Micro and Nano-Tomography of Biological Tissues

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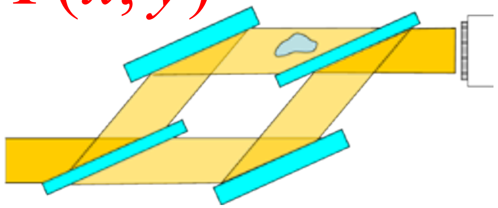
ETH-227-0965-00 L

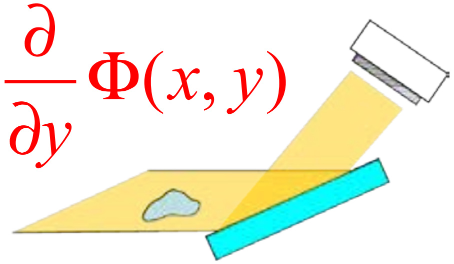
X-ray phase contrast techniques

$$\Phi(x, y)$$



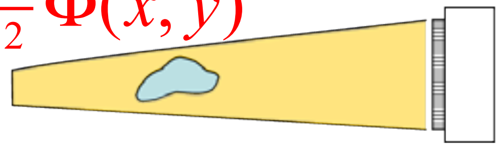
Crystal interferometry
Bonse et al. APL 6, 155 (1965)

$$\frac{\partial}{\partial y}\Phi(x, y)$$



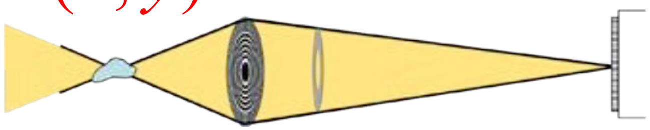
Analyser-based (DEI)
Chapman et al., *PMB,* 42, 2015 (1997)
Davis et al., JOSAA 13, 1193 (1996)

$$\frac{\partial^2}{\partial y^2}\Phi(x, y)$$



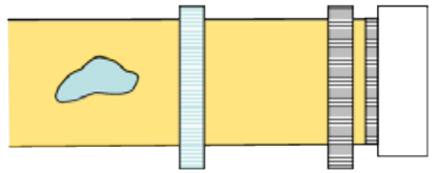
Free Space Propagation (TIE)
Snigirev et al., RSI 66, 5486 (1995)
Cloetens et al., APL 75, 2912 (1999)
Groso et al., OptExp 14, 8103 (2006)

$$\Phi(x, y)$$



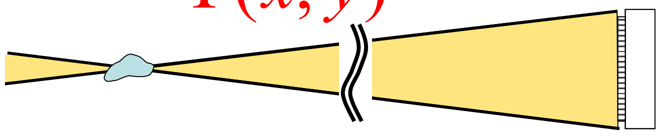
Zernike Phase Contrast
Weiss et al., UM 84, 185 (2000)
Stampanoni et al., PRB 81, 140105R (2010)

$$\frac{\partial}{\partial y}\Phi(x, y)$$



Grating interferometry (DPC)
Weitkamp et al., OptExp 13, 6296 (2005)
Pfeiffer et al., Nature Phys 2, 258 (2006)

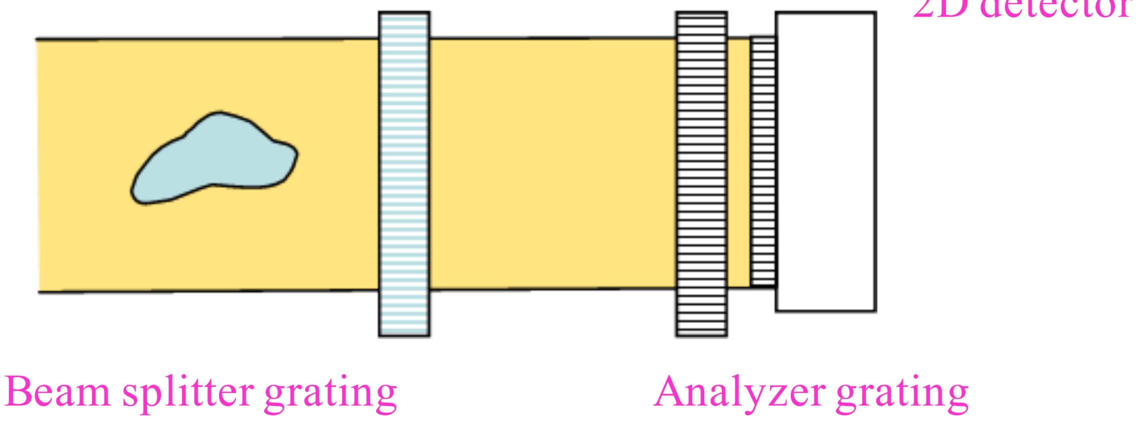
$$\Phi(x, y)$$



Coherent Diffraction Imaging (CDI)
Miao et al., Nature 400 (1999)
Thibault et al., Science, 321, 379 (2008).

Grating interferometry

Weitkamp et al., Optics Express (13)., 6296 (2005)
Pfeiffer et al., Nature Physics 2 (4): 258-261 (2006)



- The measured quantity is $(\partial\Phi/\partial y)$, as in DEI.
- Phase stepping technique followed by integration
- **Simple setup, mechanically robust**
- **Large field of view**
- **Usable with divergent and polychromatic beams**
- **Usable with standard X-ray tubes, low coherence required**

+

- **Moderate spatial resolution, limited by grid period**

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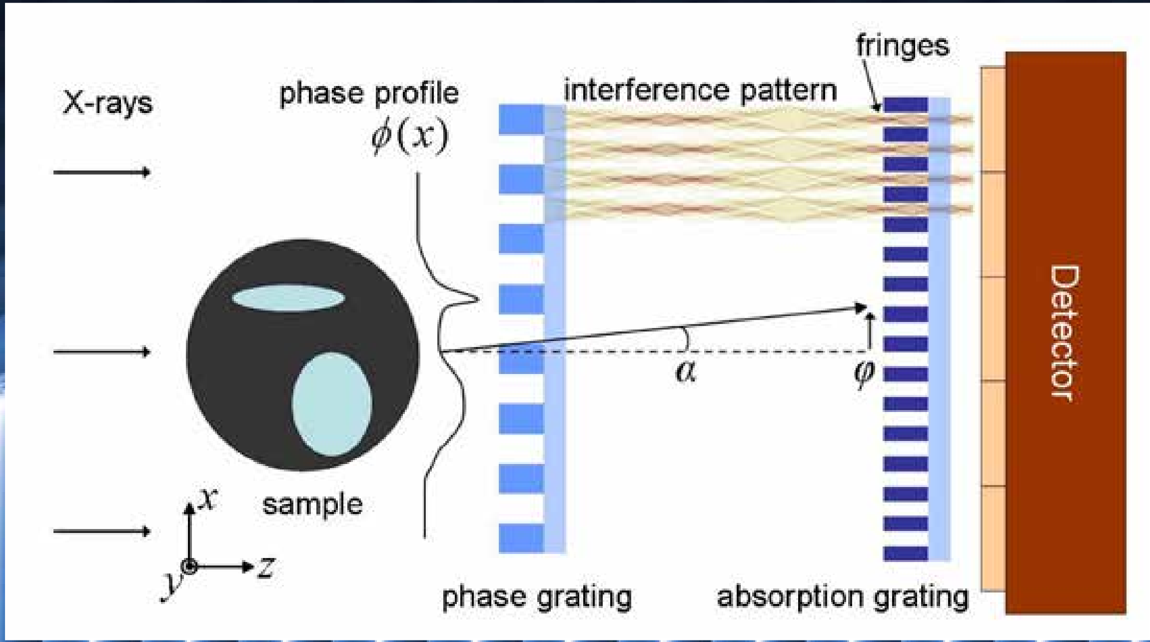
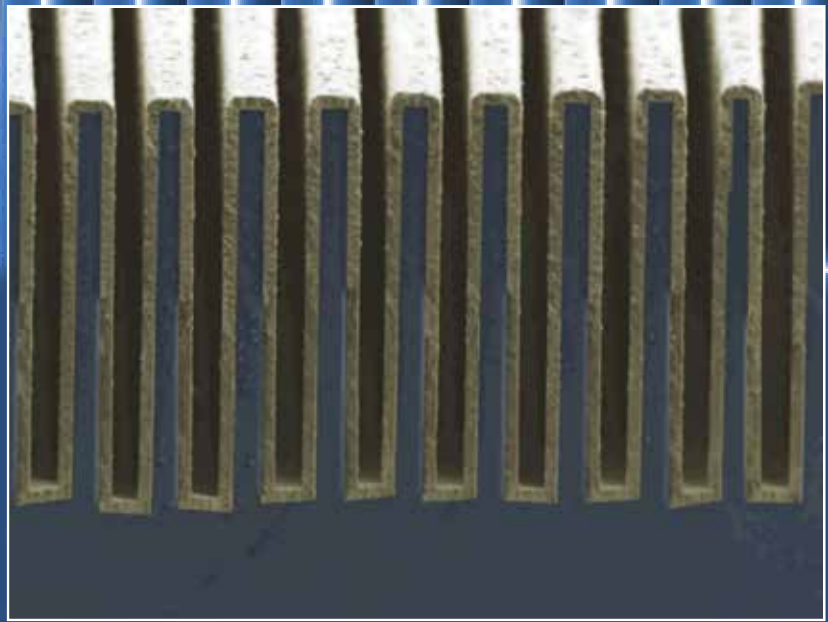
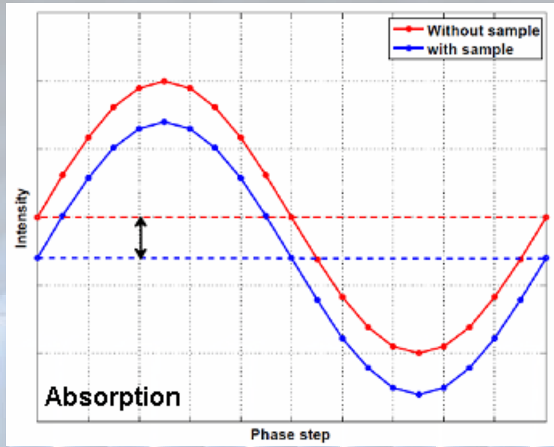
Sensing the wavefront with grating interferometry





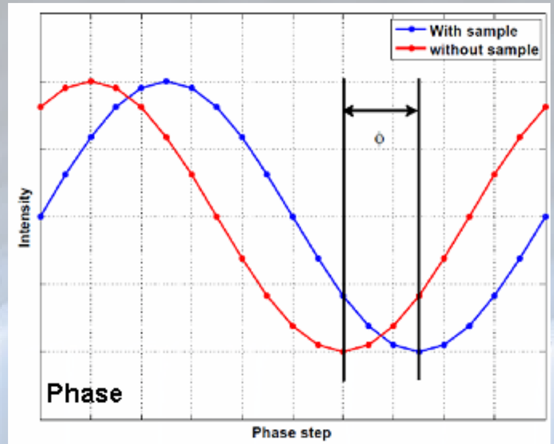
Sensing the wavefront with grating interferometry

Absorption contrast



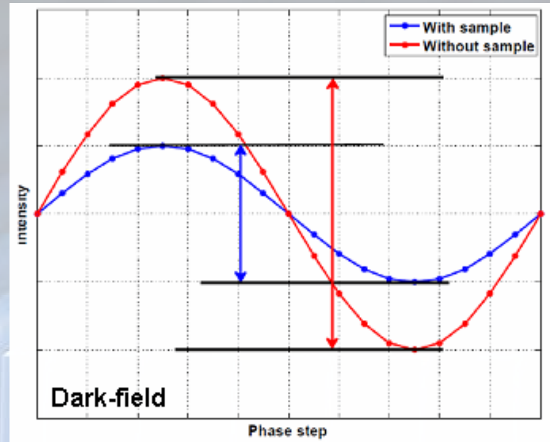
$$-\log\left(\frac{I_s}{I_b}\right)$$

Differential phase contrast



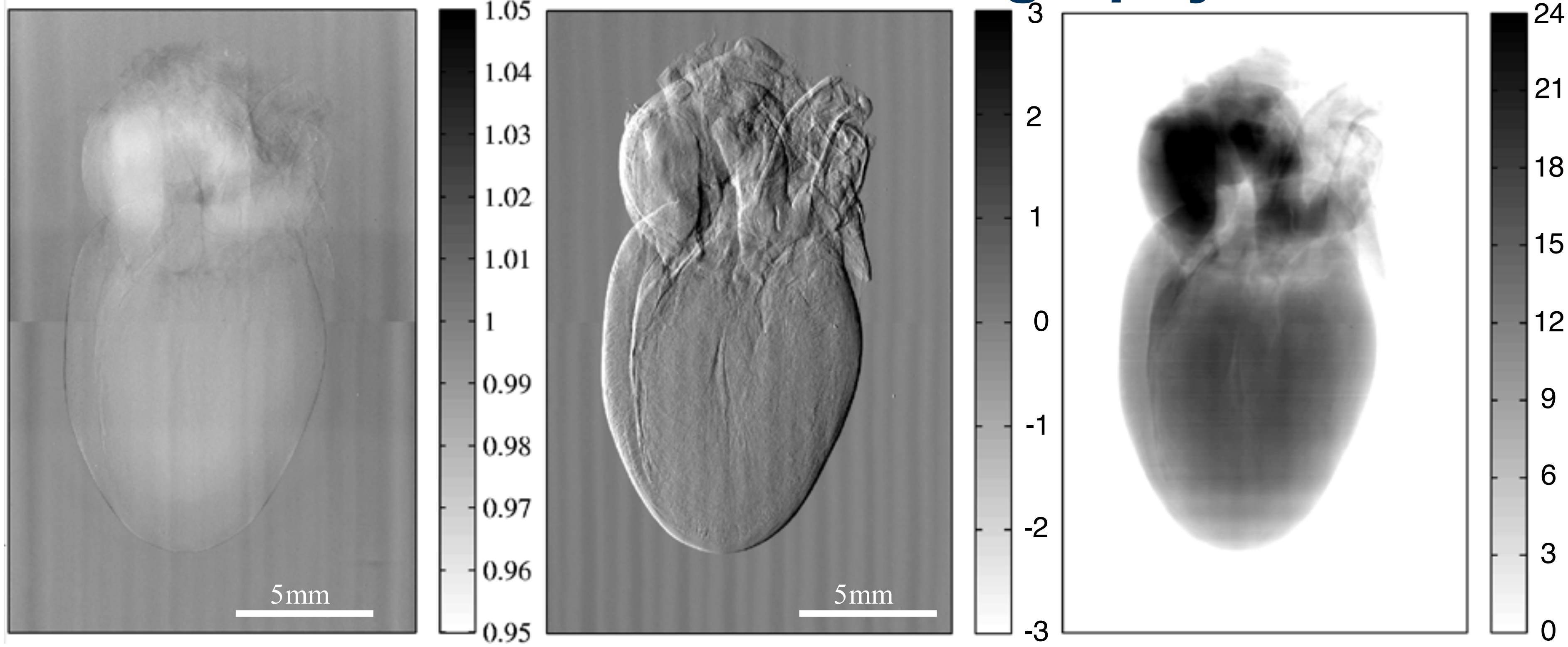
$$\Phi_s - \Phi_b$$

Dark-field contrast



$$-\log\left(\frac{V_s}{V_b}\right) \qquad V = \frac{I_{max} - I_{min}}{I_{max} + I_{min}}$$

