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# Medical imaging with synchrotron radiation

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# “ Synchrotron Radiation and Phase Contrast Imaging (PCI) ”



*Rigon L. (2014) x-Ray Imaging with Coherent Sources.  
In: Brahme A. (Editor in Chief) Comprehensive Biomedical Physics,  
vol. 2, pp. 193-220. Amsterdam: Elsevier.*

# 120 years of radiology

“



1895

- Roentgen's discovery (1895) has been **immediately** translated to clinics
  - [three weeks later it was] “used successfully by European surgeons in locating bullets and other foreign substances in human hands, arms and legs and in diagnosing diseases of the bones in various parts of the body”.

*The New York Sun*

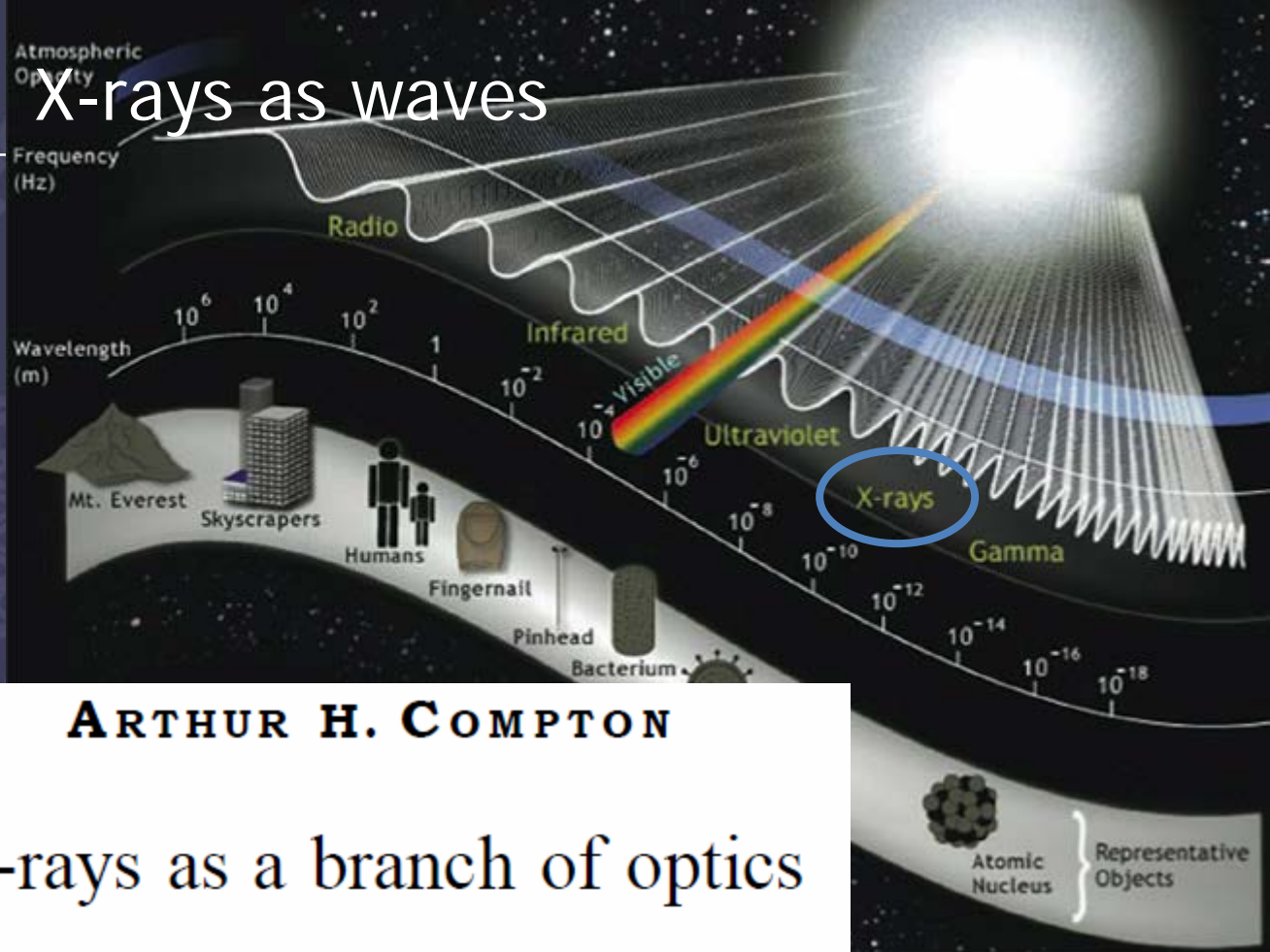
- Nowadays (120 years later):
  - image quality has much improved
  - radiation dose has been substantially reduced
  - but the physical principle remains the same, namely **X-rays absorption**



Today

”

# X-rays as waves



**ARTHUR H. COMPTON**

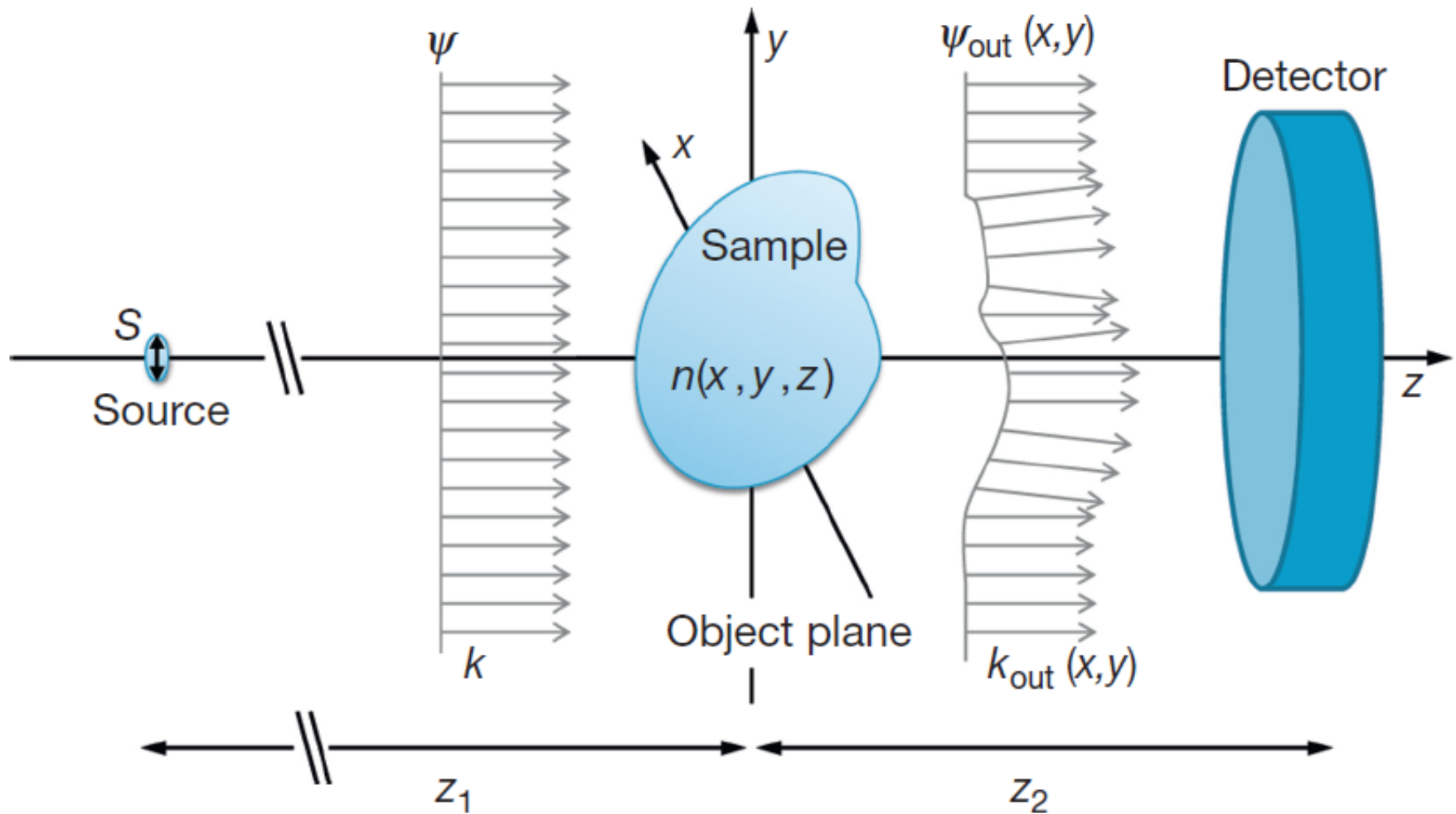
**X-rays as a branch of optics**

*Nobel Lecture, December 12, 1927*

“there is hardly a phenomenon in the realm of light whose parallel is not found in the realm of X-rays”



# X-rays as waves



# Phase-Sensitive X-Ray Imaging

- Refraction index for hard X-rays

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

phase shift      absorption

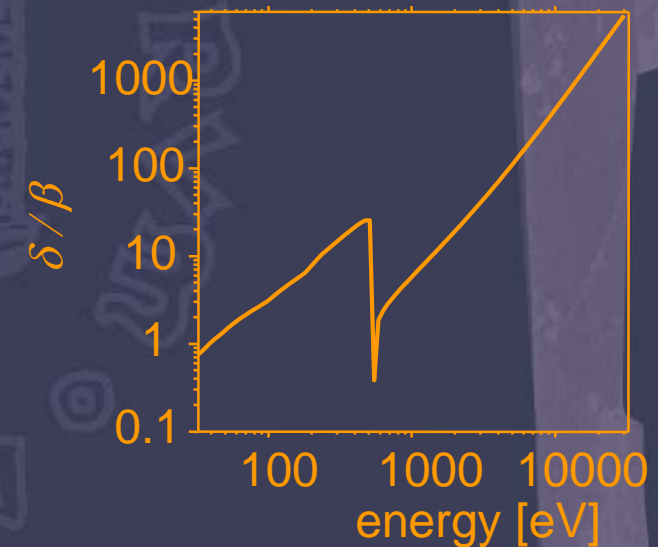
$$\mu = \frac{4\pi\beta}{\lambda}$$

- For low-Z elements  $\delta \gg \beta$

phase shift effects  $\gg$  absorption

$$\delta \propto (1/E)^2 \sim 10^{-6}$$

$$\beta \propto (1/E)^3 \sim 10^{-9}$$



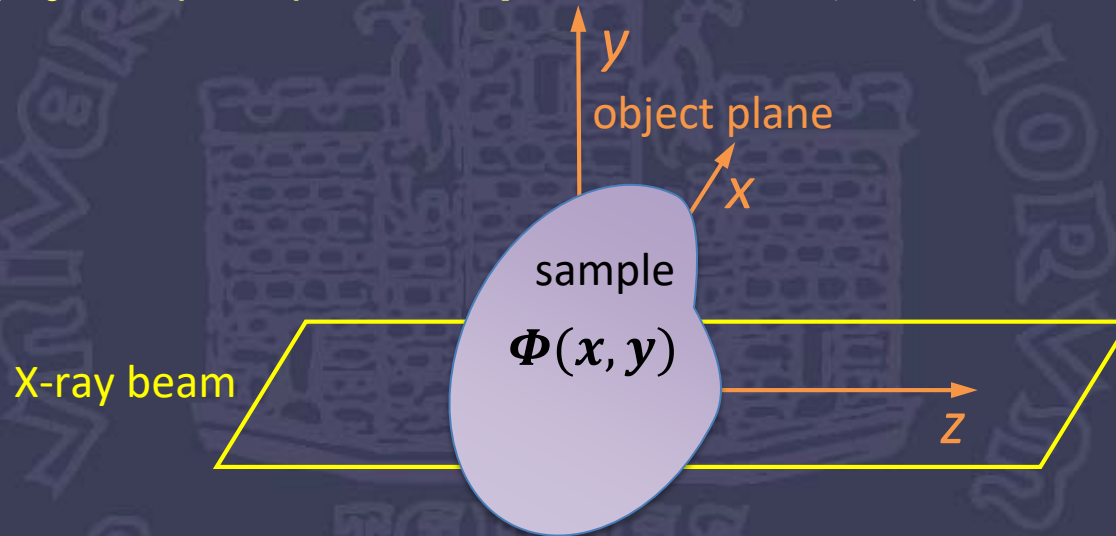
Fitzgerald, R. (2000). Phase-sensitive X-Ray imaging. *Phys. Today* **53**, 23–27.

Zhou, S.-A. and Brahme, A. (2008). *Phys. Med.* **24**, 129–148.

Bravin, A., Coan, P. and Suortti, P. (2013). *Phys. Med. Biol.* **58**, R1-R35.

# Phase Contrast Imaging Techniques

- X-rays **Phase Contrast** Imaging:
  - The physical principle is the **phase shift**  $\Phi(x, y)$  of the X-ray wave



$$\phi(x, y) = -k \int \delta(x, y, z) dz \cong -r_0 \lambda \int \rho_e(x, y, z) dz$$

- some particular **phase-sensitive techniques** are needed to transform the phase effects into a modulation of intensity on the detector

# Beamlines for Medical Imaging

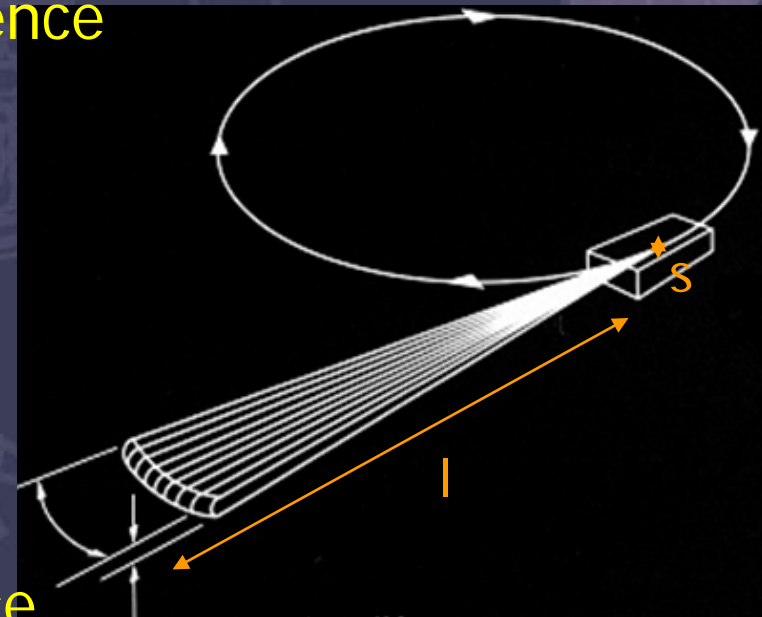
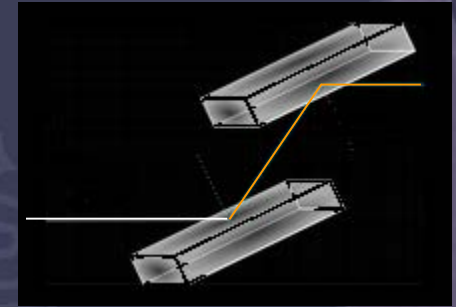
Beamline	SR Facility
X15A	NSLS (Brookhaven, NY, USA)
SYRMEP	Elettra (Trieste, Italy)
ID17	ESRF (Grenoble, France)
ID19	ESRF (Grenoble, France)
BL14C	PF-KEK (Tsukuba, Japan)
BL20B2	Spring8 (Hyogo, Japan)
BL20XU	Spring8 (Hyogo, Japan)
TOMCAT	SLS-PSI (Villigen, Switzerland)
BMIT-05B1-1	CLS (Saskatoon, Canada)
BMIT-05ID-2	CLS (Saskatoon, Canada)
Imaging and Medical Beamline	Australian Synchrotron (Melbourne, VIC, AUS)
BL10W1	SSRF (Shanghai, PRC)
I13L	Diamond (Oxfordshire, UK)



# Characteristics of synchrotron radiation (SR)

“

- High x-ray intensity on a broad energy range
  - Tunable monochromatic beam
  - High degree of **temporal coherence**
- Laminar beam geometry (the beam is naturally collimated)
  - High brilliance
- Small source size and large source-to-sample distance
  - High degree of **spatial coherence**



”

# My naive approach to coherence

- An imaging system has a certain degree of coherence if it can produce observable effects of interference and/or diffraction
- **Temporal (or longitudinal) coherence**
  - energy spectrum of the imaging system
  - the narrower the spectral bandwidth, the higher the coherence
- **Spatial (or lateral) coherence**
  - source size and geometry of the system
  - the smaller the source size and the larger the source-to-sample distance, the higher the coherence
- Perfectly coherent system: monochromatic & point-like source
- The degree of coherence of a real source depends on how well it approximates these two requirements



“

# Free-space propagation

”

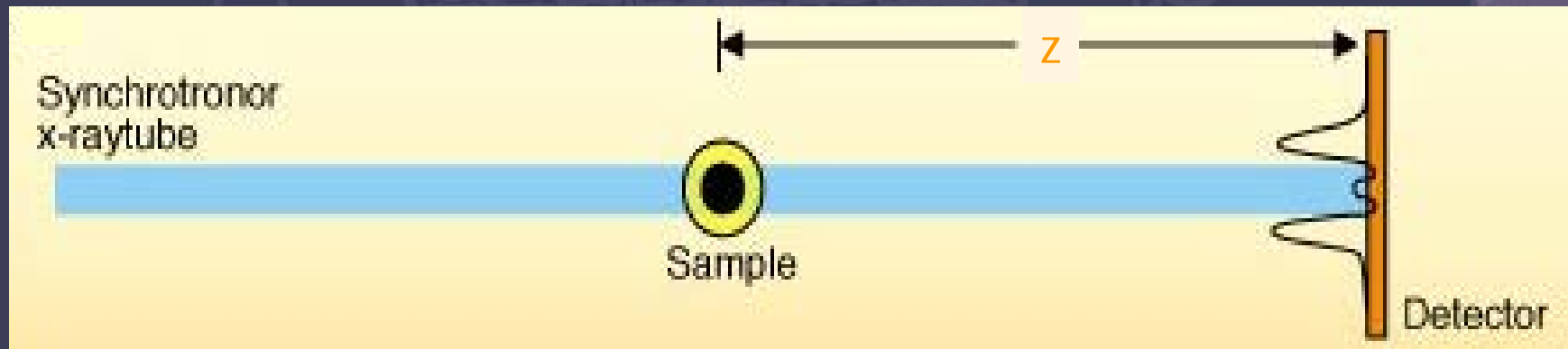
Propagation-based phase-contrast Imaging  
In-line phase-contrast Imaging



# From phase shift to image contrast

“

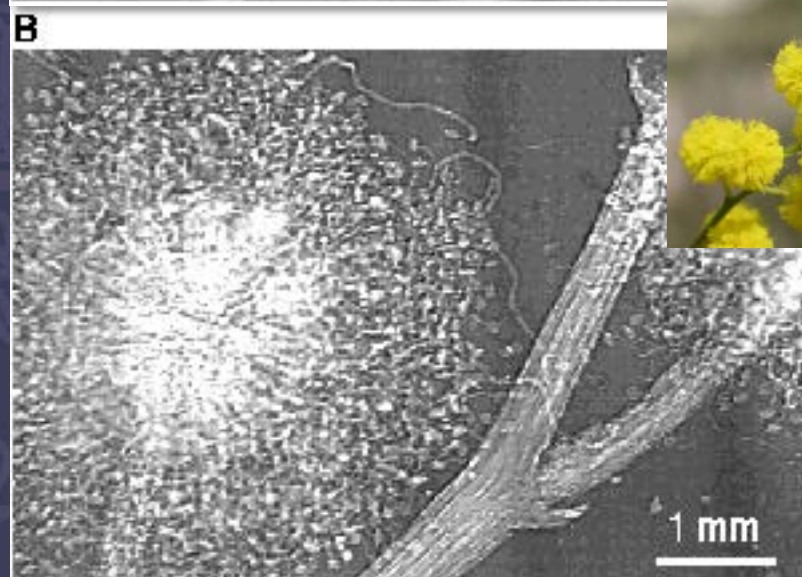
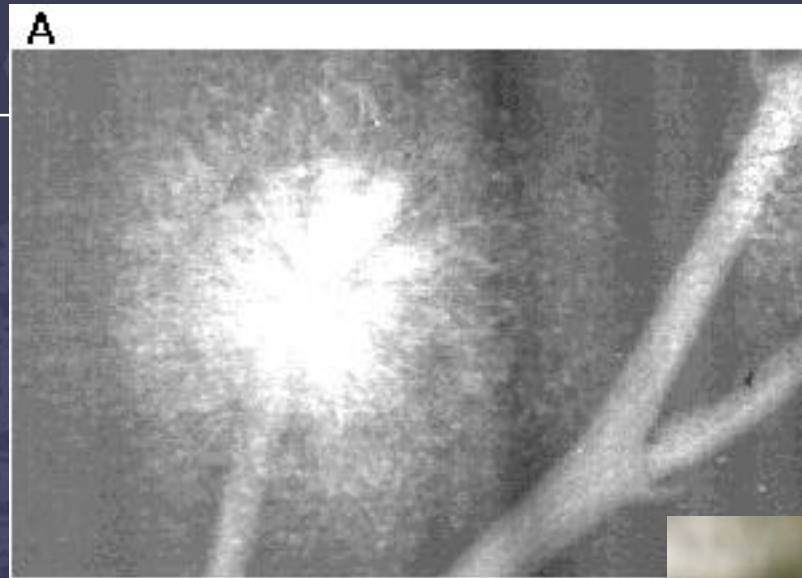
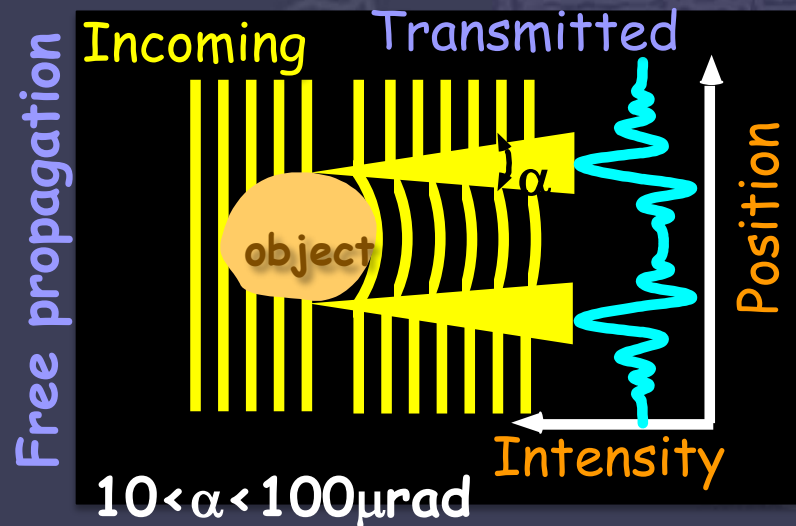
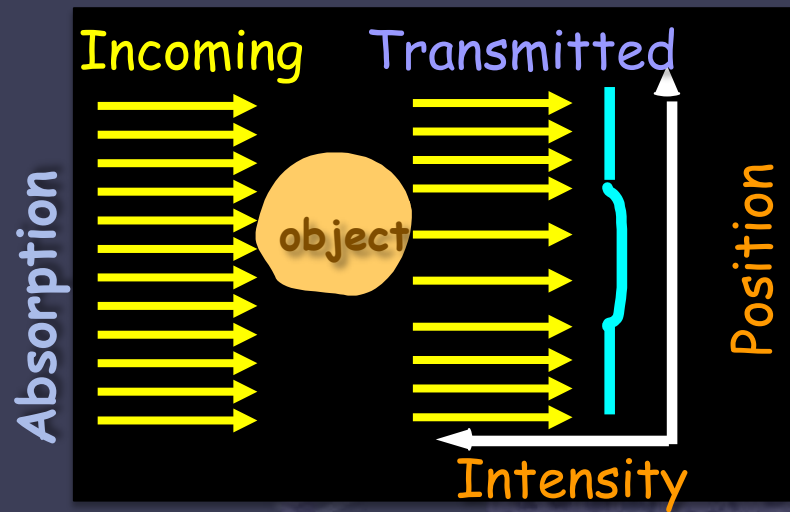
- Propagation-based phase-contrast Imaging  
(Free-space propagation)  
(In-line phase-contrast Imaging)  
is the simplest method, provided that:
  - the beam is sufficiently spatially coherent
  - the spatial resolution of the detector is sufficiently high



