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Trieste

Synchrotron Radiation for biomedical imaging

Giuliana Tromba

SYnchrotron **R**adiation for **ME**dical **P**hysics (SYRMEP) beamline

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XVI International Conference on Science, Arts and Culture

International Conference ON SESAME

In Honour of Paolo Budinich

29 August - 2 September 2016

Veli Lošinj, Croatia

ECSAC
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Outline

- Advantages of using SR for medical applications
- SR *phase contrast* imaging
- Some applications at ESRF, Spring8, Elettra
  - Mammography
  - Studies of bones, joints and cartilages
  - Lungs imaging
  - Brain studies
  - Imaging of atherosclerotic plaques
  - …..
- Final considerations

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Advantages of SR for biomedical imaging

Monochromaticity allows for:

- *optimization* of X-ray energy according to the specific case under study (dose reduction)
- quantitative CT evaluations
- no beam hardening
- convenient use of contrast agent (K-edge and L-edge imaging)

Spatial coherence enables the applications of ***phase sensitive imaging*** **techniques**

- Phase contrast overcomes the limitation of conventional radiology
- It brings to a dose reduction
- Improved contrast resolution, edges enhancement
- Use of phase retrieval algorithms

High fluxes

- Short exposure time
- Dynamic studies….

Collimation

- parallel beams, scatter reduction
- beam shaping (micro-beams)

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Imaging approaches

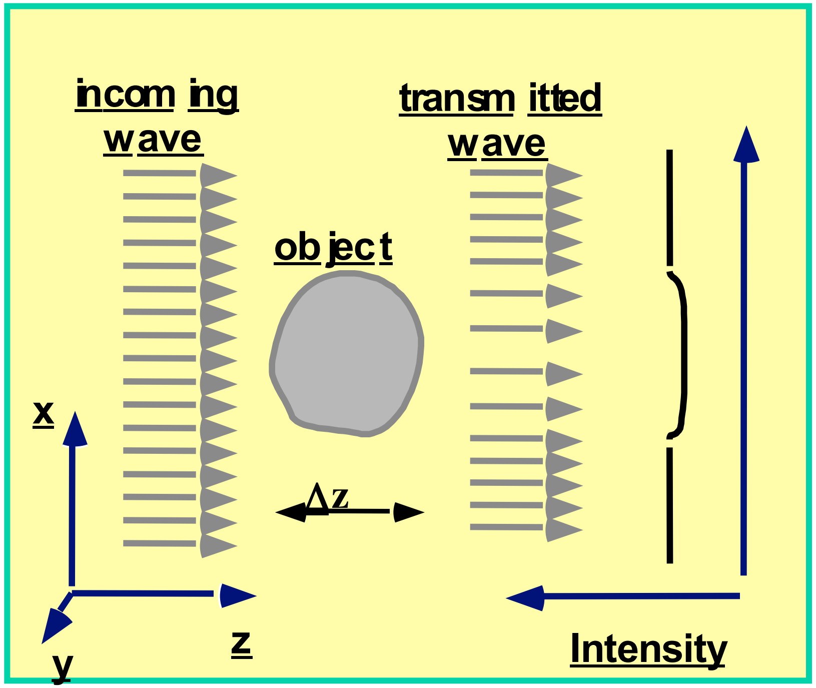
- Clinical: applications to patients
  (es. angiography, mammography, ecc.)
  *Need to **limit** radiation dose. Find best compromise between dose and image quality*

- Imaging of small animals: applied for different purposes in the development of ***animal models***
  (es. Cell tracking, Osteoporosis, genetic diseases,..)
  Research protocols, control of dose.

