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Contrast enhancement of propagation based X-ray phase contrast imaging

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ABSTRACT

We demonstrate a quantitative X-ray phase contrast imaging (XPCI) technique derived from propagation dependent phase change. We assume that the absorption and phase components are correlated and solve the Transport of Intensity Equation (TIE). The experimental setup is simple compared to other XPCI techniques; the only requirements are a micro-focus X-ray source with sufficient temporal coherence and an X-ray detector of sufficient spatial resolution. This method was demonstrated in three scenarios, the first of which entails identification of an index-matched sphere. A rubber and nylon sphere were immersed in water and imaged. While the rubber sphere could be plainly seen on a radiograph, the nylon sphere was only visible in the phase reconstruction. Next, the technique was applied to differentiating liquid samples. In this scenario, three liquid samples (acetone, water, and hydrogen peroxide) were analyzed using both conventional computed tomography (CT) and phase contrast CT. While conventional CT was capable of differentiating between acetone and the other two liquids, it failed to distinguish between water and hydrogen peroxide; only phase CT was capable of differentiating all three samples. Finally, the technique was applied to CT imaging of a human artery specimen with extensive atherosclerotic plaque. This scenario demonstrated the increased sensitivity to soft tissue compared to conventional CT; it also uncovered some drawbacks of the method, which will be the target of future work. In all cases, the signal-to-noise ratio of phase contrast was greatly enhanced relative to conventional attenuation-based imaging.

Keywords: Phase retrieval, transport of intensity, X-ray imaging

1. INTRODUCTION

Imaging using hard X-rays is a highly active field, as there are few other methods to noninvasively examine thick objects that are opaque to other forms of radiation (visible light, sound, etc.). Conventional X-ray imaging allows for interrogation of the attenuation of an object, which typically provides poor contrast between materials with similar atomic number. In applications such as security inspection, there are workarounds; for example, nitrogen is a major component of many explosives, and has a unique signature that can be detected using X-ray scatter imaging.1 For light materials and non-nitrogenous explosives, there is no easy workaround—hence the inconvenience of having to throw out water containers before security screening at airports. For medical X-ray
imaging, contrast agents are injected to enhance contrast in tissues of interest at the price of discomfort to the patient, dangers from the procedure, and nephrotoxicity of the contrast agent used.\textsuperscript{2, 3}

Phase information can provide significantly enhanced contrast for light materials without the need to stain the sample or introduce contrast.\textsuperscript{4–6} While not as straightforward as attenuation-based imaging, propagation-based techniques provide a relatively simple way to reconstruct the phase of an object. By using images taken at multiple distances along the optical axis, the system is lensless, and there is no need for a highly coherent X-ray source.\textsuperscript{7, 8} Restrictions on both the temporal and spatial coherence are relaxed with propagation based imaging, as the recovered quantity is the optical path length of the object, not its phase per se.\textsuperscript{9}

In this paper, we adopt the transport of intensity equation (TIE), which relates the measured intensity to the phase:\textsuperscript{10}

\begin{equation}
\frac{k}{\partial z} I(x, y, z) = \nabla_\perp \cdot \left[ I(x, y, z) \nabla_\perp \phi(x, y) \right], \quad \nabla_\perp = \left( \frac{\partial}{\partial x}, \frac{\partial}{\partial y} \right),
\end{equation}

where \(I(x, y, z)\) is the intensity image at the propagation distance \(z\), \(\phi(x, y)\) is the phase map (equivalently, the optical path length, or OPL) of the object, and \(k\) is the wavenumber.

By solving the TIE for a single angle of exposure, a projective phase map of the object can be obtained. Projective imaging is attractive due to the simplicity of the imaging setup, and speed at which images can be obtained. This imaging model is often-used in security applications, where object throughput demands a higher priority than exact 3D object reconstructions.