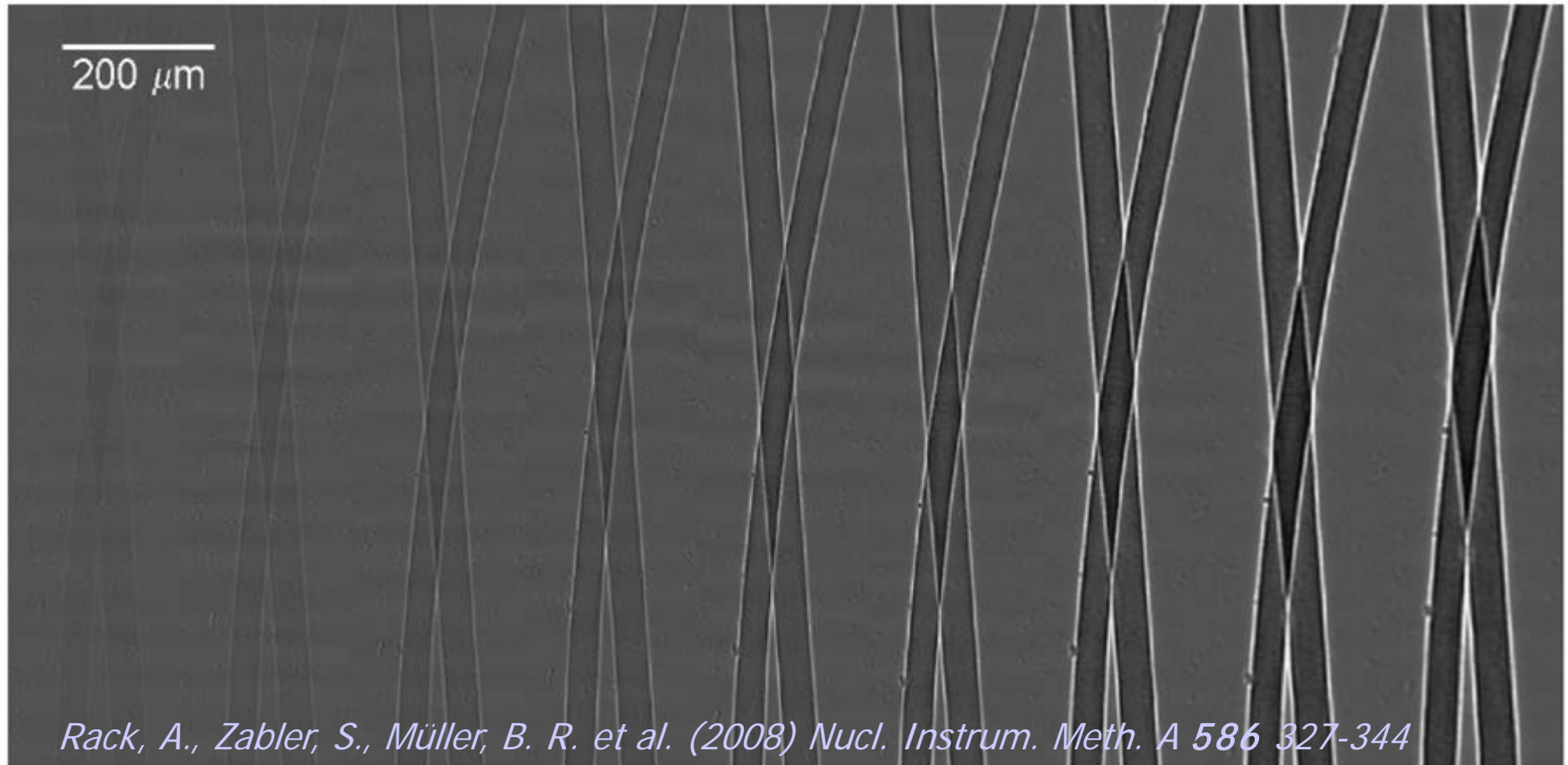
- The detector is set to a certain distance  $z$
- The recorded signal is proportional to the second (spatial) derivative of the phase term:  $\nabla_{xy}^2 \Phi(x, y)$

”





# The influence of sample-to-detector distance



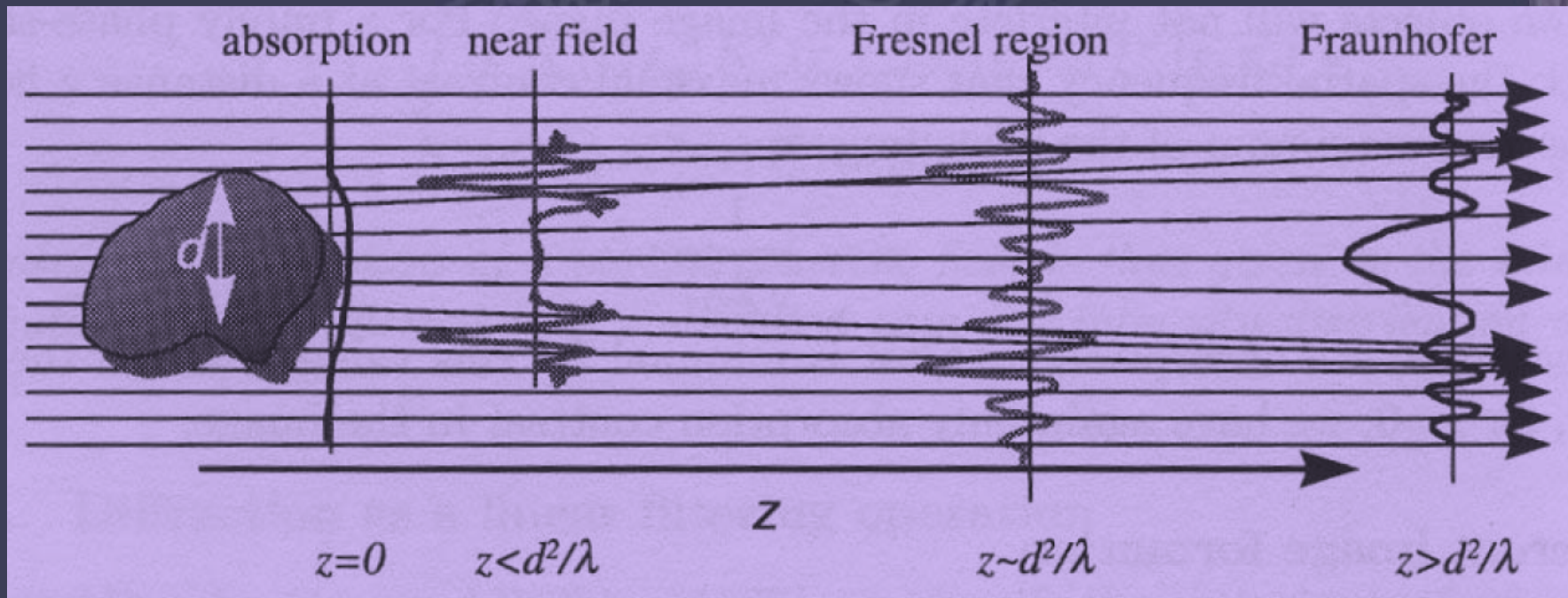
20mm



Distance

1140mm

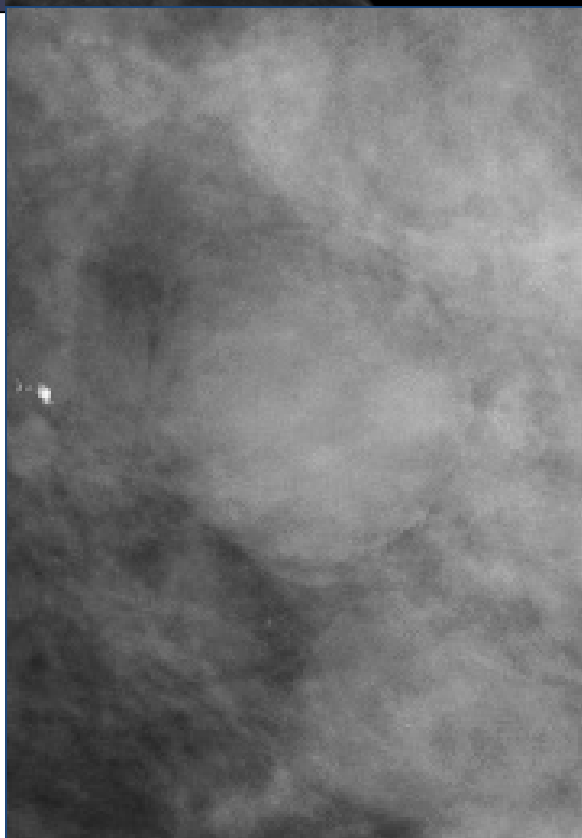
# Diffraction Regimes



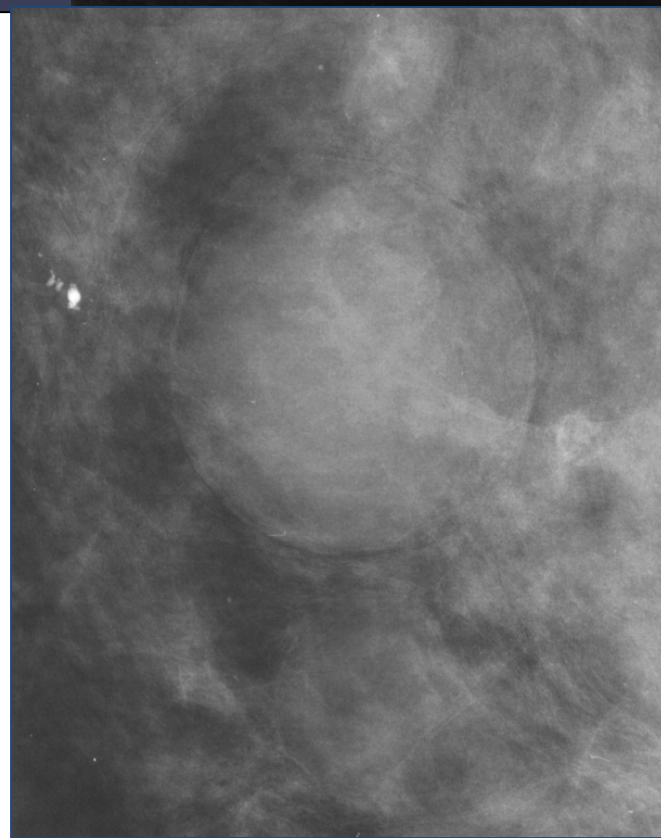
- near field: edge enhancement
- intermediate region: Fresnel diffraction or holographic regime
- far-field region: Fraunhofer diffraction (Coherent Diffractive Imaging)



# Application to Mammography (*in vivo*)



Conv



PhC



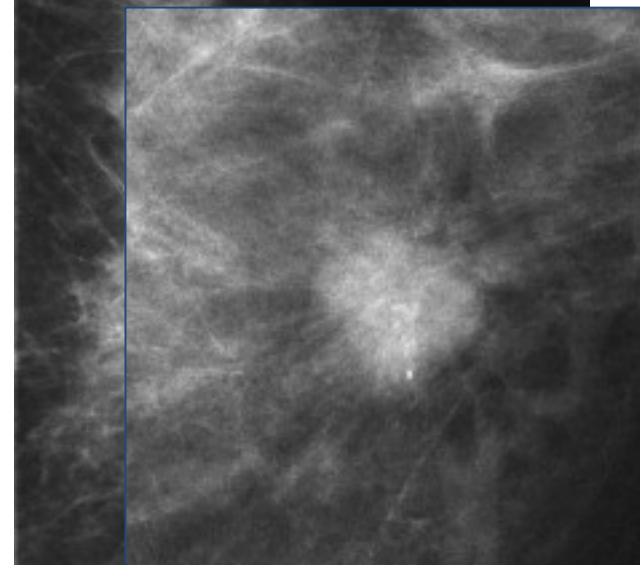
*Castelli, E., Tonutti, M., Arfelli, F. et al. (2011). Radiology 259, 684–694.*



# Application to Mammography (*in vivo*)



Conv

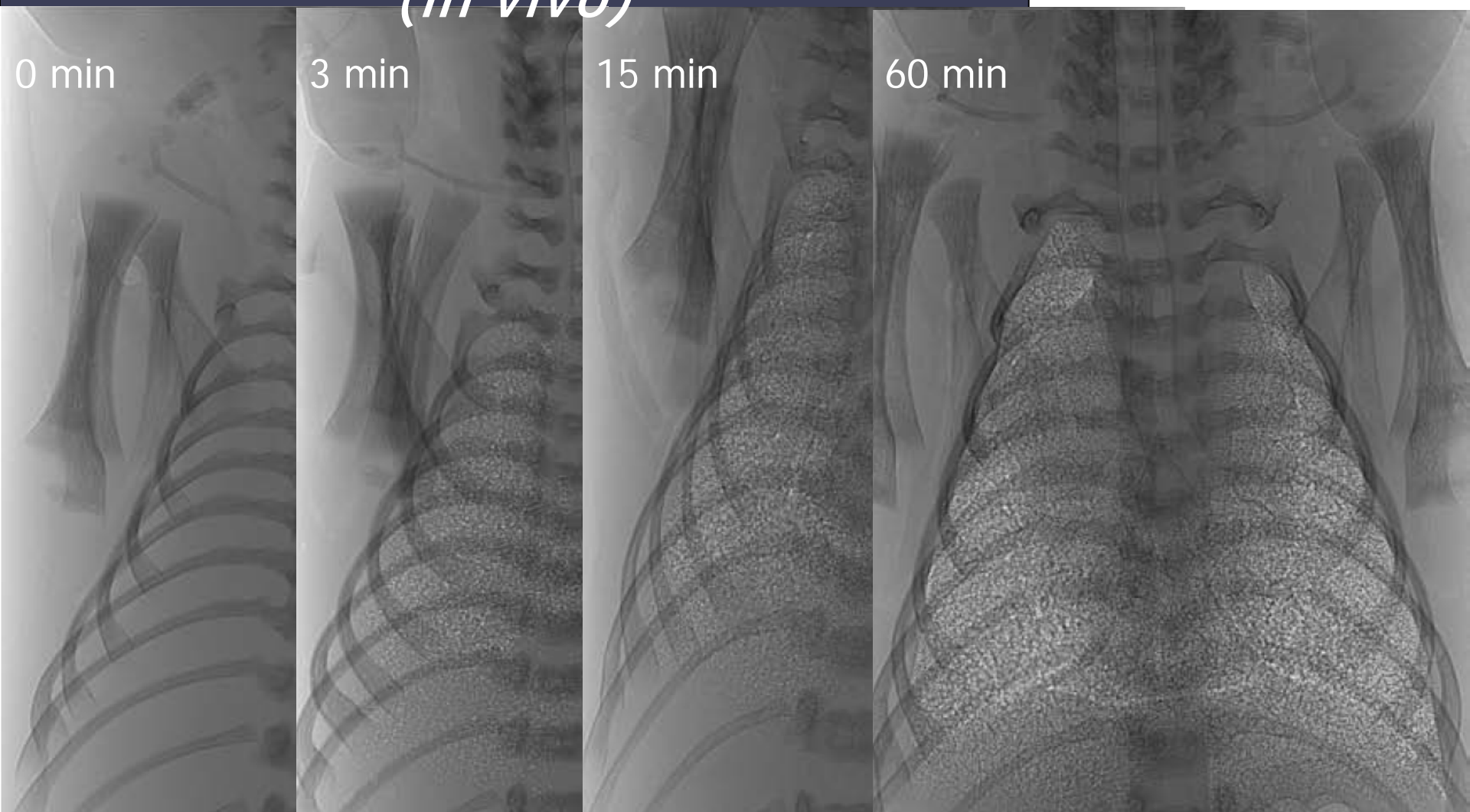


PhC



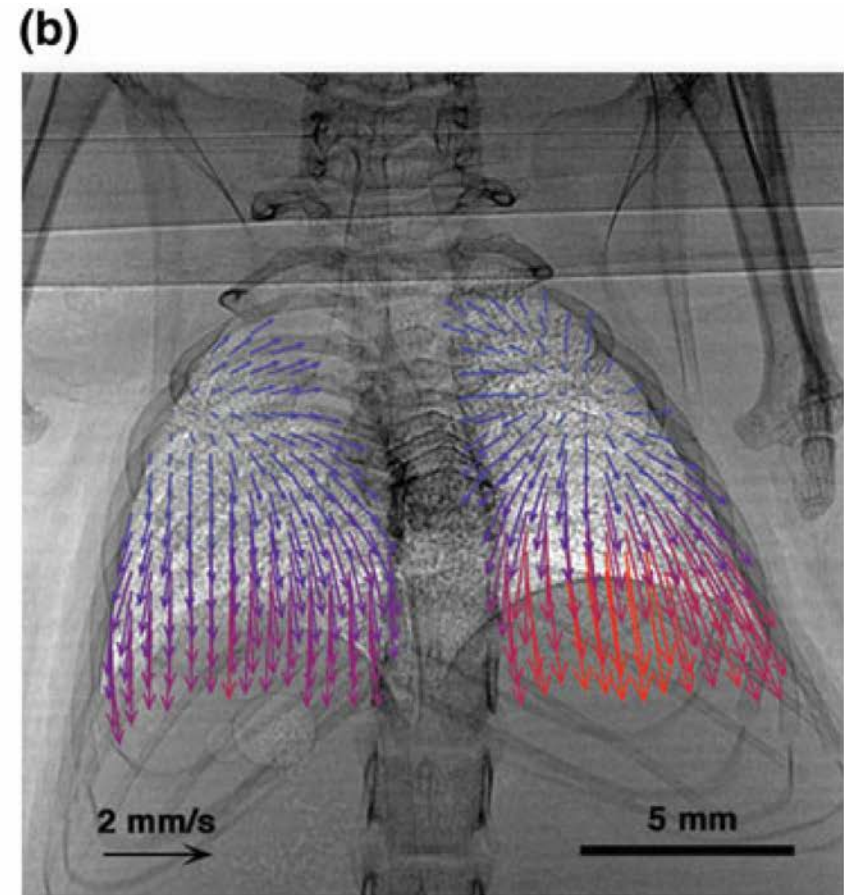
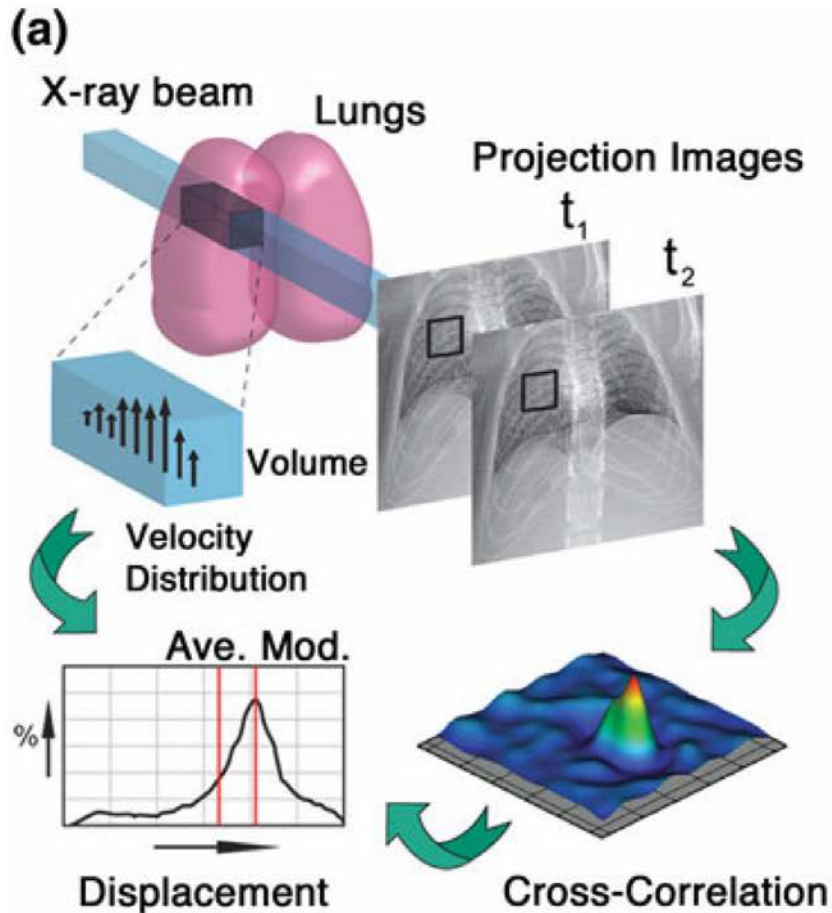
Castelli, E., Tonutti, M., Arfelli, F. et al. (2011). *Radiology* 259, 684–694.

# Lung Liquid Clearance at Birth (*in vivo*)



Hooper S B, Kitchen M J, et al. (2009). *Clin. Exp. Pharmacol. Physiol.* 36, 117–125

# Mouse model of cystic fibrosis (*in vivo*)



Fouras A, Allison B J, Kitchen M J et al. (2012)  
*Annals of Biomedical Engineering* 40, 1160–1169.

# Limitations and Requirements

“

- Spatial coherence of the beam
- Spatial resolution of the detector
  - Enough resolution to detect interference fringes (edge-enhancement)
- Exposure time related to beam intensity
- Attempt to implement it into clinics:
  - Konica-Minolta Regius 190 Pureview CR System
  - <http://www.konicaminolta.com/healthcare/technology/phasecontrast>
  - Source size 100 / 300  $\mu\text{m}$
  - 1.75x magnification (65 cm + 49 cm)
  - 43.75  $\mu\text{m}$  sampling pitch (25  $\mu\text{m}$  in the de-magnified image)

”



“

# Phase retrieval

”



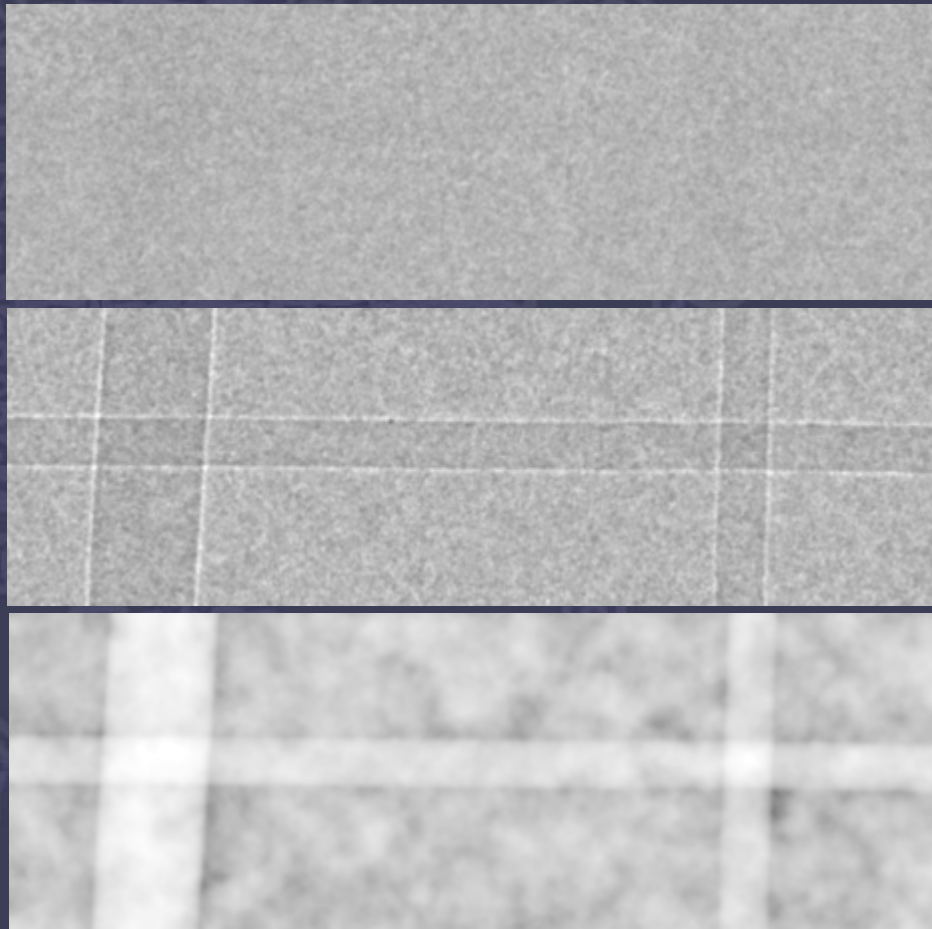
# From phase shift to image contrast

- “ – While the PB-PCI signal is proportional to  $\nabla^2_{xy} \Phi(x,y)$ ,  
Phase retrieval allows to recover  $\Phi(x,y)$

absorption  
(neglibile)

PB-PCI  
 $\nabla^2_{xy} \Phi(x,y)$

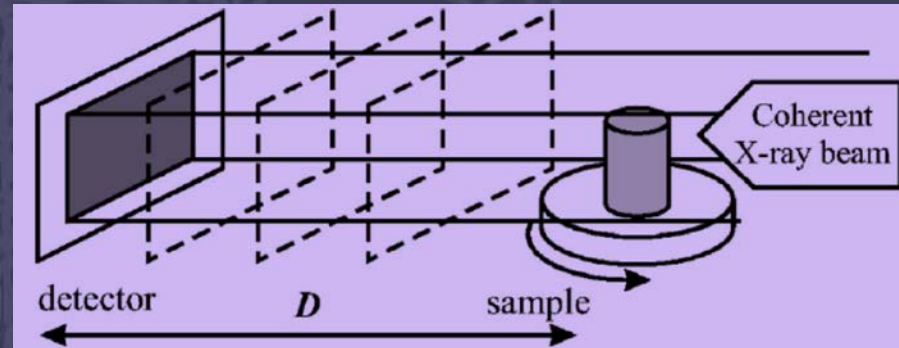
PB-PCI +  
phase retrieval  
 $\Phi(x,y)$



”

# Phase Retrieval: Methods

- “
- Phase retrieval is an inverse (and ill-posed) problem
  - In general, at least two images are needed (the more the better)
    - at different distances
    - at different energies



- Single image methods (highly desirable in CT) are possible for
  - pure-phase object (weak absorbing object)
  - phase-attenuation duality ( $\delta$  is proportional to  $\beta$ )
- Different approaches
  - direct methods (fast but more prone to noise/artifacts)
  - indirect (iterative) methods (slow but more robust – can take into account some *a priori* information)

”

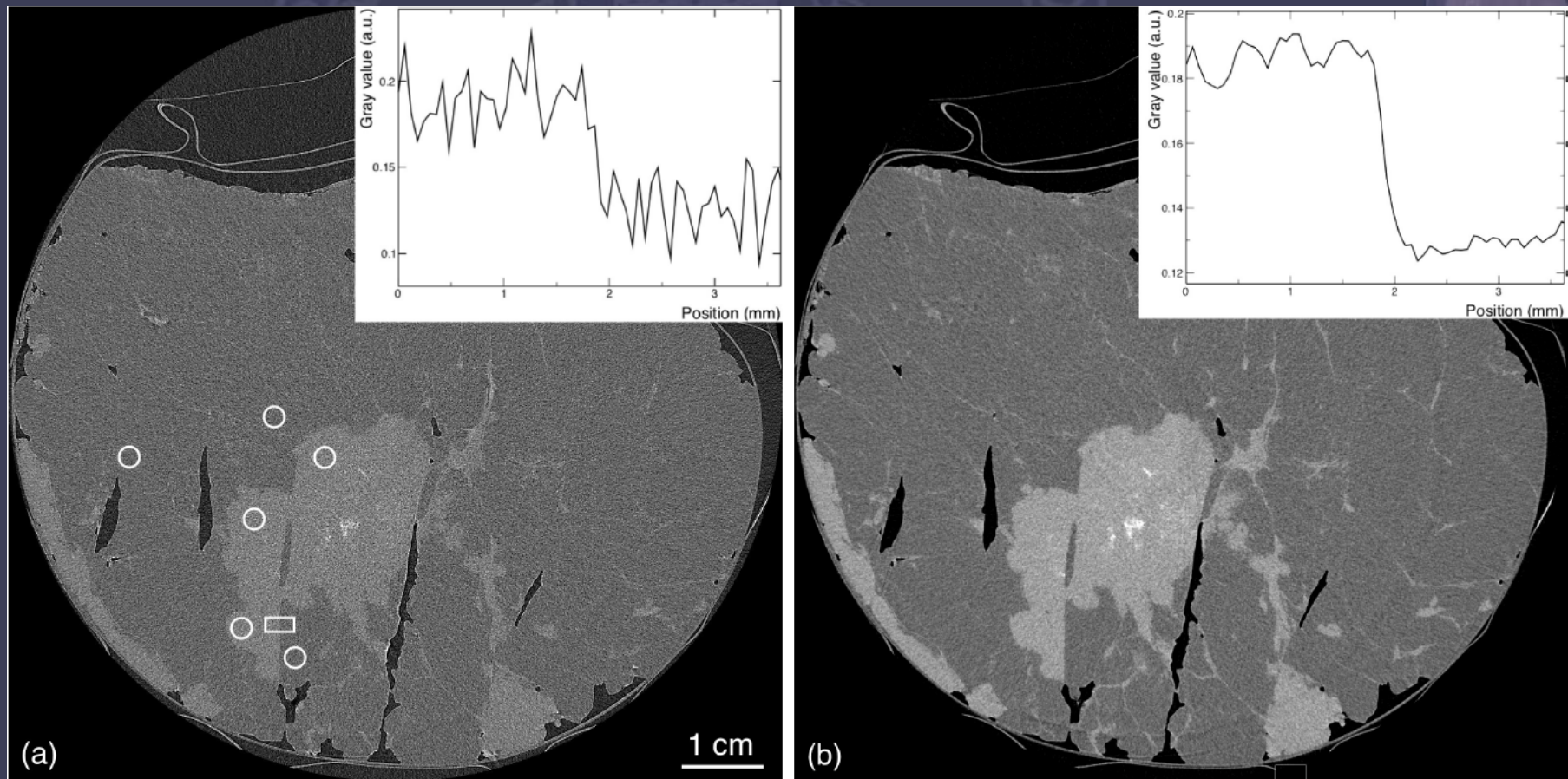


Cloetens P, et al. (1999) *Appl. Phys. Lett.* 75, 2912-2914  
Burvall A, et al. (2011) *Opt. Express* 19, 10359–10376.



