

Edge illumination and coded-aperture X-ray phase-contrast imaging: increased sensitivity at synchrotrons and lab-based translations into medicine, biology and materials science

M. Endrizzi^a, P. C. Diemoz^a, M. B. Szafraniec^a, C. K. Hagen^a, T. P. Millard^a, C. E. Zapata^a,
P. R. T. Munro^{b,c}, K. Ignatyev^d, M. Marenzana^{e,f}, R. D. Speller^a and A. Olivo^a

^aDepartment of Medical Physics and Bioengineering, University College London, Malet Place,
Gower Street, London WC1E 6BT, UK

^bOptical + Biomedical Engineering Laboratory, School of Electrical, Electronic and Computer
Engineering, The University of Western Australia, 35 Stirling Highway, Crawley, Western
Australia 6009, Australia

^cCentre for Microscopy, Characterisation and Analysis, The University of Western Australia,
35 Stirling Highway, Crawley, Western Australia, 6009, Australia

^dDiamond Light Source, OX11 0DE, Didcot, UK

^eDepartment of Bioengineering, Imperial College, London SW7 2AZ, UK

^fNuffield Department of Orthopedics, Rheumatology and Musculoskeletal Sciences, Kennedy
Institute of Rheumatology, University of Oxford, Oxford OX3 7HE, UK

ABSTRACT

The edge illumination principle was first proposed at Elettra (Italy) in the late nineties, as an alternative method for achieving high phase sensitivity with a very simple and flexible set-up, and has since been under continuous development in the radiation physics group at UCL. Edge illumination allows overcoming most of the limitations of other phase-contrast techniques, enabling their translation into a laboratory environment. It is relatively insensitive to mechanical and thermal instabilities and it can be adapted to the divergent and polychromatic beams provided by X-ray tubes. This method has been demonstrated to work efficiently with source sizes up to 100 μm , compatible with state-of-the-art mammography sources. Two full prototypes have been built and are operational at UCL. Recent activity focused on applications such as breast and cartilage imaging, homeland security and detection of defects in composite materials. New methods such as phase retrieval, tomosynthesis and computed tomography algorithms are currently being theoretically and experimentally investigated. These results strongly indicate the technique as an extremely powerful and versatile tool for X-ray imaging in a wide range of applications.

Keywords: X-ray imaging, phase contrast, edge illumination, coded apertures

1. INTRODUCTION

X-ray phase-contrast imaging (XPCI) makes use of the variations in the phase of the radiation exiting the sample for generating contrast. In conventional radiography techniques, which are insensitive to the effects related to the phase, the contrast arises only from absorption. By exploiting also the phase, XPCI is capable of visualizing low-absorption details, undetectable with a conventional radiography system, and it enhances the visibility of all the details in the X-ray image.¹ The real part of the refractive index* $\delta \sim 10^{-6}$, which governs the phase effects, can be up to 1000 times larger than the imaginary part β , related to absorption, over a wide range of X-ray energies. This makes XPCI a valuable tool which could revolutionize X-ray science,^{3,4} with emphasis on the applications that aim to study weakly-absorbing samples.

Send correspondence to M. Endrizzi

E-mail: m.endrizzi@ucl.ac.uk

*expressed as $n = 1 - \delta + i\beta$ ²

Several methods and techniques have been developed to implement XPCI: Bonse-Hart interferometry,⁵ analyser based imaging (ABI),^{1,6,7} free-space propagation (FSP)^{8,9} and grating interferometry (GI).¹⁰⁻¹² XPCI techniques were initially studied and developed at synchrotron facilities, where an X-ray beam with a high degree of coherence, both from the spatial and the temporal points of view, is available. It is worth noting that some of these techniques, as ABI,¹³ FSP⁹ and GI¹⁴ have been applied with laboratory-based X-ray tubes. Several aspects, however, limited the translation of these methods into mainstream application and clinical environments, where it is practically necessary to relax the coherence requirements. The use of crystals automatically selects a narrow range of energies and thus enforces the use of monochromatic radiation which, in turn, leads to an inefficient exploitation of the available power. FSP tolerates well polychromatic X-ray beam conditions, but still requires a high degree of spatial coherence.⁹ Those conditions are compatible with microfocal X-ray tubes which, however, still suffer an intrinsic limitation in the available flux, thus requiring very long exposure times. GI requires a very fine and stable alignment set-up,¹⁵ and the aperturing and collimation of the source result into an inefficient exploitation of the available power of a given X-ray source.