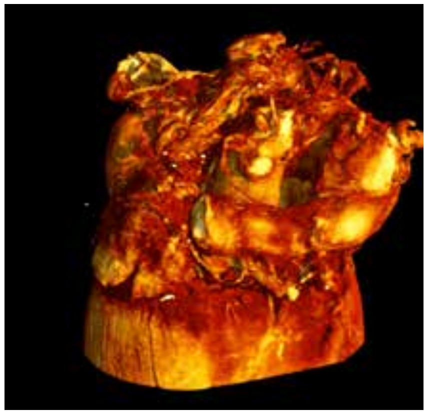
Phase contrast radiography



Absorption

Phase gradient [mrad/µm]

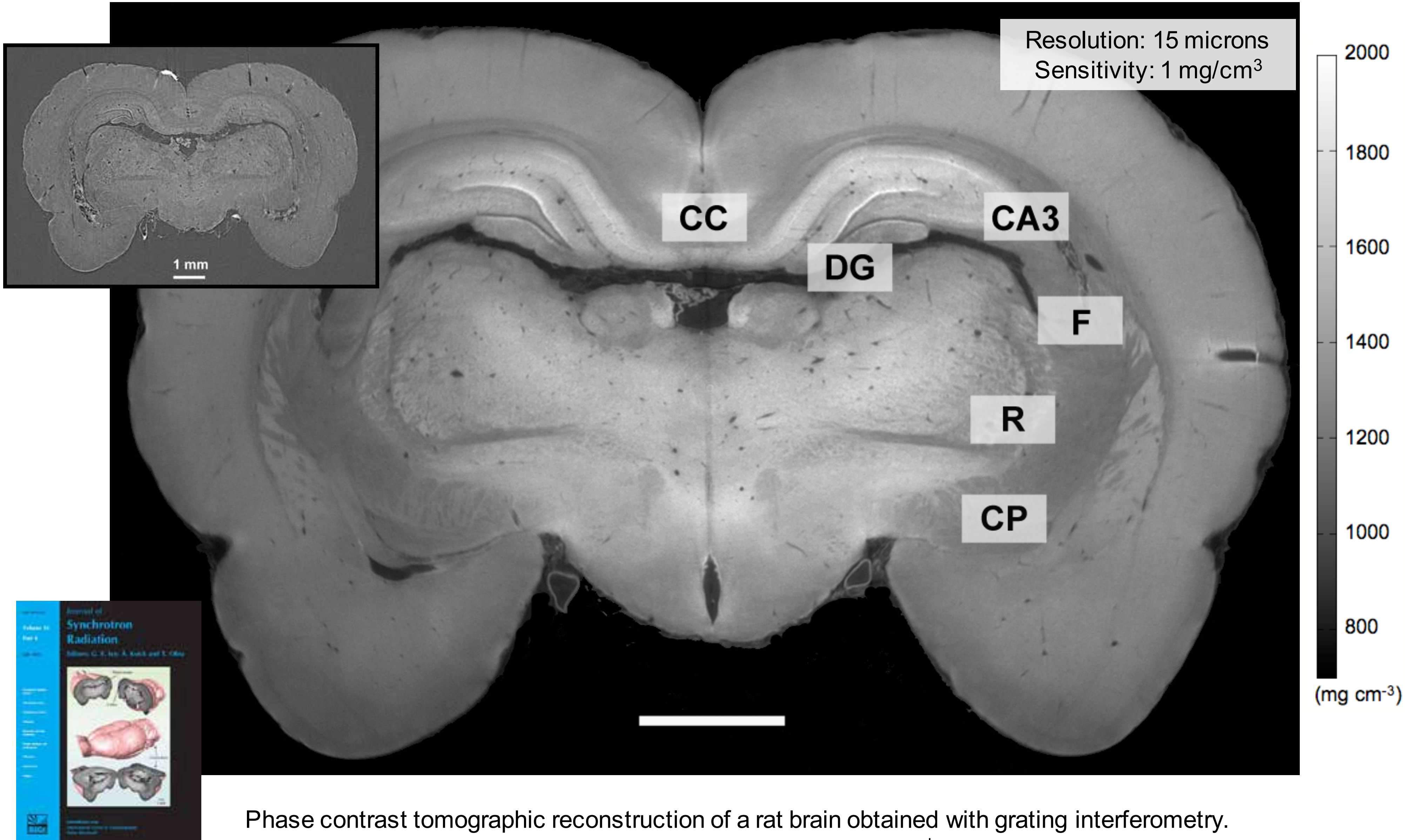
Phase [rad]



Integration

Rat heart in formalin solution, ESRF, ID19, 17.8 keV.
Images courtesy of T. Weitkamp

High sensitivity at isotropic, high resolution

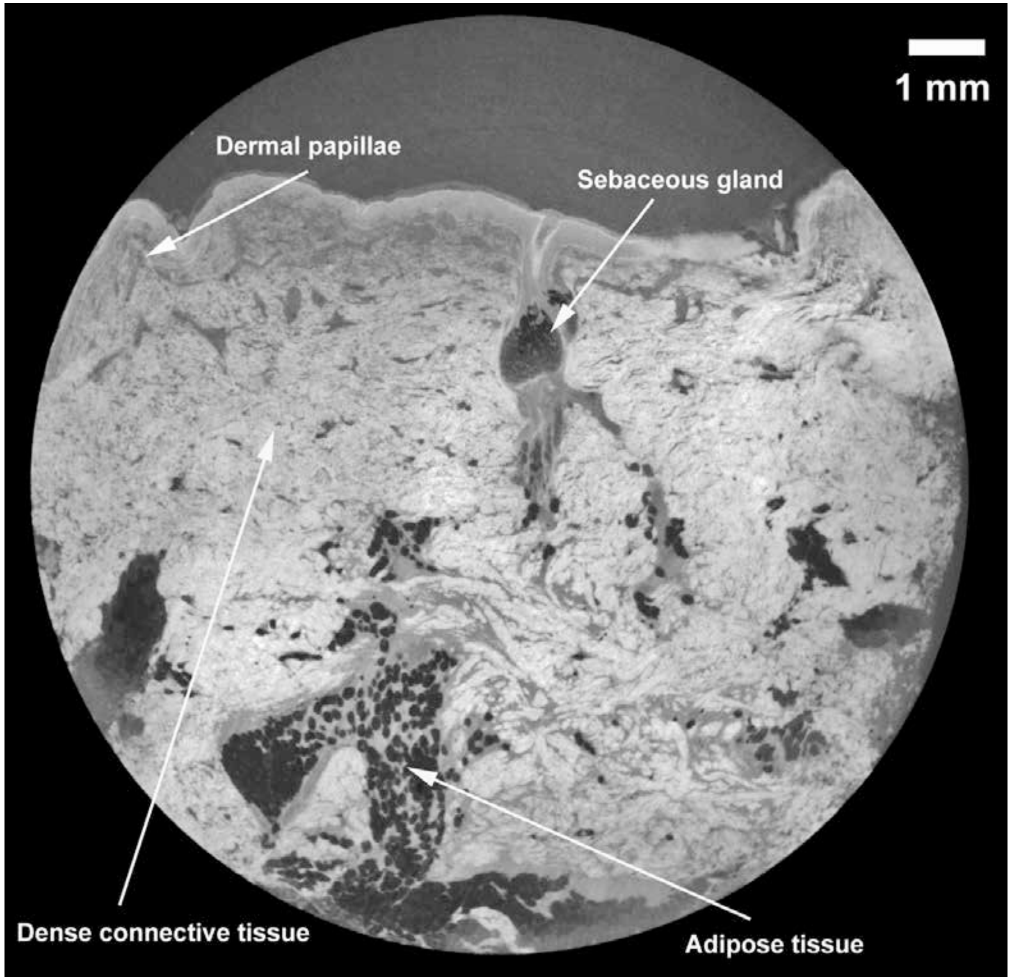


McDonald et al., JSR 2009

Phase contrast tomographic reconstruction of a rat brain obtained with grating interferometry. Scale bar 1 mm. TOMCAT Interferometer operated at 25 keV, 3rd Talbot distance.

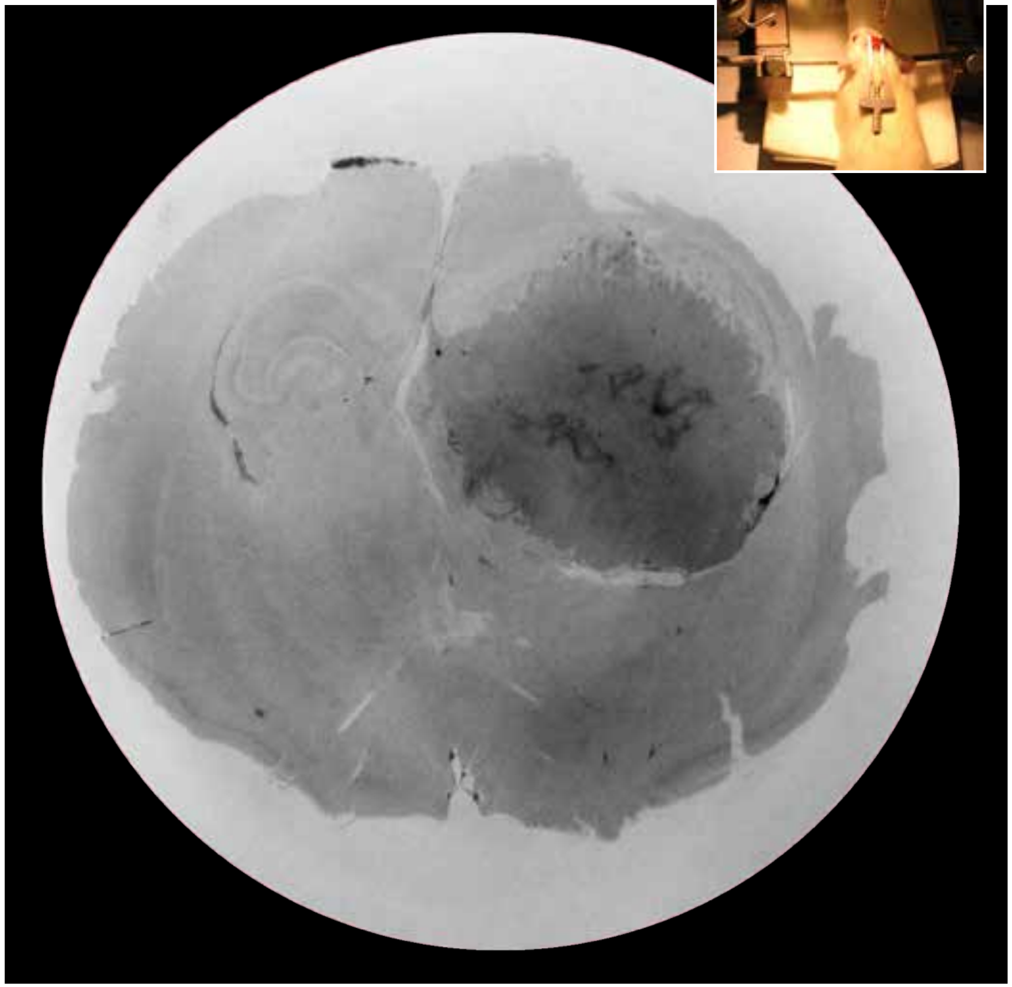
Soft-tissue sensitivity

M. Stampanoni et al., MASR 2010



Human skin tissue biopsy

E. Schültke, unpublished data

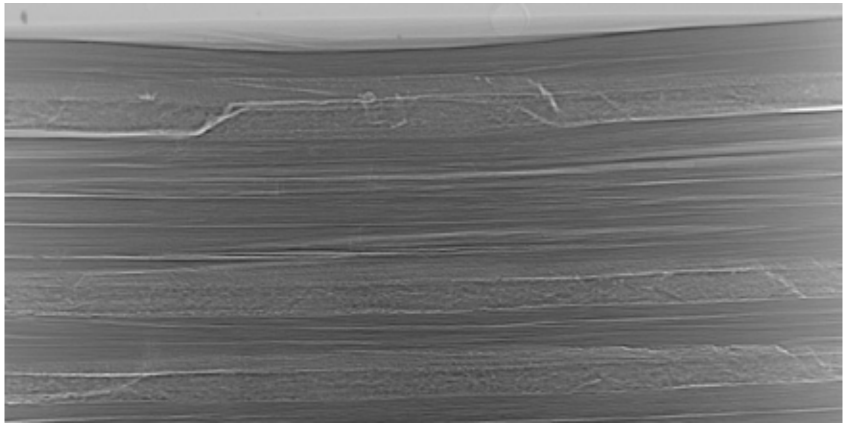


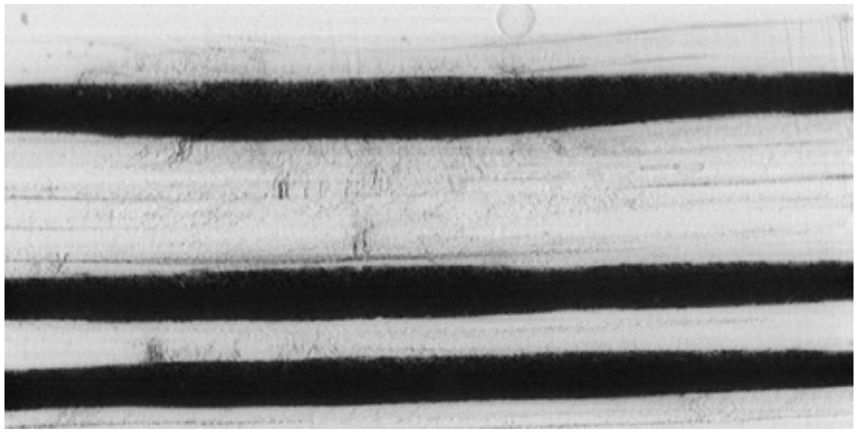
Inoculated GNP-F98 glioma

TOMCAT Interferometer: 25 keV, 3^{rd} Talbot Distance

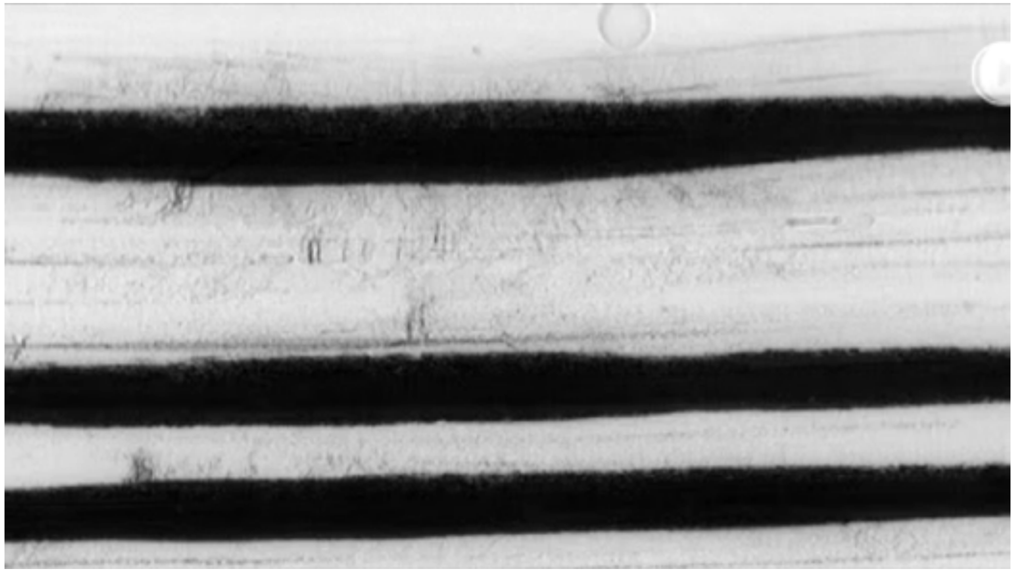
Darkfield radiology

CFRP laminated structure consisting of alternate layers of plastic matrix and fiber reinforcement





