Dark-field signal extraction in propagation-based phase-contrast imaging

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Abstract

A method for extracting the dark-field signal in propagation-based phase-contrast imaging is proposed. In the case of objects consisting predominantly of a single material, or several different materials with similar ratios of the real decrement to the imaginary part of the complex refractive index, the proposed method requires a single image for extraction of the dark-field signal in two-dimensional projection imaging. In the case of three-dimensional tomographic imaging, the method needs only one image to be collected at each projection angle. Initial examples using simulated and experimental data indicate that this method can improve visualization of small sharp features inside a larger object, e.g. the visualization of microcalcifications in propagation-based x-ray breast cancer imaging. It is suggested that the proposed approach may be useful in other forms of biomedical imaging, where it can help one to obtain additional small-angle scattering information without increasing the radiation dose to the sample.

1. Introduction

Hard x-ray phase-contrast imaging has become a popular method for non-destructive imaging of samples consisting of materials with small differences in x-ray absorption properties—see, for example, the original papers (Goetz et al 1979, Ingal and Beliaevskaya 1995, Davis et al 1995, Momose 1995, Snigirev et al 1995, Momose et al 1996, 2003, Wilkins et al 1996, Nugent et al 1996, David et al 2002, Pfeiffer et al 2008, Wen et al 2010, Olivo et al 2011, Morgan et al 2011a, 2012, Munro et al 2012, Bérujon et al 2012) or more recent reviews (Wilkins et al 2014, Wen 2019). Importantly, while hard x-rays with wavelength of 1 Å or shorter are typically needed in order to image the internal structure of biomedical samples with thicknesses of several centimetres, the resultant two-dimensional (2D), e.g. projection, images, or three-dimensional (3D), e.g. computed tomography (CT), images, tend to display weak contrast between different types of soft tissue since they tend to have similar x-ray absorption properties. In this situation, phase-contrast imaging which utilizes refraction, as well as absorption, of x-rays in the samples, has been shown to significantly increase the soft-tissue contrast under suitable experimental conditions. Since biomedical samples are often radiation sensitive, the x-ray dose also needs to be carefully controlled, and the corresponding ‘figure of merit’, which can help to objectively assess the advantages of a new method, may be represented by the contrast-to-noise ratio (CNR) or signal-to-noise ratio (SNR) per unit dose (Diemoz et al 2012, Wilkins et al 2014). However, this ‘figure of merit’ still does not present a complete picture, since the CNR and SNR can always be increased at the expense of spatial resolution, without changing the dose. Therefore, in order to evaluate the effectiveness of a particular x-ray imaging method or apparatus, it is usually necessary to take into account all three of these key parameters: CNR/SNR, x-ray dose and spatial resolution. One imaging quality characteristic that takes into account all these factors simultaneously and is invariant with respect to simple operations such as binning of the detector pixels (which increases the SNR, but lowers the spatial resolution),
is represented by ‘intrinsic imaging quality’ (Gureyev et al 2014, 2019a). Other image quality metrics can also be used in this context (Wilkins et al 2014, Mait et al 2018). We use the intrinsic imaging quality characteristic to evaluate the performance of the method proposed in the present paper.

Different modalities of x-ray phase-contrast imaging have been studied extensively in recent years, both theoretically and experimentally. The simplest such modality is propagation-based imaging (PBI) (Snigirev et al 1995, Wilkins et al 1996, Nugent et al 1996), which utilizes free-space propagation of spatially coherent transmitted x-rays from the sample to the detector as a means for visualizing the phase contrast, i.e. transforming local variations of the phase shifts in the transmitted x-ray beam in the ‘object’ plane into detectable intensity variations in the ‘image’ plane downstream the optical axis of the imaging system. Analyzer-based imaging (ABI) (Goetz et al 1979, Ingal and Beliaevskaya 1995, Davis et al 1995) uses Bragg or Laue diffraction of the transmitted beam in a high-quality ‘analyzer’ crystal in order to render the phase contrast detectable. An even more experimentally demanding, but potentially more sensitive, method is based on the use of Bonse-Hart type x-ray crystal interferometers (Bonse and Hart 1965, Momose 1995, Momose et al 1996). Other approaches, which are currently being actively developed for biomedical phase-contrast x-ray imaging include the grating-interferometer-based techniques (David et al 2002, Momose et al 2003, Pfeiffer et al 2008) and various forms of coded-aperture type methods, including the ‘edge illumination’ (EI) method (Olivo et al 2011, Munro et al 2012), 2D gratings (GB) (Wen et al 2010, Morgan et al 2011a, 2011b) and speckle-based (SB) methods (Bérubio et al 2012, Morgan et al 2012).

Most of the x-ray phase-contrast imaging methods listed above, with the notable exception of PBI, have been used both in the bright-field and dark-field modes, i.e. respectively with or without the zero-spatial-order transmitted beam contributing to the registered image (Ingal and Beliaevskaya 1995, Pfeiffer et al 2008, Munro et al 2012, Wilkins et al 2014). The dark-field mode tends to naturally emphasize the small-angle scattering (SAXS) signal, in particular (Davis 1994, Pfeiffer et al 2008, Wilkins et al 2014, Arfelli et al 2018). The methods which use gratings, coded apertures or analyzer crystals can select between the bright-field and the dark-field modes easily and naturally by changing the effective position and width of the angular transmission range of the ‘wavefront analyzer’ element with respect to the propagation direction of the undiffracted beam (zero-order Fourier component). A similar selection cannot be achieved in the PBI method since it does not involve any optical elements and therefore always includes all diffraction orders, up to the highest order determined by the resolution limit of the imaging setup, in the registered image. A very recent study however has demonstrated, via a Fokker-Planck approach (Morgan and Paganin 2019, Paganin and Morgan 2019), that the extraction of a position-dependent SAXS signal in PBI may be possible by means of numerical post-processing of two or more images collected at different propagation distances under suitable conditions. In the present work we demonstrate that it may be possible to extract the position-dependent dark-field signal, containing the SAXS contribution, using a single PBI image, provided that (1) the spatial resolution of the imaging system is sufficiently high, and (2) the sample may be considered ‘homogeneous’ in the sense that the ratio \( \gamma \) of the real decrement to the imaginary part of the complex refractive index is the same at any point inside the object (Paganin et al 2002). For such homogeneous objects, and for the case of normally-incident plane-wave illumination, the projection approximation implies that the phase, over the object’s exit-surface plane, will be proportional to the logarithm of the intensity. The class of homogeneous objects (sometimes also called ‘monomorphous’) includes all objects consisting of a single material (the density of these objects is still allowed to vary throughout the volume), and all objects consisting of low-Z elements (\( Z < 10 \)) when illuminated by x-rays with energy approximately above 60 keV (Wu et al 2005). It has also been demonstrated that many biomedical samples consisting of different soft tissues (e.g. healthy and malignant breast tissues) may be considered approximately homogeneous for the purpose of quantitative analysis of PBI images. When a sample deviates from the theoretical ‘homogeneous model’, the errors in the reconstructed values of the x-ray absorption coefficient, originating from the violation of the homogeneity condition, are typically limited to narrow vicinities of edges and interfaces between components with different \( \gamma \) ratio, as was demonstrated e.g. in Gureyev et al (2013).