Although edge illumination (EI) and coded-aperture (CA) systems take inspiration from ABI, where contrast is generated by operating a fine angular selection through a perfect crystal, it may appear that they share a superficial similarity with grating interferometry. It should be noted, however, that the Talbot self-imaging phenomenon is not exploited by the EI method or CA system. In addition, when used with rotating anode X-ray tubes, the CA systems do not require any aperturing/collimation at the source level. This is instead necessary with GI when switching from a Talbot to a Talbot-Lau configuration, a step which is required to implement this technique with conventional laboratory sources.

2. MATERIALS AND METHODS

The EI method was developed at the SYRMEP (SYnchrotron Radiation for MEDical Physics) beamline of the Elettra synchrotron in Trieste (Italy) in the late nineties.¹⁶ The underlying principle consists in illuminating only the edges of the pixels of the detector and offers the possibility to perform an angular selection while being robust with respect to relaxed spatial and temporal coherence conditions. The EI method acts in fact as a fine angular filter but without requiring the use of crystals. By using a geometrical optics approximation, the basic principle can be explained as a result of small deviations in the paths of the X-rays translating into intensity variations, as the number of photons being counted can be increased (decreased) with the deflection into (out of) the active area of the pixel of the detector.



Figure 1. Set-up for the implementation of the edge illumination method with synchrotron radiation: the beam coming from the left is shaped with a slit which is aligned with the edge of a detector pixel.

The basic set-up for the implementation of the EI method at a synchrotron facility is sketched in Fig. 1. In its essence, the beam is pre-shaped by means of an absorbing slit and the shaped beam is then aligned so as to hit the edge of a detector pixel. The sample to be imaged is placed between the slit and the detector. The representation in Fig. 1 typically extends in the direction orthogonal to the page and a two-dimensional image is obtained by scanning the sample in the vertical direction. The set-up of Fig. 1 can be extended to an array of slits (mask) so as to cover simultaneously a larger area, as depicted in Fig. 2. For each beam pre-shaping slit there is a corresponding aperture on the detector, so that the EI method is implemented on every single row of pixels. We usually refer to this configuration as a CA system. The CA system can be adapted to be used with laboratory X-ray tube sources:¹⁷ the pre-shaping mask and the detector have to be scaled in order to account for the beam divergence, as shown in Fig. 3. It has been demonstrated theoretically and experimentally that CA systems are capable of efficiently performing XPCI with source sizes up to 100 μm , which are compatible with current clinical mammography units.¹⁸ By covering a larger area with the mask and by using a two-dimensional

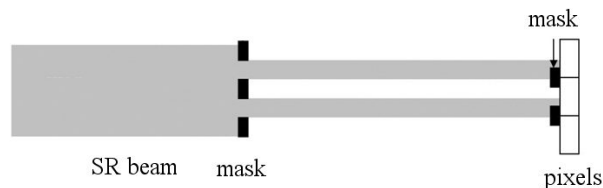


Figure 2. Extension of the EI method to an array of slits by using a pre-sample mask and a detector mask.

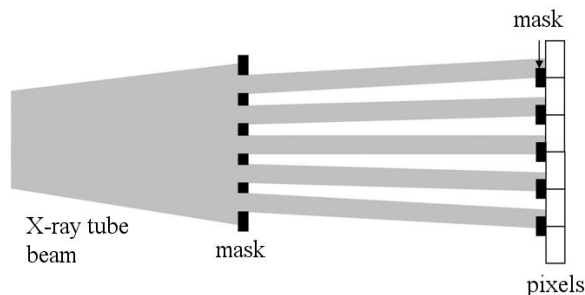


Figure 3. Adaptation of the coded-aperture system for use with laboratory X-ray tubes.

detector, scanning is no longer necessary when using a CA system; however, dithering of the sample could be used if a finer sampling is required for a particular application.¹⁹