# Phase Retrieval: Advantages

- “ • Highlight differences in the phase-shift value between the detail and the surrounding area (increasing the contrast)



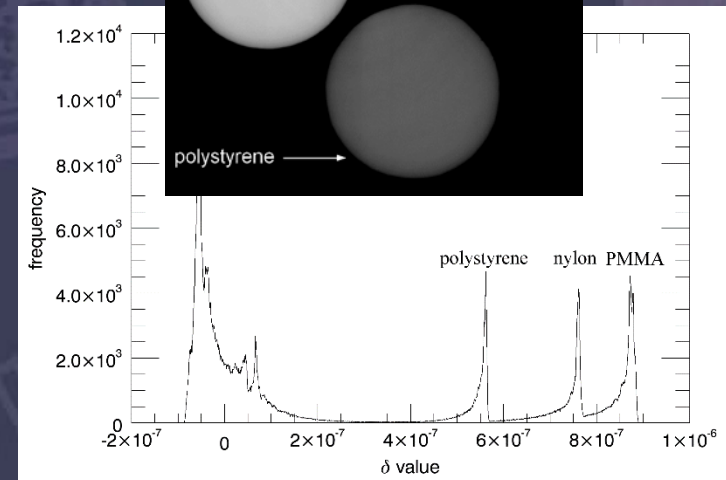
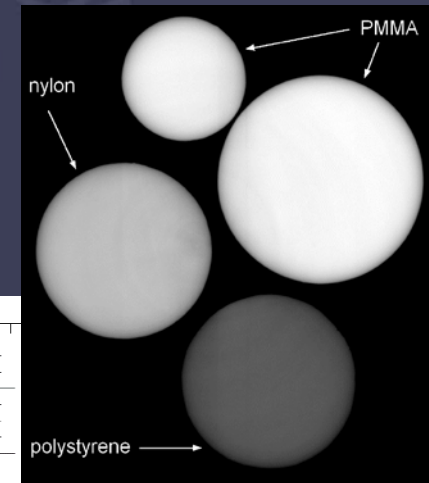
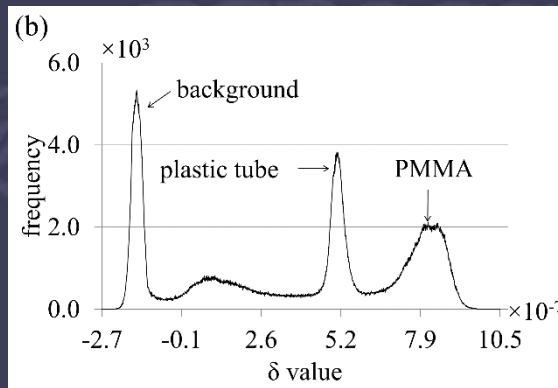
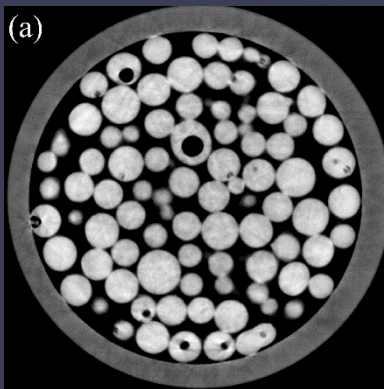
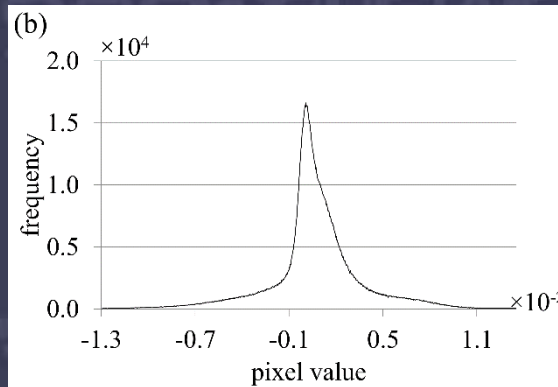
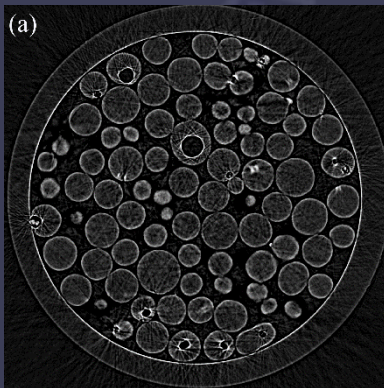
Longo R, et al. (2016) *Phys. Med. Biol.* 61, 1634  
Brombal L, et al. (2018) *J Med. Imaging* (submitted)



# Phase Retrieval: Advantages

“

- Allow tissue/material characterization, since  $\phi(x,y)$  can be related to  $\delta$ , which in turn is related to the tissue/material electron density



”

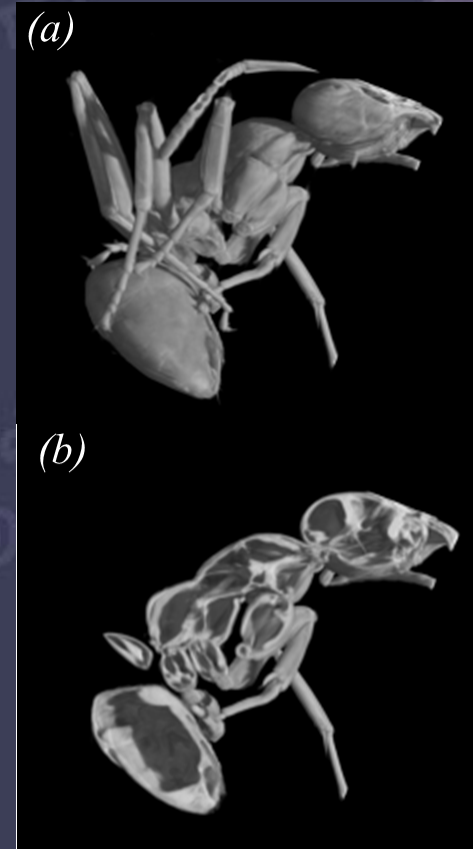
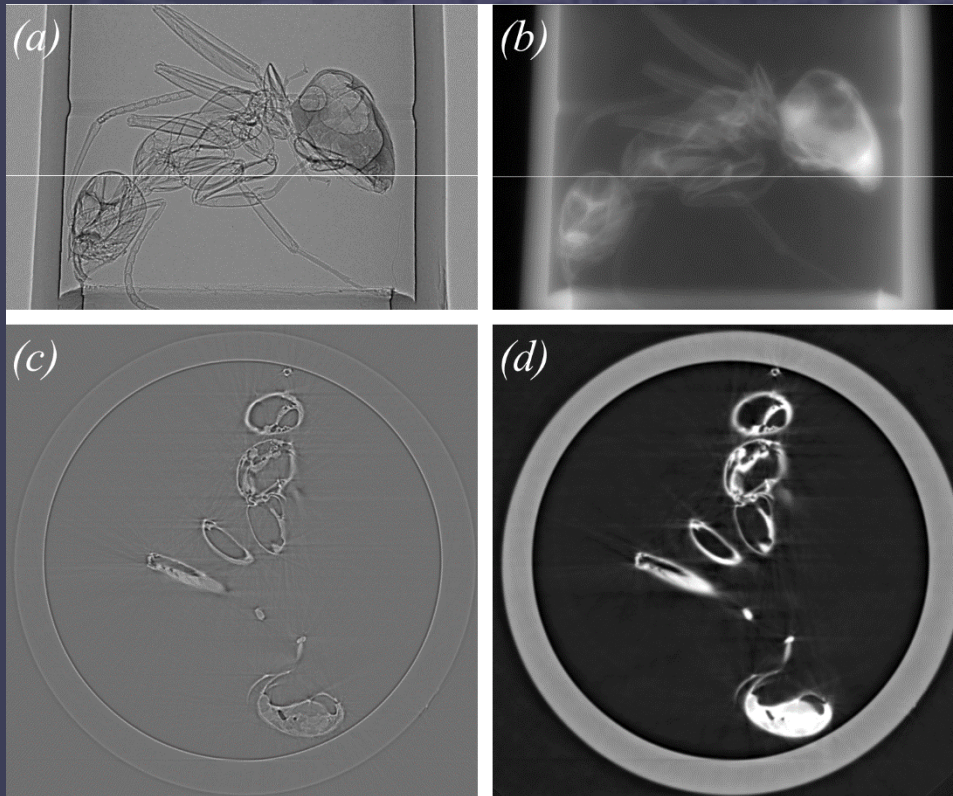


Chen R C, et al. (2011) *J. Phys. D: Appl. Phys.* 44, 495401  
 Chen R C, et al. (2011) *Opt. Lett.* 36(9), 1719-1721

# Phase Retrieval: Advantages

“

- Allow easier and more precise segmentation in 3D methods (volume rendering)



Chen R C, et al. (2012) *J. Synchrotron Radiat.* 19(5), 836-845  
Chen R C, et al. (2011) *Opt. Lett.* 36(9), 1719-1721

“

# More sophisticated PCI Techniques

”



# More sophisticated PCI techniques

- “ • In addition to Propagation-Based PCI, we have several different approaches to PCI, including:
- Analyzer-based Imaging / Diffraction Enhanced Imaging
  - Edge Illumination / Coded Apertures
  - Crystal Interferometry
  - Gratings Interferometry
  - Speckle-based PCI / Sand Paper Imaging
- All these techniques are capable of producing parametrical images, based on some characteristics of the sample
- ”



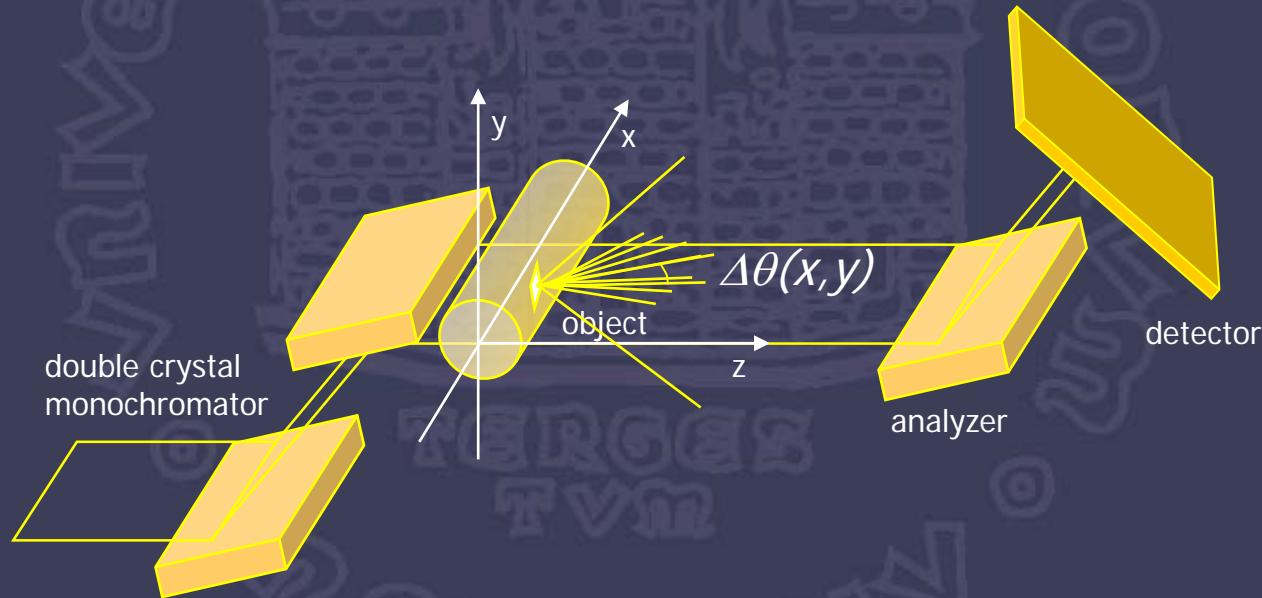
# “Analyzer-Based Imaging (Diffraction Enhanced Imaging)”



# Analyzer-based Imaging

“

- An analyzer crystal is introduced between the object and the detector to highlight tiny angular deviations  $\Delta\theta(x,y)$  (in the order of 1 – 100  $\mu\text{rad}$ ) introduced by the object in the  $yz$  plane

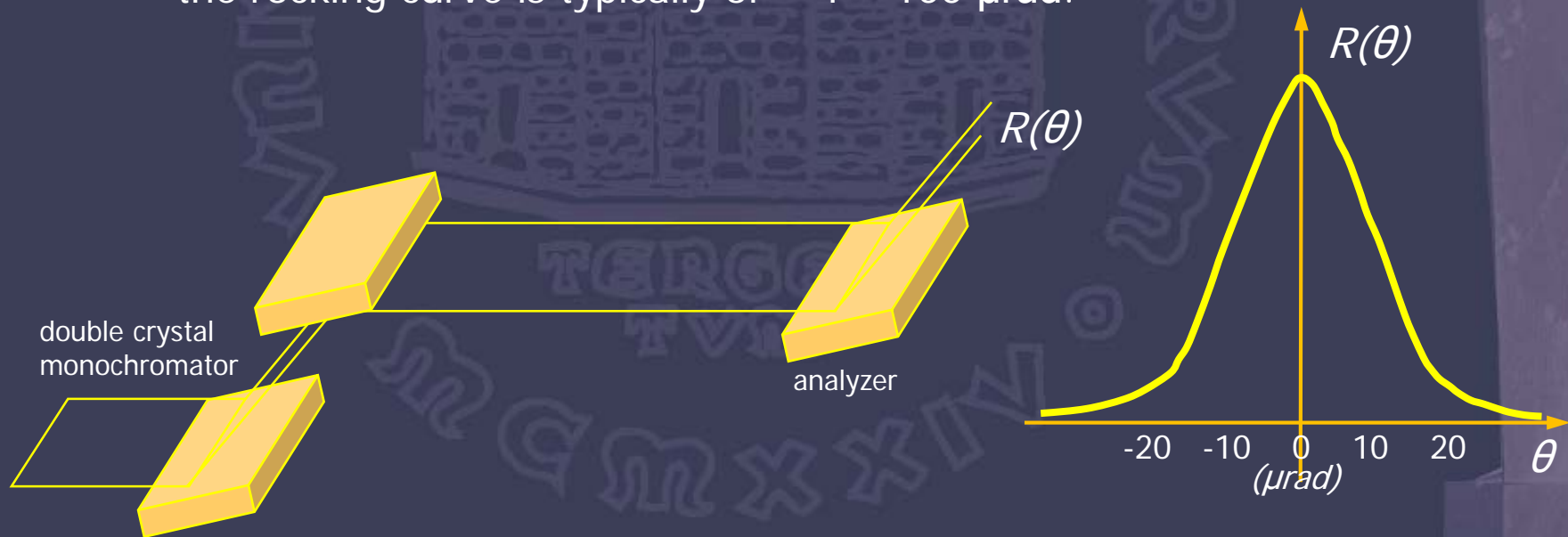


”

# The rocking curve

“

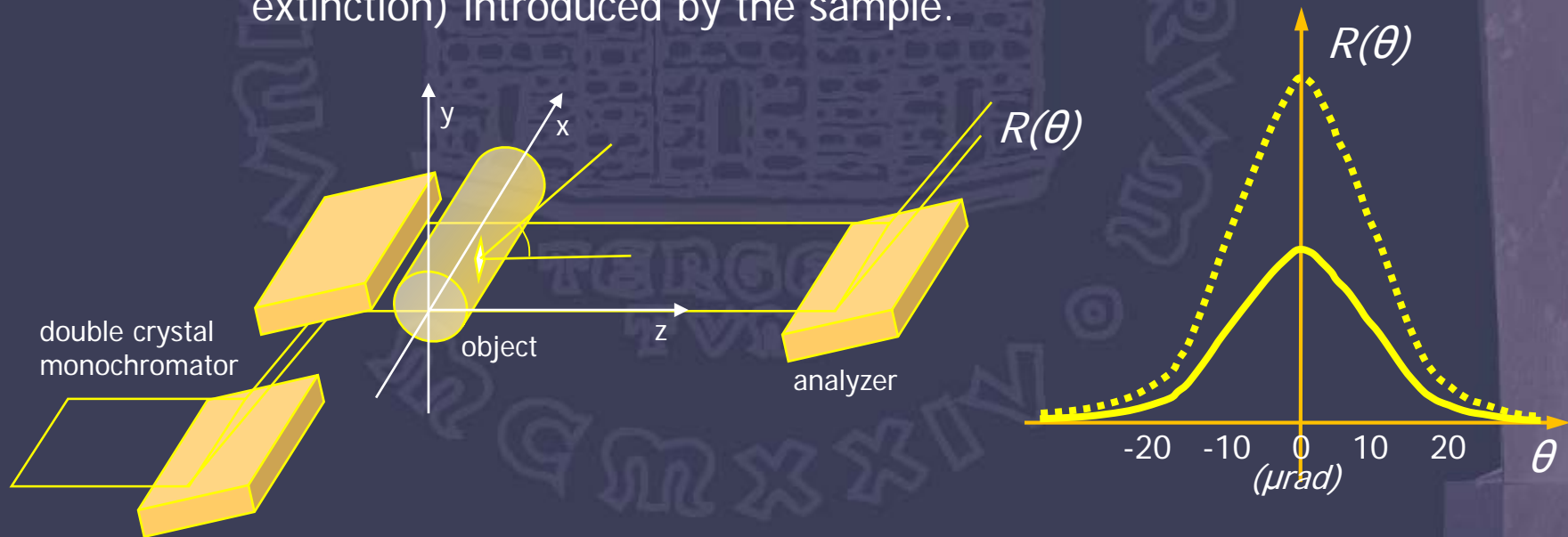
- In the absence of the object, the analyzer crystal diffracts the beam towards the detector with 100% efficiency only when perfectly aligned with the monochromator.
- The diffracted intensity  $R(\theta)$  as a function of the misalignment angle  $\theta$  defines the *rocking curve* of the system. The width of the rocking curve is typically of  $\sim 1 - 100 \mu\text{rad}$ .



”

# The local rocking curve

- “ • In the presence of the object, the rocking curve is locally altered. In particular, with respect to the intrinsic rocking curve, the **local rocking curve** can show:
- A **reduction of the height of the peak** of the rocking curve (and of the area under the rocking curve).
  - This is due to the **apparent absorption** (absorption + extinction) introduced by the sample.



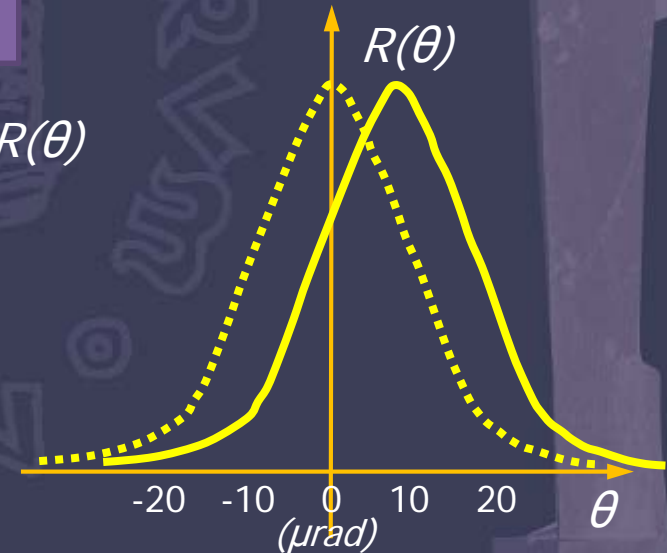
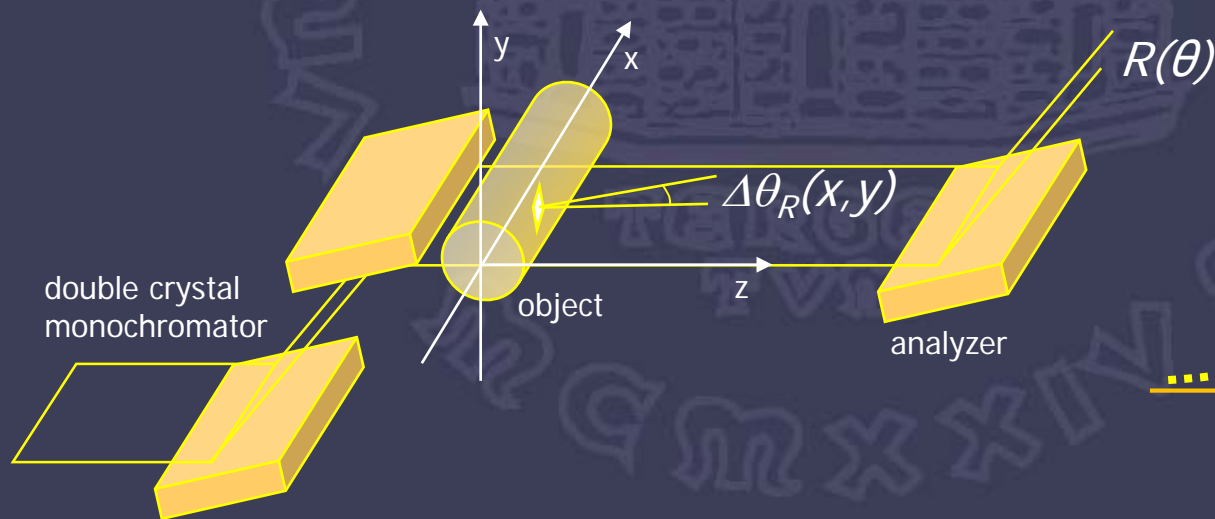
”



# The local rocking curve

- “ • In the presence of the object, the rocking curve is locally altered. In particular, with respect to the intrinsic rocking curve, the **local rocking curve** can show:
- A **shift** of the rocking curve.
  - This is due to the **refraction** introduced by the sample.

