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Refraction-based 2D, 2.5D and 3D medical imaging: Stepping forward to a clinical trial

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Abstract

An attempt at refraction-based 2D, 2.5D and 3D X-ray imaging of articular cartilage and breast carcinoma is reported. We are developing very high contrast X-ray 2D imaging with XDFI (X-ray dark-field imaging), X-ray CT whose data are acquired by DEI (diffraction-enhanced imaging) and tomosynthesis due to refraction contrast. 2D and 2.5D images were taken with nuclear plates or with X-ray films. Microcalcification of breast cancer and articular cartilage are clearly visible. 3D data were taken with an X-ray sensitive CCD camera. The 3D image was successfully reconstructed by the use of an algorithm newly made by our group. This shows a distinctive internal structure of a ductus lactiferi (milk duct) that contains inner wall, intraductal carcinoma and multifocal calcification in the necrotic core of the continuous DCIS (ductal carcinoma in situ). Furthermore consideration of clinical applications of these contrasts made us to try tomosynthesis. This attempt was satisfactory from the view point of articular cartilage image quality and the skin radiation dose.

Keywords: Synchrotron radiation; X-ray dark-field imaging (XDFI); 2D imaging; 2.5D imaging; 3D CT; Microcalcification; DEI (diffraction-enhanced imaging); Ductal carcinoma in situ (DCIS); Tomosynthesis

Novel synchrotron radiation X-ray imaging based on refraction can make major contributions to the health of society by being able to better detect early stages of disease processes such as cancer, thereby allowing earlier interventions that result in reductions of cancer mortality or early detection of articular cartilage degenerative changes, thereby allowing early interventions that reduce morbidity.

Mammography for early diagnosis of breast cancer is one of the powerful screening modalities together with ultrasonography. Since the discovery of X-rays by Roentgen in 1895 all X-ray medical imaging at hospital including mammography in the world has been based purely on absorption contrast. There are limitations in both spatial and contrast resolution using X-ray absorption. Since breast cancer is not always visible with absorption contrast one needs alternative modalities with higher contrast and with higher spatial resolution to visualize breast cancer in its early stages.

It has been well known that conventional absorption-based X-ray imaging delineates an object due to difference of X-ray

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absorption cross section that has relation to an imaginary part of the complex refractive index $n = 1 - \tilde{n} + i\kappa$. However, κ of low atomic-number elements in soft tissues of biomedicine comprising hydrogen, carbon, nitrogen, and oxygen, cannot produce sufficient contrast because $\kappa \approx 0$. In case of visualizing such objects with hard X-rays, for instance in clinical application, it is much more advantageous to detect variations of the propagation direction of incident X-rays using an analyzer with high angular sensitivity over conventional absorption contrast.

So far a variety of imaging schemes for a phase object have been proposed [1–6] including phase-interference method [7].

Following pioneering work on imaging of breast cancer by Burattini's group [8] a trial to visualize breast cancer tissue has been performed by PCI (phase contrast imaging) [9,10], DEI (diffraction-enhanced imaging) [11–14], PIC (phase-interference contrast) [15], the SMI (super magnification imaging) [16,17], XDFI (X-ray dark-field imaging) [18,19] and XRF (X-ray fluorescence) [20]. Clinical trials are already under way by the Italian team [21].

Clinical visualization of articular cartilage has also been attempted by a number of laboratories [22–24]. Furthermore tomosynthesis of articular cartilage due to X-ray refraction has been first attempted by Shimao et al. [25].

DEI [11–14], developed for refraction-based contrast by Chapman et al. [4], is the most widely used modality of X-ray optics for mammography and articular imaging. This modality is characterized by a double crystal in a parallel arrangement, where the second piece is a Bragg type angular analyzer. The refraction component can be extracted by a mathematical procedure [13]. Later XDFI [18,19] was proposed in 2002 (see in Fig. 1). This modality is characterized by a double crystal arrangement with a Laue type angular analyzer (LAA) with a specified thickness in order to allow

