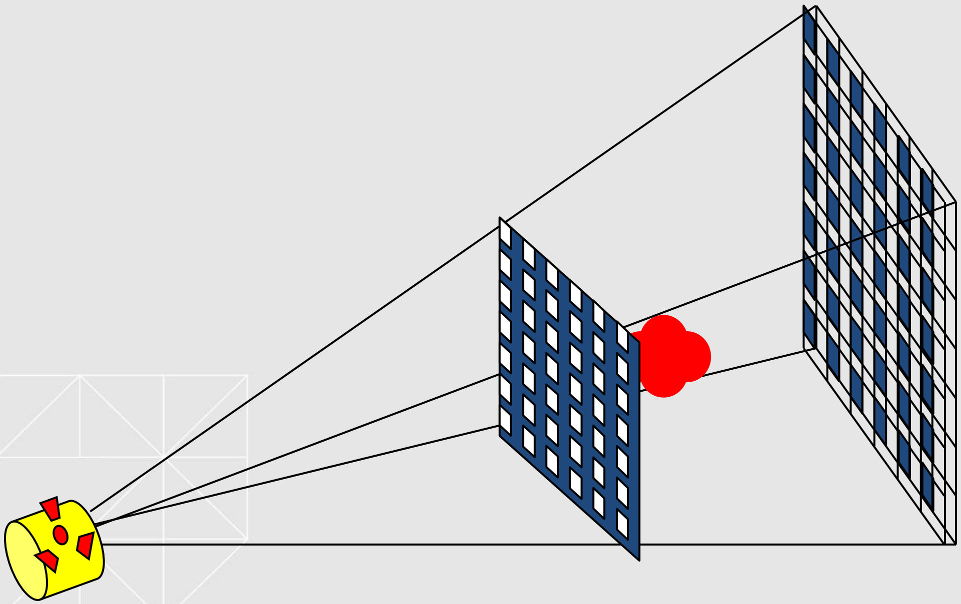
Multi-modal phase-based x-ray imaging: detecting the undetectable



Sandro Olivo, Head of the UCL XPCi group
Medical Physics and Bioemedical Engineering, UCL

UCL Institute of Biomedical Engineering

Research Complex at Harwell

John Adams Institute for Accelerator Science
Denys Wilkinson Building, University of Oxford, Oct 29 2015

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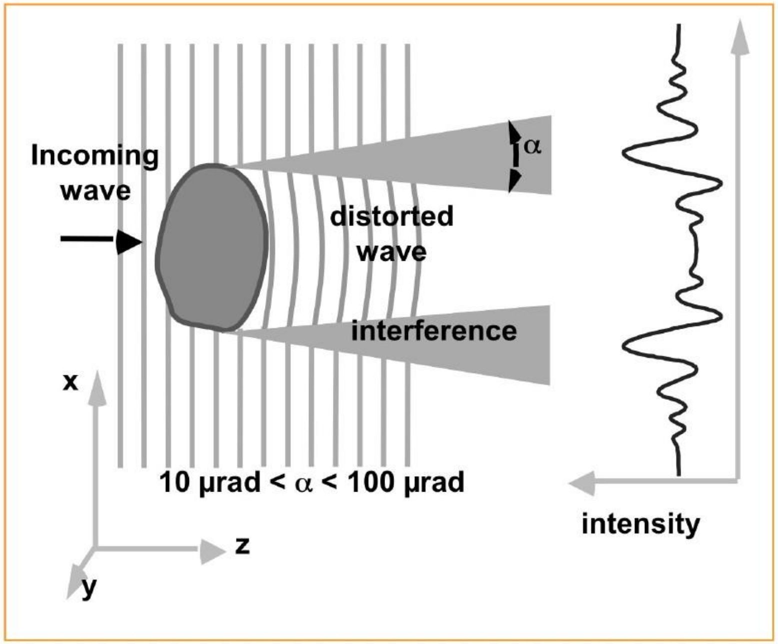
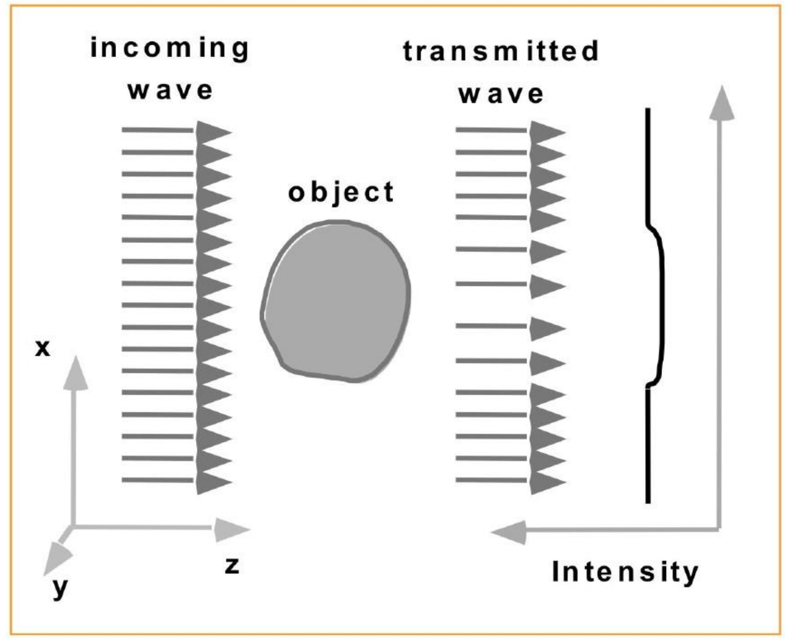
Phase Contrast Imaging vs. Conventional Radiology



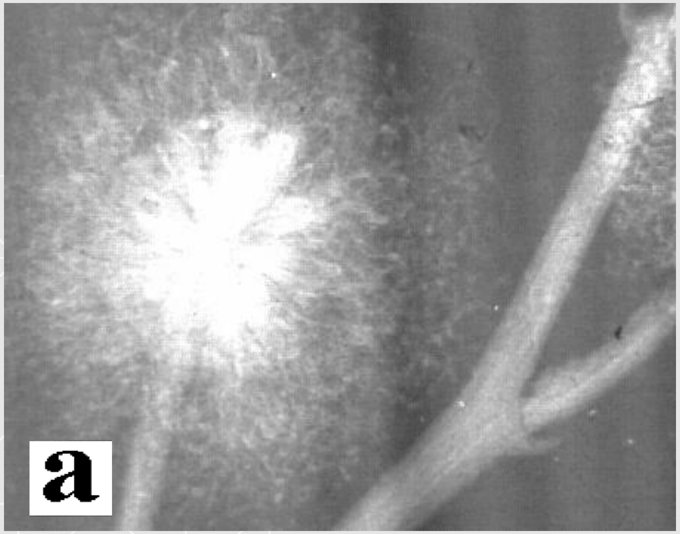


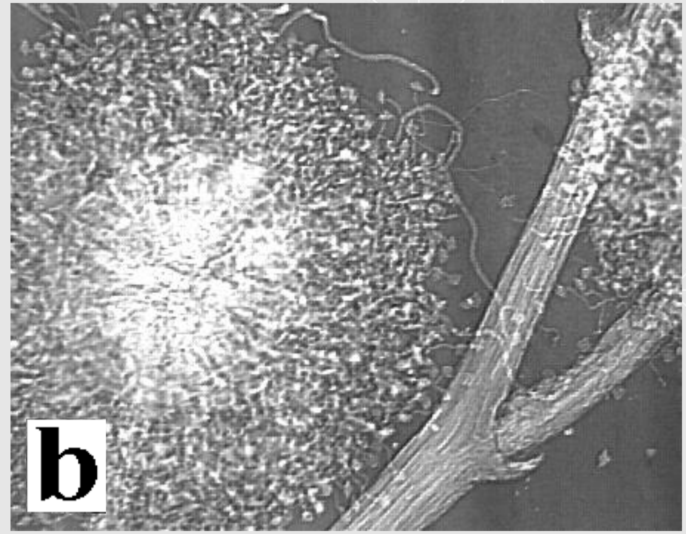
Refractive index: $n = 1 - \delta + i\beta$; $\delta >> \beta$ ->
phase contrast ($\Delta I/I_0 \sim 4\pi\delta\Delta z/\lambda$) >> absorption contrast ($\Delta I/I_0 \sim 4\pi\beta\Delta z/\lambda$)

Two possible approaches:
- **detect interference patterns**
- **detect angular deviations**

a) absorption

b) phase contrast

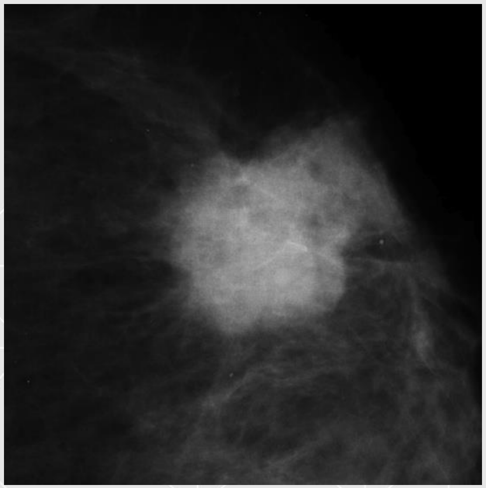




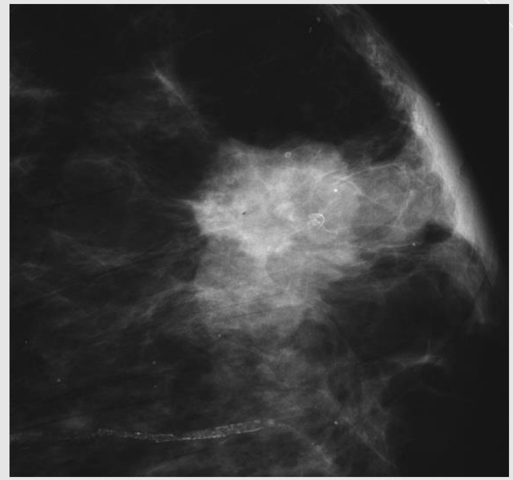
DiMichiel *et al* Proceedings of MASR1997

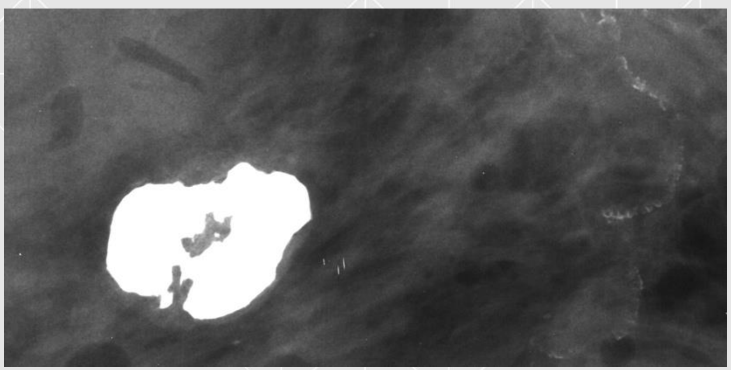
Impressive results are achieved in breast imaging

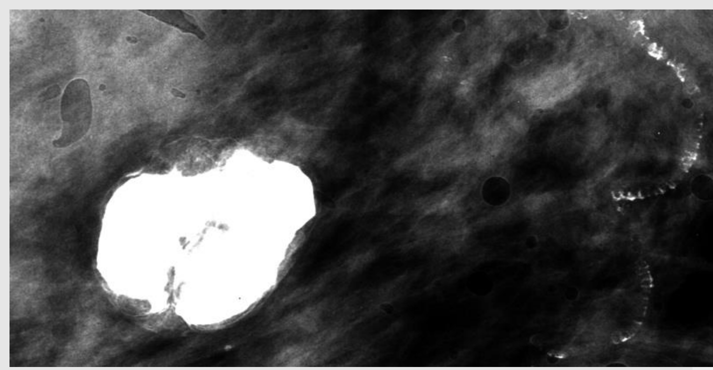
absorption



phase contrast







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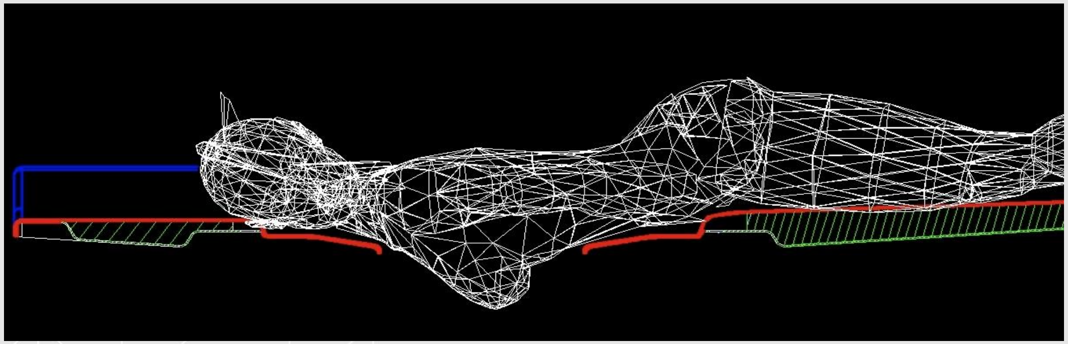
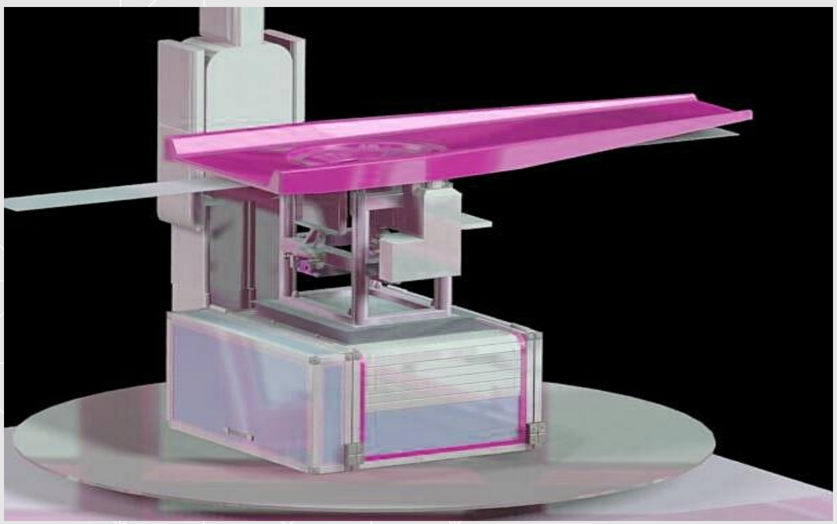
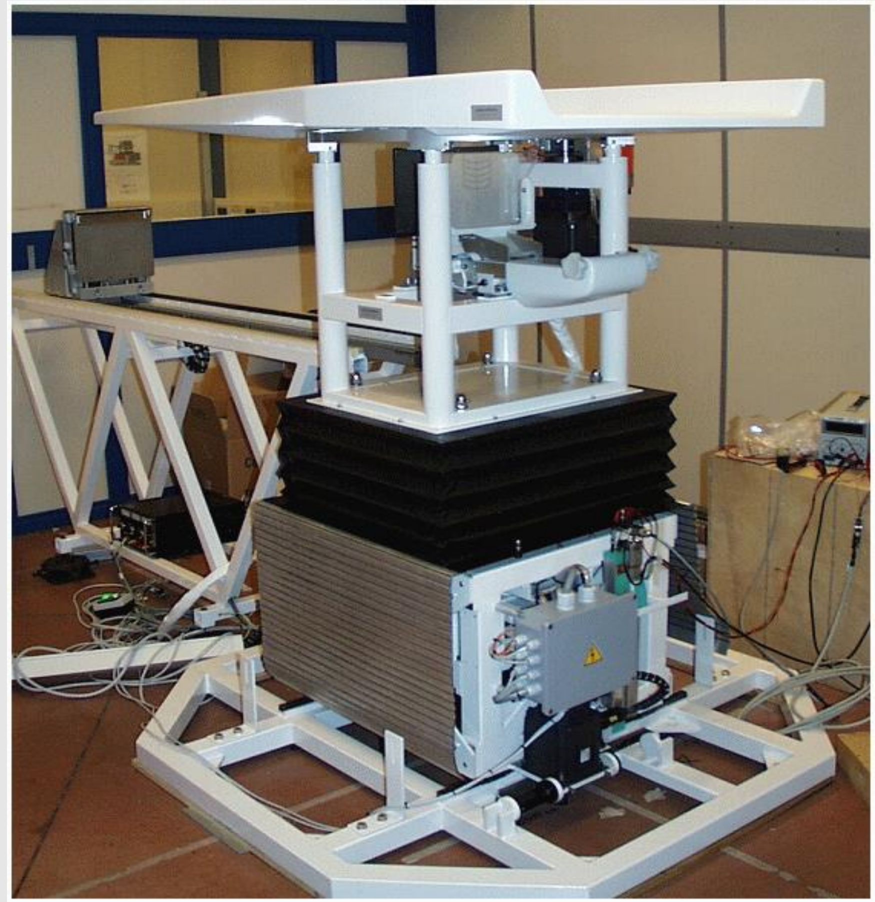
Arfelli et al. Phys. Med. Biol. 43 (1998) 2845-52

Which led to the realization of a dedicated mammography station in TS







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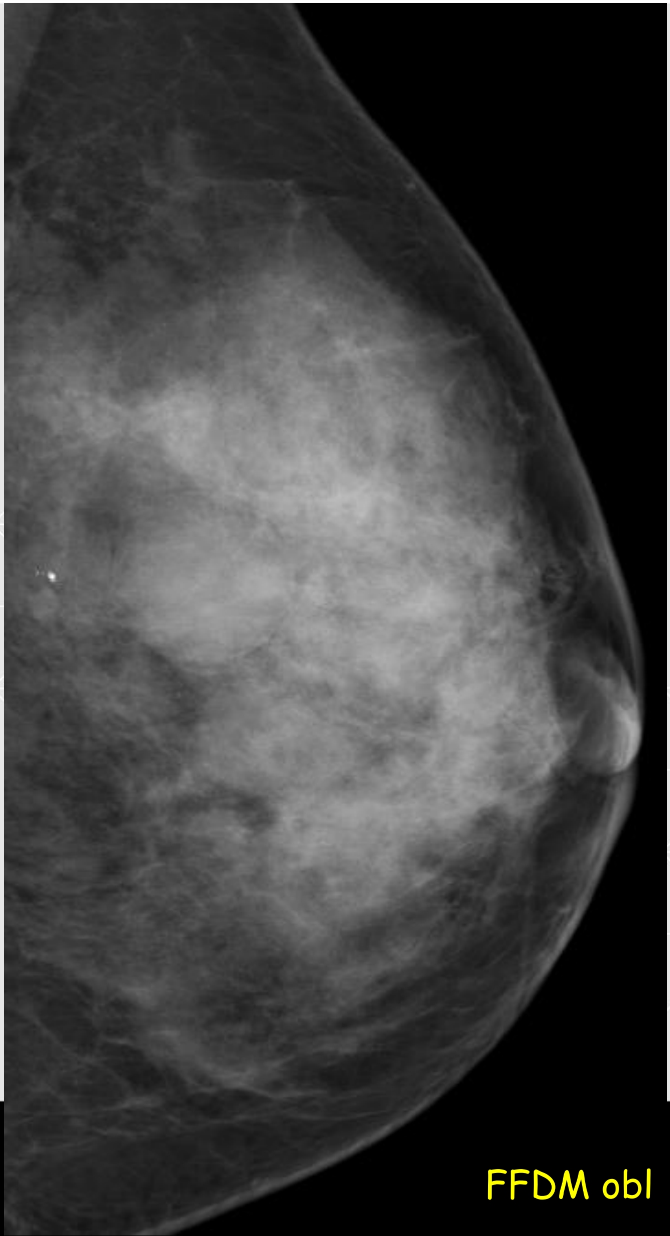
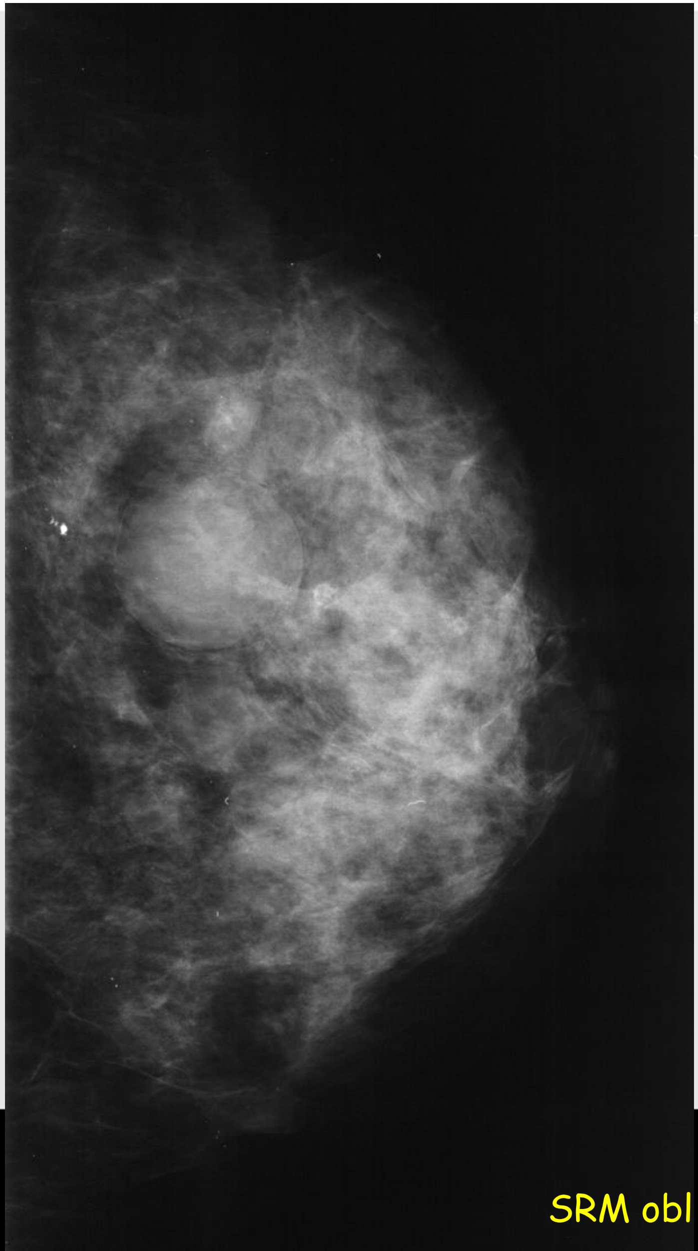
Castelli et al. Radiology 259 (2011) 684-94

