres $15 \mu\text{m}$ in diameter are shown in Fig. 10. According to increases in K with embossing, the contrast of heart muscles slightly decreased, and fine coronary arteries

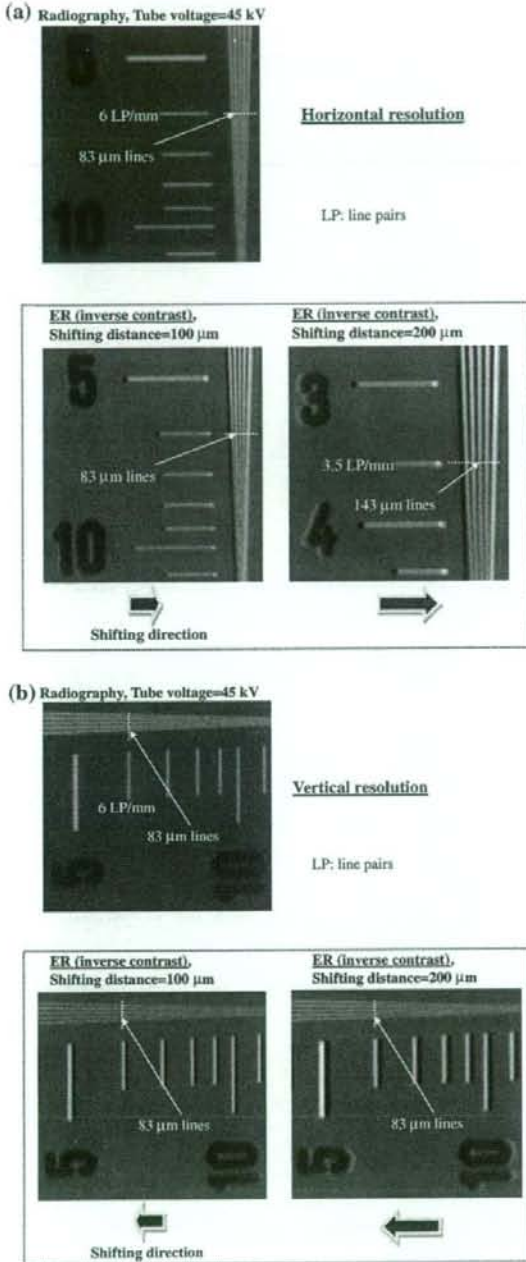


Fig. 7 Radiography and ER of a lead test chart according to changes in the shifting distance in the horizontal direction. a Horizontal spatial resolutions and b vertical spatial resolution

were clearly observed at K values ranging from 0.7 to 1.0. To observe fine blood vessels below 100 μm in diameter, the shifting dimension should be minimized to 100 μm .

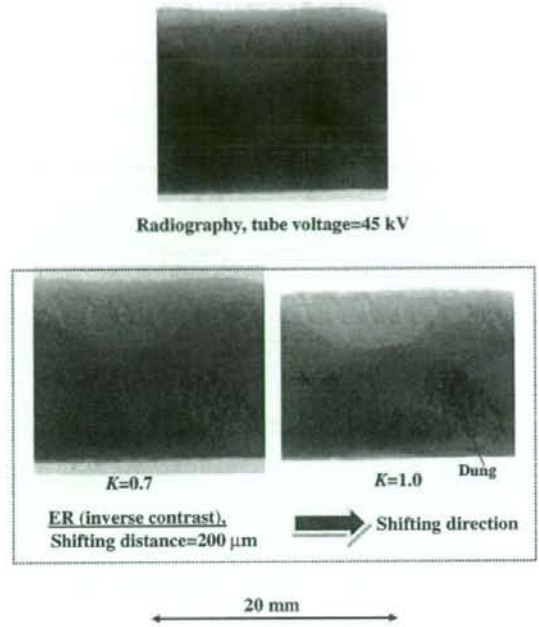


Fig. 8 Radiography of a mouse abdomen. Dung is clearly seen on ER

In radiography of a vertebra, the contrast resolution increased with embossing, and bone structures were visible (Fig. 11). In dual-energy ER for observing dry bones, because the image contrast decreased with increasing K , the single-energy ER was usable.

4 Conclusion and outlook

We performed ER by utilizing energy subtraction and image shifting. In this method of radiography, concavo-convex images were obtained by shifting of the second image, and absorption contrasts of unnecessary regions were decreased by use of energy subtraction. As compared with conventional radiography, the contrast resolution of target regions increased to approximately 1 when we used a linear-contrast system. Therefore, it was easy to observe target regions as embossed images without decreasing the spatial resolution. Currently, although spatial resolution decreases with increasing shifting distance ξ , the minimum shifting distance ξ_{\min} should be kept at approximately 100 μm to enhance embossing and is written as

$$\xi_{\min} \cong 2s_p \leq \xi \leq \xi_{\max} \tag{10}$$

where s_p is the pixel size of 48 μm and ξ_{\max} is the maximum shifting distance corresponding to the allowable spatial resolution.