By solving the TIE for multiple angles of exposure, the complex refractive index distribution of an object can be obtained through tomographic reconstruction. In this way, TIE tomographic reconstruction can be thought of as a two-step problem. While tomographic imaging introduces significant complexity and cost (gantries may make up half of the equipment cost of a CT scanner), the additional information obtained from tomographic reconstruction can be invaluable. For example, in medical imaging, 3D imaging is necessary to accurately identify and locate lesions for diagnosis, and to help guide clinical intervention.

Direct inversion of the TIE phase retrieval and tomographic reconstruction problems are ill-posed. For the TIE, the existence of a zero in the TIE transfer function results in numerical instability during inversion. The traditional choice of regularizer to relieve this ill-posedness is the Tikhonov method.\textsuperscript{11–13} However, this type of regularization also strongly deteriorates the low-frequency signal in the phase image. Myers et al. propose inversion of the TIE using prior knowledge that the sample consists of a single material of known refractive index.\textsuperscript{14}

For tomographic reconstruction, limiting the number of projections can result in undersampling of the object index of refraction distribution in radon space. The traditional solution to tomography is the filtered backprojection (FBP), often referred to as the inverse Radon transform. The drawback to this technique is that the quality of FBP reconstructions depends on having a large number of projection angles. By exploiting the sparseness present in some representation of the object, iterative solvers enable tomographic reconstruction on far fewer angles of exposure compared to the FBP.\textsuperscript{15, 16}

We have previously demonstrated the effectiveness of a single-step TIE based method for compressive X-ray phase tomography of weakly attenuating samples, wherein the TIE and tomographic reconstruction steps are computed in a combined transfer function, and solved using iterative methods.\textsuperscript{17} However, this method places a severe restriction on the class of objects suitable for imaging. Recently, we have extended this method in two ways: to account for the weak spatial correlation (i.e. the structural similarity) between absorption and phase in the object,\textsuperscript{18} and to account for samples which consist of only light materials, based on the phase-attenuation duality for light materials.\textsuperscript{19} The formulation of the TIE solvers are shown in Section 2. In this paper, we present three demonstrations of these methods, one involving projective imaging, and two involving tomographic reconstruction of objects. In Section 3, we demonstrate detection of an index matched nylon sphere in a water filled test-tube using projection based X-ray phase imaging. In Section 4, we experimentally demonstrate the use of our X-ray phase tomography technique to resolve the refractive index of water from that of chemically similar (in terms of Z number) but potentially hazardous materials, such as hydrogen peroxide and acetone; this particular application is potentially significant for security in airports and other controlled spaces. Finally, in
Section 5, we present a reconstruction of a biological specimen: a human iliac artery with atherosclerotic plaque. Soft tissue features in the specimen, including the fibroatheromatous plaque are revealed without the aid of contrast in the phase imaging study, suggesting that phase contrast X-ray tomography may expand the purview of medical X-ray imaging.

2. RECONSTRUCTION PROCESS

A schematic diagram of the imaging geometry is presented in Fig. 1. A microfocus source with a spectrally weighted mean wavelength $\lambda$ is located at the plane $z = -z_0$, and a detector is located at the plane $z = d$. The sample, centered at $z = 0$, is characterized by a complex refractive index $n(x, y, z; \lambda) = 1 - \delta(x, y, z; \lambda) + i\beta(x, y, z; \lambda)$, where $1 - \delta(x, y, z; \lambda)$ and $\beta(x, y, z; \lambda)$ are the real and imaginary parts of the refractive index, respectively. We assume that the geometry of our experiment is such that the beam passing through the object is approximated by a plane wave oriented along the optical axis, and that the interaction between the sample and the field follows the projection approximation.

