9 Medical Application

9-1 Phase-contrast X-ray Imaging Using a Two-crystal Interferometer for Biomedical Observation

Phase-contrast X-ray imaging, which detects the X-ray phase-shifts after traversing an object, was developed because the sensitivity of this technique is about 1000-fold greater than that of absorption-contrast X-ray imaging for biomedical objects composed of low atomic-number elements [1]. Phase-contrast X-ray imaging with an X-ray interferometer [2] is most sensitive for detecting minute density differences in biomedical objects [3]. The inner structures of formalin fixed biological objects such as rabbit cancer [4], rat brain and human cancer [5] can be demonstrated clearly without contrast material by this technique.

In this work, we have attempted to perform phase-contrast X-ray imaging of a live animal using a system based on the two-crystal X-ray interferometer installed at BL-14C1. The observation of live animals might be applicable to assessing tumor growth and various therapeutic effects sequentially. Fig. 1 shows a schematic view of our latest imaging system based on a two-crystal X-ray interferometer [6]. The system consists of a mechanical positioning system for mounting the crystal blocks of the interferometer, a feedback system for stabilizing the relative displacement between the blocks, a sample positioner, and CCD-based imaging detectors. A vertically polarized incident X-ray beam is horizontally expanded by the asymmetric crystal and then introduced to the interferometer, which generates two interference beams, one for CCD-based imaging detector 1 used for measuring the phase maps and the other for imaging detector 2 used for operating the feedback system. The view area was 24 × 30 mm^2 for 35 keV energy X-rays. The phase fluctuation of the interference beam during the operation of the feedback system was suppressed to within $\pi/15$ over more than three hours, which corresponds to the 0.06-nrad angle between the crystal blocks. To observe small living animals under anesthesia, the measurement time must be less than one hour. We therefore used the Fourier method, which requires an interference pattern to obtain a phase map, while the spatial resolution was limited by the interference fringe spacing. A typical measurement time was 40 min, with a projection number of 250, and the exposure time to obtain one interference pattern was 3 sec. The present study was approved by the Medical Committee for the Use of Animals in Research of the University of Tsukuba.

In-vivo phase-contrast X-ray CT imaging of a cancer implanted in a nude mouse was successfully carried out for the first time by using the two-crystal X-ray interferometer-based phase-contrast X-ray technique (Fig. 2). This image shows the location and structure of a colon cancer, thin muscle layer and hair follicles. Skin, subcutaneous thin muscle layer, and the cancer lesion show a relatively high density, whereas the subcutaneous tissue that is composed of rough fibrosis show a low density. However, the fine inner structures of cancer such as cancer cells and patched necrosis which were observed by optical microscopy could not be depicted clearly due to the low spatial resolution of 0.1 mm [7]. We are planning on using a high-speed X-ray detector to overcome this problem. This study indicated that the phase-contrast X-ray imaging with X-ray interferometer might be used to observe the *in-vivo* biological objects for future biomedical research.

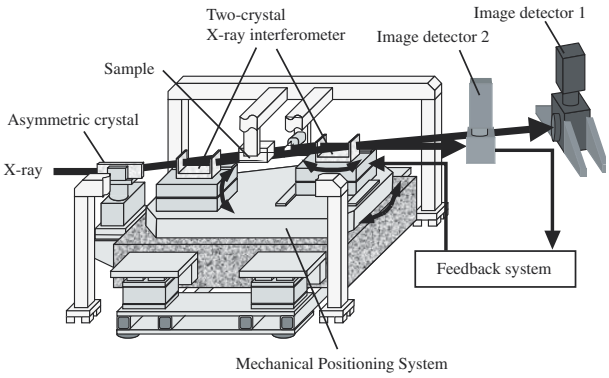

Figure 1
Schematic view of phase-contrast X-ray imaging system based on a two-crystal X-ray interferometer.

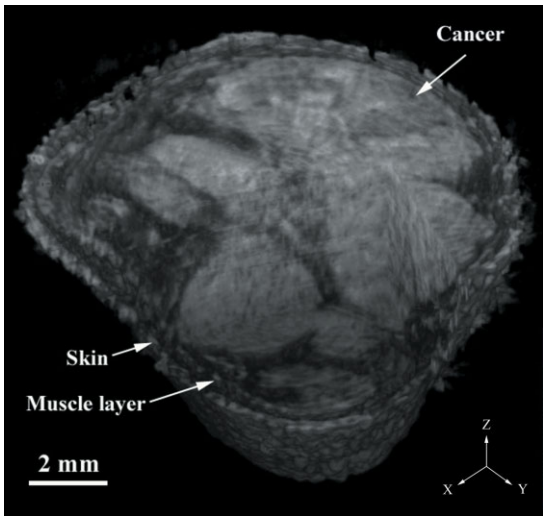

Figure 2
Three-dimensional *in-vivo* phase-contrast X-ray CT image of a colon cancer implanted in a nude mouse.

