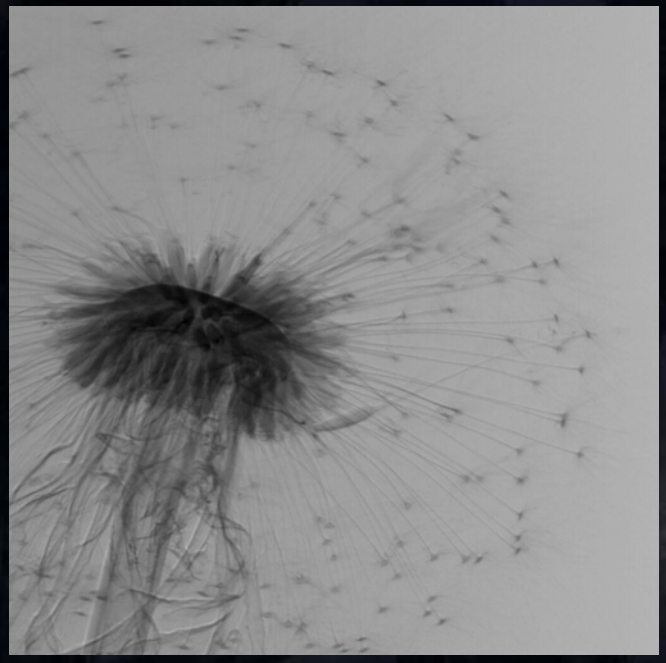
Una luce per la ricerca biomedica: i raggi X da sincrotrone



2015
UNESCO
INTERNATIONAL
YEAR OF LIGHT

Luigi Rigon

Università degli studi di Trieste
Istituto Nazionale di Fisica Nucleare

Cominciamo dall'inizio...

Wilhelm Conrad Roentgen (1845 -1923)

EINE NEUE ART
VON
STRAHLEN.

Sweden awards first Nobel Prizes

Alfred Nobel

Dec 10. The King of Sweden and the Norwegian Nobel Committee distributed the first Nobel Prizes today. These awards, according to Alfred Nobel's will, "should be annually made to those who, during the preceding year, shall have conferred the greatest benefit on mankind" in the specialized fields of physics, chemistry, medicine, literature and peace.

This year's Nobel laureates are: Wilhelm Roentgen of Germany (physics) for his discovery of X-rays; Jacobus Henricus van't Hoff of the Netherlands (chemistry) for his laws of chemical dynamics and osmotic pressure; Emil von Behring of Germany (medicine) for his work on serum therapy; and Sully Prudhomme of France (literature) for his poetry. The 1901 Nobel Peace Prize was awarded to both Jean Henri Dunant of Switzerland, who established the Red Cross in 1864, and the economist Frederic Passy, who founded the French Society of the Friends of Peace.

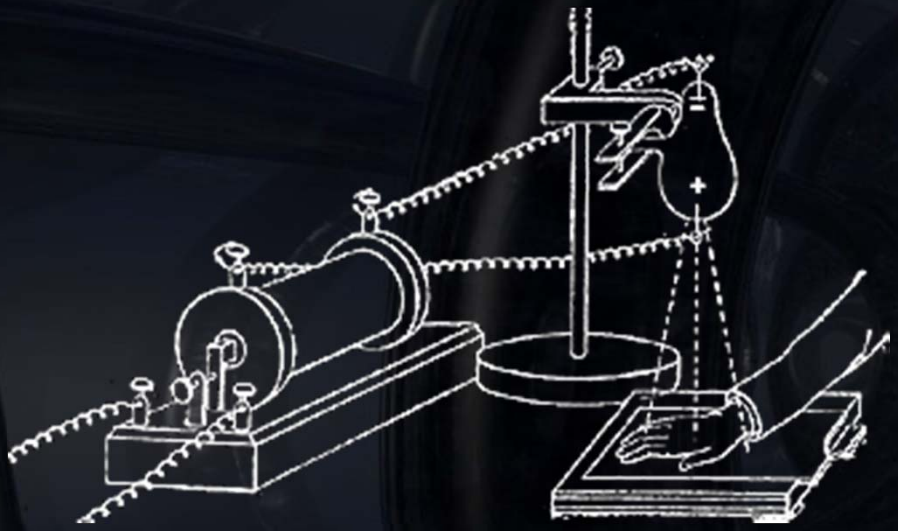
From this day forward, the prizes will be awarded by four institutions, three Swedish and one Norwegian, from a fund established under the will of Alfred Nobel. The ceremonial presentation of the prizes is to take place every year in Stockholm, Sweden, and Oslo, Norway, on December 10, the anniversary of Nobel's death.

In 1867, Nobel, a Swedish chemist, invented dynamite and later discovered many other explosive substances. As a result, he earned a fortune, which he left to a foundation when he died in 1886. The annual interest yielded by his wealth will finance the five Nobel Prizes. The Nobel Foundation is the legal owner and functional administrator of the funds, but it is not concerned with the prize deliberations, which rest exclusively with the Swedish and Norwegian institutions.

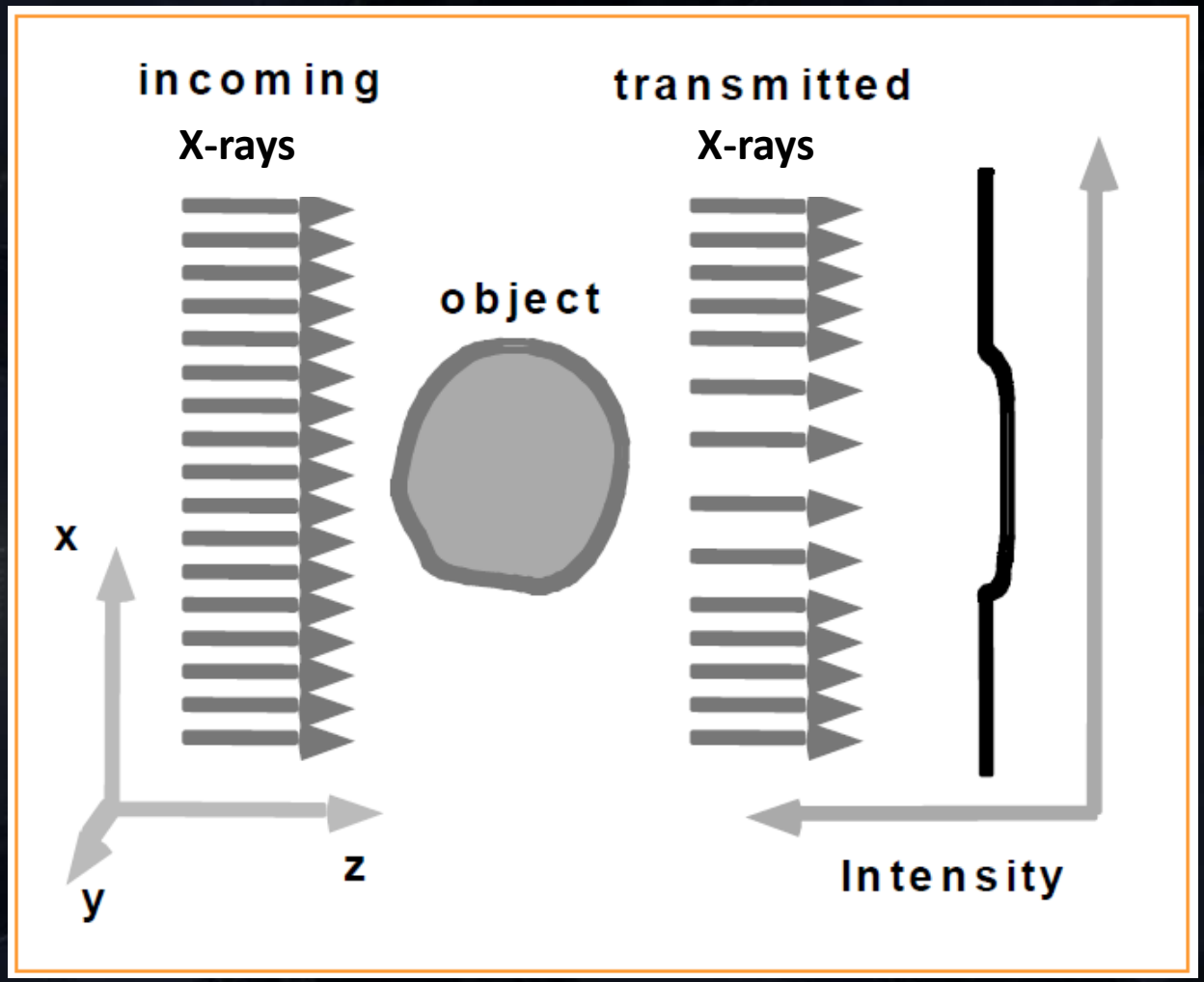
Wilhelm Conrad Roentgen, winner of the Nobel Prize in physics.

Sully Prudhomme, winner of the Nobel Prize in literature.

La radiografia della mano della signora Roentgen



Assorbimento dei raggi X

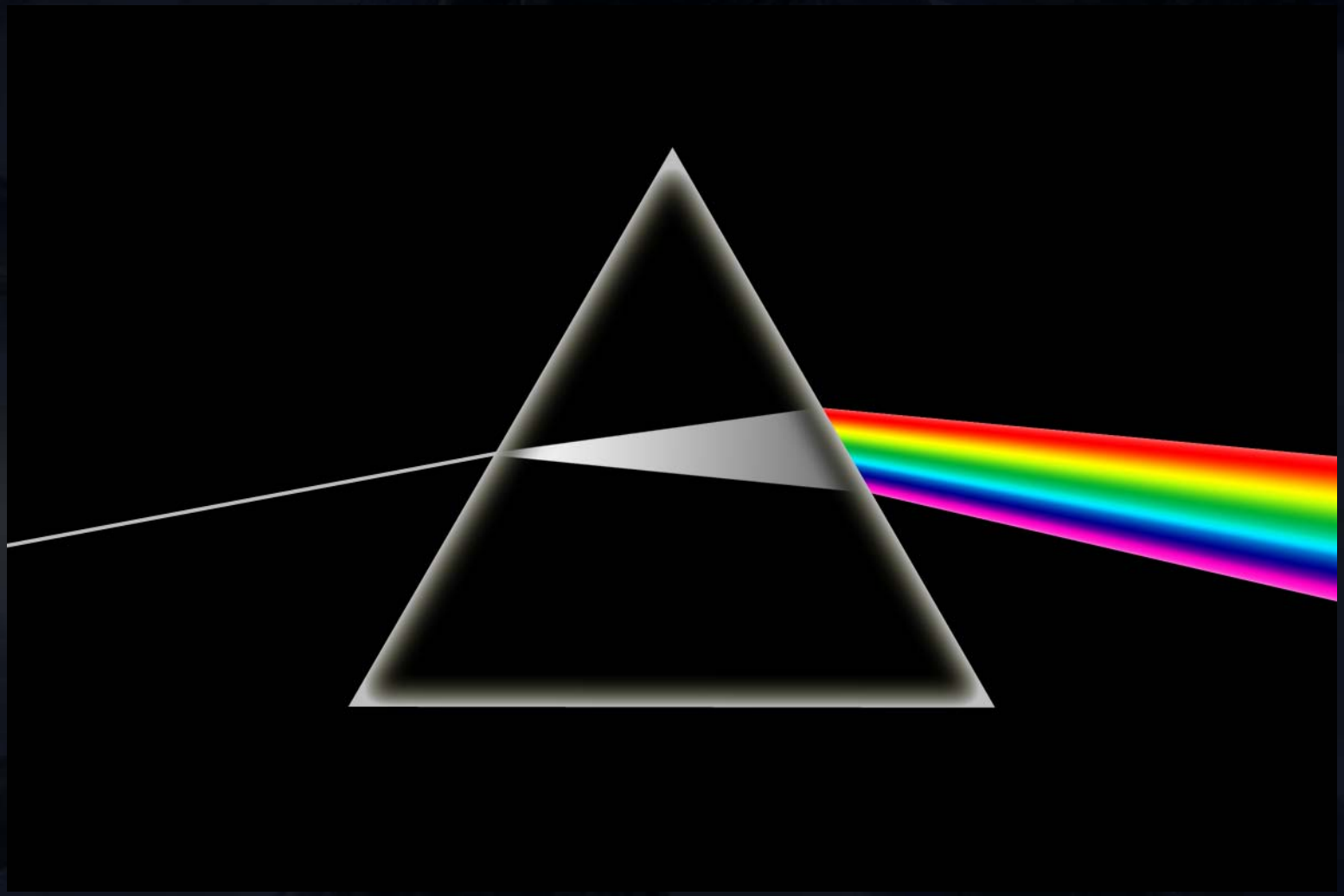


Una moderna radiografia clinica

- Ottimo contrasto e risoluzione dei dettagli per le ossa
- Solo una pallida ombra per i tessuti molli