Traditionally, the TIE is formulated using intensity measurements along two different points on the optical axis.\textsuperscript{20} Taking into account the magnification introduced by using a point X-ray source, the two-shot formulation of TIE is as follows,

$$
g(x', y') = \frac{I_2(M_2 x, M_2 y) - I_1(M_1 x, M_1 y)}{I_0(d_2 - d_1')} = \frac{\lambda}{2\pi} \nabla_{\perp} \cdot (I_1(M_1 x, M_1 y) \nabla_{\perp} \phi(x', y')),
$$

(2)

where $(x', y')$ denote the coordinates of the detector plane, $\nabla_{\perp}$ is the gradient operator in the detector plane, $\phi(x', y')$ is the projected phase map of the object, $I_1$ and $I_2$ are the two intensity images, $d_1$ and $d_2$ are their respective propagation distances, $M_1 = (z_0 + d_1)/z_0$ and $M_2 = (z_0 + d_2)/z_0$ are their respective magnification factors, and $d_1' = d_1/M_1$ and $d_2' = d_2/M_2$ are their effective propagation distances given by the Fresnel scaling theorem (page 397 in\textsuperscript{21}). Note that the retrieved phase map is not at the sample plane, but at the detector plane. However, since both intensity and phase are known after reconstruction, direct propagation can be used to determine the phase at the sample plane.\textsuperscript{22}

The phase-attenuation duality (PAD) approximation allows us to reformulate the TIE such that only one intensity measurement is necessary. We assume that electron interactions are the primary source of x-ray attenuation and phase delay, thus the real and complex components of the complex refractive index are correlated such that $\delta(x, y, z; \lambda)/\beta(x, y, z; \lambda) = \gamma(\lambda)$.\textsuperscript{23} Under paraxial and small-wavelength approximations, the TIE gives the following relationship between the projected phase map of the object, $\phi(x', y')$, and the single image of the object at the detector, $I(x', y')$,

$$
g(x', y') = \frac{I(M x, M y)}{I_0} = \left[ 1 + \frac{d' \lambda \gamma(\lambda)}{4\pi} \nabla_{\perp}^2 \right] \exp \left[ \frac{2\phi(x', y')}{\gamma(\lambda)} \right],
$$

(3)
where \( x' = Mx \) and \( y' = My \) correspond to spatial coordinates in the detector plane, \( M = (z_0 + d)/z_0 \) is the magnification at the detector plane, \( I_0 \) is the incident intensity without the object, and \( d' = d/M \) is the effective propagation distance given by the Fresnel scaling theorem. Equation (3) is the discretized form of PAD TIE which uses a single image to retrieve phase.

In a tomographic measurement, the sample is rotated about the \( x \) axis such that the projected phase \( \phi \) at a certain angle \( \theta \) is

\[
\phi(x, y; \theta) = \int \int \delta(x, y_s, z_s; \lambda) D(y - y_s \cos \theta + z_s \sin \theta) dy_s dz_s,
\]

where we use \( D(\cdot) \) to denote the Dirac delta function to avoid confusion with the real component of the refractive index. Equation (3) along with the forward Radon transform, Eq. (4), provides us with a forward model for describing the image generated on our X-ray detector by our object, and implementation of these operators in the Fourier domain is computationally efficient.\(^{24}\) To perform direct reconstruction, Eq. (3) can be inverted using the Fourier domain solution to Poisson’s equation, and Eq. (4) can be inverted using the Fourier slice theorem implementation of FBP as

\[
\phi(x, y) = \frac{\gamma(\lambda)}{2} \ln \frac{\mathcal{F}_{2D}^{-1}\left\{\frac{f(x, y)}{I_0}\right\}}{1 + \pi z \lambda \gamma(\lambda)|u^2 + v^2|},
\]

\[
\delta(x, y_s, z_s; \lambda) = \mathcal{F}_{1D}^{-1}\{|w| \mathcal{F}_{1D}\{\phi(x, y, \theta)\}|,}
\]

where \( u, v, \) and \( w \) are spatial frequency variables, and \( \mathcal{F}_{1D} \) and \( \mathcal{F}_{2D} \) both denote Fourier transforms but in two different domains: the former is for applying the Fourier slice theorem in tomography and, hence, it operates along the projection coordinate variable; whereas the latter applies to the lateral plane \( (x, y) \). The superscript \( \mathcal{F}^{-1} \) denotes the inverse Fourier transform correspondingly in the two cases.

