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ABSTRACT

Results of microtomography experiments that employ filtered radiation from the National Synchrotron Light Source X-26 Microprobe beam line are presented. These experiments have yielded images of a freeze-dried caterpillar with a spatial resolution of the order of 30 μm and show that the limit on the spatial resolution with the present apparatus will be 1 to 10 μm. Directions for improvement in synchrotron microtomography techniques and some possible applications are discussed.

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1. Introduction

The invention of computerized tomography, CT, has been an important recent advance in diagnostic radiology. CT makes it possible to image thin transverse sections of the human body with little image degradation due to scattered radiation or image information from outside the imaged slice. This is in contrast to conventional radiography where the attenuation properties of a 3-dimensional object are projected onto a plane. In clinical CT, the rotating anode X-ray tubes used as radiation sources limit the image resolution to a few millimeters. In principle it is possible to develop CT with a spatial resolution below 1 μm if only the radiation doses to the object can be tolerated. Some cases of computerized microtomography with spatial resolutions ranging from a few hundred down to about 15 μm have been reported [1-9]. The main obstacle for a higher resolution has been the limited photon fluence rates from the radiation sources used in these experiments, making the imaging time very long. However, the higher X-ray photon fluence rates available from synchrotron radiation sources make possible improved spatial resolution so that CT can be extended to the detection of details in small objects such as biopsy specimens. It also makes possible the use of monochromators for energy tuning while still maintaining a fluence rate high enough to be useful for imaging purposes. This can be used to increase the quality in imaging of humans without increasing the energy imparted, since one of the limiting factors in clinical CT is the continuous energy spectrum from rotating anode X-ray tubes.

Here computerized X-ray transmission microtomography experiments employing x-rays from the National Synchrotron Light Source (NSLS) X-26 Microprobe beam line are presented. Directions for improvements in the synchrotron microtomography techniques are discussed as well as some possible applications.

2. Principle

The main principle underlying any type of computerized tomography, whether it be transmission or emission tomography, is that if we have a two-dimensional function of a measurable quantity and can measure the line integrals of this quantity for all lines through every point in the function plane, then it is possible to reconstruct the function. In theory an infinite number of line integrals is necessary, but useful images can be obtained from a limited number of samples. For X-ray transmission tomography ,the line integrals of the linear attenuation coefficient are easily obtained in the monoenergetic case by taking the logarithms of the inverse of the relative transmissions. When polyenergetic X-rays are used and only the total photon fluence measured, this simple relation no longer holds and artifacts are introduced. Better image quality, as compared to clinical CT, is therefore possible if monoenergetic X-rays from synchrotron sources are used for imaging of humans.

The data collection in X-ray transmission CT consists of measuring the relative transmission of X-rays through the object for a number of ray paths. In the first generation of clinical CT-scanners and the type of apparatus used for these experiments, a narrowly collimated radiation beam is scanned over the object while the transmission is sampled. The object is then rotated a small angle and the translational sampling repeated. This is continued until the total rotation angle is 180 degrees. It is required that the rotation axis be orthogonal to the radiation beam and that the translation be parallel with the rotation plane. If these requirements are not fulfilled, the radiation beam will not pass through the same slice of the object for all translations.

3. Instrumentation

The micro-CT scanner used here is a slightly modified version of that developed by Carlsson et al. [2,3]. It differs from clinical CT-scanners in that the object is moved while the radiation source and the detector are stationary, for obvious reasons. Fig. 1 shows the assembly of stepper motor-driven translators (2) and rotators (2) used to move the object through the radiation beam during the sampling of the X-ray transmission. The vertical translator is used to select the slice to be imaged. A vertically mounted rotator is used to align the plane of the horizontal rotator parallel to the radiation beam. The horizontal translator is used to scan the object through the beam while the transmission is sampled. The scanning can be made either continously or stepwise. In continous mode the sampling interval is determined by feeding the stepper motor control pulses to a preset counter. In this way the translation time can be minimized. The minimum rotation angle for the vertical rotator was .001 degrees and for the horizontal .01 degrees, while the minimum step size for the translators was .5 μm. The stepper motors were controlled by a microcomputer with programs automatically placing the moving stages at the correct start position relative to the radiation beam after specifying the scan width and sampling distance.

