Hard X-Ray Phase-Contrast Imaging for Medical Applications – Physicist's Dream or Radiologist's Mainstream?

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Abstract. We briefly review currently practiced methods of X-ray phase contrast imaging and consider some of their relative features, especially in regard to applicability to clinical medical studies. Various related technological issues and promising future areas of development are also briefly discussed.

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INTRODUCTION

Conventional X-ray radiography, which has prevailed in medical diagnostic applications for the past 100 years, relies on differential absorption in a sample to produce contrast. Over the past 30 or so years, a variety of methods for producing X-ray contrast via refractive (i.e. phase) effects have been proposed and applied [1-15]. In the case of the in-line imaging approach, which is perhaps the most easily implemented, early results were obtained using high spatial coherence sources both in the laboratory [9,11] and at synchrotron radiation facilities [10]. Conventional laboratory type sources, such as microfocus tube sources, while able to give impressive results for static samples, are not yet sufficiently brilliant to facilitate routine implementation of phase-contrast imaging for medical applications. However, improvements in performance (flux) of microfocus sources, by a factor of say 3 to 5, and/or the availability of suitable high-signal-to-noise imaging detectors (e.g. those based on photon counting) could propel hard X-ray phase-contrast imaging into mainstream application in radiography. The energy spectrum from the source can be quite broad. The advent of compact synchrotrons and other moderate cost high-brilliance sources offers to facilitate a revolution in X-ray imaging in the next few years that could make phase-contrast imaging a routine tool in clinical diagnostic imaging with many potential advantages over conventional radiography including: increased contrast, improved signal-to-noise ratio, lower absorbed dose, ability to give useful information at higher X-ray energies, yield of quantitative information from intensities and attainment of higher spatial resolution.

Some recent activities and future prospects in this field will be discussed here, especially from the viewpoint of work that relates to interests and activities of the CSIRO group in Melbourne.

METHODS FOR X-RAY PHASE-CONTRAST IMAGING

The appreciation that purely refractive effects in objects could be imaged using X-rays dates back to 1965 and the use by Bonse & Hart [1-2] of an X-ray interferometer cut into a monolithic boule of perfect-crystal silicon to image a simple phase object, namely a plano-convex lens made from polymeric material. Since that time, a number of different modes for hard X-ray phase-contrast imaging have been developed and implemented, and we briefly outline some of the features of these below and especially their applicability to clinical medical-type X-ray imaging.

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Interferometer-Based X-Ray Phase Contrast Imaging (IB-PCI)

This technique can give exquisite sensitivity (e.g. $\Delta\rho/\rho \sim 10^{-9}$, where ρ is the electron density) and allow visualization of soft-tissue features (see e.g. Momose [4]). Its limitations lie in that if the phase change variation introduced by the object exceeds 2π, multiple images are required for robust phase-unwrapping. Other limitations of this technique for medical imaging lie in the typically small FoV, the need for extremely high mechanical and thermal stability, and also the need for a high brightness source.

Analyzer-Based X-Ray Phase-Contrast Imaging (AB-PCI)

This technique appears to have been first implemented by Goetz, Kalashnikov and colleagues in 1979 [5,6] and essentially involves placing the sample inside a double-crystal diffractometer, with the first crystal acting as a collimator/monochromator and the second crystal acting as an angular analyzer/filter. The rocking curve width of the analyzer bears a Fourier transform relation to the point-spread function for this crystal-based imaging system [16]. Hence, a broad rocking curve width for the analyzer crystal is required if high spatial resolution is to be achieved. This is not easily achieved with high energy X-rays and currently available X-ray optics. Advantages of this technique are that it can give high contrast, e.g. for soft-tissue features. One should note, however, that high contrast does not necessarily mean more information. Drawbacks of the method include the following: The FoV is limited by the size of available optics, e.g. perfect crystals, and by the nature of the source. For flat crystals and laboratory-type point sources, only a small angular divergence from the source is accepted by the optics. This can in principle be overcome to some extent by using curved crystals in Laue mode, but this raises other technical difficulties. Secondly, the images obtained using the AB-PCI technique do not readily yield to quantitative interpretation. In a certain regime [19], the intensities measured for a phase object depend on the phase gradient, $\nabla\phi$, where ϕ is the phase change introduced by the object, e.g. see [11]. Quantitative methods for interpretation tend to require images at multiple settings of the analyzer crystal and away from the exact matching condition for monochromator and analyzer crystal [17,18] and tend to involve high doses to the sample because of inefficient use of photons striking the sample. Further, when there is a significant distance between the sample and the analyzer crystal, the combined effects of Fresnel propagation and interaction with the analyzer crystal need to be taken into account and this adds a level of complication [20]. Other issues relate to the need for high-brilliance X-ray sources.