2. Dark-field signal in PBI

We investigate here the theoretical possibility of carrying out ‘dark-field imaging’, i.e. the extraction of a ‘dark-field signal’, in PBI. Note that by the term ‘dark-field imaging’ we understand here any imaging technique ‘in which the nondiffracted rays are removed altogether so that the image is composed solely of diffracted wave components’ (Gage 1920, Murphy and Davidson 2013). This general terminology may have a broader scope than the usage of the same term in some publications on interferometric or analyzer-based x-ray dark-field imaging, where the technique was predominantly associated with the identification of regions in the object that produce reduced visibility of interferometric fringes or broadening of the analyzer rocking curve. A particular dark-field signal mechanism that leads to these effects is typically related to the
presence of unresolved random microstructure. This mechanism makes pixels in dark-field images brighter in the regions where x-rays traverse parts of the sample with significant sub-resolution structures, indicating the increased amount of SAXS signal. Under the (historically consistent) usage of the term ‘dark field’ adopted in the present paper, another fundamentally different possible contributor to dark-field images can be related to scattering from edges (Young-Maggi-Rubinowicz boundary wave, Keller-type edge-diffracted rays—see e.g. Born and Wolf (1999)). The edge-scattering-type signal can give both positive and negative contributions. When the recovered dark-field images are replaced with their moduli, such images also appear as brighter regions on a dark field (see simulated and experimental examples in the following sections). We discuss the physical meaning of the dark-field signal in PBI further in the present section, after formally introducing the relevant generic optical setup and the corresponding mathematical model.

Let an object (scatterer) be located in the vicinity of the optic axis in the half-space \( z < 0 \) immediately before the ‘object’ plane \( z = 0 \). We assume for simplicity that the wave incident on the sample is a plane monochromatic wave with wavelength \( \lambda \) and unit intensity, propagating along the optic axis \( z \), i.e. the complex amplitude of the incident wave is \( \exp(ikz) \). Generalization of the following results to cases involving polychromatic and spatially partially coherent incident radiation can be carried out similarly to the way described in Gureyev et al (2006). The scattering properties of the object are assumed to be such that the wave transmitted through the object is paraxial, i.e. all the wavefront normals in the object plane are contained in a narrow cone around the direction of the \( z \) axis. The transmitted wave propagates in the free half-space \( z > 0 \) until it reaches a position-sensitive detector. As the transmitted wave has been assumed to be paraxial, its evolution in the free half-space \( z > 0 \) can be described by the Fresnel integral (Paganin 2006),

\[
U_p(x, y) = \frac{\exp(ikR)}{i\lambda R} \iint \exp \left\{ \frac{i\pi}{\lambda R} [(x-x')^2 + (y-y')^2] \right\} U_0(x', y') \, dx' \, dy',
\]

where \( U_0(x, y) \equiv a(x, y) \exp[i\varphi(x, y)] \) is the transmitted complex scalar amplitude of the wave in the object plane having transverse coordinates \( (x, y) \) and \( R \) is the distance between the object and image planes. The detector is assumed to be capable of measuring the spatial distribution of intensity in the image plane,

\[
I_p(x, y) = |U_p(x, y)|^2.
\]

In phase-contrast imaging and phase-contrast tomography one is often interested in finding the object-plane phase \( \varphi(x, y) \) and intensity \( I_0(x, y) = a^2(x, y) \) from the measured intensity distribution in one or more image planes (Paganin 2006). It is easy to see that equation (2) is non-linear with respect to the object-plane phase and amplitude, and as such may be challenging to solve analytically or numerically. For example, the well-known family of Gerchberg–Saxton type phase retrieval algorithms (Gerchberg and Saxton 1972, Fienup 1987) does not work well in the near-Fresnel region (Gureyev 2003). On the other hand, the linearized form (approximation) of equation (2) that will be employed below, which can be sufficiently accurate under certain well-specified conditions, can also be convenient for use in the retrieval of object-plane phase and amplitude in the Fresnel region (Gureyev et al 2004).

Let us assume that it is possible to represent the complex wave amplitude in the object plane in the following form:

\[
U_0(x, y) = U_{TIE}(x, y)U_{\text{Born}}(x, y),
\]

where \( U_{TIE}(x, y) \equiv \exp[-\mu_{TIE}(x, y) + i\varphi_{TIE}(x, y)] \) is a slowly varying ‘envelope’ function satisfying the validity conditions for the transport of intensity equation (TIE) (Teague 1983), and \( U_{\text{Born}}(x, y) = \exp[-\mu_{\text{Born}}(x, y) + i\varphi_{\text{Born}}(x, y)] \) contains small but rapidly varying absorption and phase shift components, such that \( |\mu_{\text{Born}}| \ll 1 \) and \( |\varphi_{\text{Born}}| \ll 1 \), and hence \( U_{\text{Born}}(x, y) \equiv 1 - \mu_{\text{Born}}(x, y) + i\varphi_{\text{Born}}(x, y) \). The term \( U_{\text{Born}}(x, y) \) may contain the SAXS signal, in particular. Note that the ‘Born’ subscript here refers to the first Born approximation, which is applicable in weak-scatter contexts (Paganin 2006). Note also that the following normalization can always be imposed: \( \iint |I_{TIE}(x, y)\mu_{\text{Born}}(x, y)\, dxdy = \iint I_{TIE}(x, y)\varphi_{\text{Born}}(x, y)\, dxdy = 0 \). Under these conditions it is possible to show (Gureyev et al 2004) that

\[
\hat{I}_g(\xi, \eta) = \hat{I}_{TIE}(\xi, \eta) - (R/k)[\nabla_\perp \cdot (I_{TIE}\nabla_\perp \varphi_{TIE})] (\xi, \eta) - 2\cos[\pi \lambda R(\xi^2 + \eta^2)](I_{TIE}\mu_{\text{Born}})^{\lambda}(\xi, \eta)
+ 2\sin[\pi \lambda R(\xi^2 + \eta^2)](I_{TIE}\varphi_{\text{Born}})^{\lambda}(\xi, \eta),
\]

where the overhead hat symbol denotes the 2D Fourier transform with respect to \( x \) and \( y \),

\[
\tilde{f}(\xi, \eta) = \iint \exp[-i2\pi(x\xi + y\eta)]f(x, y)\, dxdy.\]

The first two terms on the right-hand side of equation (4)
correspond to the TIE approximation (Teague 1983, Nugent et al 1996) of the intensity distribution in the image plane \( z = R \):

\[
\hat{I}_{R,TIE}(\xi, \eta) \equiv \hat{I}_{TIE}(\xi, \eta) - (R/k)[\nabla_{\perp} \cdot (I_{TIE} \nabla_{\perp} \varphi_{TIE})]^\wedge(\xi, \eta). \tag{5}
\]

