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

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X-Ray: Particle or Wave?

"If X-rays be indeed ultra-violet light, then that light must posses 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?

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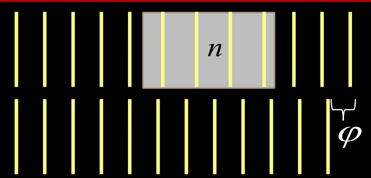
X-Ray Wave-Matter Interaction



$$\varphi = \frac{2\pi}{\lambda}(1-n)L = \frac{2\pi}{\lambda}\int_{\ell}\delta(l)dl = \lambda r_e \int_{\ell}\rho_e(l)dl$$

$$n = 1 - \delta + i\beta$$

$\delta = \frac{\rho_e r_e \lambda^2}{2\pi}$ Real Part (refraction)

Imaginary Part (absorption) $\beta = \frac{\lambda}{4\pi}(\sigma_p + \sigma_c)$

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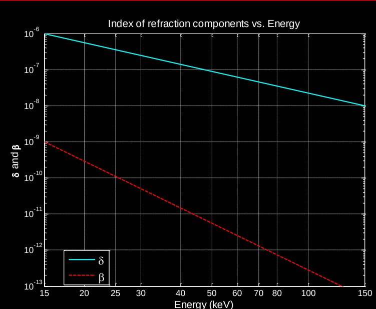
Refractive Index of Breast Tissue



The real and imaginary parts, δ (Sanchez-del-Rio and Dejus 2003) and β (Chantler, et al 2003), of the complex refractive index of breast tissue.

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Refraction of Visible Light and X-rays

600 nm Visible Light

$$n_{\text{glass}} - n_{\text{air}} = 0.5$$

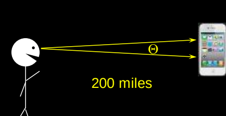
Refraction angle: as large as 50 degrees