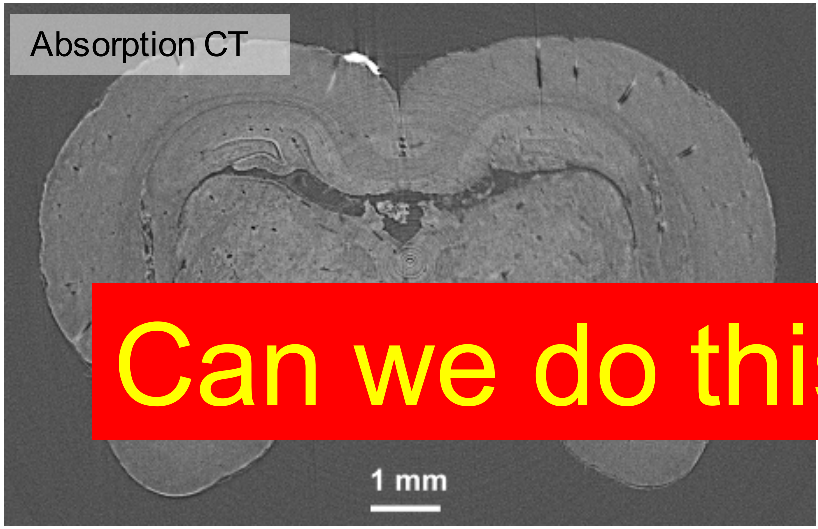
10 mm

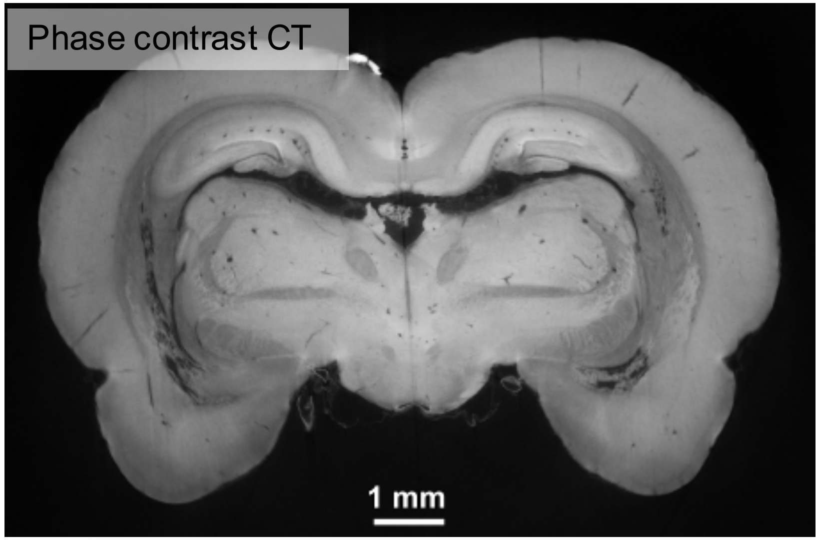


Directional dependency of the darkfield signal.
Issues with the tomographic reconstruction…

S. McDonald, M. Stampanoni et al. , Journal of Synchrotron Radiation 16, 562-572,(2009)

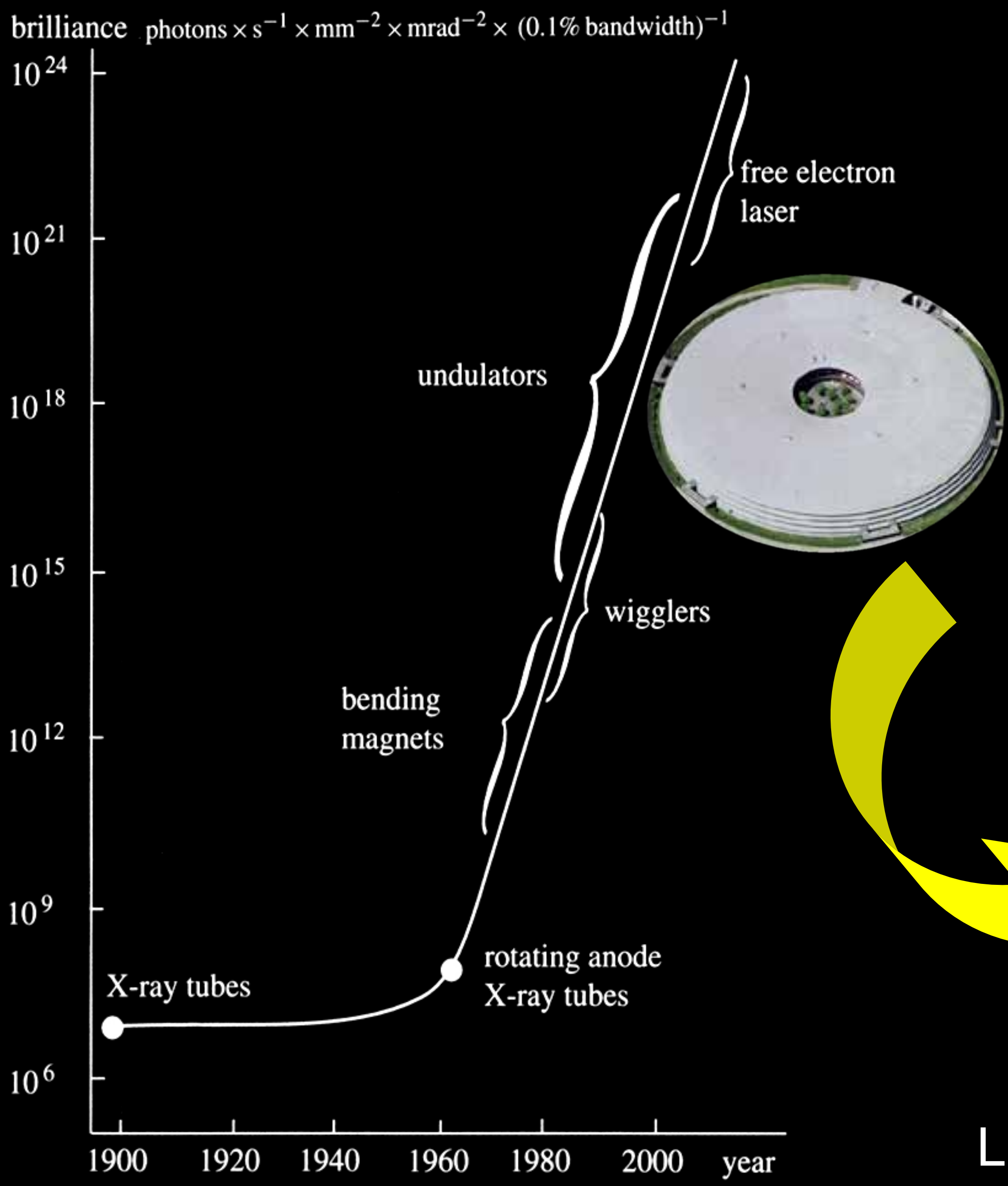
Phase contrast imaging (CT) at synchrotron
(10 microns isotropic resolution)





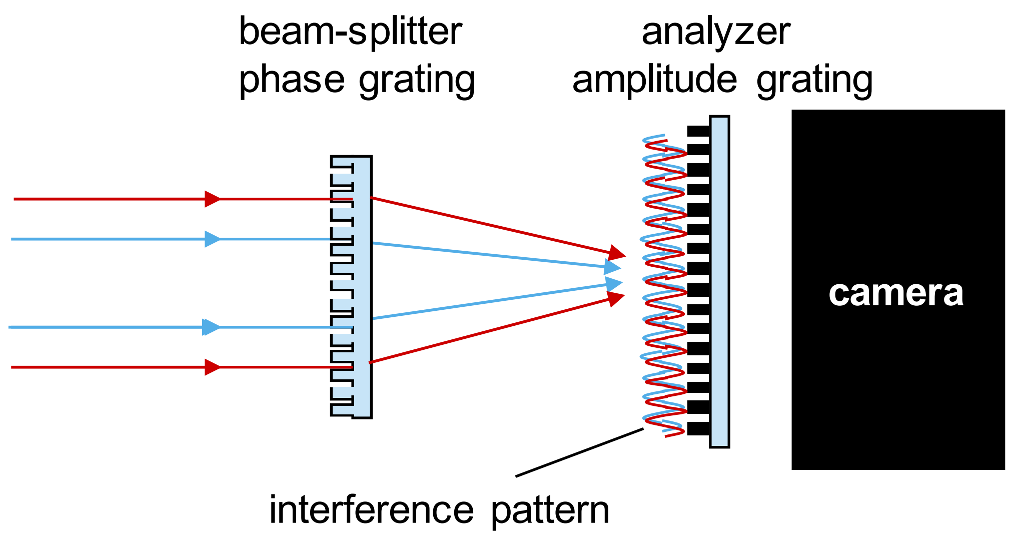
Can we do this in the clinics?

Moving back to the "origins"…



Low spatial and temporal coherence!!

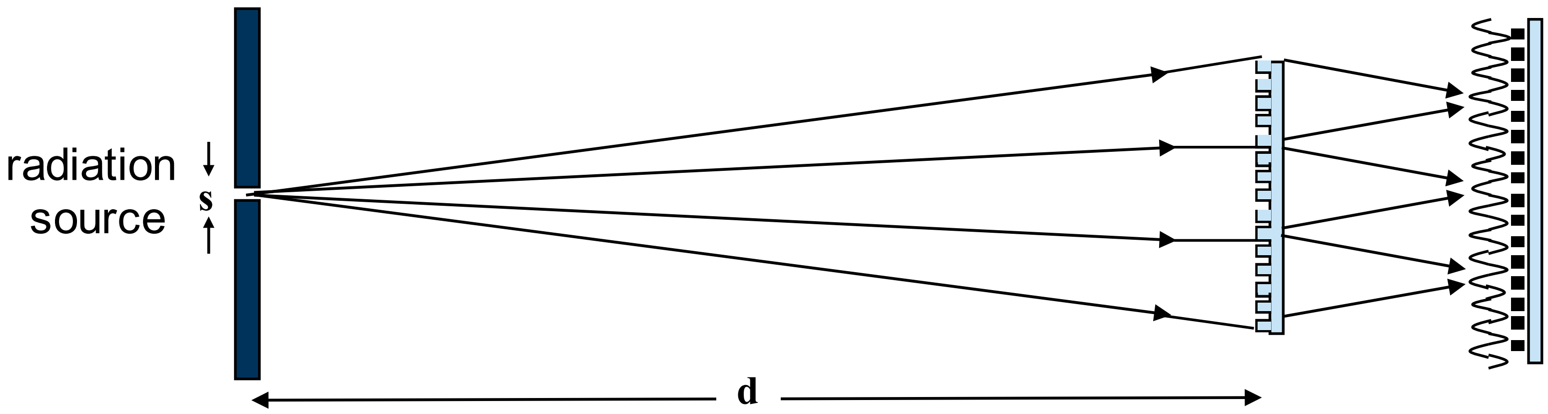
Temporal (longitudinal) coherence requirements



The position and pitch of the interference pattern does not depend on the wavelength!

10-20% bandwidth is OK

Spatial (transverse) coherence requirements



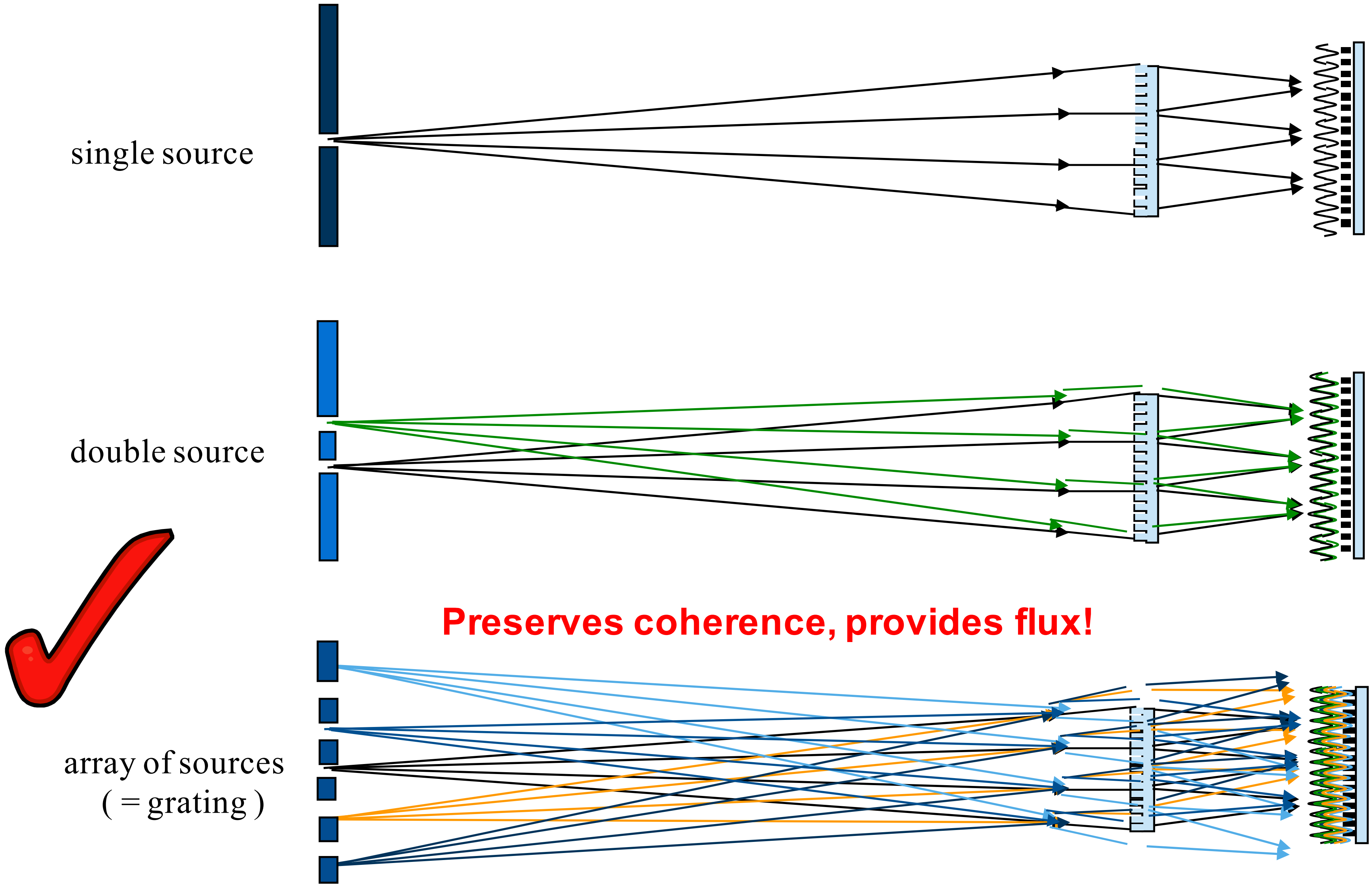
- Required in one direction

- Depends on wavelength, geometry, ….