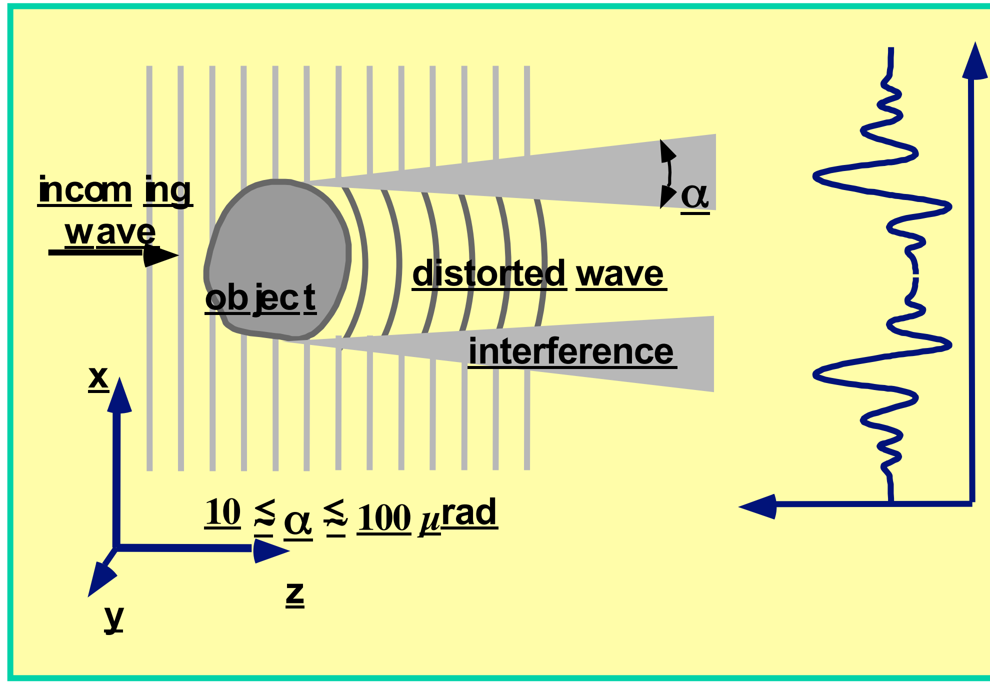
- "In vitro" imaging: it concerns the study of biological samples. (es. micro-tomography applied on bone samples, scaffolds, cartilages, etc.)
  Requirements of high resolution and high sensitivity

Increase of dose and spatial resolution

PHase Contrast (PHC) vs. absorption contrast



Absorption radiology (conventional)



PHC

In conventional radiology image formation is based on differences in X-ray absorption properties of the samples. The image contrast is generated by density, composition or thickness variation of the sample. Main limitation: poor contrast in soft tissue differentiation. ***Phase contrast* techniques** are based on the observation of the *phase shifts* produced by the object on the incoming wave. Contrast arises from interference among parts of the wave front differently deviated (or phase shifted) by the sample. Edge enhancement effects.

Refraction index for hard X-rays : $n = 1 - \delta + i\,\beta$, β = absorption term, δ = phase shift term

for soft tissue@17 keV: $\beta \sim 10^{-10}$; $\delta \sim 10^{-6}$, $\delta \propto \lambda^2$, $\beta \propto \lambda^3$

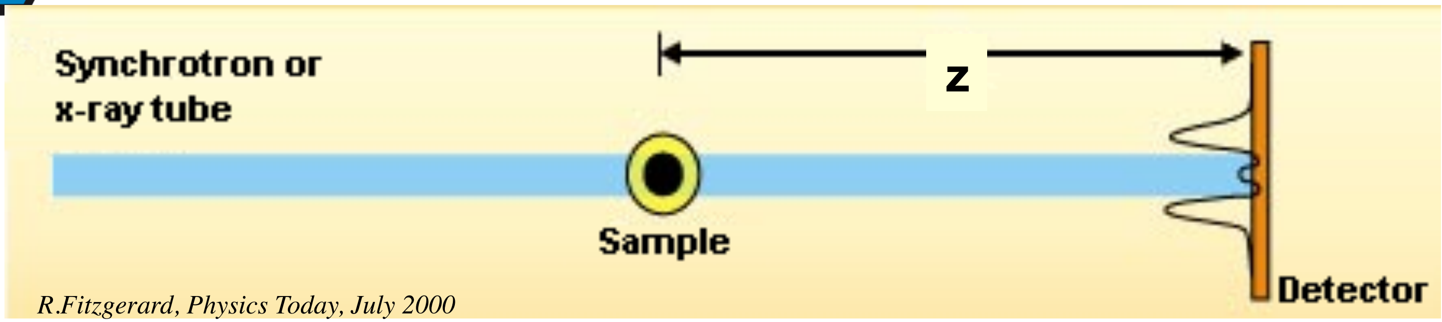
Absorption radiology -> contrast is generated by differences in the x-ray absorption ($C_{abs} \sim x\ \Delta\beta$),

Phase Radiology -> contrast is generated by phase shifts ($C_{\phi} \sim x\ \ \Delta\delta$)

x = object size // to beam direction

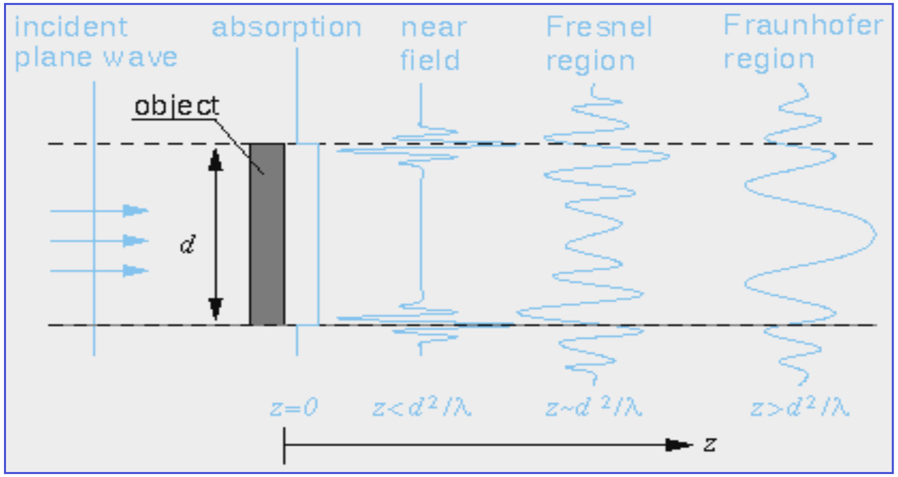
$\delta >> \beta$ ➔ phase shifts effects >> absorption