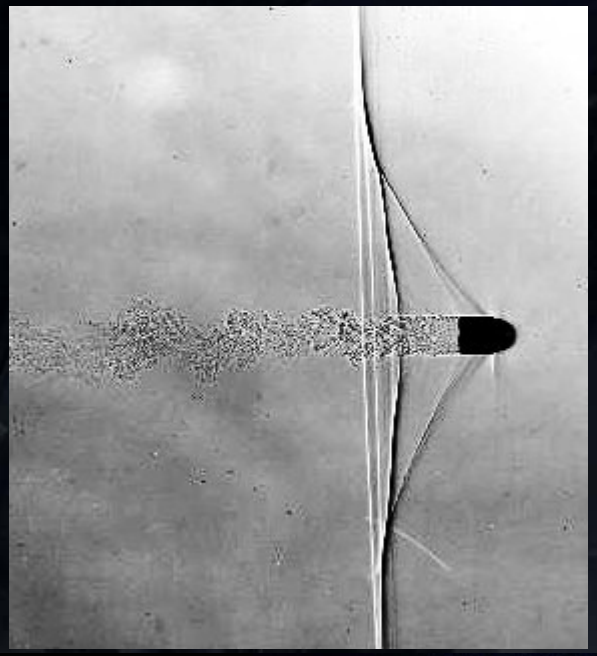
A proposito di ombre…

Rifrazione della luce

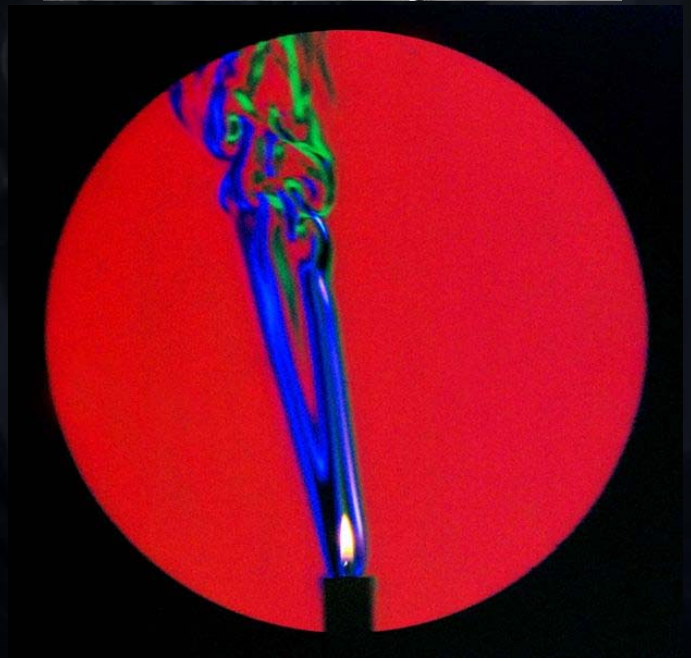


Contrasto di fase (con la luce visibile)

- Shadowgraph

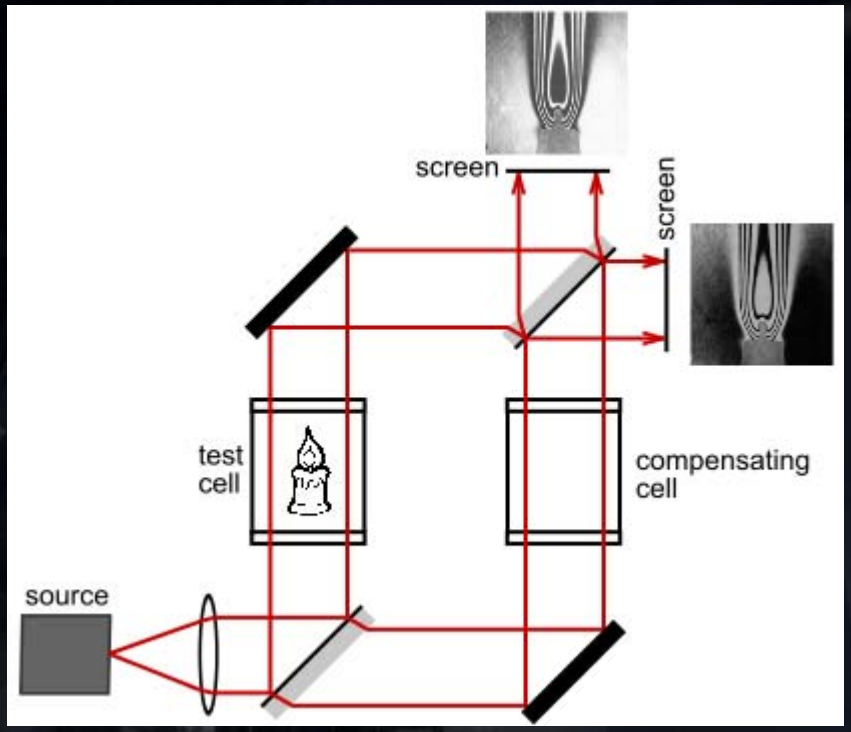


- Schlieren (August Toepler, 1864)

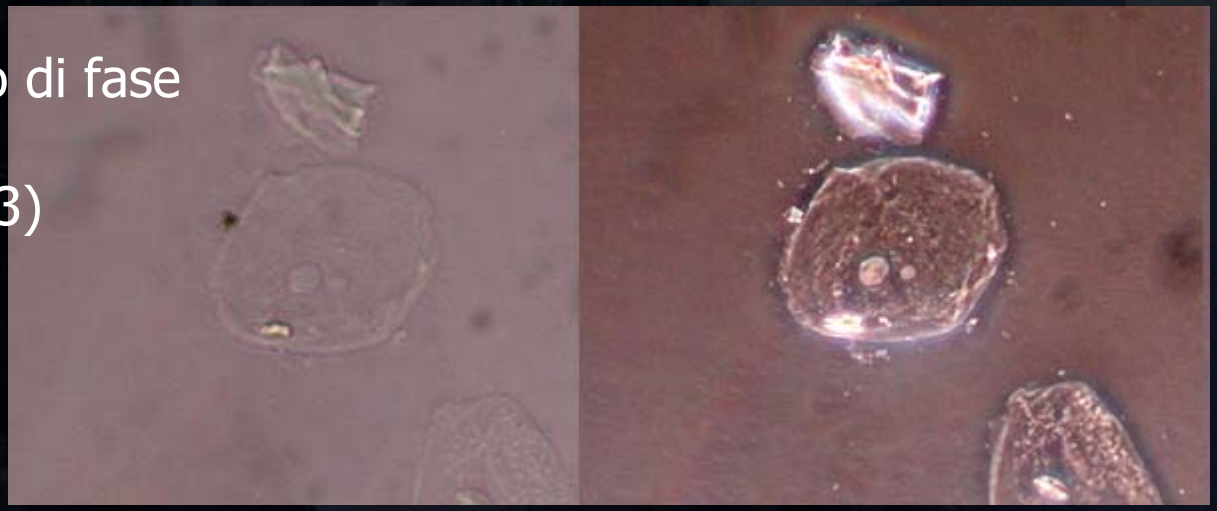


Contrasto di fase (con la luce visibile)

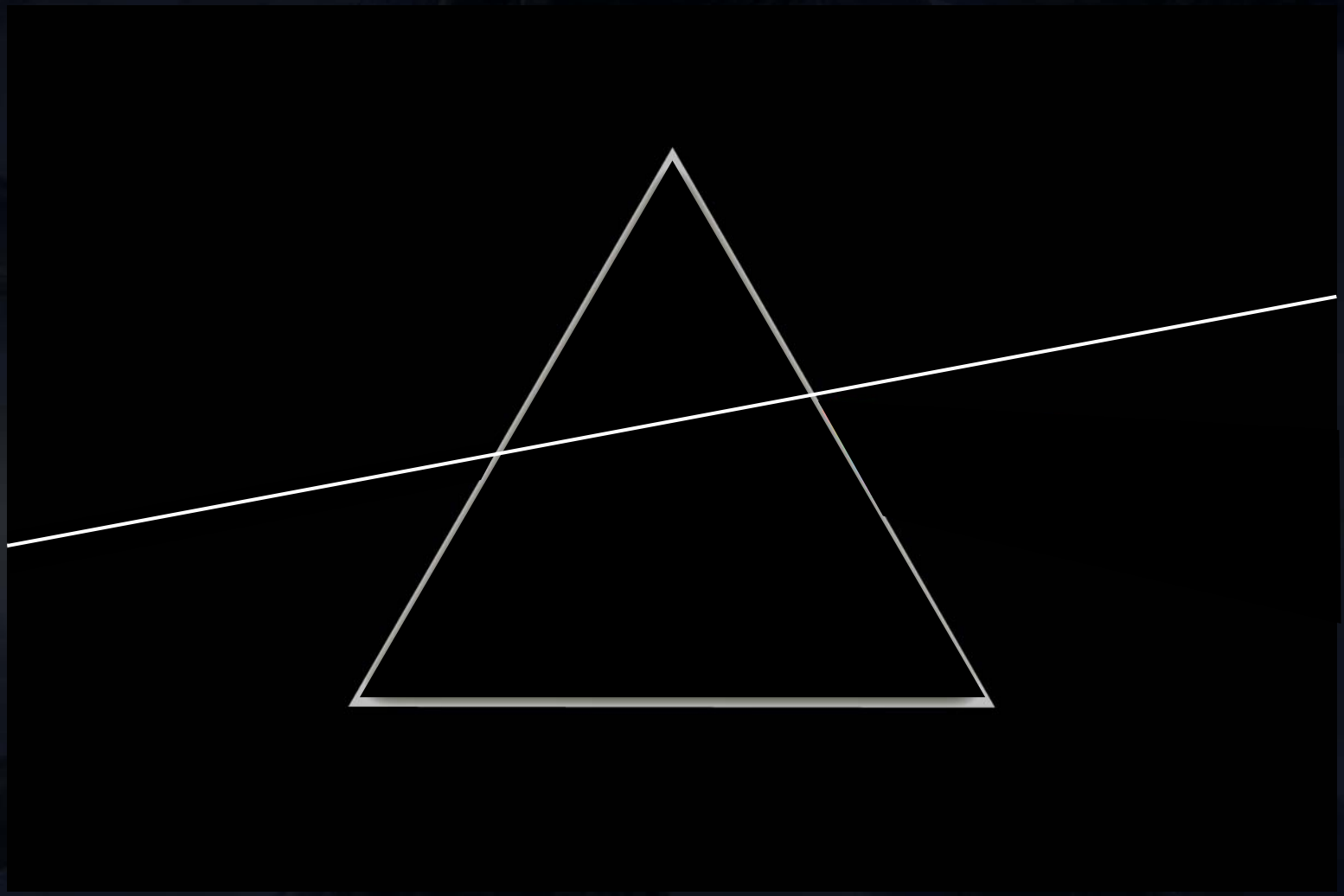
- Interferometero di Mach - Zender (1891 -1892)



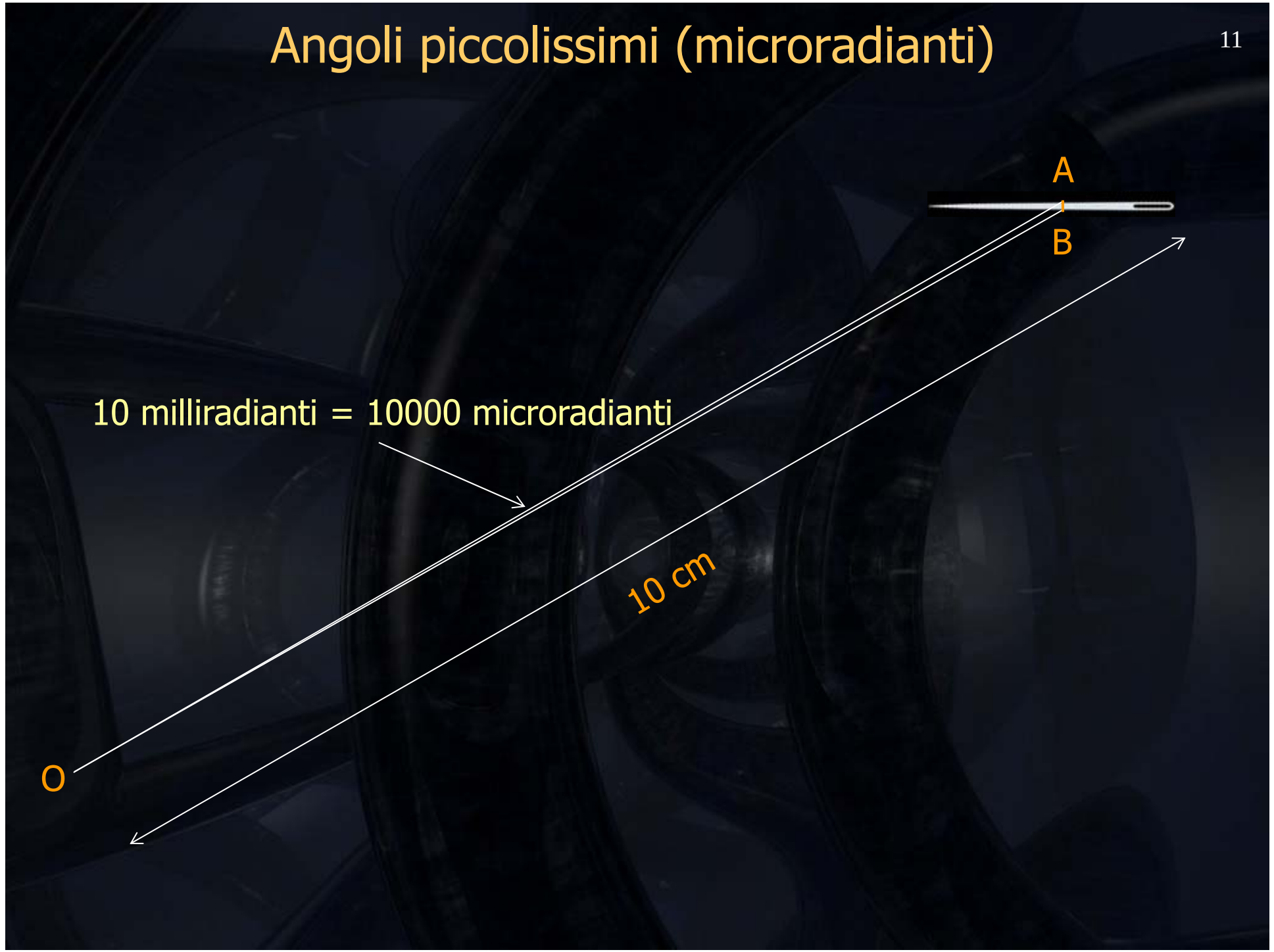
- Microscopio a contrasto di fase (Frits Zernike, Nobel per la fisica, 1953)