To perform iterative reconstruction, we utilize our approach presented in\(^{18}\) for projective imaging, and our approach presented in\(^{19}\) for tomographic reconstruction, which will be described briefly for convenience. For reconstruction of single projections, the detector is once again assumed to consist of an \( N \times N \) grid of square pixels of side length \( M_1 \Delta_1 = M_2 \Delta_2 \). The intensity term of can be arranged into a real-valued vector of length \( 2N^2 \). The refractive index of the object will also be discretized into a \( N \times N \) square, packed into a complex valued vector \( \mathbf{n} \). Let \( \mathbf{P} \) denote the projection operator specified in Eq. (2), such that

\[
\mathbf{g} = \mathbf{Pn}.
\]

In principle, the change in imaging signal, be it amplitude or phase, arises from an underlying change in sample material composition and projection thickness. Thus, edges which exist in the phase image but not in the intensity image are sparsified by solving the weighted gradient norm minimization problem

\[
\mathbf{n} = \arg\min_{\mathbf{n}} \|\mathbf{WGn}\|_1 \text{ such that } \mathbf{g} = \mathbf{Pn}
\]

where \( \mathbf{G} \) is the 2-D spatial gradient operator, and \( \mathbf{W} \) is a diagonal weighting matrix. The weighting matrix represents our prior of edge information present in the intensity image. The gradient of the intensity image is thresholded so that the strongest 10\% of all pixels are considered to contain edge information. In a typical image, only 20\% of the diagonal elements of \( \mathbf{W} \) take on a value between 0 and 1. We adapt the two-step iterative shrinkage/thresholding algorithm (TwIST) to solve the minimization.\(^{25}\)

For tomographic reconstruction, the detector is again assumed to consist of an \( N \times N \) grid of square pixels of side length \( M \Delta \). Let \( \Theta \) denote the number of angular projections. Then the measured projections \( \mathbf{g} \) at all angles may be arranged into a real-valued vector \( \mathbf{g} \) of length \( N^2 \Theta \). The refractive index of the object will also be discretized into a \( N \times N \times N \) cube width side length \( \Delta \), packed into a complex valued vector \( \mathbf{n} \). Then let \( \mathbf{P} \) and \( \mathbf{R} \) denote operators corresponding to the discretized forms of Eqs. (3) and (4), respectively, such that

\[
\mathbf{g} = \mathbf{PRn} \equiv \mathbf{An},
\]
where the operator $A$ is the cascade of the linear operators $P$ and $R$. If $n$ is sparse in some basis, as it often is the case in tomography, then Eq. (9) can be solved using compressive reconstruction. Specifically, total variation (TV) minimization has been shown to be an effective sparsity basis for tomographic reconstruction:

$$\hat{n} = \arg \min_n ||n||_{TV} \text{ such that } g = An$$

where the TV norm is defined as $||n||_{TV} = \sum_n \sqrt{(\nabla_x n)^2 + (\nabla_y n)^2 + (\nabla_z n)^2}$, and $\nabla_x$, $\nabla_y$, and $\nabla_z$ are the finite difference operators in Cartesian coordinates.

Again, we use the two-step iterative shrinkage/thresholding algorithm (TwIST) to solve the minimization.