Since \((I_{TIE,Born})^\wedge(0, 0) = (I_{TIE,\varphi,Born})^\wedge(0, 0) = 0\) due chosen normalization, the last two terms of equation (4) correspond to the first Born approximation for the dark-field part of the intensity distribution in the image plane obtained after subtracting the contribution of the TIE component:

\[
\hat{I}_{R,Born}(\xi, \eta) \equiv \hat{I}_R(\xi, \eta) + I_R(\xi, \eta) - \hat{I}_{R,TIE}(\xi, \eta) = I_0(\xi, \eta) - 2 \cos[\pi \lambda R(\xi^2 + \eta^2)](I_{TIE,\varphi,Born})^\wedge(\xi, \eta) + 2 \sin[\pi \lambda R(\xi^2 + \eta^2)](I_{TIE,\varphi,Born})^\wedge(\xi, \eta),
\]

where \(I_0 = \int \int I_0(x, y) dx dy\) (although this particular choice of constant \(I_0\) in equation (6) is not essential). We would like to emphasize that equation (6) corresponds to the contribution of the 'small, rapidly varying' (Born) component to the whole propagated image, \(I_R(\xi, \eta)\), described by equation (4). The sum of the Born component of the image, \(\hat{I}_{R,Born}(\xi, \eta)\), described by equation (6), and the TIE component of the image, \(\hat{I}_{R,TIE}(\xi, \eta)\), described by equation (5), is formally equal to the whole propagated image with an extra zero diffraction order (unperturbed beam), \(I_0(\xi, \eta) + \hat{I}_R(\xi, \eta)\), as can be seen from the first line of equation (6). This 'extra' zero order appears here, because equation (6) emulates the complete usual first Born approximation to propagated images (Cowley 1995, Pogany et al 1997), including its zero order which was already included in the TIE approximation as well in equation (5).

Equations (4)–(6) suggest the following phase retrieval procedure (Gureyev et al 2004), which is reminiscent of the well-known Gerchberg–Saxton–Fienup type phase retrieval algorithms (Gerchberg and Saxton 1972, Fienup 1987). First, we take an initial approximation \(\hat{I}_R(\xi, \eta) \approx \hat{I}_{R,TIE}(\xi, \eta)\) and solve the TIE equation (5) for \(I_{TIE}\) and \(\varphi_{TIE}\). Note that in general this requires two or more measurements of the propagated intensity distribution \(I_R(x, y)\) at different defocus distances \(R_n, n = 1, 2, \ldots, \) (Teague 1983, Paganin 2006). In the second step, we take the difference \(I_R(\xi, \eta) - \hat{I}_{R,TIE}(\xi, \eta)\) for each \(R = R_n\) and solve the conventional first Born (also known as 'Fourier optics') equation, i.e. equation (6), for \(I_{TIE,Born}\) and \(I_{TIE,\varphi,Born}\) (Pogany et al 1997, Gureyev et al 2004). The complex amplitude in the object plane is then obtained using equation (3). The second step can be easily iterated multiple times, if desired (Gureyev et al 2004). This algorithm becomes simpler in the case of homogeneous objects, where it requires only a single defocused image for the reconstruction of both the absorption and the phase shift in the object plane.

As mentioned in the Introduction, homogeneous objects are characterized by the proportionality relationship between the attenuation and the phase in the object plane, \(\varphi_0(x, y) = (\gamma/2)\ln I_0(x, y)\), with the proportionality constant \(\gamma\) equal to the ratio of the real decrement to the imaginary part of the complex refractive index \(n(x, y, z) = 1 - \delta(x, y, z) + i\beta(x, y, z)\) inside the object, i.e. \(\gamma = \delta(x, y, z)/\beta(x, y, z) = const\) (Paganin et al 2002, 2004). In the case of a homogeneous object, equation (4) becomes

\[
\hat{I}_R(\xi, \eta) = [1 + \gamma \pi \lambda R(\xi^2 + \eta^2)] I_{TIE}(\xi, \eta) - 2 \{\cos[\pi \lambda R(\xi^2 + \eta^2)] + \gamma \sin[\pi \lambda R(\xi^2 + \eta^2)]\}(I_{TIE,\varphi,Born})^\wedge(\xi, \eta).
\]

Here the two unknown distributions, \(I_{TIE}(x, y)\) and \(\mu_{Born}(x, y)\), can be uniquely reconstructed from a single propagated image, \(I_R(x, y)\), if the supports \(\Sigma_{TIE}\) and \(\Sigma_{Born}\) of the Fourier transforms, \(I_{TIE}(\xi, \eta)\) and \((I_{TIE,\varphi,Born})^\wedge(\xi, \eta) = (I_{TIE} * \mu_{Born})(\xi, \eta)\) (where the asterisk denotes convolution), are disjoint, i.e. \(\Sigma_{TIE} \cap \Sigma_{Born} = 0\). For example, \(\Sigma_{TIE}\) could correspond to the low-spatial-frequency Fourier-space domain \(\xi^2 + \eta^2 \leq C_1\), with \(\Sigma_{Born}\) corresponding to the high-frequency domain \(\xi^2 + \eta^2 \geq C_2\), where \(C_1\) and \(C_2\) are positive constants and \(C_1 < C_2\). Given the disjoint nature of these supports, the distribution \(I_{TIE}(x, y)\) can be reconstructed from the restriction of equation (7) onto \(\Sigma_{TIE}\):

\[
\hat{I}_{TIE}(\xi, \eta) = \hat{I}_R(\xi, \eta)/[1 + \gamma \pi \lambda R(\xi^2 + \eta^2)], \quad (\xi, \eta) \in \Sigma_{TIE}.
\]

For \((\xi, \eta) \in \Sigma_{TIE}\), equation (8) coincides with equation (7), because \((I_{TIE,\varphi,Born})^\wedge(\xi, \eta) = 0\) at such points by assumption. After \(I_{TIE}(x, y)\) is found, the distribution \(\mu_{Born}(x, y)\) can be obtained from the equation

\[
(I_{TIE,\varphi,Born})^\wedge(\xi, \eta) = 0.5\hat{I}_R(\xi, \eta)/\{\cos[\pi \lambda R(\xi^2 + \eta^2)] + \gamma \sin[\pi \lambda R(\xi^2 + \eta^2)]\}, \quad (\xi, \eta) \in \Sigma_{Born}.
\]

At points \((\xi, \eta) \in \Sigma_{Born}\), equation (9) coincides with equation (7), because \(\hat{I}_{TIE}(\xi, \eta) = 0\) at such points by assumption. In practice, equation (9) is regularized to prevent the denominator on the right-hand side from going to zero.

Note that in this formalism, in principle, the values of the constant \(\gamma\) can be different between the Born and TIE components appearing in equation (3). Consequently, one can assume \(\gamma = \gamma_1\) in equation (8) and
γ = γ2 in equation (9), with γ2 ≠ γ1. Since these equations are applied to non-overlapping subsets of the input distribution \( I_0(\xi, \eta) \), the two constants do not have to be the same. Such a modification of the above algorithm can be useful in the case of samples consisting essentially of two distinct materials, one for the 'large, slowly varying' (TIE) component, and another for the 'small, rapidly changing' (Born) component. Samples of this type are considered in sections 3 and 4 below.