Rifrazione (???) dei raggi X

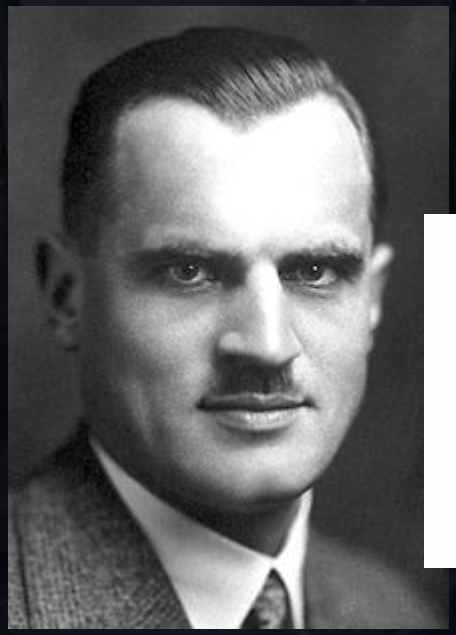


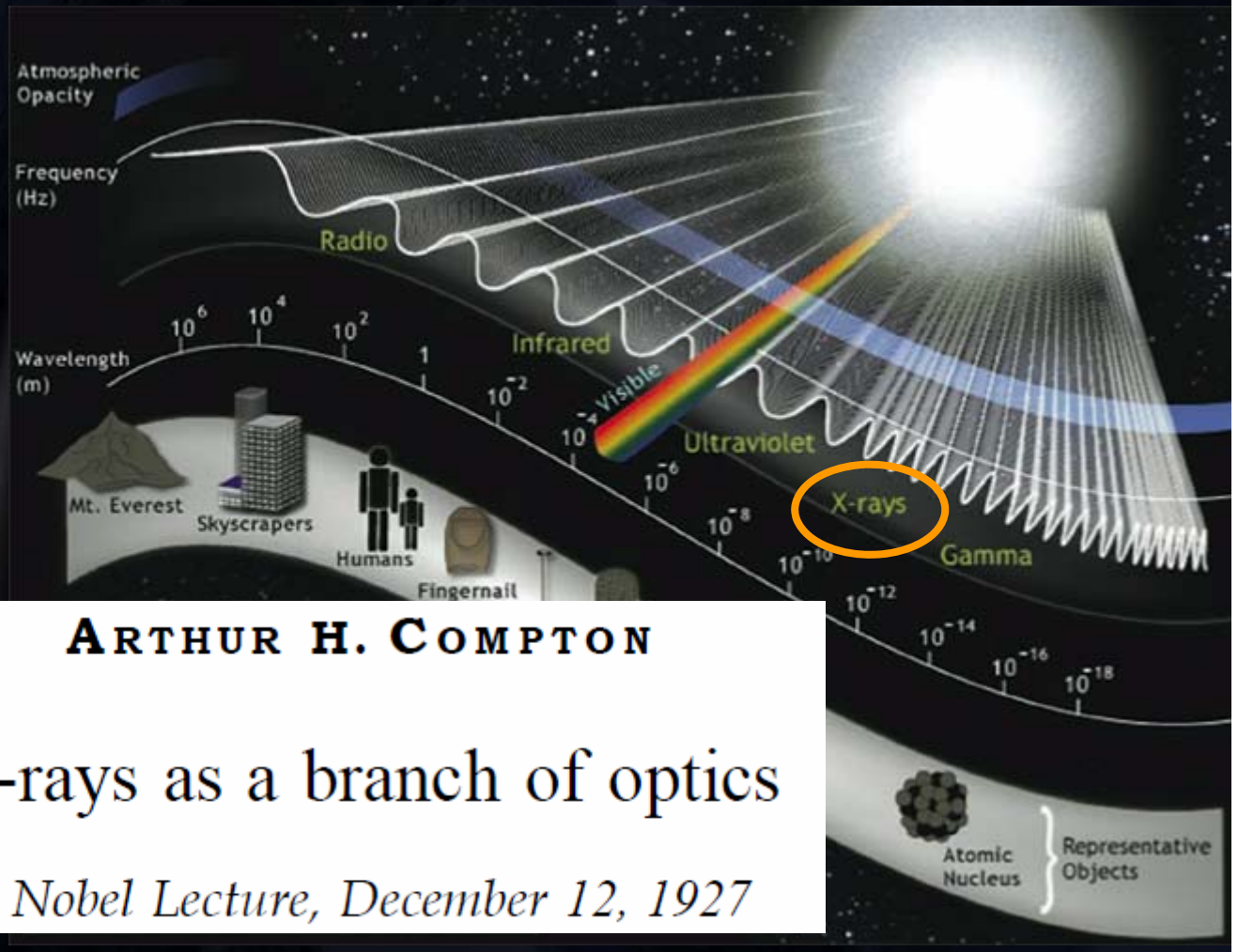
Angoli piccolissimi (microradianti)



Angoli piccolissimi (microradianti)

I raggi X come onde elettromagnetiche





ARTHUR H. COMPTON

X-rays as a branch of optics

Nobel Lecture, December 12, 1927

One of the most fascinating aspects of recent physics research has been the gradual extension of familiar laws of optics to the very high frequencies of X-rays, until at the present there is hardly a phenomenon in the realm of light whose parallel is not found in the realm of X-rays. Reflection, refraction, diffuse scattering, polarization, diffraction, emission and absorption spectra, photoelectric effect, all of the essential characteristics of light have been found also to be characteristic of X-rays. At the same time it has been found that some of these phenomena undergo a gradual change as we proceed to the extreme frequencies of X-rays, and as a result of these interesting changes in the laws of optics we have gained new information regarding the nature of light.

It has not always been recognized that X-rays is a branch of optics. As a result of the early studies of Röntgen and his followers it was concluded that X-rays could not be reflected or refracted, that they were not polarized on transversing crystals, and that they showed no signs of diffraction on passing through narrow slits. In fact, about the only property which they were found to possess in common with light was that of propagation in straight lines. Many will recall also the heated debate between Barkla and Bragg, as late as 1910, one defending the idea that X-rays are waves like light, the other that they consist of streams of little bullets called "neutrons". It is a debate on which the last word has not yet been said!

Contrasto di fase

Elettra (Trieste)

Elettra (Trieste)

Elettra (Trieste)

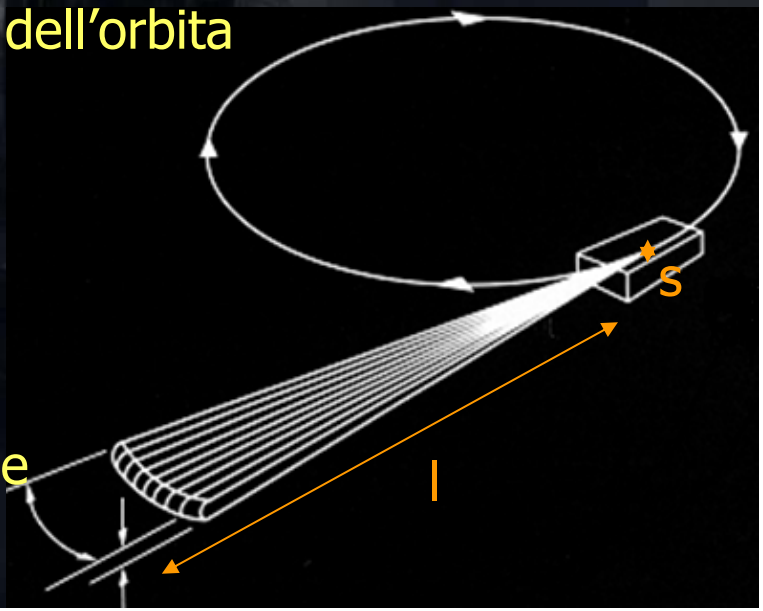
Elettra (Trieste)

courtesy of Elettra

Caratteristiche dei raggi X da sincrotrone

- Elevata intensità
  - Fascio monocromatico di energia selezionabile a piacere
  - Energia ottimale per ogni singolo esame

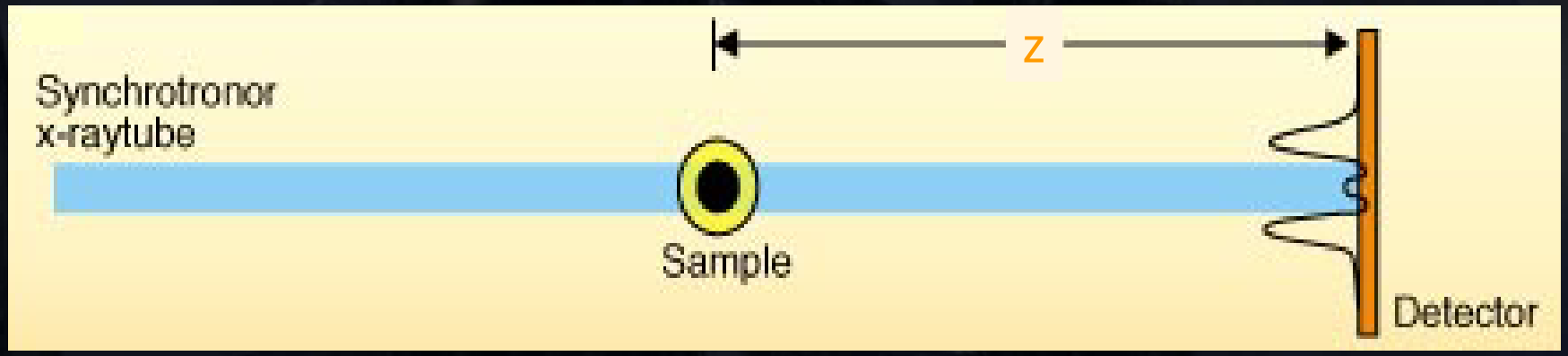
- Geometria laminare
  - Fascio naturalmente collimato sul piano dell'orbita



- Alta coerenza spaziale
  - Sorgente di piccole dimensioni
  - Grande distanza tra sorgente e campione

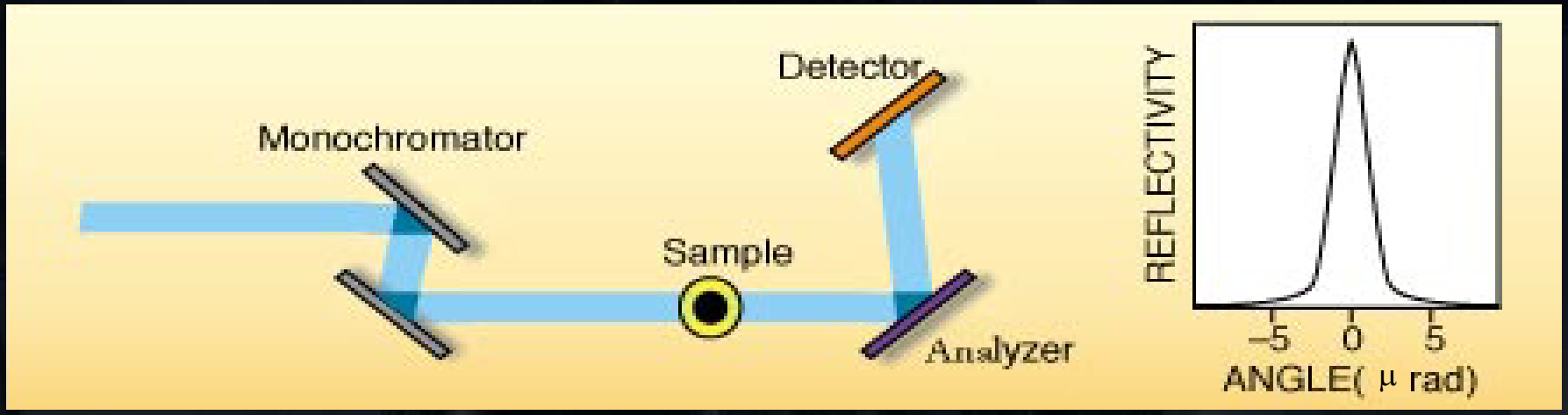
Propagazione libera

- Il rivelatore viene posto ad una certa distanza *z* in modo da raccogliere la figura di interferenza tra i raggi X rifratti e quelli non rifratti (contrasto in prossimità dei bordi)