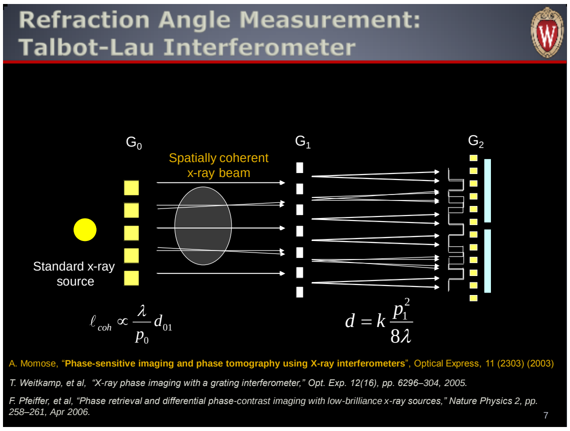
30 keV X-Ray

$$n = 1 - \delta$$

$$\delta_{\text{glass}} - \delta_{\text{air}} = 0.0000007$$

Refraction angle: about one millionth of a degree




Refraction Angle Measurement:
Talbot-Lau Interferometer
G0
G1
G2
Spatially coherent
x-ray beam
Standard x-ray
source
$\ell_{coh} \propto \frac{\lambda}{p_0} d_{01}$
$d = k \frac{p_1^2}{8\lambda}$
A. Momose, "Phase-sensitive imaging and phase tomography using X-ray interferometers", Optical Express, 11 (2303) (2003)
T. Weitkamp, et al, "X-ray phase imaging with a grating interferometer," Opt. Exp. 12(16), pp. 6296–304, 2005.
F. Pfeiffer, et al, "Phase retrieval and differential phase-contrast imaging with low-brilliance x-ray sources," Nature Physics 2, pp. 258–261, Apr 2006.
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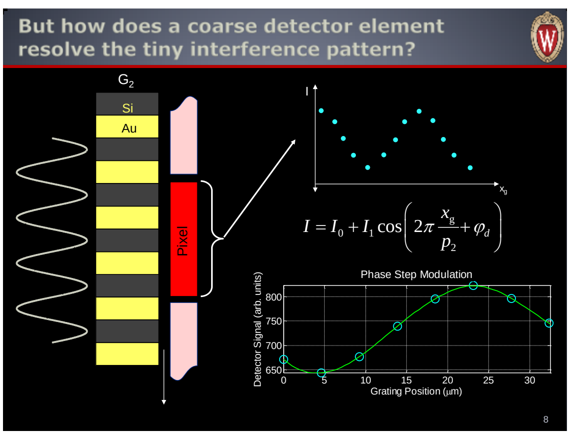
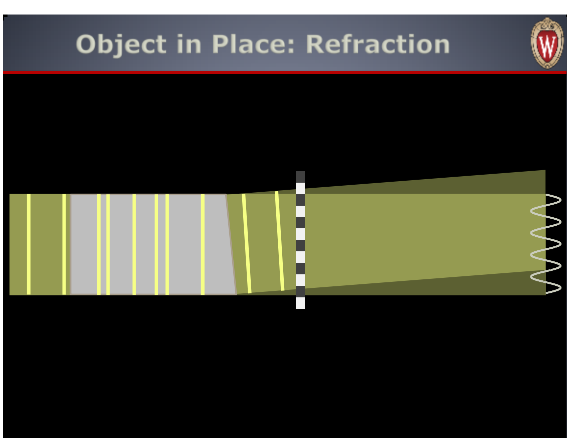
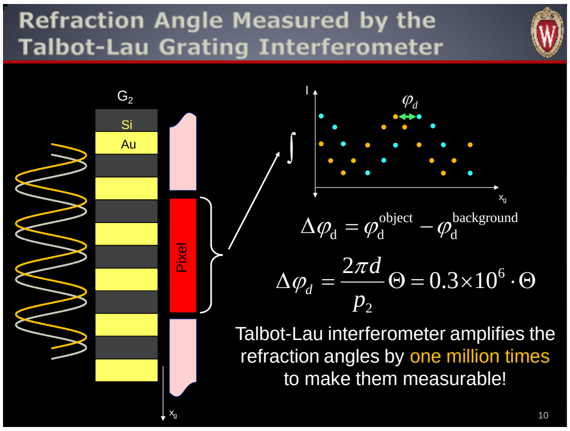

But how does a coarse detector element
resolve the tiny interference pattern?
G2
Si
Au
Pixel
I
xg
$I = I_0 + I_1 \cos\left(2\pi \frac{x_g}{p_2} + \varphi_d\right)$
Phase Step Modulation
Detector Signal (arb. units)
800
750
700
650
0
5
10
15
20
25
30
Grating Position (μm)
8


Object in Place: Refraction


Refraction Angle Measured by the Talbot-Lau Grating Interferometer
G_2
Si
Au
Pixel
I
x_0
φ_d
$\Delta\varphi_\mathrm{d} = \varphi_\mathrm{d}^\mathrm{object} - \varphi_\mathrm{d}^\mathrm{background}$
$\Delta\varphi_d = \frac{2\pi d}{p_2}\Theta = 0.3\times10^6\cdot\Theta$
Talbot-Lau interferometer amplifies the refraction angles by one million times to make them measurable!
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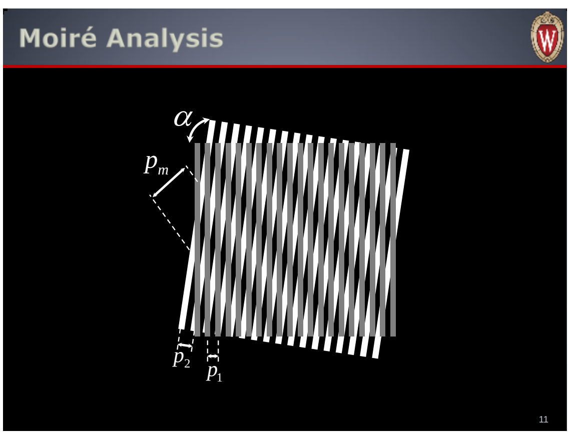
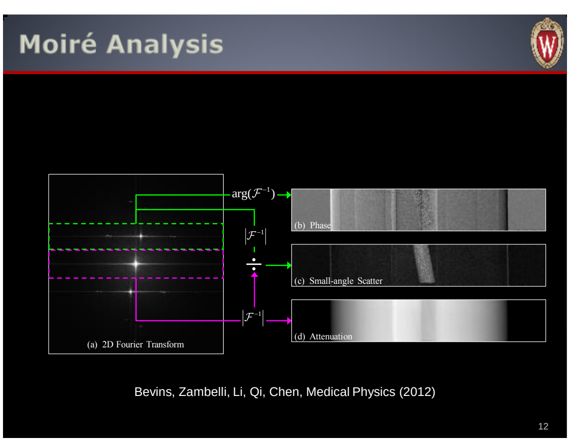