If the assumption about the supports of the distributions \( \hat{I}_{\text{TIE}}(\xi, \eta) \) and \( (I_{\text{TIE}})_{\text{Born}} \wedge(\xi, \eta) \) being completely disjoint is relaxed, and some (small) overlap of the two supports is allowed, then the algorithm can be modified (Gureyev et al 2004). The first step is still performed according to equation (8), but on the second step, equation (9) is replaced with the following homogeneous version of equation (6):

\[
(\hat{I}_{\text{TIE}})_{\text{Born}} \wedge(\xi, \eta) = 0.5[\hat{I}_R(\xi, \eta) - \hat{I}_{R,\text{TIE}}(\xi, \eta)]/\{\cos[\pi \lambda R(\xi^2 + \eta^2)] + \gamma \sin[\pi \lambda R(\xi^2 + \eta^2)]\},
\]

where \( \hat{I}_{R,\text{TIE}}(\xi, \eta) \) can be defined either as in equation (5), or, more generally, by the full Fresnel propagation from the plane \( z = 0 \) to the plane \( z = R \) of the complex amplitude \( U_{\text{TIE}}(x,y) = \hat{I}_{\text{TIE}}(x,y) \exp[\gamma \ln I_{\text{TIE}}(x,y)] \) constructed from the distribution \( I_{\text{TIE}}(x,y) \) that was found on the first step of the algorithm.

Expanding the sine and cosine in equation (7) into a Taylor series, we obtain:

\[
\hat{I}_R(\xi, \eta) = [1 + \gamma \pi \lambda R(\xi^2 + \eta^2)] \hat{I}_{\text{TIE}}(\xi, \eta) - 2[\hat{I}_{\text{TIE}})_{\text{Born}} \wedge(\xi, \eta)] \sum_{m=0}^\infty (-1)^m \pi \lambda R(\xi^2 + \eta^2)]^{2m} \left[ 1 + \gamma \pi \lambda R(\xi^2 + \eta^2) \right].
\]

Note that different powers of the reciprocal-space variables \( \xi \) and \( \eta \) on the right-hand side of equation (11) correspond to different 'diffraction orders', even though it may not be immediately obvious. Conventionally, diffraction orders with integer indices \( (m, n) \) are associated with the Fourier components, \( U_0^{(m,n)}(x,y) = \exp[2\pi/m(A + my/B)] \), of a complex amplitude in the object plane, where the amplitude is assumed to be identically zero outside a rectangle \( (-A/2 ≤ x ≤ A/2) × (-B/2 ≤ y ≤ B/2) \). The Fourier transform of \( U_0^{(m,n)}(x,y) \), i.e. \( \hat{I}_R^{(m,n)}(\xi, \eta) = \delta(\xi - m/A)\delta(\eta - n/B) \), is non-zero only at the point \( (\xi, \eta) = (m/A, n/B) \). It is easy to see, however, that, if the Fourier spectrum \( [I_{\text{TIE})_{\text{Born}} \wedge(\xi, \eta)] \) behaves similarly to a Gaussian distribution \( \exp(-(\xi^2 + \eta^2)/(2\sigma^2)) \), the terms \( \hat{I}_R^{(m,n)}(\xi, \eta) \equiv (\xi^2 + \eta^2)^m[I_{\text{TIE})_{\text{Born}} \wedge(\xi, \eta)] \), with different indices \( m = 0, 1, 2, \cdots \), reach their maxima at the circles \( (\xi^2 + \eta^2)/(2\sigma^2) = m \). This can be verified by noting that the function \( (\xi^2 + \eta^2)^m \exp(-(\xi^2 + \eta^2)/(2\sigma^2)) \) is equal to zero both at the origin of coordinates and at infinity, and the partial derivatives \( \partial_i \hat{I}_R^{(m,n)}(\xi, \eta) = [2m(\xi^2 + \eta^2)^{-1} - \sigma^{-2}]\xi^{(m,n)}(\xi, \eta) \) and \( \partial_i \hat{I}_R^{(m,n)}(\xi, \eta) = [2m(\xi^2 + \eta^2)^{-1} - \sigma^{-2}]\eta^{(m,n)}(\xi, \eta) \) are both equal to zero when \( (\xi^2 + \eta^2)^m = m, 1, 2, \cdots \), on the right-hand side of equation (11).

As discussed at the beginning of this section, in the approach adopted in the present paper, the x-ray dark-field signal may contain components of two different physical types (Yashiro et al 2015, Morgan and Paganin 2019, Paganin and Morgan 2019). The first type of dark signal is generated by 'random microscopic' (unresolved) features with characteristic lengths smaller than the width of the point-spread function (PSF) of the imaging system. This type of dark-field signal in PBI can be associated with SAXS. A physically different type of dark-field signal originates from weak but relatively sharp 'macroscopic' (i.e. resolvable at the current spatial resolution) edges and interfaces in the object, which generate higher-order diffraction terms in equation (11) because of their sharpness, i.e. due to rapid variation of x-ray absorption and refraction properties. In order to see how the SAXS signal, in particular, can be incorporated in the 'TIE + Born' approach described above, we consider the following reduced version of equation (11), with only the zero and second orders retained (in particular, keeping only the term with \( m = 0 \) in the sum over \( m \)):

\[
\hat{I}_R(\xi, \eta) = [1 + \gamma \pi \lambda R(\xi^2 + \eta^2)]\hat{I}_0(\xi, \eta),
\]

where we have used the relationship \( \hat{I}_0(\xi, \eta) = \hat{I}_{\text{TIE}}(1 - 2\mu_{\text{Born}}) \wedge(\xi, \eta) = \hat{I}_{\text{TIE}}(\xi, \eta) - 2[I_{\text{TIE})_{\text{Born}} \wedge(\xi, \eta)]. \) It is known (Gureyev and Nesterets 2017) that for homogeneous objects equation (12) can be derived from equation (2) assuming only that \( I_0(x,y) \) satisfies Guigay-type conditions (Guigay 1977). The latter is equivalent to assuming that the transmitted intensity in the object plane can be represented as \( I_0(x,y) = \exp(-2\mu_{\text{TIE}}(x,y) - 2\mu_{\text{Born}}(x,y)) \), where \( \mu_{\text{TIE}}(x,y) \) is a (possibly large) slowly varying function and \( \mu_{\text{Born}}(x,y) \) is a small (but possibly rapidly varying) function, which was previously stated in conjunction with equation (3) above. Now, however, we apply the second-order Born approximation, \( I_{\text{Born}}(x,y) \equiv 1 - 2\mu_{\text{Born}}(x,y) + 2\mu_{\text{Born}}(x,y) \), in the expression \( I_0(x,y) = \hat{I}_{\text{TIE}}(x,y) \hat{I}_{\text{Born}}(x,y) \), and substitute the result back into equation (12):

\[
\hat{I}_R(\xi, \eta) \equiv [1 + \gamma \pi \lambda R(\xi^2 + \eta^2)]\hat{I}_{\text{TIE}}(\xi, \eta) - 2[1 + \gamma \pi \lambda R(\xi^2 + \eta^2)](I_{\text{Born}}) \wedge(\xi, \eta) + 2[1 + \gamma \pi \lambda R(\xi^2 + \eta^2)](I_{\text{TIE}})_{\text{Born}} \wedge(\xi, \eta).
\]
Take the inverse Fourier transform of the above expression and convolve both sides with the PSF \( P(x,y) \), to represent the effect of finite spatial resolution of the imaging system, where the width of the PSF is much larger than the characteristic length of variation of the rapidly varying component \( \mu_{\text{Born}}(x,y) \), while being much smaller than the characteristic length of the slowly varying component \( I_{\text{TIE}}(x,y) \). Then equation (13) becomes:

\[
(I_R \ast P)(x,y) \approx [1 - \frac{\gamma}{2}](R/k)\nabla_\perp^2 I_{\text{TIE}}(x,y) + \gamma(R/k)\nabla_\perp^2 [(I_{\text{TIE}}\mu_{\text{Born}}^2 \ast P)](x,y),
\]