SRM: findings

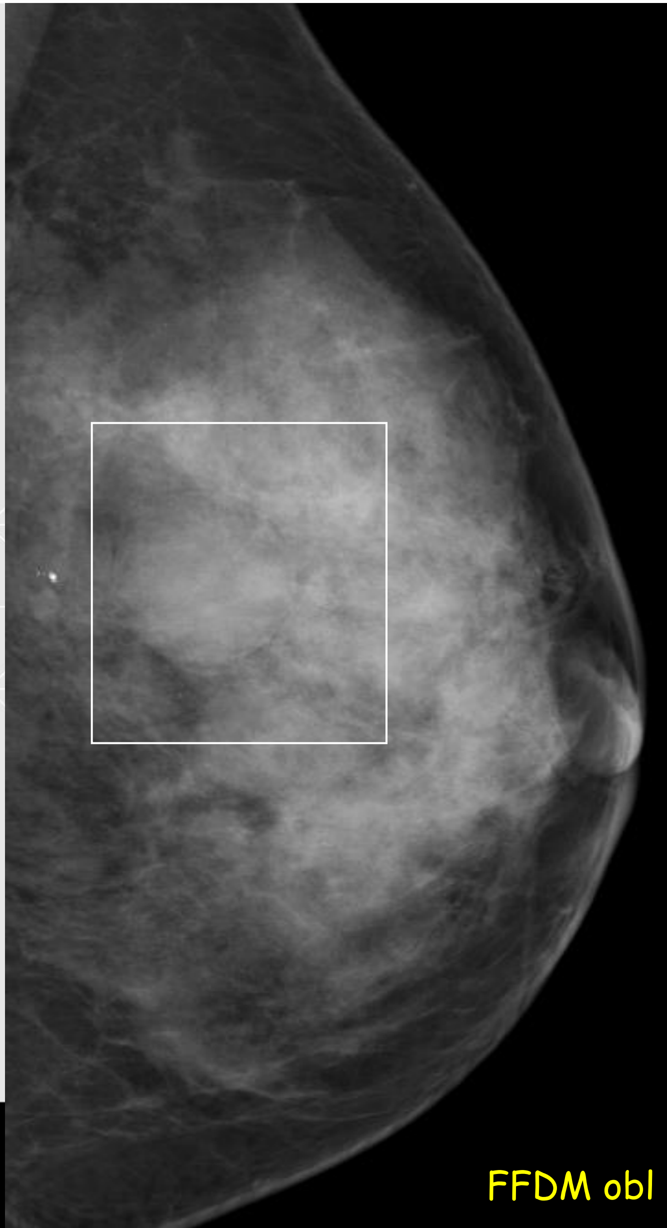


FFDM obl

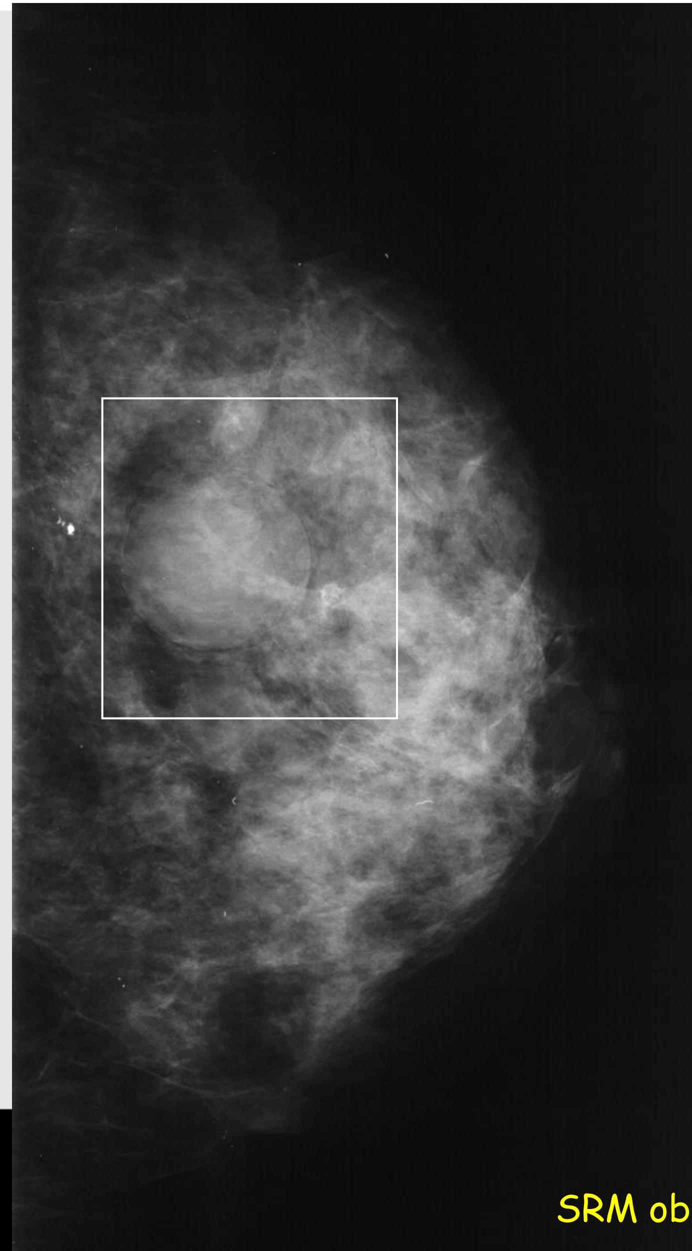


SRM obl

SRM: findings



FFDM obl



SRM obl

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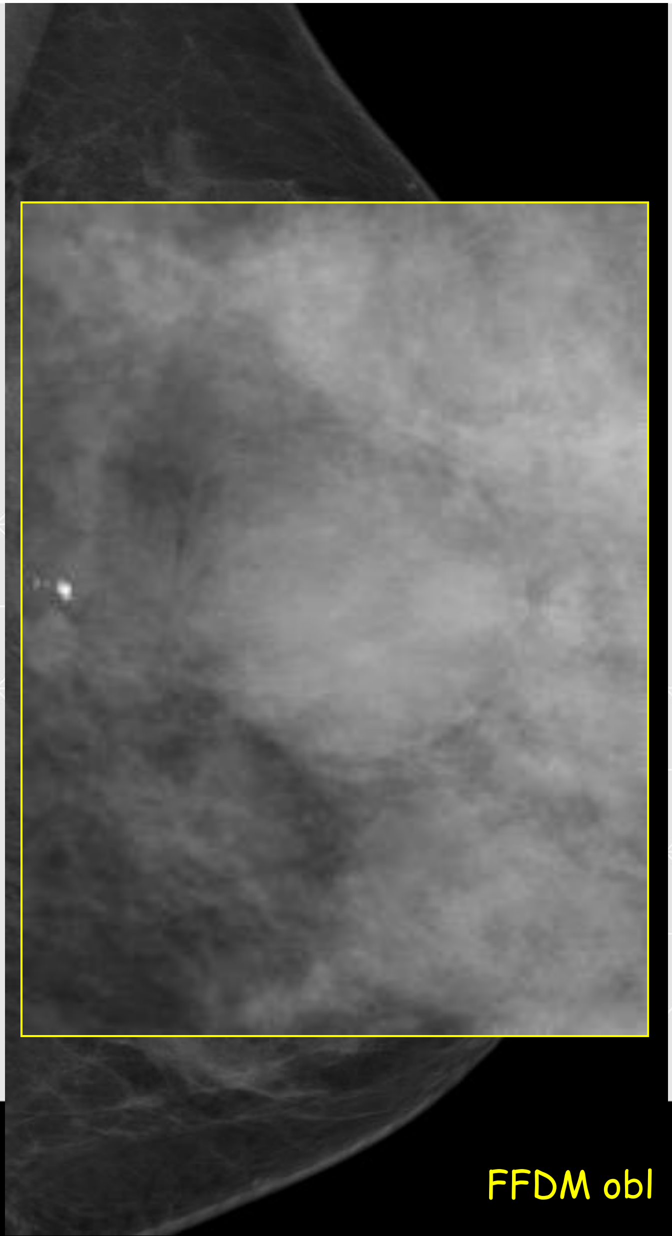
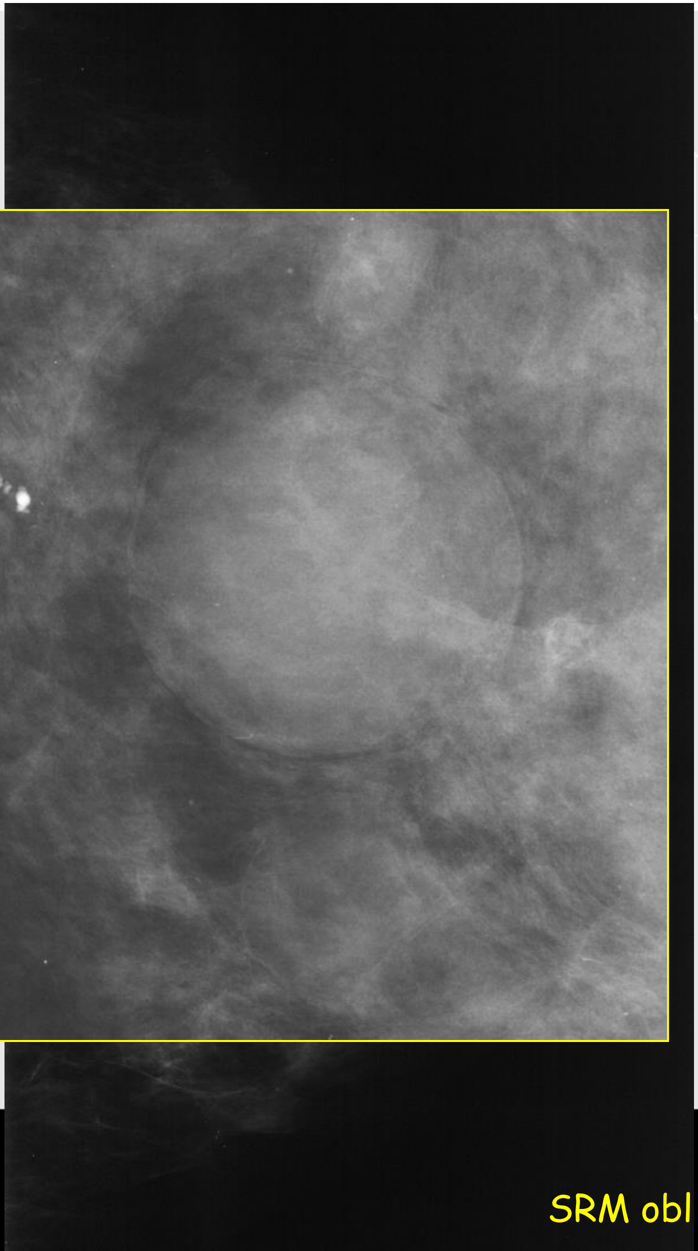
SRM: findings



FFDM obl



SRM obl

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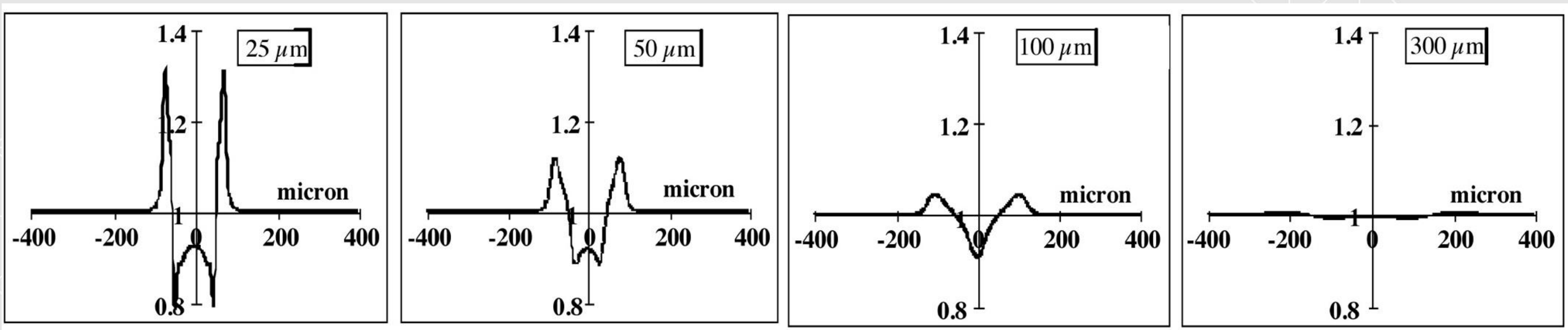
FSP works wonders when implemented with a spatially coherent source – why ask for more?

- It suffer immensely when transferred to conventional sources:

the spread associated with projected source size becomes too large and kills the signal.



Moreover:

The system has little flexibility - only d_{sd} can be changed

But:

Amazing stuff @ synchrotrons, e.g. check out Cloetens' work at the ESRF
+ straightforward use e.g. coupled with Paganin's single distance phase retrieval

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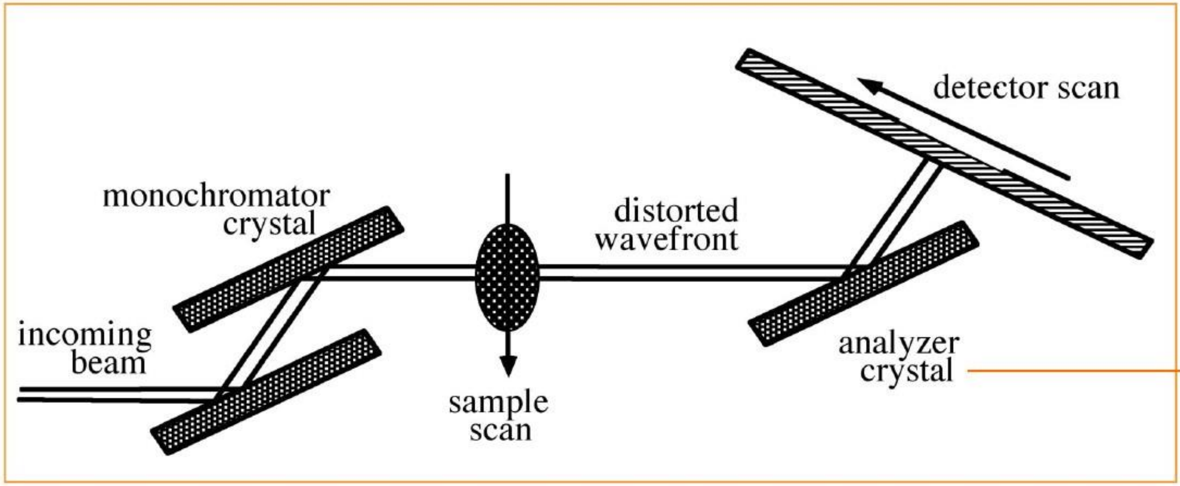
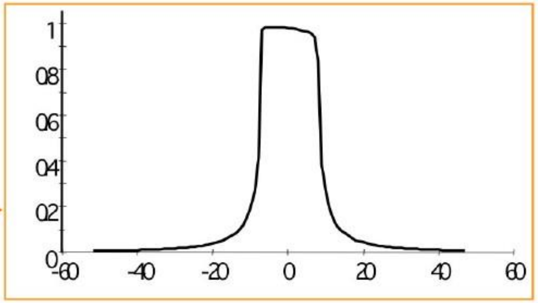
Olivo *et al.* Med. Phys. 28 (2001)1610-19

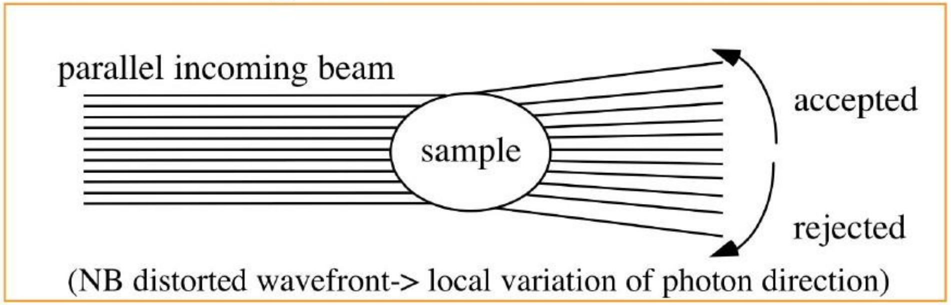
Other methods to perform phase contrast imaging:

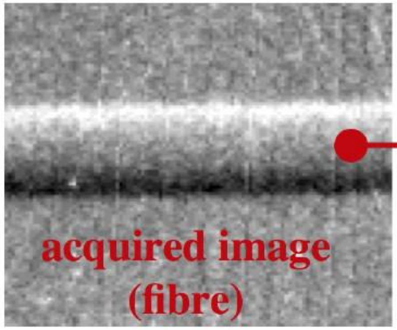
"Analyzer Based Imaging"





a small misalignment makes it more sensitive:



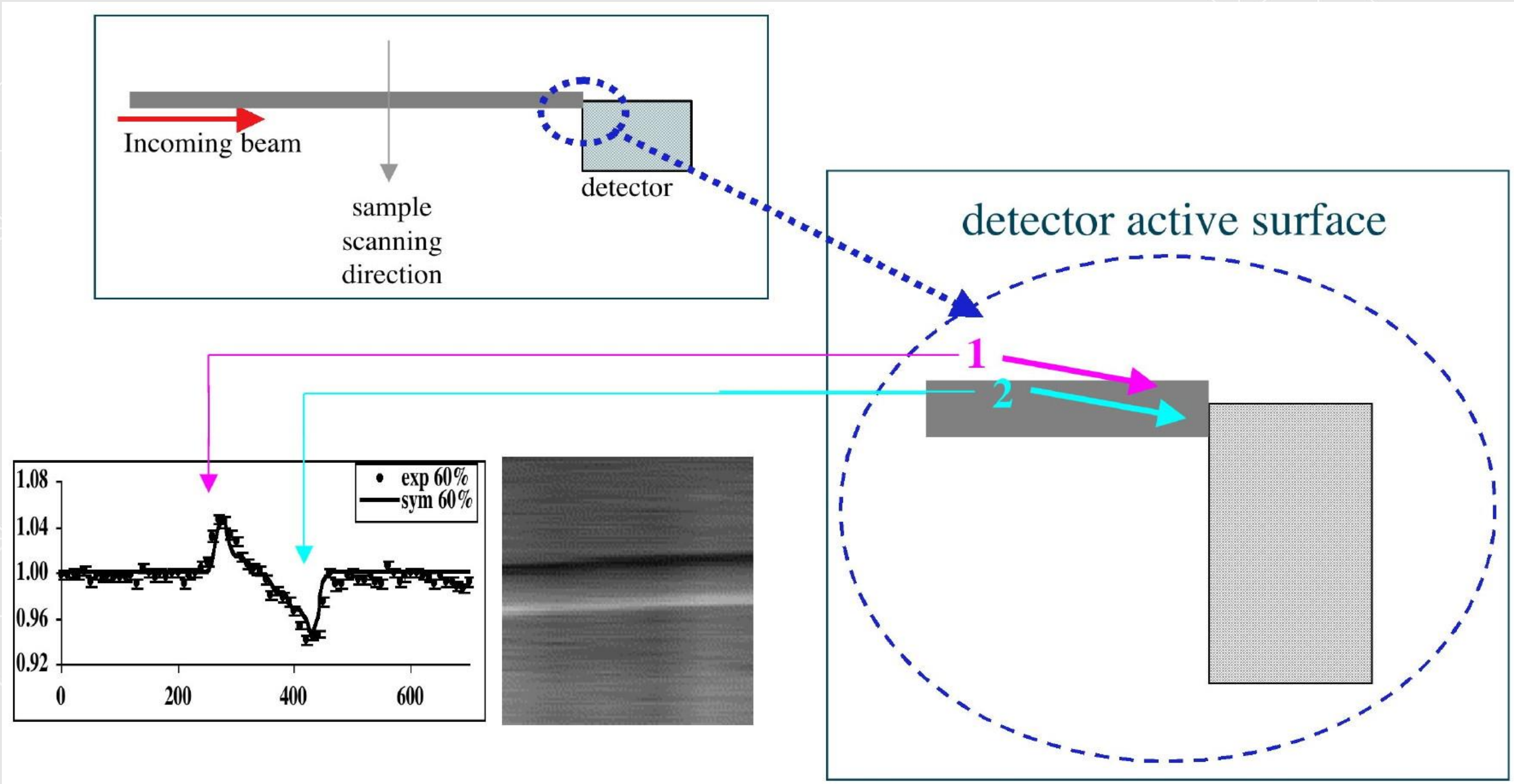


NOTE: NO ABSORPTION

Davis et al, Nature 373 (1995) 595-8; Ingal & Beliaevskaya, J. Phys. D 28 (1995) 2314-7, Chapman *et al*, Phys. Med. Biol. **42** (1997) 2015-25 - **but even before that Forster**

A different way to obtain a similar effect:

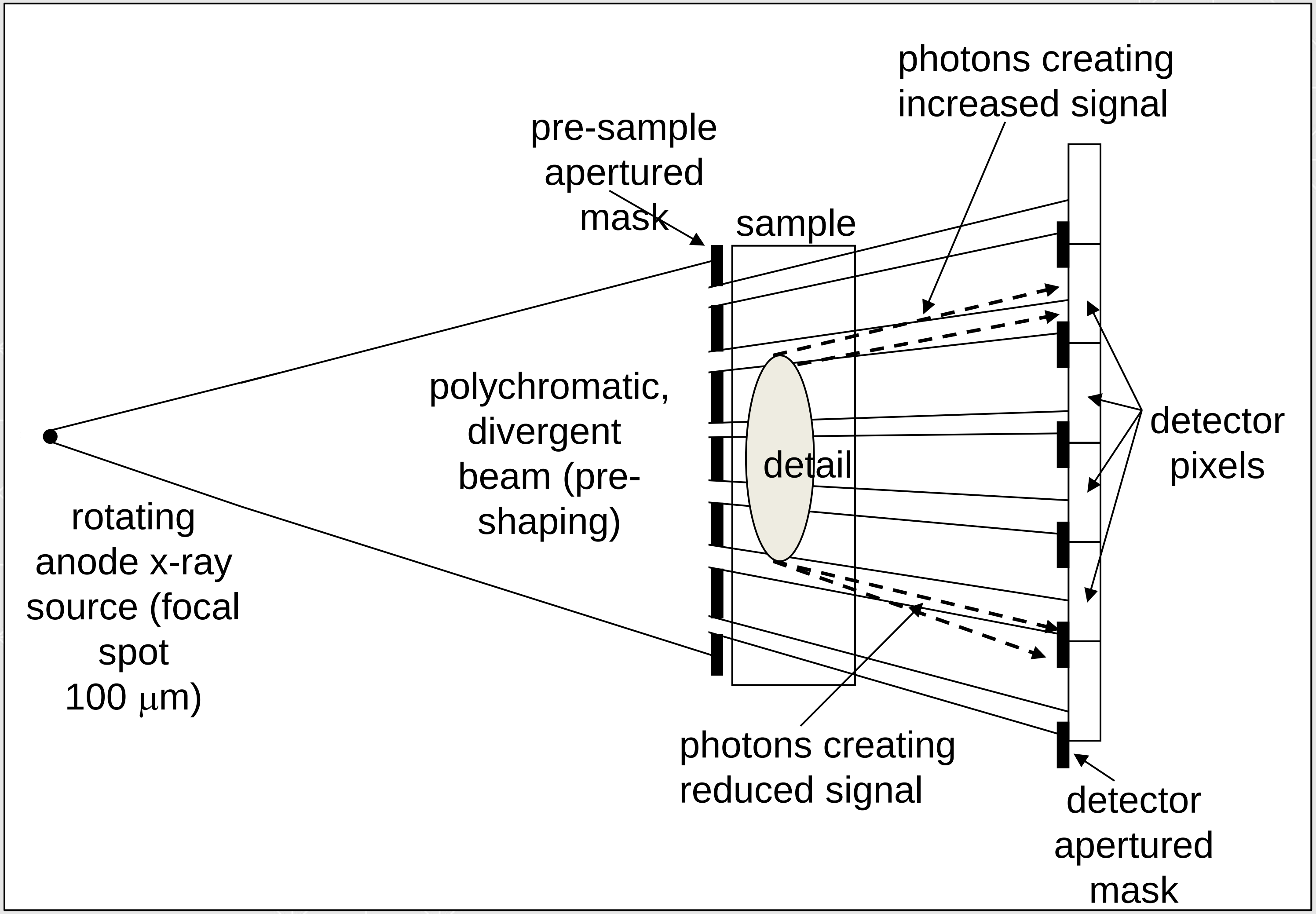
The Edge Illumination Technique



Provides results similar to ABI but opens the way to the use of **divergent** **and** **polychromatic** **beams**

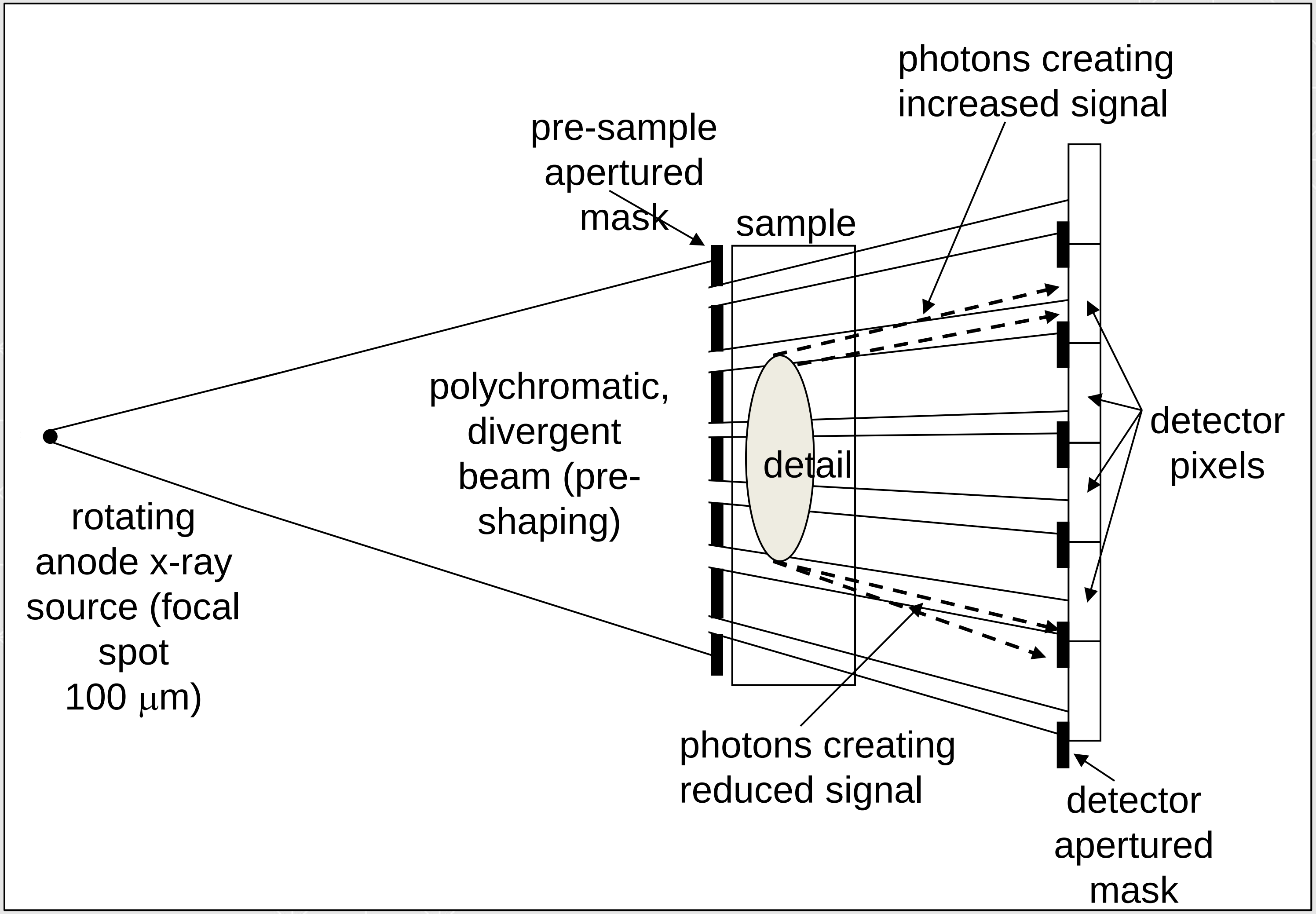
Olivo *et al.* Med. Phys. 28 (2001)1610-19