Moiré Analysis
α
p_m
p_2
p_1
11


Moiré Analysis
$\arg(\mathcal{F}^{-1})$
$|\mathcal{F}^{-1}|$
$\div$
(a) 2D Fourier Transform
(b) Phase
(c) Small-angle Scatter
(d) Attenuation
Bevins, Zambelli, Li, Qi, Chen, Medical Physics (2012)
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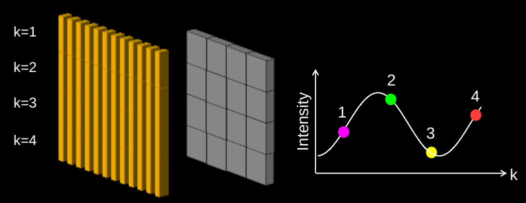
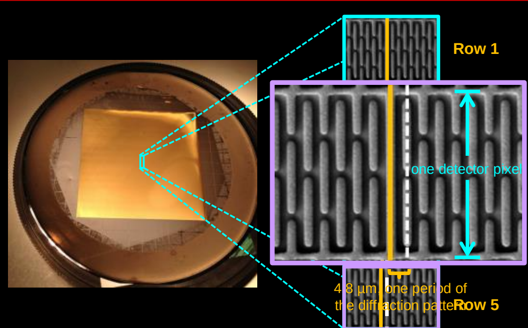
Staggered Analyzer Grating



Y. Ge, K. Li, J. Garrett, G.-H. Chen, Optics Express (2014)

Staggered Analyzer Grating



Scanning electron microscope (SEM) image

A third contrast mechanism: Small angle scattering contrast

- One term of the equation describing the measured intensity has not been used.

$$I = I_0 + I_1 \cos\left(2\pi \frac{x_g}{p_2} + \varphi_d\right)$$

- 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?

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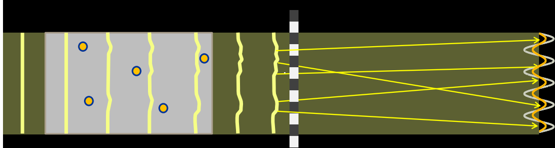
Small Angle Scatter Effect (SAS)



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Small Angle Scatter Imaging (a.k.a. Dark-Field Imaging)

- The dark field image can be extracted using the normalized oscillation amplitude

$$\varepsilon \equiv \frac{I_1}{I_0}, \qquad V_{SAS} = \frac{\varepsilon^{obj}}{\varepsilon^{bkgd}} = \frac{I_0^{bkgd}}{I_0^{obj}} \frac{I_1^{obj}}{I_1^{bkgd}}$$

Pfeiffer et al, Nature Materials (2008)

$$\ln\left(V_{\mathrm{SAS}}\right) = -\frac{r^2}{4}\int dz\, \frac{\sigma_{\mathrm{SAS}}\rho_{\mathrm{SAS}}}{R^2(z)}$$

Chen, Bevins, Zambelli, Qi, Opt. Express (2010)

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Fringe Visibility and Phase Contrast Imaging Performance