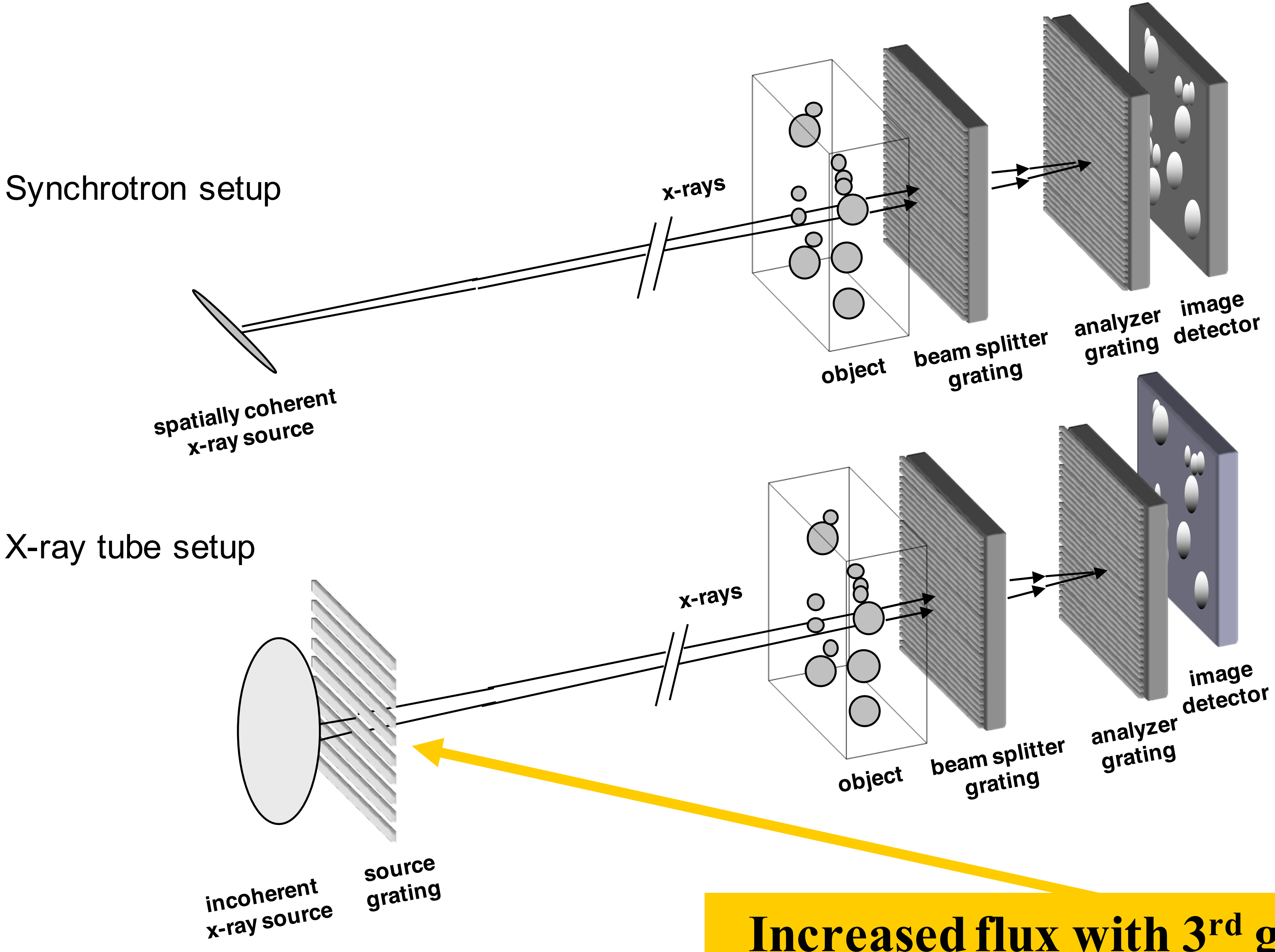
- For Energy = 20 keV, d=1m, → **s < 10-20 µm**

→ **LOW FLUX !!**

The Talbot-Lau interferometer



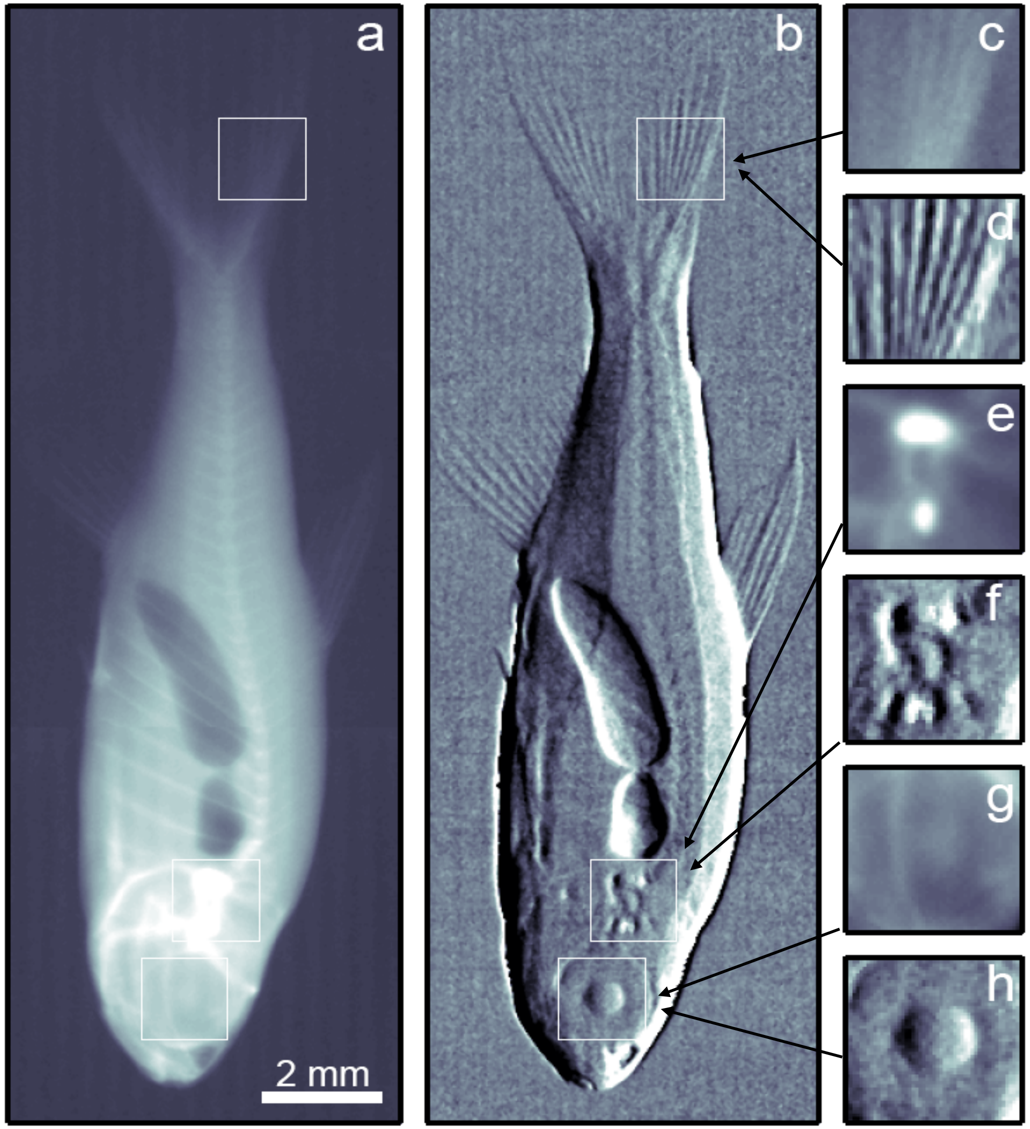
The Talbot-Lau interferometer



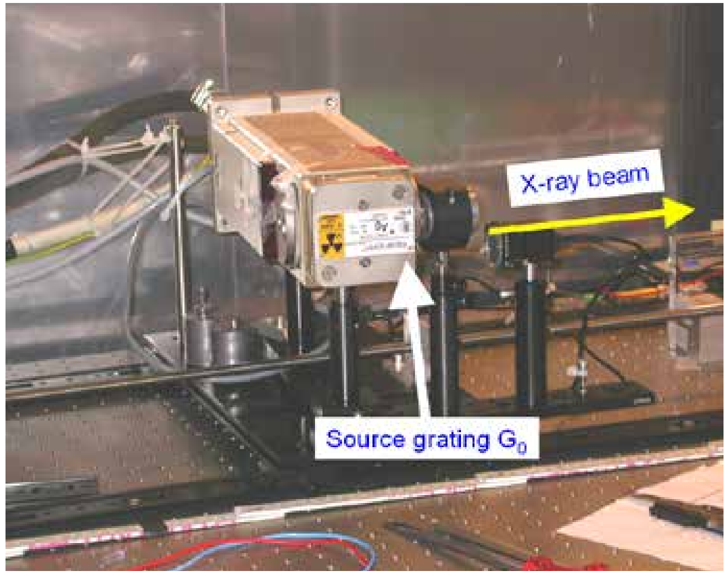
Increased flux with 3rd grating

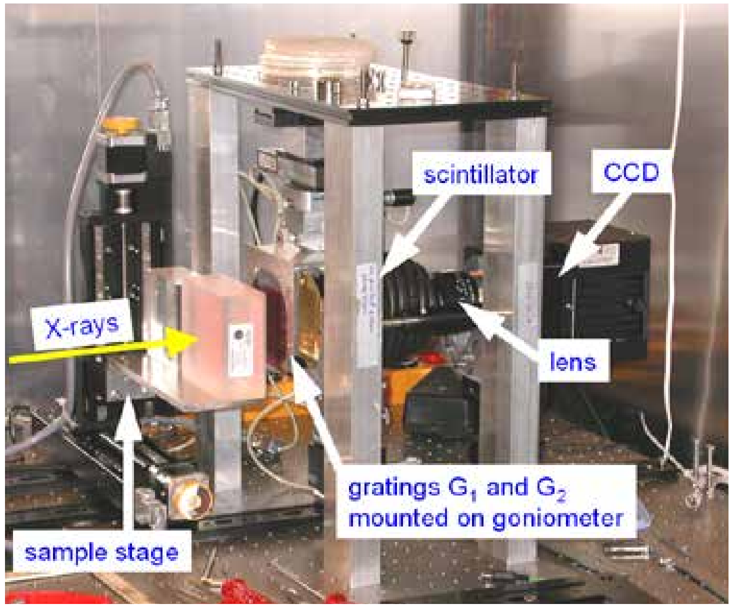
DPC on a X-ray tube

Amplitude Phase (gradient)



F. Pfeiffer et al., NATURE PHYSICS 2, (2006)

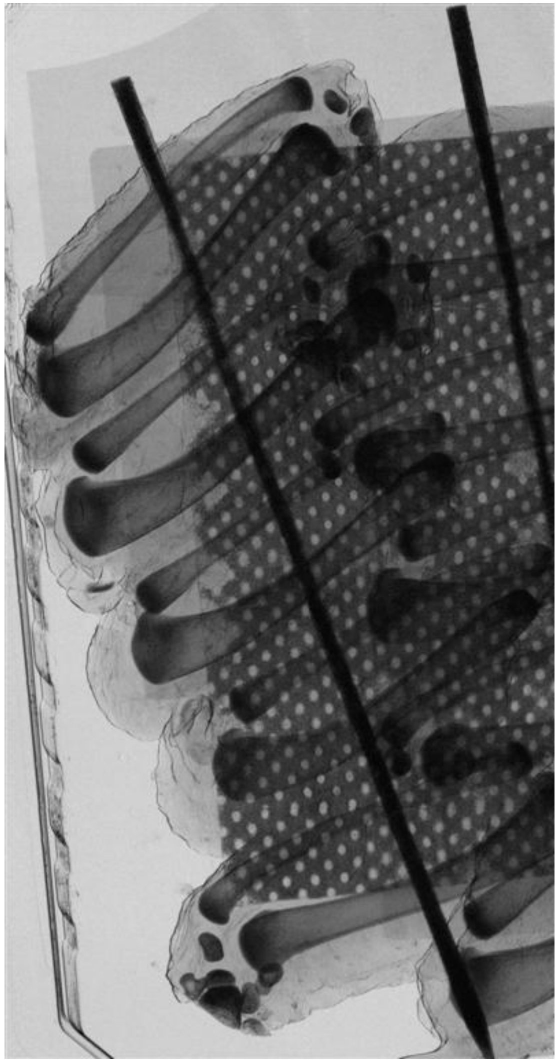




Advanced imaging of large samples

Absorption

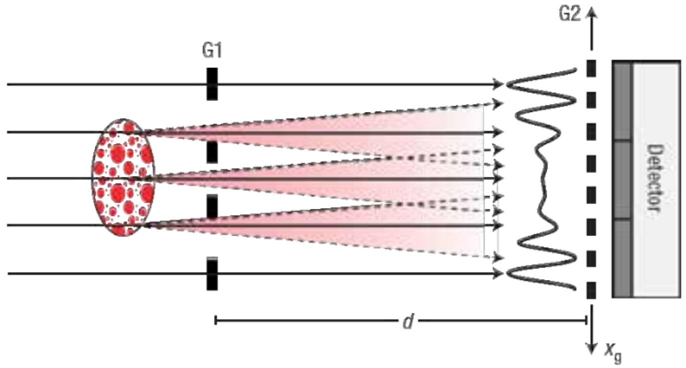
Differential Phase contrast

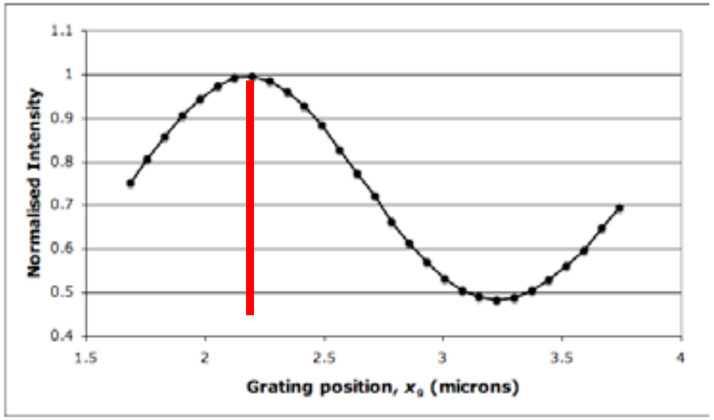


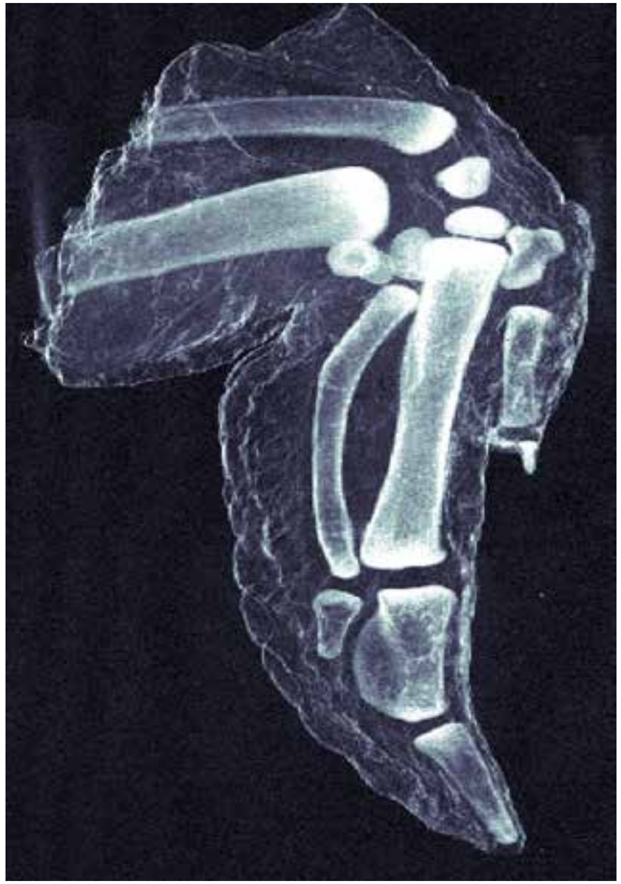
Dark Field

Data courtesy of Z. Wang, TOMCAT Group

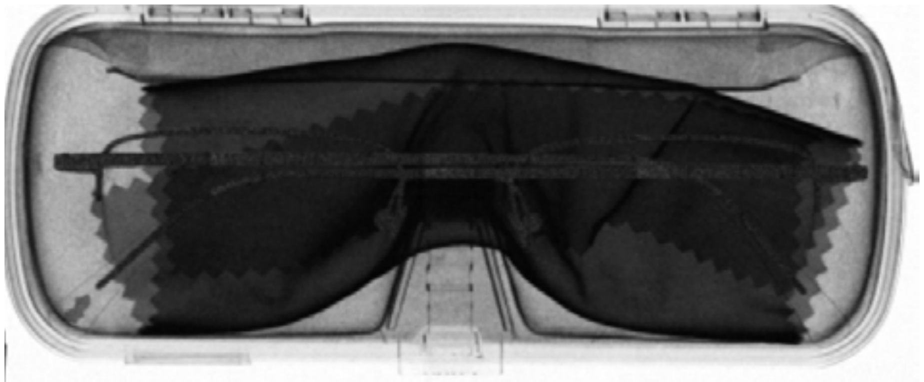
Absorption vs. dark-field imaging







Transmission image



Darkfield image

New radiological capabilities

Exploit these additional physical signals to improve (early) breast cancer detection