Commercially available detectors are routinely used in the two prototypes in our laboratory: an indirect detection passive pixel CMOS sensor with directly deposited structured CsI (Hamamatsu C9732DK), and a direct detection a-Se (ANRAD SMAM). The pixel sizes are $50\ \mu\text{m}$ and $85\ \mu\text{m}$ for the indirect and direct detector, respectively. The Hamamatsu detector exhibits a considerable spill-out of the signal in neighbouring pixels, which causes a degradation of the image quality for a CA system when a full mask is used. This problem can however be overcome by means of a slightly different mask design (line-skipped), at the expenses of the exposure time required to image the entire sample.²⁰ This kind of problem is not encountered for the ANRAD detector, where the spillover of the signal between neighbouring pixels is negligible for most applications. The two rotating anode X-ray tubes operational in our laboratories are a Rigaku M007, with a Mo target and a focal spot of about $70\ \mu\text{m}$, and an X-Tek source, which features a W target and a focal spot of about $50\ \mu\text{m}$.

Based on the EI method, robust phase retrieval algorithms have been developed that allow for quantitative non-interferometric XPCI.^{21–23} Using two complementary positions of the pre-sample mask in a CA system it is possible to invert the signal arising from phase effects, while the contributions due to absorption remain unchanged. By means of two images acquired in those complementary positions, the quantitative differential phase image can be retrieved both in a point source approximation and when an extended source is used.²¹ The EI method proved to be extremely sensitive when implemented with synchrotron radiation, enabling unprecedented angular resolution ($\leq 2\ \text{mrad}$)²³ and the amplification of the phase-contrast signal at high energy ($85\ \text{keV}$).²⁴ Quasi three-dimensional methods (tomosynthesis) have been developed and tested on several applications including breast imaging. Depth discrimination for XPCI images acquired with a laboratory based CA system have been demonstrated on numerical simulations and experimental data. The discrimination is achieved preserving the phase-contrast signal, leading to enhanced detail visibility in the plane of interest.²⁵ The EI method was also extended to computed tomography which allows, beside reconstructing the retrieved absorption and phase signals, the possibility of reconstructing a mixed phase and absorption signal, as it was shown by Diemoz et al.^{26,27}

3. APPLICATIONS AND RESULTS

Laboratory based CA systems have been demonstrated to be potentially useful in security applications,^{19,28,29} also thanks to the robustness of the method with respect to the increase of the energy of the X-ray beam. CA

systems can in fact be used with laboratory sources operated up to 100 kV with acceptable exposure times.³⁰ The contrast of the details in the experimental images produced at high energy was compatible with the value theoretically predicted on the basis of the behaviour of δ with the X-ray energy, with no additional image degradation mechanisms.

Cartilage imaging in murine models has been successfully performed³¹ with a laboratory-based CA system. A thin (about 100 μm thick) cartilage layer was clearly visualized in a rat femur head, as shown in Fig. 4. It is also

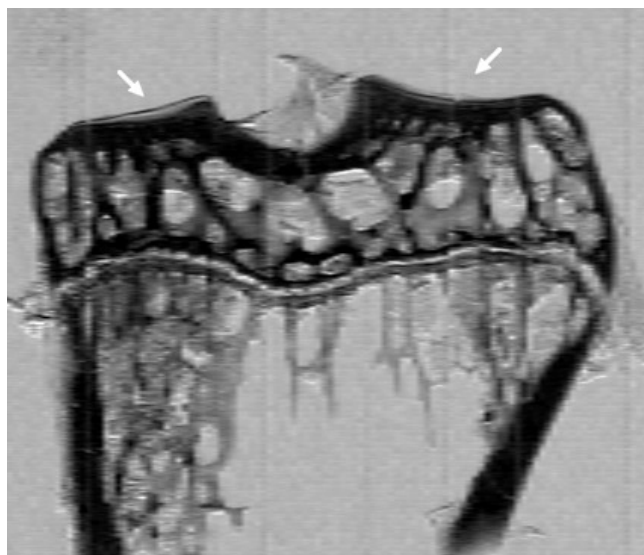


Figure 4. Laboratory based CA image of a rat femur head: the thin cartilage layer is well visible and a small defect in the cartilage layer is also detectable, as indicated by the white arrows.

possible to appreciate small defects on the cartilage surface, as highlighted by the arrow on the right-hand side of Fig. 4. Most studies aiming at a studying osteoarthritis, and the effects of a treatment on its progression, are conducted on murine models, but they currently suffer from the lack of a technique capable of visualizing the thin cartilage layers involved.^{32,33} The effective visualization of murine cartilage layers, by means of laboratory-based CA system, offers the possibility to overcome this problem.

