Physica Medica 32 (2016) 1801–1812

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Dark-Field Imaging: Recent developments and potential clinical applications

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ARTICLE INFO

Article history:
Received 13 May 2016
Received in Revised form 10 November 2016
Accepted 13 November 2016

Keywords:
X-ray dynamical diffraction
Monochromator
Laue angle analyzer
Refraction contrast
Phase contrast
Medical imaging
Human soft tissue
Breast cancer
Articular cartilage
Artery damage
Synchrotron radiation
High contrast
High spatial resolution

ABSTRACT

This paper describes an X-ray phase contrast imaging technique using analyzer-based optics called X-ray Dark-Field Imaging that has been under development for the past 10 years. We describe the theory behind XDFI, the X-ray optics required for implementing it in practice, and algorithms used for 2D, 2.5D, and 3D image reconstruction. The XDFI optical chain consists of an asymmetrically cut, Bragg-type monochromator-collimator that provides a planar monochromatic X-ray beam, a positioning stage for the specimens, a Laue-case angle analyzer, and one or two cameras to capture the dark and bright field images. We demonstrate the soft-tissue discrimination capabilities of XDFI by reconstructing images with absorption and phase contrast. By using a variety of specimens such as breast tissue with cancer, joints with articular cartilage, ex-vivo human eye specimen, and others, we show that refraction-based contrast derived from XDFI is more effective in characterizing anatomical features, articular pathology, and neoplastic disease than conventional absorption-based images. For example, XDFI of breast tissue can discriminate between the normal and diseased terminal duct lobular unit, and between invasive and in-situ cancer. The final section of this paper is devoted to potential future developments to enable clinical and histo-pathological applications of this technique.

Key points

- XDFI can dramatically increase sensitivity of phase detection.
- XDFI can provide enhanced soft tissue discrimination.
- With XDFI, anatomical features can be visualized with high spatial/contrast resolution.

1. Introduction

Clinical soft-tissue imaging using traditional X-ray fluoroscopy, radiography or computed tomography (CT) uses absorption or attenuation differences between tissues as the primary contrast mechanism [1]. X-ray absorption, arising primarily from photo-electric absorption and Compton scattering, is markedly different between bones, soft tissues and air [2]. However, among the different soft tissue types, the attenuation coefficient is very similar;

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http://dx.doi.org/10.1016/j.ejmp.2016.11.103
1120-1797/

thus, conventional X-ray imaging cannot adequately differentiate between them [2]. For example, while a calcified atherosclerotic plaque can be differentiated from a non-calcified plaque using traditional CT, the soft tissue components of the plaque such as the fibrous cap and atheroma are essentially indistinguishable [3]. Similarly, one cannot delineate a tumor from surrounding healthy tissue using conventional CT unless the tumor is calcified, distorts the tissue architecture, or has dense cell packing that increases its density over the surrounding tissue. For these purposes, we must administer iodinated contrast agents [4], or use alternative imaging techniques such as MRI [5,6].

To overcome this limitation in conventional X-ray imaging, a variety of phase contrast imaging (PCI) methods, e.g., crystal interferometry [7,8], Bragg analyser-based imaging [9,10], grating-based systems [11], and others [12,13], have been proposed. 'The X-ray Dark-Field Imaging (XDFI)' technique, a type of analyser-based imaging using a Laue (transmission) angle analyser, was proposed in 2002 [14]. While all PCI methods can be performed using synchrotron X-ray radiation, PCI techniques using traditional X-ray sources have also been proposed [15–17]. Recent review articles [18,19] provide a more complete list and detailed description of the existing PCI techniques.

In the XDFI imaging geometry, two beams emanate from the Laue angle analyser (LAA): one traveling in the direction of original incident beam (forward diffraction: FD) and the other traveling in the direction of diffraction (D). The FD and D beams contain complementary contrast information, and the use of two cameras allows for capture of both absorption and phase images in a single exposure, reducing measurement time and skin radiation dose compared to other methods. Furthermore, thinning the LAA improves the spatial resolution of XDFI, an important consideration in pathology.

In principle, the electron density of a specimen causes small angular deviations on the order of 10^{-4}–10^{-5} degrees in the incident beam as it travels through the specimen. The relative change in such angular deviations (i.e., the phase contrast) for different soft tissues is much higher than the relative change in absorption. Therefore, for soft tissue discrimination over the energy range used for medical imaging, phase contrast provides a much stronger signal than absorption contrast. While the relative change in phase is high, the overall magnitude of the phase change or angular deviation (10^{-4}–10^{-5} degrees) is quite small. As a result, it cannot be directly measured with a conventional X-ray imaging system. Nevertheless, a perfect single crystal, due to its high angular sensitivity, is well suited for detecting such small angular deviations in a refracted X-ray beam.