THE METHOD CAN BE ADAPTED TO A DIVERGENT AND POLYCHROMATIC (=conventional) SOURCE



Olivo and Speller Appl. Phys. Lett. 91 (2007) 074106

THE METHOD CAN BE ADAPTED TO A DIVERGENT AND POLYCHROMATIC (=conventional) SOURCE



NB for those of you who are familiar with grating (or Talbot, or Talbot-Lau) interferometers **this isn't one!**

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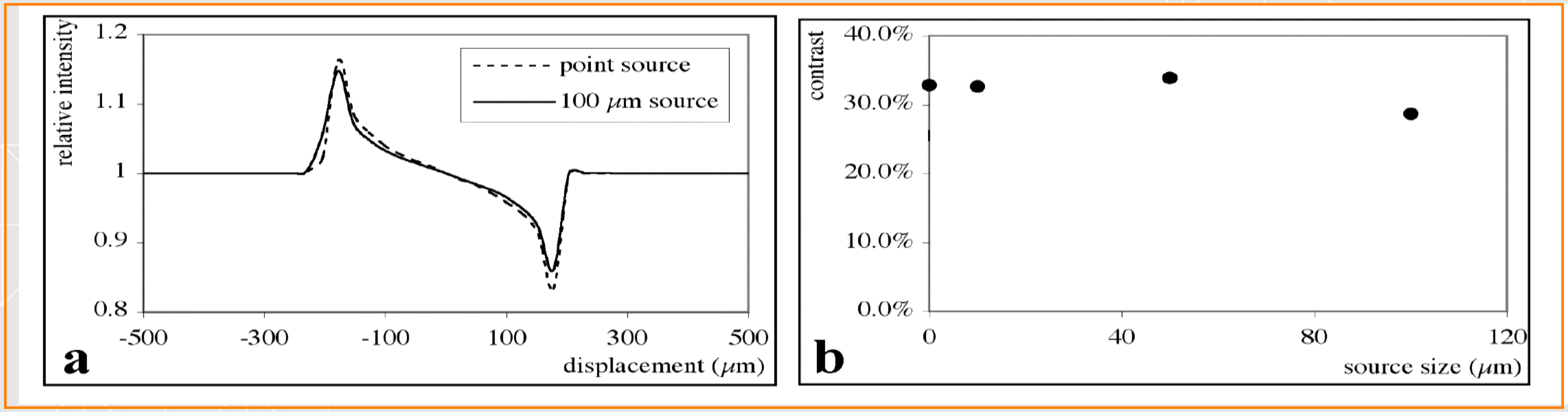
Olivo and Speller Appl. Phys. Lett. 91 (2007) 074106

Little loss of signal intensity for source sizes up to 100 µm



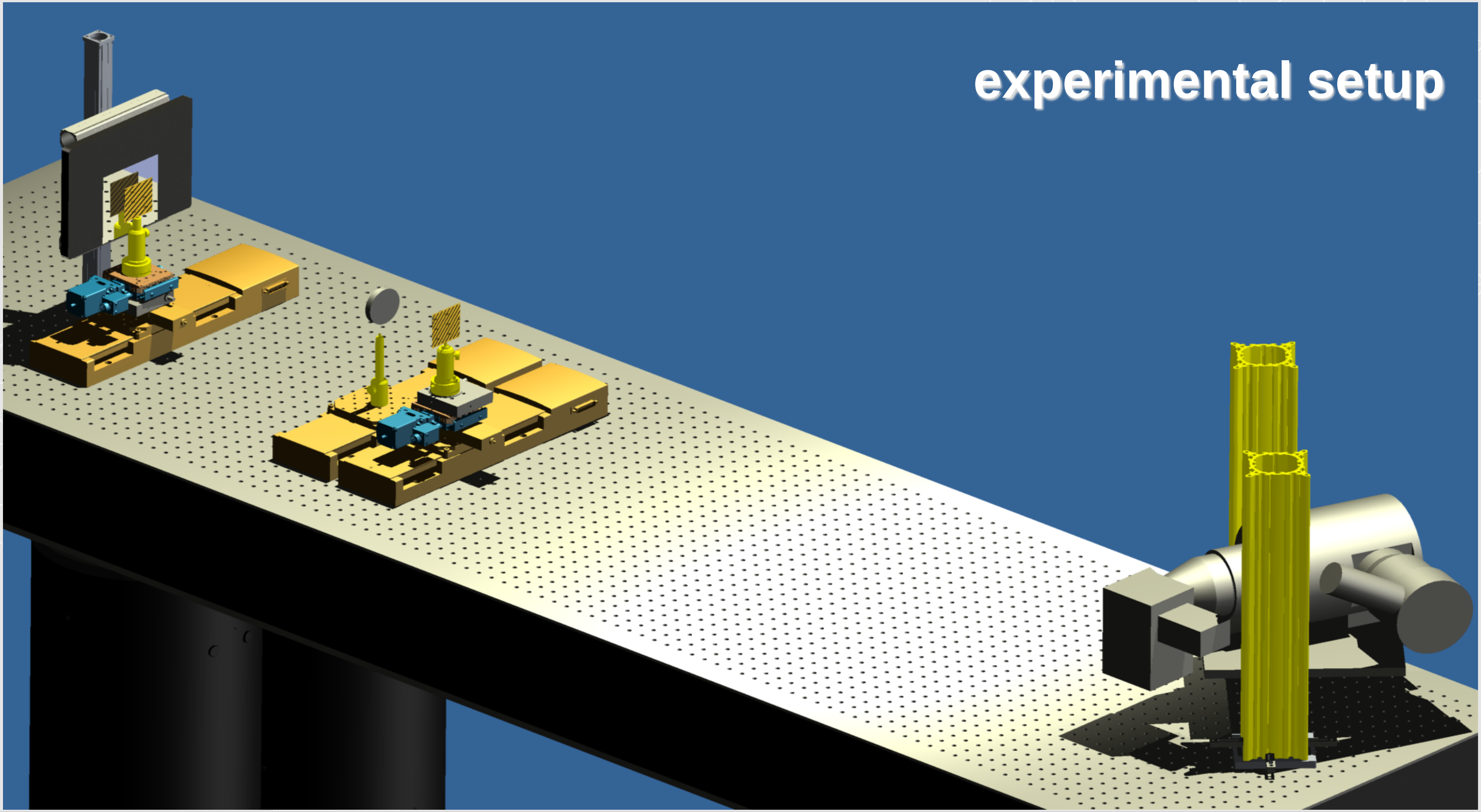
Which can be achieved with state-of-the-art mammo sources

Why?

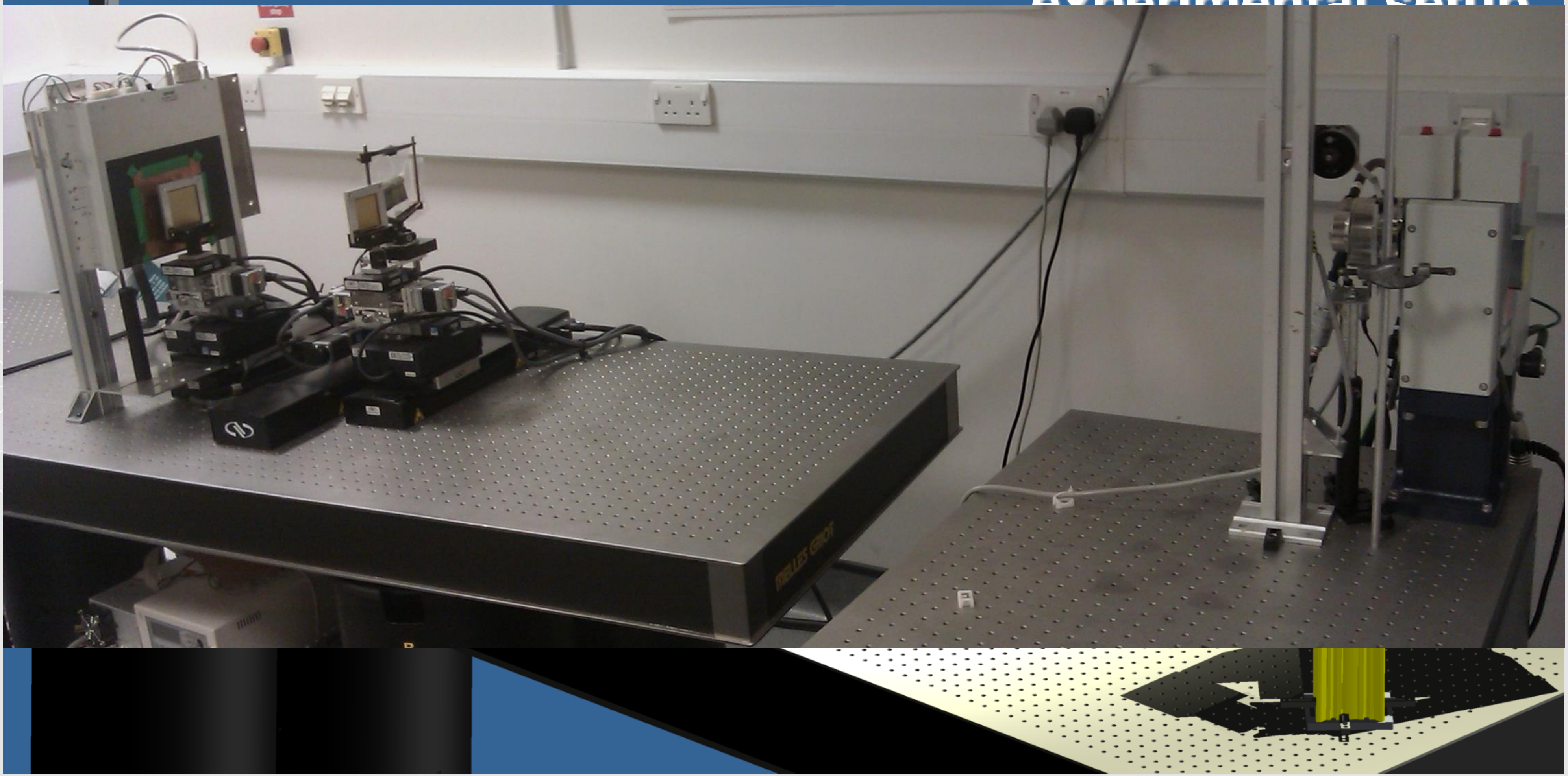
1) Because we are only relying on refraction, which survives under relaxed coherence conditions;
2) Because we are use aperture pitches matching the pixel size, i.e. BIG: the projected source size remains < pitch, and therefore blurring does "not" occur.

Olivo and Speller Phys. Med. Biol. 52 (2007) 6555-73

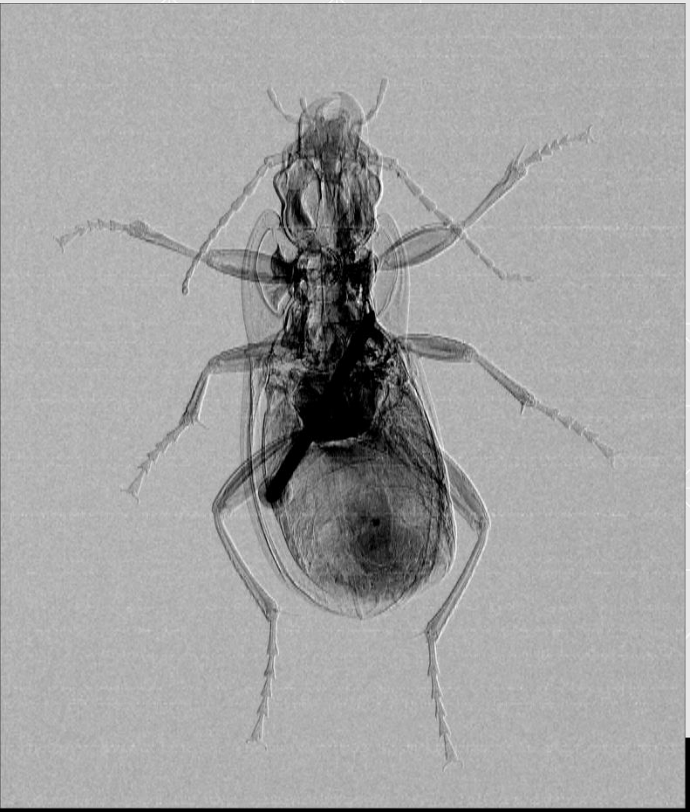
experimental setup



experimental setup

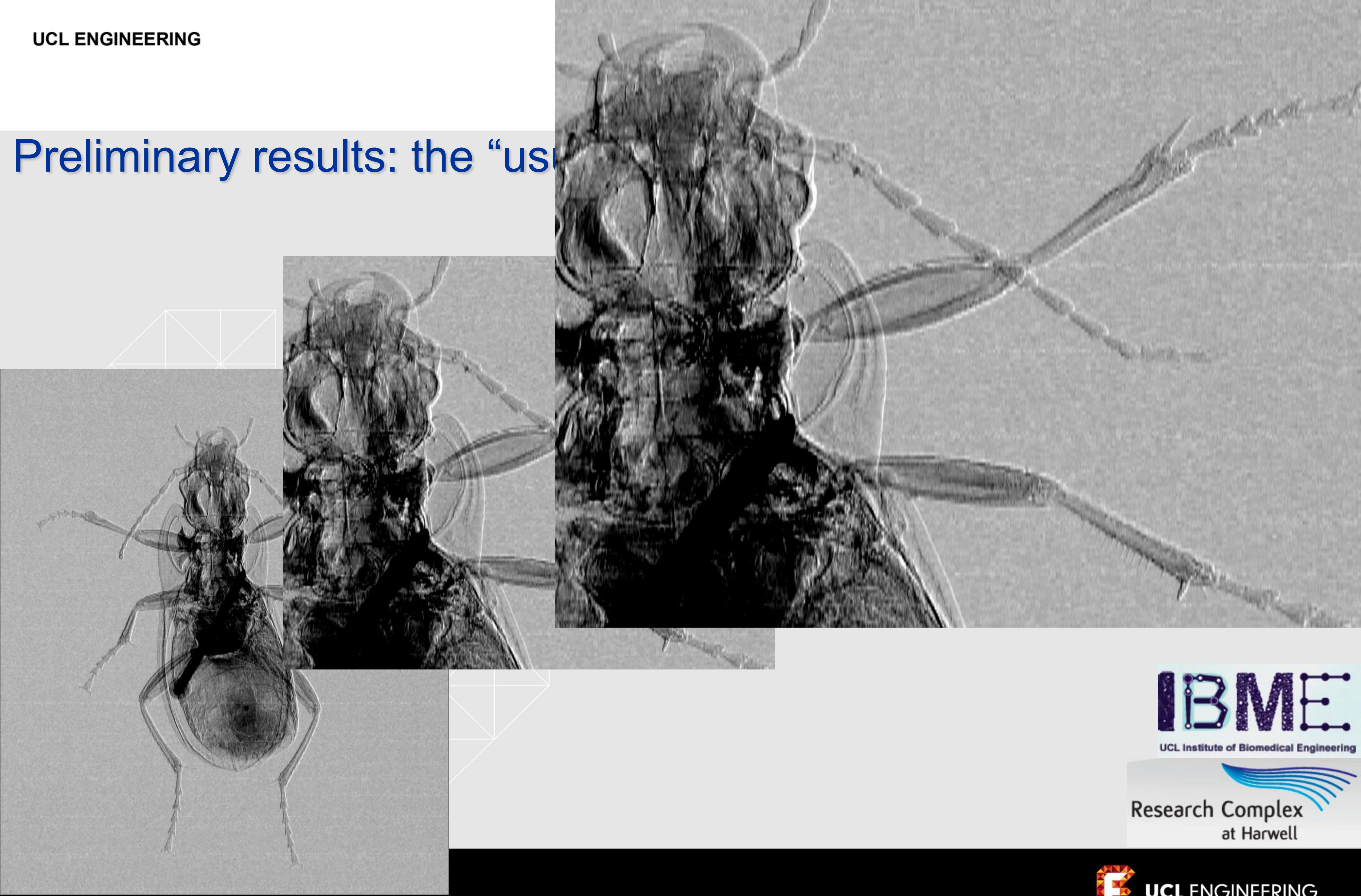


Preliminary results: the “usual” insects (but a bit faster)



Preliminary results: the “usual” insects (but a bit faster)

Preliminary results: the "usu



Prelimir

RESEARCH HIGHLIGHTS Selections from the scientific literature

APPLIED PHYSICS

Better X-ray vision

A new technique allows fainter features to be imaged by X-rays.

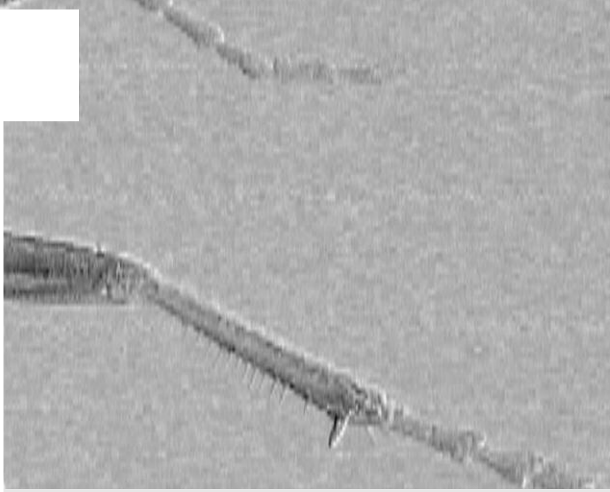
Conventional X-ray imaging relies on the absorption and scattering of X-ray photons by the object being imaged. But X-ray phase-contrast imaging instead detects changes in the photons' direction and velocity.

A. OLIVO ET AL.

Alessandro Olivo and his colleagues at University College London used a conventional X-ray source outfitted with grated masks — one in front of the object for imaging and one behind it. The masks were offset slightly from one another so that they filtered out some of the photons, reducing background noise. The detector measures by how much photons have deviated from their path, capturing different image data from conventional X-ray imaging and boosting the visibility of fine detail.

The team used its technique to image biological specimens such as a beetle (pictured), as well as samples of interest for medical imaging, materials science and security inspection.

Appl. Optics 50, 1765–1769 (2011)



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Nature 472 (2011) p. 392

PHYSICS

Can You See Me Now?

A new x-ray technique may herald improved baggage screening and mammograms

X-rays can help reveal anything from bombs hidden in luggage to tumors in breasts, but some potentially vital clues might be too faint to capture with conventional methods. Now a new x-ray technique adapted from atom smashers could resolve more key details.

Conventional x-ray imaging works much like traditional photography, relying on the light—in this case, x-rays—that a target absorbs, transmits and scatters. To make out fine details, one typically needs a lot of x-rays, either over time, which can expose targets to damaging levels of radiation, or all at once from powerful sources such as circular particle accelerators, or synchrotrons, which are expensive.

Instead physicist Alessandro Olivo of University College London and his colleagues suggest imaging an object by looking for very small deviations in an x-ray's direction as it moves through that object. Their idea is to take such x-ray phase-contrast imaging, which has been used in synchrotrons for more than 15 years, and use it with conventional x-rays.

The scientists rig conventional x-ray sources with gold grates that are 100 microns or so thick—one in front of a target and one behind it. The holes on one grate do not line up exactly with the holes on the other, meaning x-rays that passed in straight lines through the first grate would get filtered out by the second, lowering background noise. The detector then analyzes only the photons that deviated in direction as they passed through the object. This can lead to at least 10 times greater contrast than conventional imaging—"all details are more clearly visible, and details classically considered very hard to detect become detectable," Olivo says of findings reported recently in *Applied Optics*. Whereas bombs are usually visible in conventional x-ray imaging, they can be confused with other materials such as plastics or liquids. The scientists are now pushing imaging sensitivity even further with new grating designs and are working on 3-D scanning techniques by coming at the target from multiple angles.

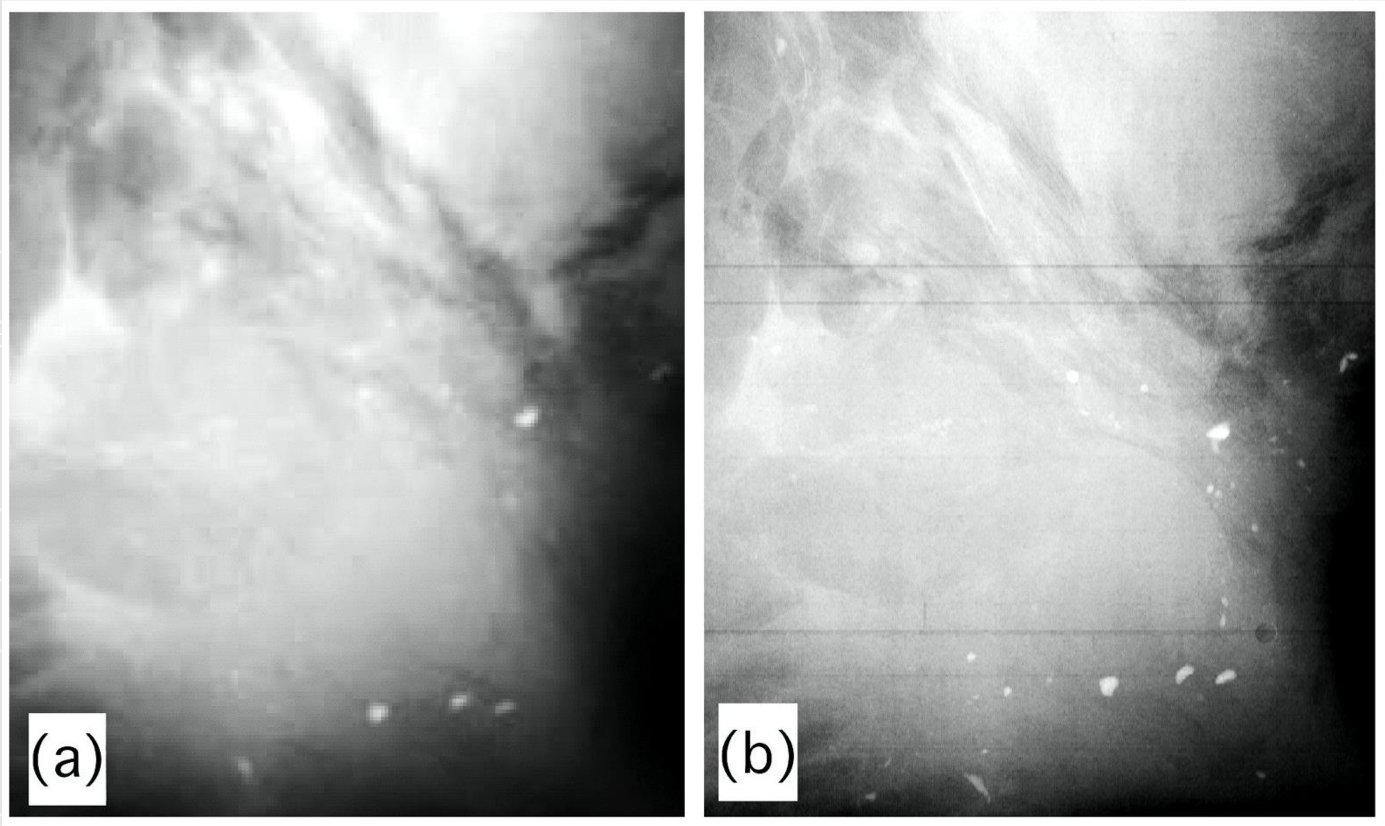
This system can generate images in just seconds, far quicker than other x-ray phase-contrast techniques, which cannot exert as much power during scanning and thus require minutes, says radiation physicist David Bradley of the University of Surrey in England, who did not take part in this study. But it remains unclear if this system could work fast enough for security scanning, says materials scientist Philip Withers of the University of Manchester in England. Withers does think the technology could lead to better medical imaging, as well as improvements in detecting defects in materials used in aerospace work.

—Charles Q. Choi

Olivo's x-ray of a chive plant

Scientific American 305 (2011) p. 14

Preliminary results - mammo



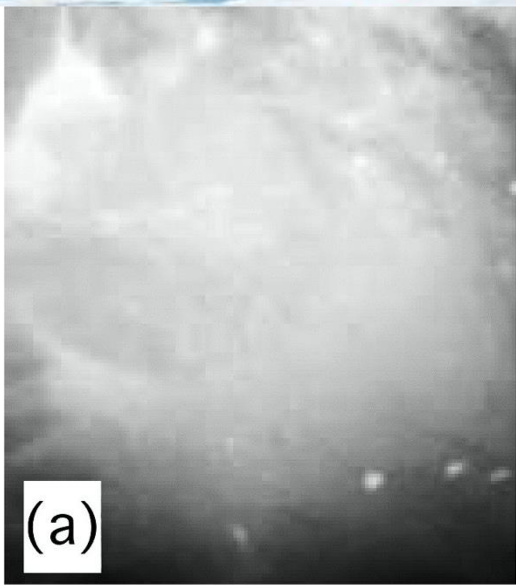
(a): GE senographe Essential ADS 54.11; 25 kVp, 26 mAs

(b): coded-aperture XPCi, 40 kVp, 25 mA – **ENTRANCE** dose 7 mGy (< mammo!)