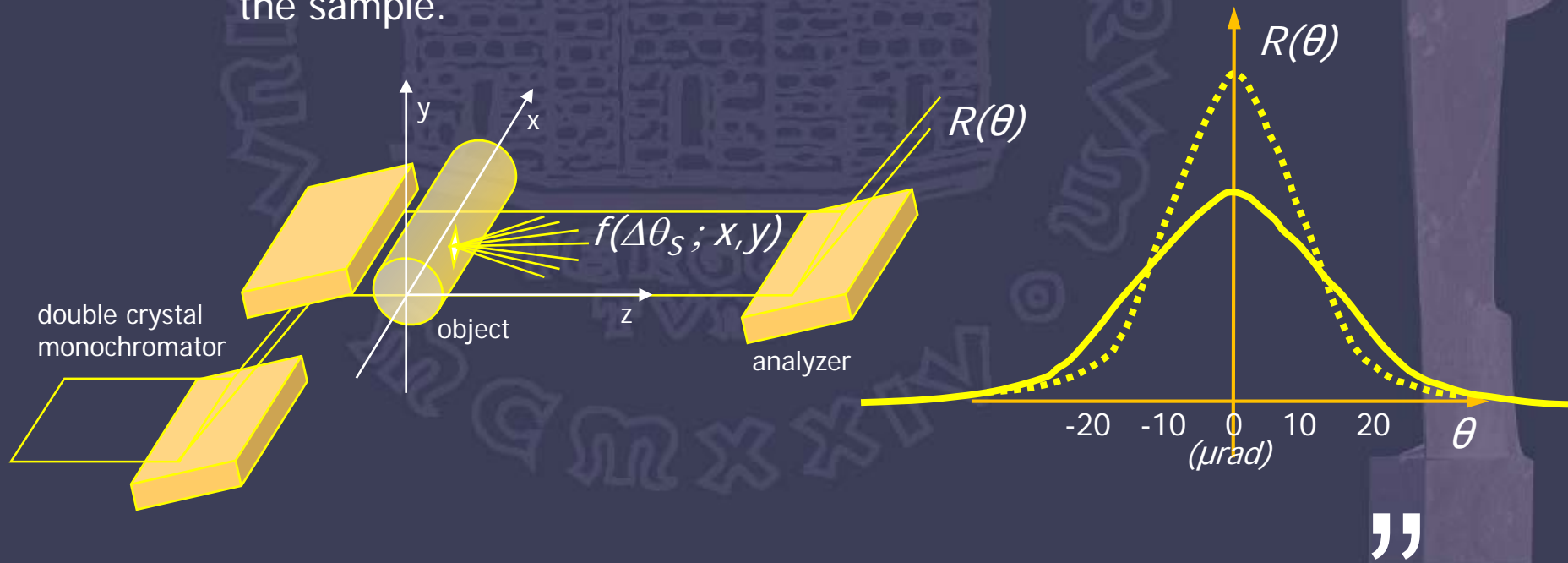
$$\Delta\theta_R(x, y) = \frac{1}{k} \frac{\partial}{\partial y} \phi(x, y)$$



”

# The local rocking curve

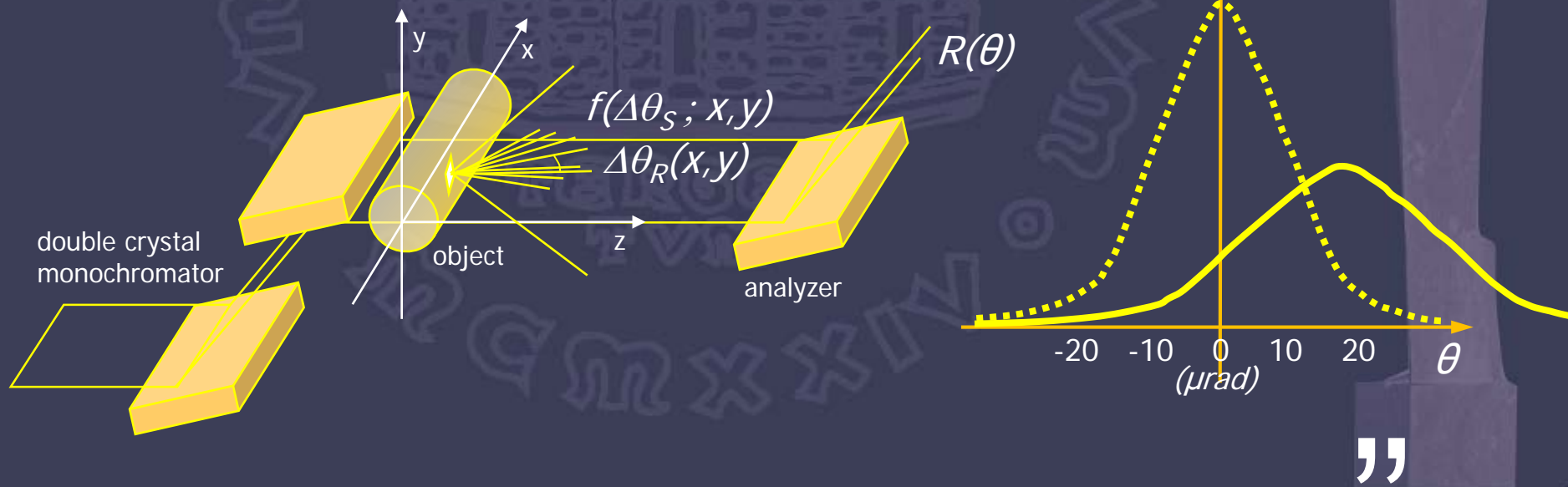
- “ • In the presence of the object, the rocking curve is locally altered. In particular, with respect to the intrinsic rocking curve, the **local rocking curve** can show:
- An **increment of the width** of the rocking curve (keeping the same area under the rocking curve).
  - This is due to the ultra-small-angle scattering introduced by the sample.



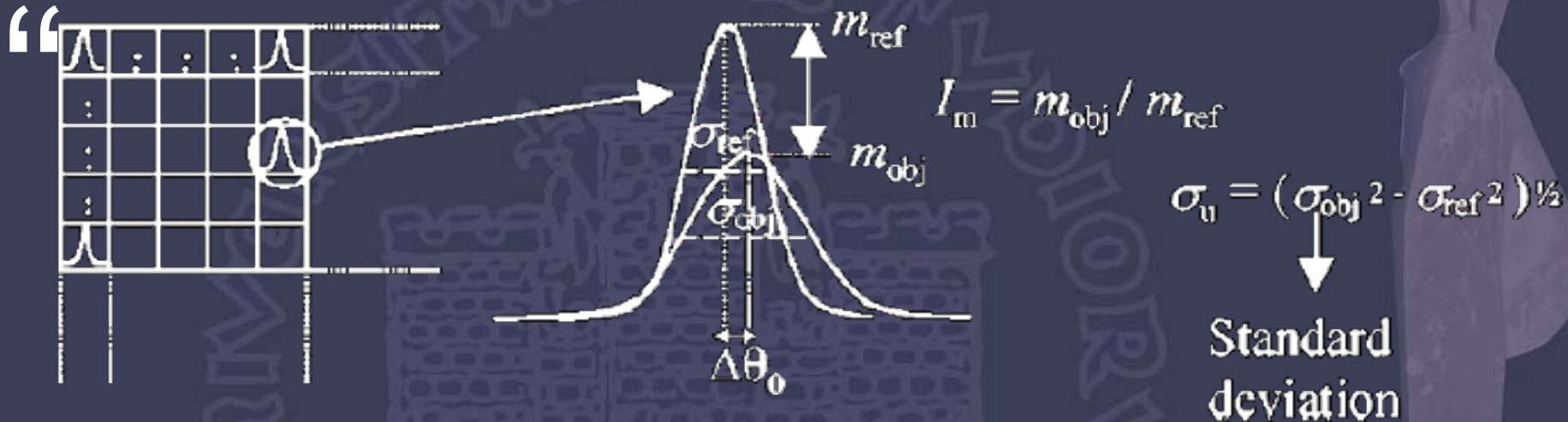
”

# The local rocking curve

- “ • In general, all these effects co-exist, and the **local rocking curve** is therefore
- Reduced in height (due to apparent absorption)
  - Shifted (due to refraction)
  - Widened (due to ultra small angle scattering)
- The amount of these effects can be calculated on a pixel-per-pixel basis



# Sampling the local rocking curve



- A local rocking curve is obtained on a **pixel-per-pixel** basis
- Comparing the characteristics of the local Vs the intrinsic rocking curve, 3 **parametric** images can be obtained:
  - area or height: **(apparent) absorption image**
  - shift: **refraction (differential phase contrast) image**
  - width: **ultra-small-angle scattering (dark field) image**



Oltulu O, et al. (2003) *Journal of Physics D: Applied Physics* 36: 2152–2156.  
 Pagot E, et al. (2003) *Applied Physics Letters* 82: 3421–3423  
 Wernick MN, et al. (2003) *Physics in Medicine and Biology* 48: 3875–3895



# Sampling the local rocking curve

“

- Parametric images can be evaluated:
  - by means of numerical and statistical methods
  - by analytically curve-fitting the local rocking curve on a pixel-per-pixel basis
- Both approaches typically require to collect a high number of images (3-24)
  - long exposure time
  - possibly high dose
- Curve-fitting also require considerable computing power

”



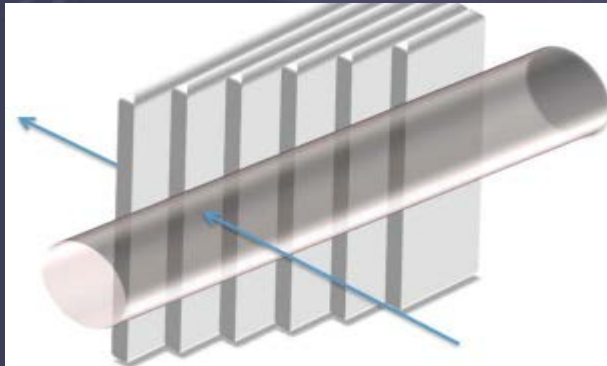
*Diemoz PC, et al. (2010) Optics Express 18: 3494–3509.*

*Diemoz PC, et al. (2010) Physics in Medicine and Biology 55: 7663–7679.*

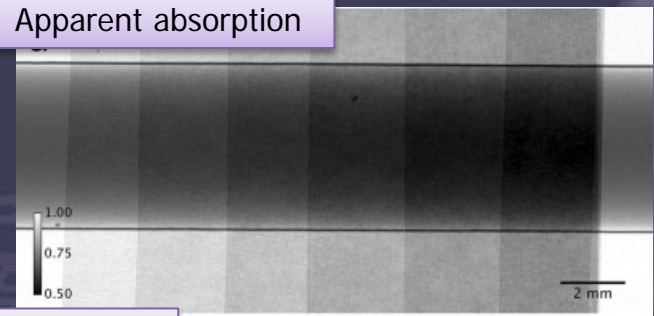
# Generalized DEI algorithms

“ • Similar results can be obtained with Generalized Diffraction Enhanced Imaging algorithms

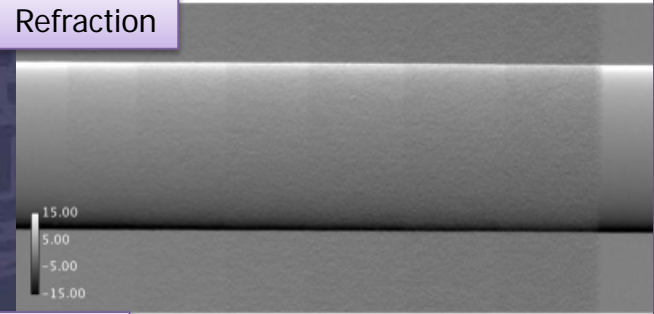
- Only 3 images, collected at 3 different rocking curve positions, are needed
- Parametric images are obtained applying specific equations on a **pixel-per-pixel** basis



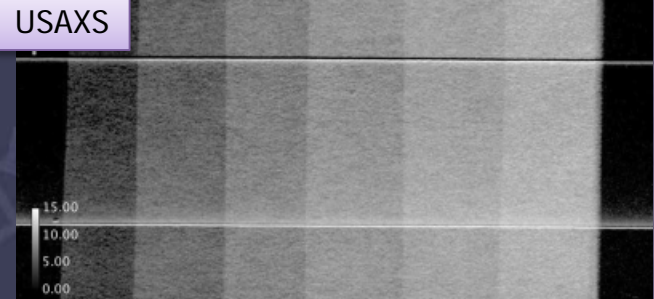
Apparent absorption



Refraction



USAXS

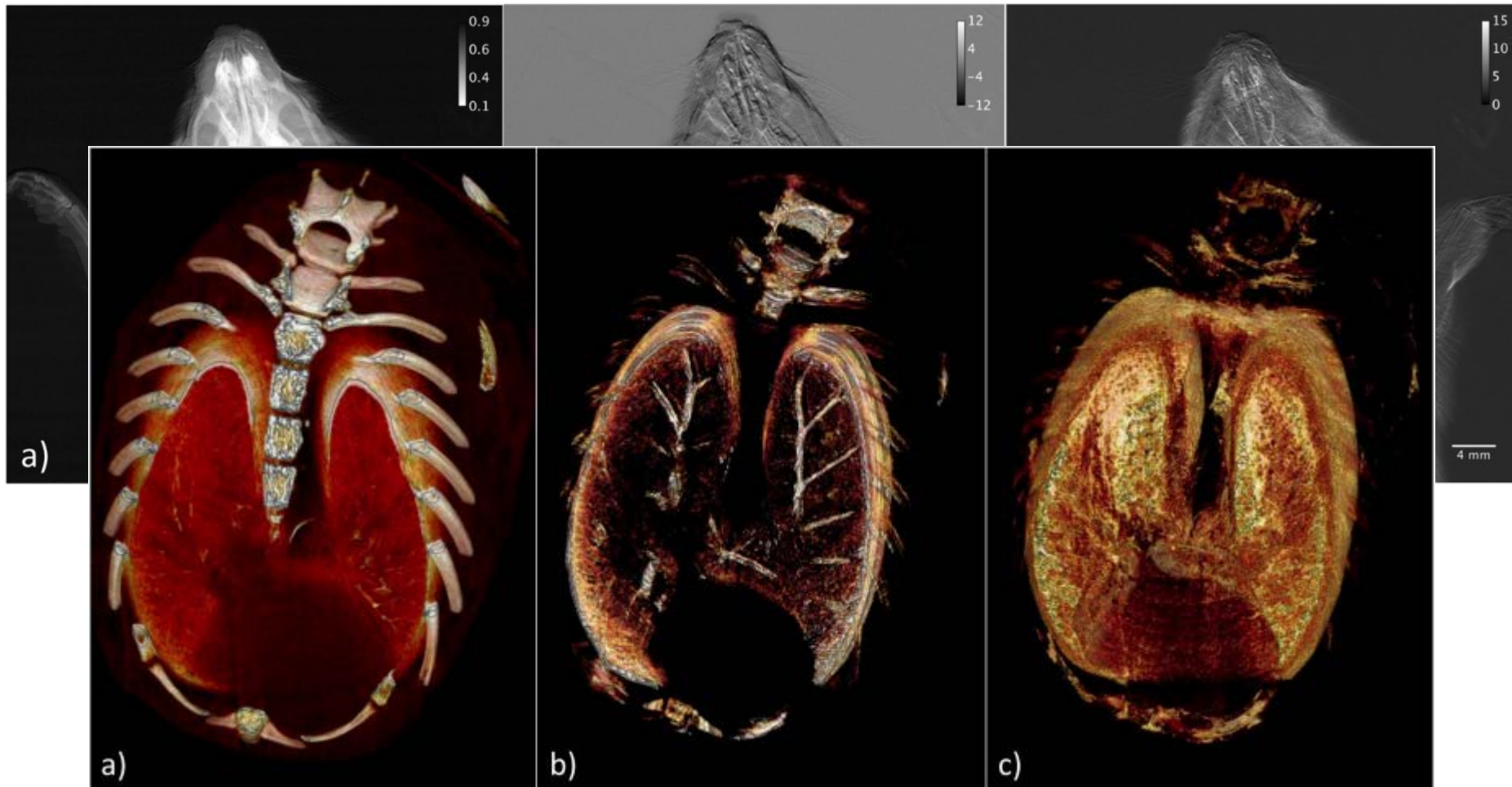


”



*Rigon L, et al. (2007) Appl. Phys. Lett. 90, 114-102*  
*Arfelli F, et al. (2018) Scientific Reports 8, 362*

# Small animal Imaging

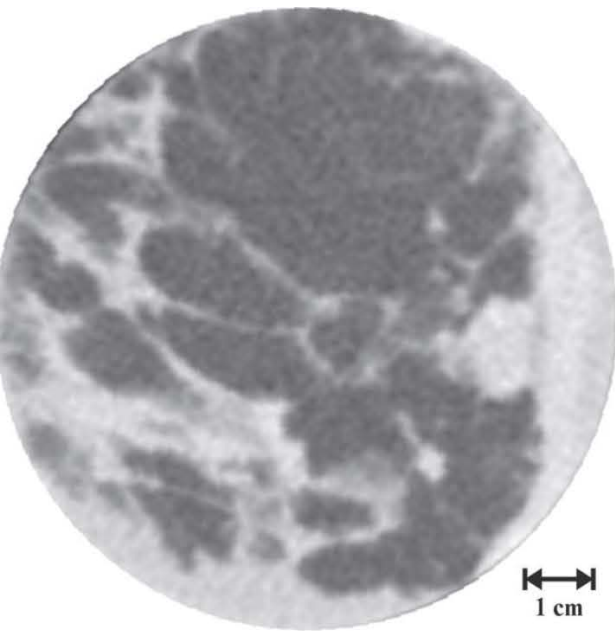


Luigi Rigon  
 University of Trieste & INFN, Sezione di Trieste  
*XV Seminar on Software for Nuclear, Subnuclear and  
 Applied Physics – Alghero (Italy) - 31 MAY 2018*

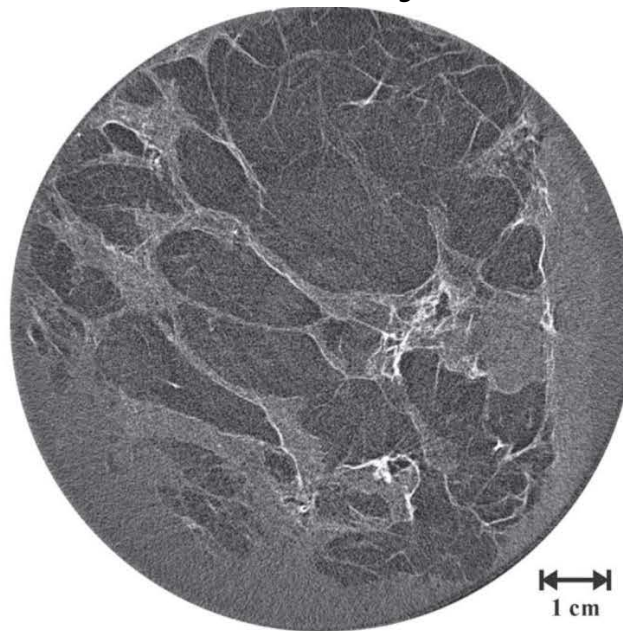


# CT of Breast Tissue Sample

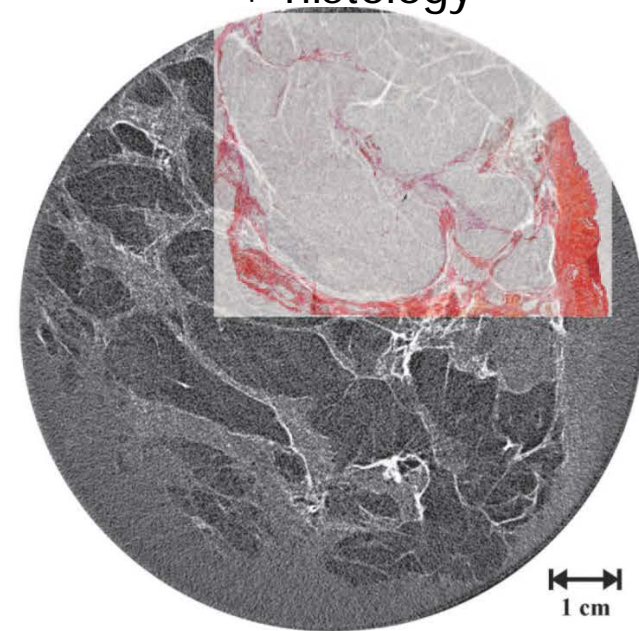
Conventional  
6.9 mGy



ABI at peak of RC  
1.9 mGy



ABI  
+ histology



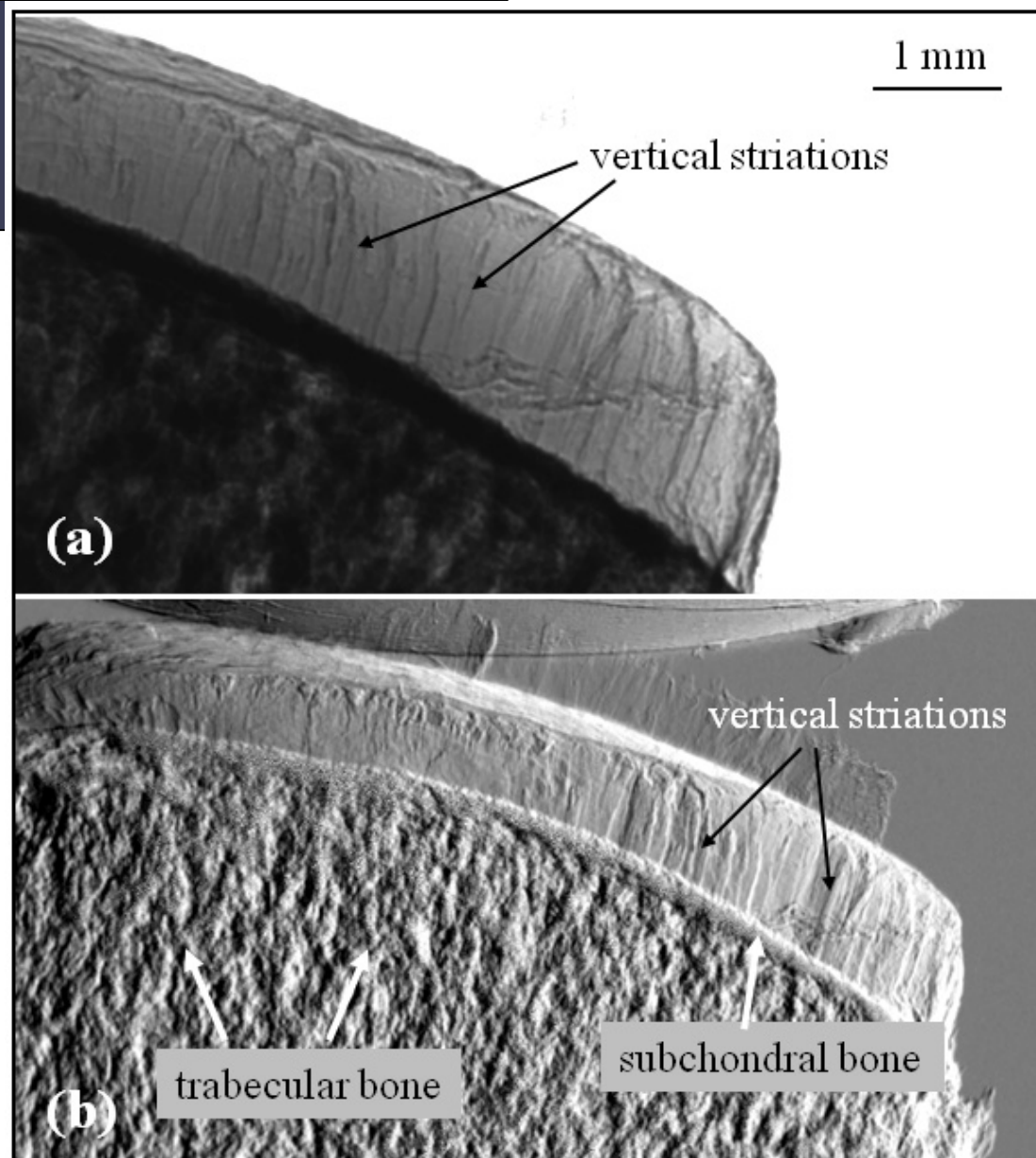
*Keyriläinen, J., Fernandez, M. et al. (2008). Radiology 249, 321–327.*





# Articular Cartilage

- first radiographic detection of the structural orientation and organization of joint cartilage
- depict simultaneously cartilage and bone
- inspect and correlate features on the whole joint structure
- longitudinal studies of osteoarthritis development in small-animal models



*Muehleman, C., Majumdar, S. et al. (2004). Osteoarthritis Cartilage 12, 97–105.*

# ABI: Limitations and Requirements

- “
  - Monochromatic and parallel beam
    - Synchrotron beam is the “natural” choice
  - Mechanical stability ( $\sim 1 \mu\text{rad}$ )
  - Multiple acquisitions ( $\sim 3$  working points on the RC)
  - ABI with X ray tubes
    - the challenge of low flux/long acquisition time”



Faulconer L., Parham C. et al. (2009). *Acad. Radiol.* **16** 1329–1337

Parham C., Zhong Z. et al. (2009). *Acad. Radiol.* **16** 911–917

Muehleman C., Li J., Connor D. M. et al. (2009). *Acad. Radiol.* **16** 918–923

Nesch I., Fogarty D. P., Tzvetkov T. et al. (2009). *Rev. Sci. Instrum.* **80** 93702”

“

## Other sophisticated PCI Techniques

”



“

# Edge Illumination

”

Coded Apertures X-ray Phase Contrast Imaging  
(CAXPCI)





# CAXPCI Basics

“

- Coded Apertures X-ray Phase Contrast Imaging (CAXPCI)
  - produces images similar to ABI:
    - Apparent absorption
    - Refraction
    - USAXS

... but ...