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

Diffraction Enhanced Imaging
Analyzer Based Imaging

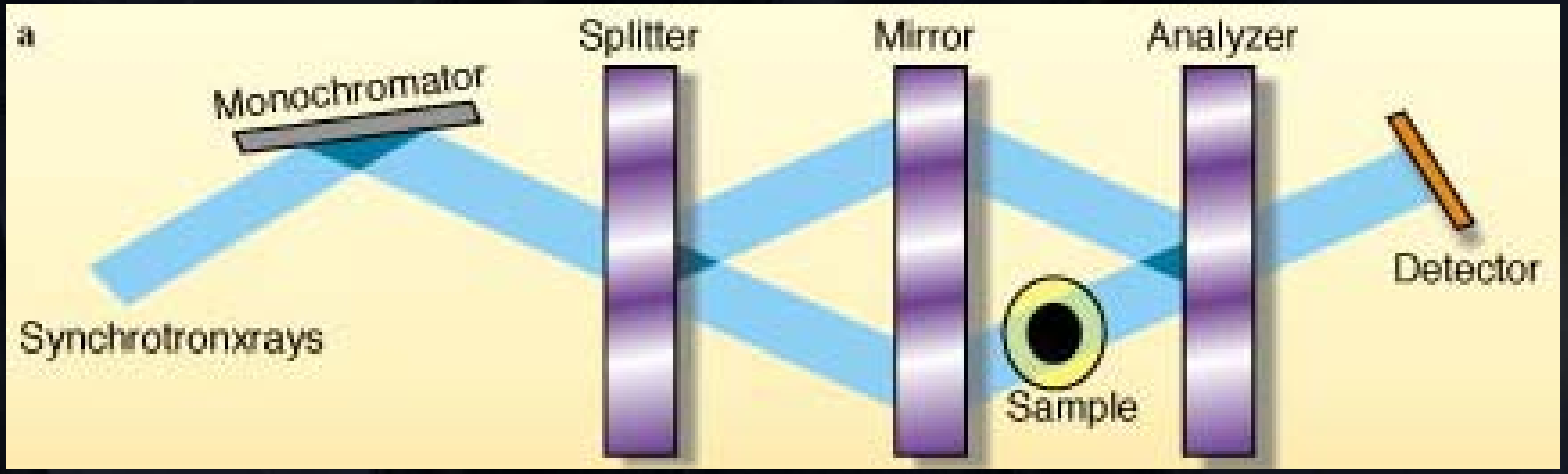


- Si pone un cristallo analizzatore tra l'oggetto ed il rivelatore
  - Il cristallo riflette perfettamente i raggi X *non* rifratti verso il rivelatore, mentre i raggi X che sono stati deviati vengono riflessi verso il rivelatore con minore probabilità

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

Interferometria

- Si utilizza un interferometro concettualmente analogo a quello di Mach-Zender per la luce visibile

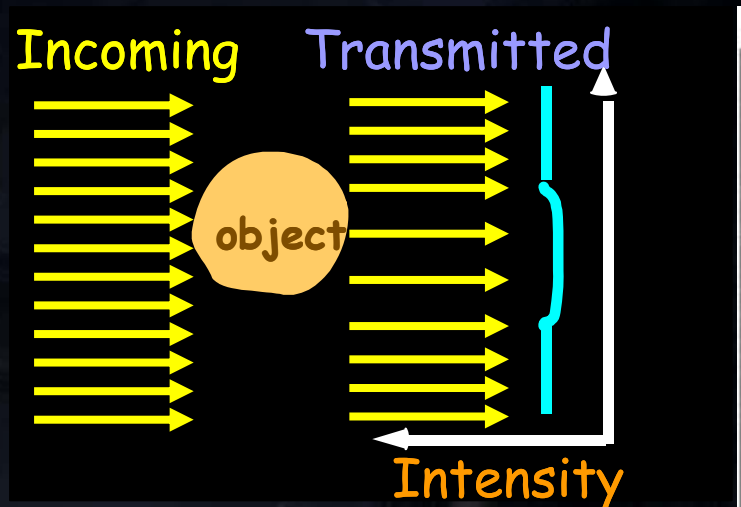


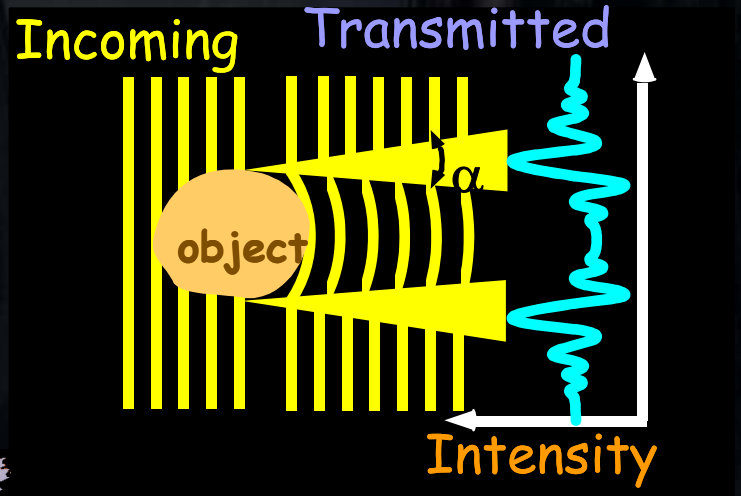
  - Per i raggi X si utilizzano dei cristalli al posto degli specchi

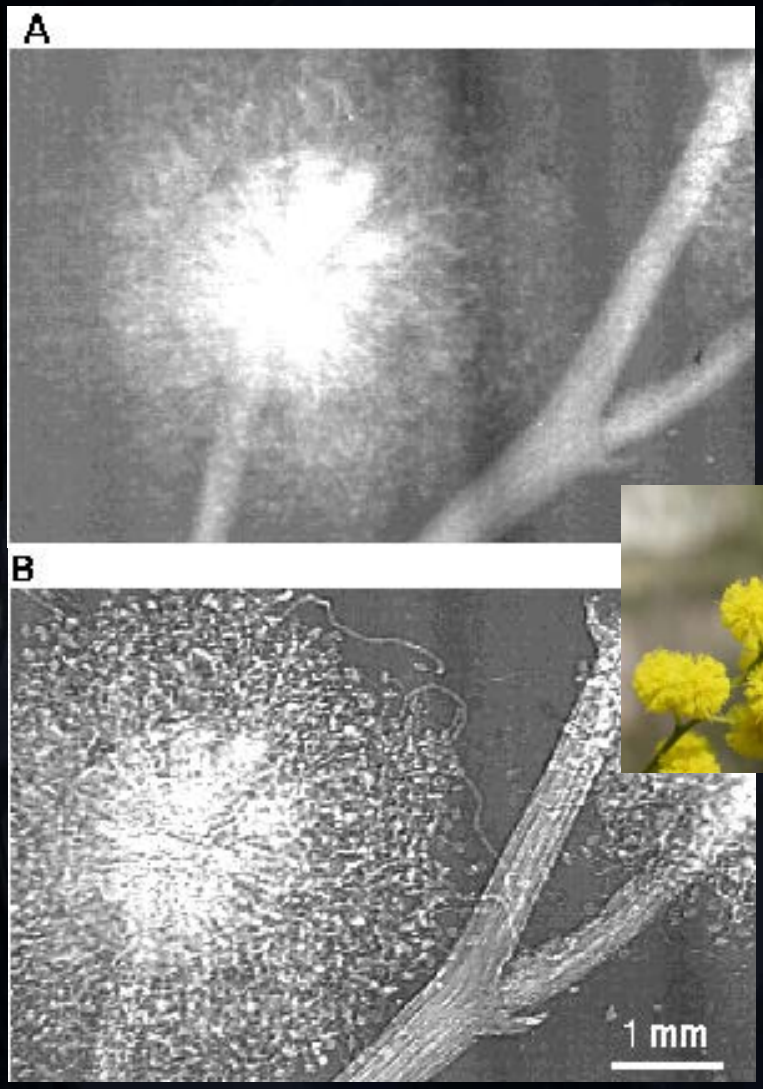
Fitzgerald, R. (2000). Phase-sensitive X-Ray imaging. Phys. Today ***53****, 23–27.*


CINEMA
IN CINEMA TODAY
INTRO E TEORIA
APPLICAZIONI

Confronto tra contrasto in assorbimento (A) e contrasto di fase in propagazione libera (B)