In typical analyser-based imaging (ABI) [9], an analyser crystal is used in reflection mode (also known as Bragg mode) in a setup referred to as DEI (diffraction enhanced imaging). The angular sensitivity of DEI can be increased by adopting multiple crystals [20] to increase the slope at both sides of the reflection curve. However, this gain trades off spatial resolution because of beam diffusion at multiple surfaces of the crystal and intensity reduction that is approximately proportional to 0.9^n where n is the number of successive reflections. We describe an alternate technique that employs a thin crystal in transmission Laue mode. We call this technique XDFI (X-ray dark field imaging) [14] and show that one can achieve both high angular sensitivity and high spatial resolution using such a setup.

The overall setup in our PCI methodology consists of a monochromator crystal in the Bragg mode and an analyser crystal in the Laue mode. When the setup is aligned in this approach, the image formed by transmitted X-ray beams appears dark in the absence of a sample interposed between the monochromator and the analyser crystals. With an object in the beam path, the forward diffracted image is intensity modulated according to the refraction by the object. Takagi-Taupin equation predicts that XDFI can concomitantly increase both angular sensitivity and spatial resolution by carefully choosing the diffraction index and the LAA thickness, respectively [21–23]. Computational evidence for this claim was demonstrated by Suzuki et al. [24].

In this paper, we describe the overall XDFI setup, summarize most recent advancements in it, and demonstrate its efficacy by applying it to a variety of human and other tissue specimens. We show that by reducing the thickness of the Laue mode analyser crystal employed by XDFI to 170 μm, one can obtain a spatial resolution of 2.6 μm and 17 μm in the vertical and horizontal directions, respectively. In addition, we adopt an asymmetric-cut monochromator-collimator, an arrangement that enables full-field imaging of large specimens without the need for rastering or scanning the beam across the specimen. As demonstrated in the results section of this paper, XDFI optics can simultaneously increase angular sensitivity, spatial resolution, and field of view. The resulting phase contrast images have unprecedented soft tissue discrimination capability in distinguishing structures with similar X-ray attenuation.

2. Methods and materials

2.1. X-ray Dark-Field Imaging (XDFI) system

The optical setup for XDFI, schematically shown in Fig. 1, consists of an X-ray source, an asymmetrically-cut Bragg-type monochromator-collimator (MC), a specimen, a Laue-case angle analyser (LAA) and two CCD cameras. The X-ray beam from the synchrotron is reflected by MC and passes through the specimen and thus to be angle analysed by LAA. The specimen is placed between the MC and the transmission mode of LAA. All the X-ray photons are first reflected by the 440 planes of the MC (in the reflection mode); when there is no specimen in between MC and LAA, all of these photons are again reflected by the 440 planes of the LAA into the diffracted beam, also known as the bright field. The specimen alters the Bragg condition for some of the photon and these photons constitute the forward diffracted (FD) beam, also known as the dark field. The dark field is so named because without the specimen this image is completely dark when the MC and LAA are set at the Bragg condition. It can be shown that the intensity of any pixel in the dark field is proportional to the angle of refraction imparted by the specimen [25]. If the rocking curve of the LAA is known, one can convert the pixel intensity in the dark field to numerical differential phase signal for that ray.

We have tested the XDFI setup using two different synchrotron light sources: the beamline BL14C on a 2.5 GeV storage ring (KEK Photon Factory (PF), Tsukuba, Japan) and the beamline BL6C on a 3.0 GeV storage ring (Pohang Light Source (PLS), Pohang, Korea).

At BL14C in the Photon Factory, the magnetic field of the 5.0 T superconducting wiggler is horizontally orientated. This facility, therefore, provides a vertically-polarized X-ray beam. When such a vertically polarized beam interacts with the MC, it is displaced horizontally. Similarly, the monochromatic beam coming from the MC is split by LAA into horizontally separated forward and diffracted beams. Such horizontal separation makes the overall setup on a horizontal optical table simpler in comparison to a vertically split beam. The critical photon energy is 20 keV and the heat load onto a 1st piece of pre-monochromator is approximately 300 W; this amount of heat load can be removed by water cooling in order to avoid monochromator distortion.

On the other hand, at BL6C in the Pohang Light Source the magnetic field of the 2.0 T by 16 pole permanent magnets is vertically oriented. BL6C, therefore, produces a horizontally polarized X-ray beam. Despite the difficulties inherent in a horizontally polarized