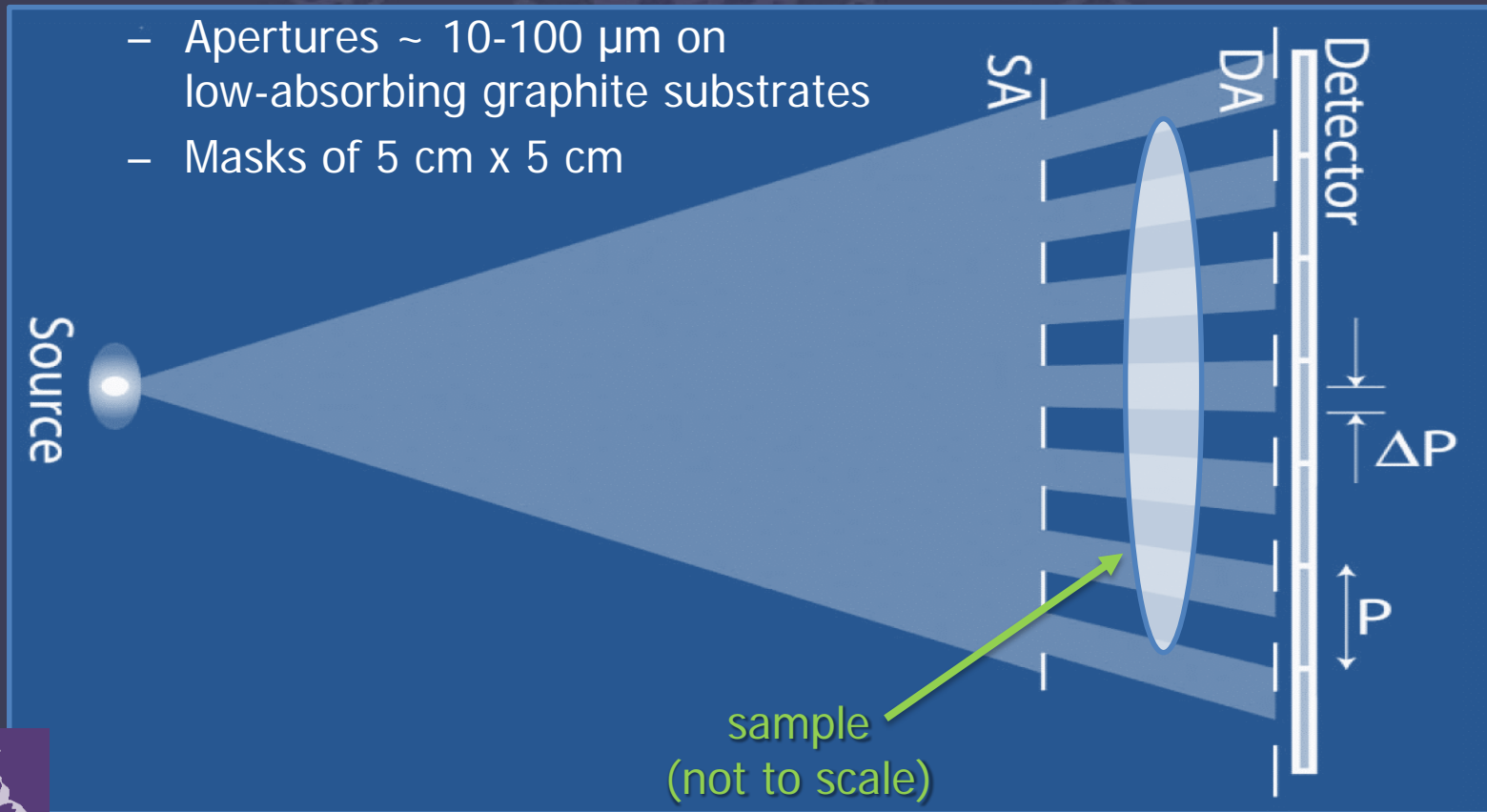
- does not use crystals
- two masks are used instead
  - pre-sample apertures (in front of the sample)
  - detector apertures (in front of the detector)
- conventional sources can be used since no coherence is required

”

# Coded Apertures

“

- Conventional sources can be used
  - Apertures  $\sim 10\text{-}100\text{ }\mu\text{m}$  on low-absorbing graphite substrates
  - Masks of  $5\text{ cm} \times 5\text{ cm}$

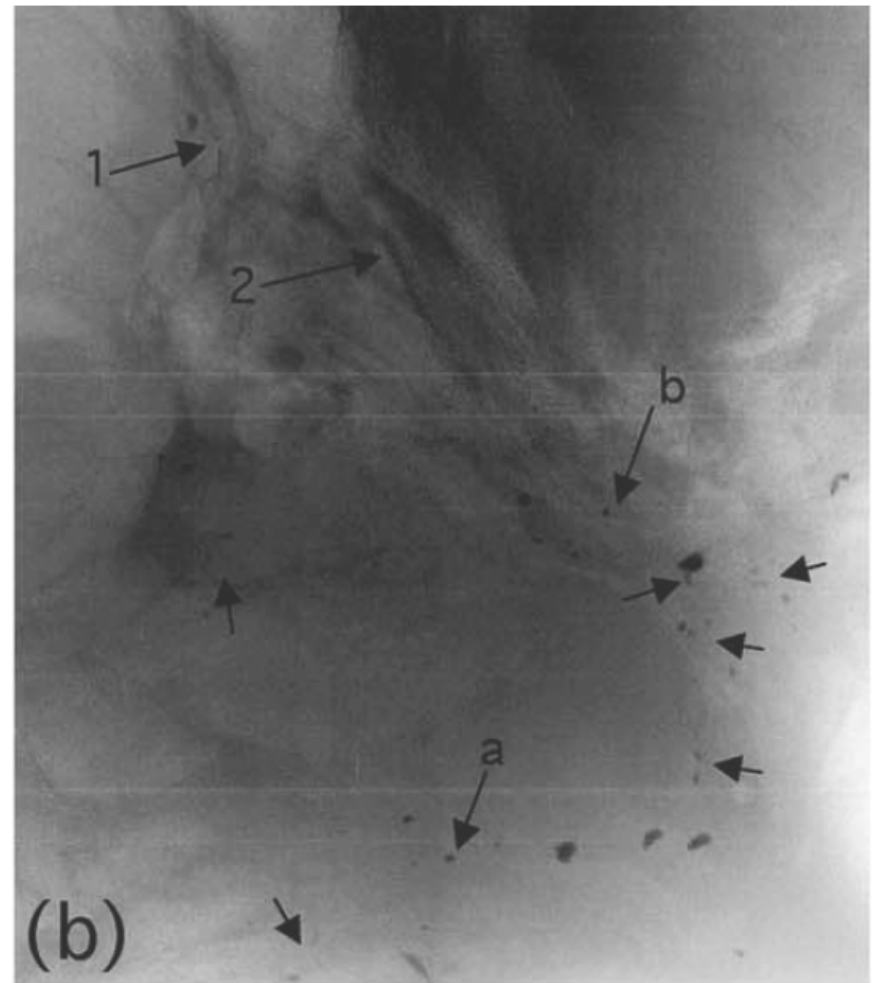
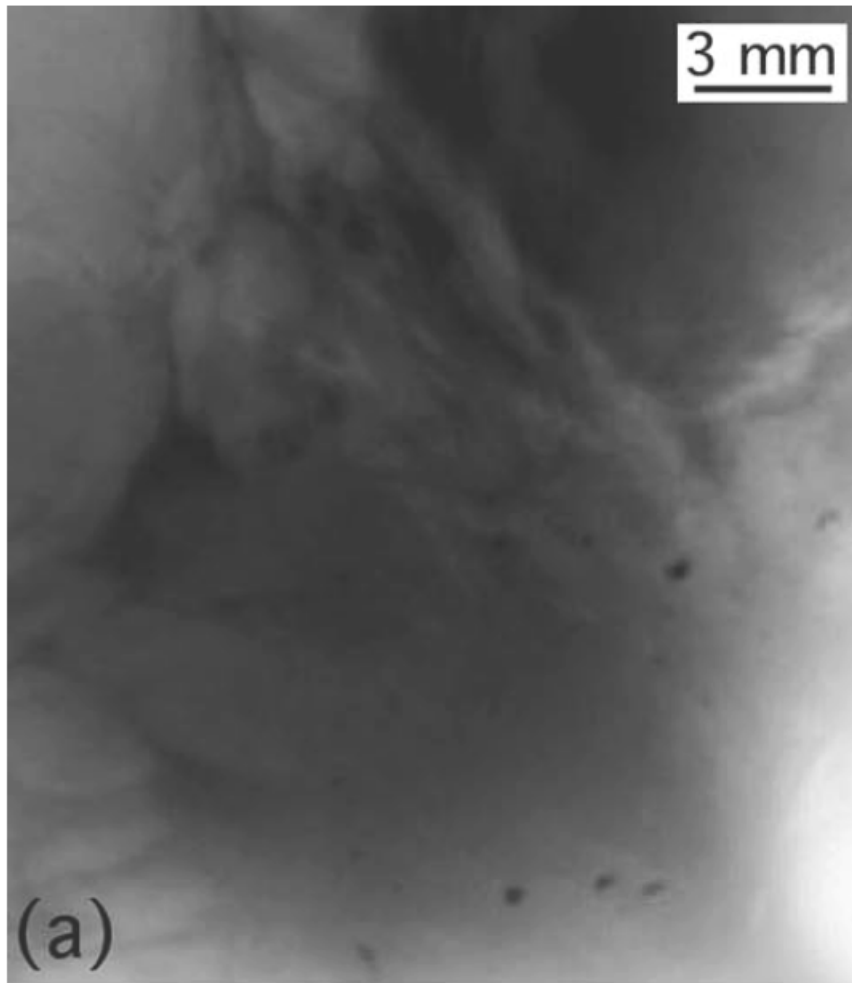


Olivo, A. and Speller, R. (2007). *Appl. Phys. Lett.* **91**, 074106.

”

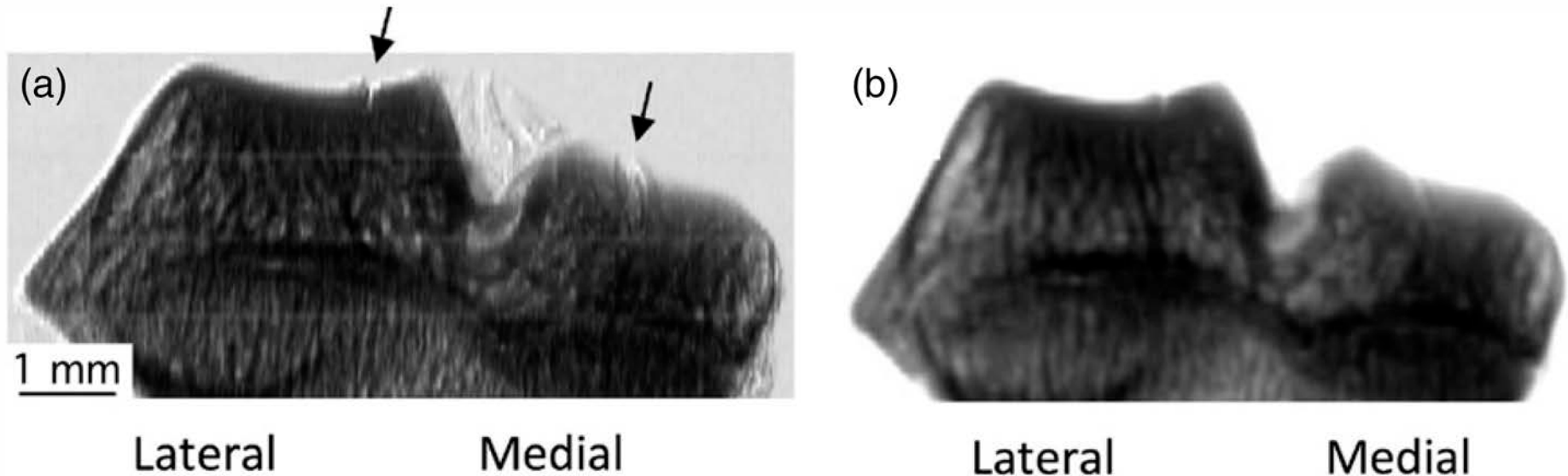


# Application to mammography



*Olivo, A., Gkoumas, M., Endrizzi, M. et al. (2013). Med. Phys. 40, 090701*

# Cartilage



Excised rat tibia  
imaged using a conventional x-ray tube (source size of 75  $\mu\text{m}$ ).  
Small surgically induced are more clearly visible  
than in the absorption image



*Marenzana, M., Hagen, C. K., et al. (2012). Phys. Med. Biol. 57, 8173–8184*



# CAXPCI: Limitations and Requirements

“

- Basically no spatial/temporal coherence of the beam is needed (applicable to conventional X-ray tubes)
- Modest mechanical requirements
- Field of view can be increased to clinical size
  - At the moment 5 cm x 5 cm
- Limited exploitation of X-ray output
  - 20% - 50%

”



Olivo, A. and Speller, R. (2007). *Appl. Phys. Lett.* **91**, 074106.

Olivo, A., Bohndiek, S. E., et al. (2009). *Appl. Phys. Lett.* **94**, 044108.

Olivo, A., Ignatyev, K., et al. (2011). *Appl. Opt.* **50**, 1765–1769.

“

# Grating Interferometry

”



# GI Basics

“

- Grating Interferometry
  - produces images similar to ABI:
    - (Apparent) absorption
    - Differential Phase (Refraction)
    - Dark field (USAXS)

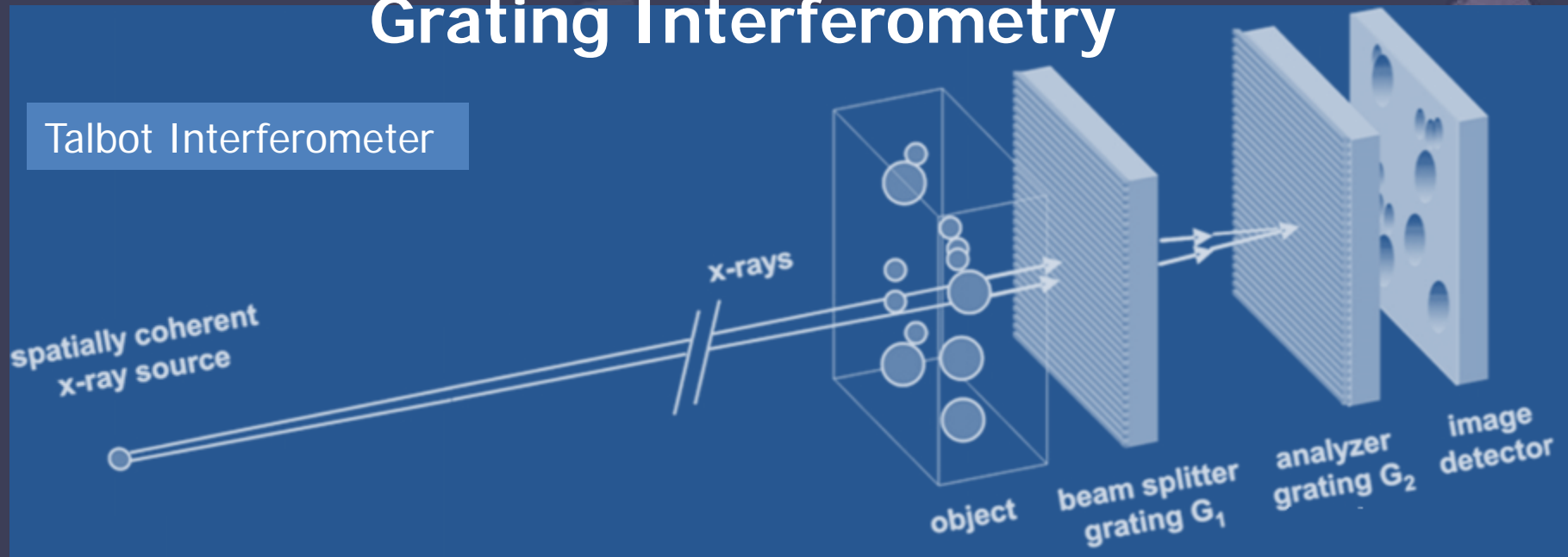
... but ...

- does not use crystals
- two gratings between sample and detector are used instead
  - splitter grating  $G_1$  (phase grating)
  - analyzer grating  $G_2$  (absorption grating)
- a certain degree of spatial coherence is required, but conventional sources can be used with a mask (Talbot-Lau)

”

# Grating Interferometry

## Talbot Interferometer

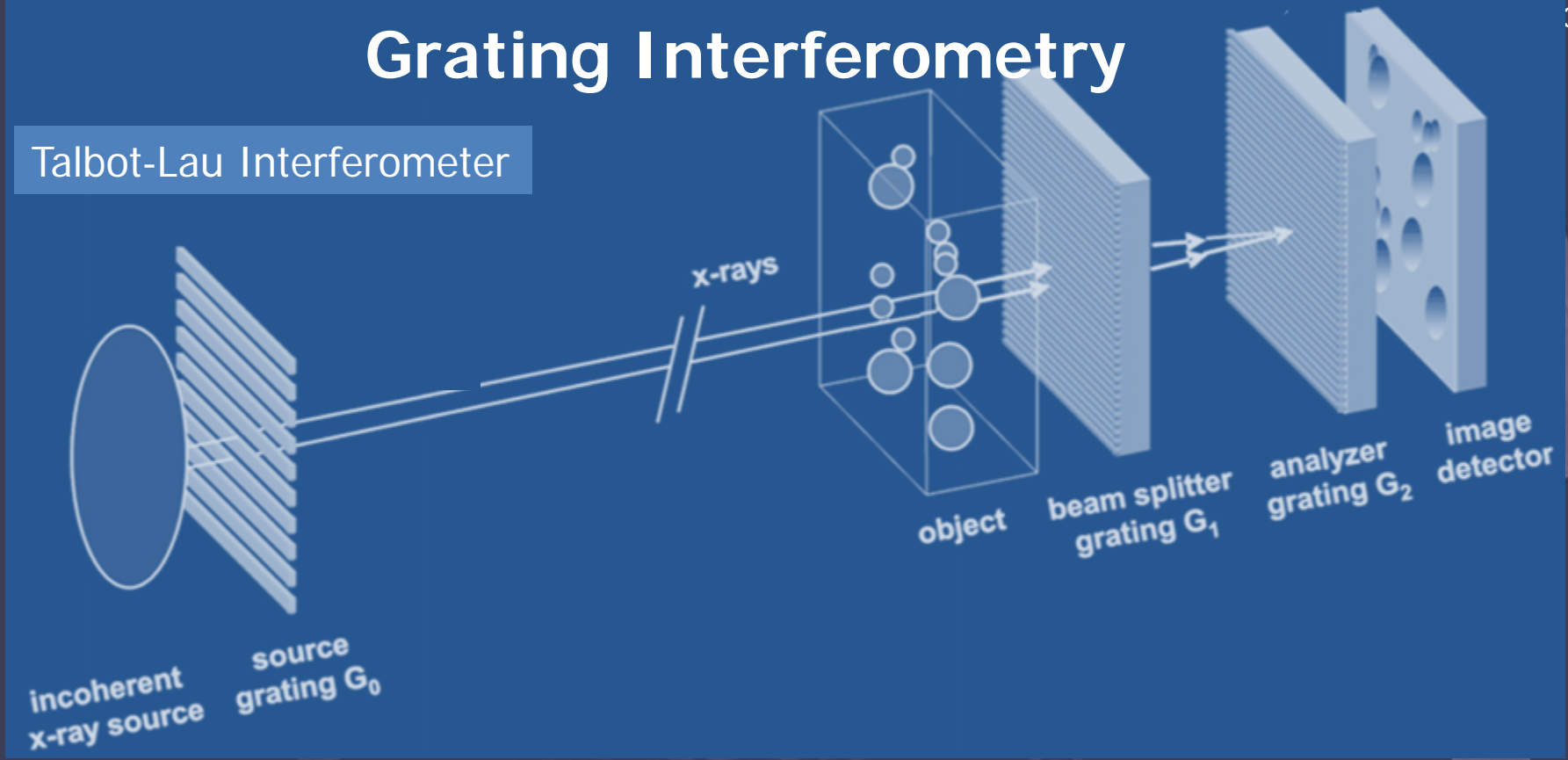


- Two beams are created at the splitter grating  $G_1$  (phase grating)
  - the two beams are only sheared by a small angle so that they almost overlap
  - downstream of the splitter, the beams interfere and form periodic fringe patterns
- The analyzer grating  $G_2$  (absorption grating) can reveal the high-spatial-frequency fringe pattern
  - either by scanning it at a very fine step (phase stepping)
  - or by a slightly misalignment with respect to  $G_1$  (moiré pattern)



# Grating Interferometry

## Talbot-Lau Interferometer

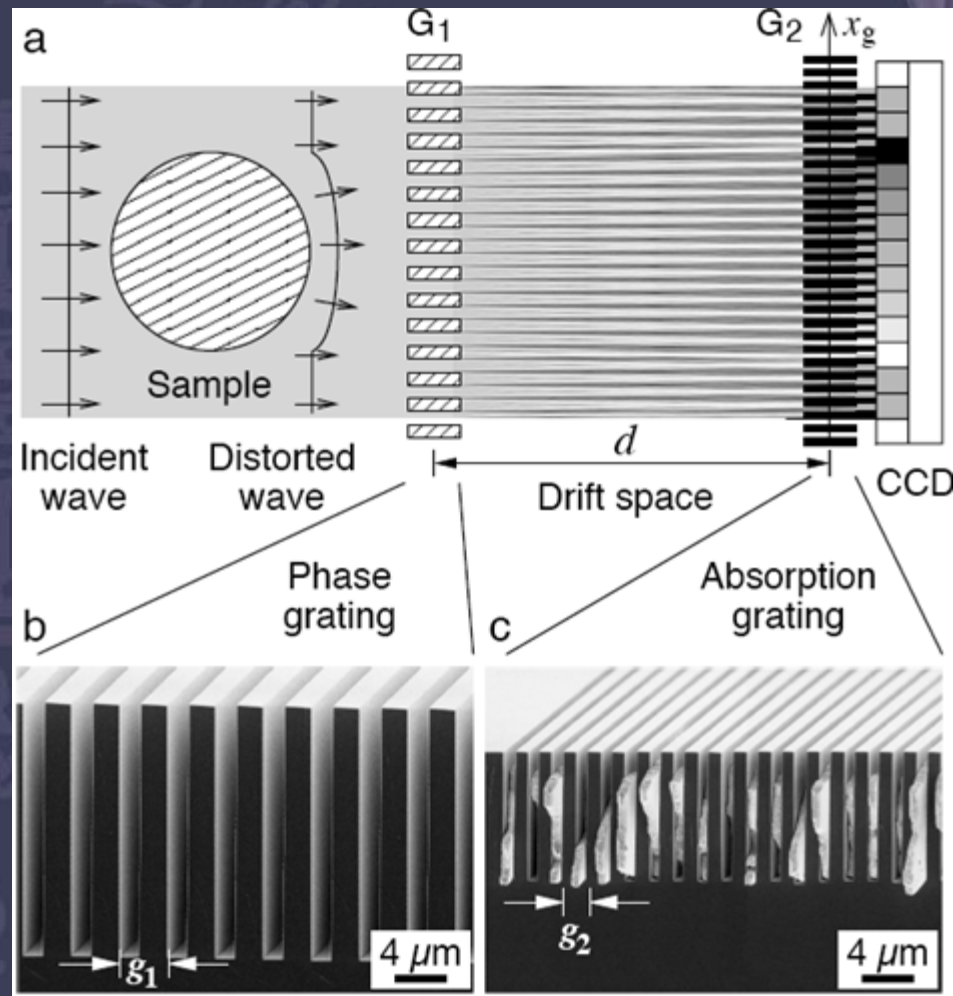


- The principle can be implemented also with spatially incoherent sources
  - an absorbing mask with transmitting slits is placed near the source (source grating  $G_0$ )
  - The source grating  $G_0$  creates an array of individually coherent, but mutually incoherent sources (Talbot-Lau interferometer)

# Grating Interferometry- Limitations

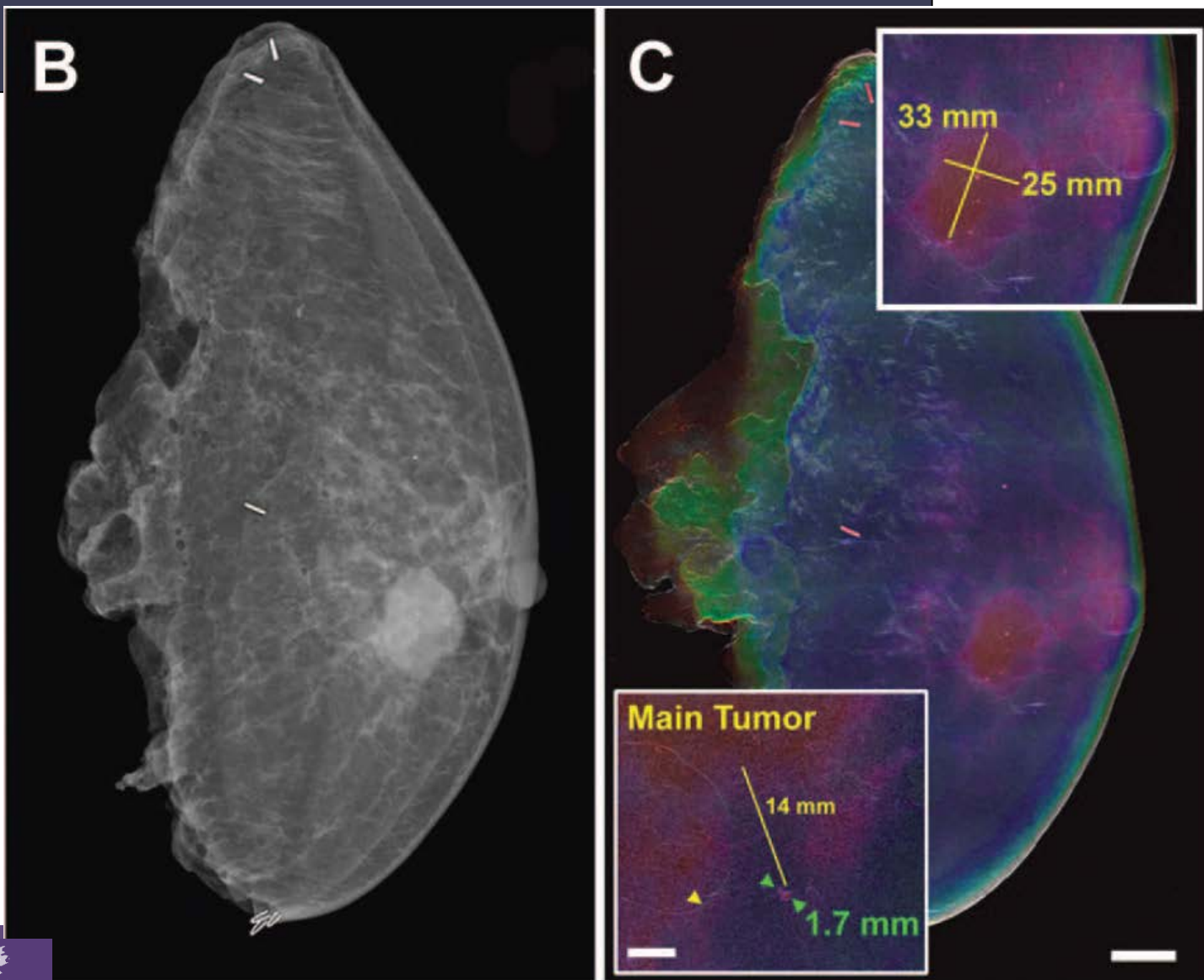
“

- Demanding mechanical requirements (precision ~ 20-30 nm)
  - Field of view must be increased to clinical size
  - At the moment 5 cm x 5 cm
- Limited exploitation of X-ray output
  - 20% - 30% due to source grating
  - grating silicon substrates (~ 300  $\mu\text{m}$ )
- Long exposure time and high delivered dose