Composite materials are expected to play a key role in important industrial sectors as, for example, transport and energy. Their very nature (i.e. being composed of several layers) poses severe problems to testing methods, especially in terms of being able to detect fine defects or blemishes. An example is here reported in Fig. 5. The small blemishes, which can be seen in the synchrotron radiation image recorded with the FSP technique (Fig. 5(a)), are undetectable in the absorption image acquired in the laboratory (Fig. 5(b)). However, they become visible again in the image obtained with a laboratory-based CA system (Fig. 5(c)). The horizontal lines in Fig. 5(c) are artefacts due to defects in the mask prototypes which would be eliminated in a commercial system.

In order to evaluate the potential of CA systems applied to breast imaging, a trial on ex-vivo samples has been conducted. The study encompassed about 100 human tissue specimens, affected by several types of tumours. We have preliminary evidence indicating that CA systems can produce enhanced detail visibility at doses that are compatible with clinical mammography. The full set of images is currently under review by a pool of radiologists in order to fully assess the clinical relevance of the trial.

4. CONCLUSION

Edge illumination and coded-aperture systems proved to be an extremely powerful and flexible tool for X-ray phase-contrast imaging, with applications over a wide range of fields such as medicine, material science and security. The laboratory-based CA systems built at UCL are actively characterized and optimized and intensive testing of applications is currently taking place, while novel methods for improving detail visibility and extending

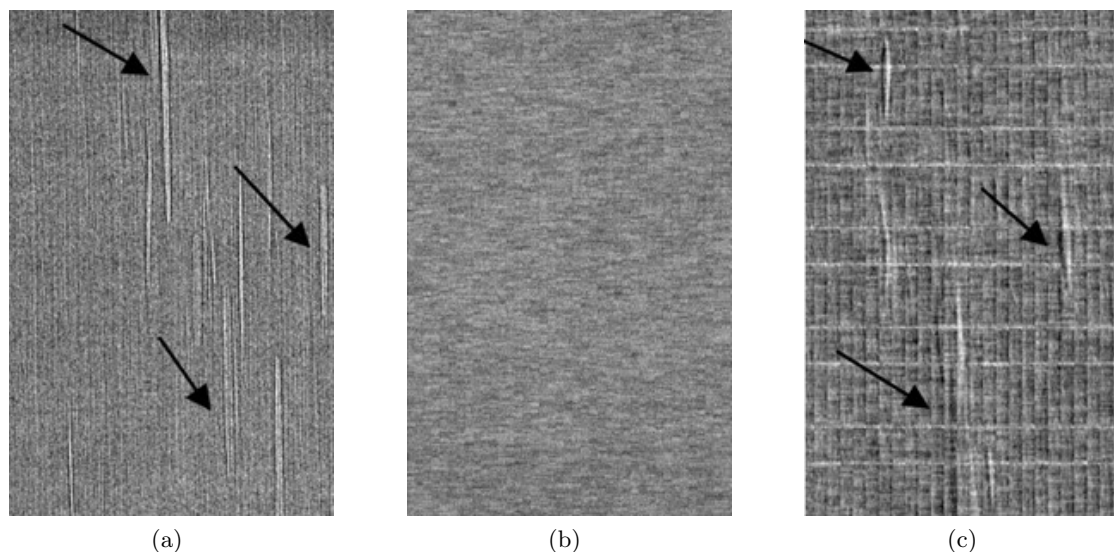


Figure 5. Image of a composite material: in the synchrotron radiation FSP image (a) small blemishes are visible, they are undetectable in a laboratory absorption radiography (b) while they can be appreciated in a laboratory-based CA image (c).

the technique to three-dimensional imaging are under exploration and test. On the one hand, edge illumination provides a very high sensitivity when implemented with synchrotron radiation and offers the possibility to amplify phase-contrast signals at high X-ray energies. On the other, coded-apertures systems can operate under relaxed coherence conditions, making feasible a translation of the technique into an environment compatible with laboratory and clinic conditions.