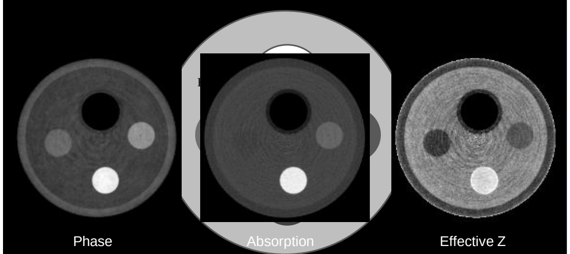
- Noise variance of phase contrast signal is inversely proportional to the square of visibility

$$\sigma^2 \propto \frac{1}{\varepsilon^2}$$

- 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)

Multi-Contrast CT Images



Qi, Zambelli, Bevins, and Chen, PMB, Vol. 55:2669-2677 (2010)

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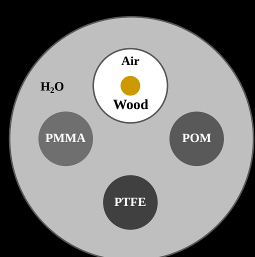
Phantom Results



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 .

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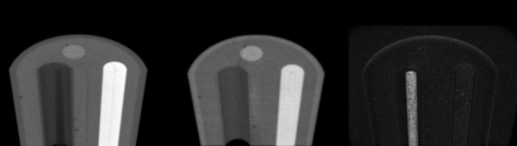
Multi-Contrast CT Images



Absorption Phase Contrast Dark Field

Bevins, Zambelli, Qi, and Chen, Proc SPIE (2010)

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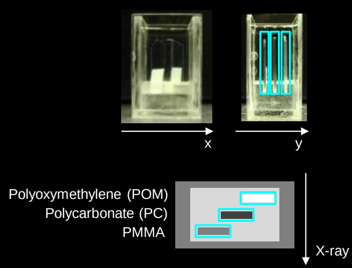
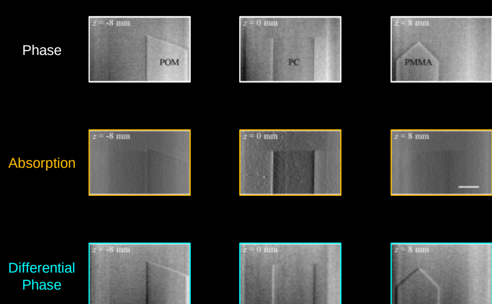
Multi-Contrast Tomosynthesis Imaging



Li, Ge, Garrett, Bevins, Zambelli, Chen, Medical Physics (2014)

Multi-Contrast Tomosynthesis Images

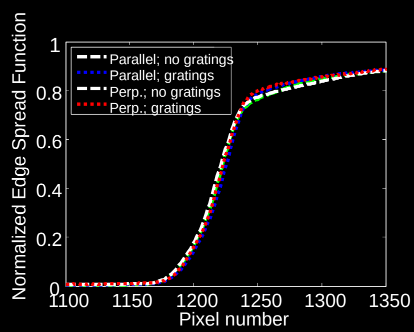


Li, Ge, Garrett, Bevins, Zambelli, Chen, Medical Physics (2014)

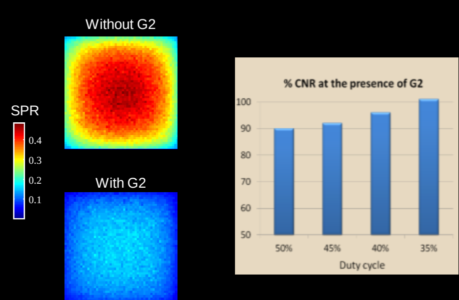
The Author's Position Statement

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".