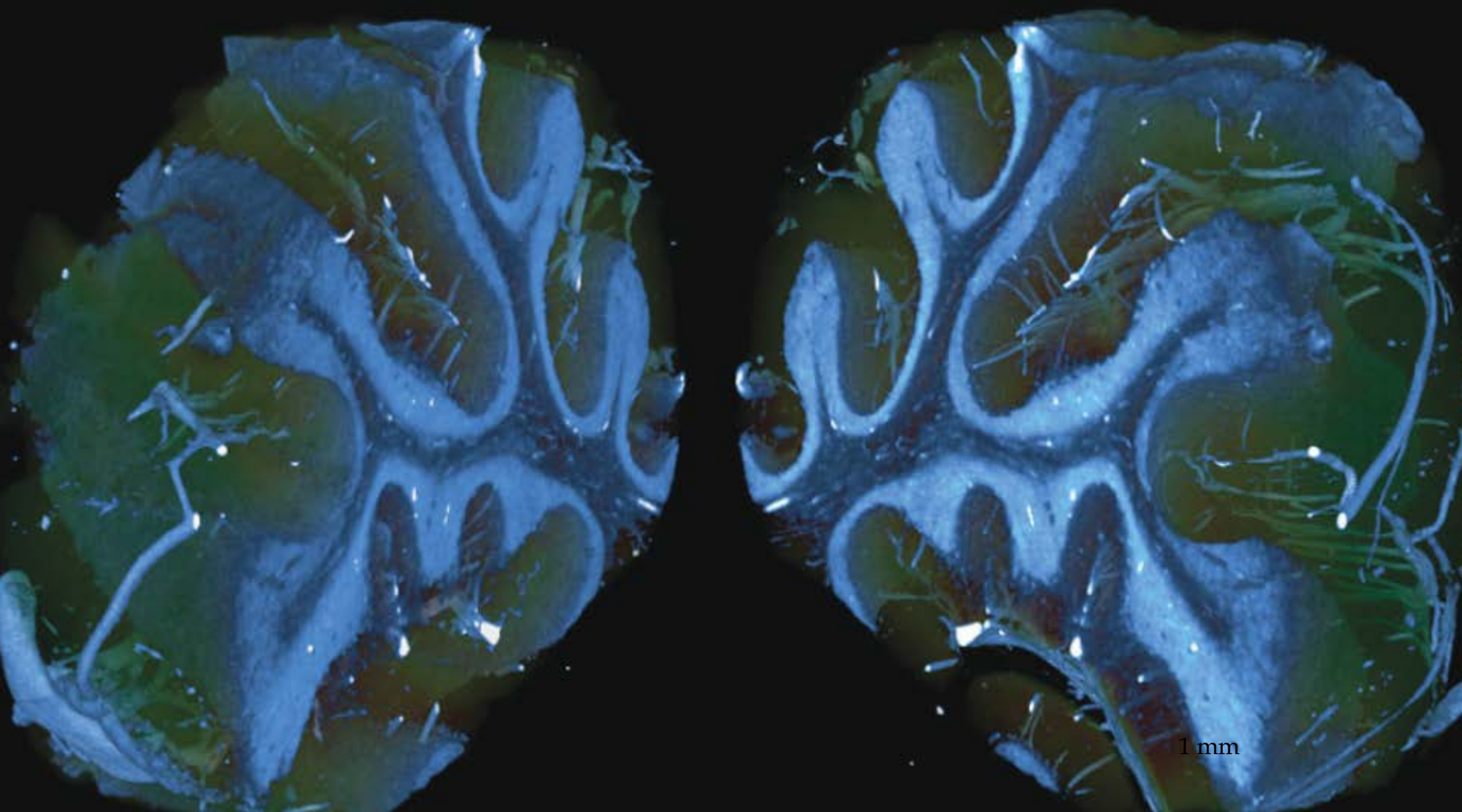
”

# Application to mammography (*ex vivo*)





# High-resolution tomographic imaging of a human cerebellum



*Schulz, G., Weitkamp, T. et al. (2010) J. R. Soc. Interface 7, 1665–1676*



“

# Speckle-Based Phase Contrast Imaging

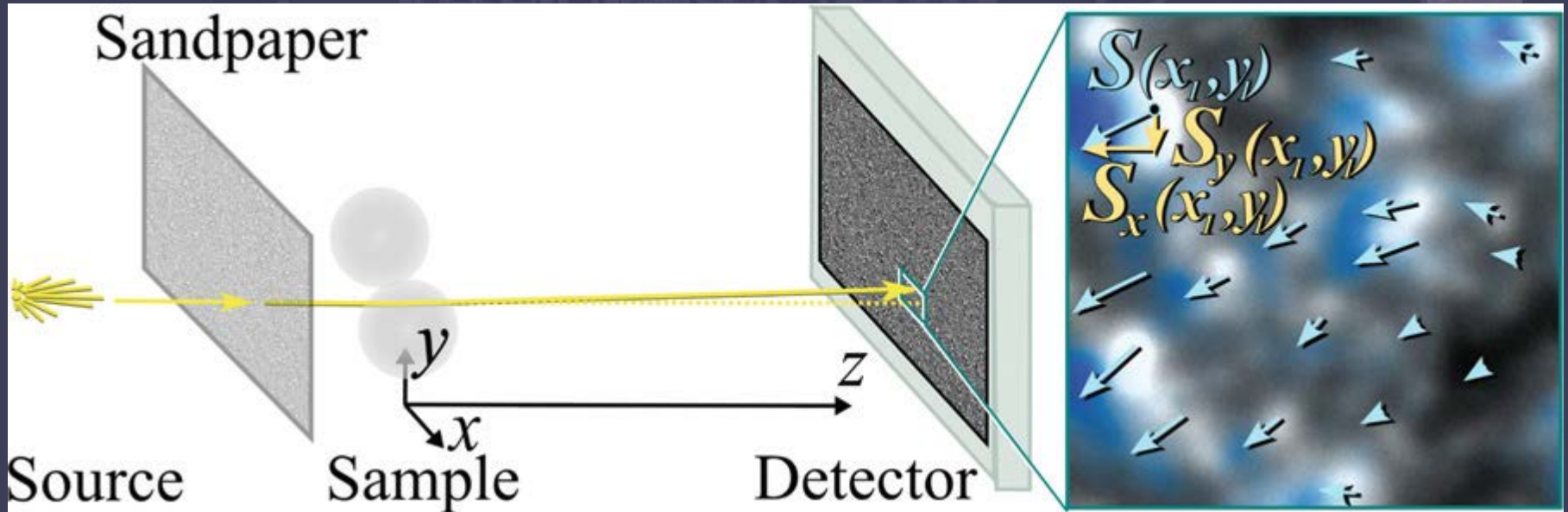
”

## Sandpaper Imaging



# Speckle-Based PCI - Basics

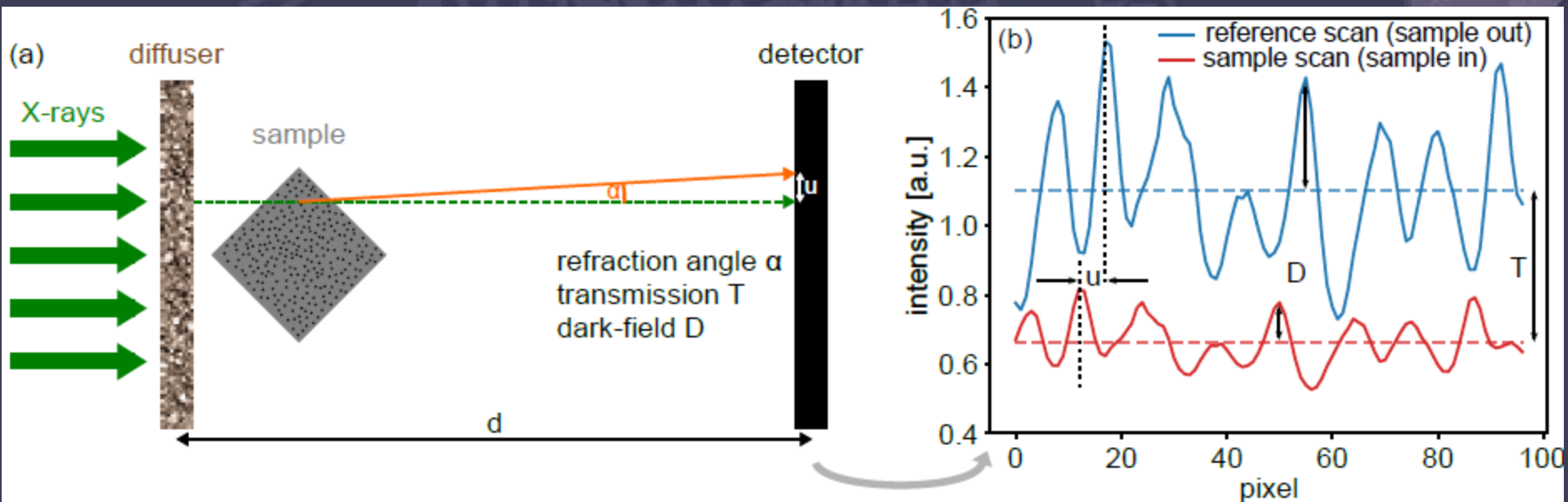
- “
- An object capable of generating a strong speckle pattern (e.g. sandpaper) is put in the beam
  - The sample introduces a distortion of the X-ray wavefront, altering the speckle pattern
  - By correlating the speckle pattern with and without the sample, PCI can be obtained



Morgan KS, Paganin DM, Siu KW (2012) *Appl. Phys. Lett.* 100, 124102  
Berujon S, Wang H, Sawhney K (2012) *Phys. Rev. A* 86, 063813

# Speckle-Based PCI - Basics

- “ • Comparison of a line profile (blue = reference, red = sample in)
  - Reduced in intensity (  $T$  - due to absorption)
  - Shifted (  $u$  - due to refraction)
  - Smoothed (  $D$  - due to ultra small angle scattering)
- sample, PCI can be obtained



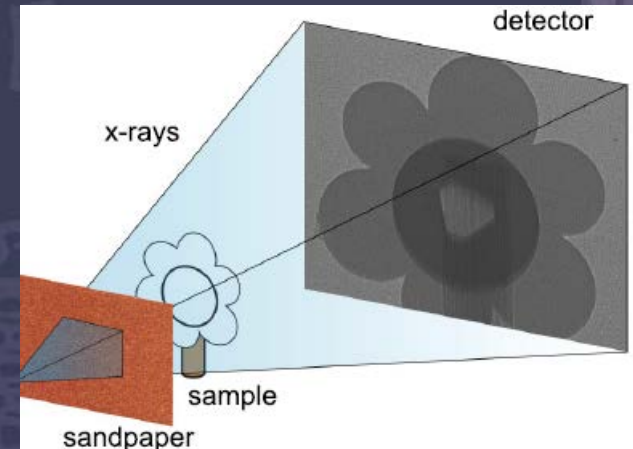
Zanette I, et al. (2014) *Phys. Rev. Lett.* 112, 253903

Zdora M-C (2018) *J Imaging* 4, 60; doi:10.3390/jimaging4050060

# Speckle-Based PCI - Basics

“

- Several operational modes have been developed
- Different parametric images can be obtained
- Can be performed with compact X ray sources



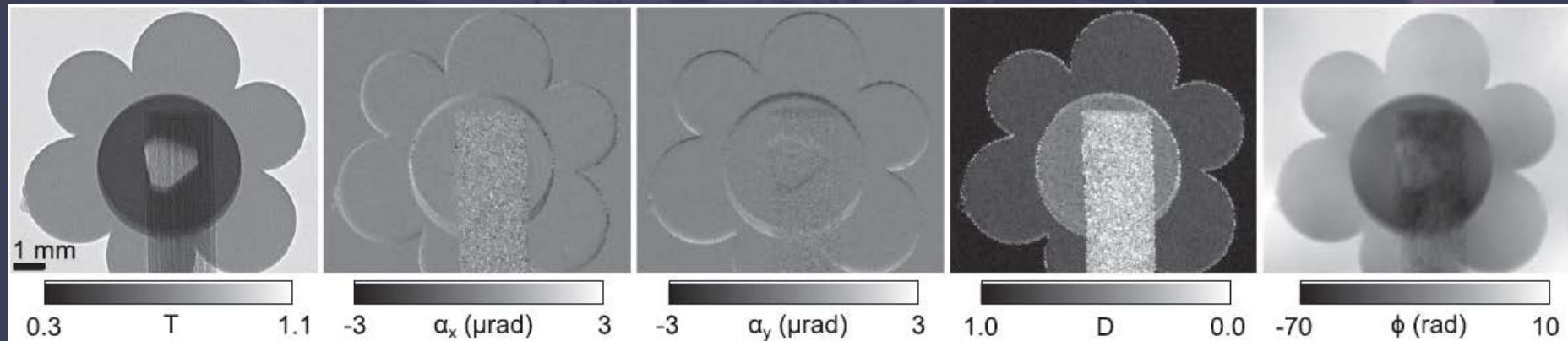
transmission

refraction x

refraction y

dark-field

phase shift



”



Zanette I, et al. (2014) *Phys. Rev. Lett.* 112, 253903

Zdora M-C (2018) *J Imaging* 4, 60; doi:10.3390/jimaging4050060



# The last slide

“

- Several different Phase Sensitive techniques have been presented
  - Propagation-Based PCI
  - Analyzer-Based PCI
  - Edge Illumination
  - Grating Interferometry
  - Speckle-Based PCI
- All of them show improved image quality with respect to conventional X-ray imaging
- Some of them could arguably be translated soon to clinics or to small-animal imaging applications

”





Thanks for your attention

Luigi Rigon  
University of Trieste & INFN, Sezione di Trieste  
*XV Seminar on Software for Nuclear, Subnuclear and  
Applied Physics – Alghero (Italy) - 31 MAY 2018*



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DI TRIESTE



“

Back-up

”



# My naive approach to coherence (at the SYRMEP beamline)

- We can define two coherence lengths:
- **Temporal (or longitudinal) coherence length**
  - length up to which the beam can be considered as coherent along the propagation direction

$$L_t = \lambda^2 / \Delta \lambda$$

- At SYRMEP,  $L_t = \lambda \cdot \lambda / \Delta \lambda = 10^{-10} m \cdot 10^4 = 10^{-6} m$

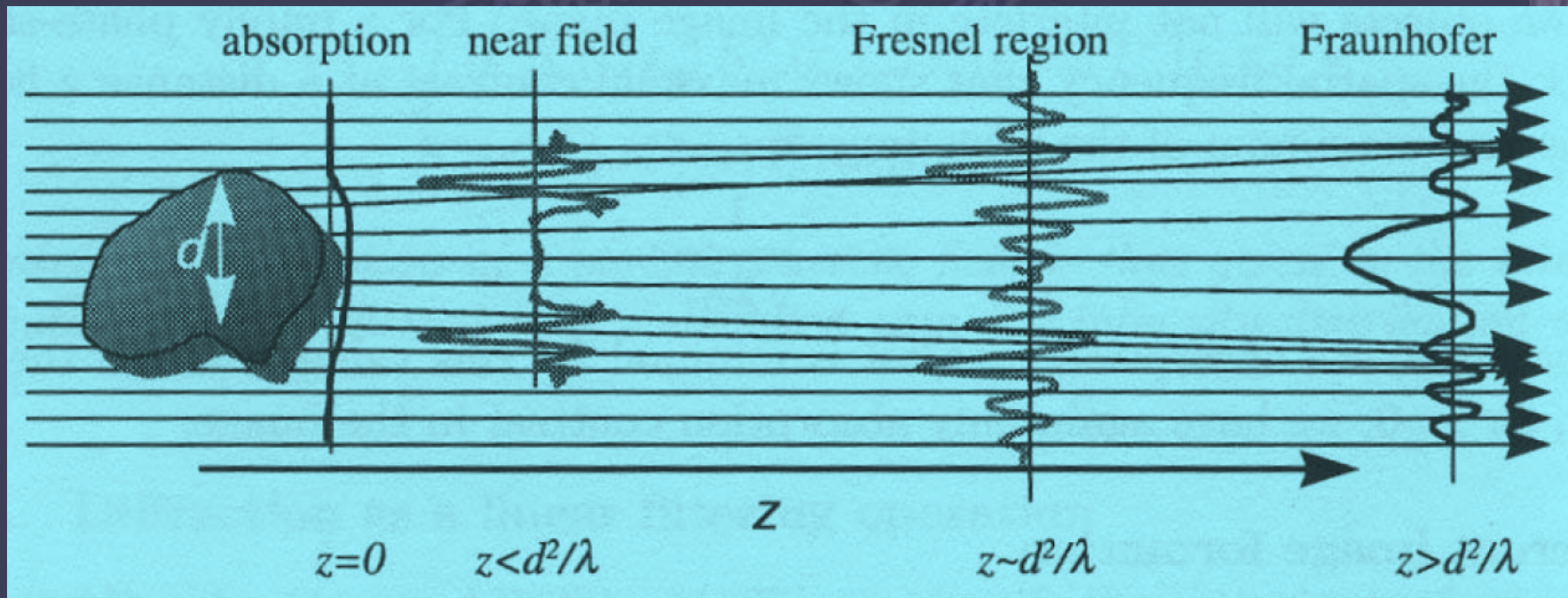
- **Spatial (or lateral) coherence length**
  - Reference length for the coherence on the object plane, perpendicular to the beam propagation direction

$$L_s = \lambda z_1 / S$$

- At SYRMEP,  $L_s = 10^{-10} m \cdot 30 m / 3 \cdot 10^{-4} m = 10^{-5} m$

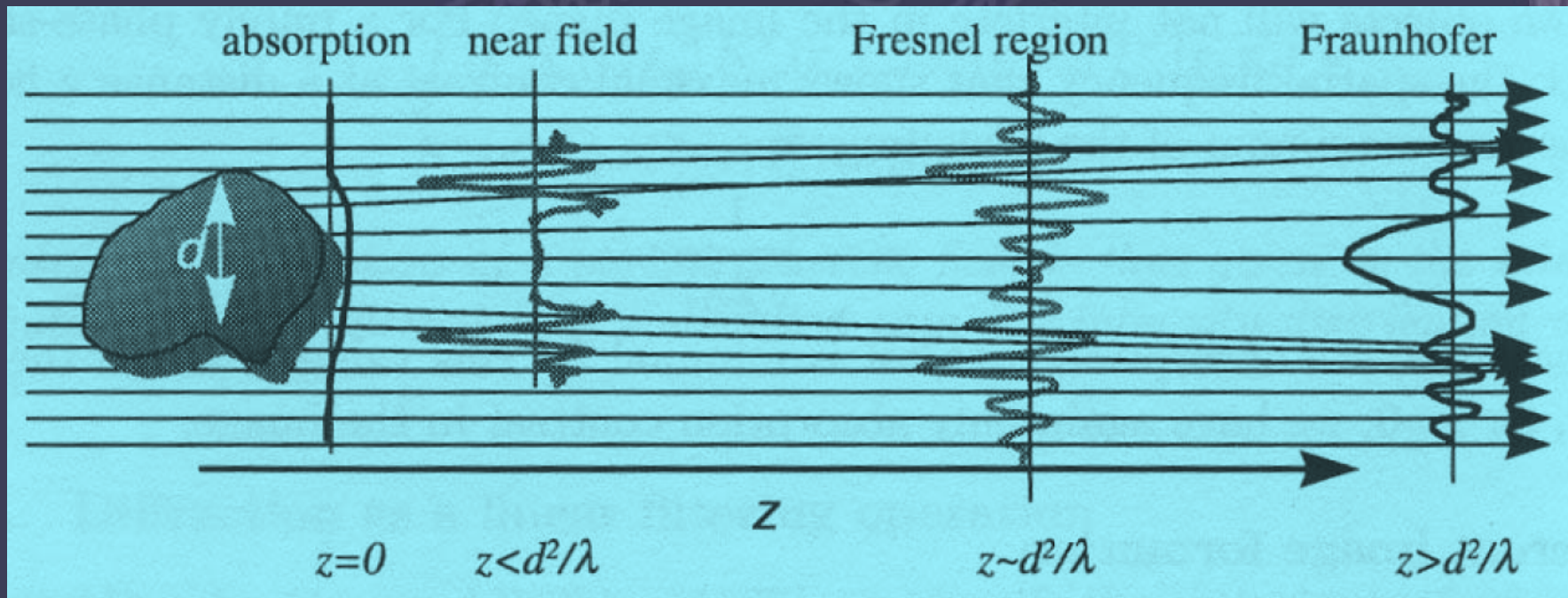


# Diffraction Regimes at SYRMEP



- Let us suppose  $d \sim 10^{-5} \text{ m}$ 
  - Comparable with  $L_s$  and with the spatial resolution of the CCD
- Then the near field region is limited by
  - $z \sim (10^{-5} \text{ m})^2 / 10^{-10} \text{ m} = 1 \text{ m}$

# Diffraction Regimes at SYRMEP



- If we set  $z > 1 \text{ m}$ , the Fresnel region is in principle accessible, but secondary peaks are anyway not visible because the signal must be convolved with the re-scaled source size:
  - $S z_2/z_1 = 3 \cdot 10^{-4} \text{ m} \cdot 1/30 = 10^{-5} \text{ m}$



# PB-PCI: Limitations and Requirements

“

- Spatial coherence of the beam
- Spatial resolution of the detector
- Attempt to implement it into clinics:
  - Konica-Minolta Regius 190 Pureview CR System
  - Source size 100 / 300  $\mu\text{m}$
  - 1.75x magnification (65 cm + 49 cm)
  - 43.75  $\mu\text{m}$  sampling pitch (25  $\mu\text{m}$  in the de-magnified image)

$$L_t = \lambda \cdot \lambda / \Delta \lambda = 10^{-10} \text{m} \cdot 1 = 10^{-10} \text{m}$$

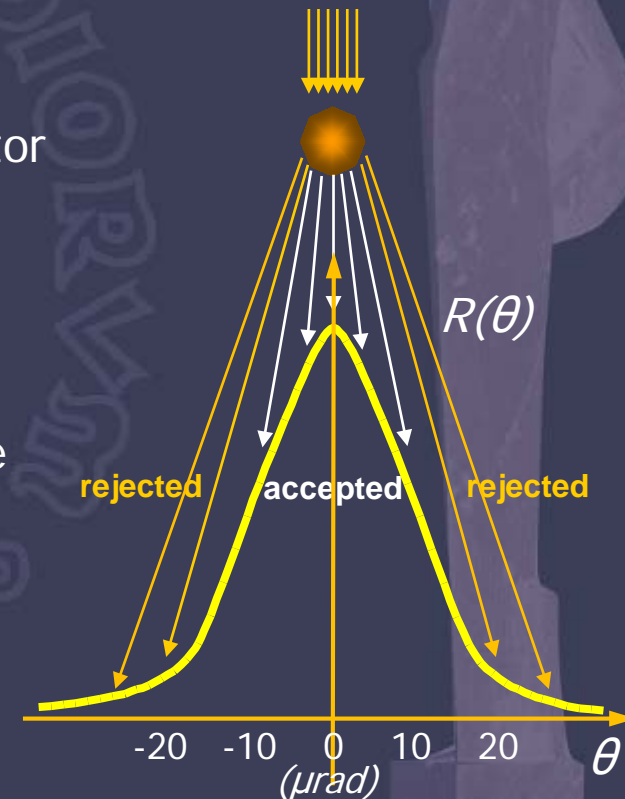
$$L_s = \lambda z_1 / S$$

$$L_s = 10^{-10} \text{m} \cdot 1 \text{m} / 10^{-4} \text{m} = 10^{-6} \text{m}$$

”

# Extinction and Refraction Contrast

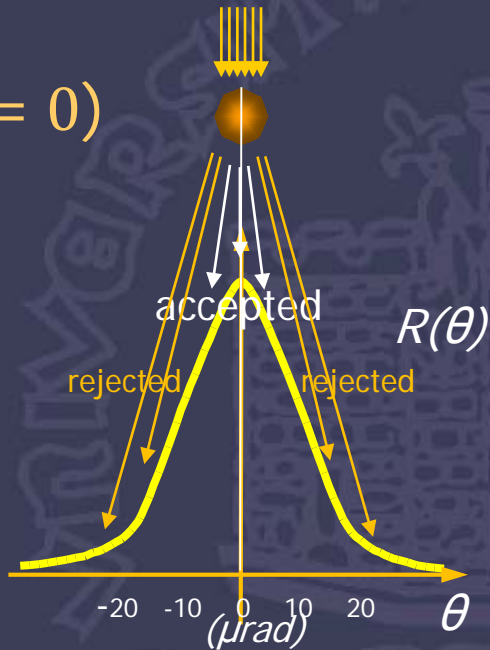
- The analyzer crystal acts as an angular band-pass filter, the filtering function being the rocking curve
  - Photons deviated outside the rocking curve width are not diffracted by the analyzer towards the detector
    - » Extinction contrast
  - Photons deviated within the rocking curve width are diffracted by the analyzer towards the detector, the probability being modulated by the rocking curve
    - » Refraction contrast
- Extinction and refraction contrast depend on the position of the analyzer on the rocking curve



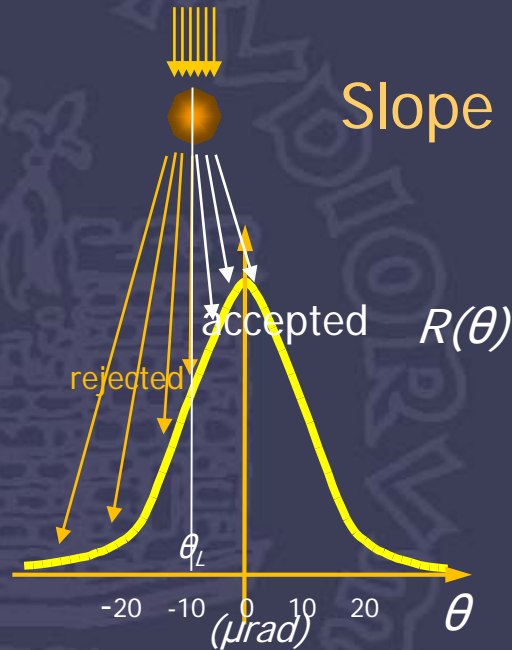


# Analyzer Tuning

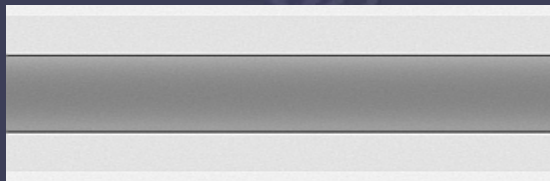
Top ( $\tilde{\theta} = 0$ )