Fig. 9 Radiograms of a rabbit kidney. In ER, a renal pelvis is visible with gadolinium oxide nano-particles

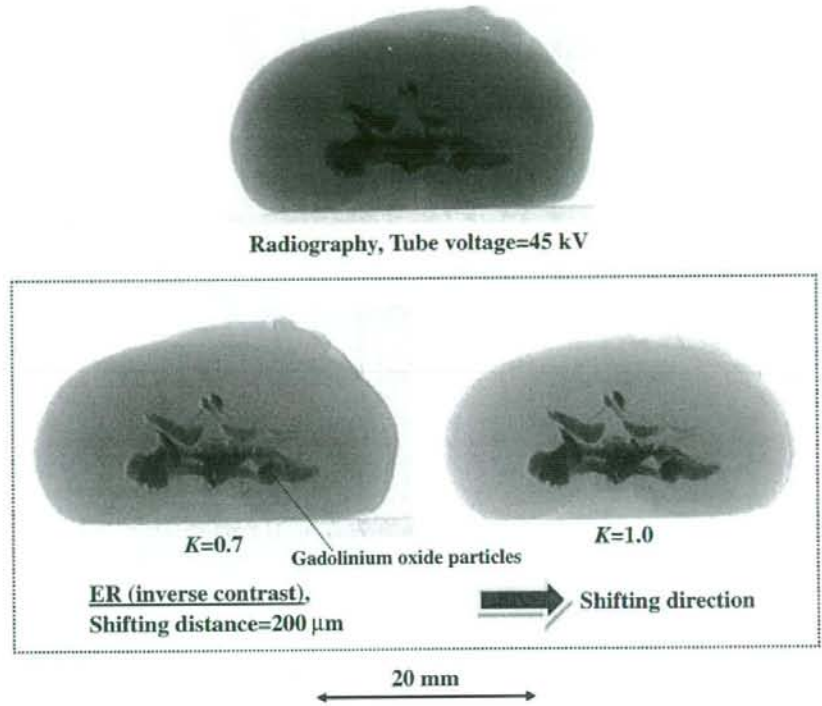


Fig. 10 Radiography of a rabbit heart using iodine-based microspheres. Coronary arteries are clearly observed in ER.