3. PROJECTION IMAGING OF INDEX MATCHED SOLIDS

We configured the setup as in Fig. 1 to allow only one angle of exposure, translating the object along the optical axis to obtain two separate intensity images. A microfocus source (Hamamatsu L8121-03) located at $z = 0$ m was operated at 150 kVp and 66 mA to produce a circular focal spot 7 $\mu$m in diameter. The resulting X-ray beam has a spectrally weighted mean wavelength of $\lambda = 0.0210$ nm. Intensity images were taken with a CMOS photodiode image sensor (Rad-icon, Shad-o-Box 4K, 2000 $\times$ 2048 pixels, 48 $\mu$m pixel size). The scintillator was placed at a fixed location 2.00 m away from the X-ray source. The intensity of the incident beam $I_0$ was calibrated by taking a single background image without the sample in place. Intensity images were obtained with the sample placed at two different positions along the optical axis ($d_1 = 1.50$ m; $d_2 = 0.7$ m), resulting in two different magnifications and effective pixel sizes ($M_1 = 4$, $\Delta_1 = 12$ $\mu$m; $M_2 = 1.54$, $\Delta_2 = 31.2$ $\mu$m). $I_2$ was registered and scaled to $I_1$ to allow for finite differencing.

The imaging phantom consists of a rubber and a nylon sphere inside a water-filled test tube. A single projection image, $I_1$, shown in Figure 2, demonstrates the range of attenuation throughout the sample. Note

![Figure 2. Raw intensity image of sample. Scale bar denotes 2 mm.](image)

![Figure 3. Experimental results of a rubber and nylon sphere in a water-filled test tube, showing (a) a Tikhonov regularized direct inversion of TIE, (b) a single-shot reconstruction using the phase attenuation duality, and (c) an iterative reconstruction using a structural similarity promoting regularizer. Scale bars denote 2 mm.](image)
Figure 4. Image profiles along the dashed blue line in Figure 3, showing our iterative compressive method compared to: (a) raw intensity; (b) Wiener filtered intensity; (c) single-shot phase retrieval.\(^{18}\)

that while the rubber sphere is clearly visible in this image, the nylon sphere is index-matched, and produces a very weak intensity signal. Figure 3 shows reconstruction results from Tikhonov regularized direct inversion of TIE, single-shot reconstruction using the phase attenuation duality, and iterative reconstruction using a structural similarity promoting regularizer.\(^{18}\) From Figure 4, we see that the structural similarity-promoting regularizer significantly enhances the profile of the nylon sphere compared to other methods. Direct intensity measurement does not provide sufficient visual information to distinguish a sphere from the water in the test tube, and Wiener filtering distorts the profile of the sphere, flattening the profile of the sphere while simultaneously rounding the sharp phase edge introduced by the bubble. Compared to direct single-shot phase retrieval, the iterative reconstruction shows a marked decrease in noise across the profile of the sphere.

4. DISCRIMINATION OF LIQUIDS USING X-RAY PHASE CONTRAST COMPUTED TOMOGRAPHY

To investigate tomography and identification of liquids with similar density profiles but differing chemical compositions, we imaged four Eppendorf tubes containing water, hydrogen peroxide, acetone, and air. Water and hydrogen peroxide possess similar atomic densities, and therefore their absorption signatures are very difficult to separate from one another. Additionally, acetone and hydrogen peroxide are both common components used in explosive synthesis, and thus of interest in security applications. An empty, air-filled tube was used as a control.

A total of 72 projections were taken, with source-to-detector distance 2.159 m and source-to-object distance 0.635 m. The X-ray microfocus source (Hammamatsu L812103) was set to 7 \(\mu\)m spot size, 100 kVp, and 100 \(\mu\)A. The spectrally weighted mean wavelength was 0.0269 nm.

Figure 5. A projection image of the sample (a), with its profile (b) showing significant white noise at the detector level. The liquids occupy the upper portions of the tubes, and air bubbles occupy the lower portions of the tubes.\(^{19}\)
These experiments demonstrate the higher sensitivity that compressive X-ray phase imaging provides, far exceeding that of standard absorption contrast (Figs. 5 and 6). In Fig. 6, we see that absorption based FBP reconstruction is heavily noise-corrupted, and does not provide sufficient visual information to distinguish between water and hydrogen peroxide, while compressive phase reconstruction can clearly distinguish between the two samples. To quantify this difference, we measured a peak signal-to-noise ratio (PSNR) of 3 dB in a conventional CT, while obtaining a PSNR of 38 dB in our phase CT, with all other experimental parameters constant, a SNR gain of 35 dB.\textsuperscript{19}

