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Original paper

Imaging with ultra-small-angle X-ray scattering using a Laue-case analyzer and its application to human breast tumors

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ABSTRACT

Purpose: In this study, we demonstrate a novel imaging technique, based on ultra-small-angle X-ray scattering (USAXS) that uses a Laue-case Si wafer as the angle analyzer. Methods: We utilized the (1 1 1) diffraction plane of a 356 μm thick, symmetrically cut Si wafer as the angle analyzer, denoted by A[L]. With this device, we performed USAXS imaging experiments using 19.8 keV synchrotron X-rays. The objects we imaged were formalin-fixed, paraffin-embedded breast tumors (an invasive carcinoma and an intraductal papilloma). During image acquisition by a charge-coupled device (CCD) camera, we varied the rotation angle of the analyzer in 0.02″ steps from −2.40″ to +2.40″ around the Bragg angle. The exposure time for each image was 2 s. We determined the amount of ultra-small-angle X-ray scattering from the width of the intensity curve obtained for each local pixel during the rotation of the analyzer. Results: We acquired USAXS images of malignant and benign breast tumor specimens using the A[L] analyzer; regions with larger USAXS form brighter areas in the image. We varied the sensitivity of the USAXS image by changing the threshold level of the object rocking curve. Conclusions: The USAXS images can provide information about the internal distribution of closely packed scattering bodies in a sample with reasonable sensitivity. This information differs from that obtainable through refraction-contrast imaging. Although further validation studies will be necessary, we conclude that USAXS imaging using a Laue-case analyzer may have significant potential as a new diagnosis technique.

1. Introduction

When an object is irradiated by X-rays, three types of interactions occur: absorption, refraction, and scattering. X-ray imaging has been used ever since its discovery by Wilhelm Röntgen in 1895 with the image contrast determined by differential X-ray absorption by the internal structures in the object being studied (absorption contrast). Various modalities of X-ray imaging have been proposed—ranging from fluoroscopy to computed tomography—and they have become integral parts of modern medicine; all are based on the concept of absorption contrast. However, the difference in attenuation coefficients is small for the soft tissues of which living organisms are composed. This hinders the absorption contrast and limits the value of these techniques for medical diagnostics. Efforts to compensate for this shortcoming have included the use of a contrast agent, or low-energy X-rays particularly for mammography.

Over the past 20 years, alternative imaging techniques based on X-ray refraction (phase shift) and scattering have been intensively explored and developed [1,2]. For soft tissues and with the X-ray energies generally used for diagnostics, the angle of refraction of the X-rays is at most 0.1″ (1 arc-second = 1″ ≈ 4.85 μrad). This is so small that it is not usually detected and is thus ignored. However, the cross section for this interaction is approximately 1000 times larger than that for absorption, and it may therefore result in higher-sensitivity imaging than can be obtained using absorption contrast [3,4]. Methods for detecting X-ray refraction include crystal interferometry [5–7], propagation-based methods [8–10], angle-analyzer-based methods [11–14], and grating interferometry [15–17]. All succeed in making visible internal structures that cannot be detected using absorption contrast methods. Scattered radiation, such as Compton scattering, causes a decrease in

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the image quality, but this can be managed using an anti-scatter grid. However, it has been found that ultra-small-angle X-ray scattering (USAXS) can determine the distribution of strong scattering centers within objects [18–21]. Wernick et al., Khelashvili et al. and Suhonen et al. elucidated the differences between the contrast produced by refraction and that obtained using USAXS with Bragg-case angle-analyzer crystals [18–20]. Stutman et al. extracted USAXS images using grating interferometry and noted its diagnostic usefulness [21]. To our knowledge, however, there has been no previous study of USAXS imaging using a Laue-case angle analyzer.

In the present study, we have developed a USAXS imaging device using a Laue-case angle-analyzer crystal and we have obtained USAXS images of malignant and benign breast-tumor specimens. We also discuss possible usages of USAXS imaging in medicine, particularly its application for the imaging of breast-tumor specimens.

2. Methods and materials

2.1. Concept of USAXS imaging

When X-rays travel through an object, they are subject to absorption, refraction, and scattering (Compton scattering and USAXS). Fig. 1 illustrates these interactions using the simplified example of parallel X-rays incident on a homogeneous object. If they are separately illustrated except for Compton scattering (gray arrows), the three interactions are easy to understand (Fig. 2). Arrows of different lengths indicate the varying magnitude of X-ray absorption within the object; see Fig. 2(a), –(c). Deflected arrows indicate X-ray refraction, which occurs easily around the border of an object, where X-rays are incident obliquely [Fig. 2(b)]. The refraction angle is around 0.1″ for soft tissues and an X-ray energy of a few tens of keV. Fig. 2(c) illustrates USAXS, which causes expansion of the X-ray beam by scattering bodies; the scattering angle for this process is also around 0.1″. We can detect both X-ray refraction and USAXS using the methods mentioned above [5–21].