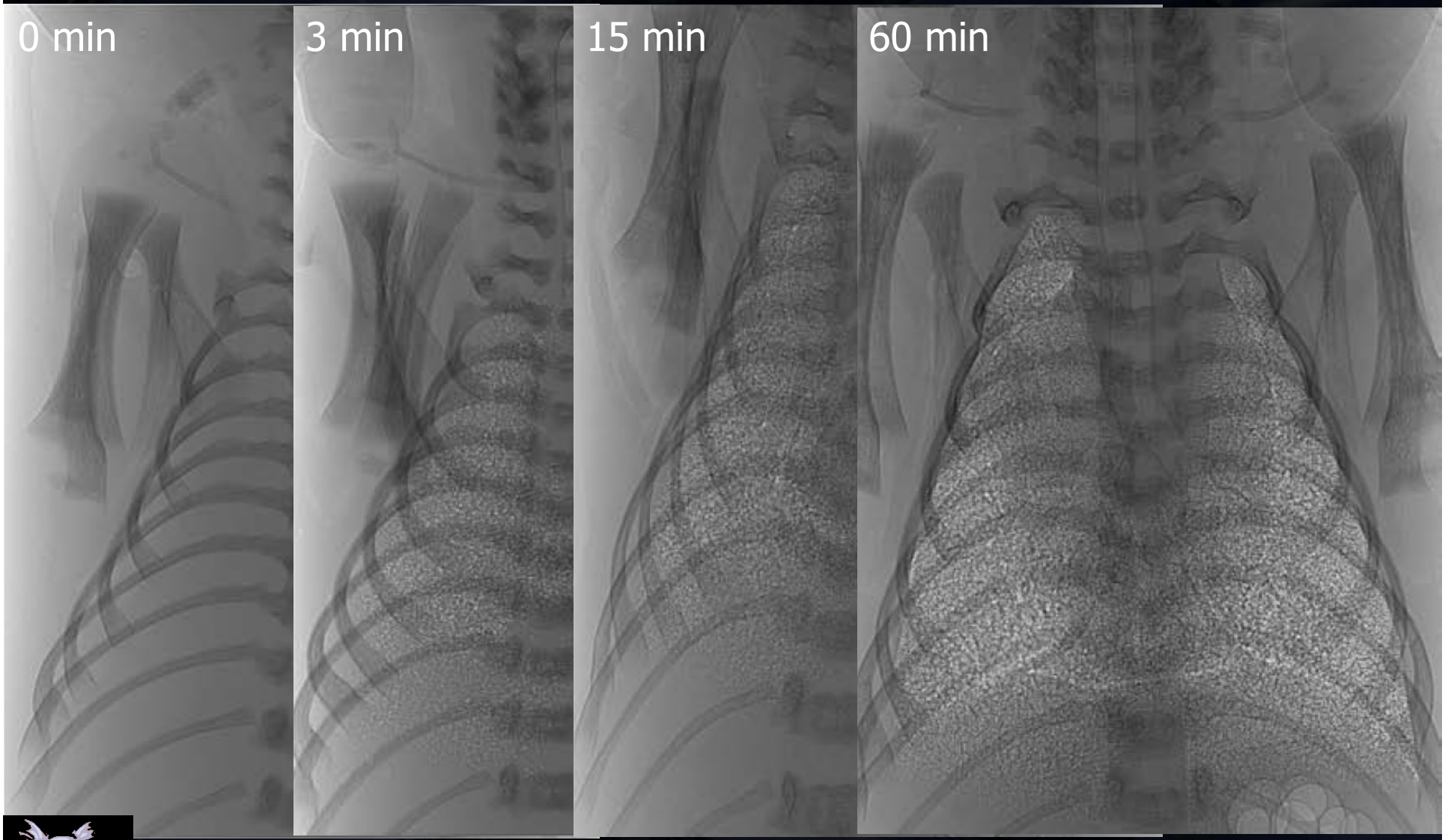




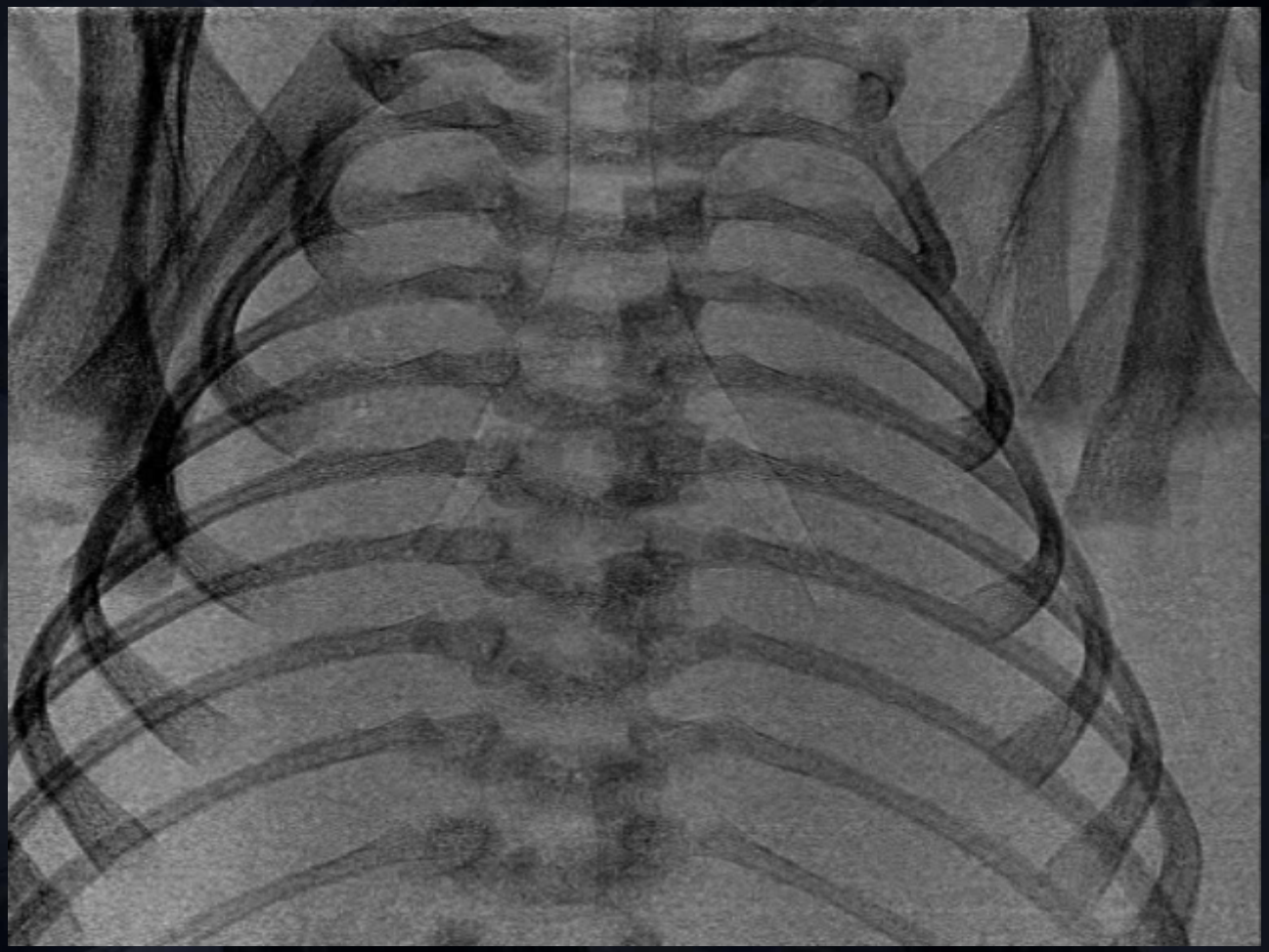


Di Michiel M, et al. in Medical applications of synchrotron radiation. Tokyo, Japan: Springer-Verlag, 1998; 78–82.

In vivo Lung Liquid Clearance at Birth

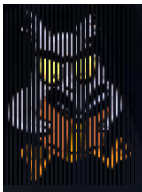


Kitchen M J, et al. (2008) Phys. Med. Biol. ***53****, 6065-77*
Hooper S B, Kitchen M J, et al. (2009). Clin. Exp. Pharmacol. Physiol. ***36****, 117–125*



courtesy of M. J. Kitchen, Monash University, Australia

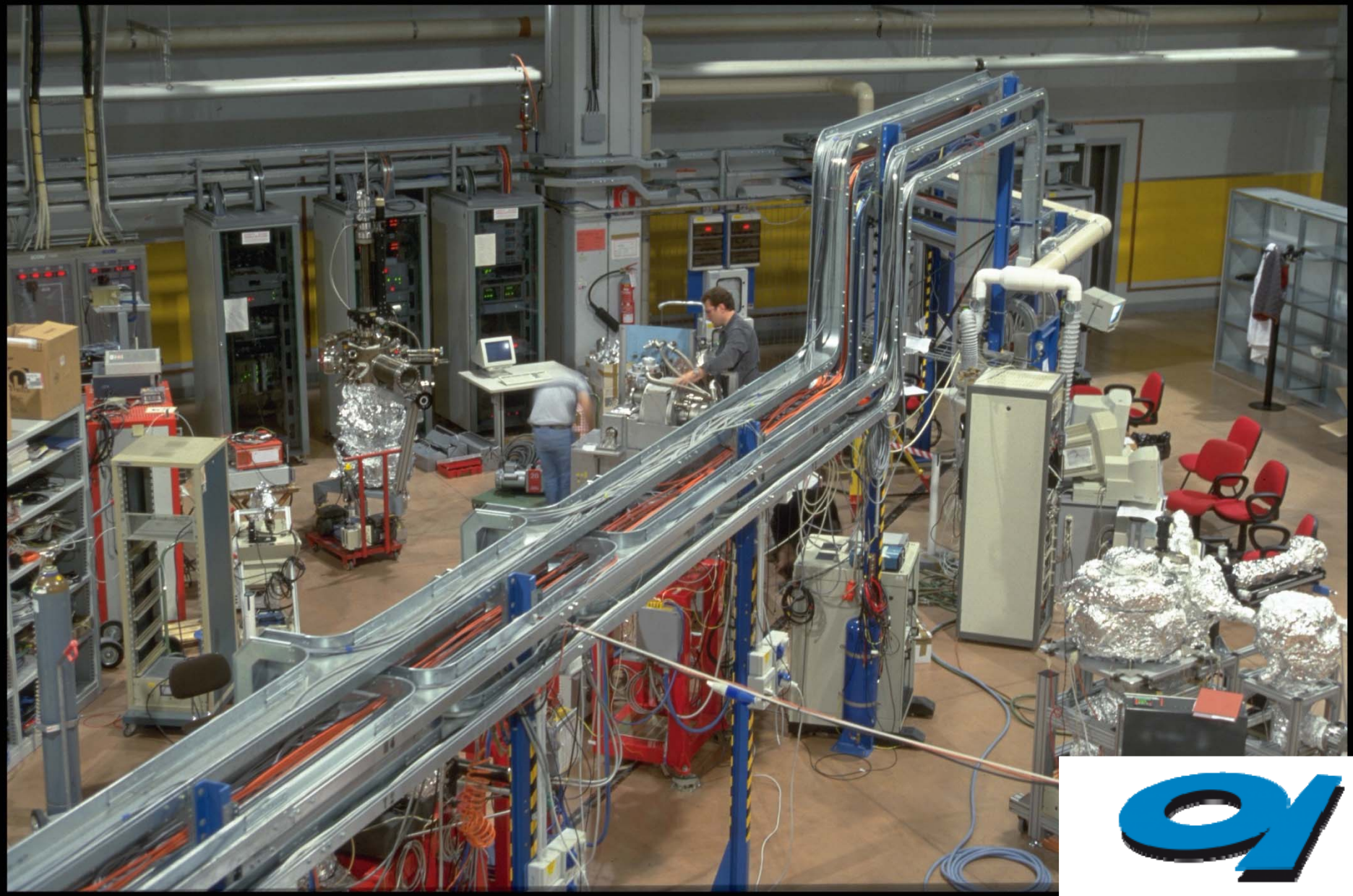
Kitchen M J, et al. (2008) Phys. Med. Biol. ***53****, 6065-77*
Kitchen M J, et al. (2014). PLOS One ***9****, e93391*



Kitchen M J, et al. (2008) Phys. Med. Biol. ***53****, 6065-77*
Kitchen M J, et al. (2014). PLOS One ***9****, e93391*

courtesy of M. J. Kitchen, Monash University, Australia

Meanwhile at Elettra...



courtesy of Elettra

Elettra Sincrotrone Trieste

SYRMA
(synchrotron radiation for mammography)

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(synchrotron radiation for mammography)

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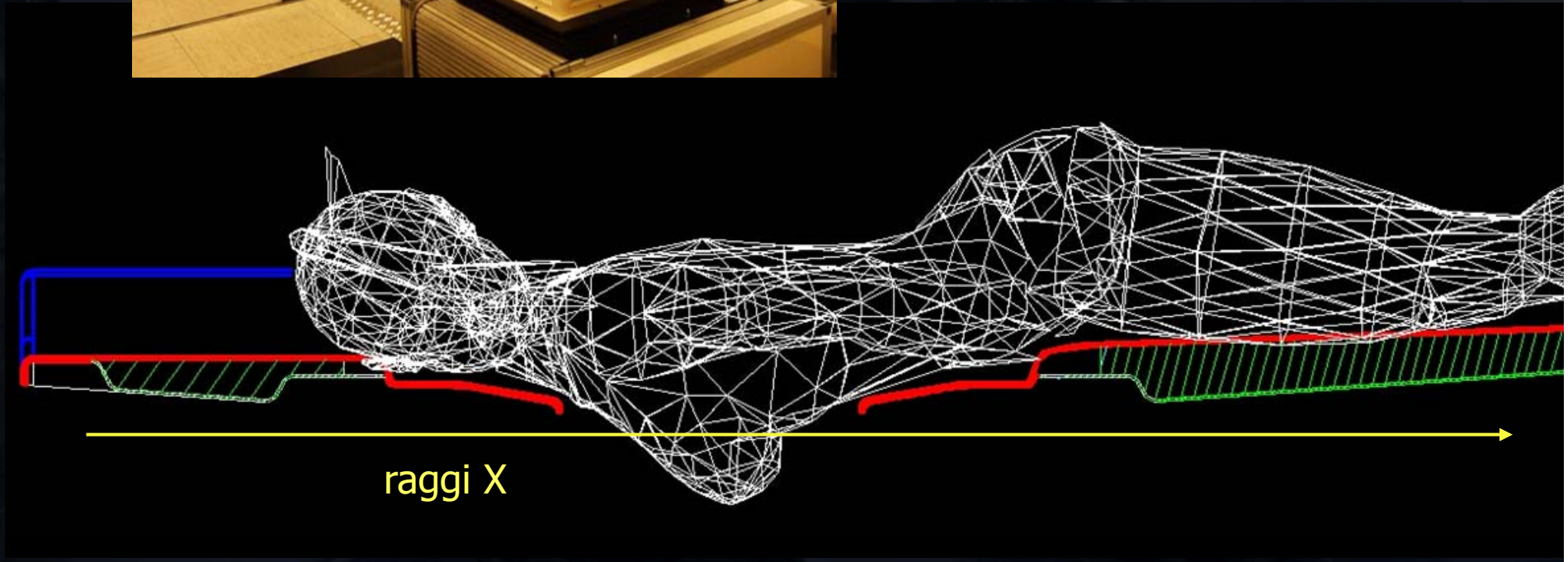
(synchrotron radiation for mammography)

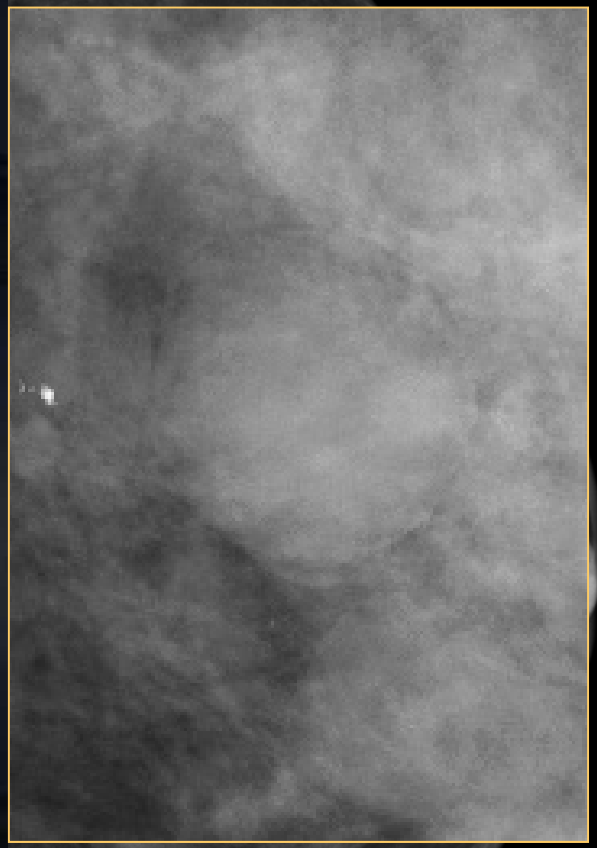



E. Castelli, R. Longo,
F. Arfelli, L. Rigon
Physics Departement,
University
and INFN
INFN
Istituto Nazion
di Fisica Nucle
SYRMA
(synchrotron radiation for mammography)
OSPEDALI RIUNITI DI TRIESTE
M.A. Cova, E. Quaia, M. Tonutti,
F. Zanconati, P. Bregant
Radiology Department, University
and Hospital of Trieste
G. Tromba, D. Dreossi, A. Abrami,
K. Casarin, V. Chenda, R.-H. Menk,
E. Quai, A. Vascotto
Sincrotrone Trieste ScPA (ELETTRA)
Elettra Sincrotrone Trieste

SYRMA
(synchrotron radiation for mammography)