Preservation of Spatial Resolution for Absorption Contrast Imaging

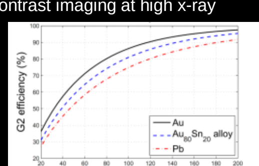


Preservation of CNR per Dose for Absorption Contrast Imaging



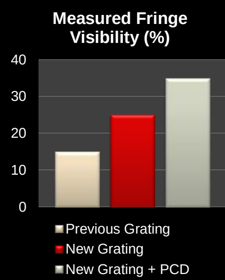
Methods to Improve Fringe Visibility

- Improved grating fabrication methods
  - Reznikova et al., Soft X-ray lithography of high aspect ratio SU8 submicron structures. Microsystem Technologies (2008)
  - 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)

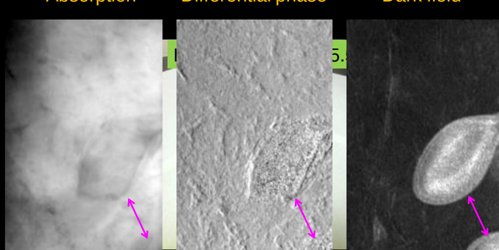


Potential Clinical Applications

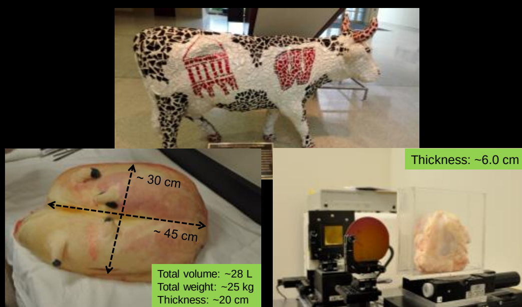
- Brain imaging
  - Brain tumor, Alzheimer's disease
- Lung imaging
  - Emphysema and fibrosis
- Musculoskeletal imaging
  - Osteoarthritis and rheumatoid arthritis
- Abdominal imaging
  - Kidney stone
- Breast imaging

Biological Samples

Absorption Differential phase Dark field



Fresh Udder Specimen

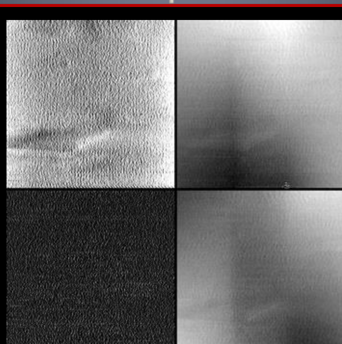


Multi-Contrast Images of the Fresh Udder Specimen

Absorption | Differential Phase | Dark Field

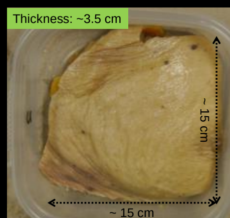
Multi-contrast Tomosynthesis Images of the Fresh Udder Specimen

Absorption | DPC



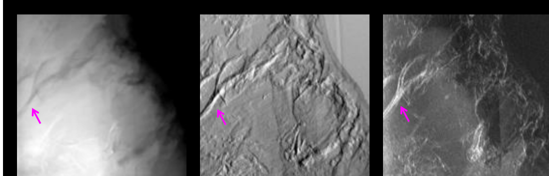
Dark Field | Phase

Human Cadaver Breast Specimen

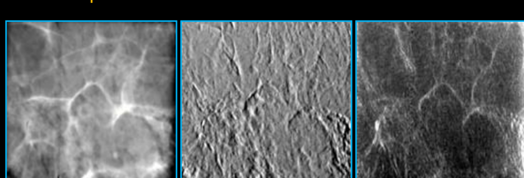


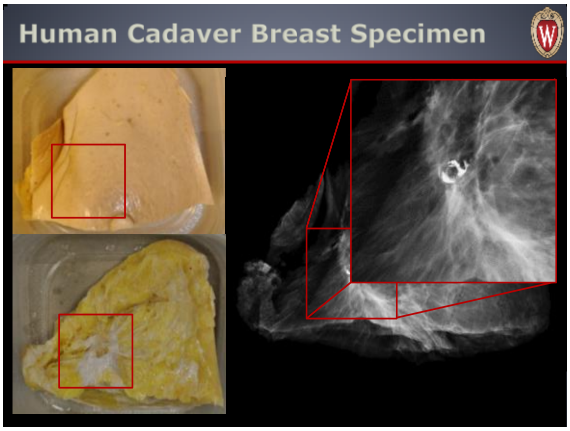
Human breast cadaver specimen, dissected