Absorption image
Conventional radiography
(since 1895…)

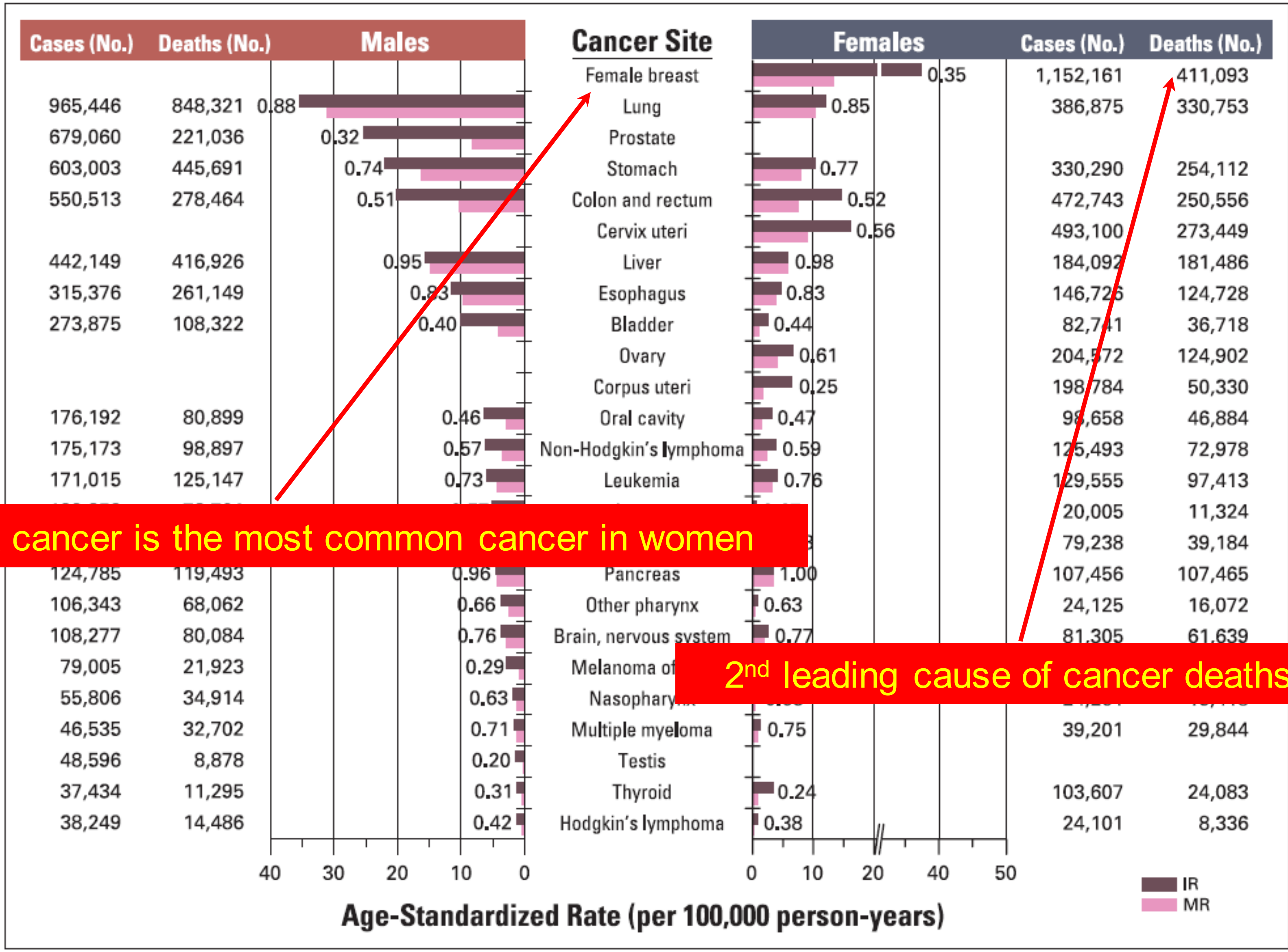
"Differential Phase image"

"Scatter image"

Index of refraction: $n = 1 \underbrace{- \delta}_{\text{Phase}} + \underbrace{i\beta}_{\text{Absorption}}$

Phase contrast mammography: why?

Worldwide annual number of cancer cases and cancer deaths, incidence rates and mortality rates

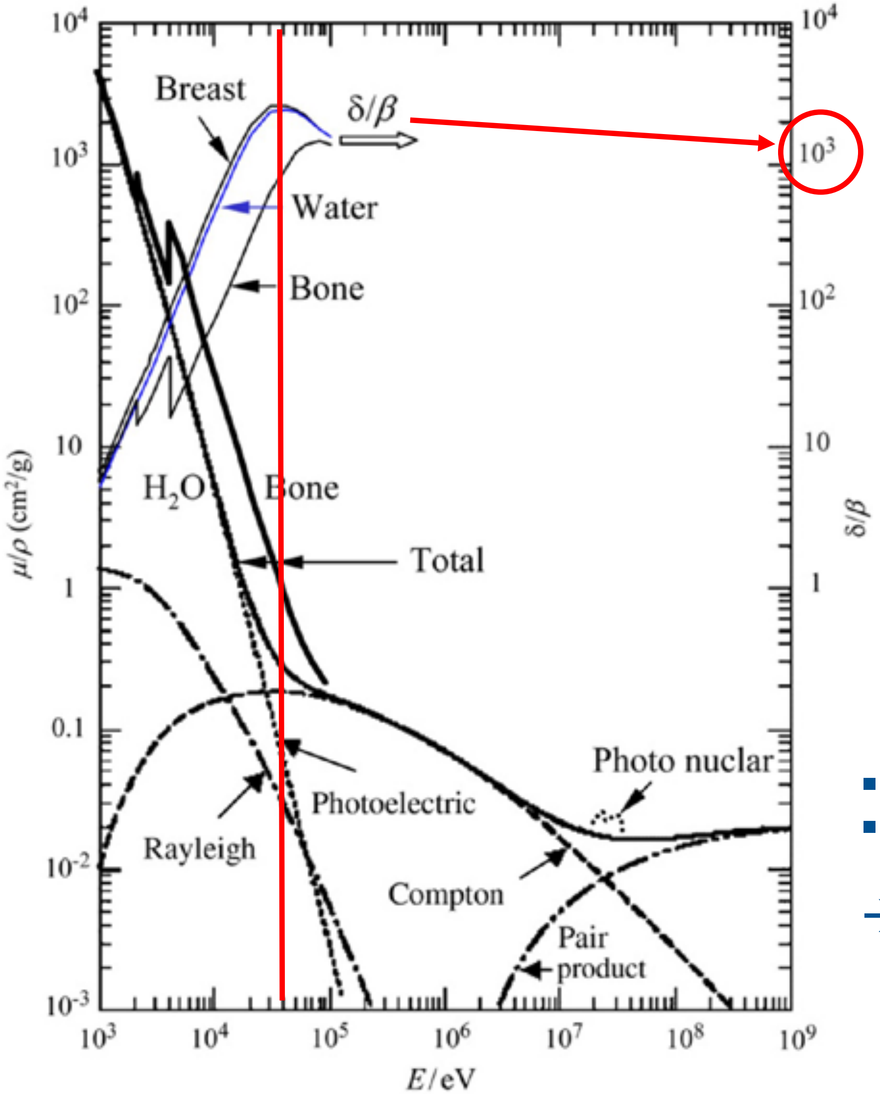


Breast cancer is the most common cancer in women

2nd leading cause of cancer deaths

F. Kamangar *et al.*, Journal of Clinical Oncology, 24(14), 2137-2150 (2006)

Towards clinical phase contrast mammography



Zhou et al., Physica Medica (2008) 24, 129-148

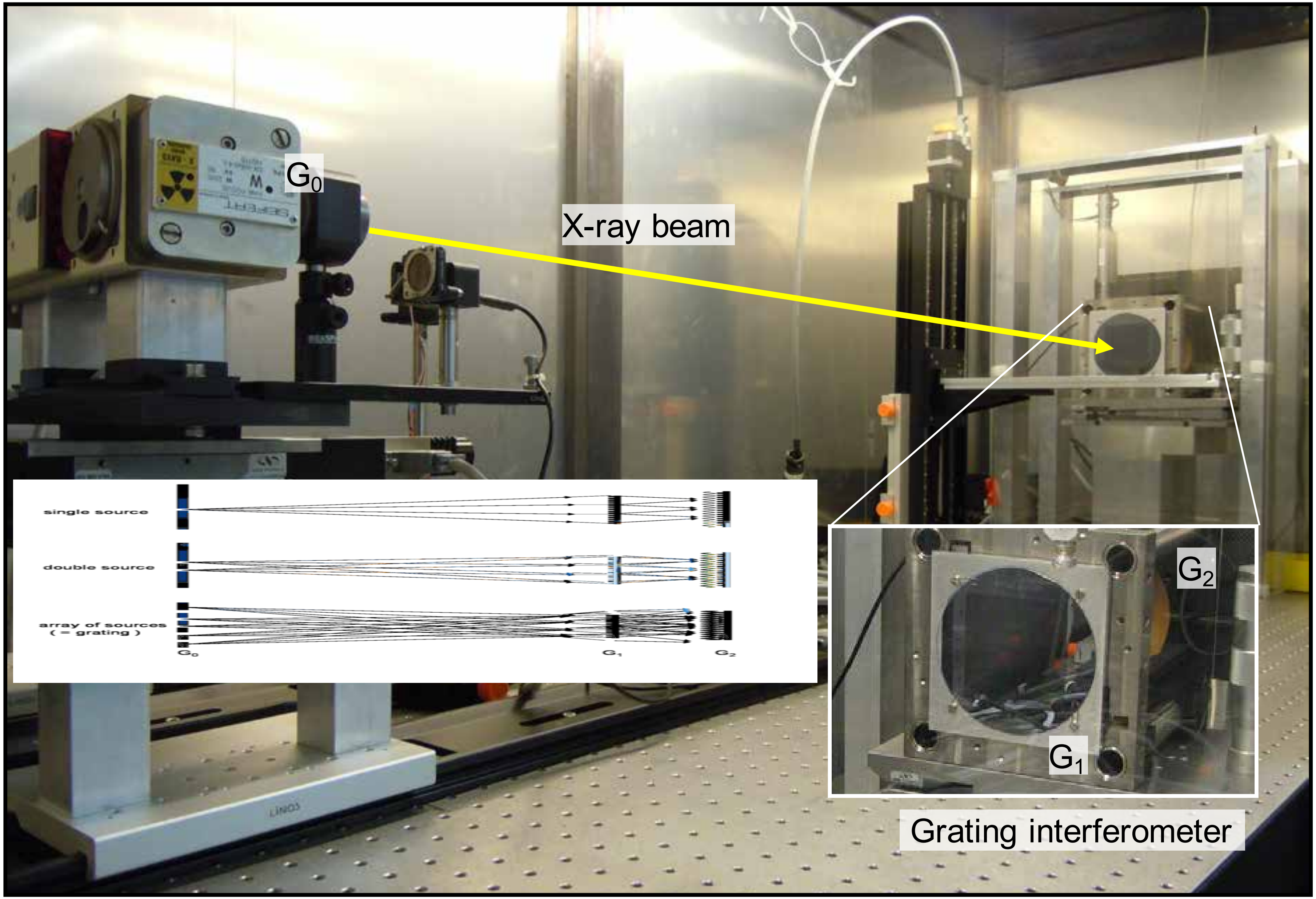
Index of refraction: $n = 1 - \underbrace{\delta}_{\text{Phase}} + \underbrace{i\beta}_{\text{Absorption}}$

- Working energy for mammography: 20-30 keV
- For 20-30 keV, $\delta/\beta > 1000$

→ When comparing various tissue samples, relative differences in angular deviations are larger than the corresponding relative changes in attenuation

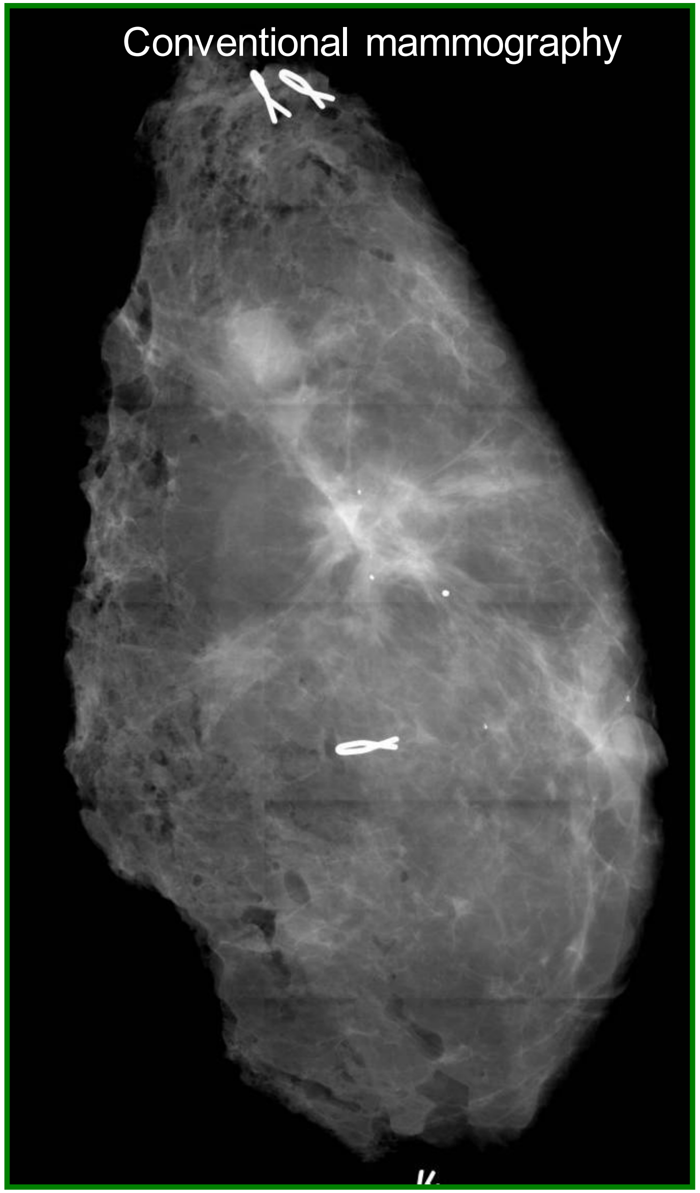
→ We expect improved diagnostic capabilities when compared to conventional methods