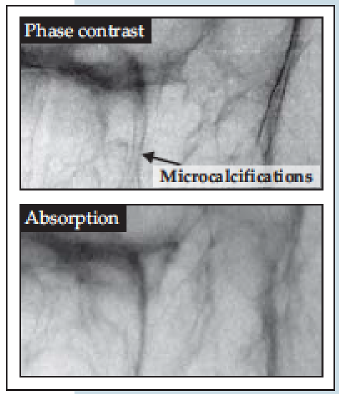
It has to be said the tissue was 2.5 cm thick -> we expect ~ same dose for thicker tissues

Olivo et al Med. Phys. (letters) 40 (2013) 090701

www.physicstoday.org
physics today
A publication of the American Institute of Physics
October 2013
volume 66, number 10



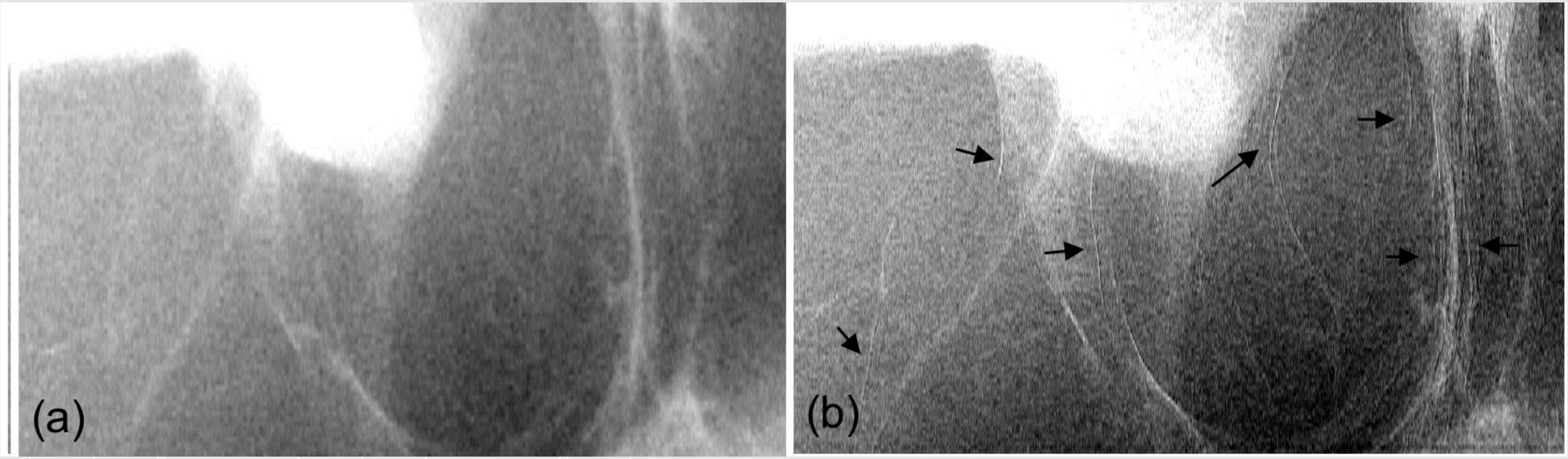
Low-dose phase-contrast mammography. Small, treatable tumors are difficult to spot in mammograms because healthy and cancerous tissues differ little in how they absorb x rays. But absorption isn't the only source of contrast. As x rays pass through an inhomogeneous medium, they can acquire differences in phase—even if the medium is a uniform absorber. Early attempts at phase-contrast imaging required a synchrotron or other bright, coherent source of x rays. Now Alessandro Olivo of University College London and his collaborators have built a prototype machine that performs phase-contrast mammography with a conventional x-ray tube at clinically acceptable doses. The setup works by masking the x-ray source with an array of hundreds of narrow, closely spaced holes. Each beam that emerges points at a single pixel of a flat-panel detector. The detector is also masked—such that half the x rays from each beam are prevented from reaching their designated pixel. When an object is placed between the source and the detector, the beams suffer either absorption or, thanks to a change in phase, refraction. Because of the setup's geometry and the small angles of refraction involved, some refracted photons will still reach their pixel, but others will miss and hit the mask. Enough photons are diverted to the mask that they boost the contrast of what would otherwise be a conventional absorption image. Olivo's team tested its setup on donated samples of cancerous breast tissue. Microcalcifications that presage cancer showed up more clearly in the phase-contrast image than in an absorption image.
(A. Olivo et al., *Med. Phys.* **40**, 090701, 2013.) —CD



(a): GE senographe Essential AD
(b): coded-aperture XPCi, 40 kVp < mammo!)

It has to be said the tissue was 2.5 cm th… s

Preliminary results - mammo



(a): GE senographe Essential ADS 54.11; 25 kVp, 26 mAs

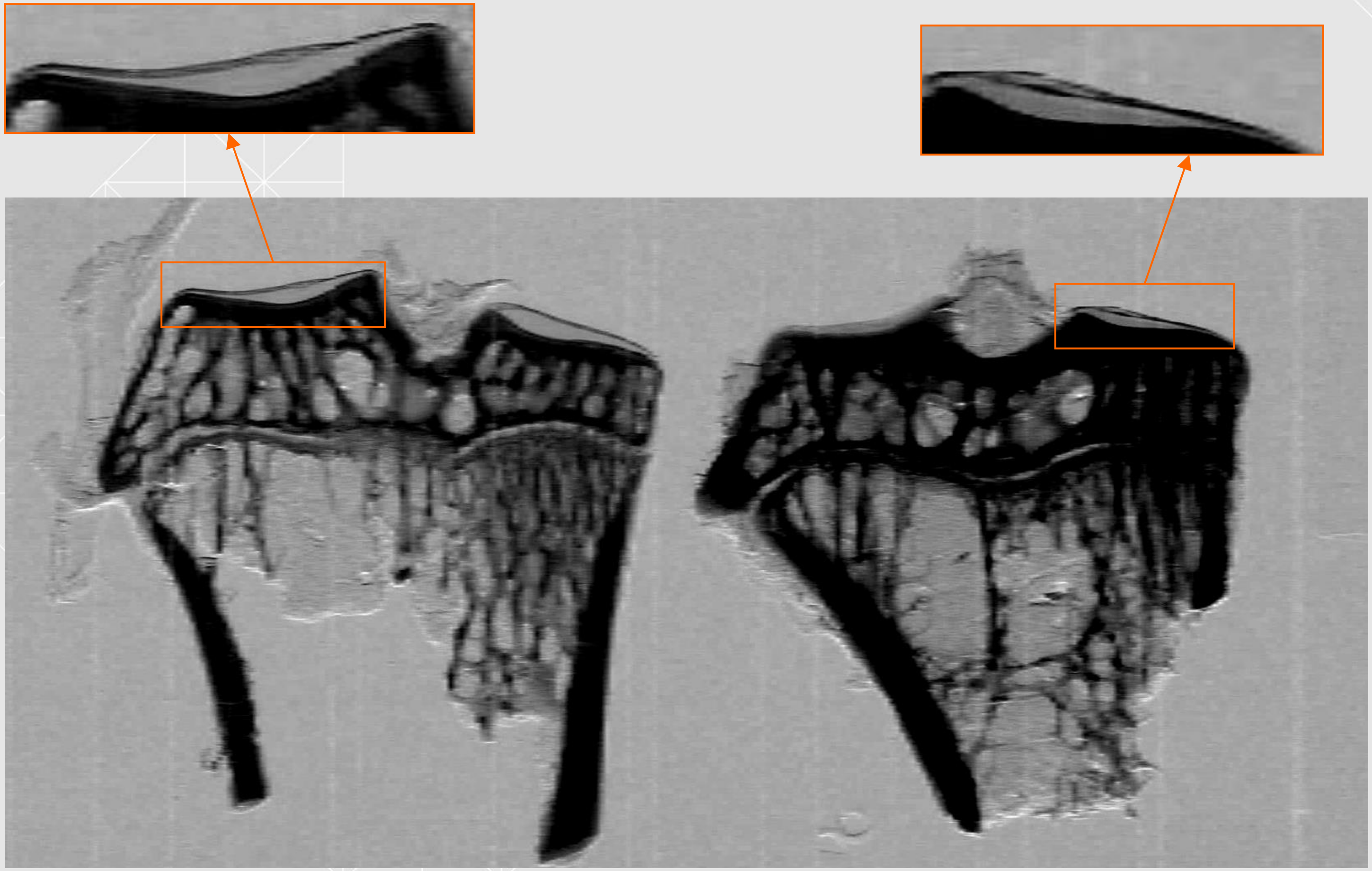
(b): coded-aperture XPCi, 40 kVp, 25 mA – **ENTRANCE** dose 7 mGy (< mammo!)

Tissue thickness 2 cm-> extrapolation leads to ~standard mammo dose for thicker (4-5 cm) tissues

unpublished

Preliminary results - cartilage imaging

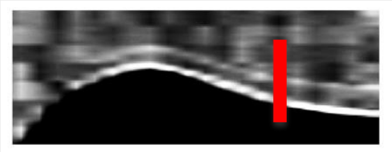
Rat cartilage, ~ 100 µm thick, invisible to conventional x-rays



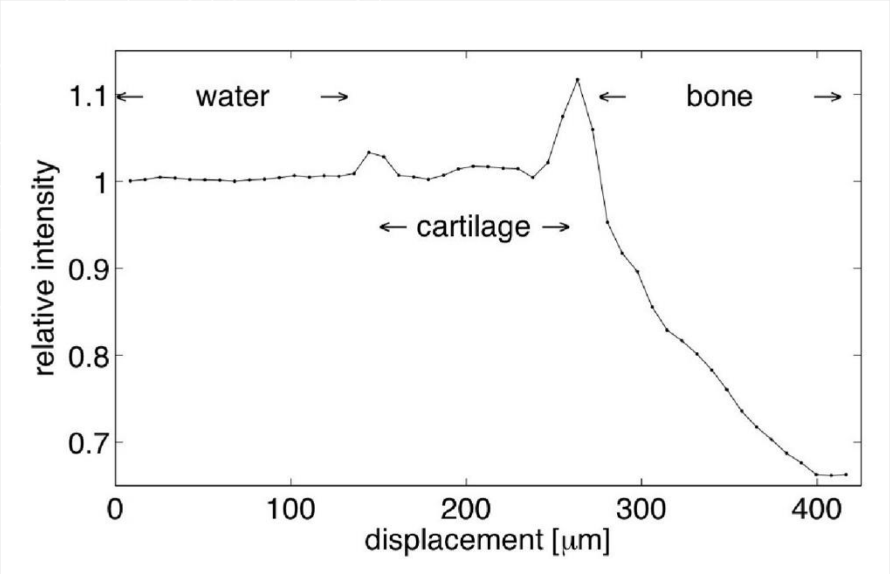
Marenzana *et al*, Phys. Med. Biol. 57 (2012) 8173-84

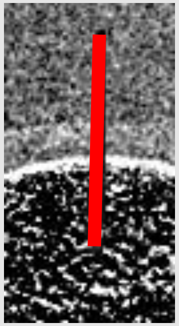
Cartilage in water:

Tells us a lot about CAXPCi vs Talbot/Lau sensitivity:

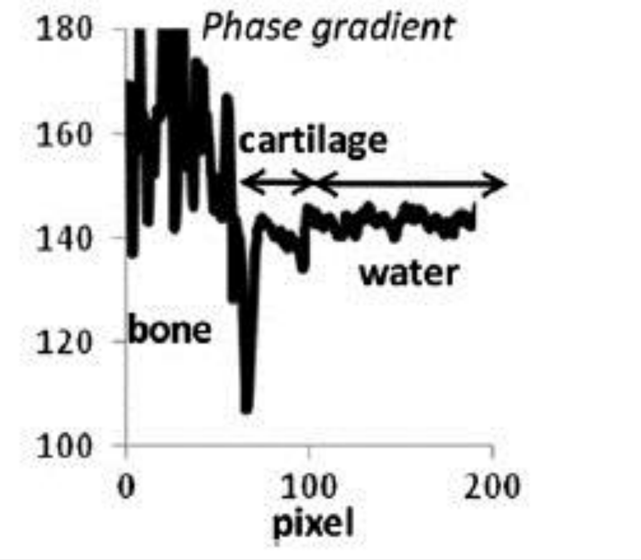


CAXPCI
(RAT cartilage)



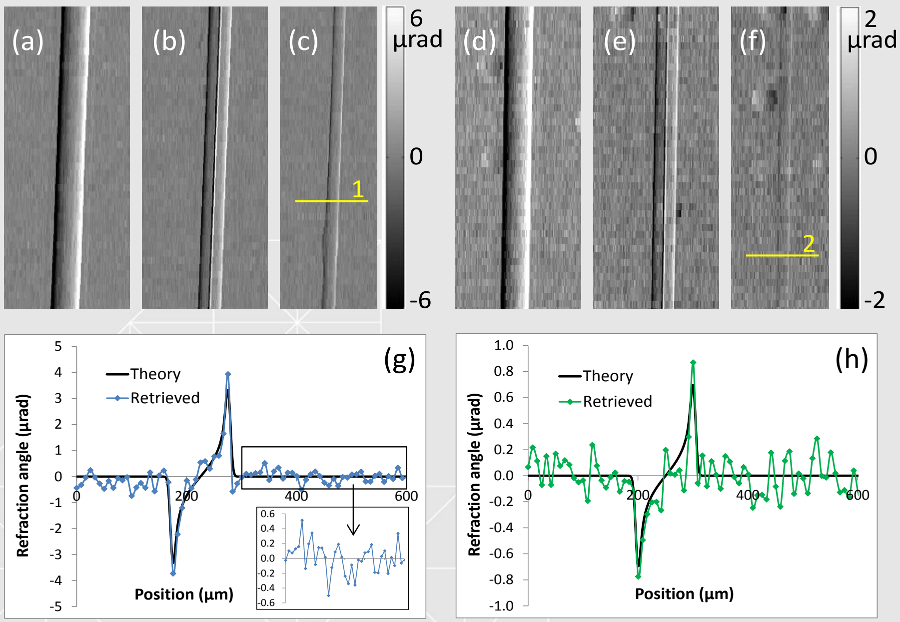


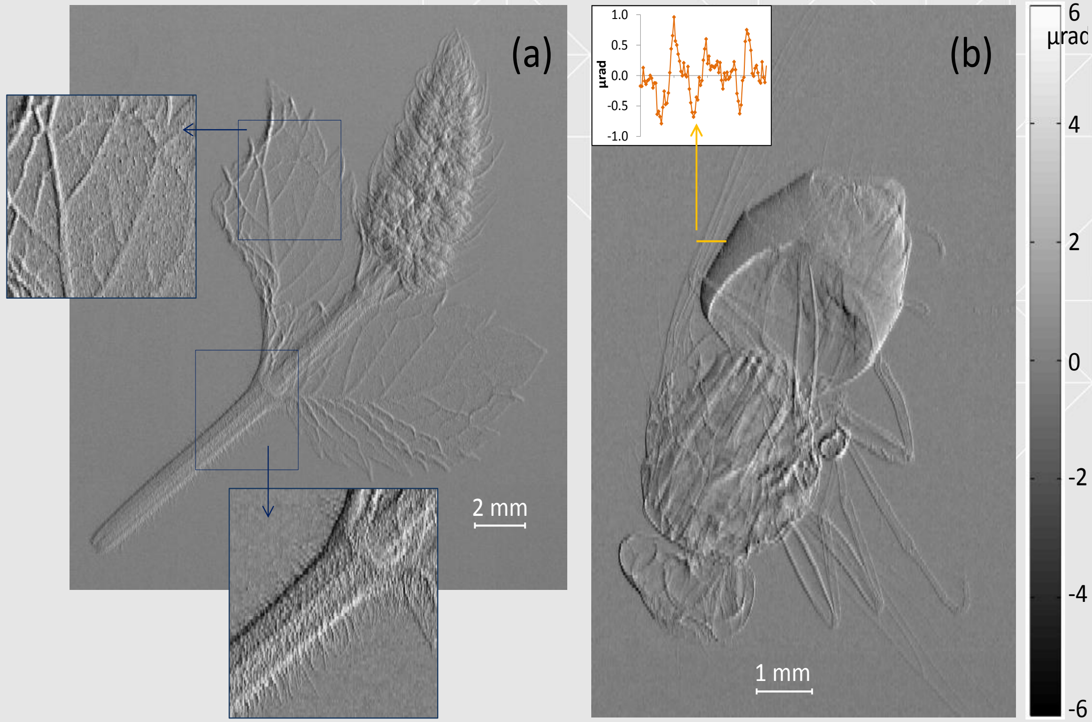
TALBOT/LAU
(PORK cartilage)
from Stutman *et al*, Phys. Med. Biol. 56 (2011) 5697-720



- SAME signal (despite thicker cartilage for T/L);
- on **3rd** Talbot order (cartilage in water invisible on 1st order)

More on the sensitivity of the lab system:



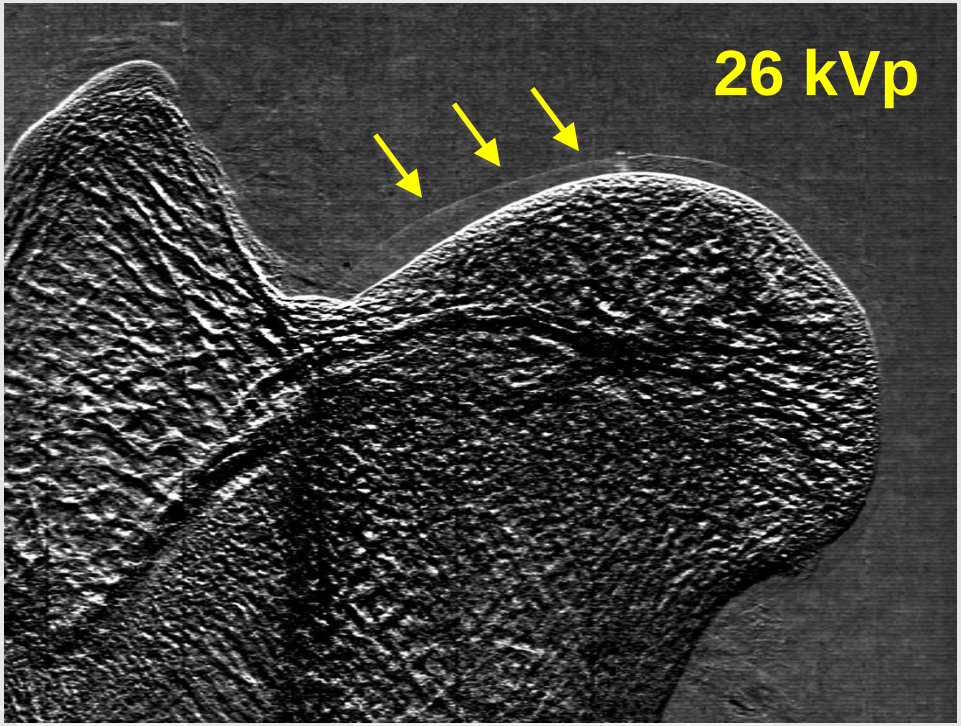


$$\Delta\theta_{x,eff} = \frac{1}{z_{od}} R^{-1}\left(\frac{I_{obj,+}}{I_{obj,-}}\right) \Rightarrow \sigma\left(\Delta\theta_{x,eff}\right);\ \frac{\sqrt{C\left(x_{e,+}\right)}}{z_{od}\sqrt{2TI_0}\left[\rho_{ref,n}\left(x_{e,+}\right)-\rho_{ref,n}\left(x_{e,+}+d\right)\right]}$$

This gives a phase sensitivity of ~ 270 nRad, with only 2 images x 7s exposure each; same as reported by Thuring (Stampanoni’s group) for GI. Revol reported a sensitivity of about 110 nRad but with 12 x 7s frames – as one can expect the value to scale with sqrt(exp time), that also fits.

Diemoz *et al*, Appl. Phys. Lett. 103 (2013) 244104

Actually we've done much better on cartilage, in collaboration with PIXIRAD (Bellazzini *et al.*)

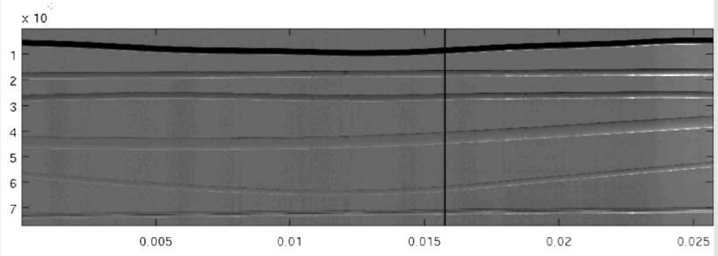


Underpins sensitivity better than 270 nrad – indeed we've recently measured 150-200 and are putting measures in place to improve it even further.

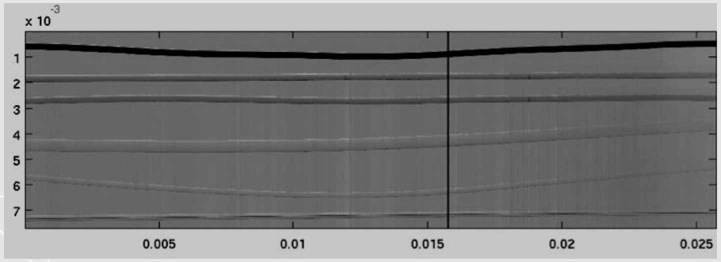
Endrizzi *et al*, JINST 9 (2014) C11004

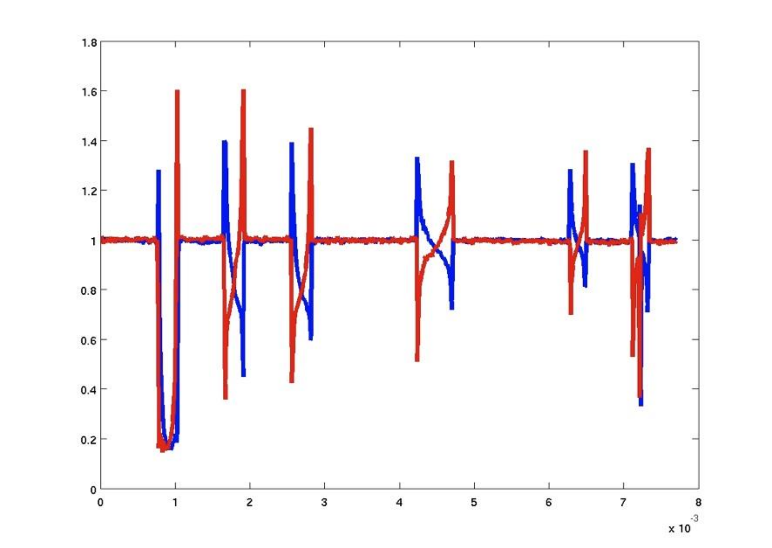
Quantitative phase contrast imaging

“SLOPE -”

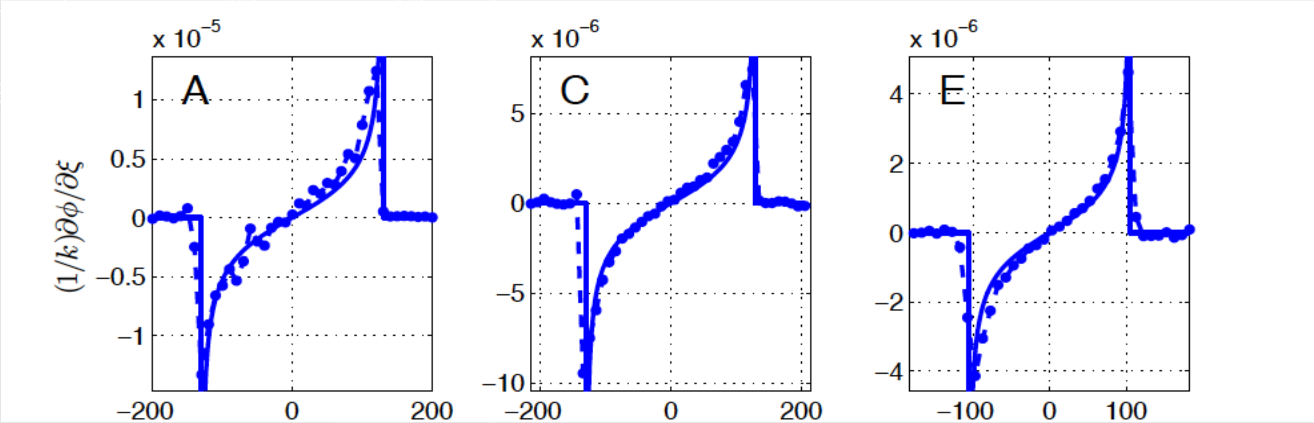


“SLOPE +”





Titanium Aluminum PEEK

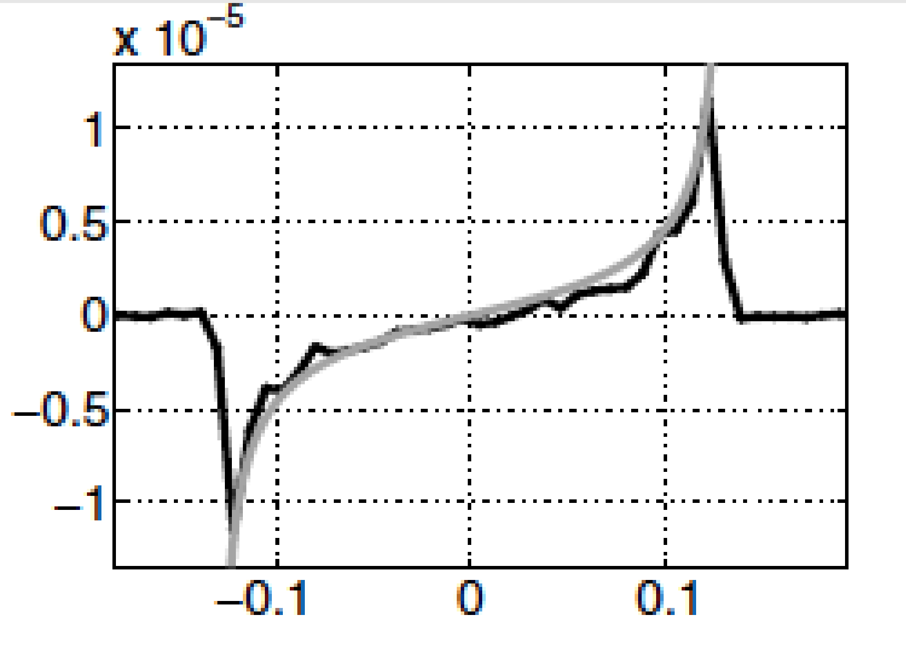


Highly precise retrieval, for both high and low Z materials, up to high gradients where other methods break down

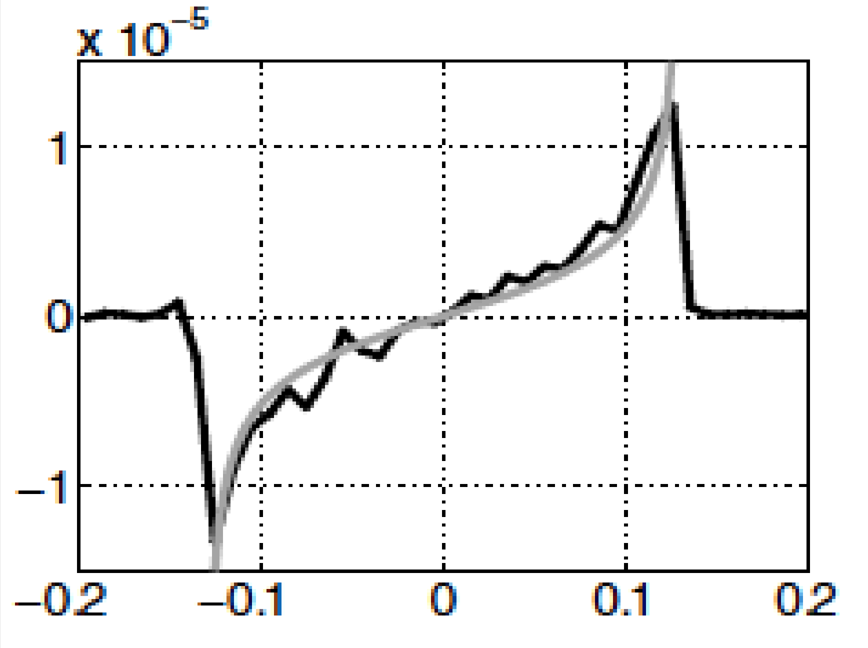
Munro *et al* Opt. Exp. 21 (2013) 647-61

Phase retrieval with synchrotron and conventional sources:

Ti filament: retrieved @ synchrotron



and with conventional source!