The radiation source was the X26-C Microprobe beam line at the National Synchrotron Light Source (NSLS), Brookhaven National Laboratory [10,11]. This beam line produces unfocussed synchrotron radiation from a bending magnet. The size of the radiation beam was defined by two pairs of perpendicularly-oriented 1-mm thick Ta-slits. The photon energy distribution of the primary beam is shown in fig. 2. For this pilot study no monochromator was available. Instead, metal foils were used as absorbers to shape the energy spectrum of the beam. An Ar-filled proportional counter was used as a radiation detector.

The imaging time with the above equipment ranges from about 1000-4000 seconds depending on the size of the imaged object, the required spatial resolution, and the attenuation contrast in the object. Over such time periods the electron storage ring current decays significantly. In ordinary CT, reference detectors are used to measure fluctuations in the incident photon flux. Here we used instead the normalization method descibed by Carlsson et al. [2,3], which utilizes the fact that for each measuring angle the beam passes through the entire object. The sum of the measured line integrals at each measuring angle should therefore be constant. This normalization technique works well since the beam current decays smoothly, although not linearly, with time.

4. Alignment

One of the most important requirements for successful micro-CT is to accurately align the sample stage assembly with the radiation beam. The basic requirements are that the translation is orthogonal to the rotation axis and that the rotation axis is orthogonal to the radiation beam. Since the reconstruction algorithm we have used requires that the number of samples are equal on each side of the rotation axis, it was also necessary to determine the translator position for which the radiation beam and the rotation center coincided. This position was calculated from two determinations of the position of a vertical edge of a highly attenuating material. The coordinates of the edge, this placed eccentric on the rotator, were determined for two rotation angles 180 degrees apart. The edge coordinates could simply be found by scanning the object through the radiation beam. The translator position where the beam and the rotation center coincide is equal to the mean of the two edge coordinates. The orthogonality of the rotation axis and the

radiation beam was checked by determining the vertical coordinates of an eccentric horizontal edge for two rotation angles, also 180 degrees apart. If these two coordinates were not identical within the desired tolerance, the vertical rotation stage was moved (fig. 1) and the procedure repeated until orthogonality was achieved. The orthogonality between the translation and the rotation axis can be checked in a similar manner. These edge searches are easy to do, and we have developed computer programs which automatically perform the alignment.

5. Experiments

In order to illustrate the capabilities of micro-CT with synchrotron radiation, the head of a freeze-dried caterpillar was imaged. A 200-μm thick Zn filter was used to shape the spectrum. The resulting photon energy distribution is shown in fig 2. X-rays with energies just below the K absorption edge of Zn were close to the optimum energy [cf. 12,13] for the caterpillar, as judged from the transmission measurements. However, this filter gives a relatively high photon fluence rate in the energy range 20-50 keV. These photons, however, did not contribute significantly to the measured signals since the Ar-filled proportional counter was insensitive to these high energy X-rays (cf. fig 2). For imaging of living objects, one would have to be concerned about the energy imparted by this radiation.

The radiation field used during the imaging was about 12 μm wide and 20 μm high at the slits situated 540 mm from the object. This field size was chosen to assure that the count rate was within the linear range of the proportional counter and resulted in a maximum count rate of about 220000 pulses/s during the experiment. At the object the field size is somewhat larger, about 30 × 40 μm^2 including penumbras totaling 10 and 30 μm for the horizontal and vertical sides, respectively since the radiation source has a

dimension of the order of 0.5 × 1.5 mm^2 20 m before the slits [10]. The resolution on the translation stage was 30 μm. At each of 163 angles, 177 transmission measurements were made, the number of angles smaller than optimum [13] because of limited computer memory. The counting time was 0.1 s for each transmission measurement. After normalization of the data, a filtered back projection algorithm [13] was used to reconstruct the image.