Propagation based imaging (PBI)



- The technique exploits the high spatial coherence of the X-ray source.
- z =0 -> absorption image
- For z > 0 -> interference between diffracted and un-diffracted wave produces edge and contrast enhancement. A variation of δ is detected
- Measure of $\nabla^2\Phi(x,y)$
- The technique requires a high spatial coherence source and detectors with adequate spatial resolution. Monochromaticity is not needed
- Phase effects visible also at low dose (mammography trial @ SYRMEP)

Regimes



Snigirev A. et al., Rev. Sci. Instrum. 66, 1995
Wilkins S. W. et al., Nature 384, 1996
Cloetens P. et al., J. Phys D: Appl. Phys. 29, 1996
Arfelli F et al., Phys. Med. Biol. 43,1998

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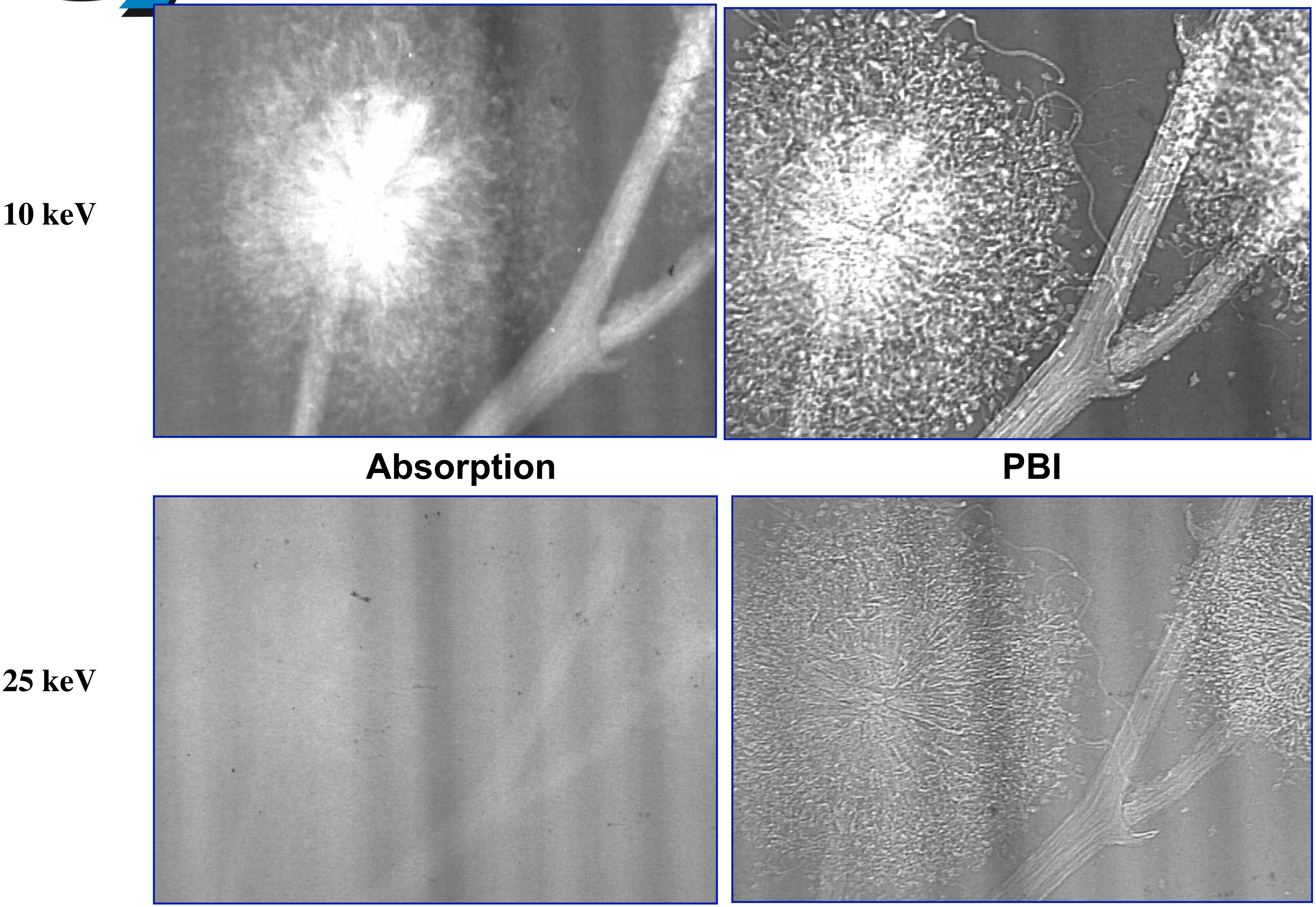
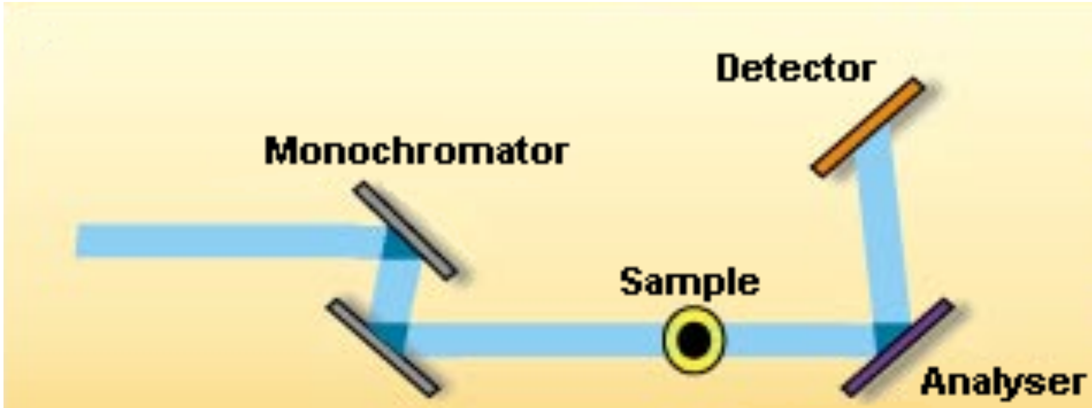
Imaging a Mimosa flower….