In a Student’s T-test comparison between phase and attenuation based imaging, both methods were able to achieve discrimination with the full CT data, though phase was able to provide much higher certainty in the signal region ($P < 0.010$ for absorption, $P < 6.79 \times 10^{-7}$ for phase). Taking only 100 randomly sampled voxels from each CT (after segmentation), intensity based CT could only distinguish water and peroxide in 26% of tests, meaning rejection of the null hypothesis at the 5% significance level, while phase based CT could distinguish the two liquids in 100% of tests.\textsuperscript{19}

Figure 6. Reconstruction results. (a) Filtered backprojection, (b) compressive PAD TIE, (c) plot along line in (a), and (d) plot along line in (b). These reconstructions show cross sections of the Eppendorf tubes containing the liquids taken along the plane coinciding with the line in Fig. 5(a).\textsuperscript{19}
5. PHASE CONTRAST COMPUTED TOMOGRAPHY OF A HUMAN ARTERY SPECIMEN

There exists a large, unmet need for high quality noninvasive imaging techniques for visualizing atherosclerotic disease. In the following section, we present the results of a proof-of-concept experiment for extending X-ray phase imaging to cardiovascular studies. In this experiment, an *ex vivo* section of an atherosclerotic human common iliac artery was encased in paraffin wax and imaged using both conventional and phase contrast CT. A total of 90 projections were taken, with source-to-detector distance 1.537 m and source-to-object distance 0.768 m. The X-ray microfocus source (Hammamatsu L812103) was operated at a spot size of 7 µm, with a tube voltage of 100 kVp, and a tube current of 100 µA. The spectrally weighted mean wavelength was 0.0269 nm.

The results of both conventional X-ray CT and compressive X-ray phase CT are presented in Fig. 7. From a purely qualitative standpoint, the phase CT in Fig. 7(b) provides significantly better visualization of the artery structure than the absorption CT in Fig. 7(a). To provide a point of reference, a histological sample of the same artery (stained using hematoxylin and eosin, a standard histology stain) was prepared (Fig. 7(c)). The phase

![Figure 7](https://www.spiedigitallibrary.org/conference-proceedings-of-spie)
image shows very strong correlation with the histologic images, accurately representing the major components of the atherosclerotic plaque: the fibrous cap and lipid core (along with artifacts due to fixation). The artery is also clearly distinguishable from the surrounding wax, allowing for estimation of the lumenal dimensions and artery wall thickness. However, a drawback is the apparent artifact generated around the calcification near the bottom of the artery specimen. This artifact is caused by a violation of the phase attenuation duality assumption, as calcium is not a light material, and thus, the assumed ratio of $\gamma$ is incorrect for this region of the object. In reality, elements with higher atomic numbers will have much higher absorption than their electron density would suggest and, as a result, PAD ascribes a much higher value of phase than usual. This results in a “phase sink” in the reconstructed image, where edges around a material with high atomic number become smeared.

These results are show that X-ray phase contrast tomography has significant potential in the medical imaging applications. In the future, X-ray phase CT may find many applications in diagnostic medicine. For example, a clinician can evaluate a patient’s entire coronary vascular tree for lesions from a single X-ray phase CT angiography, without the need for invasive procedures or contrast enhancement. In another scenario, radiologists can use X-ray phase CT as part of pulmonary exams, to differentiate between a variety of possible causes of dyspnea (e.g. asthma, pneumonia, cardiac ischemia, interstitial lung disease, congestive heart failure, or chronic obstructive pulmonary disease, to name a few)\textsuperscript{27} some of which may look similar on a chest X-ray, but may be easily distinguished on X-ray phase CT.

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REFERENCES