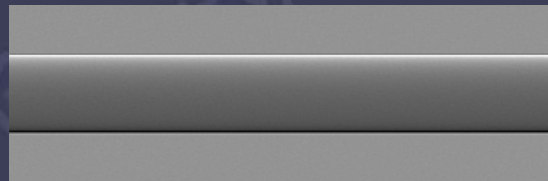
Slope ( $\tilde{\theta} = \theta_L$ )



$$R(0 + \Delta\theta(x,y)) < R(0)$$



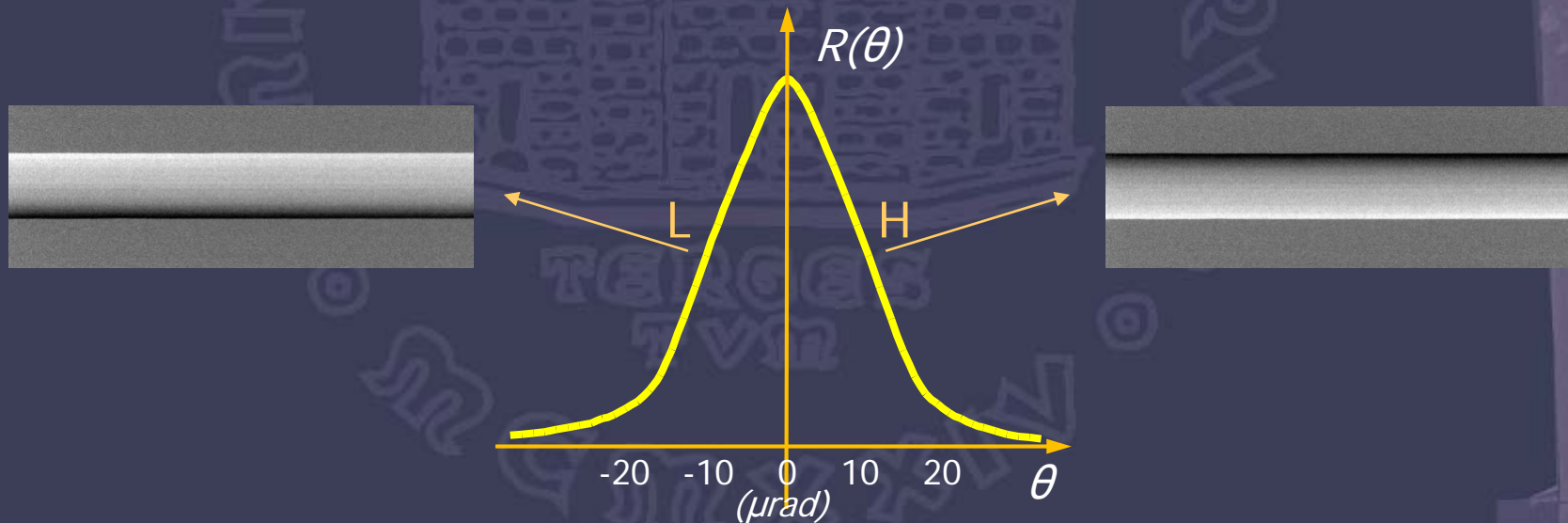
$$R(\theta_L + \Delta\theta(x,y)) \begin{matrix} < \\ > \end{matrix} R(\theta_L)$$



# The «conventional» DEI algorithm (I)

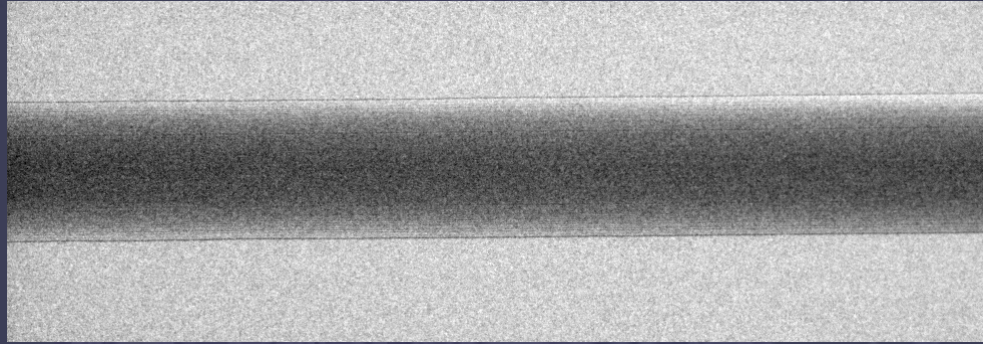
– D.Chapman *et al.*, Phys.Med.Biol. **42** 2015 (1997)

- Data acquisition and modeling:
  - Two images are acquired at the slopes of the rocking curve
  - The rocking curve is approximated with a first order Taylor expansion

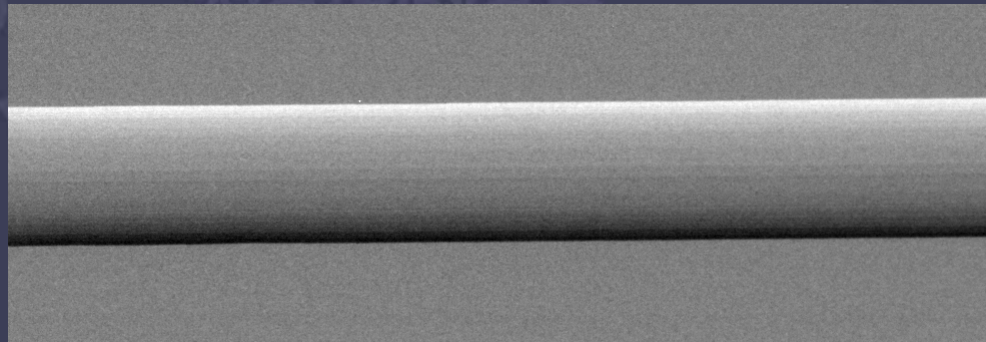


# The «conventional» DEI algorithm (II)

- The two equations can be solved to yield two images:
  - apparent absorption image (**absorption** + **extinction**)

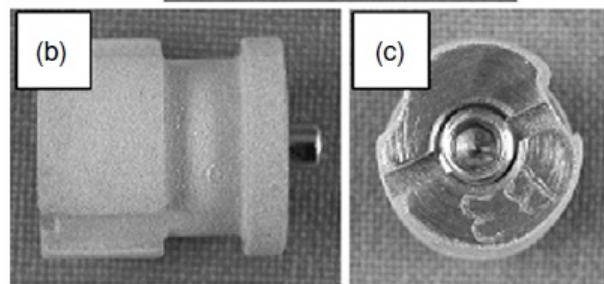


- refraction image (i.e. a map of the width of the **refraction** angle)





# Implants

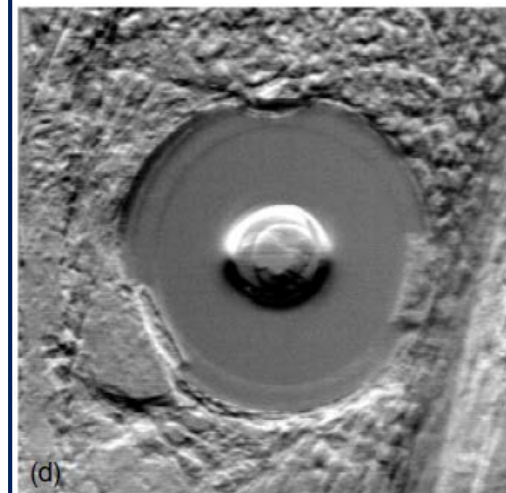
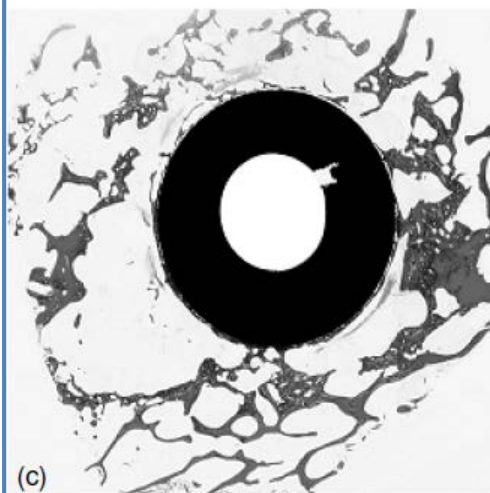


destruction-free and longitudinal evaluation of the quality of integration of metal implants into bone

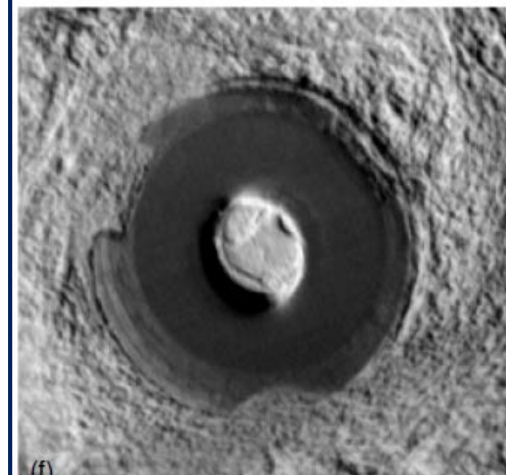
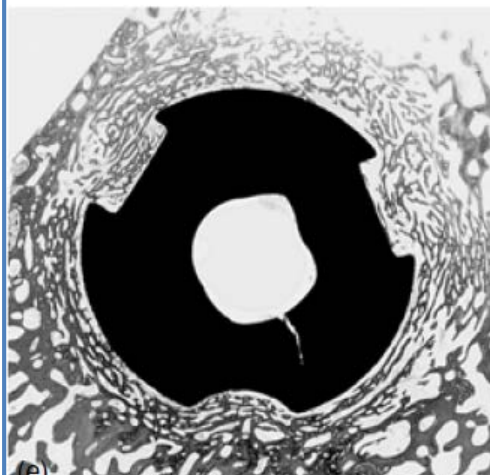
## Histology

## DEI

W/O BMP-2



BMP-2



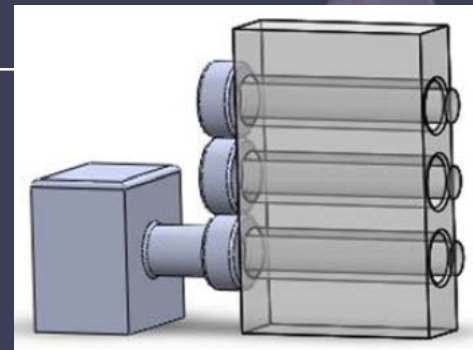
Wagner, A., Sachse, A., Keller, M. et al. (2006). *Phys. Med. Biol.* 51, 1313–1324.  
Coan, P., Wagner, A., Bravin, A., et al. (2010). *Phys. Med. Biol.* 55, 7649–7662.



# Contrast Agents for DEI

“

- Contrast media based on gas-filled microbubbles, normally used in ultrasound imaging ( $2\text{--}8\ \mu\text{m}$ ).

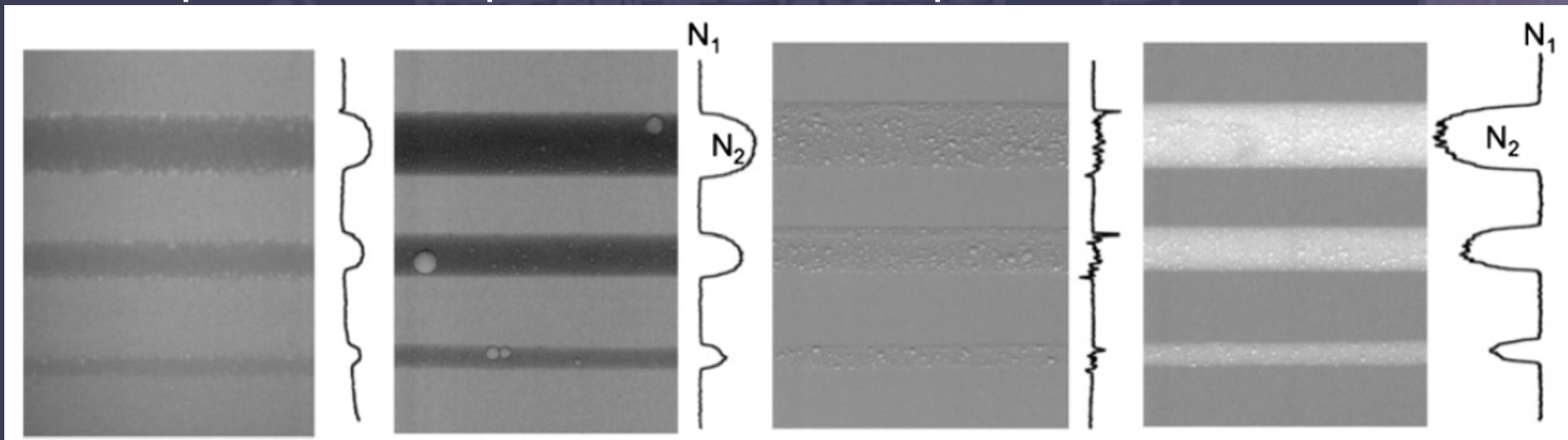


absorption

peak

slope

toe

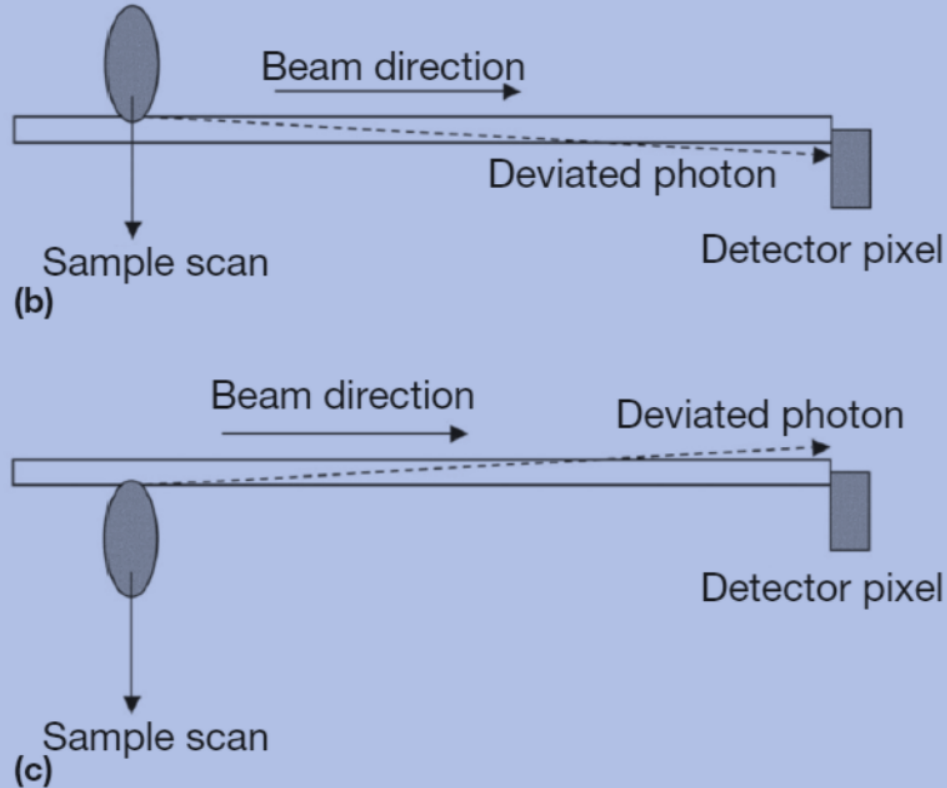
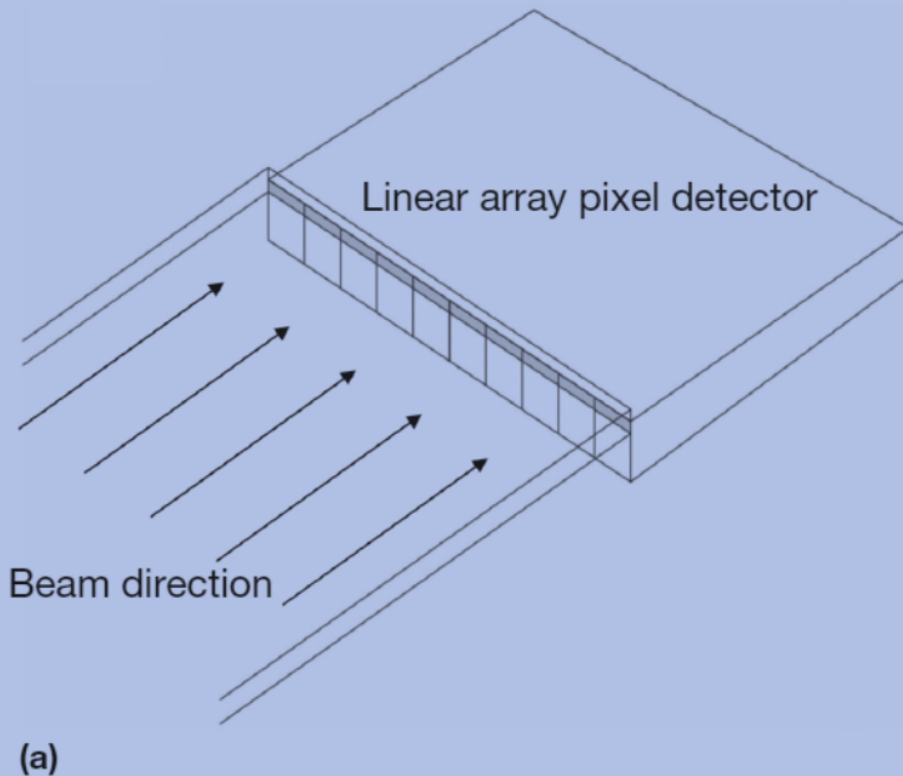


Arfelli F, Rigon L, and Menk RH (2010) *Physics in Medicine and Biology* 55: 1643–1658.  
 Arfelli F, et al. (2003) *Proc. SPIE* 5030I 274–83

”

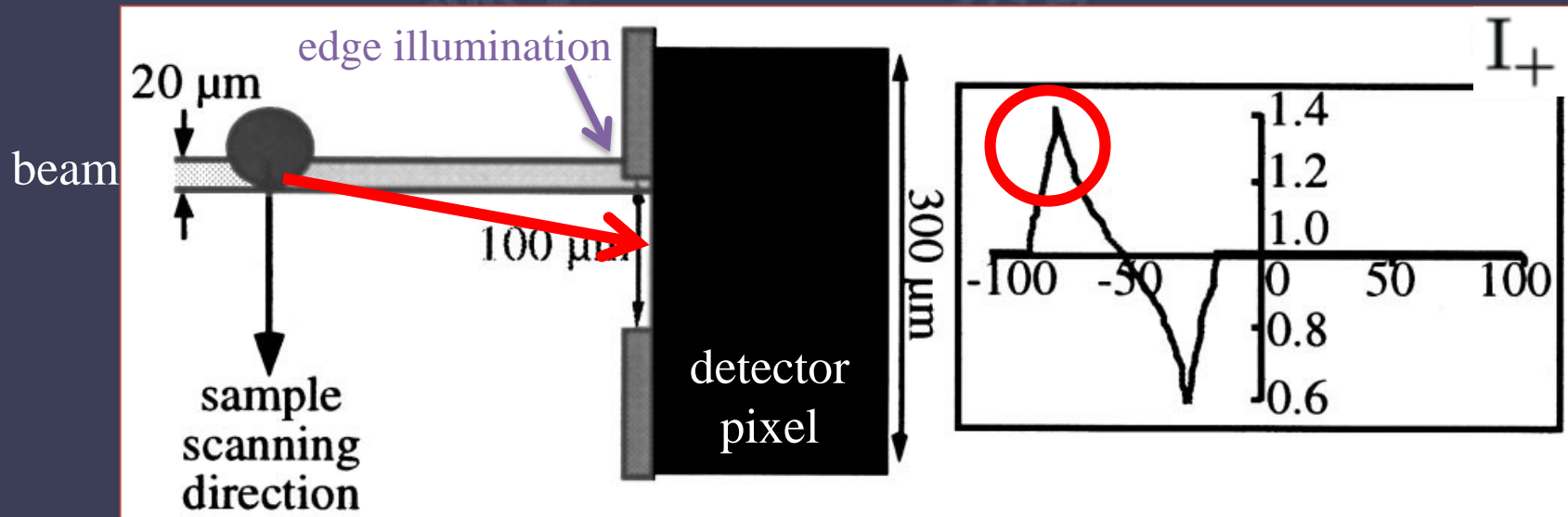
# Edge-illumination principle

- “ • This technique exploits the so-called edge-illumination principle, that was invented by A. Olivo at Elettra (2001)

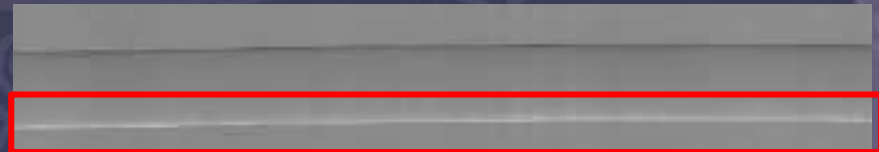


Olivo, A., Arfelli, F., Cantatore, G. et al. (2001). *Med. Phys.* 28, 1610

# The edge-illumination principle

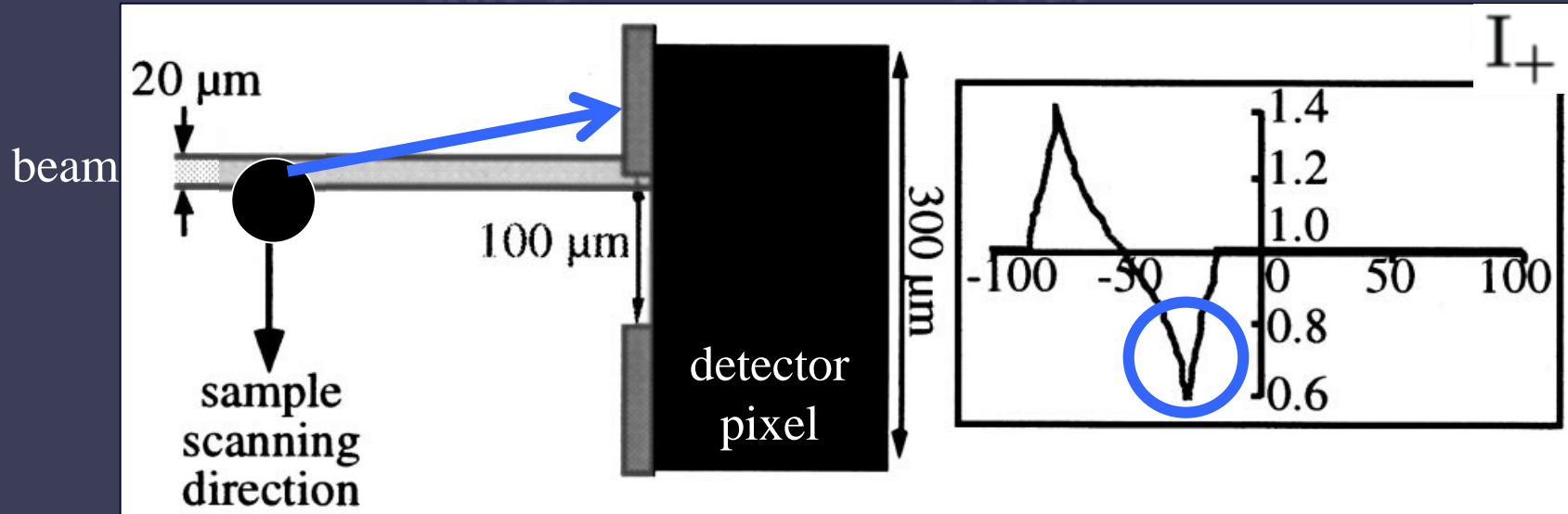


nylon wire ( $\varnothing\ 450\ \mu\text{m}$ )

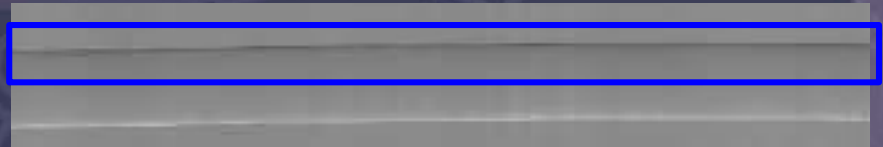


Olivo, A., Arfelli, F., Cantatore, G. et al. (2001).  
*Med. Phys.* **28**, 1610-1619.

# The edge-illumination principle



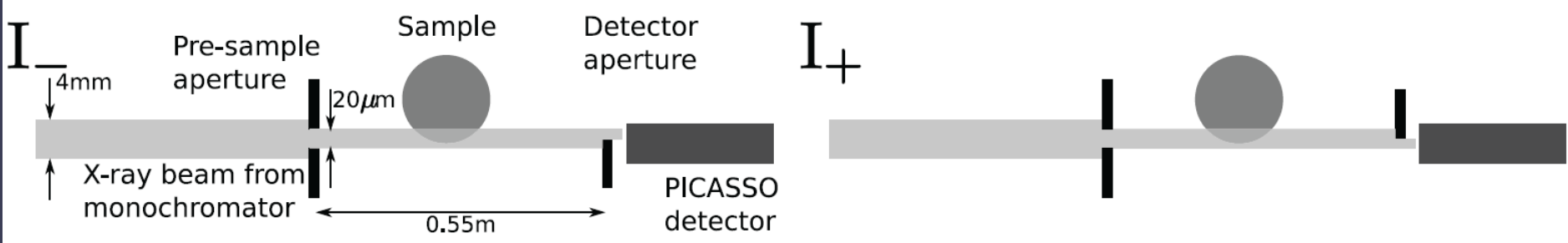
nylon wire ( $\varnothing\ 450\mu\text{m}$ )



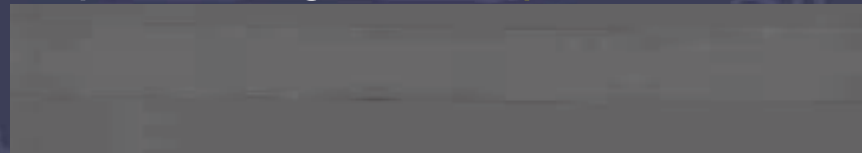
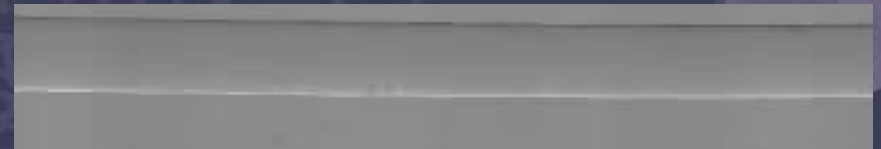
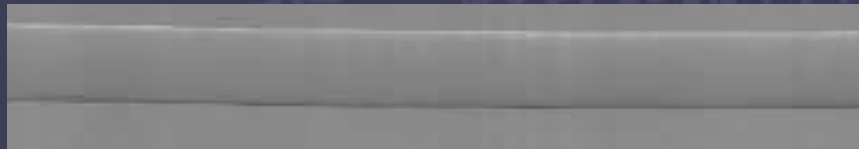
Olivo, A., Arfelli, F., Cantatore, G. et al. (2001).  
*Med. Phys.* **28**, 1610-1619.