6. Results

Fig. 3 shows the reconstructed image of a slice through the head of the freeze-dried caterpillar. Each picture element shows the reconstructed relative linear attenuation coefficient averaged over a volume element nominally 20 × 30 × 30 μm^3 where the penumbra is neglected. Black represents low, and white represents high attenuation. Observe that the thickness of the imaged slice is approximately equal to the side of the picture element. In clinical CT the slice thickness is in most cases 5 to 10 times the pixel side. The total imaging time was 53 minutes, determined mainly by the count-rate capability of the proportional counter.

7. Discussion

Fig. 3 gives a good indication of the great potential of synchrotron-based micro-CT which, as long as the radiation damage is not present, is a nondestructive imaging method. Since we are not close to being limited by low photon fluence rates, these initial experiments show that considerably higher spatial resolution can be achieved. The alignment procedures we have used allow the slice thickness to be of the order of 1 μm, and a spatial resolution of this order of magnitude should be possible to reach. In order to accurately collimate the radiation beam to below 10 μm, pinhole collimators have to be used. These will be relatively transparent to the high energy

photons in the white synchrotron spectrum which may mask the detector signal from the photons which pass through the pinhole. The use of a monochromator before the pinhole eliminates this problem. The pinhole should be placed as close to the imaged object as possible to reduce the influence of beam divergence on the field size.

The main disadvantage with the present equipment is the long imaging time. For objects exceeding a few millimeters in size, the time is limited by the count-rate capability of the detector. This rate capability can be increased by use of other detectors, i.e., a scintillation detector operated in current mode. For objects of the size of a mouse, the rate limitations on the translator stage contribute about 20 minutes to the imaging time. The use of a detector array, like a charge-coupled device (CCD), and with wide radiation field covering the whole slice to be imaged, could reduce this time to a few minutes. Since it has been shown that CT-images of mice having a spatial resolution of the order of 100 μm and showing good detail can be generated [2,3,7,8], and since mice can be anaestesized for more than half an hour, such a short imaging time would make imaging of live mice convenient. However, no X-ray detector array exists having a spatial resolution below about 10 μm. For such high resolution imaging the first generation type of CT-scanner therefore still has to be used.

Micro-CT with a spatial resolution below 10 μm has a great potential in many areas of research which can only be touched upon here. For example, such high resolution imaging of biopsies can be used to study how tumors invade normal tissues. This might be interesting not only in connection with tumor therapy research, but also for clinical purposes since it might be possible to extract information about a patient's prognosis from micro-CT of excised tumor specimens. The advantage of the method as compared to other microscopy

methods is that the specimen can be imaged without any histochemical preparation which often inadvertently disrupts some of its micro-anatomical features. The ability to image live mice has the potential to considerably improve the quality of some biomedical research utilizing mice, for example tumor therapy research, since it makes it possible to follow the mice individually instead of sacrificing them at different times during the course of an experiment.

Elemental analysis by subtraction of images generated above and below a photoelectric absorption edge of an element has been suggested [15] and can be done with the above equipment. The main problem with this technique is that the size of the object will be limited by the energy of the absorption edge, since the imaging time varies rapidly with the photon energy [2,12]. Another possibility for elemental mapping is to detect the characteristic X-rays emitted from the element. Tomographic techniques can also speed up two-dimensional mapping of thin samples in X-ray fluorescence analysis when low concentration samples are used, since the sampling can be done with a long but narrow radiation field instead of a small field scanned over the object. Because of the larger radiation field, the synchrotron radiation and the detectors are then more efficiently used.

8. Conclusions

The experiment described here yielded tomograms with a spatial resolution of the order of 30 μm. It also demonstrates that with the present equipment it should be possible to reach spatial resolutions well below 10 μm when synchrotron radiation is used for CT imaging of small objects.

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Figure Captions

Figure 1. The rotator and translator assembly used for moving the imaged object through the radiation beam during the transmission measurements. The radiation beam is incident from the left. To the right is a radiation detector.

Figure 2. From top to bottom: primary X-ray spectrum, spectrum after 200-μm thick Zn filter and the energy distribution of the photons detected with the Ar detector. Calculated at sample position 20 m from source.

Figure 3. Micro-CT image of a lateral section of the head of a freeze-dried caterpillar, approximately at the height of the mouth. Diameter 5 mm, pixel size 30 × 30 μm, slice thickness nominally 20 μm, 177 × 177 matrix, sampled at 163 angles.