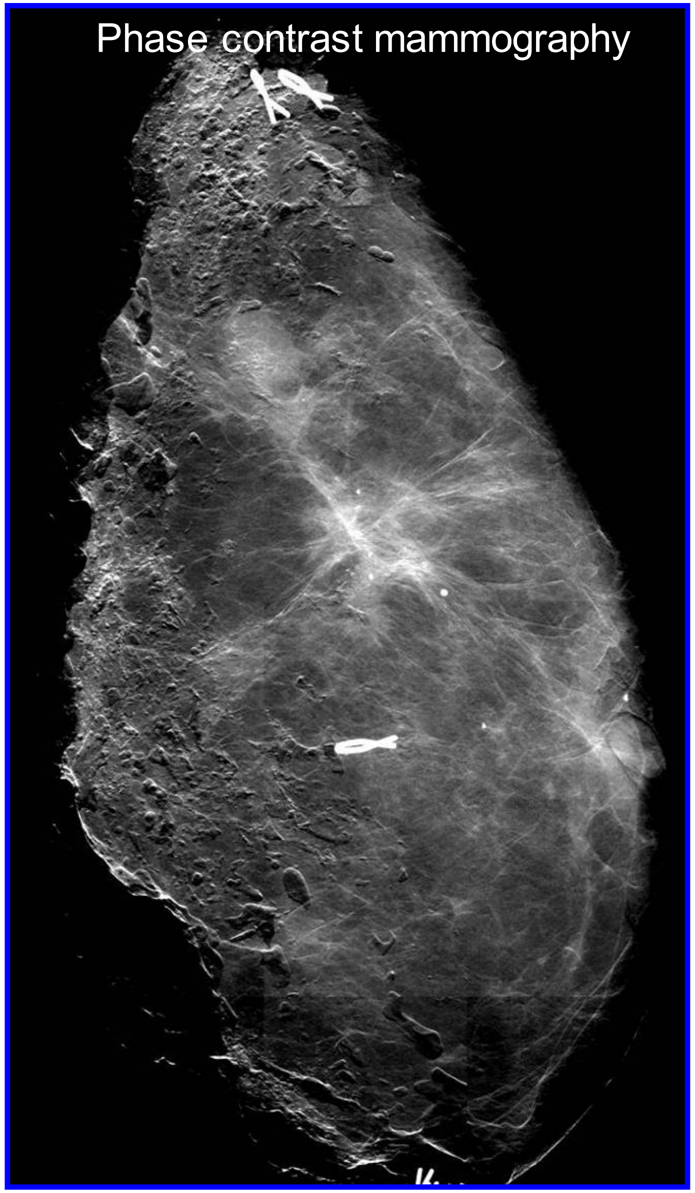
Phase contrast mammography demonstrator



M. Stampanoni et al., Investigative Radiology, 46,801, (2011)

Differential phase signal enhances *spiculations* visibility





M. Stampanoni et al., Investigative Radiology, 46,801, (2011)

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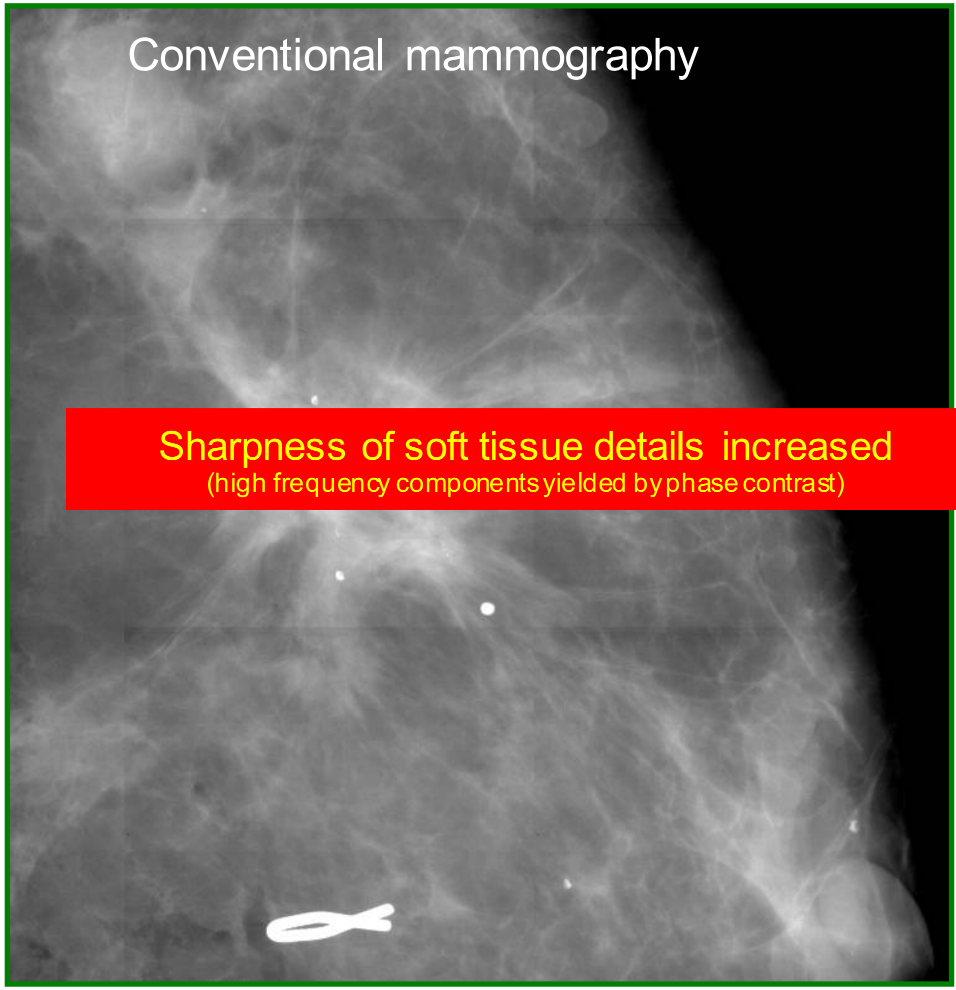
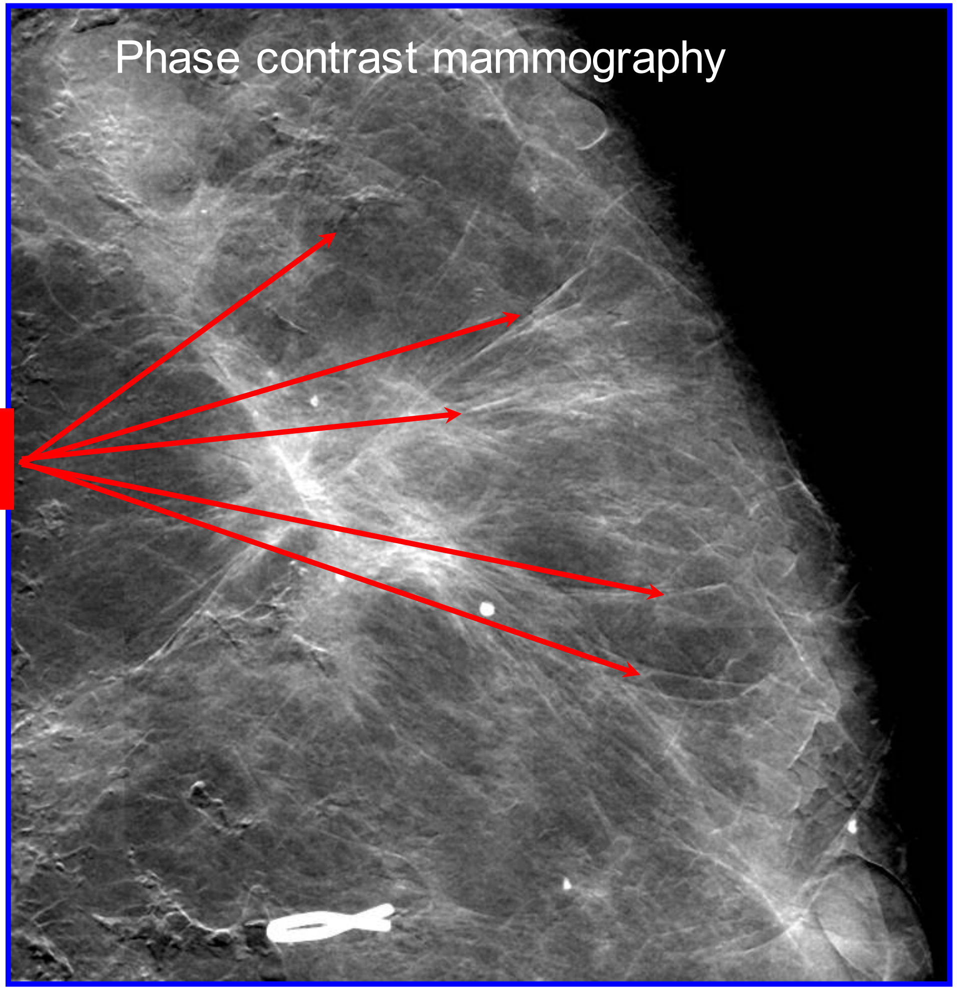




Sharpness of soft tissue details increased
(high frequency components yielded by phase contrast)

Same dose!

M. Stampanoni et al., Investigative Radiology, 46,801, (2011)

Phase contrast enhanced mammography

ORIGINAL ARTICLE

A Study on Mastectomy Samples to Evaluate Breast Imaging Quality and Potential Clinical Relevance of Differential Phase Contrast Mammography

TABLE 2. Statistical Outcome Showing the Criteria Under Which mammoDPC Is Superior to Absorption-Based Mammography

Evaluated Criteria (mammoDPC Is Superior)	*P**	IQR
General quality of image	<0.001	2–3†
Sharpness and lesion delineation	<0.001	2–3
Delineation of surface structures	<0.001	2–3
Sharpness of microcalcifications	<0.001	2–2
General visibility of microcalcifications	<0.001	2–3
Potentially clinically relevant information	<0.001	4–5‡
Identification of spiculations	<0.015§	

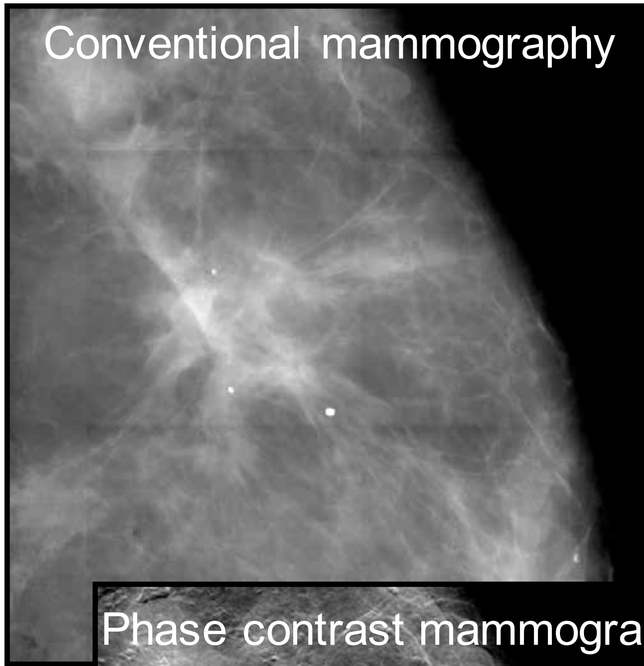
*$P < 0.005$ is considered to be significant with Bonferroni correction.

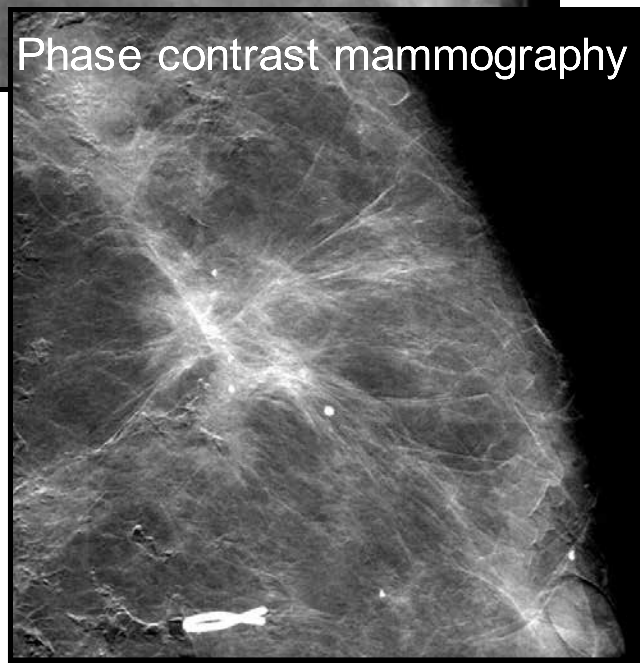
†2 being "superior" and 3 being "equivalent" quality.

‡4 being "11% to 20% superior" and 5 being "1% to 10% superior."

§This criterion was evaluated in study 2. $P < 0.025$ is significant with the Bonferroni correction.

IQR indicates interquartile range; mammoDPC, phase contrast-enhanced mammography.