(14)

where use has been made of the assumptions that: (a) the slowly varying TIE component is approximately invariant with respect to convolution with this PSF, i.e. \( I_{\text{TIE}} \ast P \approx I_{\text{TIE}} \); (b) since \( \mu_{\text{Born}}(x,y) \) is a small, but rapidly varying function, we have \( \mu_{\text{Born}}^2 < \gamma(R/k)\nabla_\perp^2 \mu_{\text{Born}} \); (c) \( [(I_{\text{TIE}}\mu_{\text{Born}}^2 \ast P)](x,y) \approx 0 \) in the case of microscopic unresolved features. The last of these three assumptions physically corresponds to the fact that: (i) \( \mu_{\text{Born}}(x,y) \) will oscillate many times over the width of the PSF, while \( I_{\text{TIE}}(x,y) \) will remain approximately constant over the same distances; and (ii) \( I_{\text{TIE}}(x,y) \) will by construction average to zero, since the mean value has been included in the slow TIE signal. The first term on the right-hand side of equation (14) describes coherent TIE-type energy flow downstream of the sample, with the second term describing diffuse energy flow associated with unresolved microstructure. The term \( \mu_{\text{Born}}^2(x,y) \), averaged over the width of the PSF, effectively represents the source of the local SAXS signal in PBI (Paganin and Morgan 2019). Such an expression for the position-dependent SAXS signal is physically intuitive: the local variance of the PSF, effectively represents the source of the local SAXS signal in PBI (Paganin and Morgan 2019). Provided that the effective diffusion coefficient \( D_{\text{eff}}(x,y) \)—which quantifies the position-dependent local SAXS blurring in the Fokker–Planck formalism—is taken to be

\[
D_{\text{eff}}(x,y) = (\gamma/k)(\mu_{\text{Born}}^2 \ast P)(x,y).
\]

Note that in the approach described in this section, while the ‘large slowly varying (TIE)’ component of the object is retrieved according to equation (8) and the ‘small rapidly varying (Born)’ component is retrieved using equation (9) or (10), the ‘unresolved random subpixel (SAXS)’ component cannot be quantitatively reconstructed, since, according to the assumption used in the present mathematical model, this component falls below the spatial resolution of the imaging system. Just as in some other x-ray dark-field imaging methods where the source of the SAXS signal is usually only identified as regions in the object which produce locally-increased dark-field signal, similarly, in the present method the SAXS signal is expected to be visualized in the form of increased noise-like ‘mottle’ with characteristic ‘grain’ size comparable to the width of the PSF. This expected behaviour is confirmed by the examples presented in the subsequent sections.

3. Computer simulations

In this section we carry out computer simulation aimed at testing and illustrating the theoretical considerations presented in the previous section. We extract the dark-field signal by solving equation (8) for \( I_{\text{TIE}} \) and then equation (10) for \( I_{\text{TIE}}\mu_{\text{Born}} \) in a two-step procedure, as explained above (see also Gureyev et al (2004)). For the simulation study, we have used two well-known images, ‘Peppers’ and ‘Resolution chart’, from the USC-SIPI Image Database (SIPI 2020). These images have a broad variety of resolution and texture features which make it easy for an observer to notice the distortions that a particular image processing algorithm may introduce into the images. The ‘Peppers’ image was bi-linearly interpolated to a 4096 × 4096 uniform discrete Cartesian grid with a grid step size of 1 \( \mu \)m, so that the whole distribution had a physical size of approximately 4.1 × 4.1 mm\(^2\). The interpolated ‘Peppers’ image was then convolved with a Gaussian PSF \( P_{\text{Gauss}}(x,y) \) with 4 \( \mu \)m standard deviation in order for the result to represent the ‘large slowly varying’ distribution (which we will call component C1 below) satisfying the TIE approximation in the subsequent free-space propagation. The C1 component was also scaled by multiplying all pixel values by such a constant that the maximum pixel value became \( I_{\text{Lmax}} = 1.1 \times 10^4 \) \( \mu \)m. The resultant values in each pixel represented the projected thickness \( t_1(x,y) \) of a ‘material’ with a constant relative x-ray complex refractive index, \( n = 1 - \delta_1 + i\beta_1 \), corresponding to glandular tissue embedded in adipose tissue and illuminated by monochromatic x-rays with energy \( E = 34 \text{ keV}; \delta_1 = 2.02 \times 10^{-8}, \beta_1 = 2.14 \times 10^{-11} \) and \( \gamma_1 = 942.01 \) (see e.g. TS Imaging (2020)).

A ‘random microscopic’ component (C3), with projected thickness \( t_3(x,y) \), was generated at each one of 4096 × 4096 numerical pixels by taking a sample value of a Gaussian random distribution with zero mean and standard deviation equal to 0.05\( t_1(x,y) \), i.e. 5% of the local value of the component C1 at the pixel. Note that component C3 is not homogeneous and its contribution is treated in a similar manner to additive image noise. Figure 1(a) shows the sum, C1 + C3, of these two components, after masking off a 512 pixel wide strip.
Figure 1. Original components of the simulated test object represented here as transverse spatial distributions of projected thickness, $t(x, y)$, of materials specified in the text: (a) large slowly varying component C1, with $4096 \times 4096$ pixels and $t_{\text{max}} = 10972 \, \mu m$; (b) ‘random microscopic component’ C3, having $4096 \times 4096$ pixels with $t$ values sampled from normal distributions with zero mean and standard deviation equal to 0.05 times the thickness of the ‘large slowly varying component’ from (a) in each pixel; (c) one ‘building block’ of the ‘regular, small, rapidly varying component’ C2, with $256 \times 256$ pixels and $t_{\text{max}} = 200 \, \mu m$; (d) cross-section along the dashed line shown in (a), after the addition of the ‘random microscopic distribution’ from (b). The size of numerical pixels (grid step) in all images was assumed to be $1 \, \mu m$.

at all four sides of the image with zero values, $t(x, y) = 0$, in order to enforce the periodic boundary conditions needed for subsequent modelling of free-space propagation and phase retrieval. Figure 1(b) shows the component C3 (after the masking) separately, while figure 1(d) presents a linear cross-section through the C1 + C3 distribution along the dotted line shown in figure 1(a).

Finally, figure 1(c) depicts one ‘building block’ of the ‘small rapidly varying macroscopic’ component (C2) which has relatively small $t$ values, but contains multiple sharp edges expected to produce high-order diffraction components in the subsequent free-space propagation. The image used for generating the C2 component was the ‘Resolution chart’ image bi-linearly interpolated to a grid with $256 \times 256$ numerical pixels, masked with zero values at the edges and scaled to achieve $t_{2,\text{max}} = 2.0 \times 10^2 \, \mu m$. The resultant pixel values represented the projected thickness $t_2(x, y)$ of a ‘material’ with relative x-ray complex refractive index corresponding to calcium embedded in adipose tissue and illuminated by monochromatic 34 keV x-rays: $\delta_2 = 9.35 \times 10^{-8}$, $\beta_2 = 1.18 \times 10^{-9}$ and $\gamma_2 = 79.00$ (TS Imaging 2020). The complete C2 component was formed by taking one ‘building block’, made from the scaled and masked ‘Resolution chart’ image, and replicating it repeatedly inside three horizontal strips across the C1 + C3 image, with one additional single ‘building block’ placed at the top left corner.