# Quantitative Edge-illumination PCI



- The two images  $I_-$  and  $I_+$  can be combined to yield:
  - apparent absorption image (**absorption** + **extinction**)
  - refraction image (i.e. a map of the width of the **refraction** angle)



“

# Interferometry

”



# From phase shift to image contrast

“

- Interferometry is a family of techniques in which waves are superimposed in order to extract information.
  - Widely used in optics (visible light)
  - It can be used in X-ray phase contrast imaging to transform the phase shift introduced by the object into image contrast
- Two different interferometric approaches:
  - Crystal interferometry
    - (Bonse and Hart, 1965)
  - Grating interferometry
    - (David et al, 2002; Momose et al., 2003)



*Bonse, U. and Hart, M. (1965). Appl. Phys. Lett. 6, 155–156.*

*David, C., Nöhammer, B. et al. (2002). Appl. Phys. Lett. 81, 3287–3289*

*Momose, A. et al. (2003). Japan J. Appl. Phys.: 2 Lett. 42, L866–L868*

”

Luigi Rigon  
Physics Dept. University of Trieste & INFN

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“

# Crystal Interferometry

”



Luigi Rigon  
University of Trieste & INFN, Sezione di Trieste  
*XV Seminar on Software for Nuclear, Subnuclear and  
Applied Physics – Alghero (Italy) - 31 MAY 2018*



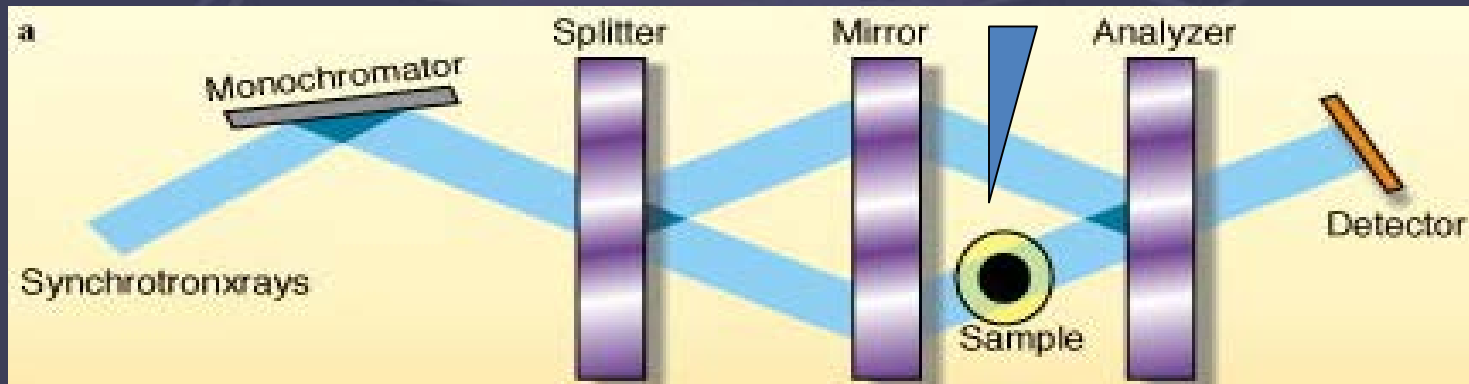
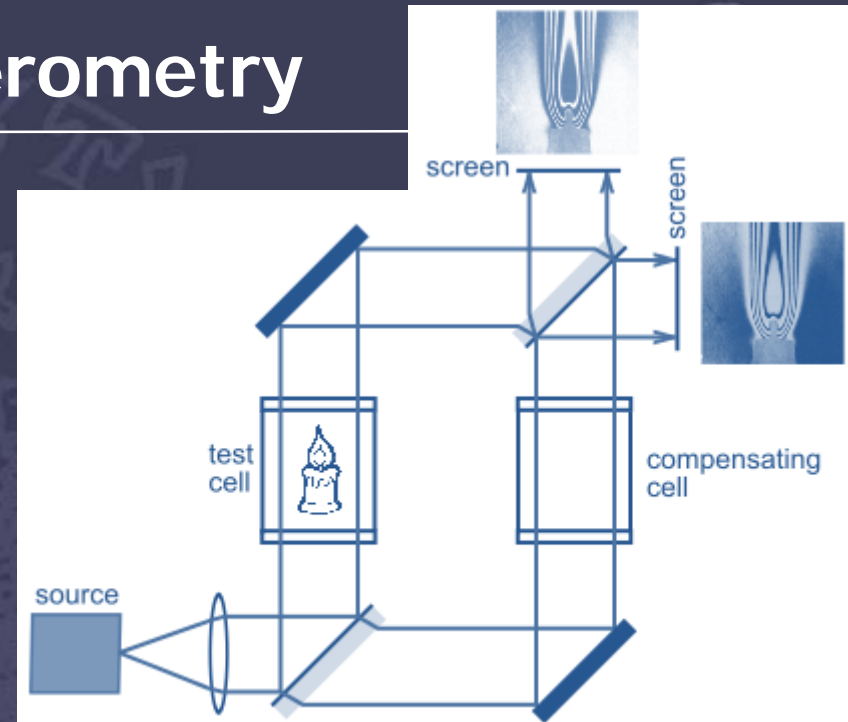
UNIVERSITÀ  
DEGLI STUDI  
DI TRIESTE



# Crystal Interferometry

“

- Mach-Zehnder interferometer used in optics (with visible light), 1892.
- Bonse-Hart X-ray interferometer, 1965.



”

# Crystal Interferometry

- “
- Extracting the phase shift introduced by the object
  - Phase wrapping:

- wrapped phase map



- unwrapped phase map

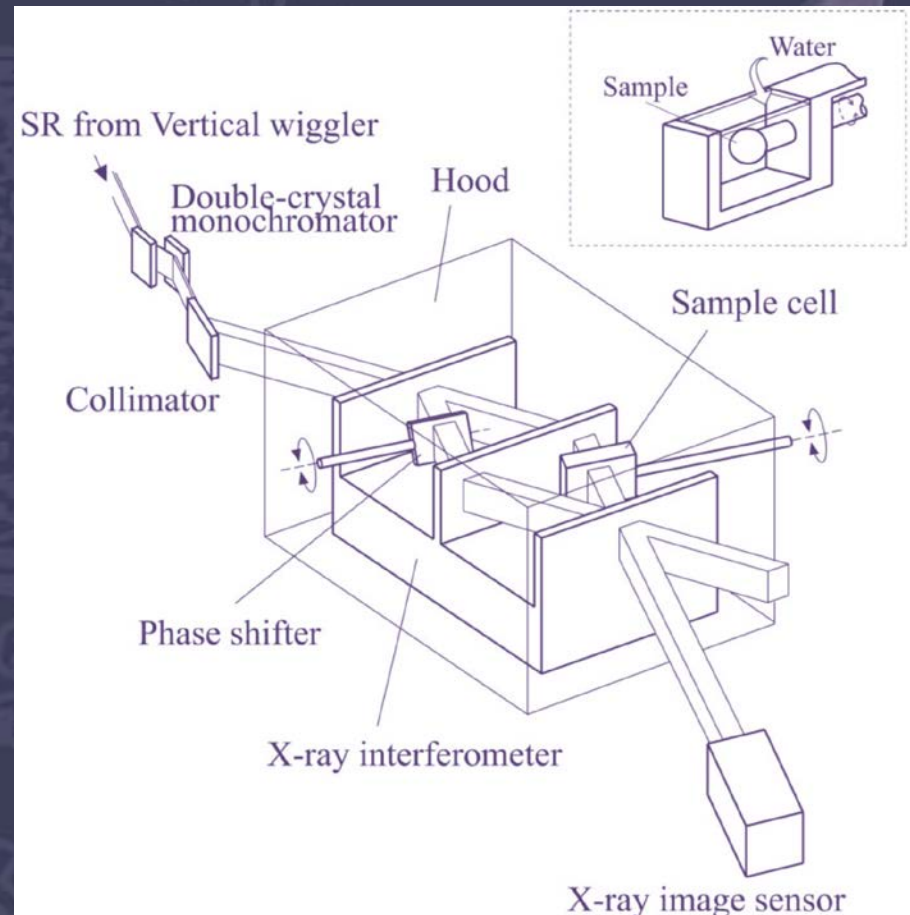


”

# Crystal Interferometry - Limitations

“

- Monochromatic and parallel beam
  - Synchrotron beam is basically the only choice
- Extreme Mechanical stability ( $\sim 1 \text{ \AA}$ )
  - the three crystals are typically obtained by grooving a single-crystal monolith
  - Limited field of view (25 mm x 30 mm)
  - sample in a water cell to avoid large phase jumps
  - *in vivo*, the heat from the small-animal can cause thermal instability



”

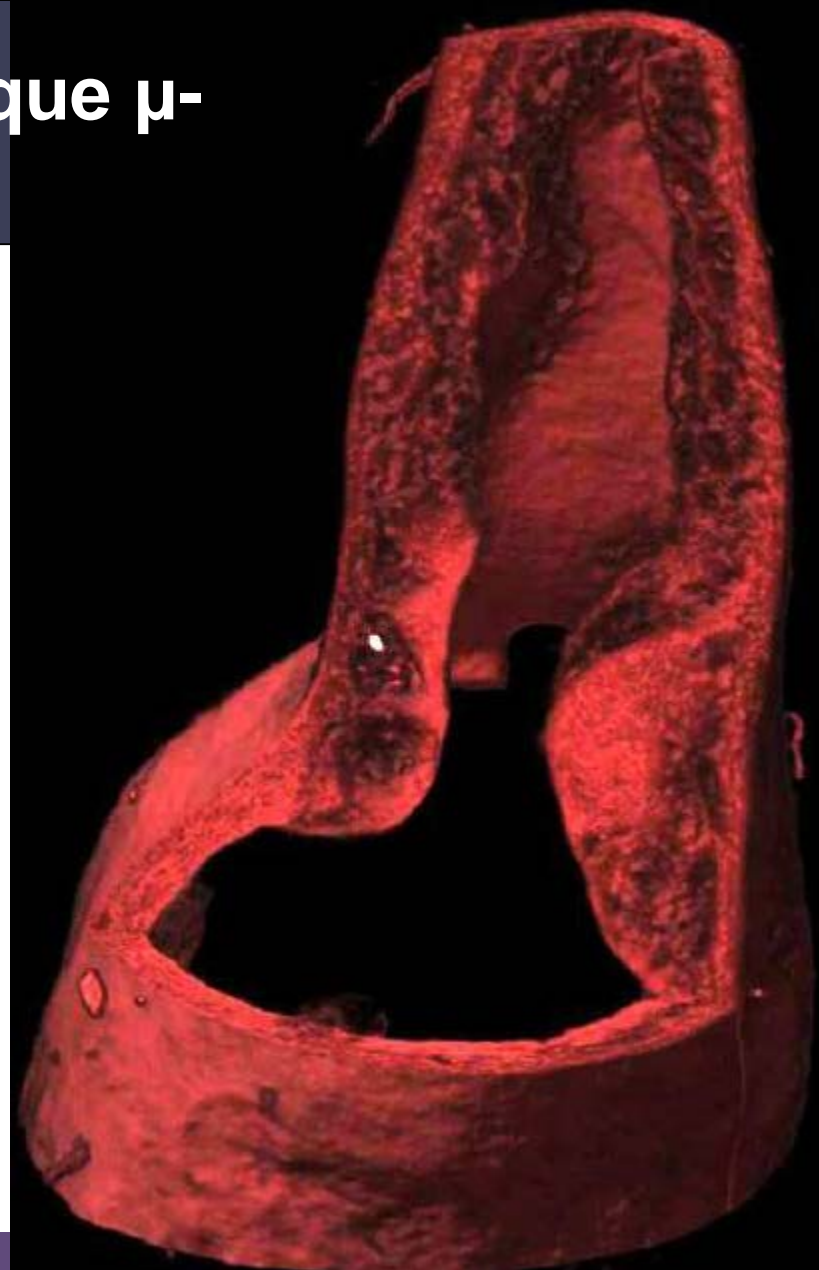
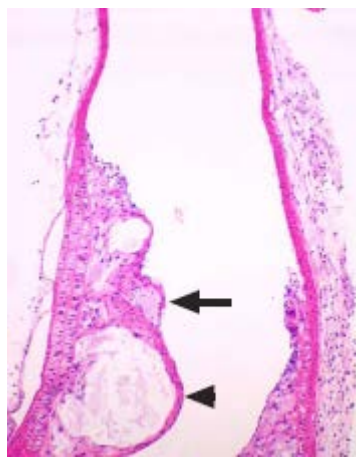
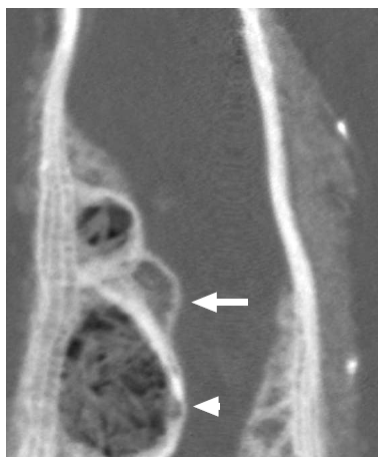
# *Ex vivo* atherosclerotic plaque $\mu$ -CT imaging

non-calcified components are visible with improved sensitivity with respect to absorption-based  $\mu$ -CT

investigate the effect of anti-platelet therapies in small-animal models:

by quantifying the plaque volume

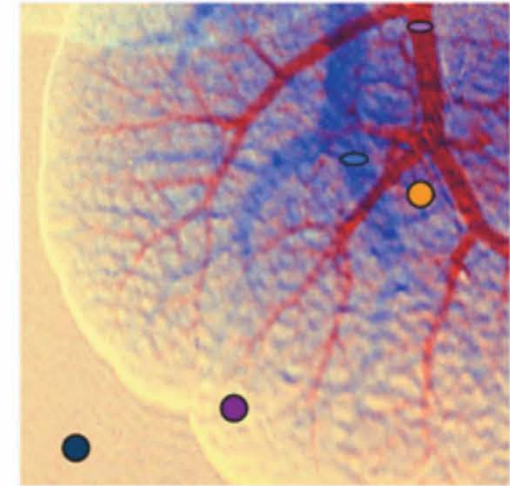
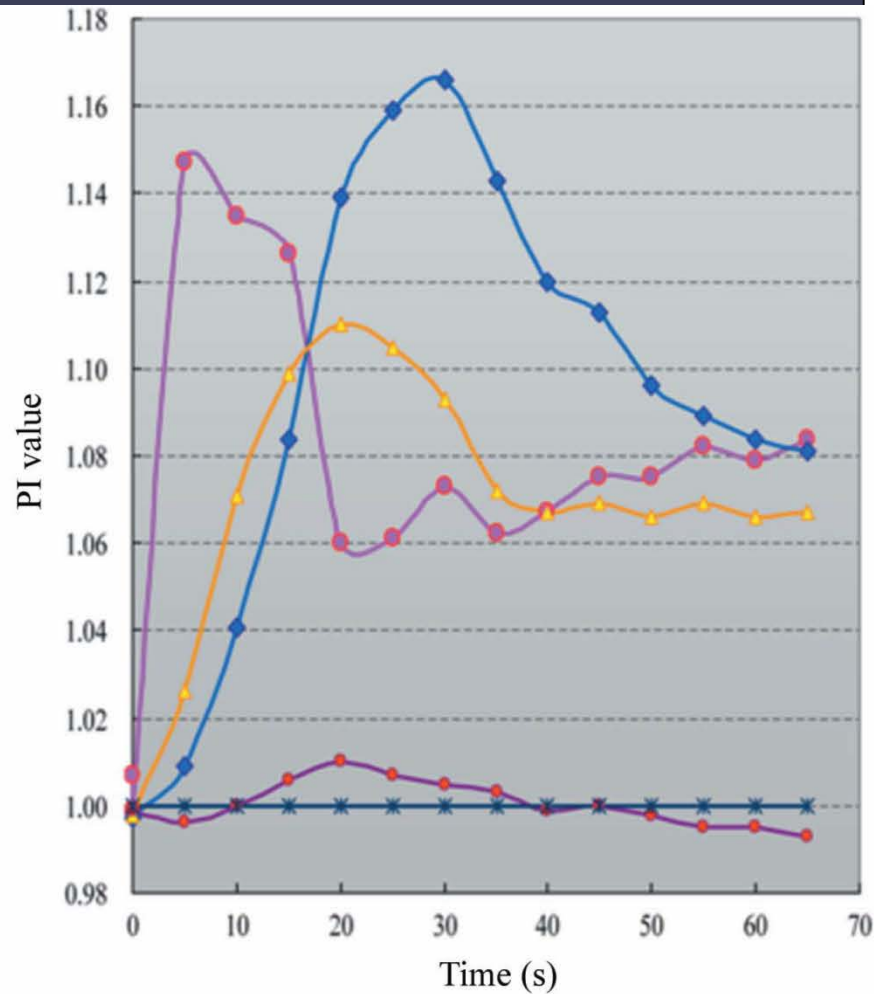
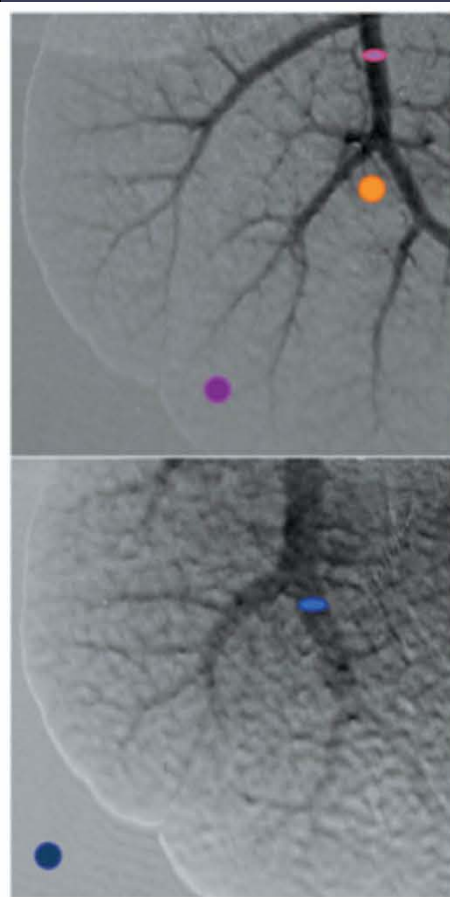
by qualifying the plaque components



*Shinohara, M. et al. (2008) Am. J. Physiol. Heart Circ. Physiol. 294, H1094–H1100*  
*Takeda, M. et al. (2012). Int. J. Cardiovasc. Imaging 28, 1181–1191.*



# *In-vivo* hepatic vessel imaging with Physiological saline as contrast agent



Overlapped image

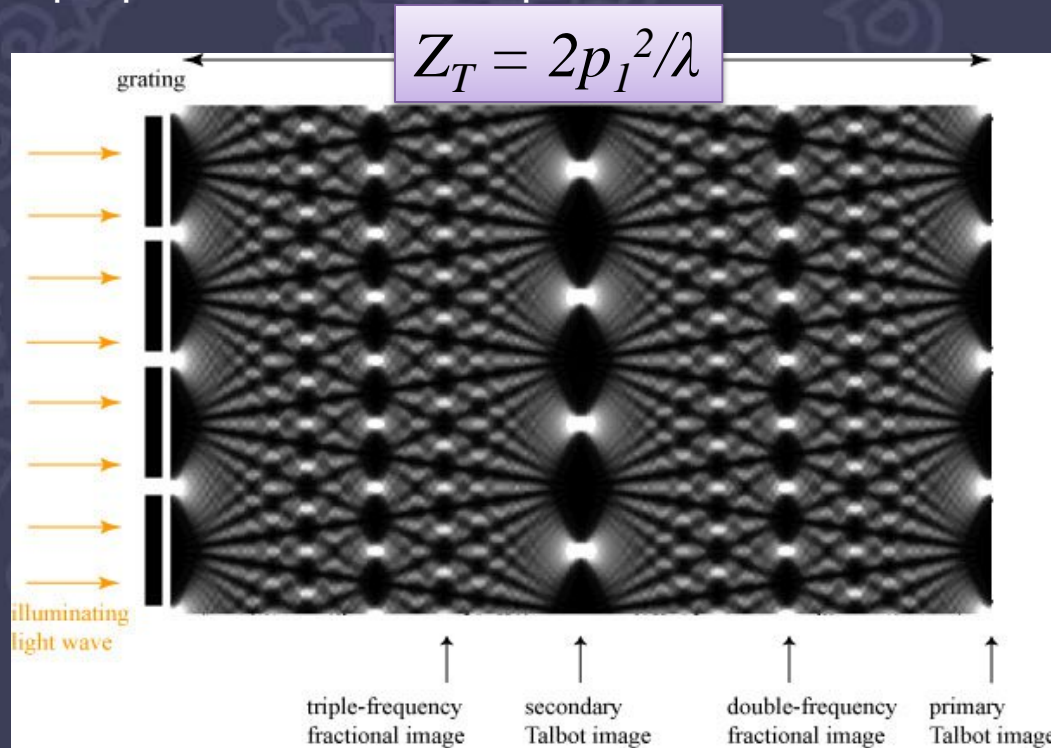
- Portal vein
- ◆— Hepatic vein
- ▲— Small vessel area
- Peripheral small vessel
- \*— Background



Takeda, T., Yoneyama, A., et al. *J. Synchrotron Radiat.* 19, 252–256.

# Talbot self-imaging effect

- “ • The diffracted beams interfere and form periodic fringe patterns in planes perpendicular to the optical axis



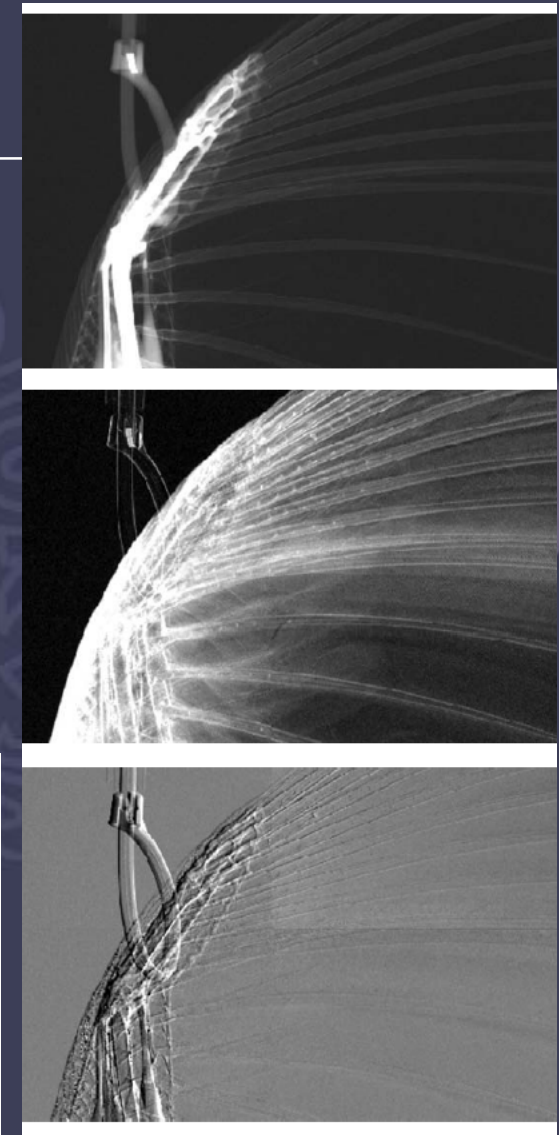
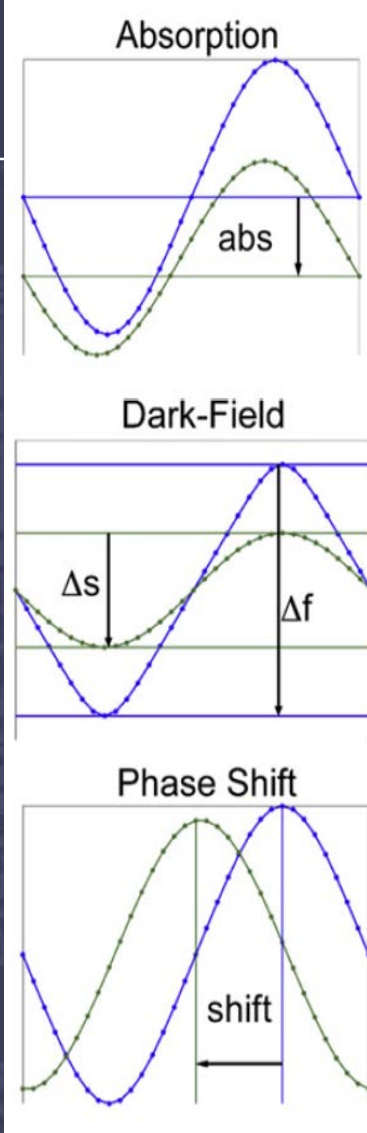
- Intensity pattern with period  $p_2 = p_1$  or  $p_2 = p_1/2$  observed at fractional Talbot distances

”

# Phase Stepping

“

- The high-spatial-frequency fringe pattern can be scanned by the analyzer grating  $G_2$
- The oscillations of the fringe pattern with and without the object are compared to yield:
  - Absorption image
    - Mean intensity
  - Dark-Field (USAXS)
    - Amplitude
  - Differential Phase (refraction)
    - Phase shift



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Pfeiffer, F. et al. (2008). *Nat. Mater.* 7, 134–137.

Scattarella, F. et al. (2013). *Phys. Med.- Eur. J. Med. Phys.* 29, 478-486.