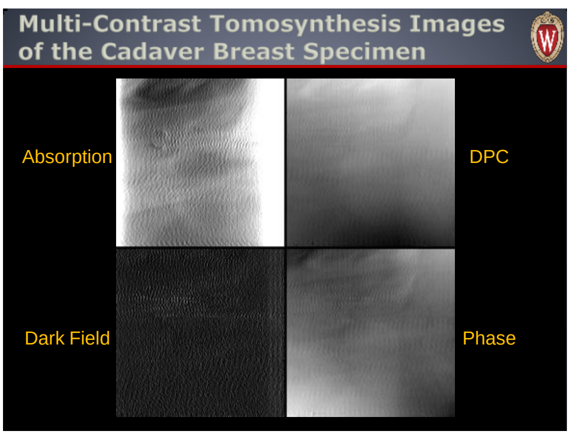
Multi-Contrast Images of the Human Cadaver Breast

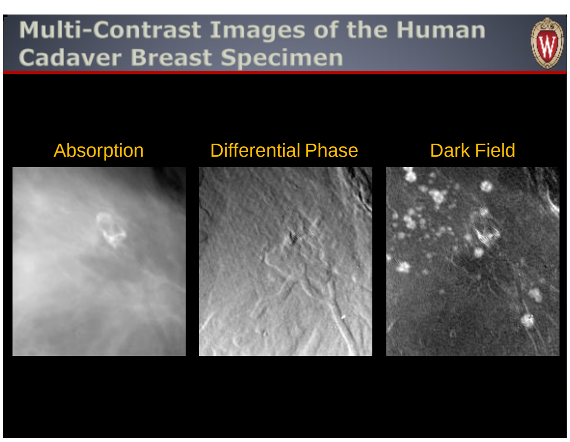


Multi-Contrast Images of the Human Cadaver Breast

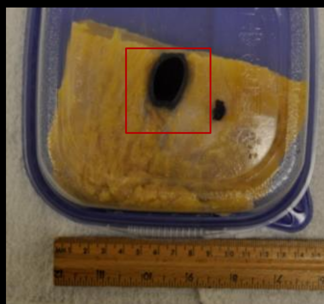



Human Cadaver Breast Specimen

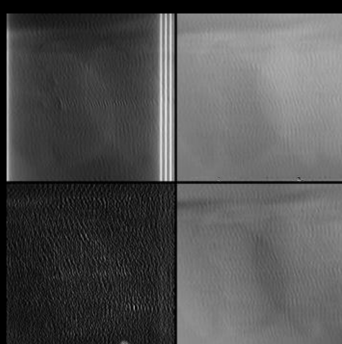

Multi-Contrast Tomosynthesis Images of the Cadaver Breast Specimen
Absorption
DPC
Dark Field
Phase


Multi-Contrast Images of the Human Cadaver Breast Specimen
Absorption
Differential Phase
Dark Field

Human Cadaver Breast Specimen with Simulated Lesion



Multi-contrast Tomosynthesis Images of the Human Cadaver Breast with Simulated Lesion

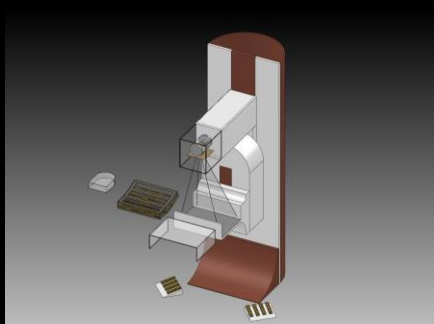


Multi-contrast Images of the Human Cadaver Breast with Simulated Lesion

Summary

- 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 performance evaluations in a clinical setting and without sacrificing the performance of absorption imaging

Future System Design



Future system design

Thank You