The structure of the total resultant combined image containing the three ‘material’ components C1, C2 and C3, can be seen clearly in the propagated and reconstructed images, as described next.

We calculated the result of transmission of a plane monochromatic incident wave $U_\text{in}(x, y) = \exp(ikz)$, with $k = 2\pi / \lambda$, $\lambda = 0.36 \, \text{Å}$ (this wavelength corresponds to x-rays with $E = 34 \, \text{keV}$), through an object with the complex transmission function...
\[
T(x, y) = \exp\{-(2\pi/\lambda)[(\beta_1 + i\delta_1)(t_1(x, y) + t_3(x, y)) + (\beta_2 + i\delta_2) t_2(x, y)]\},
\]
so that the transmitted complex amplitude in the object plane was \(U_0(x, y) = U_{0x}(x, y) T(x, y)\). The simulated image intensity distribution, \(I_G(x, y)\), after \(R = 1\) m free-space propagation of the amplitude \(U_0(x, y)\) and convolution of the resultant propagated intensity with the PSF \(P_{\text{A,G}}(x, y)\), is shown in figure 2(a). The latter convolution emulated the effect of the finite spatial resolution of the imaging system: it resulted in the 'effective pixel' size of approximately \(10 \times 10 \mu m^2\), in accordance with the full width at half maximum of the PSF \(P_{\text{A,G}}(x, y)\).

Figure 2. (a) PBI image intensity distribution obtained after simulated free-space propagation by \(R = 1\) m of the complex wave amplitude \(U_0\), which resulted from the simulated transmission of a monochromatic plane wave with unit amplitude and wavelength \(\lambda = 0.3647\) Å through an object with the transmission function \(T(x, y)\) (described in the main text) and a subsequent convolution with a Gaussian PSF with 4 \(\mu m\) standard deviation. (b) A zoomed 1.4 \(\times\) 1.4 mm\(^2\) sample of the distribution of \(P_{\text{A,G}}(x, y)\) (which corresponds to the source of the SAXS signal, according to equation (14)), obtained from the random microscopic component shown in figures (1b) and (a) Gaussian PSF with 4 \(\mu m\) standard deviation.

We then applied the retrieval algorithm based on equations \(8\) and \(10\), as described in the previous section, to the simulated PBI image. At the first step of the algorithm, we applied the TIE-Hom retrieval method (Paganin et al 2002, 2004), with \(\varphi_{\text{TIE}}(x, y) = \langle \gamma_1/2 \rangle \ln I_{\text{TIE}}(x, y)\), to reconstruct the distribution \(I_{\text{TIE}}(x, y)\) in the object plane from the propagated intensity shown in figure 2(a). The result of these calculations is presented in figures 3(a) and (c) in the form of reconstructed projected thickness \(t_{\text{TIE}}(x, y) = -\lambda(4\pi\beta_1)^{-1} \ln I_{\text{TIE}}(x, y)\), which can be directly compared with the original projected material thicknesses shown in figure 1. It is obvious that, while the details of the 'large slowly varying' component \(C_1\) have been reconstructed with good accuracy, the 'small, rapidly varying components' \(C_2\) and \(C_3\) are strongly blurred in this TIE-based reconstruction and are difficult to discern. The error in the reconstruction of the object components \(C_2\) and \(C_3\) was large primarily because these components did not satisfy the validity conditions of the TIE approximation.

At the next step, we applied the first Born retrieval method (Gureyev et al 2004), in accordance with equation \(10\) with \(\varphi_{\text{Born}}(x, y) = \gamma_2 \mu_{\text{Born}}(x, y)\), to reconstruct the distribution of \(\mu_{\text{Born}}(x, y)\) in the object plane from (i) the propagated intensity \(I_G(x, y)\) shown in figure 2(a), and (ii) the TIE-Hom reconstructed intensity \(I_{\text{TIE}}(x, y)\) from figure 3(a) re-propagated to the image plane \(z = R\). The result of this reconstruction step is presented in figures 3(b) and (d) in a way that formally corresponds to the projected thickness \(t_{\text{Born}}(x, y) = -\lambda(4\pi\beta_3)^{-1} \ln I_{\text{Born}}(x, y)\), and can be compared with the components \(C_2\) and \(C_3\) in figure 1 and the expected SAXS signal in figure 2(b). Note however that the absolute values of the reconstructions in figures 3(b) and (d) cannot be interpreted literally as the projected thickness \(t_2(x, y)\) or \(t_3(x, y)\), because this reconstruction is strongly 'contaminated' by the first type of dark-field signal that was mentioned in the previous section. Namely, the edges of the strong component \(C_1\) clearly also contributed to the reconstruction in figures 3(b) and (d). While the presence of additional information about such edges and interfaces in these images can actually be quite useful in practice, it makes the quantitative reconstruction of the weak rapidly varying components very difficult. In this sense, unlike the TIE-Hom reconstruction shown in figures 3(a) and (c), the Born reconstructions in figures 3(b) and (d) are mostly qualitative. On the positive side, one can see that the rapidly varying weak components \(C_2\) and \(C_3\) are still visualized much
Figure 3. Images reconstructed from the single simulated PBI image shown in figure 2(a). (a) TIE-Hom reconstructed projected thickness distribution obtained according to the 'homogeneous version' of equation (5); (b) first Born reconstructed projected thickness distribution obtained according to the 'homogeneous' version of equation (6); (c) zoomed image of an area bounded by the dotted square in (a); (d) zoomed image of the same area in (b), showing some SAXS-type signal in particular; (e) absolute values of pixels in (b) (with the maximum brightness reduced for presentation purposes) demonstrating a more conventional version of the expected dark-field image.

better in figures 3(b) and (d), compared to the initial TIE-Hom reconstruction in figures 3(a) and (c). In particular, the C2 component has visibly higher contrast and spatial resolution in figures 3(b), (d), compared to 3(a), (c). The C3 (SAXS) component is also clearly visible in figure 3(b), and particularly in the magnified
image in figure 3(d), where the similarity of the background texture with that in figure 2(b) becomes apparent. Note that the SAXS signal was practically invisible in the initial TIE-Hom reconstruction shown in figures 3(a),(c) due to the strong smoothing (blurring) effect of the TIE-Hom retrieval, which can be seen in equation (8). Finally, figure 3(e) provides a different perspective on the reconstructed dark-field signal by depicting the modulus (absolute values) of the distribution from figure 3(b). One can see that in figure 3(e) all the pixels with substantial dark-field signal appear bright on the dark background. In agreement with the theory presented in the previous section, this image allows a particularly clear identification of: (a) sharp edges of the large component C1, (b) the rapidly varying weak macroscopic component C2, and (c) image ‘mottle’ associated with the random unresolved (SAXS) component C3.