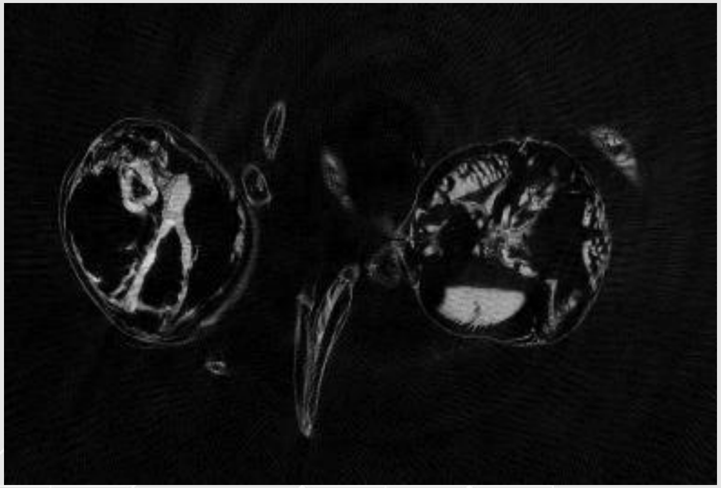
@ conventional source: incoherence modelled as beam spreading – the movement of the "spread" beam is then tracked and referred back to the phase shift that caused it.

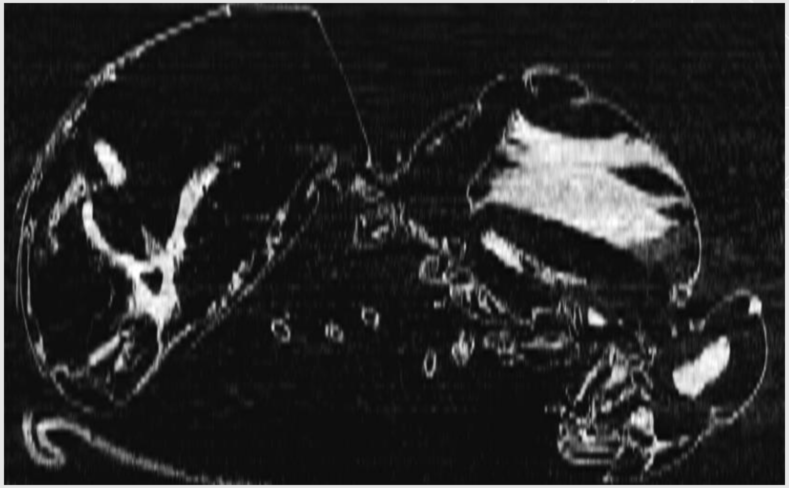
But with lots of care as far as "effective energy" is concerned!

(See Munro & Olivo Phys. Rev. A **87** (2013) 053838)

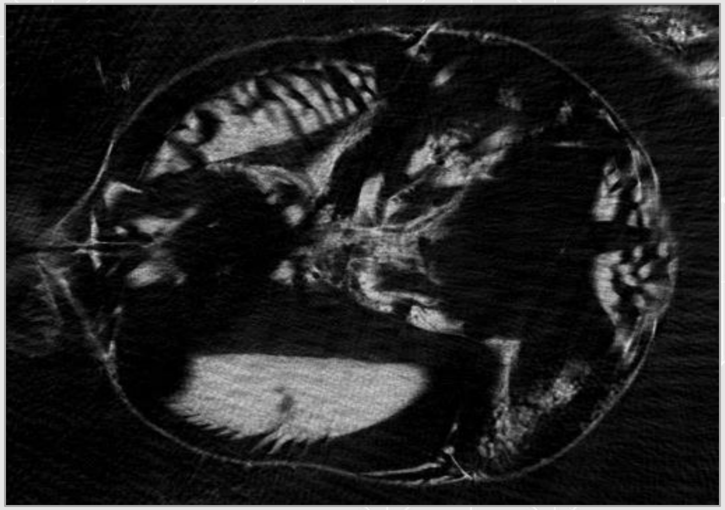
Munro *et al*, *PNAS* 109 (2012) 13922-7

preliminary CT results





Soft tissue inside wasp thorax resolved



Dose **tens of mGy**, instead of tens of Gy!

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Hagen et al, Med. Phys. (letters) 41 (2014) 070701

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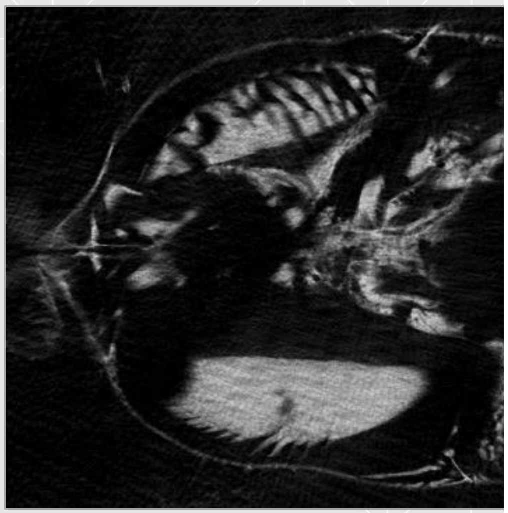
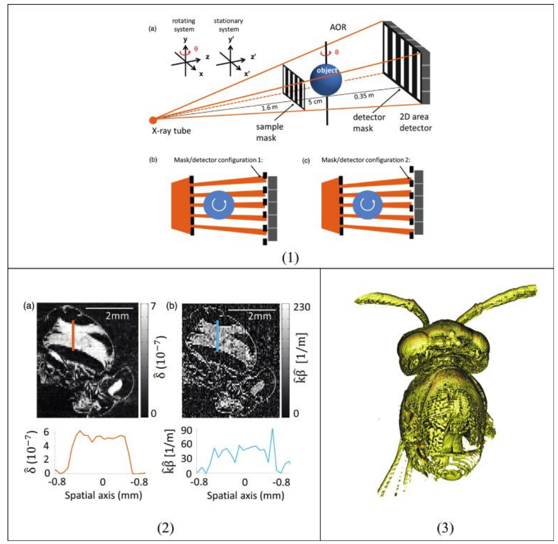


Medical Physics

AVAILABLE ONLINE—See http://www.medphys.org July 2014 Volume 41, Number 7

The International Journal of Medical Physics Research and Practice



First experimentally acquired x-ray phase-contrast images acquired with ordinary x-ray source using edge-illumination method (EI PCi). (1) 3D schematic view of the laboratory implementation of tomographic EI XPCi. (a) Views from top showing two opposing edge illumination conditions, (b,c), achieved by shifting the sample mask appropriately. (2) Coronal tomographic images of a wasp showing the phase shift (a) and attenuation (b) images within the insect with profiles extracted across the indicated thorax region. (3) 3D volume rendering of the wasp derived from phase shift images.

[Figures 1, 2, and 3 from Hagen, Munro, Endrizzi, Diemoz, and Olivo, "Low-dose phase contrast tomography with conventional x-ray sources," Med. Phys. 41, 070701 (5pp.) (2014)].

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Soft tissue inside wasp thorax resolved

Dose **tens of mGy**, instead of tens of Gy!

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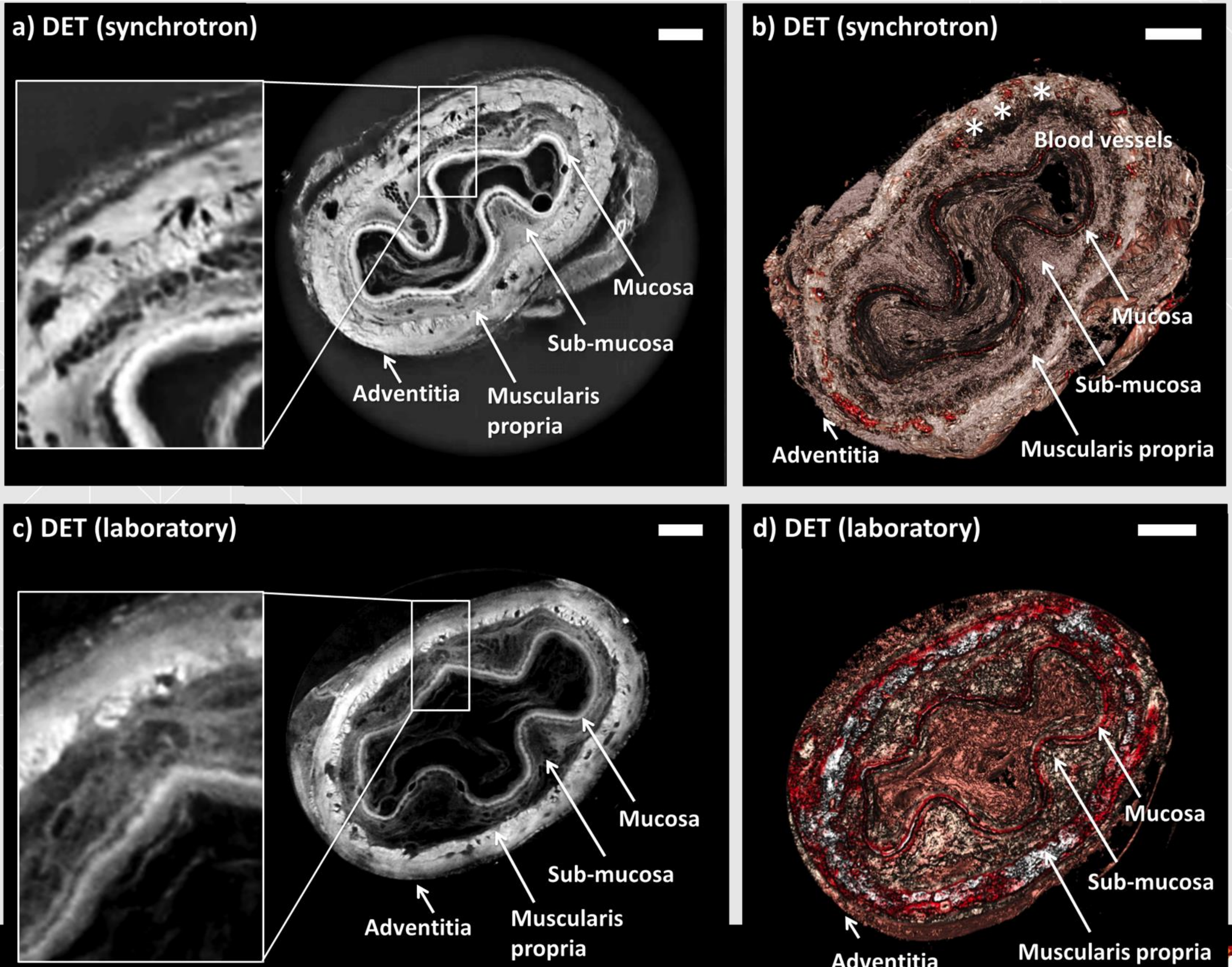
Hagen et al, Med. Phys. (lett

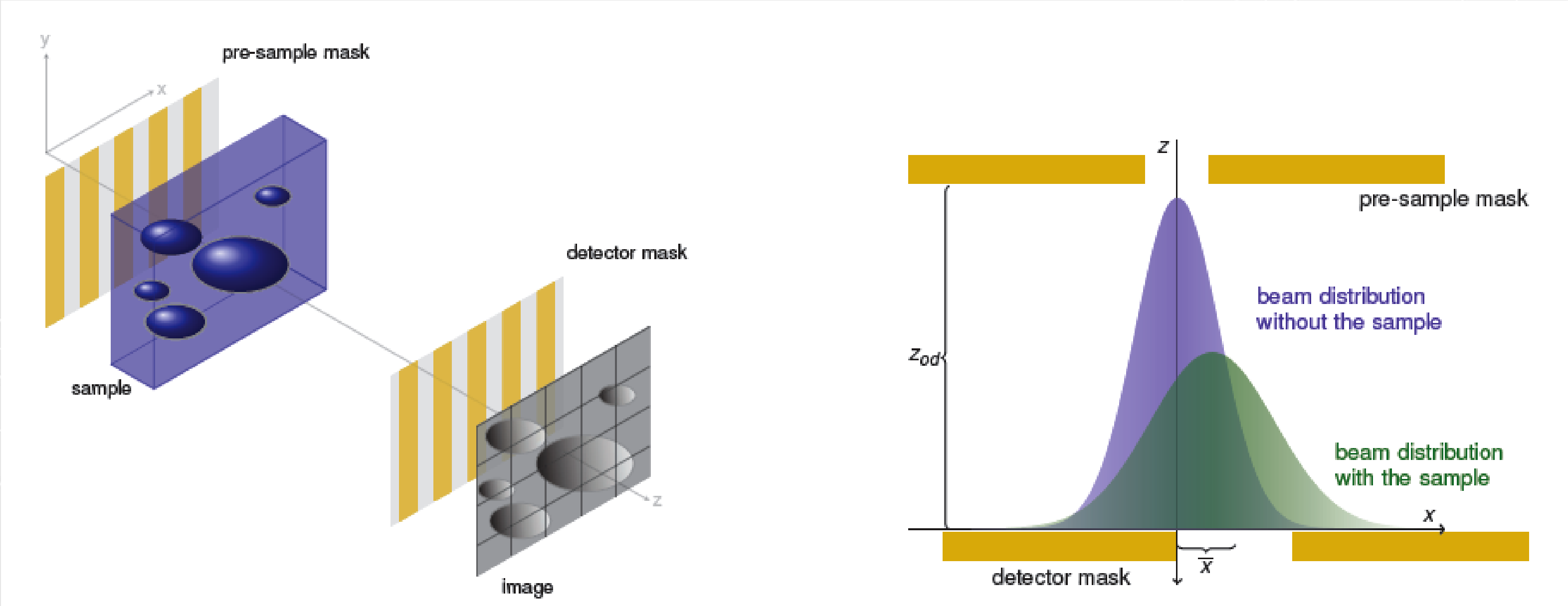
preliminary CT results

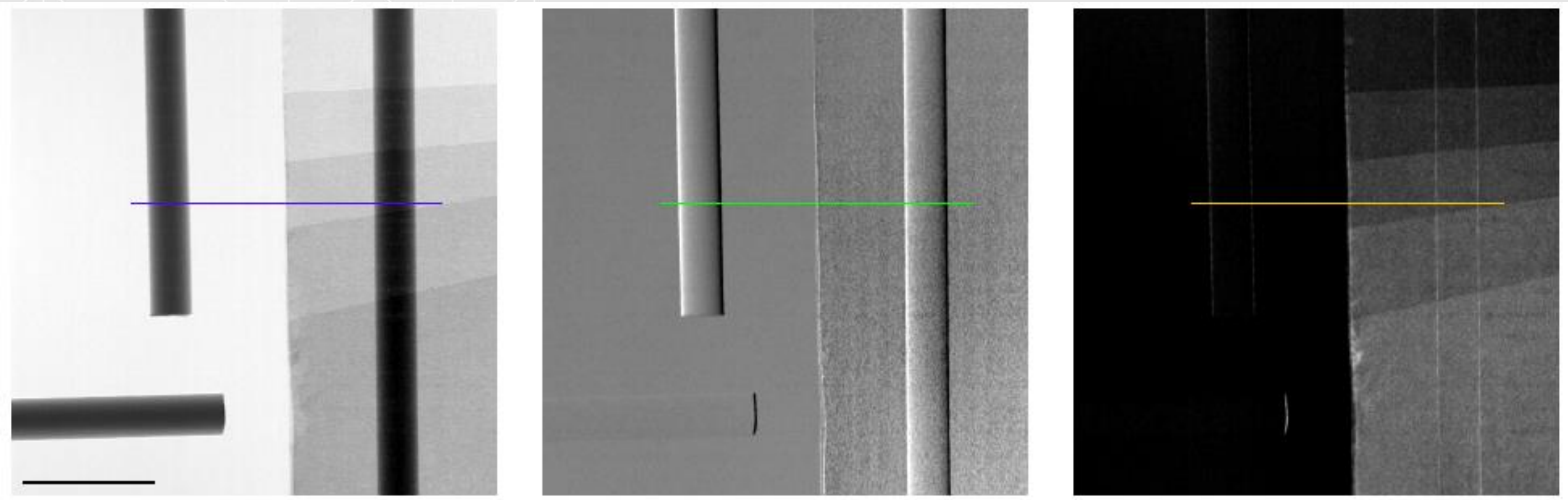
Rabbit oesophagous



Hagen *et al*, submitted to Sci. Rep.

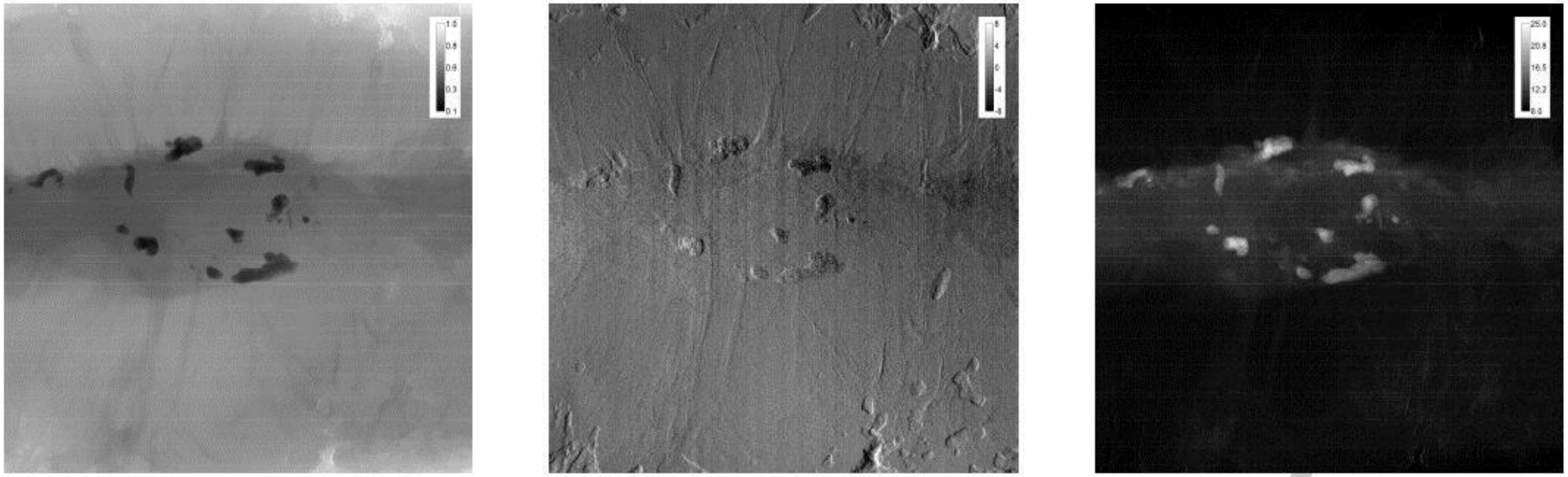
Three-shot DARK FIELD IMAGING retrieval





Endrizzi *et al*, Appl. Phys. Lett. 104 (2014) 024106

DARK FIELD IMAGING of breast calcifications
3 images only, still within clinical dose limits!