Propagation-Based X-Ray Phase-Contrast Imaging (PB-PCI)

This is by far the simplest approach, since it involves no X-ray optics. It simply uses Fresnel propagation to yield phase contrast and resembles in-line holography developed by Denis Gabor in 1948 [21] to improve the resolution obtained in electron microscopy/diffraction. In the X-ray context, early developments were made by Wilkins and colleagues from 1995 [9,11] in the context of polychromatic sources and by Snigirev and colleagues [10], also from 1995, in the context of synchrotron sources.

Apart from its simplicity, features of the method include the ability to use broad-band polychromatic sources such that all photons in the FoV are essentially available for contributing to image formation. Other features are that the FoV is not limited by optics and the method can operate at high X-ray photon energies, such as might be required for various types of whole body clinical medical radiography. Also, a single exposure can be sufficient to obtain quantitative information under certain conditions [22,23].

Disadvantages lie with the low sensitivity to slowly varying features, since in the near-field regime of Fresnel diffraction, intensity for a pure phase object is proportional to the Laplacian of the phase, viz $\nabla^2\phi$. This can be ameliorated to a certain extent by going to large projection distances.

This method appears to be the only one that has already been demonstrated in the clinical medical context for *in vivo* imaging; especially of note are the recent mammography studies at *Sincrotrone Elettra* using the *SYRMEP* beamline [24]. This was not an optimized PB-PCI set-up and so there remains much opportunity for improved performance [25,26]. Nonetheless, these early results are extremely promising for the widespread application of PB-PCI in the clinical medical context.

Grating-Based X-Ray Phase-Contrast Imaging (GB-PCI)

This method bears some resemblance to both IB-PCI and AB-PCI. It involves 2 or more (linear) gratings operating as an interferometer. An early development of this type of approach was described by Clauser in 1997 [12], but apparently without any experimental demonstration by him using X-rays. Subsequent development and demonstration of the method was carried out by Swiss and Japanese groups using both synchrotron and laboratory sources: see in particular, David, Weitkamp, Pfieffer and colleagues at the Swiss Light Source [13-14] Momose and colleagues at the University of Tokyo and the Photon Factory in Tsukuba [15].

Features of the method include the ability to image with reasonable sized field of view, limited by the ability to micromanufacture gratings of sufficiently high quality. They also include the ability to use polychromatic radiation. Because the method essentially gives information on $\partial\phi/\partial x$ (or $\partial\phi/\partial y$), it can be sensitive to slowly varying features. Speed of recording images can be increased by use of broader high-power X-ray sources and by using a third grating in front of the source, but at the expense of spatial resolution.

Difficulties with GB-PCI for *in vivo* clinical medical applications include: i) the need to record multiple images in a very short time frame (typically less than 1 second) in order to determine $\partial\phi/\partial x$ or related quantities that are independent of the position of the absorber grating (in front of the detector). This places extremely stringent demands on the detector if high spatial resolution, large area and high readout speed are to be achieved. ii) determination of ϕ from $\partial\phi/\partial x$ requires the careful consideration of appropriate mathematical boundary conditions in the case of objects that either partially or completely extend beyond the boundaries of the FoV. In this case, inevitable approximations can lead to significant artifacts. Other difficulties relate to the problems of making high-aspect-ratio absorber gratings if high energy photons are to be utilized.

TECHNOLOGICAL ISSUES AND FUTURE PROSPECTS

New Types of X-Ray Sources

All the X-ray phase-contrast imaging techniques described in this paper can benefit from the availability of improved (especially high-brilliance laboratory-based) X-ray sources. As examples of the progress in this area, we note that new types of electron-impact sources are being developed [27], high-power pulsed-laser sources [28], as well as compact and portable synchrotron sources [29].

X-Ray Detector Developments

X-ray phase-contrast imaging methods, and especially PB-PCI and GB-PCI, will benefit greatly from improved types of 2D electronic detectors and particularly, from the availability of high detective quantum efficiency (DQE) detectors with large area and good spatial resolution (say 50 micron or better). Recent developments in photon-counting detectors, see for example [30,31], are of considerable interest and promise in this regard and can essentially eliminate electronic noise and enable short exposure times and very low-dose radiography.

High speed readout or image acquisition is also required if multiple frames are required, such as in GB-PCI if the phase gradient is to be determined.