We introduced a Laue-case wafer crystal, denoted by A[L], as an analyzer to extract USAXS data, and we define maps of the magnitude of expansion of the X-ray beam as "USAXS images". Fig. 3 shows

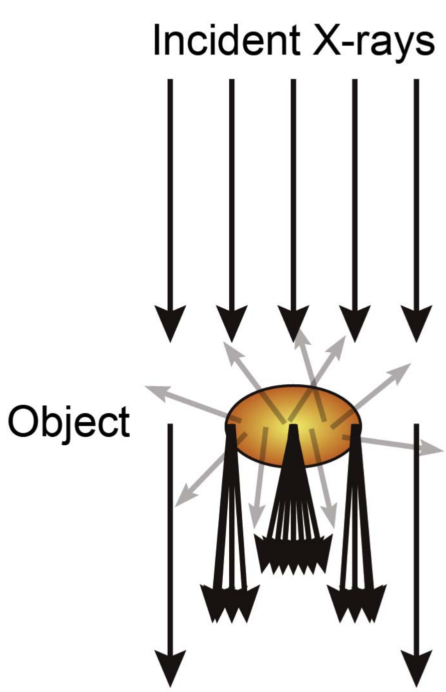

Fig. 1. Simplified illustration of the interactions between parallel X-rays and a homogeneous object. Note that gray arrows indicate Compton scattering.

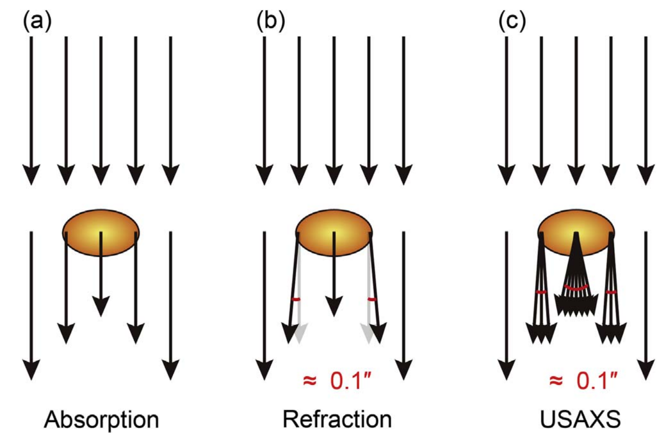

Fig. 2. Separate illustrations of (a) absorption, (b) refraction, and (c) USAXS.

variations in the magnitude of the USAXS expansions produced by "object rocking curves" (defined below) of diffracted X-rays for different samples. The rocking curve for diffracted X-rays is obtained by plotting the intensity of the diffracted X-rays obtained during the rotation of the analyzer crystal A[L] around the Bragg condition [Fig. 3(a)]. When a homogeneous object (orange ellipsoidal body) is placed upstream of A[L], the oscillation at the base of the curve disappears, and the curve is broadened; this is defined as the "object rocking curve" [Fig. 3(b)]. When a different homogeneous object (red ellipsoidal body), which induces more USAXS than does the orange ellipsoidal body, is placed in the beam, the object rocking curve is broadened further [Fig. 3(c)]. When an object is a complex body, one must calculate pixel-by-pixel measurements of the object rocking curves for the entire set of two-dimensional images taken at different angular positions of the A[L] analyzer to acquire the USAXS image (Fig. 4).

Mathematically, the object rocking curve is represented as

$$R_O(\varphi) = \int_{-\infty}^{+\infty} f(\theta) R_A(\varphi-\theta) d\theta$$

where θ and φ are the angle of divergence from the incident X-ray direction and the rocking angle around the Bragg condition, respectively; $R_O(\varphi)$, $R_A(\varphi)$, and $f(\theta)$ are the object rocking curve, the rocking curve of the A[L] analyzer, and the beam expansion caused by the object, respectively. Namely, $R_O(\varphi)$ is derived as a form of a convolution of $R_A(\varphi)$ and $f(\theta)$. The observed function $R_O(\varphi)$ thus involves information about the scattering nature of object through the function $f(\theta)$.

Generally, $f(\theta)$ is a smooth, unimodal function like a Gaussian. The object rocking curve $R_O(\varphi)$ is also a unimodal function if the full width at half maximum (FWHM) or full width at quarter maximum (FWQM) of $f(\theta)$ is sufficiently large compared with the oscillation period on both sides of $R_A(\varphi)$. We can thus obtain information about the nature of the scattering objects by measuring the FWHM or FWQM of $R_O(\varphi)$; that is, when an object has a strong scattering nature, the measured FWHM and FWQM are large, and vice versa.

2.2. USAXS imaging system and specimen preparation

To perform USAXS imaging using a Laue-case analyzer A[L], we need a nearly parallel and monochromatic X-ray beam. At present, such beams can only be obtained from synchrotron radiation. Our USAXS imaging experiment was therefore performed at Beamline BL14B using synchrotron X-rays from the vertical wiggler of the Photon Factory (PF) at the High Energy Research Accelerator Organization (KEK) in Tsukuba, Japan. The accelerator was operated in the top-up mode with an initial ring current of 450 mA and 2.5 GeV acceleration. The X-ray energy was selected to be 19.8 keV by a Si (1 1 1) double-crystal