(a) transmission (relative intensity) (b) refraction (μrad) (c) scatter (μrad)

ENTRANCE dose 12 mGy (still compatible with mammo)

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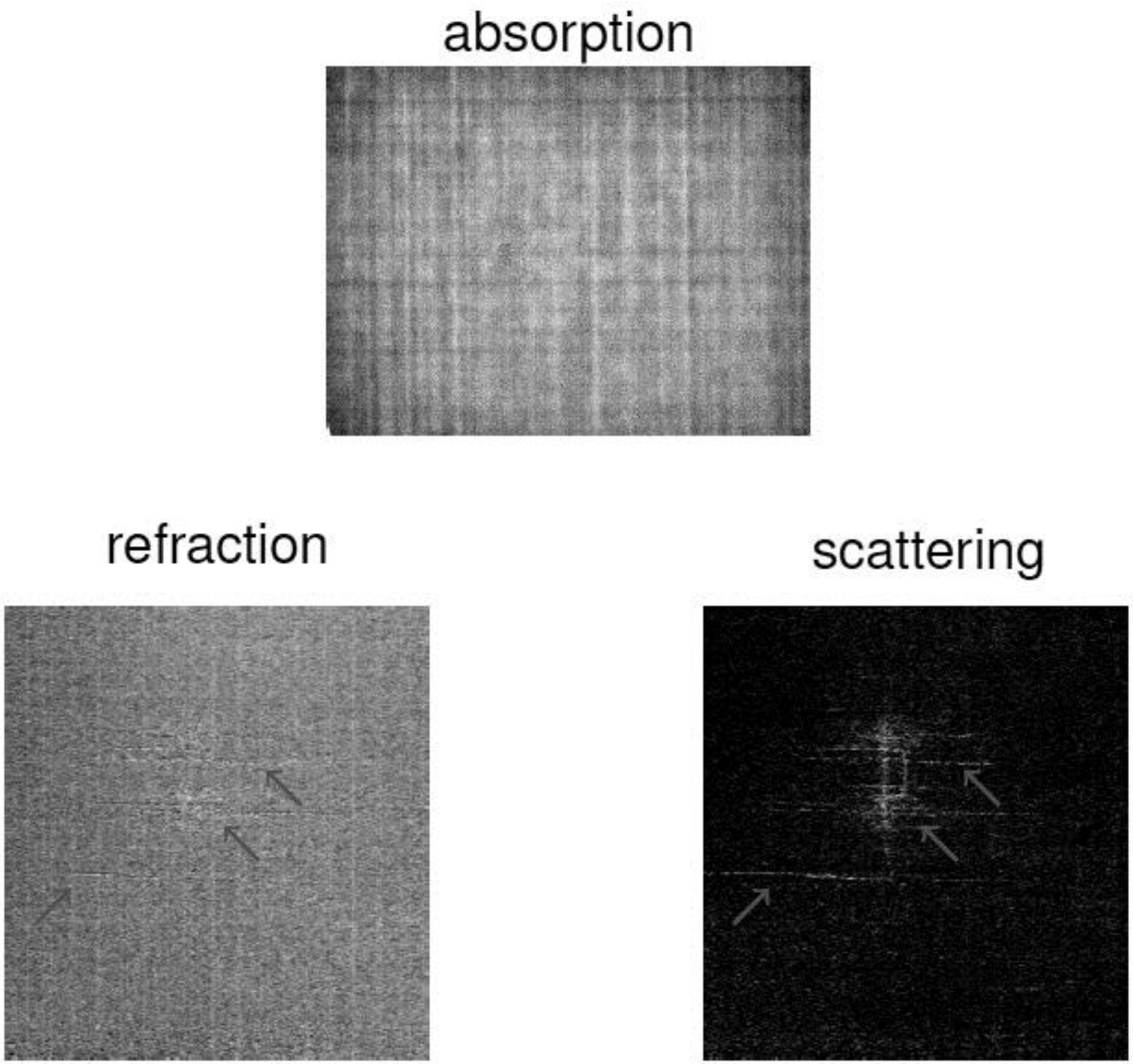
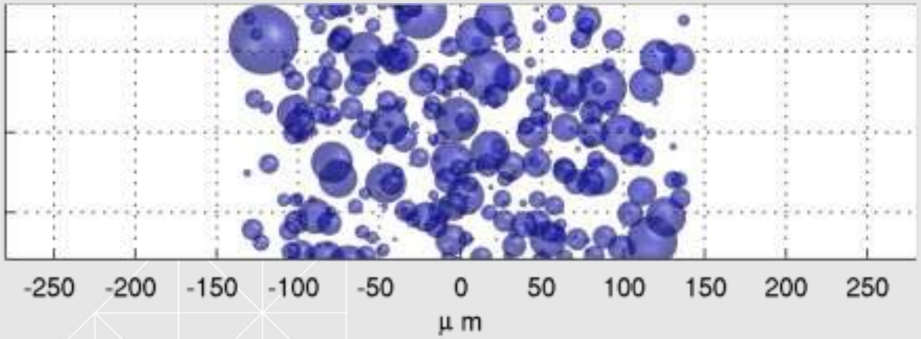
Endrizzi *et al*, Appl. Phys. Lett. 104 (2014) 024106

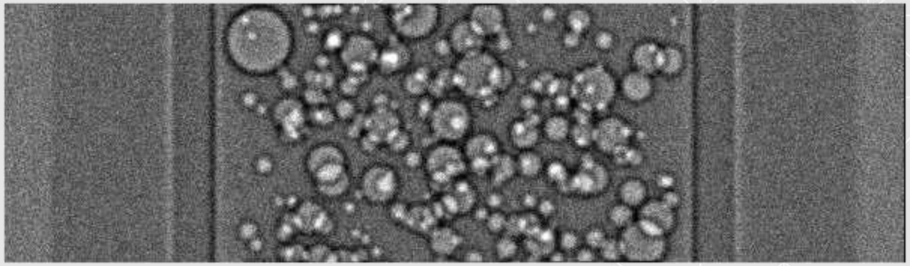


Non-medical applications: testing of composite materials

Endrizzi *et al*, Compos. Struct. 134 (2015) 895-9

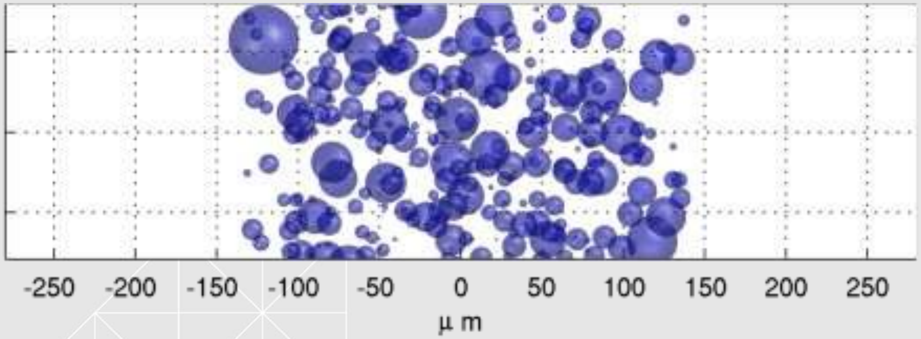
Microbubbles:
a new concept of "phase-based" x-ray contrast agent

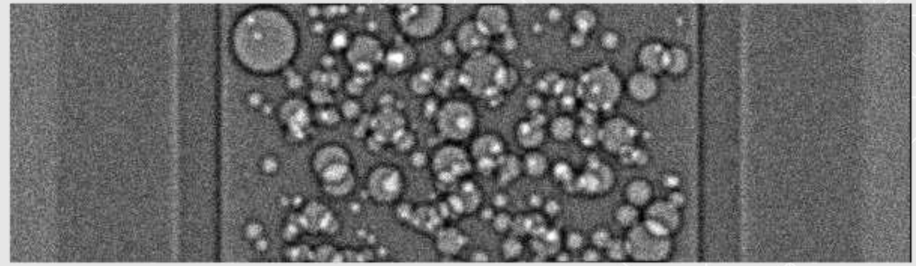




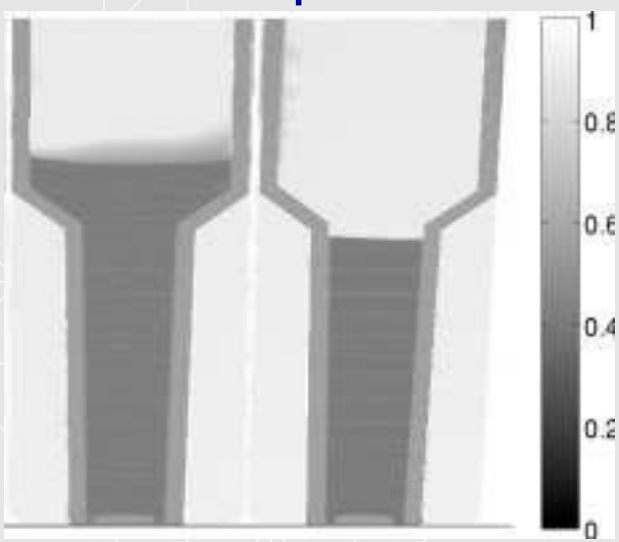
Millard et al. Appl. Phys. Lett. 103 (2013) 114105

Microbubbles:
a new concept of “phase-based” x-ray contrast agent



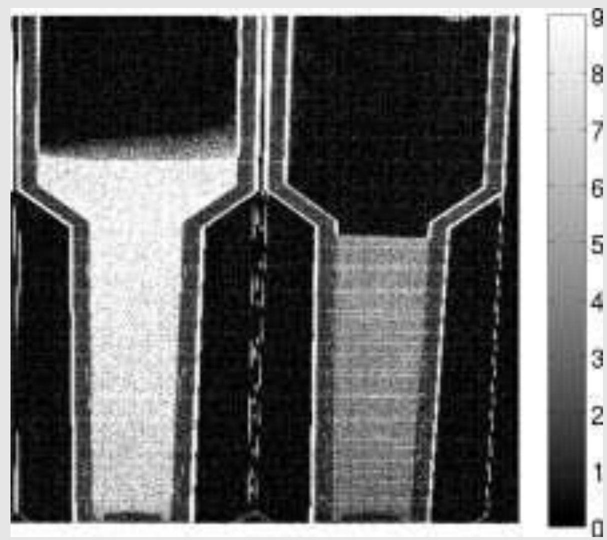


absorption



bubbles no bubbles

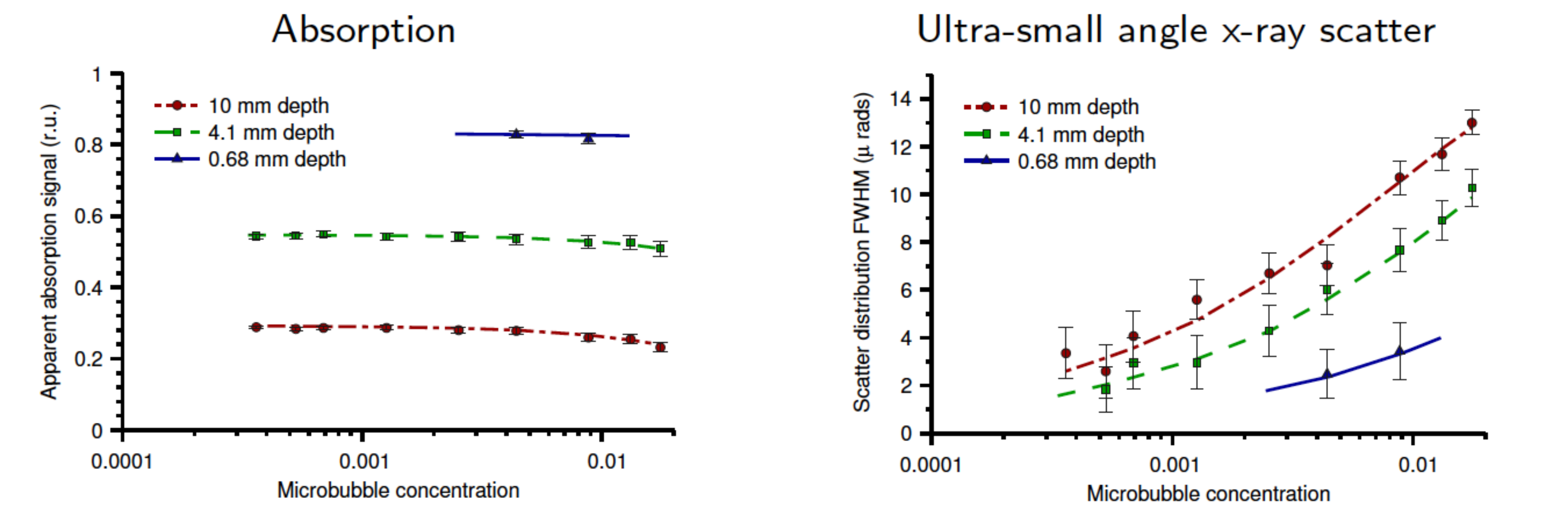
dark field



bubbles no bubbles

Millard et al. Appl. Phys. Lett. 103 (2013) 114105

Quantitative extraction of microbubble concentration



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Millard et al. Appl. Phys. Lett. 103 (2013) 114105

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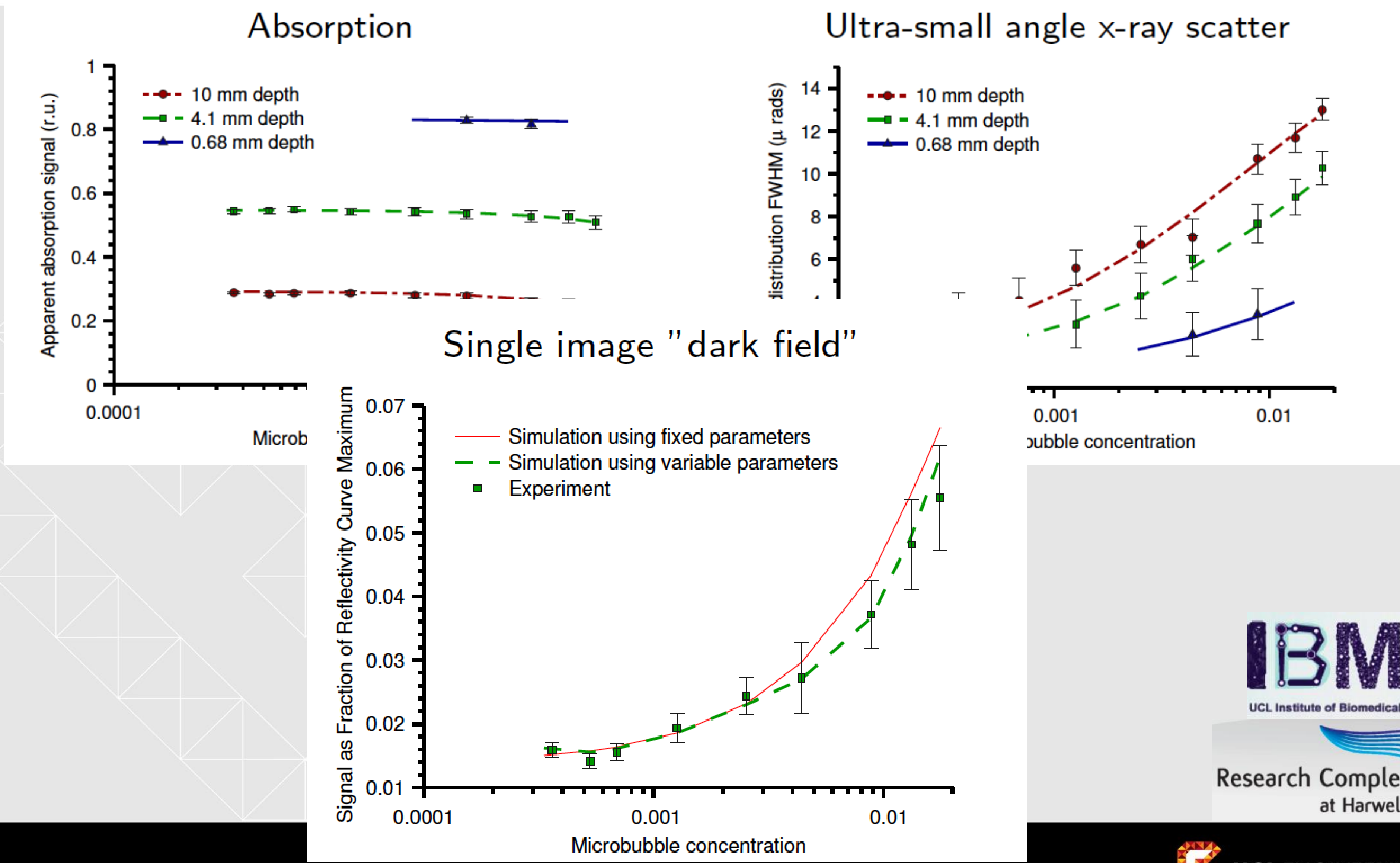

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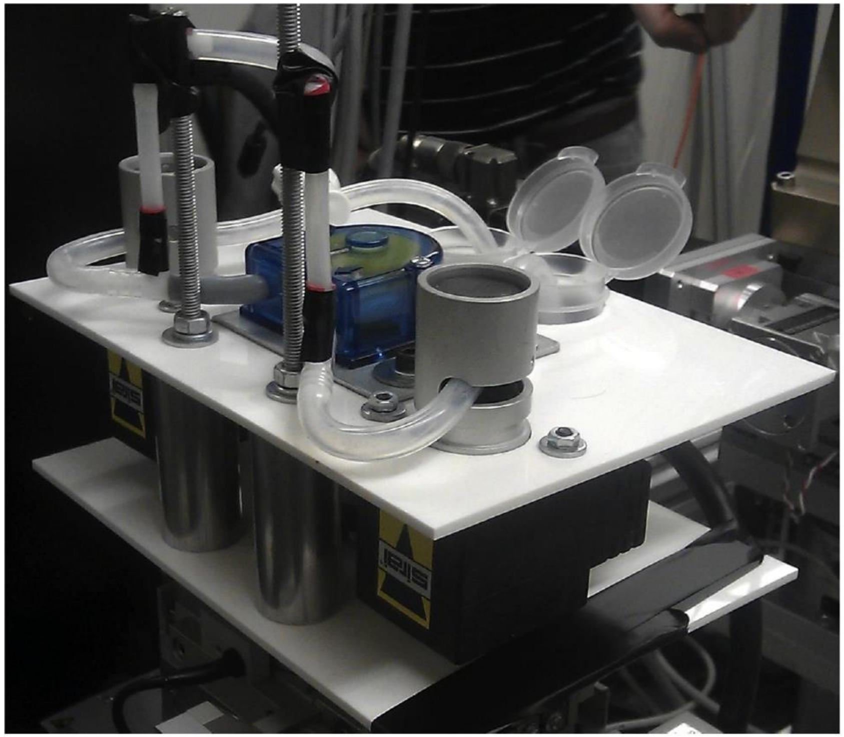
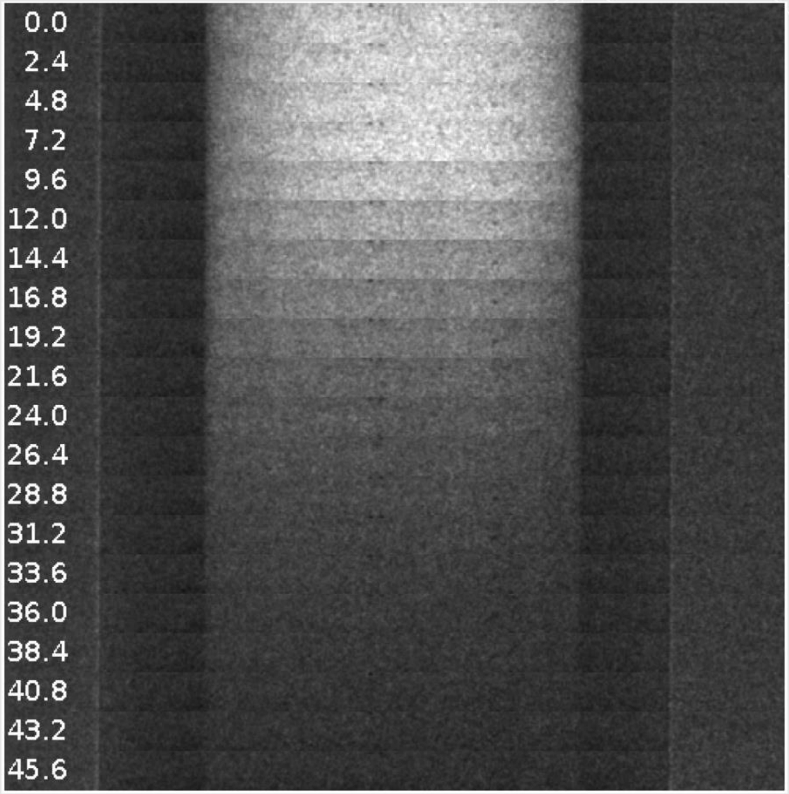
Millard et al. Appl. Phys. Lett. 103 (2013) 114105

DYNAMIC
quantitative extraction of microbubble concentration





IBME
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Millard et al., Sci. Rep. 5 (2015) 12509

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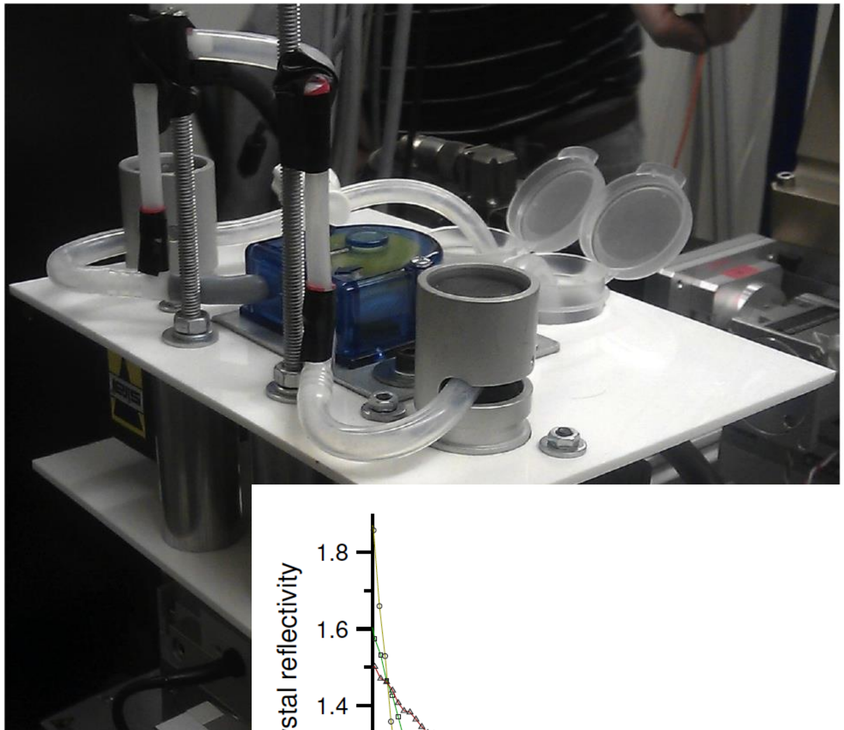
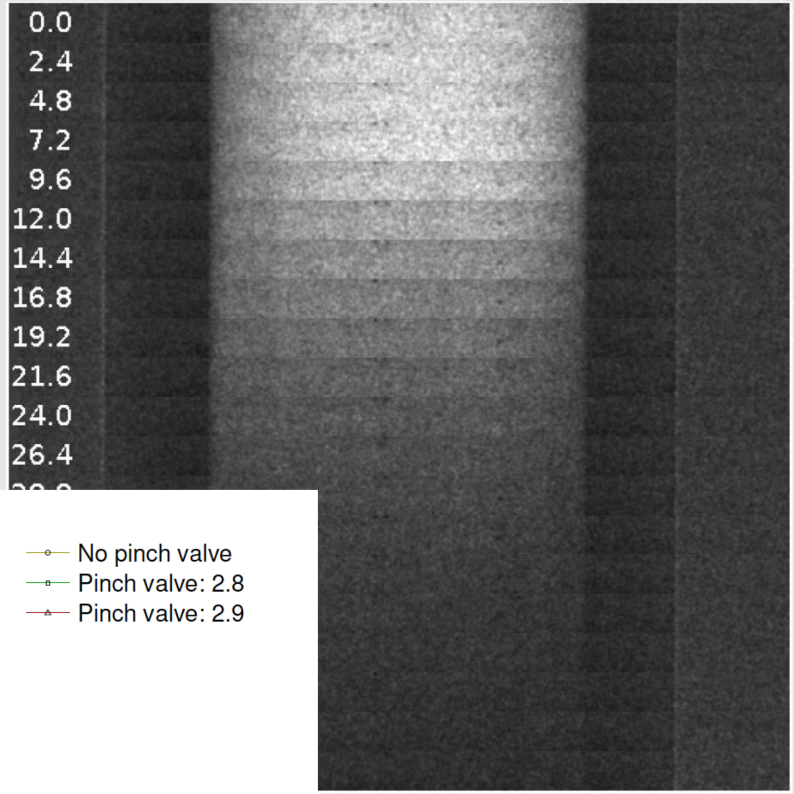
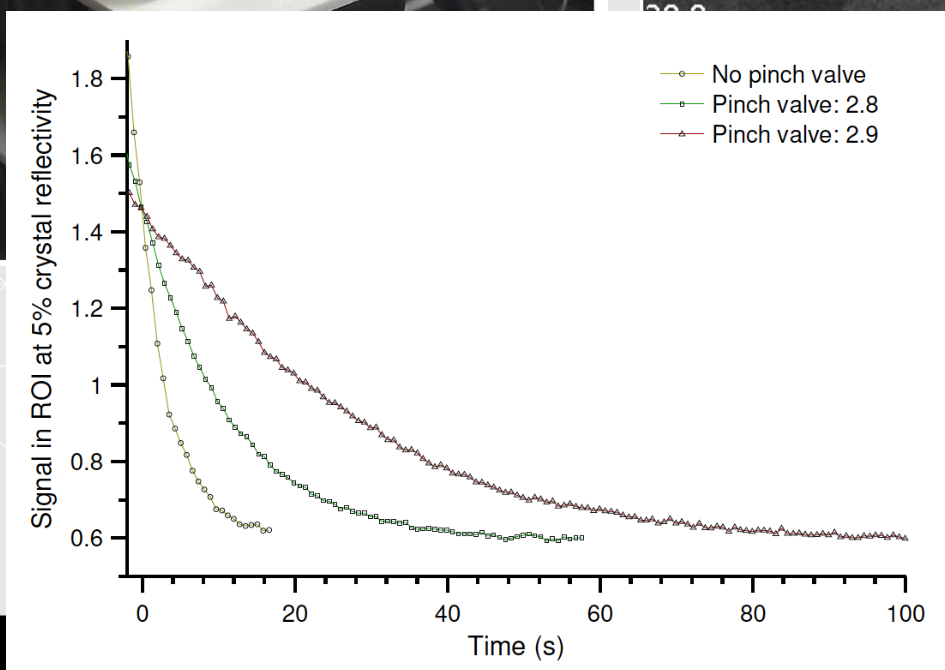
DYNAMIC
quantitative extraction of microbubble concentration