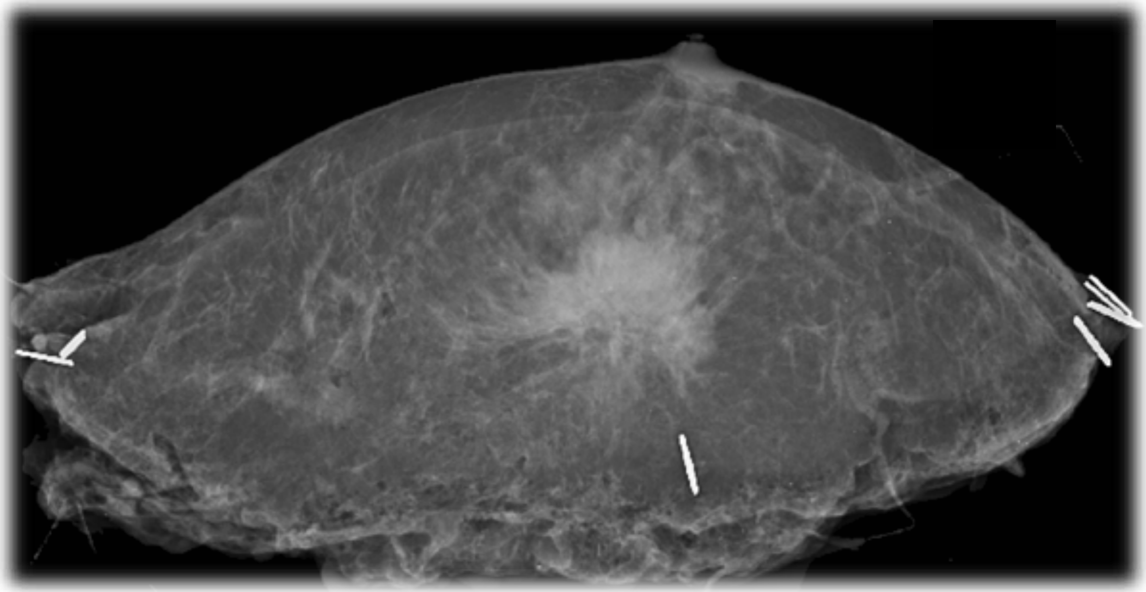


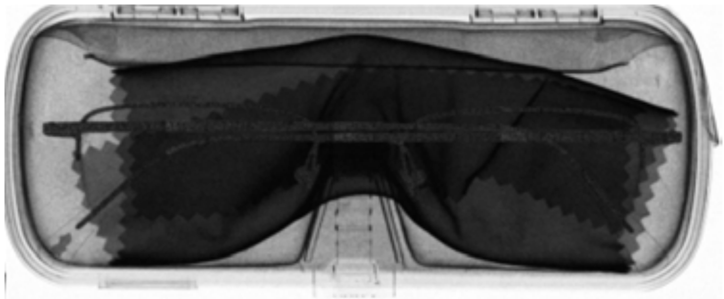


N. Hauser et al., Investigative Radiology 49 (3) 2014

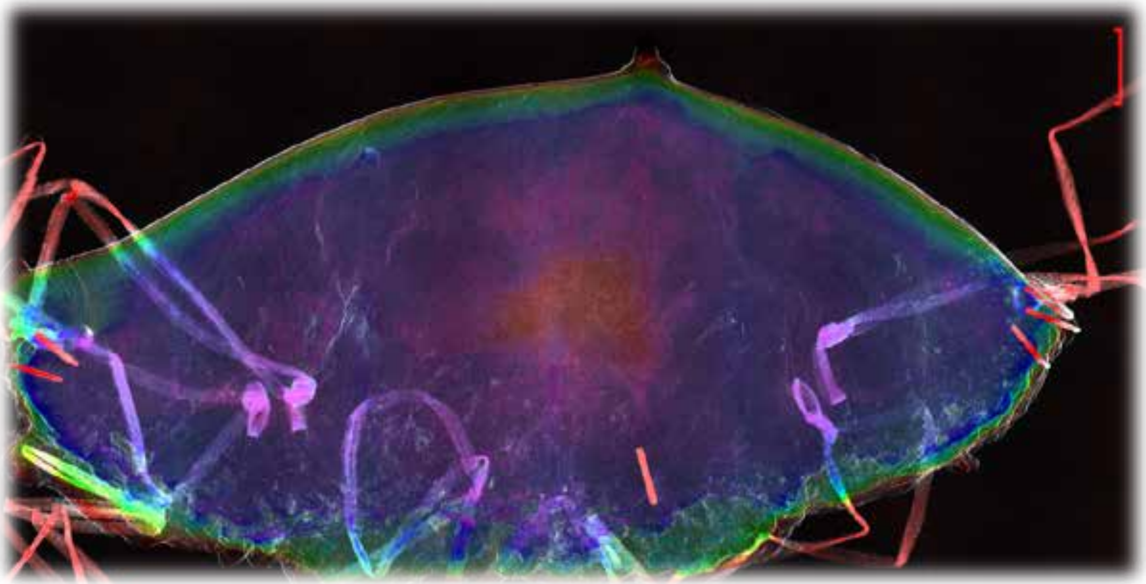
Dark field signals…

Absorption

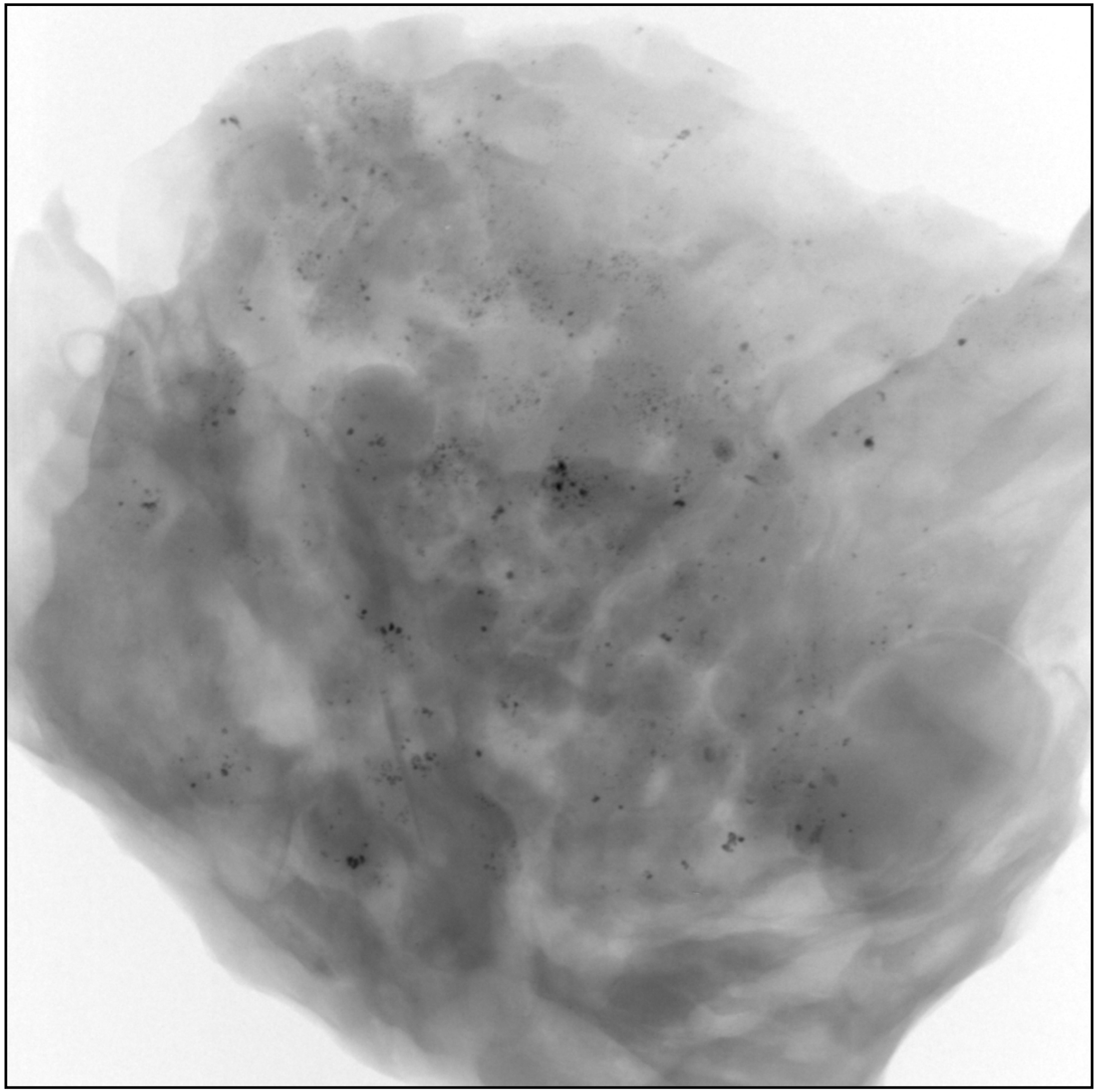


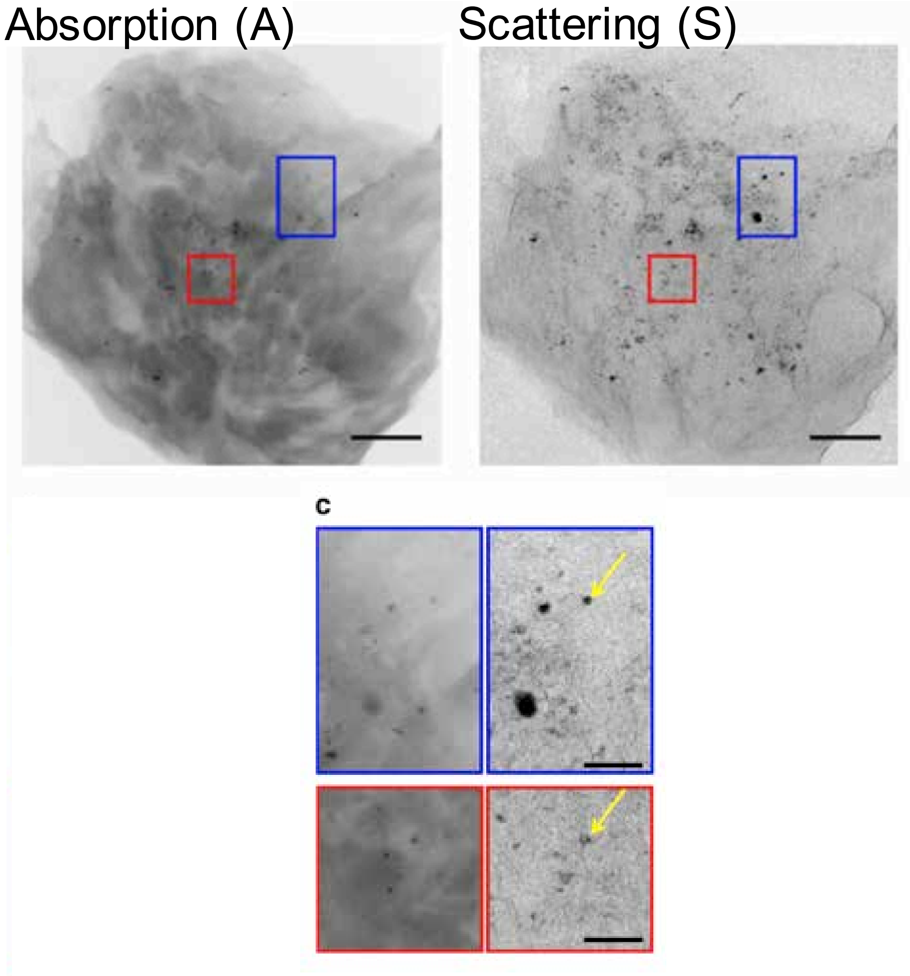


Scattering



Dark-field: the key for microcalcs discrimination?



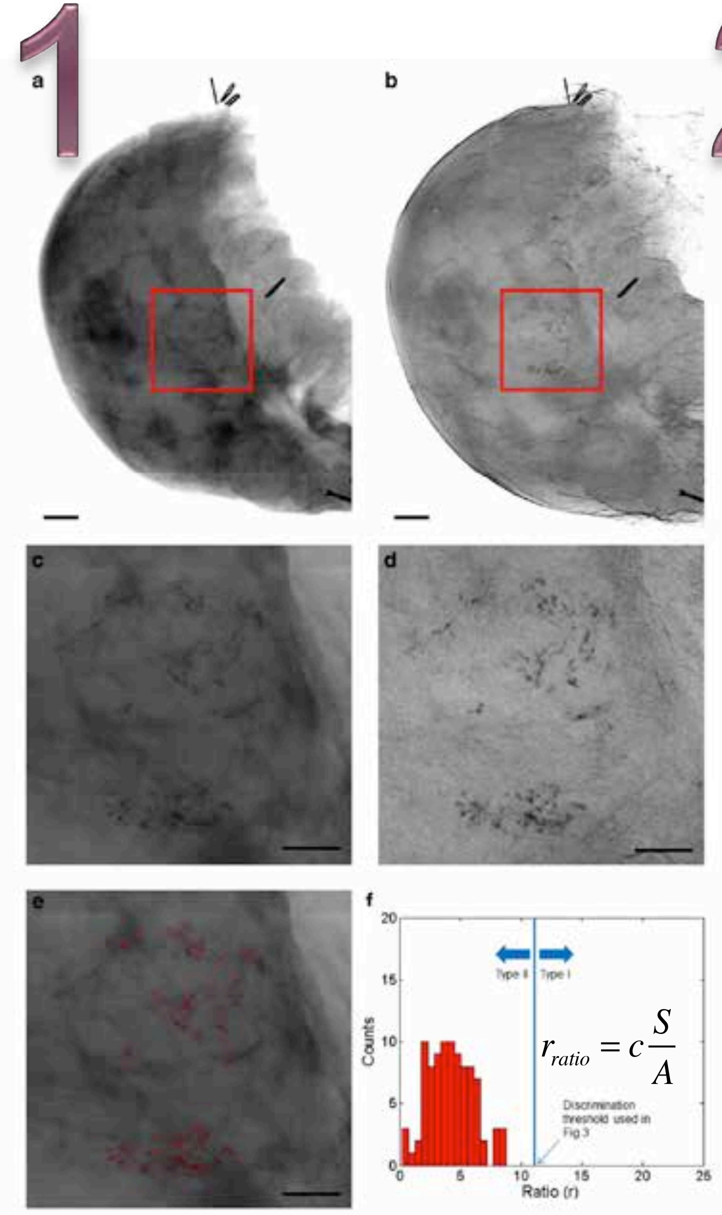


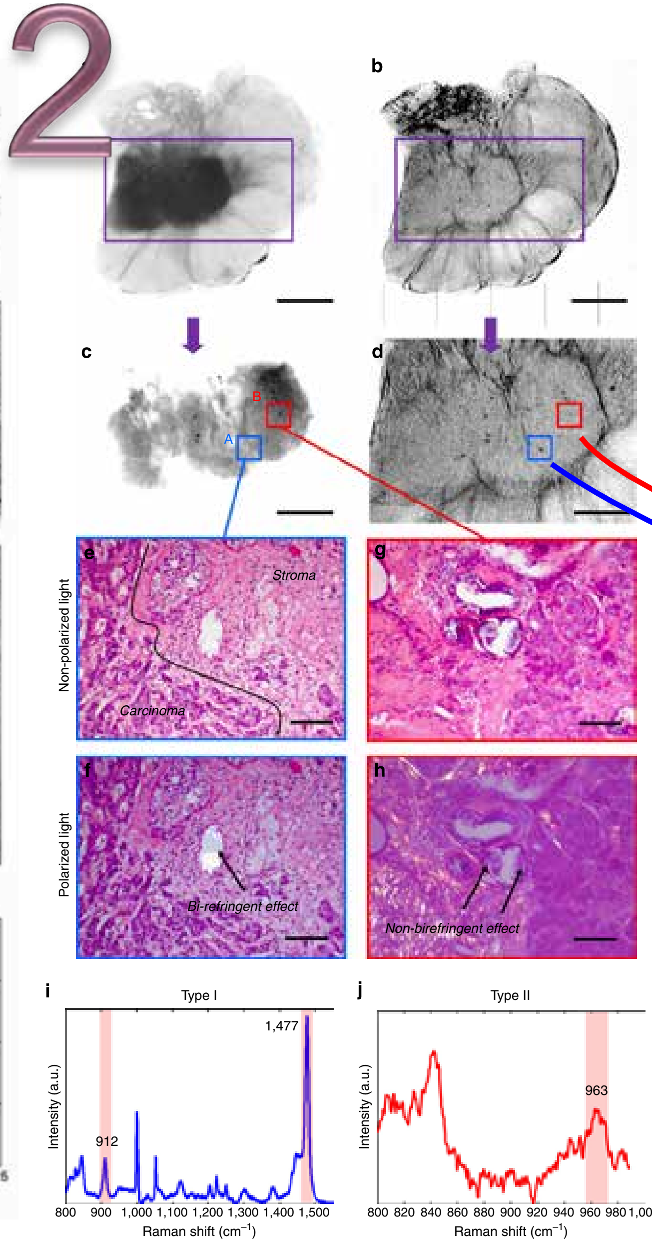
Observation: Opposite behaviors of A and S