REFERENCES

1. Davis, T. J., Gao, D., Gureyev, T. E., Stevenson, A. W., and Wilkins, S. W., "Phase-contrast imaging of weakly absorbing materials using hard X-rays," *Nature* **373**, 595–598 (Feb. 1995).
2. Paganin, D., [*Coherent x-ray optics*], Oxford series on synchrotron radiation, Oxford University Press (2006).
3. Fitzgerald, R., "Phase-sensitive x-ray imaging," *Physics Today* **53**(7), 23–26 (2000).
4. Lewis, R. A., "Medical phase contrast x-ray imaging: current status and future prospects," *Physics in Medicine and Biology* **49**(16), 3573 (2004).
5. Bonse, U. and Hart, M., "An x-ray interferometer," *Appl. Phys. Lett.* **6**, 155–156 (1965).
6. Foerster, E., Goetz, K., and Zaumseil, P., "Double crystal diffractometry for the characterization of targets for laser fusion experiments," *Kristall und Technik* **15**(8), 937–945 (1980).
7. Ingal, V. N. and Beliaevskaya, E. A., "X-ray plane-wave topography observation of the phase contrast from a non-crystalline object," *Journal of Physics D Applied Physics* **28**, 2314–2317 (Nov. 1995).
8. Snigirev, A., Snigireva, I., Kohn, V., Kuznetsov, S., and Schelokov, I., "On the possibilities of x-ray phase contrast microimaging by coherent high-energy synchrotron radiation," *Review of Scientific Instruments* **66**, 5486–5492 (Dec. 1995).
9. Wilkins, S. W., Gureyev, T. E., Gao, D., Pogany, A., and Stevenson, A. W., "Phase-contrast imaging using polychromatic hard x-rays," *Nature* **384**, 335–338 (1996).
10. David, C., Nohammer, B., Solak, H. H., and Ziegler, E., "Differential x-ray phase contrast imaging using a shearing interferometer," *Applied Physics Letters* **81**(17), 3287–3289 (2002).
11. Momose, A., Kawamoto, S., Koyama, I., Hamaiishi, Y., Takai, K., and Suzuki, Y., "Demonstration of X-Ray Talbot Interferometry," *Japanese Journal of Applied Physics* **42**, L866–L868 (July 2003).
12. Weitkamp, T., Diaz, A., David, C., Pfeiffer, F., Stampanoni, M., Cloetens, P., and Ziegler, E., "X-ray phase imaging with a grating interferometer," *Opt. Express* **13**, 6296–6304 (Aug 2005).