Conv

PhC

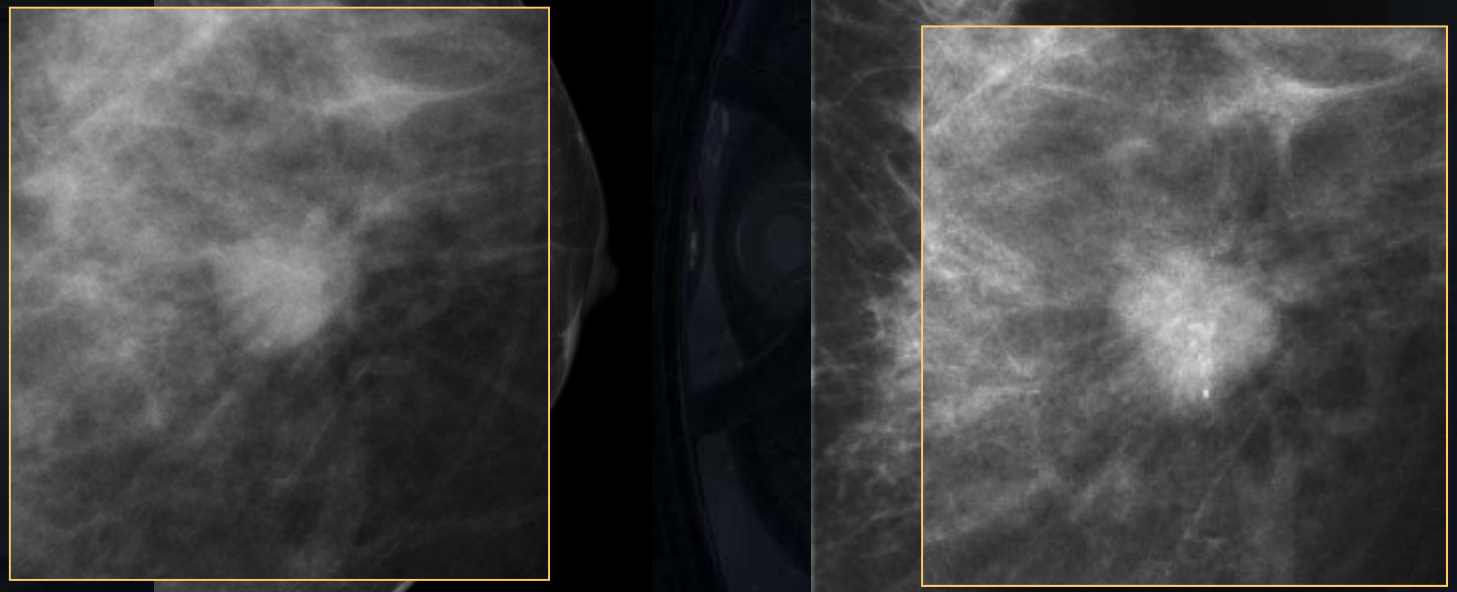


*Castelli, E., Tonutti, M., Arfelli, F. et al. (2011). Radiology **259**, 684–694.*

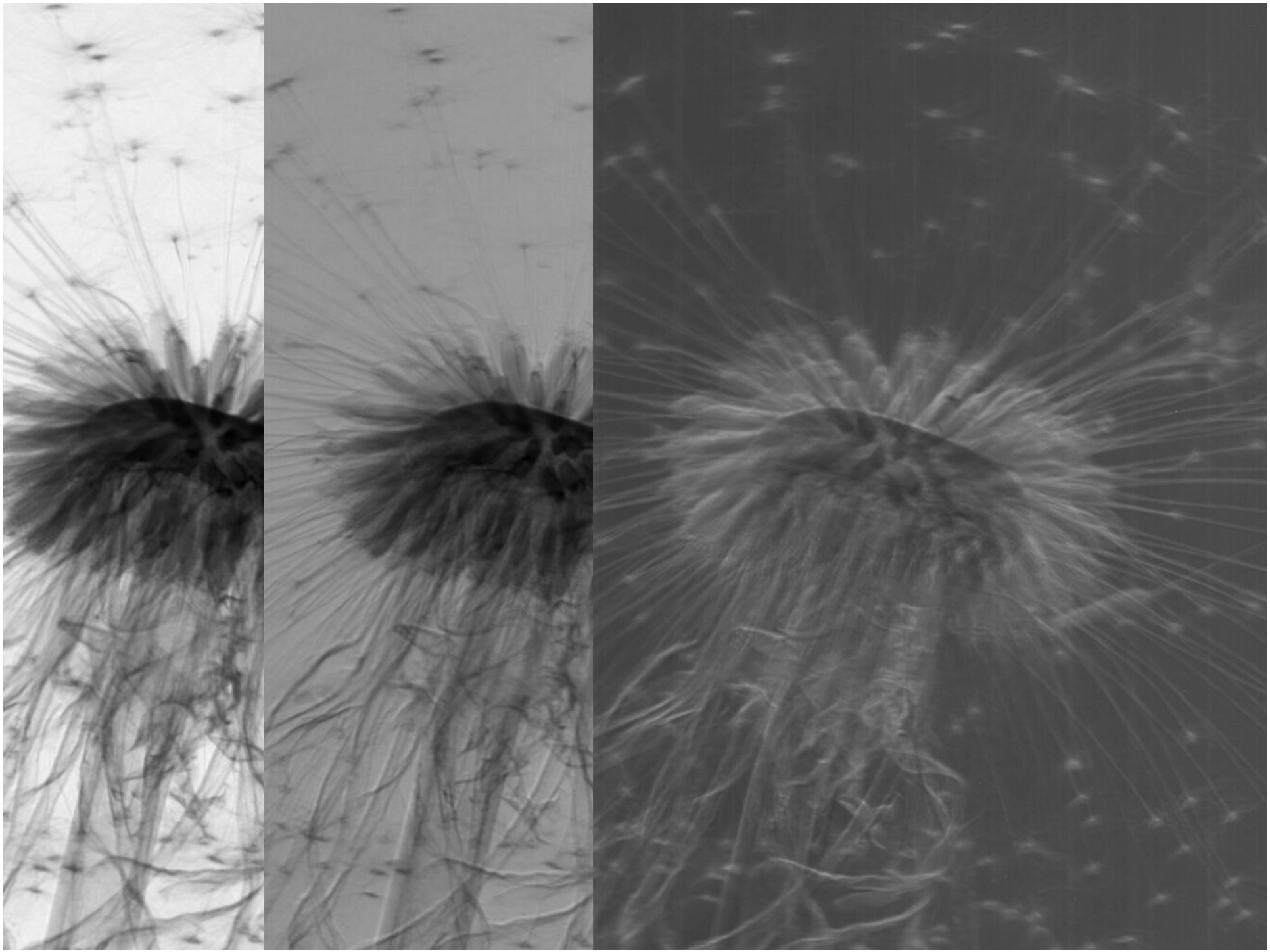
SYRMA
(synchrotron radiation for mammography)

Conv

PhC



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

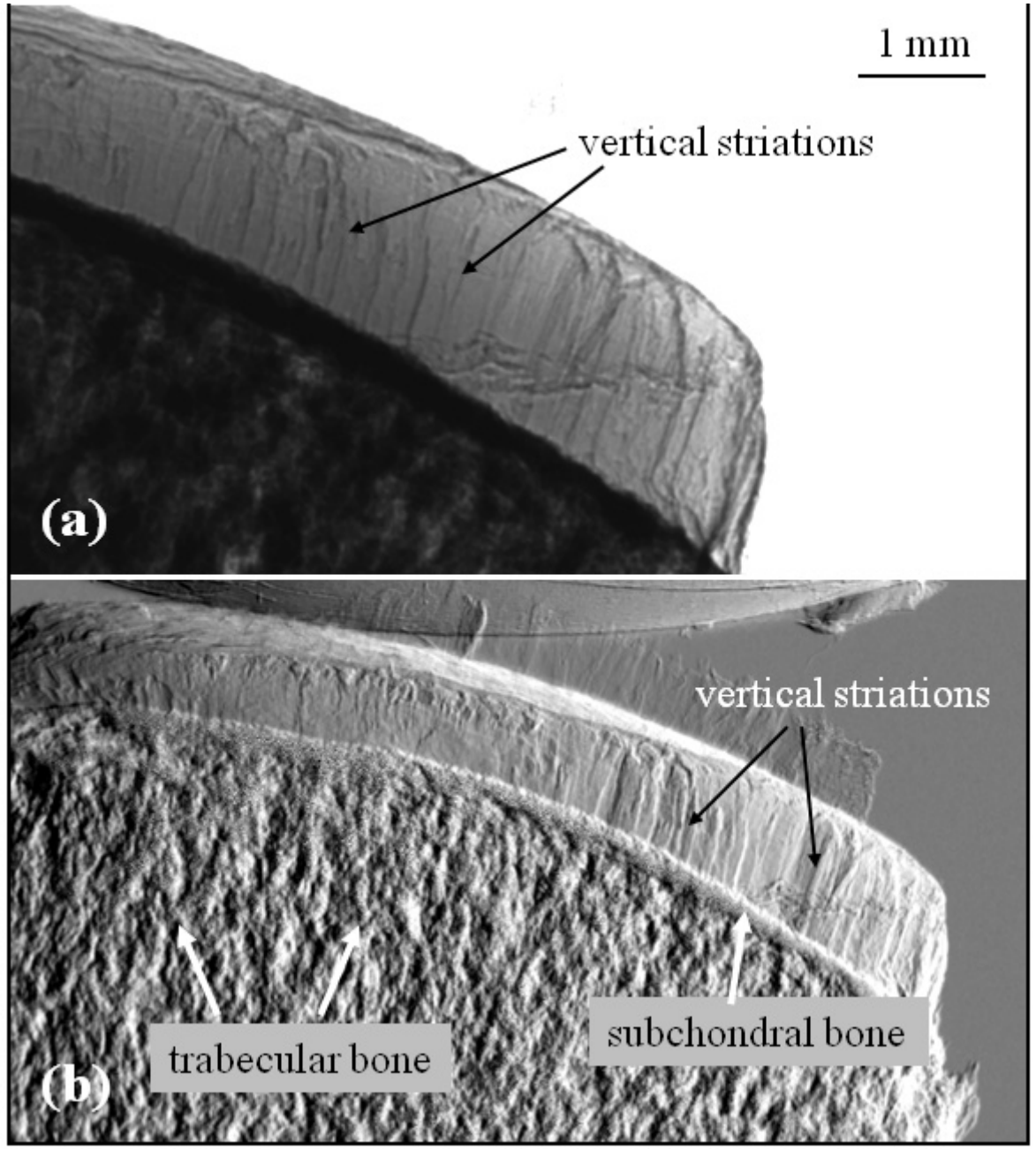


Cartilagini

- la cartilagine assorbe poco i raggi X e quindi non si vede con la radiologia convenzionale

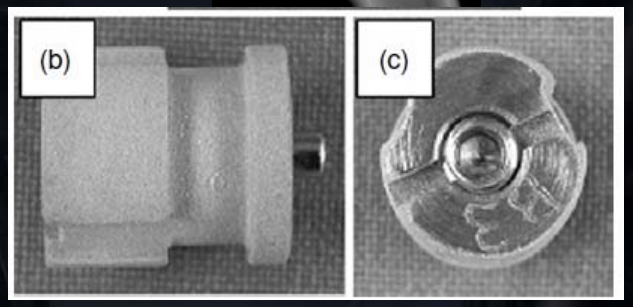
- con la DEI non solo si vede, ma si riesce a visualizzare contemporaneamente anche il tessuto osseo

- si possono così correlare alterazioni della cartilagine a quelle del tessuto osseo, ottenendo una visione unitaria dell'articolazione

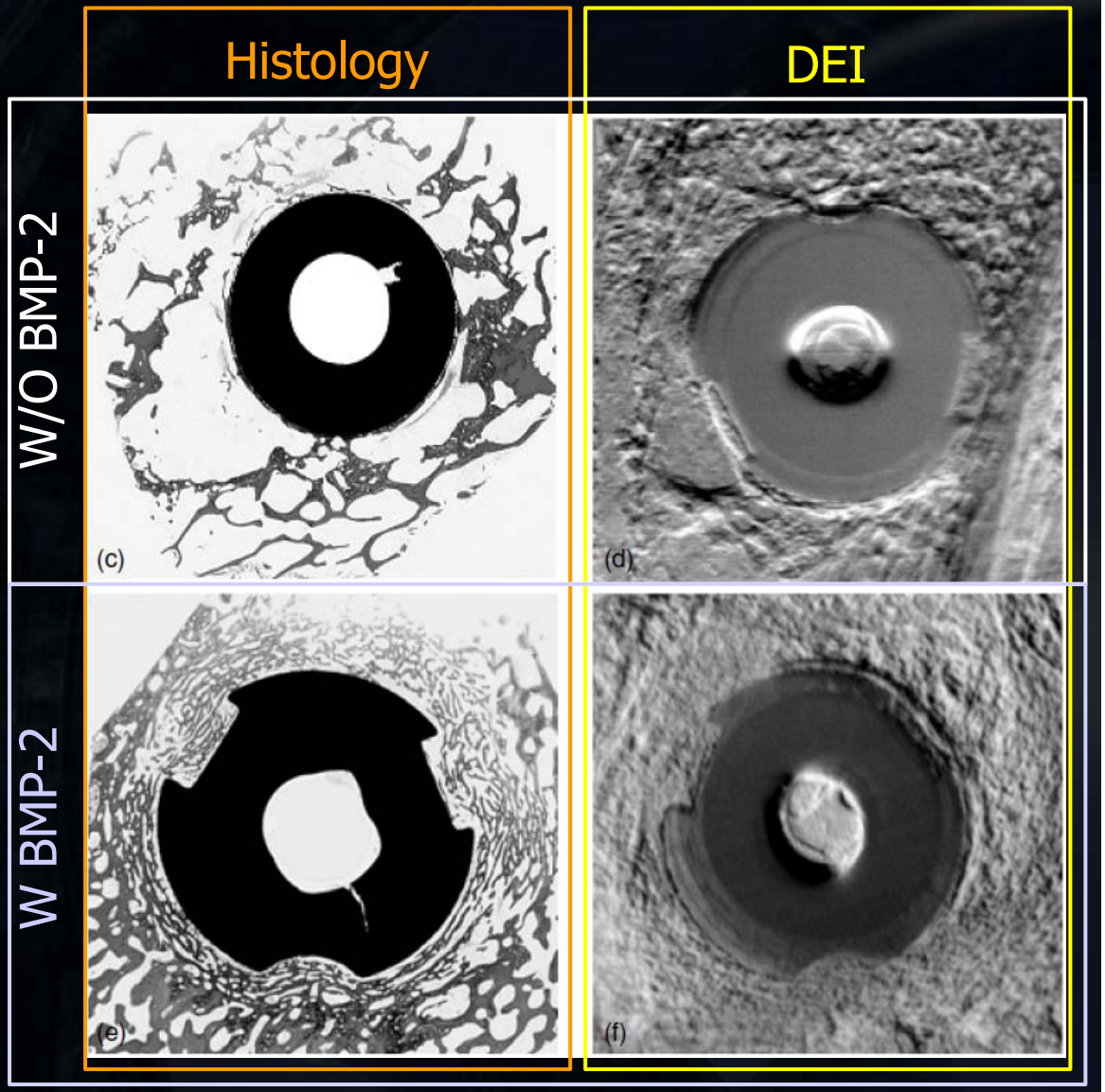


Muehleman, C., Majumdar, S. et al. (2004). Osteoarthritis Cartilage ***12****, 97–105.*