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9-2 Depiction of the Human Joint Structure by Means of X-ray Refraction-contrast with a Laue-type Analyzer

X-ray refraction-contrast imaging with a Laue-type analyzer using synchrotron radiation is a newly developed X-ray imaging technique to visualize the distribution of the X-ray refractive index in an object. With this method, high-definition X-ray images can be acquired from the soft tissues that cannot be obtained with the conventional X-ray absorption contrast method. In this research, the diagnostic ability of X-ray refraction contrast imaging with a Laue-type analyzer [1] was investigated by applying the technique to a human femur specimen [2]. If clinical imaging with this method could be used practically, the application of X-ray image diagnosis will be expanded drastically.

Refraction-contrast imaging with a Laue-type analyzer is explained as follows. A high intensity monochromatic X-ray beam with a small angular divergence is necessary for good imaging. Synchrotron radiation is the most suitable for this purpose. The experiment was carried out at BL-14C1 of the Photon Factory, and the experimental arrangement of the imaging is shown in Fig. 3. An asymmetrical diffraction crystal was employed to extend the area of the horizontal exposure field, and to improve the angular divergence of incident X-rays. The energy of X-rays used for the imaging was either 15 or 30 keV. The area of the exposure field was 30 mm vertically and 70 mm horizontally. The X-ray images were recorded on mammography film without an intensifying screen. The sample used here was the distal end region of a human femur specimen with thickness of about 8 mm which was chemically fixed with formalin. The incident X-rays were altered from their original direction by the difference of the X-ray refraction index of the sample (refraction phenomenon). Since the degree of the refraction angle is dependent on the difference of the electric density of the sample organ, the difference of refraction angle includes the structural information of the sample organ. In order to observe minute differences in refraction angle, a silicon single crystal analyzer of thickness 1 mm was placed between the sample and the X-ray film. By the diffraction effect of the analyzer crystal, differentiation of X-rays between a specific direction and any other direction can be performed. The former X-rays contribute to image formation as diffracted X-rays, the latter as forward diffracted X-rays. The forward diffracted X-ray image obtained with this method [Fig. 4(b)] is clearer and sharper than that obtained using a conventional X-ray method [Fig. 4(a)].

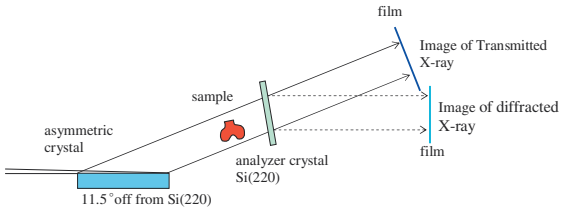

Figure 3
Experimental apparatus for refraction contrast imaging with a Laue-type analyzer installed at BL-14C1.

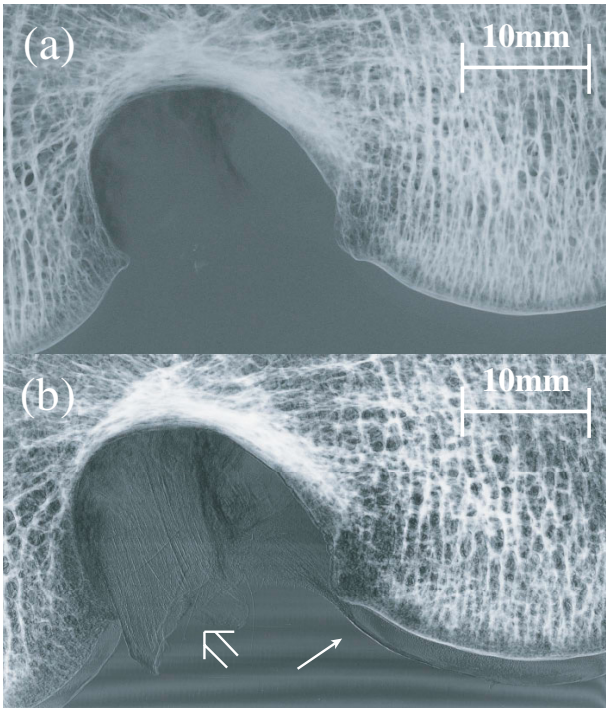

Figure 4
(a) X-ray image of the distal end region of a human femur specimen using conventional mammography equipment. The crucial ligament and articular cartilage are hardly visible by the conventional X-ray imaging.
(b) The Laue-type refraction contrast image of the corresponding area to Fig. 4(a). This is the projection image formed on the forward diffracted X-rays. The crucial ligament (⇒) and articular cartilage (→) of the soft tissues are clearly visible with this X-ray method. In particular, fine fibril structures are clearly observed in the crucial ligament image. The high-depiction ability of the new method will reveal a partial tear of the ligament and minute changes on the surface of cartilage. Such imaging has never been achieved with current clinical MRI techniques.

The crucial ligament and articular cartilage are clearly visible only in Fig. 4(b).

Sometimes a crucial ligament may be torn by an excessive joint movement, and the articular cartilage can be destroyed by aging and/or specific joint diseases. These organs can currently only be observed with the magnetic resonance imaging method (MRI) which provides little diagnostic information. The detailed structural information provided by this new X-ray imaging method will be useful for the early checkup and confirmed diagnosis of joint diseases. Furthermore, the high depiction ability of the new method may be applicable to the evaluation of reconstructive operations on the ligament and articular cartilage.

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