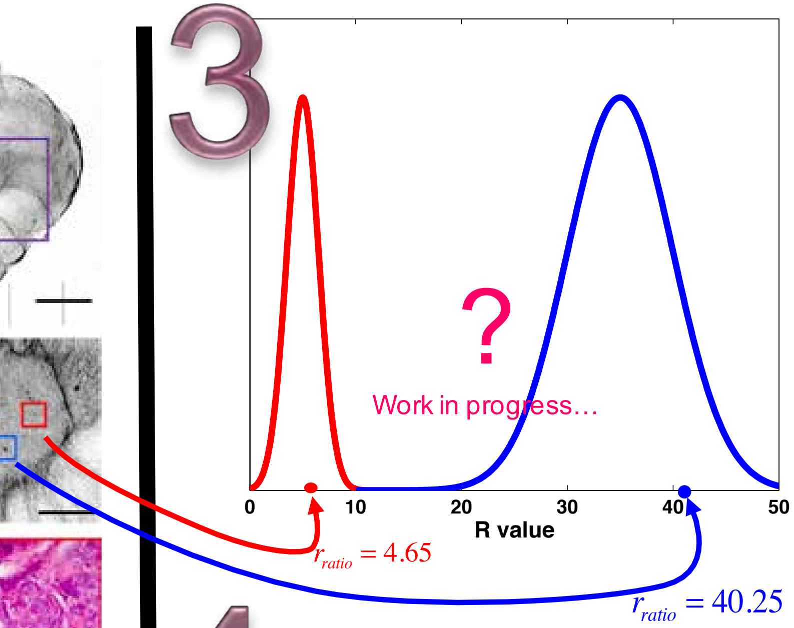
Type I: calcium oxalate dehydrate, $CaC_2O_4(2H_2O)$
Type II: calcium hydroxyapatite, $Ca_5(PO_4)_3(OH)$

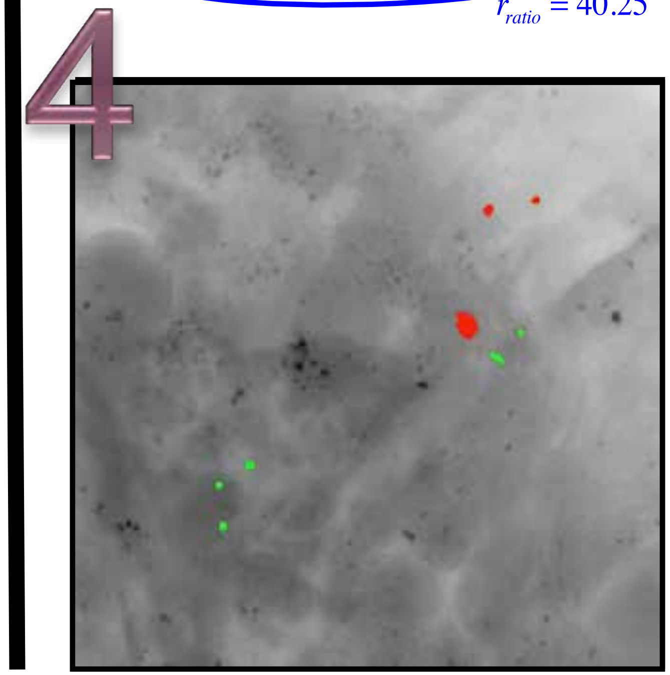
Can we discriminate between Type I (benign) and Type II (malignant) micro-calcifications *non-invasively* ?

Our hypothesis



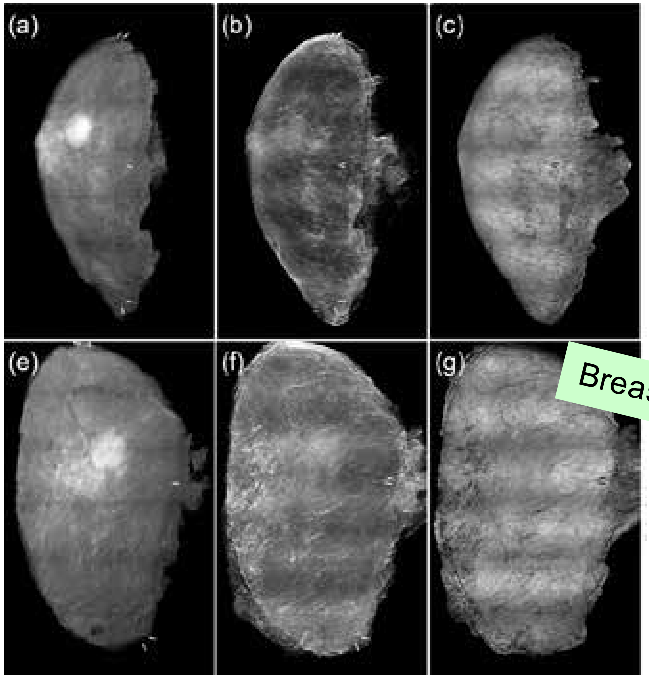




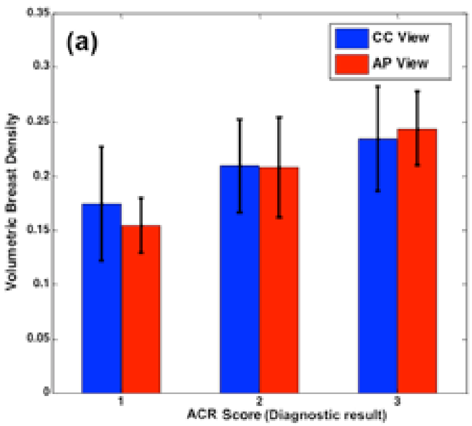


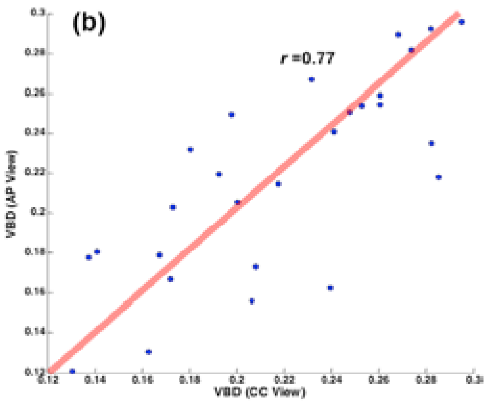
Z. Wang et al., Nat. Communications 5:3797 (2014)

Dark-field signal: the key for improved diagnostic?



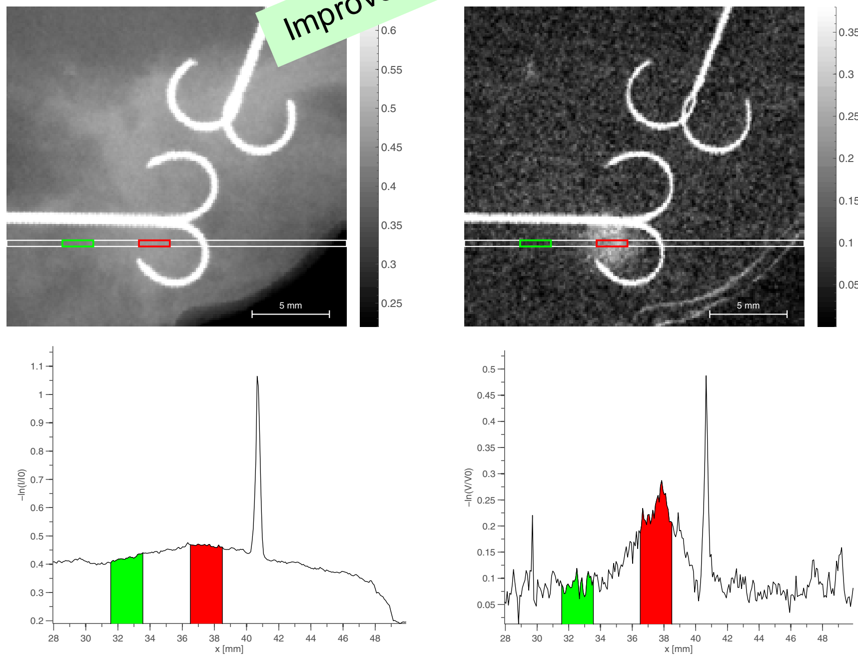
Breast density estimation?





Wang et al, PMB 2015

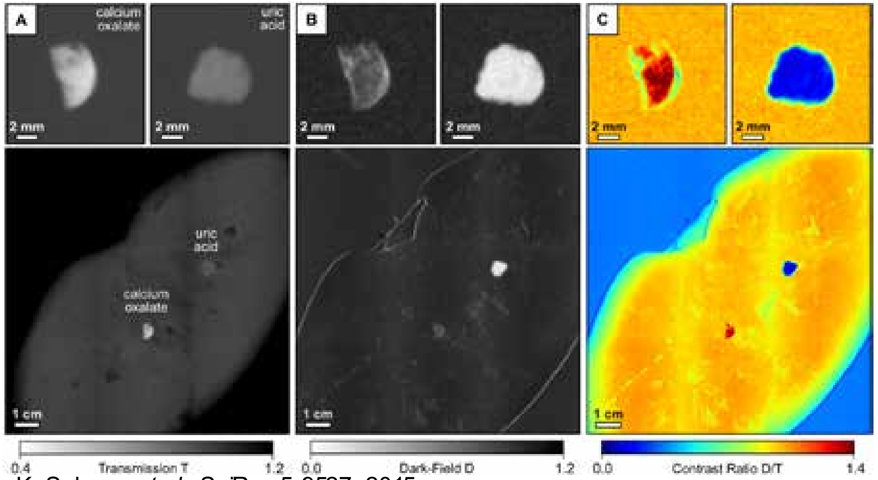
Improved tumor localization?



Michel et al., PMB 2012

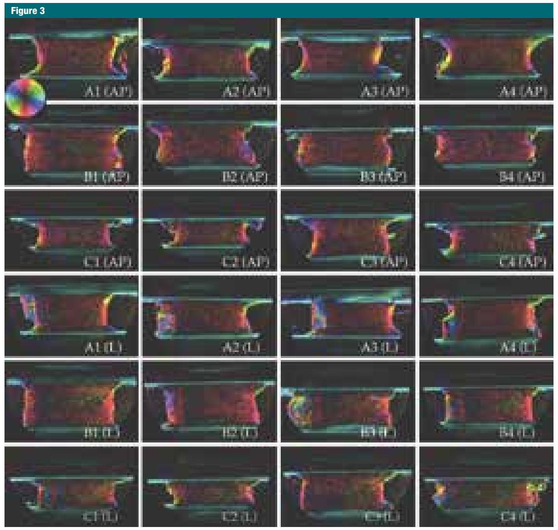
Clinical applications of dark-field imaging

Non-invasive kidney stone differentiation



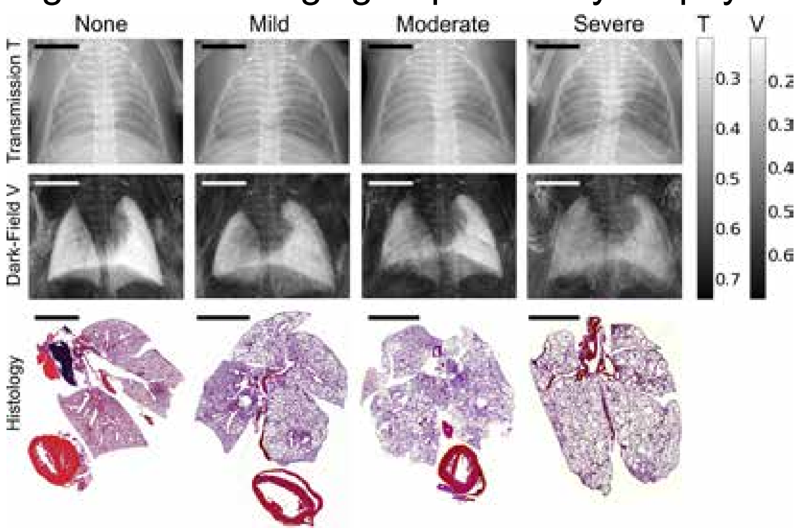
K. Scherer *et al.*, SciRep 5:9527, 2015

Prediction of bone failure load with XVR



E. Eggl et al., Radiology 275:2, 2015

Diagnosis and staging of pulmonary emphysema

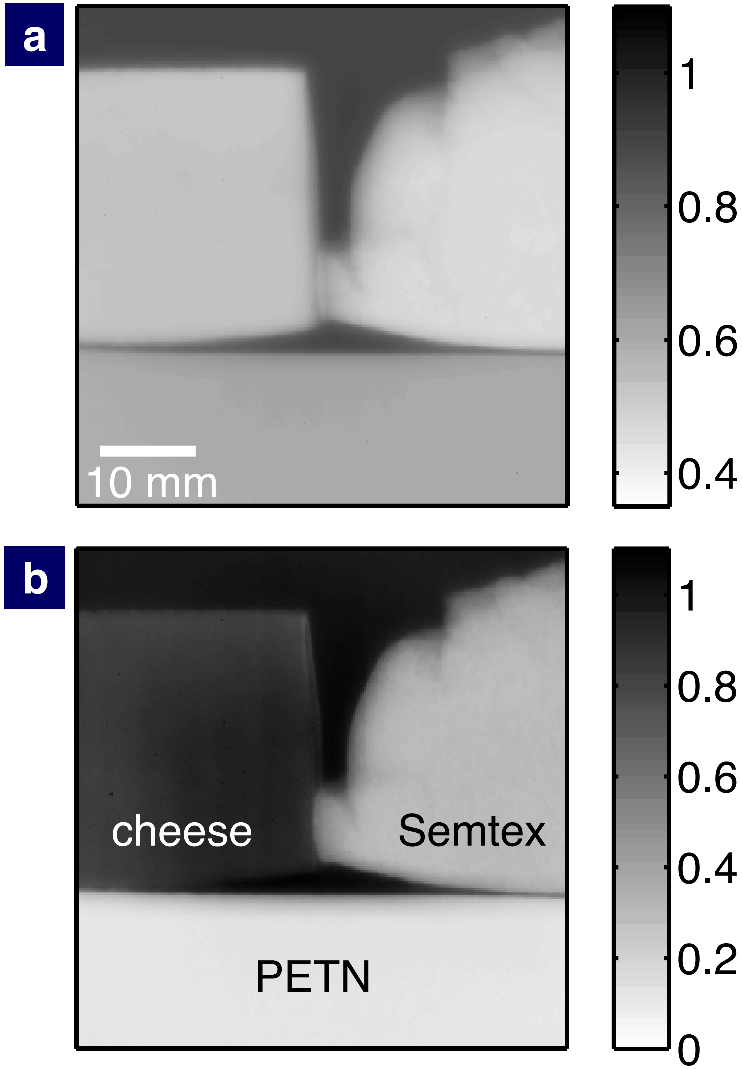


K. Hellbach, Investigative Radiology, 50(7):430-5, 2015

Cheese or not cheese? That's the (homeland) problem

250g of SEMTEX are sufficient to fully destroy an airliner

F. Pfeiffer et al., Nature Methods, 7, 134 - 137 (2008)



Different granular microstructures distinguish high-performance explosives from good cheese…