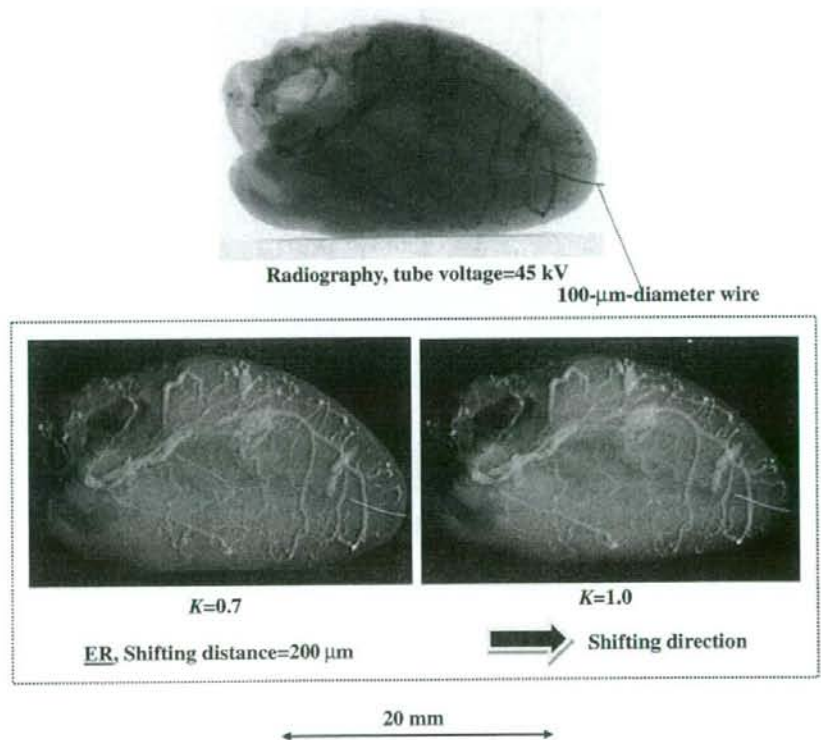
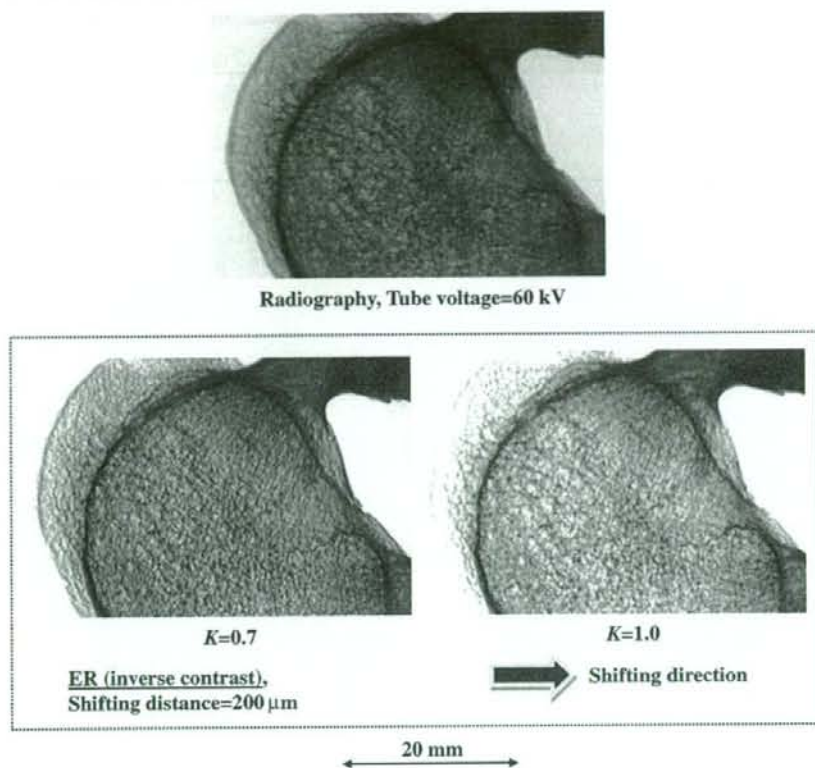


Fig. 11 Radiograms of a vertebra. With embossing, contrast resolution in the vertebra improves



To image a target region in vivo, we have to confine the X-ray spectra to optimal distributions for energy subtraction, and unnecessary regions for diagnosis should be deleted from radiograms. However, in cases where we carry out only embossment, single energy subtraction is usable. The tube voltage should be selected corresponding to radiographic objectives, and we have to use an optimal-element filter and to determine its effective thickness.

With this FPD, the exposure time was 5.0 s because the exposed dose rate from the 100- μm -focus tube was low owing to the maximum tube current of 0.5 mA. In addition, focal spot diameters below 1.0 mm are usable, and the exposure time decreases substantially with increasing spot diameter. Recently, a program for two-dimensional pixel shifting has been developed, and one-shot ER is realizable with single-energy subtraction.

Magnification radiography [19, 20] is useful for improving the spatial resolution in digital radiography. The spatial resolution improves with increasing magnification ratio, and the maximum ratio increases with decreasing focus diameter. Therefore, magnification ER utilizing energy subtraction can be performed, and a program for digital subtraction including a pixel-shifting function is useful for composing embossed images.

As compared with conventional radiography, the advantages of dual-energy ER are as follows: (1) contrast resolution can be increased up to approximately 1.0. (2) Edge-enhancement radiography such as phase-differential imaging is realizable. (3) Hard tissues are imaged effectively as compared with phase imaging. (4) Nano-particles and liquid contrast media in medical angiography can be observed as concavoconvex images with high contrast.

In human imaging, a computed radiography system is usable, and various applications will become possible as follows: angiography with iodine and gadolinium media, cancer diagnosis with nano-particles, hard-tissue (bone) imaging, and various radiographies with high contrast resolutions. In addition, an energy discriminating FPD system that can get spectral data is very useful for carrying out single-shot dual-energy subtraction with short exposure times.

This ER utilizing dual-energy subtraction is usable in various digital radiography systems, including a CR system. Therefore, we developed an ER program for CR utilizing a two-dimensional image-shifting function. However, it was difficult to carry out dual-energy ER precisely by using two imaging plates. We are currently developing a multi-slice mini-focus X-ray CT system

utilizing a 100- μm -focus tube, and embossed tomography with use of single- and dual-energy subtractions would be employed for increasing the contrast resolution of the target region. In our research, energy subtraction has been effective for imaging iodine contrast media and gadolinium oxide nano-particles, and ER is useful for edge enhancement radiography like phase imaging and for increasing the contrast resolution without a decrease in the spatial resolution.

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