We have also compared the objective image quality of the reconstructed component C2 in the TIE and Born images in terms of the ‘intrinsic imaging quality’ characteristic described in the Introduction. One version of this quality characteristic can be expressed as the ratio of the contrast to the standard deviation of pixel values within a given local feature, normalized by the square root of the incident photon fluence (Gureyev et al 2014, 2019a). Our measurements have shown that the dark-field (Born) image in figure 3(b) had higher contrast (∼0.11) for the elements of the C2 component, compared to the contrast (∼0.04) of the same features in the bright-field (TIE) image in figure 3(a). This difference in contrast can be readily seen on a qualitative level in figures 3(c) and (d). The dark-field image also had lower standard deviation of local pixel values in the background adjacent to C2 features (∼1 × 10⁻³) compared to the bright-field image (∼3 × 10⁻³), which means that the ratio of contrast to the standard deviation was ∼110 in the dark-field image and ∼13.3 in the bright-field image. The stronger local standard deviation of pixel values in the TIE-Hom retrieved image in figure 3(a) can be attributed to the presence of low-order spatial Fourier harmonics in this image, unlike the Born retrieved image in figure 3(b) where such harmonics are absent, because they have been subtracted out in equation (10). In addition, the dark-field image also had better spatial resolution (∼80 μm), compared to the bright-field image (∼180 μm), as measured via the correlation length method (Gureyev et al 2019a) in figures 3(a) and (b), respectively. This improved spatial resolution is associated with the amplification of high-order spatial Fourier harmonics in equation (10). The dark- and bright-field images were both reconstructed from the same propagated image in figure 2(a), and hence the nominal ‘incident photon fluence’ was the same for these images. Thus the dark-field image in this example had almost 19 times higher objective imaging quality of the weak rapidly-varying component C2, compared to the bright-field image: (110/80)/(13.3/180) ≃ 18.6.

4. Experimental demonstration

Phase-contrast breast cancer imaging is an emerging medical imaging technology that is currently being developed and tested in several countries (Taba et al 2018). Because it requires intense spatially-coherent x-rays in order to be used effectively with humans, the method is predominantly implemented with synchrotron radiation (Longo et al 2019, Gureyev et al 2019b), although experimental systems with micro-focus laboratory x-ray sources are also being tested (Havariyoun et al 2019). The dark-field modality of the GB phase-contrast imaging method has been reported to be effective for analysis of microcalcifications (Rauch et al 2020).

Here we demonstrate the improved visualization of microcalcification clusters in PBI CT breast cancer imaging performed at the Imaging and Medical beamline (IMBL) of the Australian Synchrotron. The key experimental details are listed below and additional details about the experimental setup can be found e.g. in Gureyev et al (2019b). The imaging experiment was conducted under a Human Ethics Certificate of Approval from Monash University and with written consent from the patients to image their clinical specimens. The breast mastectomy samples were obtained from a breast cancer surgery operation and were imaged on the same day in a complete, intact, unfixed state at IMBL using the PBI CT technique. The professional pathology analysis of the first sample (2145659R) later reported invasive carcinoma of no specific type and scar tissue formation with calcifications. The histology report for the second specimen (4607971L) listed a high-grade ductal carcinoma in situ and extensive microcalcifications. The histology report for the second specimen (4607971L) listed a high-grade ductal carcinoma in situ, invasive carcinoma of non-specific type and scar tissue formation with calcifications. The specimens contained several surgical clips that were clearly visible in the CT images. The primary question that we intended to address by the present study was how to improve the assessment of micro-calcifications, which are not always easy to resolve and evaluate in detail in conventional absorption CT or bright-field PBI CT images.

The PBI CT scans of both samples analyzed here were collected at a clinically-relevant 4 mGy mean glandular dose distributed evenly between 4800 projections over 180 degrees. The scans were carried out using quasi-plane monochromatic x-rays with energy E = 34 keV and a free-space propagation distance of 6 m between the sample and the detector (which corresponded to the effective defocus distance of 5.748 m when the relevant geometric magnification of the imaging setup was taken into account). The x-ray detector
Figure 4. PBI CT reconstructed distribution of the imaginary part of absorption index, $\beta(x,y) \times 10^{11}$, in a 100 $\mu$m thick coronal slice of mastectomy sample 2145659R, obtained from x-ray projections collected at 34 keV energy, 6 m sample-to-detector distance and 4 mGy dose: (a) a slice from the reconstructed bright-field (TIE) CT image stack; (b) the same slice from the dark-field (Born) reconstructed stack; (c) magnified version of the upper-right part of the slice shown in (a) after adjustment of the image histogram settings to maximize the visibility of the microcalcifications; (d) magnified version of the upper-right part of the slice shown in (b), without any adjustment of the image histogram. The dashed-line boxes outline areas with microcalcifications.

used for these scans was a Hamamatsu CMOS Flat Panel Sensor C10900D with pixel size 100 $\mu$m $\times$ 100 $\mu$m and field of view 12.16 cm (horizontal) $\times$ 12.32 cm (vertical). The spatial resolution of approximately 170 $\mu$m (horizontal) $\times$ 150 $\mu$m (vertical) was determined predominantly by the detector’s PSF, while the slight asymmetry of the resolution was due to the anisotropic x-ray source at IMBL.

Figure 4 presents the bright-field PBI CT image of a single coronal slice of the first mastectomy sample (2145659R) reconstructed using the TIE-Hom method (Paganin et al 2002) (see also equation (8)) and the two-step Born (dark field) method described above (represented by equations (8) and (10)). While the microcalcifications are not well visualized in the default image setting in the bright-field image shown in figure 4(a), the same microcalcifications are well resolved in the default settings of the dark-field image in figure 4(b). The images in figures 4(c) and (d) show magnified regions of the slices from figures 4(a) and (b), respectively, after the histogram was specifically adjusted in figure 4(c) to maximize the visibility of the microcalcifications, while the histogram in figure 4(d) remained the same as in figure 4(b) (since we did not find any need for further adjustments of the dark-field image).

Figure 5 depicts an example of a coronal slice of the second mastectomy sample (4607 971L) reconstructed using the bright-field method (figure 5(a)) and the dark-field method (figure 5(b)). The images in figures 5(c) and (d) show magnified regions of the slices from figures 5(a) and (b), respectively, after the histogram was specifically adjusted in figure 5(c) (but not in figure 5(d)) to maximize the visibility
Figure 5. PBI CT reconstruction distribution of the imaginary part of absorption index, $\beta(x, y) \times 10^{11}$, in a 100 µm thick coronal slice of mastectomy sample 4607971L, obtained from x-ray projections collected at 34 keV energy, 6 m sample-to-detector distance and 4 mGy dose: (a) a slice from the reconstructed bright-field (TIE) CT image stack; (b) the same slice from the dark-field (Born) reconstructed stack; (c) magnified version of the upper-central part of the slice shown in (a) after adjustment of the image histogram settings to maximize the visibility of the microcalcifications; (d) magnified version of the upper-central part of the slice shown in (b), without any adjustment of the image histogram; (e) same image as in (c), but after averaging over 20 adjacent reconstructed slices; (f) absolute values of pixels in (d), demonstrating a more conventional version of the corresponding dark-field image. The dashed-line box outlines an area with calcifications. The blue arrow points to a surgical clip.
of the microcalcifications. The overall visibility of the microcalcification cluster is already reasonably good in the default image setting here (figure 5(a)), but the shape of individual microcalcifications is resolved better in figures 5(b) and (d), compared to figures 5(a) and (c), which is important for breast cancer diagnosis (Nalawade 2009, Rauch et al 2020). Note also, that the two ‘legs’ of the surgical clip indicated by a blue arrow in each pane of figure 5 are not resolved in the bright-field images, but they are clearly resolved in the dark-field images, even at the lower magnification and without any special histogram adjustments. This illustrates the fact that the dark-field images have better spatial resolution, compared to the bright-field ones, as was already demonstrated in the simulated images in section 3. As an aside, we would like to mention that even though the calcifications and the surgical clip have similar appearance in terms of their grey-scale values in the images in figure 5, a line plot through these images readily reveals a significant difference in the reconstructed local $\beta$ values for the surgical clip and the calcifications.