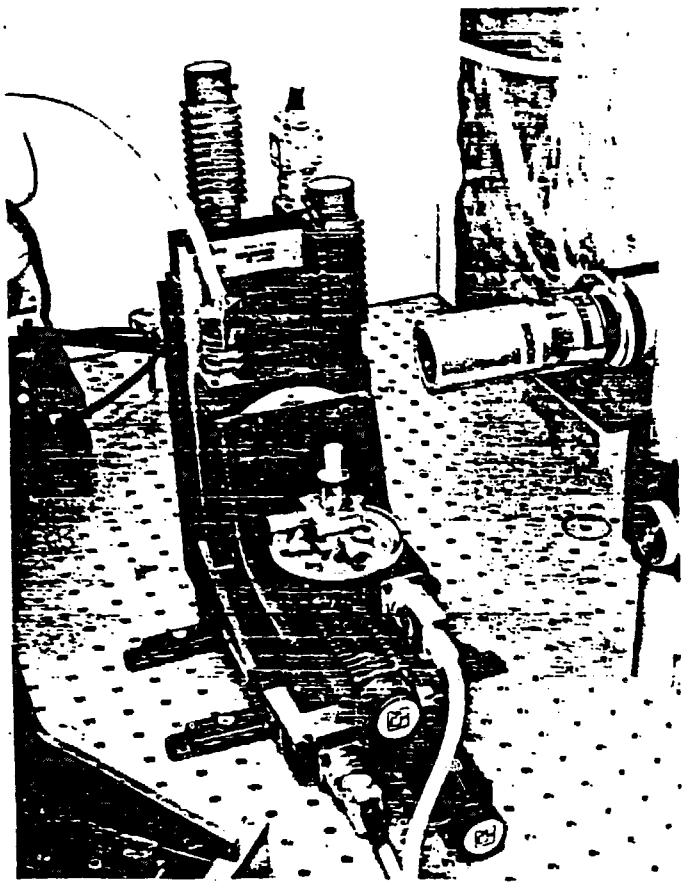

Figure 1

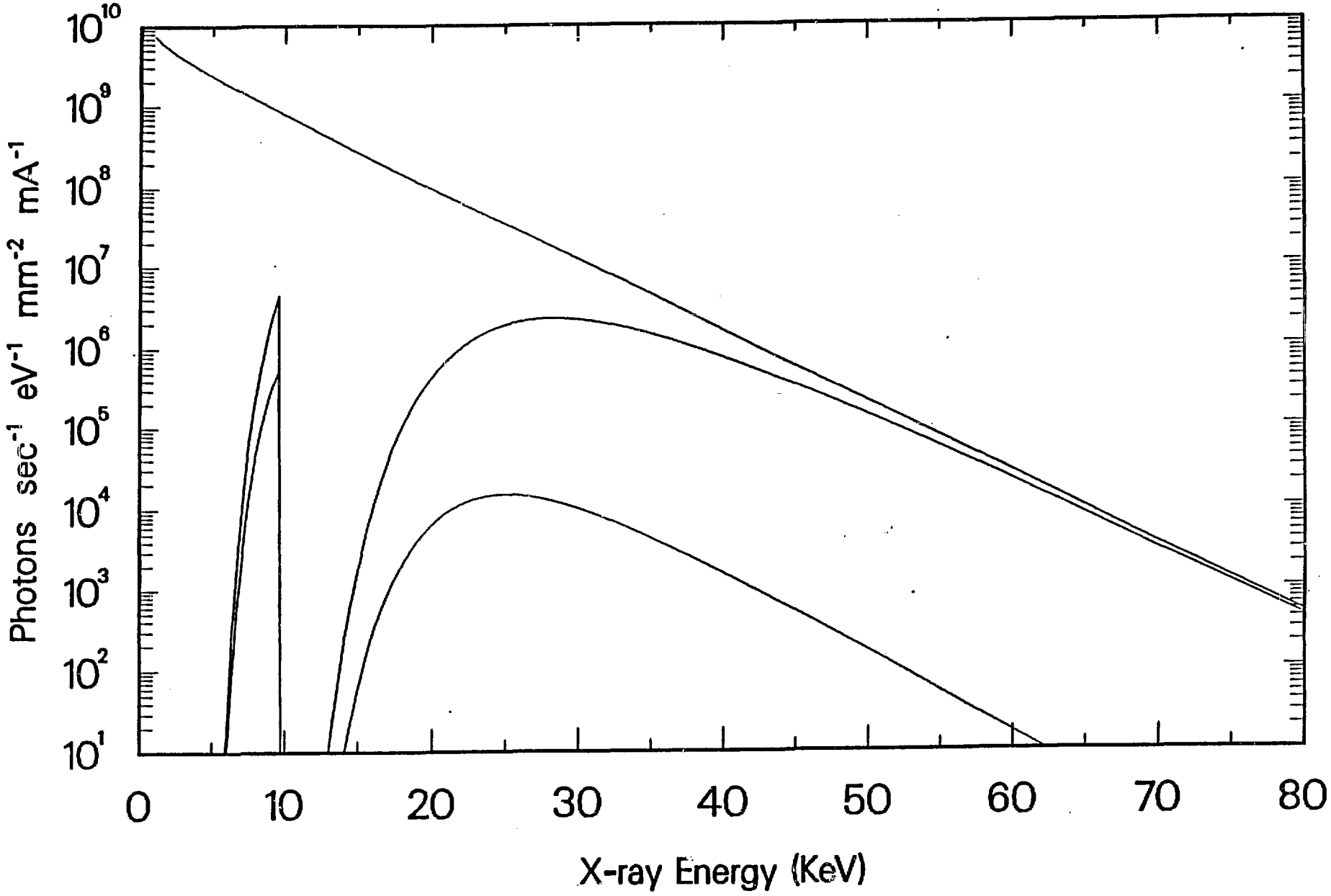
Photons sec^{-1} eV^{-1} mm^{-2} mA^{-1}