Protesi



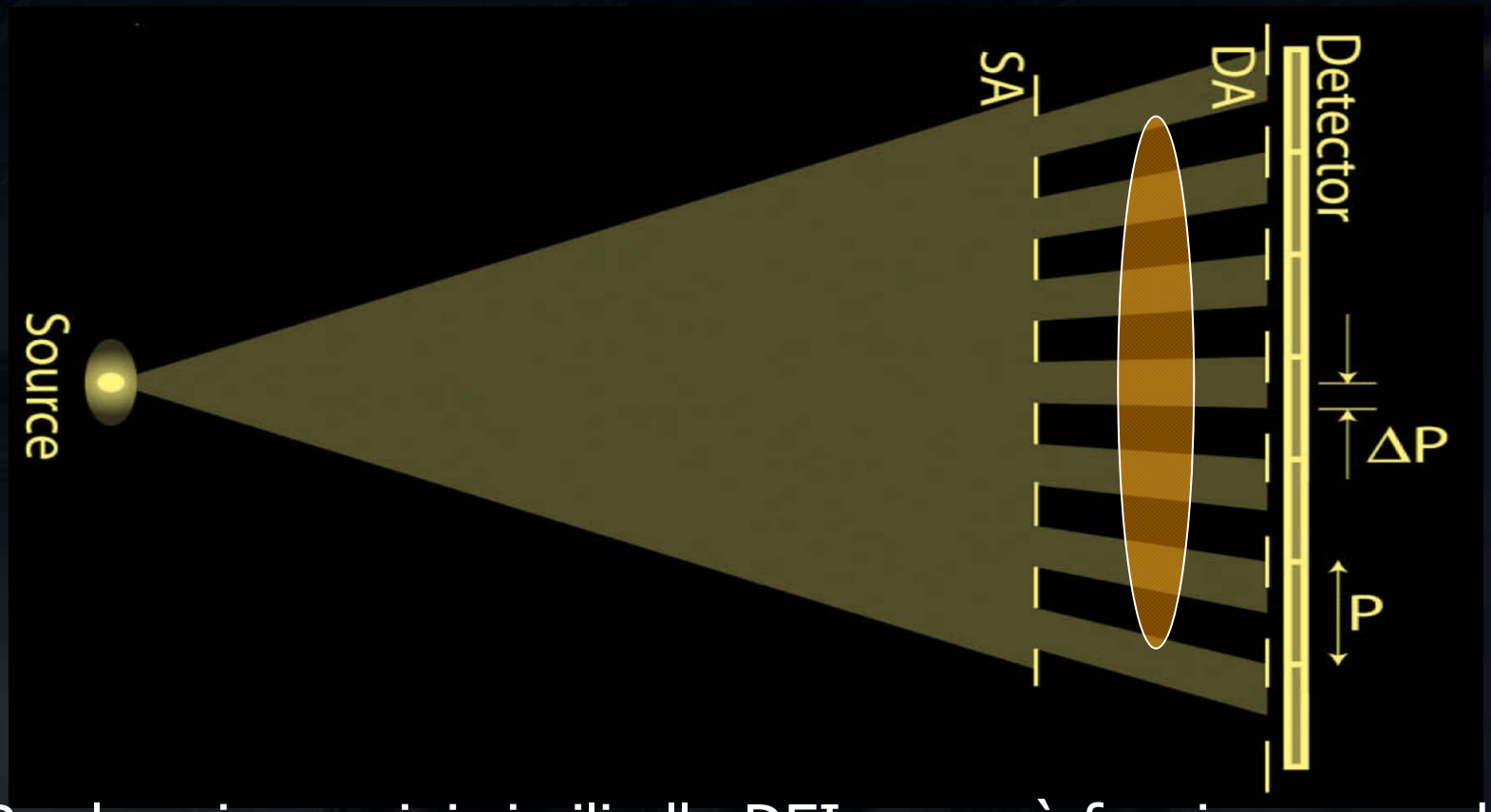
- Valutazione della qualità dell'integrazione della protesi metallica nel tessuto osseo in modo non-distruttivo



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.*

Verso la clinica ?

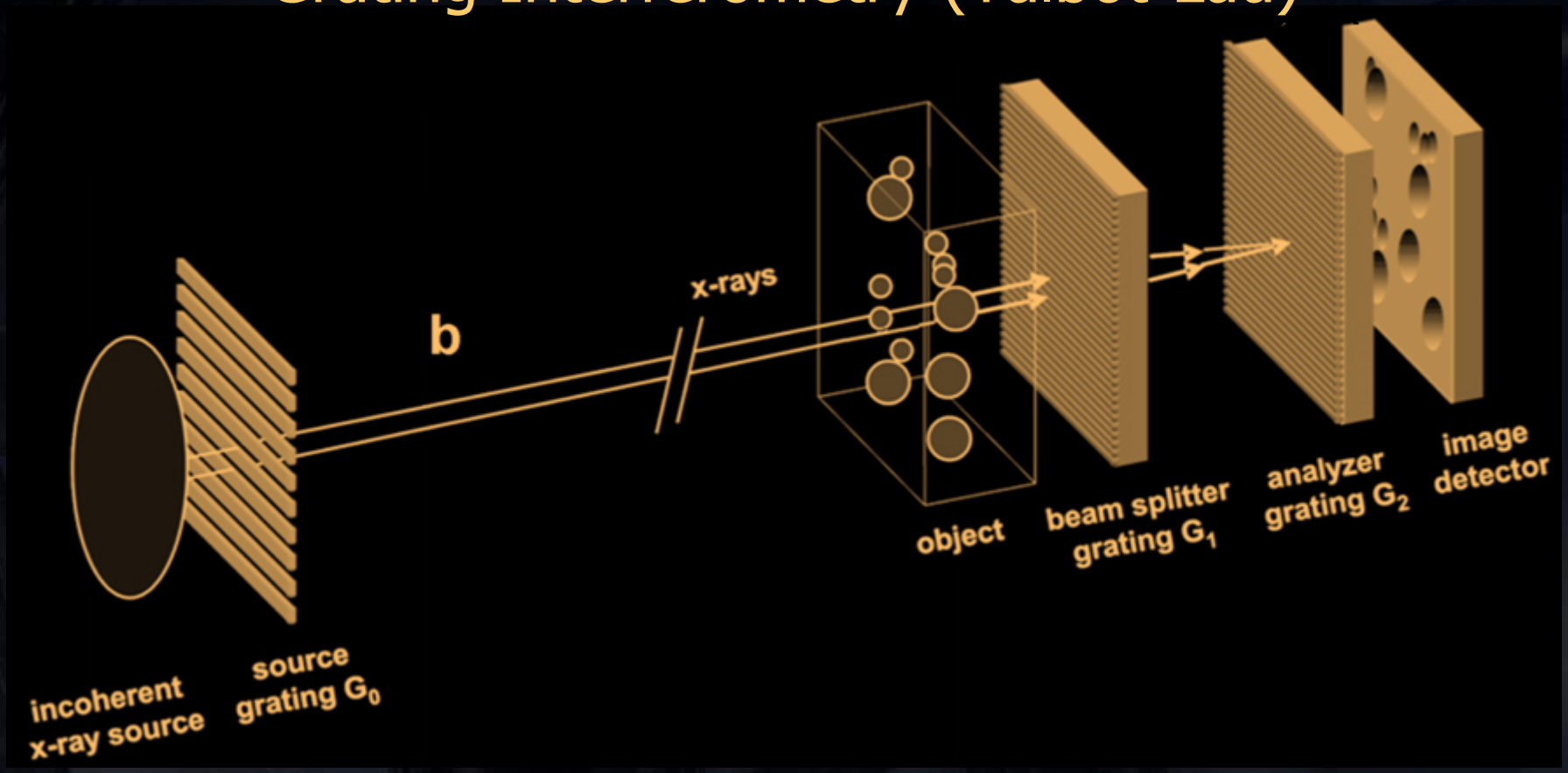
Coded Apertures



- Produce immagini simili alla DEI ma può funzionare anche con sorgenti convenzionali
  - Aperture di circa 10-100 μm su maschere che assorbono in raggi X
  - Dimensioni maschere: 5 cm x 5 cm ma anche più grandi

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

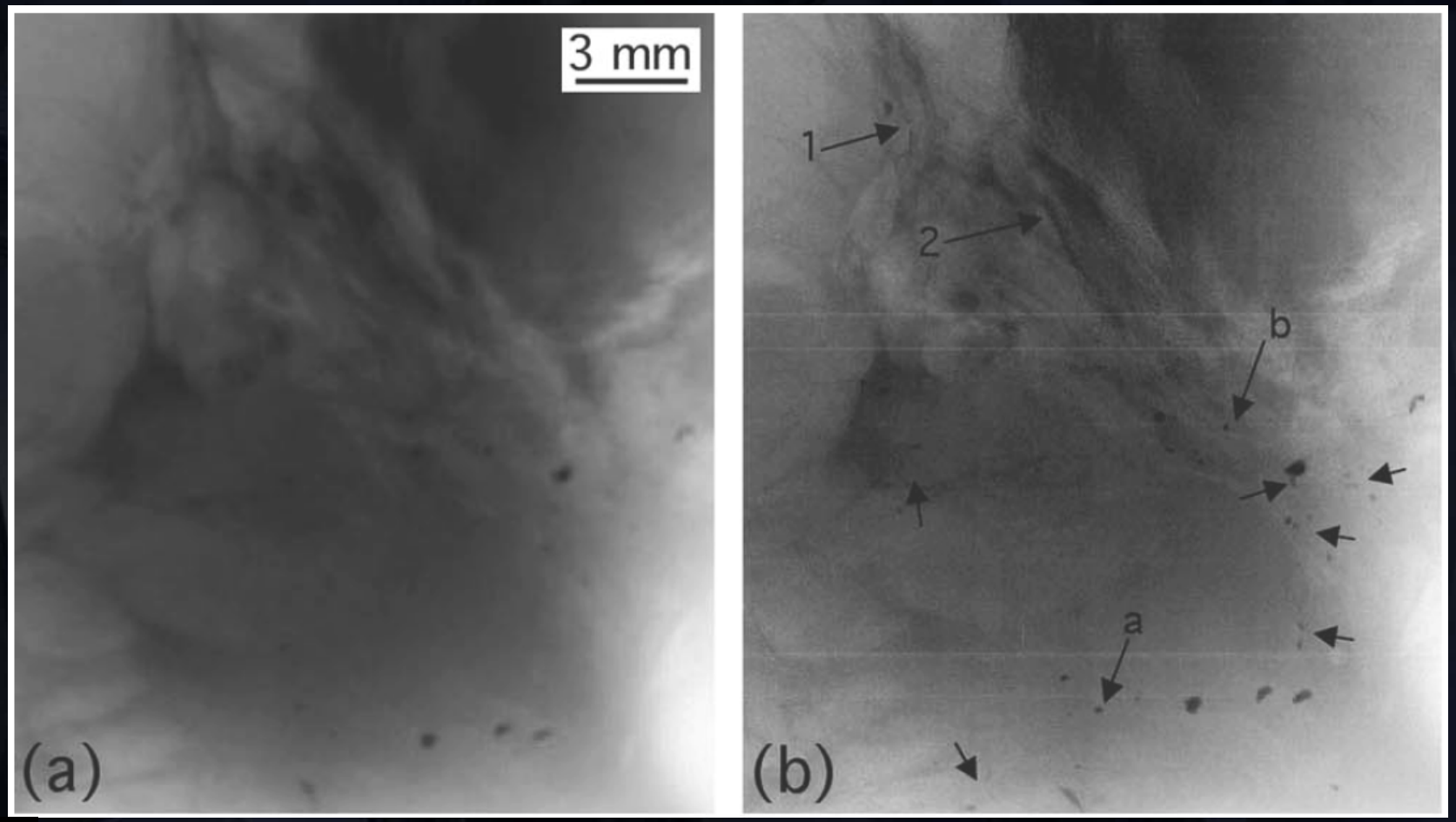
Grating Interferometry (Talbot-Lau)