In a real-life radiological examination setting a successful histogram adjustment may require the observer to detect the microcalcifications in the default setting in the first place (where the microcalcifications may be partially masked by the dense glandular or cancerous tissue and by the CT artefacts produced e.g. by the adjacent surgical clips), and then adjust the image display parameters accordingly. Such requirements may lead to missed features and to extra time spent on the examination. Note also that the CT slices presented in figures 4(a)–(d) and 5(a)–(d) are only 100 $\mu$m thick, which considerably reduces the degree of possible masking of microcalcifications by overlying glandular tissues, compared to 1 mm thick slices that are more likely to be examined in a real-life scenario (Taba et al 2018). Consider the fact that there are over 600 slices, each 100 $\mu$m thick, in the CT stacks reconstructed for a single medium-size mastectomy sample in our examples. A routine examination of 600 slices would require a significant amount of time from a professional observer (unless, perhaps, automated software could be used for the initial selection of ‘suspect’ slices), while the examination of $60 \times 1$ mm thick slices represents a much easier scenario. Figure 5(e) provides one example of the 1 mm thick slice, produced by averaging ten 100 $\mu$m thick slices adjacent to the slice shown in figures 5(a)–(d). One can see that, in comparison with the 100 $\mu$m thick slice in figure 5(c), the microcalcifications have become blurrier in figure 5(e), which is potentially detrimental for cancer diagnosis. However, as this particular microcalcification cluster appears to be quite strong, it has not become obscured by overlapping tissues as the result of slice averaging. Finally, figure 5(f) presents the modulus of the dark-field image shown in figure 5(d). As in the simulated example in the previous section (figure 3(e)), this image modality depicts the regions with significant dark-field signal as white pixels on a dark background. This representation appears to be particularly effective in terms of delineating edges and internal structure of individual elements of the microcalcification cluster, which can be potentially useful for cancer diagnosis. In this representation, dark lines appear on a white background at places where the original dark-field signal (as shown in figure 5(d)) changes sign from positive to negative or vice versa. Note that these dark line contours appear to outline the cross-sections of the ‘legs’ of the surgical clip (pointed to by the blue arrow in figure 5(f)) particularly well. Note also that the bright areas outside the yellow dashed box in figure 5(f), which appear as regions with significant dark-field signal, are mostly associated with the walls of the plastic container which was used for scanning the mastectomy sample, and with small air pockets in the sample. Such artefacts are not expected to be present in real medical breast PBI CT scans of live patients. Further details of this mode of representation of the PBI dark-field signal may be worth investigating in a future study involving a larger set of breast tissue samples.

Objective measurements of CNR and spatial resolution in these experimentally reconstructed slices have shown that the imaging quality of microcalcifications is slightly higher in the dark-field reconstructed images, compared to the bright-field images. For example, the dark-field images shown in figure 4(a) have much higher contrast ($\sim 1$) of the microcalcifications, compared to the contrast ($\sim 0.5$) of the same microcalcifications in the bright-field images in figure 4(b). This can be readily seen on a qualitative level in figures 4(a), (c) and (b), (d). On the other hand, the dark-field images have higher standard deviation of noise ($\sim 1.4 \times 10^{-7}$) compared to the bright-field images ($\sim 7.6 \times 10^{-8}$), which means that the ratio of contrast to noise is approximately the same in the two types of images here. However, the dark-field images also have better spatial resolution ($\sim 160$ $\mu$m), compared to the bright-field images ($\sim 180$ $\mu$m), and therefore, given the same incident photon fluence, the dark-field images in this example have higher objective imaging quality of microcalcifications compared to the bright-field images. There are also some indications, that for human observers, a higher level of image contrast may play a more important role, compared to the level of noise, thus possibly giving a further advantage to the dark-field PBI images, compared to the bright-field images, in a human observer context when the detection and assessment of microcalcifications is required.
5. Discussion

We have proposed a method for dark-field signal extraction from 2D and 3D PBI images, which does not require any additional image acquisitions compared to the usual bright-field imaging implementation of this method. Instead, our method employs a specialized algorithm for image processing that allows one to extract high-spatial-order diffraction components from the bright-field images. In particular, in the case of samples that can be considered approximately homogeneous for the purpose of PBI image analysis, the new method requires only a single image in a 2D setting and only one image per projection angle in a 3D PBI CT setting. This may represent an important practical advantage compared to dark-field imaging modalities previously described in the context of other x-ray phase-contrast methods, such as GB, EI, SB or ABI, where the acquisition of dark-field images inevitably required different positioning of the ‘wavefront analyser’ elements compared to bright-field imaging. Our method extracts both the bright-field and the dark-field images of the sample from a single experimental image collected in a conventional PBI setting. The dark-field images tend to show more of the SAXS signal, compared to bright-field images, when a non-negligible amount of SAXS signal is actually produced by a given sample. The fact that the proposed dark-field PBI method visualizes SAXS signals more clearly, compared to bright-field PBI, can be beneficial for medical imaging of lungs and other vital organs where the increased scattering may point to areas of abnormal tissue.

As a first example of a potential practical application, we have demonstrated that, in the case of human breast cancer imaging, the proposed dark-field method is capable of delivering images better showing the shape and quantity of microcalcifications which are often used to differentiate between benign and malignant tissues in breast cancer diagnosis. Whilst one may argue that with conventional windowing solutions available on any CT console, visualisation of the microcalcifications is possible, this relies on two assumptions. Firstly that the operator or clinician has the skills to use the appropriate windowing level, and secondly that there is enough time to make these adjustments. With regard to the latter, clinicians are often under immense pressure to read a very large number of images, with 400 slices not being uncommon for one CT run, therefore having the luxury of windowing appropriate slices in a comprehensive way may not be possible. Instead clinicians need rapid presentations of important pathologies and having a dark-field mode available with a single button highlighting important calcification clusters presents a reasonable and potentially very useful solution. This dark-field facility would also encourage more rapid identification of the microcalcification features that describe malignant lesions such as clustering, pleomorphism and rod shapes. The method has the potential to improve imaging of breast cancers in patients with breast tissue that presents challenges for conventional imaging, such as recurrent cancers along scar lines, and cancers in tissue treated with radiation therapy. The usefulness of this alternative approach for clinicians will need to be confirmed to make sure that opting for a micro-calcification visualiser does not in any way have an inadvertent affect on normal expert behaviour and recognition of other important features. Our subsequent work will involve a systematic analysis of the radiological value of the dark-field method in breast PBI CT imaging, in particular. Applications to PBI imaging of the lungs are likely to be of interest as well, as indicated by recent publications (Wagner et al 2018, Fingerle et al 2019).

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