Millard et al., Sci. Rep. 5 (2015) 12509

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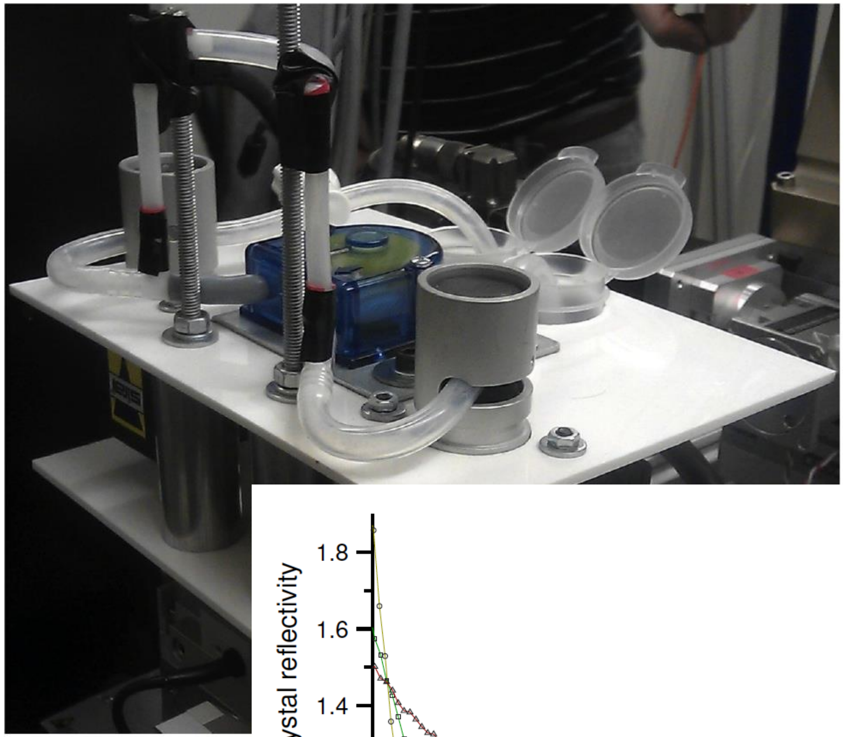
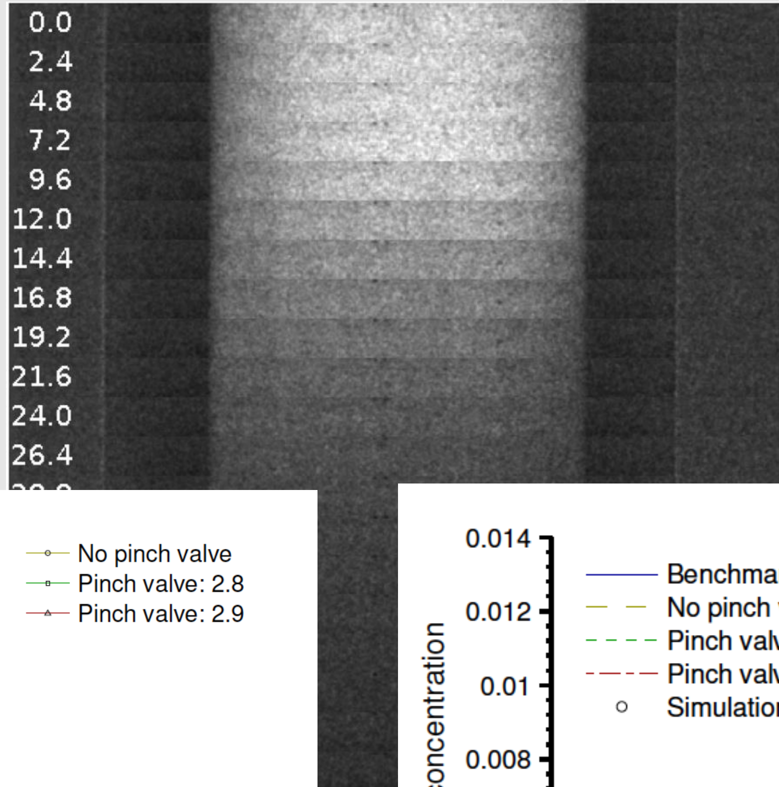
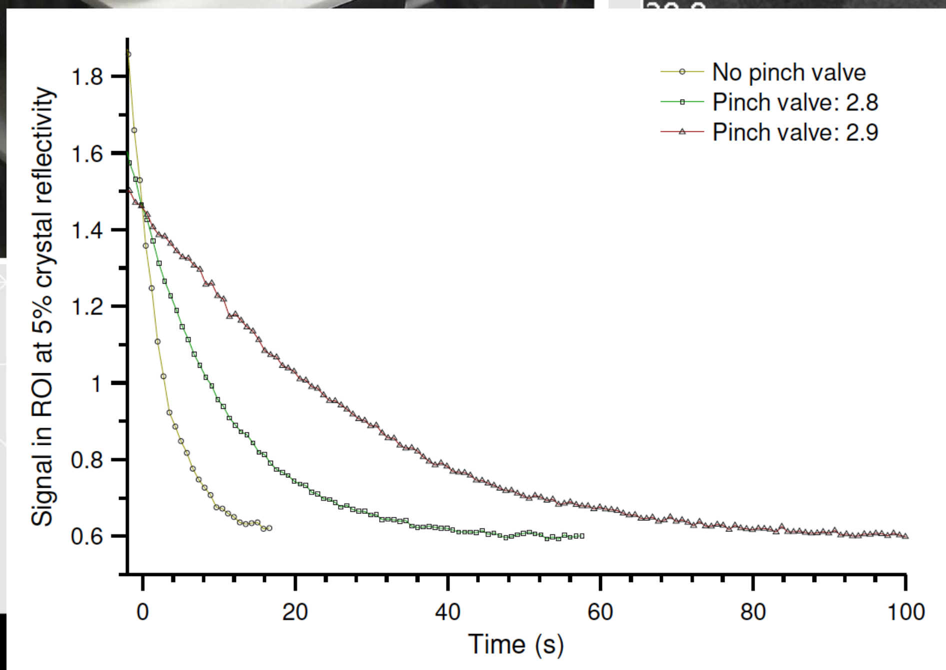
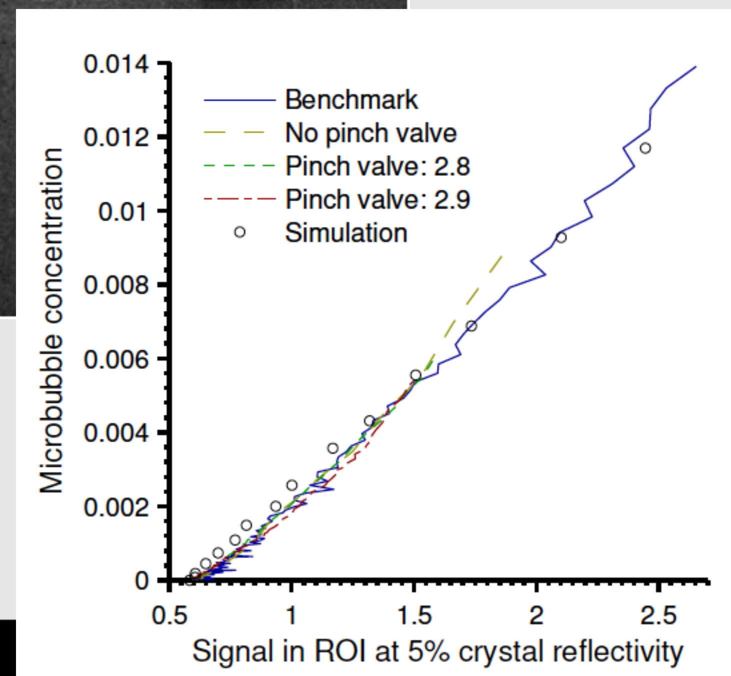
DYNAMIC
quantitative extraction of microbubble concentration





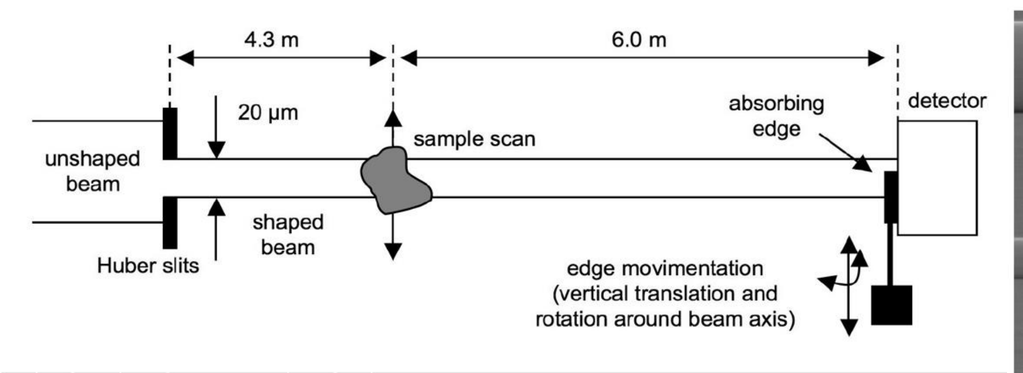


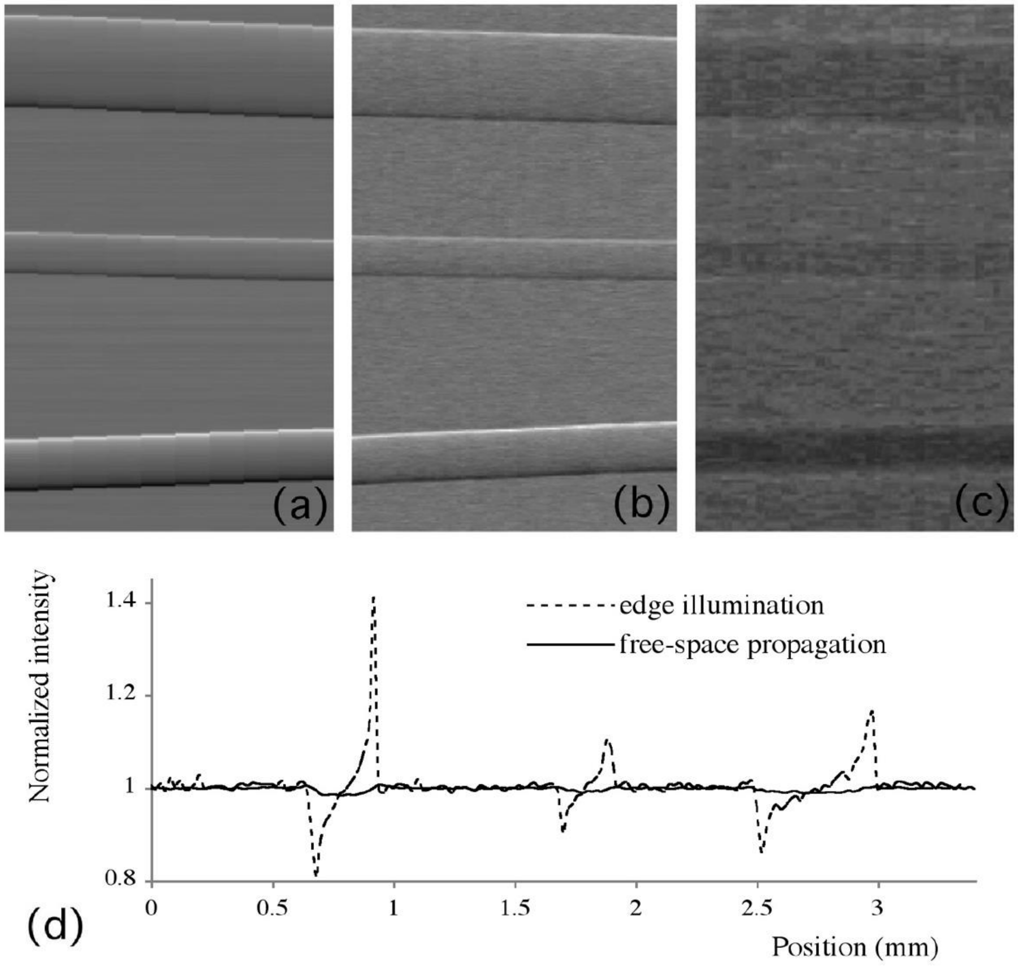


Millard et al., Sci. Rep. 5 (2015) 12509

Very high (monochromatic) energy - ESRF, 85 keV

very simple set-up… -> highly increased contrast!

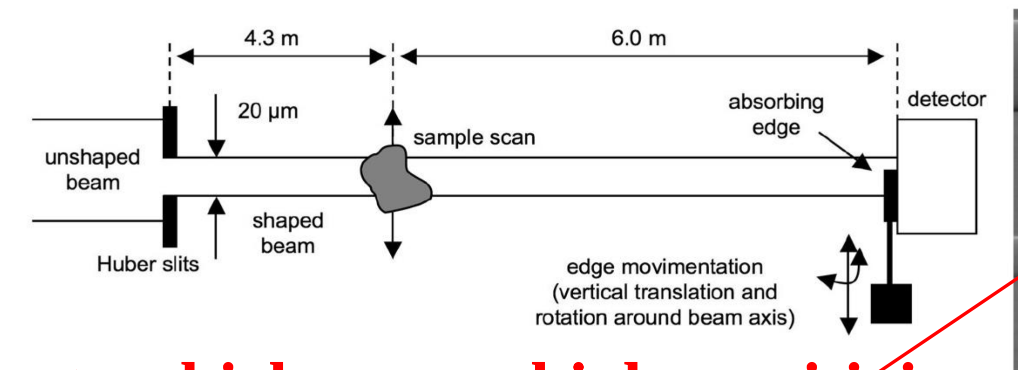


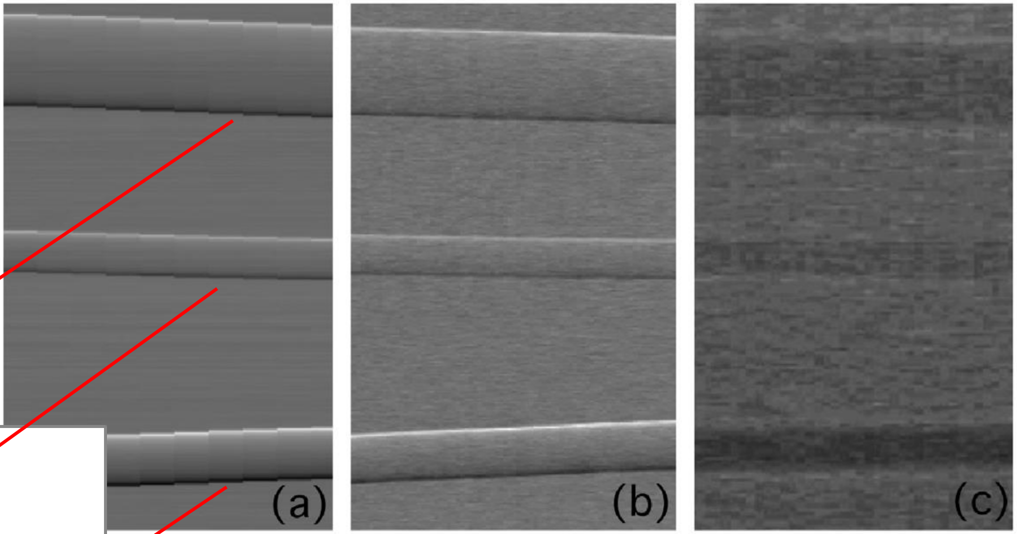


Olivo *et al*, Opt. Lett. 37 (2012) 915-7

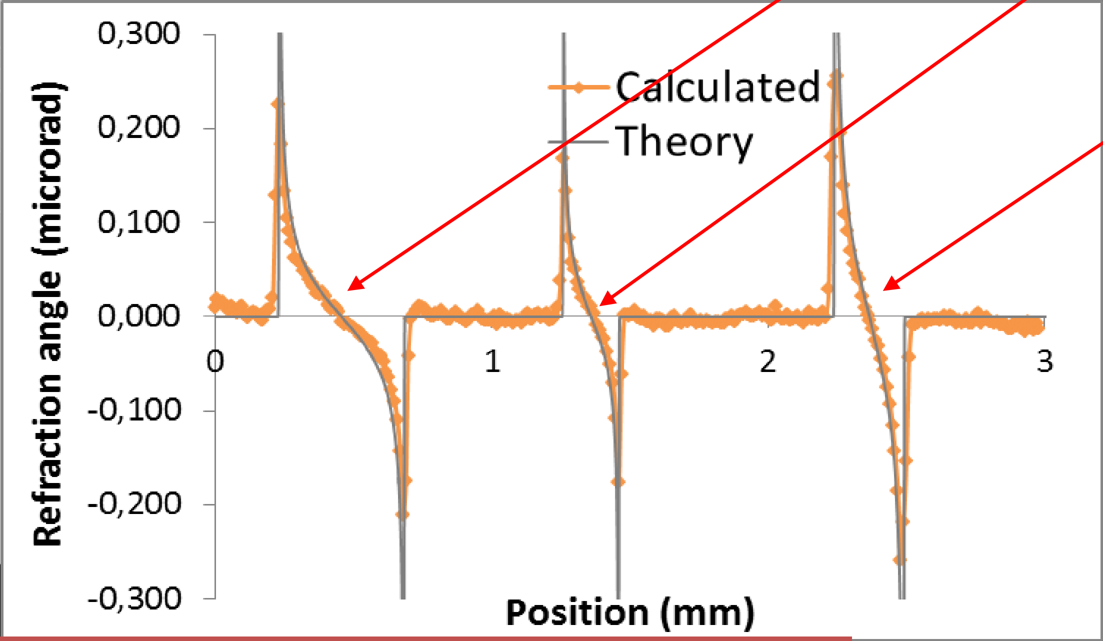
Even higher (monochromatic) energy - ESRF, 85 keV

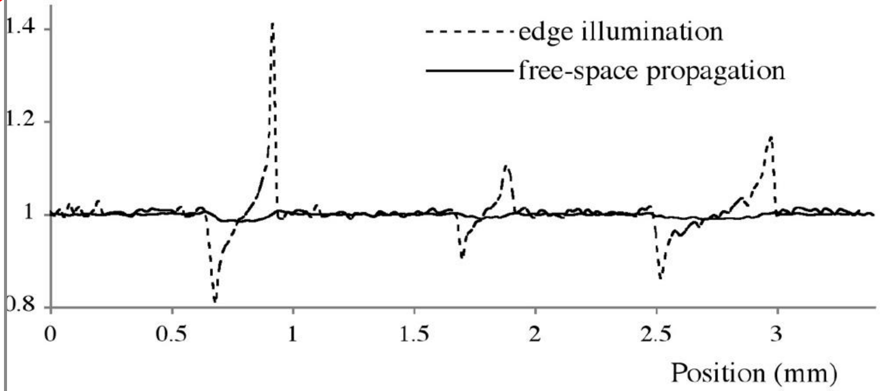
very simple set-up… -> highly increased contrast!





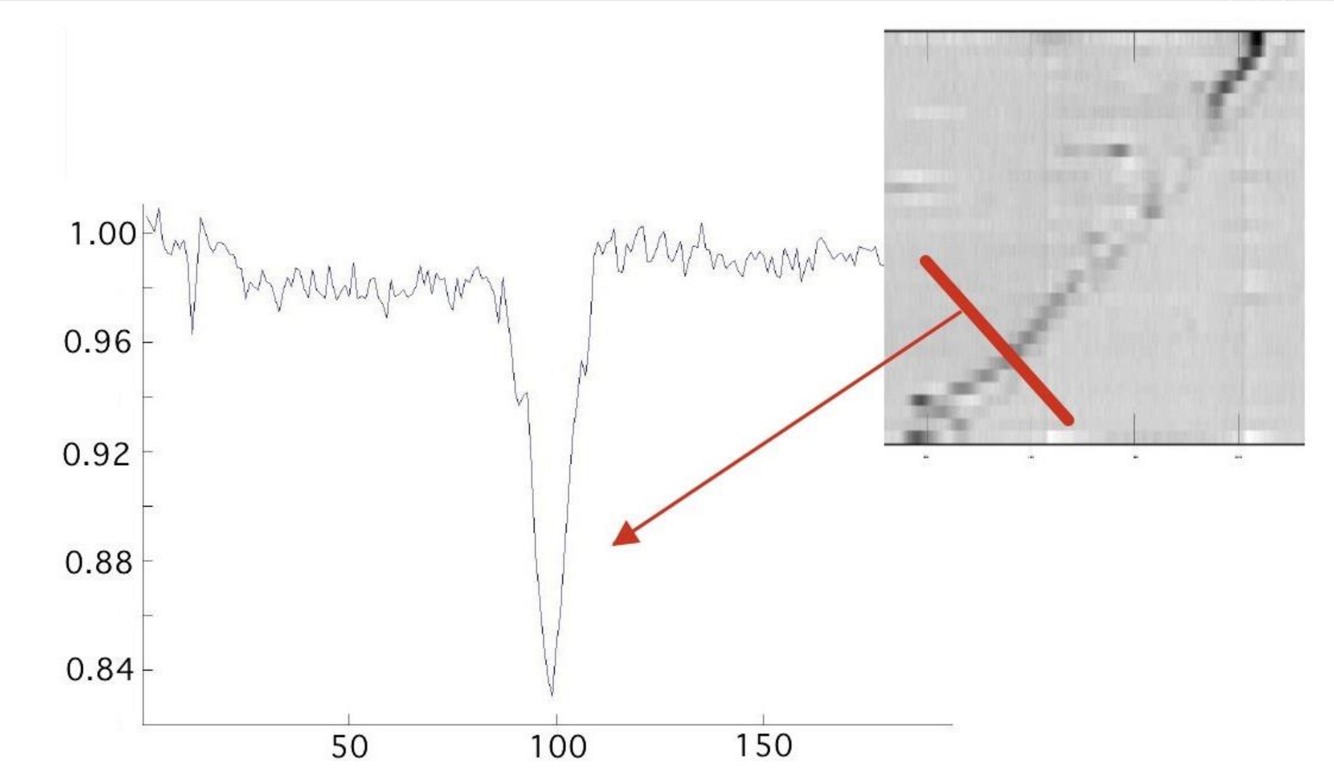
-> which means high sensitivity





Diemoz *et al*, Phys. Rev. Lett. 110 (2013) 138105

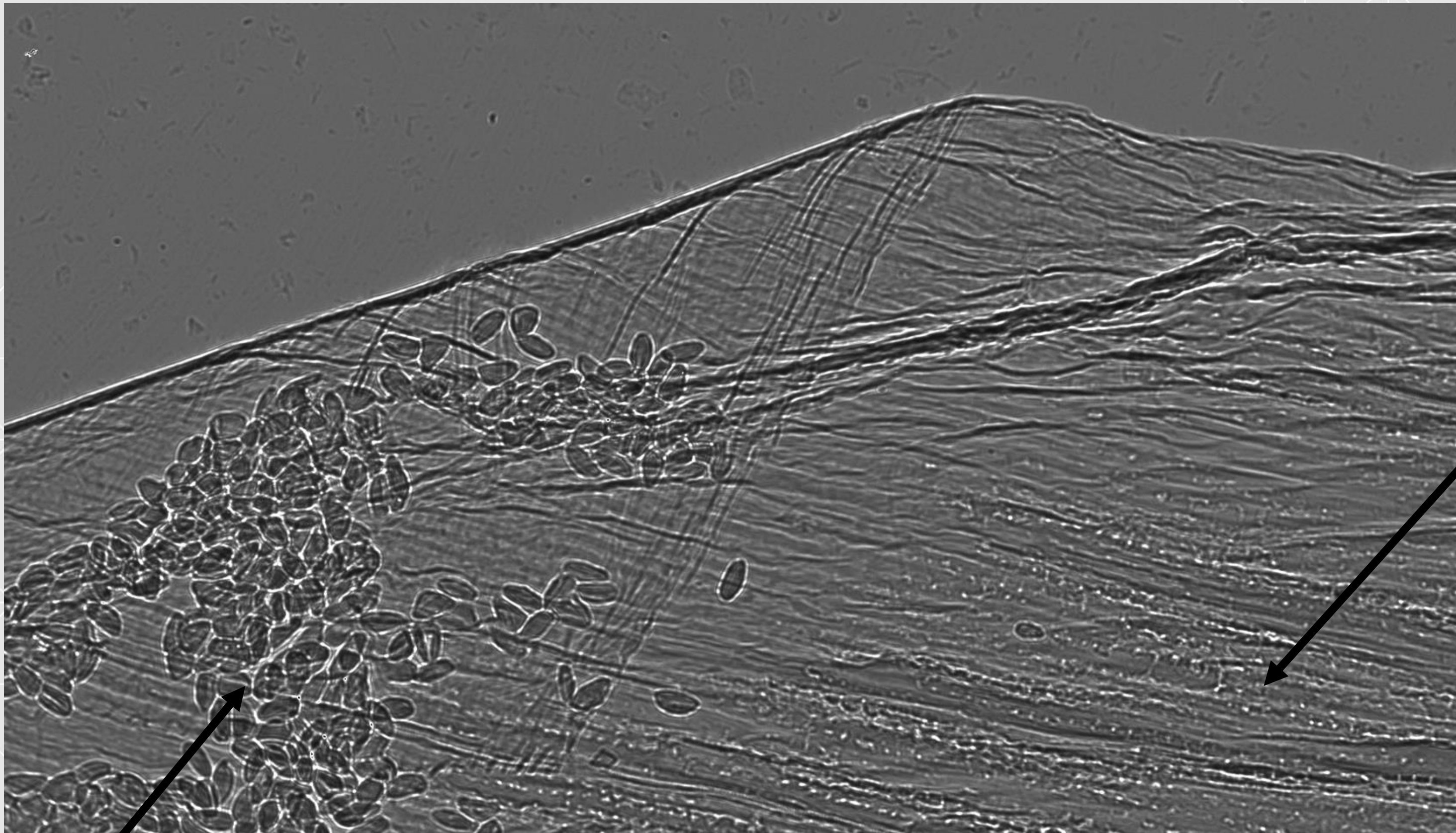
Exploitation of additional sensitivity to push the detection threshold further:



A 10 micron thick polyethilene foil immersed in water (-> matching refractive index!) generates an unprecedented **16%** image contrast!