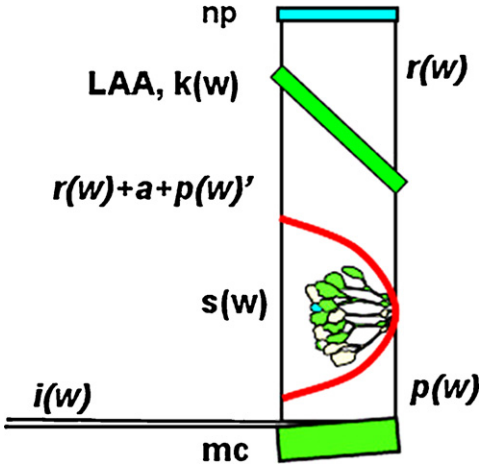

Fig. 1. X-ray optics of XDFI. A specimen $s(w)$ DCIS was illuminated by plane wave $p(w)$ that was made by the monochro-collimator (mc). LAA is a Laue case analyzer with a special thickness of 2.124 mm for 35 keV. The diffracting planes of mc and k are 2 2 0 in a parallel arrangement. The beam carrying both information $r(w)$ due to refraction, a due to absorption of the sample and the partial of the illuminating light $p(w)$ onto a specimen $s(w)$ either breast tissue or articular tissue has been analyzed by k with function of $k(w)$. Only refracted component $r(w)$ can pass through k as dark-field image that is stored in nuclear plate (np).

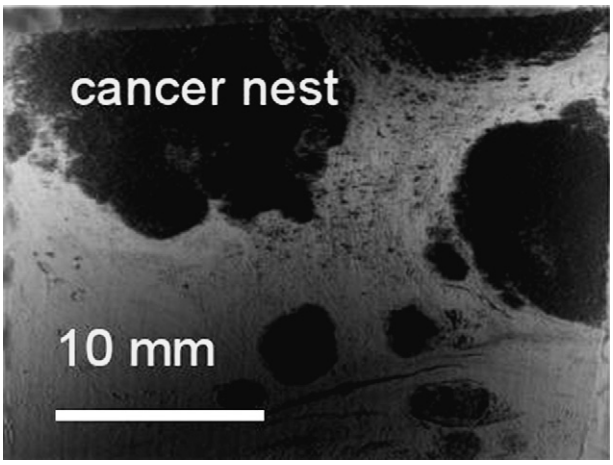

Fig. 2. X-ray dark-field image of a specimen of micropapilary carcinoma that clearly shows several islands of breast cancer nests whose size ranges from a few millimeters to over 1 mm, stroma, muscle and adipose.

only the refracted component to pass through to an imaging detector. The incident plane wave incident onto a specimen is produced by an asymmetric diffraction [26]—see mc in Fig. 1.

In Fig. 1 the refracted component $r(w)$ from object $s(w)$ has been angularly analyzed by LAA that has a specified thickness of 2.124 mm for 35 keV. Only $r(w)$ will be able to pass through LAA towards the forward direction while the beam that does not interact the specimen will be diffracted towards the same direction as the incident beam onto mc.

Fig. 2 clearly delineates breast cancer nests with sizes ranging from sub-millimeter to over 10 mm, comprised of muscle, stroma and adipose. This image was taken with XDFI with an X-ray energy of 35 keV. The black part showing excess of X-rays exactly corresponds to production of fluorescence X-rays of Ca atoms [20]. The specimen of micropapilary carcinoma with thickness of 2.4 mm was sealed with wax. Ordinary mammography shows these black spots in a very weak white contrast. One may find application of this system to articular cartilage in the papers by Shimao et al. [27] and the other by Kunisada et al. [28] in these proceedings.

An algorithm for 3D CT has been developed, following the pioneering work by Dilmanian et al. [29] in the anticipation of a need for 3D information on diseased tissues. Our reconstruction can be characterized with a complex expression of refraction angle. Maksimenko et al. [30], Yuasa et al. [31] and Huang et al. [32] have recently proposed a novel tomographic imaging protocol based on a physico-mathematically defined reconstruction algorithm with a paraxial-ray approximation in the domain of a geometrical optics. This has experimentally obtained a satisfactory result. We start outlining the principle with the ray equation as follows:

$$\frac{\mathrm{d}}{\mathrm{d}s} n(r)t(r) = n(r) \tag{1}$$

where r is a spatial coordinate, $n(r)$ is a refractive index distribution, $t(r)$ is a unit tangential vector of ray propagation and s