- Produce immagini simili alla DEI ma può funzionare anche con sorgenti convenzionali
  - Fenditure di circa 2-5 μm su maschere che assorbono in raggi X
  - Dimensioni maschere: 5 cm x 5 cm

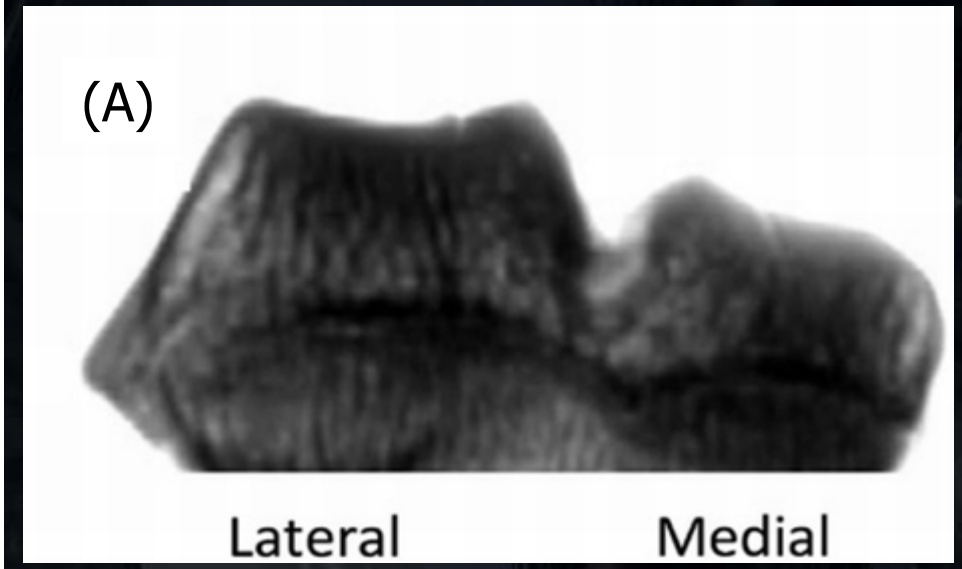
Pfeiffer, F., Weitkamp, T., Bunk, O. and David, C.(2006). Nat. Phys. ***2****, 258–261.*

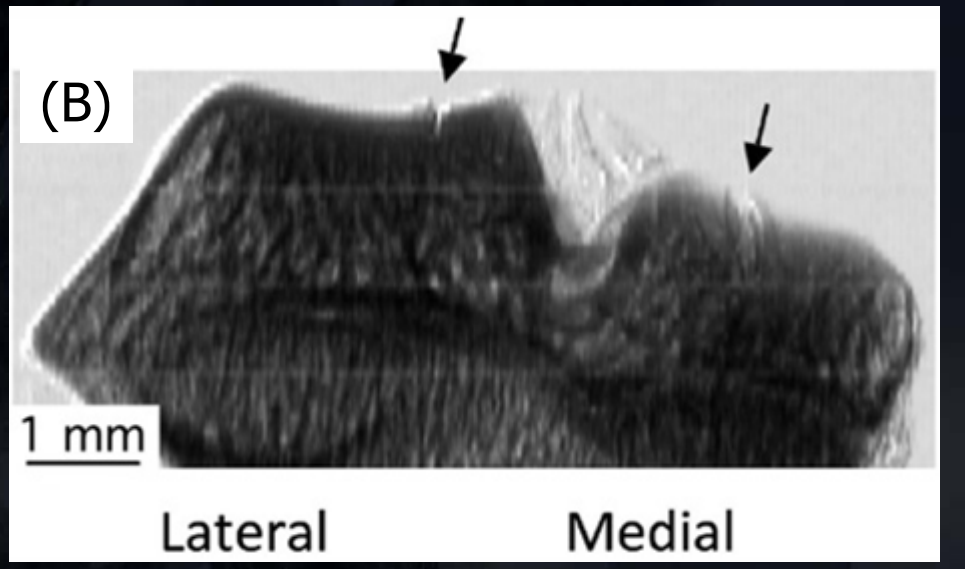
Confronto tra contrasto in assorbimento (A) e contrasto di fase con coded apertures (B): mammografia



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

Confronto tra contrasto in assorbimento (A) e contrasto di fase con coded apertures (B): cartilagini

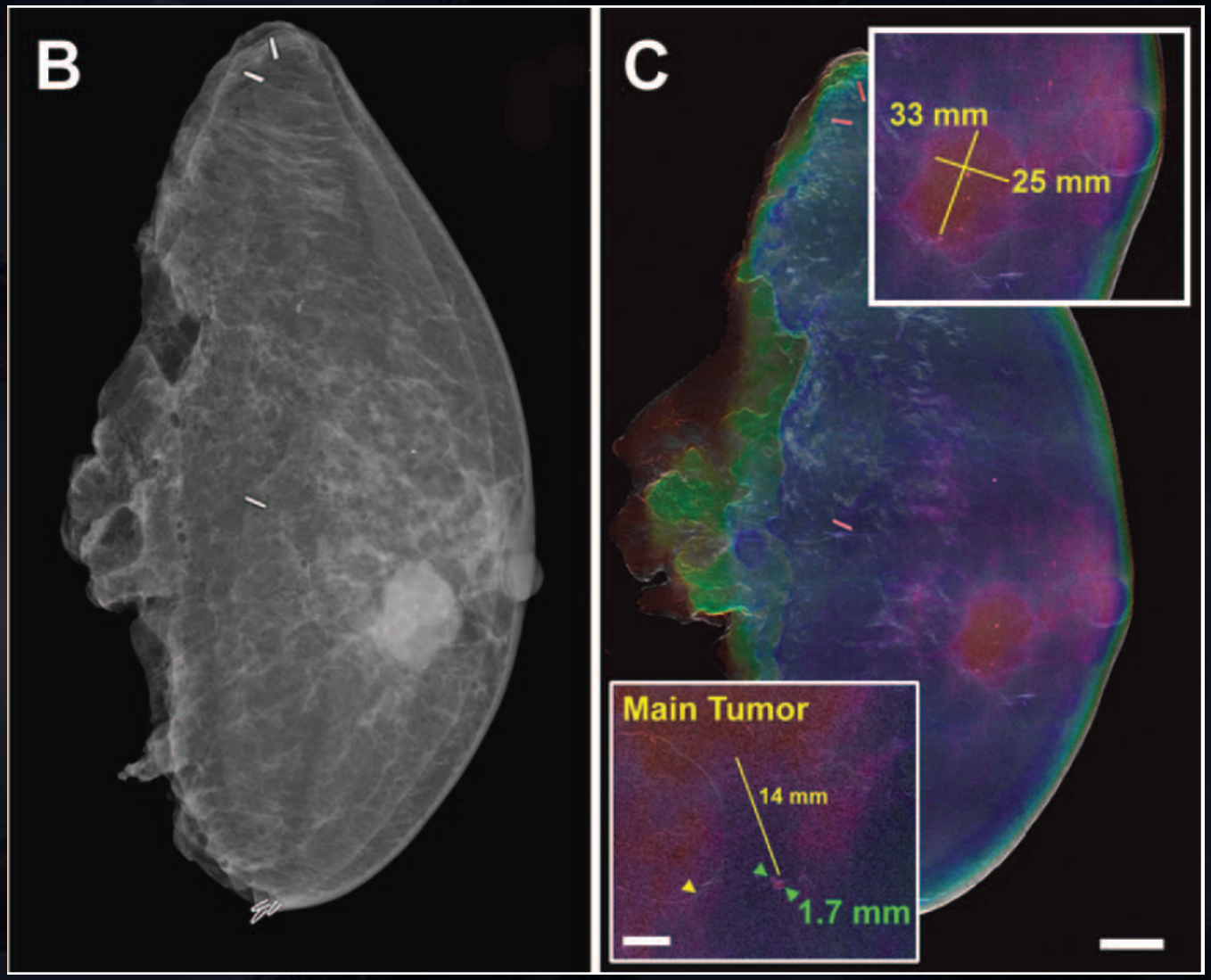




- Immagini di una tibia di ratto ottenute con sorgente convenzionale
- Le frecce indicano lesioni indotte chirurgicamente, la cui visibilità migliora con l'uso delle coded apertures

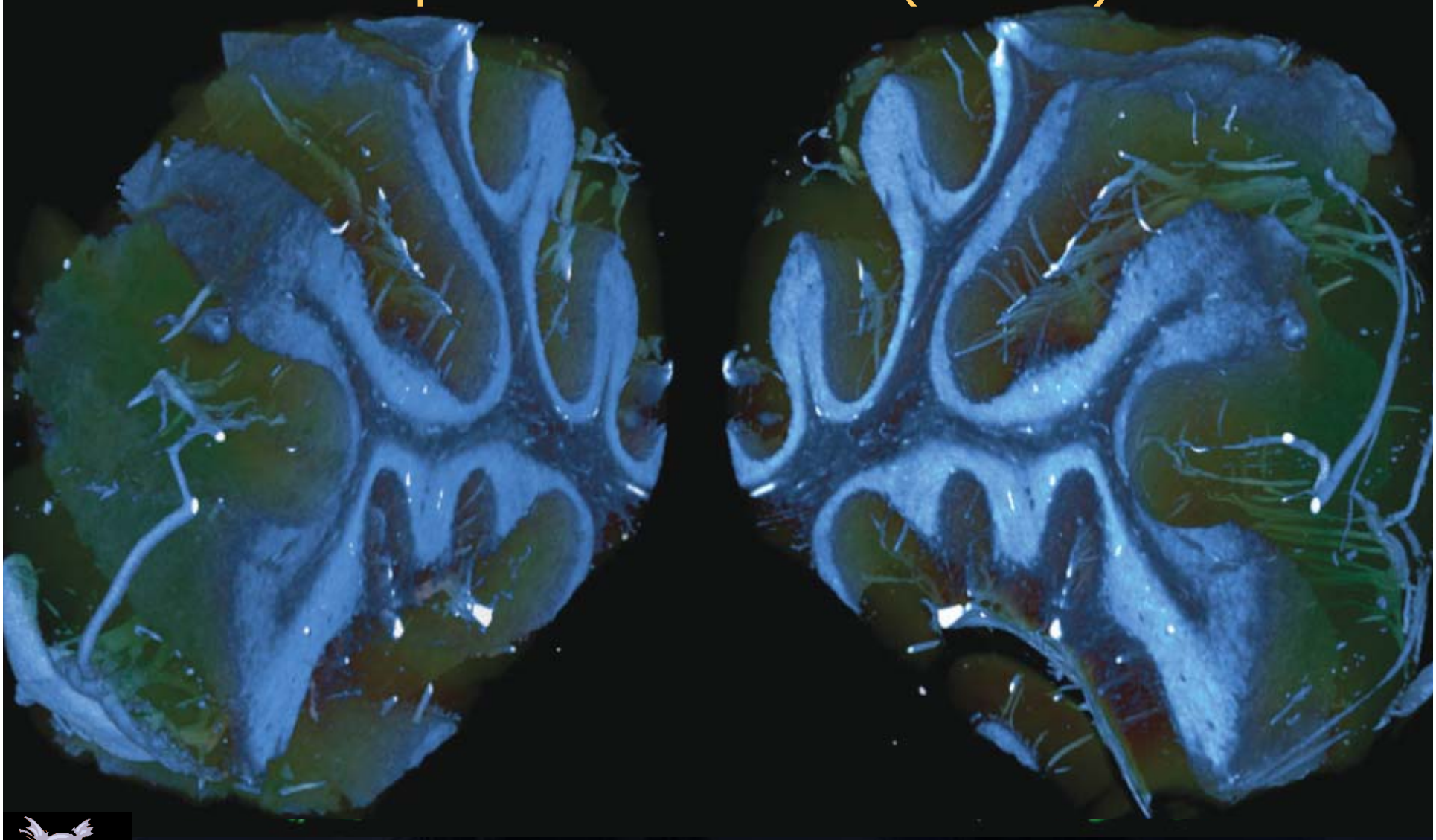
Marenzana, M., Hagen, C. K., et al. (2012). Phys. Med. Biol. ***57****, 8173–8184.*

Applicazione della Grating interferometry alla mammografia (*ex vivo*)



Stampanoni, M., Wang, Z. T. et al. (2011). Invest. Radiol. ***46****, 801–806.*

Applicazione della Grating interferometry ad un campione di cervelletto (ex vivo)



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

Conclusioni

- Abbiamo visto che i raggi X sono piuttosto simili alla luce, forse più di quanto credessimo
  - Rifrazione (anche se su angoli piccolissimi), interferenza, etc.
  - Possibilità di ottenere immagini in contrasto di fase con opportune tecniche
- Le tecniche di fase con i raggi X sono state sviluppate negli ultimi 20 anni presso i laboratori di luce di sincrotrone
  - I risultati ottenuti hanno avuto implicazioni cliniche, sia direttamente che indirettamente
- La traslazione di questi risultati verso la clinica è già cominciata e potrebbe produrre risultati significativi in futuro