SUMMARY

X-ray phase-contrast imaging appears poised for a major advance in the area of *in vivo* clinical medical applications with PB-PCI already having been demonstrated in clinical practice, albeit in significantly sub-optimal form. Advances in X-ray sources and availability of improved low-noise photon counting detectors will greatly help to make X-ray phase-contrast imaging a mainstream technology in clinical applications and offer the promise of significantly increased diagnostic information and reduced dose to the patient. Naturally, radiologists need to be informed and educated on these technological advances, in order to ensure that these new X-ray imaging capabilities reach their full potential in the field of clinical medicine.

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REFERENCES

1. U. Bonse & M. Hart. *Appld. Phys. Letts.* **6,** 155-6 (1965).
2. U. Bonse & M. Hart. *Z. Phys.* **188**, 154-64 1965).
3. U. Bonse & M. Hart. *Acta Cryst.* **A 24**, 240-5 (1968).
4. A. Momose *J. Synchr. Radn,* 9, 136-42 (2002).
5. K. Goetz, M.P. Kalashnikov, et al *Sov. J. Quantum Electron.* 9 607-10 (1979).
6. E. Forster, K. Götz & P. Zaumseil, *Kristall und Technik*, **15**, 937-45 (1980).

7. V.N. Ingal & E.A. Beliaevskaya, *J. Phys. D: Appld. Phys.* 28, 2314-7 (1995).
8. T.J. Davis, D. Gao, T.E. Gureyev, A.W. Stevenson, and S.W. Wilkins, *Nature* **373**, 595-8 (1995).
9. S.W. Wilkins *Aust. Pat Applicn* (28 March, 1995) PN 2112/95; PCT/AU96/00178; USA Patent 6,018,564.
10. A. Snigirev, I. Snigireva, V. Kohn, S. Kuznetsov and I. Schelokov, *Rev. Sci. Instrum.* **66**, 5486-92 (1995).
11. S.W. Wilkins, T.E. Gureyev, D. Gao, A. Pogany, and A.W. Stevenson, *Nature* **384**, 335-8 (1996).
12. J.F. Clauser US Pat. 5,812,629 (30 April, 1997).
13. C. David et al *App. Phys. Letts.* **81**, 3287-9 (2002).
14. T. Weitkamp, et al, *Optics Express* **13,** 6296-304 (2005).
15. A Momose et al *Jpn. J. Appl. Phys*. **42** L866-68 (2003).
16. T.J. Davis J. *X-Ray Sci & Techn.* **6,** 317-42. (1996).
17. V.N.Ingal, E.A.Beliaevskaya & V.P.Efanov. RU patent No. 2012872 (1994). US patent No. 5579363 (1995).
18. D. Chapman, W. Thomlinson, R. E.Johnston, et al. *Phys. Med. Biol.*, **42**, 2015-25 (1997).
19. Gureyev, T. E. and Wilkins, S. W. (1997). *Il Nuovo Cimento* **D19**, 545-552.
20. P. Coan, E. Pagot, S. Fiedler, P. Cloetens, J. Baruchel, and A. Bravin, J. Synchrotron Rad. **12,** 241-245 (2005).
21. D. Gabor, *Nature* **161,** 777-8 (1948).
22. K.A. Nugent, T.E. Gureyev, D. Cookson,, D.Paganin, & Z. Barnea, *Phys. Rev. Letts.* **77,** 2961-4 (1996).
23. D. Paganin et al, J.Micros. 206, 33-40 (2002).
24. A. Abrami, K. Casarin, et al, Elettra Facility Highlights 2005-06 (2006) pp 119-22.
25. A. Pogany, D. Gao, & S.W. Wilkins, *Rev. Sci Instrums.* **68,** 2774-82 (1997).
26. Ya.I. Nesterets, S.W. Wilkins, T.E. Gureyev, A. Pogany and A.W. Stevenson. *Rev. Sci. Instrums,* **76** Article.no: 093706, 1-16 (2005).
27. M. Otendal, T. Tuohimaa, & M. Hertz, *J. Appl. Phys. Letts.,* **101,** 026102 (2007).
28. J.C. Kieffer, A. Krol, Z. Jiang, et al *Appl. Phys.* **B 74** S75-81 (2002).
29. T. Hirai, H. Yamada, M. Sasaki et al *J. Synchrotron. Rad,* **13**, 397-402 (2006).
30. C. Broennimann, E.F. Eikenberry, B. Henrich, et al. *J.Synchrotron Rad.* **13,** 120-30. (2006).
31. A. Maidement, M. Albert, S. Thunberg et al, *SPIE Medical Imaging: Physics of Medical Imaging* ed by M. Flynn **5745**, pp572-82 (2005).
32. XRT Limited, http://www.xrt.com.au.