Clinical applications of x-ray differential phase contrast imaging: Where do we stand?

Ke Li, PhD
1. Department of Medical Physics, University of Wisconsin, Madison, WI
2. Department of Radiology, University of Wisconsin, Madison, WI

Acknowledgements

- Basic Science Team
  - Dr. Guang-Hong Chen
  - Dr. Ran Zhang
  - John Garrett
  - Yongshuai Ge
  - Dr. Joe Zambelli
  - Dr. Nick Bevins
  - Dr. Zhihua Qi
  - Dr. Pascal Theriault-Lauzier

- Clinical Team
  - UW Radiology
    - Dr. Wendy DeMartini
    - Dr. Amy Fowler
  - UW Pathology
    - Dr. Andreas Friedl
  - UW Surgery
    - Dr. Lee Wilke

- Industrial Partner
  - Dr. Zhenxu Jing (Hologic Inc.)
  - Dr. Baorui Ren (Hologic Inc.)

X-Ray: Particle or Wave?

“If X-rays be indeed ultra-violet light, then that light must possess the following properties...It is not refracted in passing from air into water, carbon bisulphide, aluminum, rock-salt, glass or zinc.”

-W.C. Roentgen, translated from “On a New Kind of Rays,” 1896

However, based on quantum mechanics developed after Roentgen discovered x-rays, we now understand that just like any other form of electromagnetic radiation, x-rays can also be described as a wave and should be able to refract.

Our question is to ask how to use the wave nature of x-rays to generate images for future medical applications?”
The real and imaginary parts, $\delta$ (Sanchez-del-Rio and Dejus 2003) and $\beta$ (Chantler, et al 2003), of the complex refractive index of breast tissue.

The real part (refraction) is given by $\delta = \frac{n_e r \lambda^2}{2 \pi}$ and the imaginary part (absorption) is given by $\beta = \frac{\lambda}{4 \pi} (\sigma_e + \sigma_a)$.

The index of refraction components vs. Energy chart shows the variation of $\delta$ and $\beta$ with energy. The graph indicates that $\delta$ is significantly larger than $\beta$ across the energy spectrum.

The refractive index of breast tissue is particularly high at lower energies, which can lead to significant refraction effects.

For visible light at 600 nm, the refractive index difference $n_{\text{glass}} - n_{\text{air}} = 0.5$ results in a large refraction angle of about 50 degrees, allowing light to bend significantly.

In contrast, for X-rays at 30 keV, the refractive index difference $\delta_{\text{glass}} - \delta_{\text{air}} = 0.0000007$ results in a refraction angle of about one millionth of a degree, indicating minimal bending compared to visible light.

Spatially coherent x-ray beam

\[ d = k \frac{\lambda}{N \Delta} \]


But how does a coarse detector element resolve the tiny interference pattern?

\[ I = I_0 + I_1 \cos \left( \frac{2 \pi}{P_2} x + \phi \right) \]

Object in Place: Refraction

Phase Step Modulation

Detector Signal (arb. units)

Grating Position (µm)
Refraction Angle Measured by the Talbot-Lau Grating Interferometer

\[ \Delta \phi_d = \phi_d^{\text{object}} - \phi_d^{\text{background}} \]

\[ \Delta \phi_d = \frac{2 \pi d}{p_2} \Theta = 0.3 \times 10^6 \cdot \Theta \]

Talbot-Lau interferometer amplifies the refraction angles by one million times to make them measurable!

Moiré Analysis

\[ \alpha \]

\[ p_m \]

\[ p_1 \]

\[ p_2 \]

\[ \Theta \]

Bevins, Zambelli, Li, Qi, Chen, Medical Physics (2012)
One term of the equation describing the measured intensity has not been used.

\[ I = I_0 + I_1 \cos \left( \frac{2\pi x}{p_2} + \phi_2 \right) \]

This term reflects the amplitude of the intensity change as phase measurement is performed.

Two factors: grating & beam quality (extrinsic), and sample characteristic (intrinsic).

What kind of intrinsic characteristic of the image object does this term offer?
The dark field image can be extracted using the normalized oscillation amplitude

\[ \varepsilon = \frac{I_1}{I_0} \quad V_{SAS} = \frac{\varepsilon^{\text{obs}}}{\varepsilon^{\text{meas}}} = \frac{I_1^{\text{meas}}}{I_0^{\text{meas}}} \]


\[ \ln(V_{SAS}) = -\frac{r^2}{4} \int \frac{d\zeta}{R^2(\zeta)} \sigma_{SAS} \rho_{SAS} \]


Noise variance of phase contrast signal is inversely proportional to the square of visibility

\[ \sigma^2 \propto \frac{1}{\varepsilon^2} \]

Maximizing fringe visibility is the key in improving the imaging performance of phase contrast imaging

Chen et al., Med Phys (2011)
Li et al., Med Phys (2013)
The same phantom as previously described is used again, however this time with the addition of a 2.3 mm diameter wooden dowel in the air-filled insert to provide a small-angle scattering structure.
In a realistic clinical multi-contrast x-ray imaging system, the absorption contrast mechanism should not be relegated to a secondary position; its performance should be maintained as much as possible, allowing the complementary information provided by phase contrast and dark field contrast “free of charge”.
**Methods to Improve Fringe Visibility**

- Improved grating fabrication methods
  - Bevins, grating fabrication using liquid metal filling technique, UW-Madison (2012)
- Improved interferometer setup
  - Stutman and Finkenthal, Glancing angle Talbot-Lau grating interferometers for phase contrast imaging at high x-ray energy, APL (2012)
- Combination with single photon counting detector
Methods to Improve Fringe Visibility

- 15 cm x 15 cm total imaging area, 100 um pixel size (XCounter AB, Sweden)

**Measured Fringe Visibility (%)**

- Previous Grating
- New Grating
- New Grating + PCD

Potential Clinical Applications

- Brain imaging
  - Brain tumor, Alzheimer’s disease
- Lung imaging
  - Emphysema and fibrosis
- Musculoskeletal imaging
  - Osteoarthritis and rheumatoid arthritis
- Abdominal imaging
  - Kidney stone
- Breast imaging

Biological Samples

- Absorption
- Differential phase
- Dark field
Total volume: ~28 L
Total weight: ~25 kg
Thickness: ~20 cm

Absorption
Differential Phase
Dark Field

Multi-contrast Tomosynthesis Images of the Fresh Udder Specimen

Absorption
DPC
Dark Field
Phase
Human breast cadaver specimen, dissected

Thickness: ~3.5 cm

Absorption  Differential Phase  Dark Field

Multi-Contrast Images of the Human Cadaver Breast

Absorption  Differential Phase  Dark Field

Multi-Contrast Images of the Human Cadaver Breast
Human Cadaver Breast Specimen

Multi-Contrast Tomosynthesis Images of the Cadaver Breast Specimen

Multi-Contrast Images of the Human Cadaver Breast Specimen
X-ray differential phase contrast imaging is an innovative method that is sensitive to x-ray refraction in matter. The method is particularly adapted to visualize weakly x-ray absorbing soft tissues and may provide complementary information to conventional absorption contrast imaging. The key factor of the performance of phase contrast imaging is fringe visibility, which has been significantly improved through recent technical advances. To fully understand the clinical benefit of this method, it is essential to perform evaluations in a clinical setting and without sacrificing the performance of absorption imaging.