Practically corresponds to a single cell in water

Which of course can be generalized to other biological applications, etc

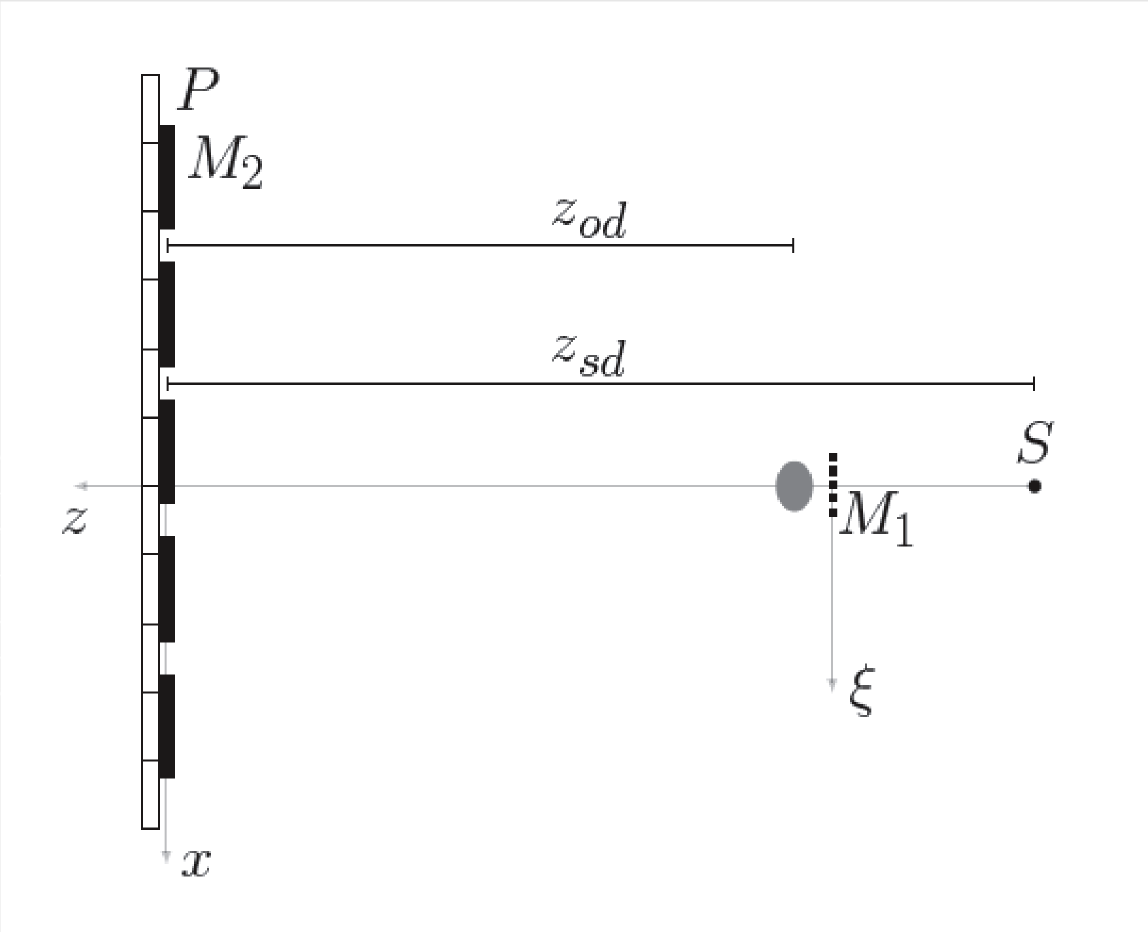


Individual lines of cells along petal veins

pollen

Unpublished

Can we hope to translate this into the lab?



Endrizzi *et al*, Opt. Lett. 39 (2014) 3332-5

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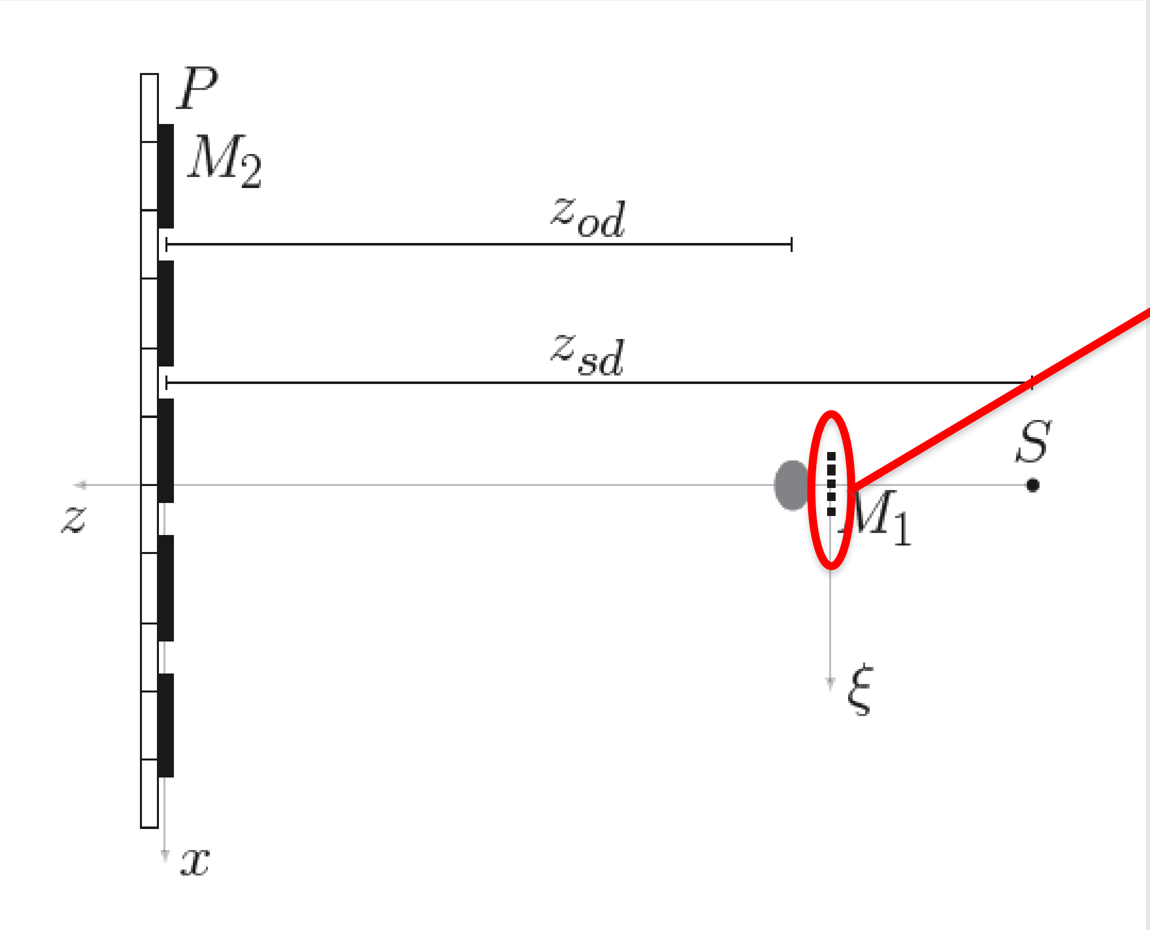

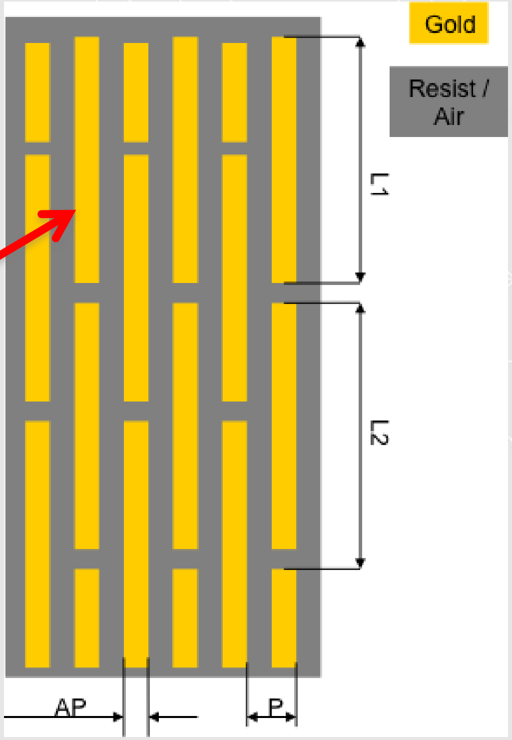

Endrizzi *et al*, Opt. Lett. 39 (2014) 3332-5

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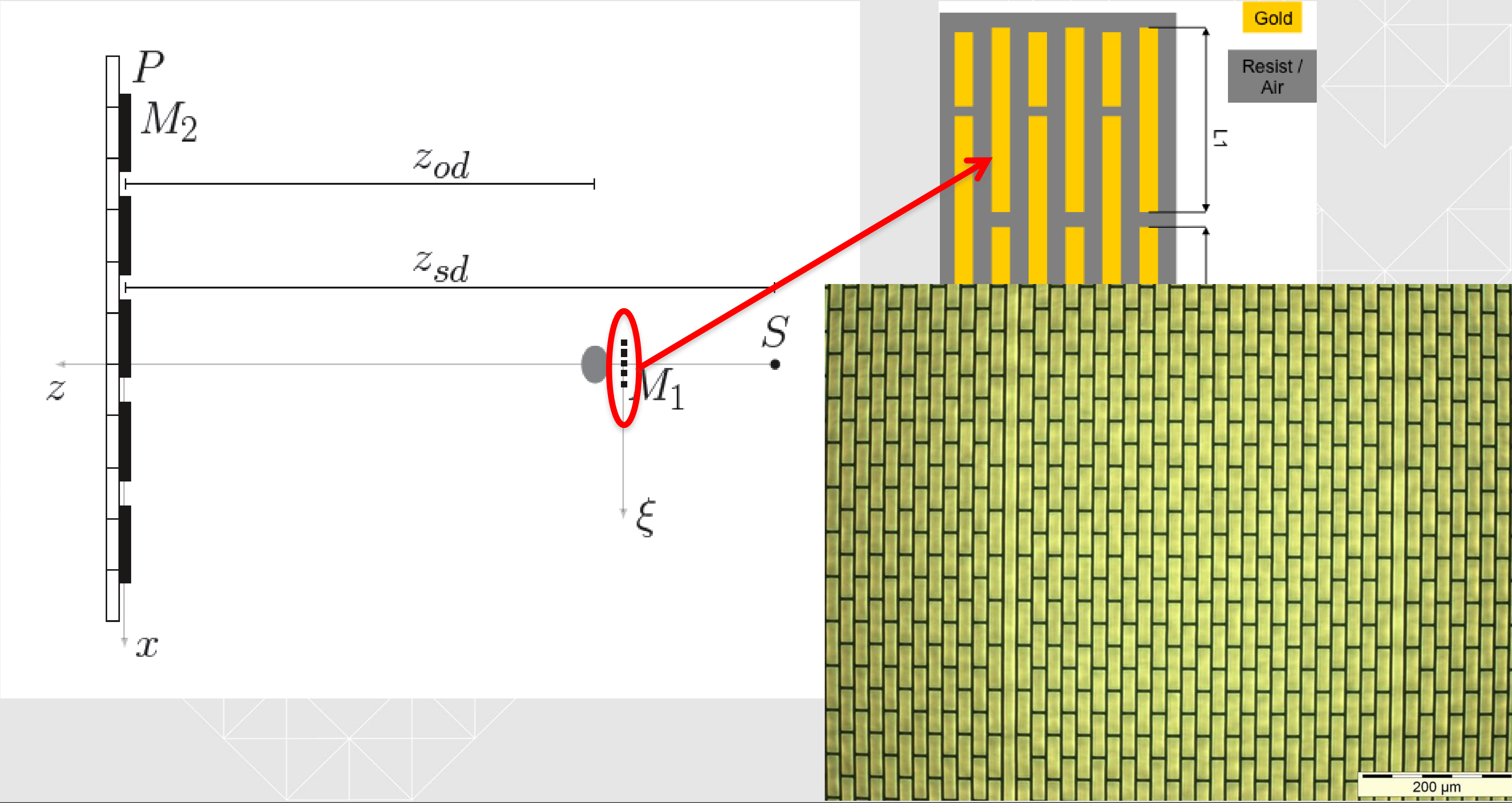

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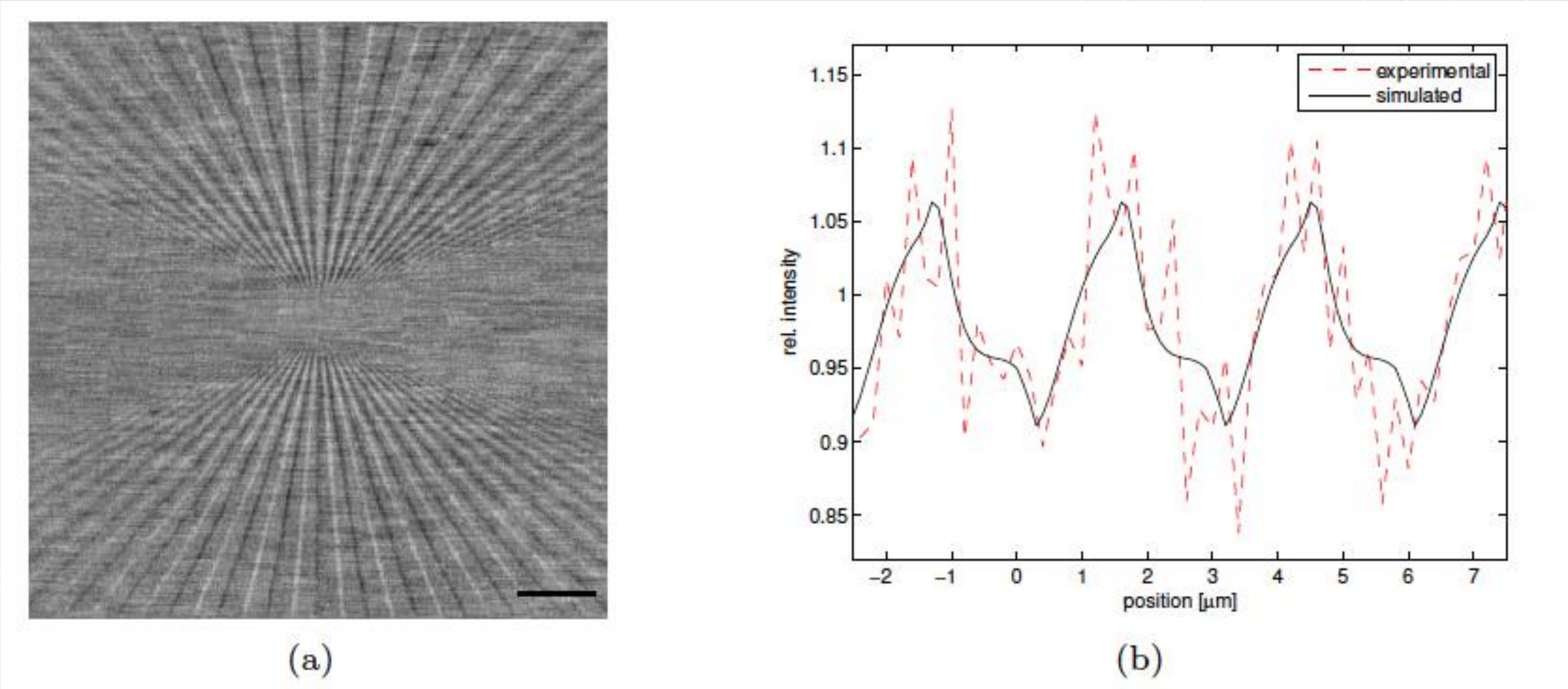
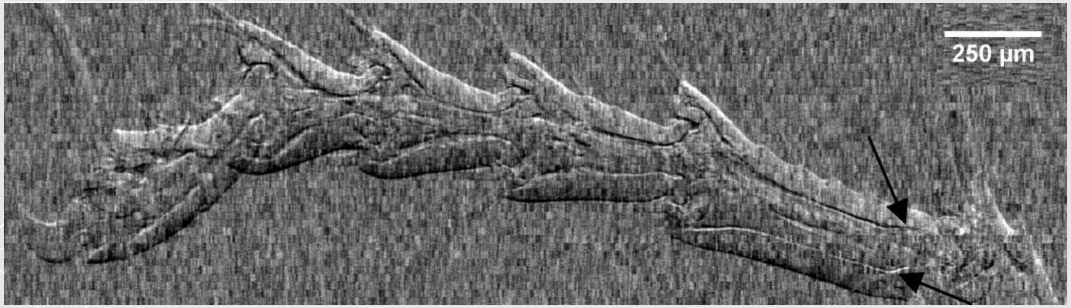


NB both pure "phase" objects (80 kVp were used)



Endrizzi *et al*, Opt. Lett. 39 (2014) 3332-5

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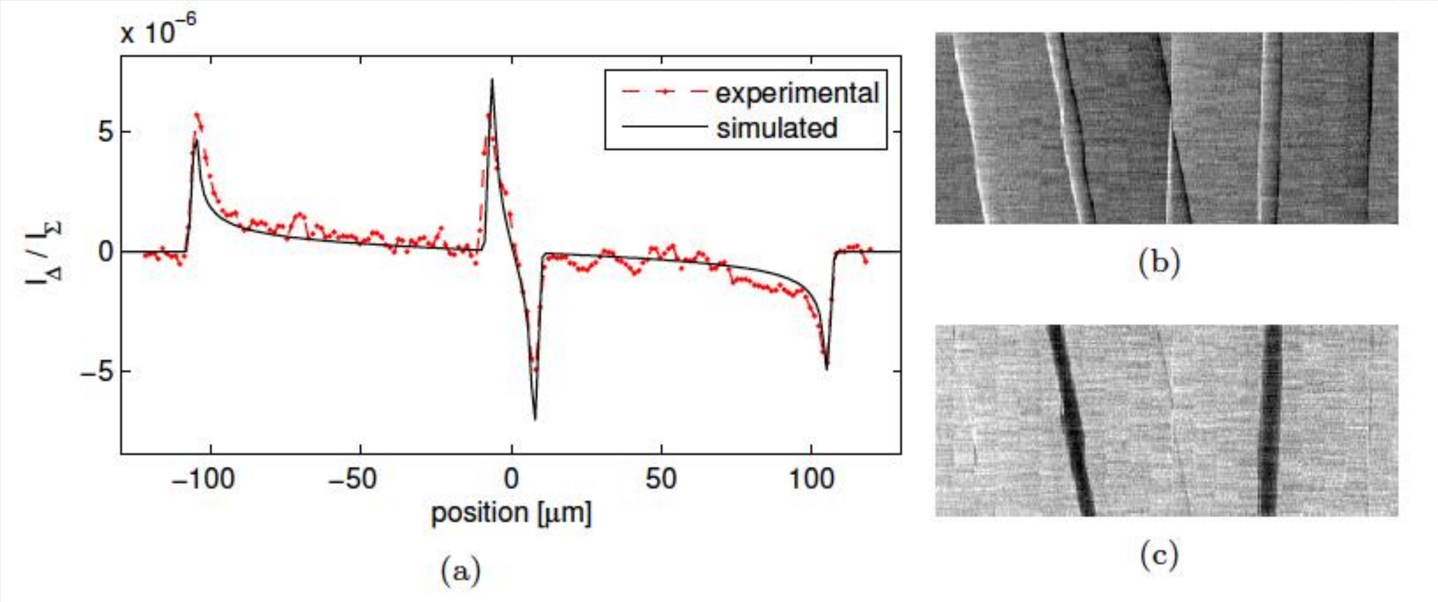
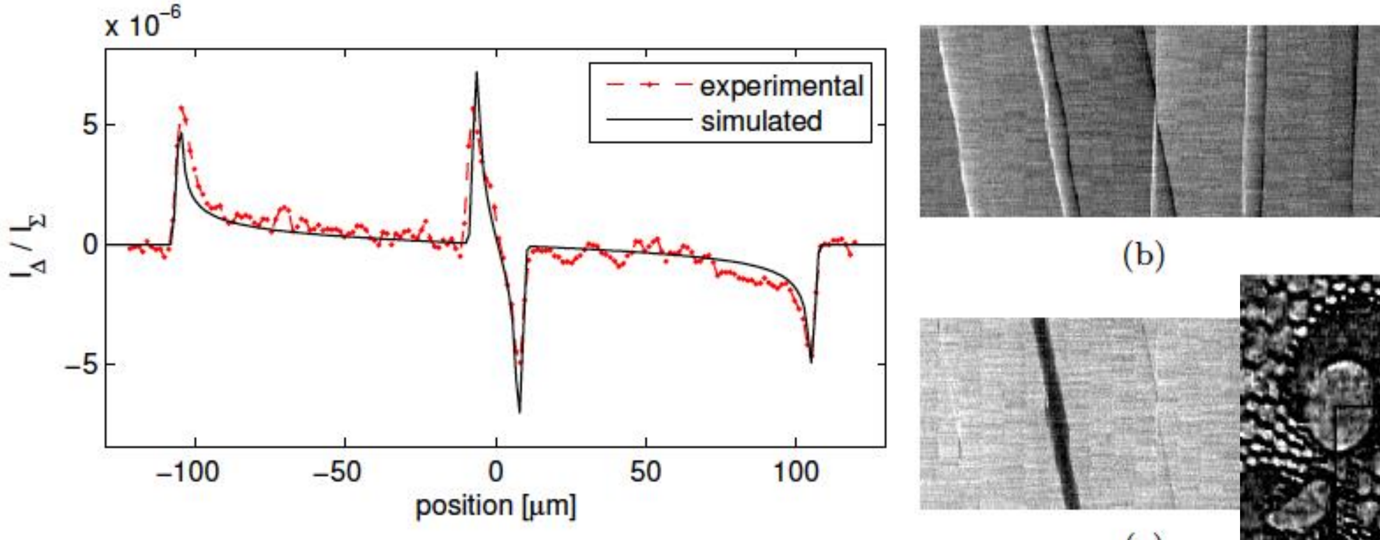


still quantitative…

Endrizzi *et al*, Opt. Lett. 39 (2014) 3332-5

Can we hope to translate this into the lab?

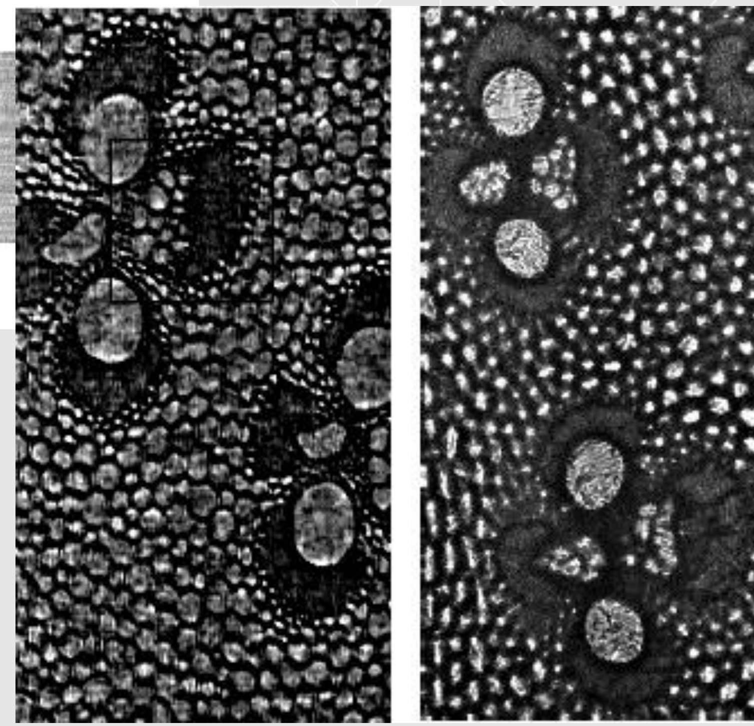


(a)

(b)

(c)

still quantitative…



Lab

Synchro

microstructure of bamboo wood
(nature-inspired engineering project)

Endrizzi *et al*, Opt. Lett. 39 (2014) 3332-5

Conclusions:

Edge-illumination XPCi is a NON-INTERFEROMETRIC, TOTALLY INCOHERENT, QUANTITATIVE x-ray phase contrast method working with conventional sources which:

allows the use of fully divergent, fully polychromatic x-ray sources with focal spots of up to at least 100 μm - with no additional collimation/aperturing; **the use of large apertures in thin gold layers** (-> no angular filtration)**, low-absorbing graphite substrates, moderate misalignments between masks allowed achieving a reduction in the exposure times -** although demanding medical applications require further developments. Most of all they keep the **dose at acceptable levels**.

requires aperture pitches of the order of ~50-100 μm - therefore making fabrication, alignment and scale-up (masks are available up to 30 cm) easier.

has been described both by wave & geometrical optics (but for source sizes like the ones we use they give the same results) and **robust phase retrieval was achieved.**

Translated "back" to a coherent source, it enables **unprecedented phase sensitivity** which opens the way to **NEW, PREVIOUSLY INACCESSIBLE SCIENTIFIC APPLICATIONS**