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10^{1}
0
10
20
30
40
50
60
70
80
X-ray Energy (KeV)

Figure 2

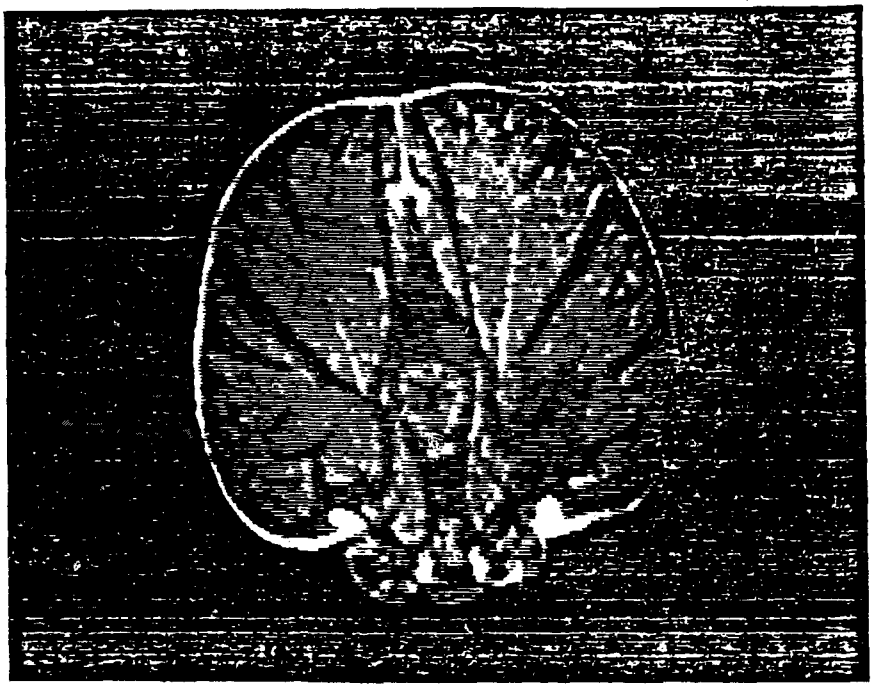

Figure 3