13. Vine, D. J., Paganin, D. M., Pavlov, K. M., Kräußlich, J., Wehrhan, O., Uschmann, I., and Förster, E., "Analyzer-based phase contrast imaging and phase retrieval using a rotating anode x-ray source," *Applied Physics Letters* **91**, 254110 (Dec. 2007).
14. Pfeiffer, F., Weitkamp, T., Bunk, O., and David, C., "Phase retrieval and differential phase-contrast imaging with low-brilliance X-ray sources," *Nature Physics* **2**, 258–261 (Apr. 2006).
15. Zambelli, J., Bevins, N., Qi, Z., and Chen, G.-H., "Radiation dose efficiency comparison between differential phase contrast CT and conventional absorption CT," *Medical Physics* **37**, 2473 (2010).
16. Olivo, A., Arfelli, F., Cantatore, G., Longo, R., Menk, R. H., Pani, S., Prest, M., Poropat, P., Rigon, L., Tromba, G., Vallazza, E., and Castelli, E., "An innovative digital imaging set-up allowing a low-dose approach to phase contrast applications in the medical field," *Medical Physics* **28**, 1610–1619 (Aug. 2001).
17. Olivo, A. and Speller, R., "A coded-aperture technique allowing x-ray phase contrast imaging with conventional sources," *Applied Physics Letters* **91**, 074106 (Aug. 2007).
18. Munro, P. R. T., Ignatyev, K., Speller, R. D., and Olivo, A., "Source size and temporal coherence requirements of coded aperture type x-ray phase contrast imaging systems," *Optics Express* **18**, 19681 (Sept. 2010).
19. Olivo, A., Ignatyev, K., Munro, P. R. T., and Speller, R. D., "Noninterferometric phase-contrast images obtained with incoherent x-ray sources," *Applied Optics* **50**, 1765 (Apr. 2011).
20. Ignatyev, K., Munro, P. R. T., Speller, R. D., and Olivo, A., "Effects of signal diffusion on x-ray phase contrast images," *Review of Scientific Instruments* **82**, 073702 (July 2011).
21. Munro, P. R., Ignatyev, K., Speller, R. D., and Olivo, A., "Phase and absorption retrieval using incoherent X-ray sources," *Proc. Natl. Acad. Sci. U.S.A.* **109**, 13922–13927 (Aug 2012).
22. Munro, P. R., Rigon, L., Ignatyev, K., Lopez, F. C., Dreossi, D., Speller, R. D., and Olivo, A., "A quantitative, non-interferometric x-ray phase contrast imaging technique," *Opt. Express* **21**, 647–661 (Jan 2013).
23. Diemoz, P., Endrizzi, M., Zapata, C., Pešić, Z., Rau, C., Bravin, A., Robinson, I., and Olivo, A., "x-ray phase-contrast imaging with nanoradian angular resolution," **under review**.
24. Olivo, A., Diemoz, P. C., and Bravin, A., "Amplification of the phase contrast signal at very high x-ray energies," *Optics Letters* **37**, 915 (Mar. 2012).
25. Szafraniec, M. B., Millard, T. P., Ignatyev, K., Speller, R. D., and Olivo, A., "Theoretical and experimental bases of coded-aperture phase-contrast tomosynthesis," **under review**.
26. Diemoz, P. C., Coan, P., Zanette, I., Bravin, A., Lang, S., Glaser, C., and Weitkamp, T., "A simplified approach for computed tomography with an x-ray grating interferometer," *Opt. Express* **19**, 1691–1698 (Jan 2011).
27. Endrizzi, M., Diemoz, P. C., Munro, P. R. T., Hagen, C. K., Szafraniec, M. B., Millard, T. P., Zapata, C. E., Speller, R. D., and Olivo, A., "Applications of a non-interferometric x-ray phase contrast imaging method with both synchrotron and conventional sources," *Journal of Instrumentation* **in publication**.
28. Olivo, A., Ignatyev, K., Munro, P. R. T., and Speller, R. D., "Design and realization of a coded-aperture based X-ray phase contrast imaging for homeland security applications," *Nuclear Instruments and Methods in Physics Research A* **610**, 604–614 (Nov. 2009).
29. Ignatyev, K., Munro, P. R. T., Chana, D., Speller, R. D., and Olivo, A., "A New Generation of X-ray Baggage Scanners Based on a Different Physical Principle," *Materials* **4**, 1846–1860 (Oct. 2011).
30. Ignatyev, K., Munro, P. R. T., Chana, D., Speller, R. D., and Olivo, A., "Coded apertures allow high-energy x-ray phase contrast imaging with laboratory sources," *Journal of Applied Physics* **110**, 014906 (July 2011).
31. Marenzana, M., Hagen, C. K., Borges, P. D. N., Endrizzi, M., Szafraniec, M. B., Ignatyev, K., and Olivo, A., "Visualization of small lesions in rat cartilage by means of laboratory-based x-ray phase contrast imaging," *Physics in Medicine and Biology* **57**(24), 8173 (2012).
32. Muehleman, C., Majumdar, S., Issever, A. S., Arfelli, F., Menk, R.-H., Rigon, L., Heitner, G., Reime, B., Metge, J., Wagner, A., Kuettner, K. E., and Mollenhauer, J., "X-ray detection of structural orientation in human articular cartilage," *Osteoarthritis and Cartilage* **12**(2), 97 – 105 (2004).
33. Glasson, S., Chambers, M., Berg, W. V. D., and Little, C., "The oarsi histopathology initiative recommendations for histological assessments of osteoarthritis in the mouse," *Osteoarthritis and Cartilage* **18**, **Supplement 3**(0), S17 – S23 (2010). OAC Histopathology Supplement.