Analyzer Based Imaging (ABI)



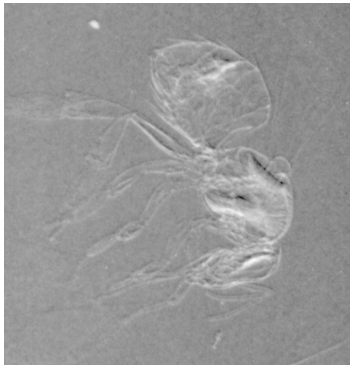
R.Fitzgerard, Physics Today, July 2000

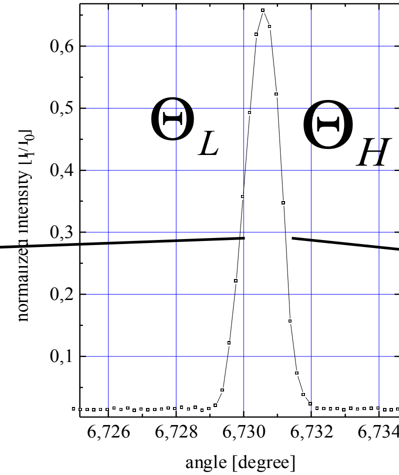
- Sensitive to refraction of X-rays
- A perfect crystal is used as an angular filter to select angular emission of X-rays. The filtering function is the rocking curve (FWHM: 1-20 μrad)
- Image formation with ABI is sensitive to a variation of δ in the sample. Indeed, **refraction angle is roughly proportional to the gradient of δ**
- Analyzer and monochromator aligned -> X-ray scattered by more than some tens μrad are rejected
- Small misalignments -> investigation of phase shift effects
- With greater misalignments the primary beam is almost totally rejected and pure refraction images are obtained
- Sensitive to $\nabla\Phi(x,y)$
- The technique requires the beam monochromaticity, spatial coherence is less stringent.

Podurets K. M. et al., Sov. Phys. Tech. Phys. 34(6), 1989
V. N. Ingal and E. A. Beliaevskaya, J. Phys. D: Appl. Phys. 28, 1995
Chapman D et al., Phys. Med. Biol. 42, 1997

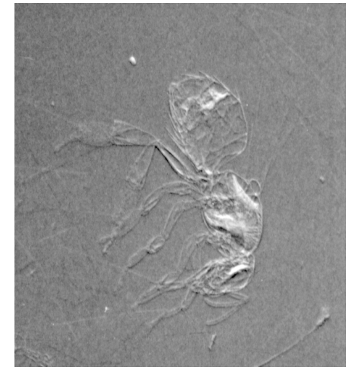
ABI image manipulation (original algorithm)

I_L





I_H



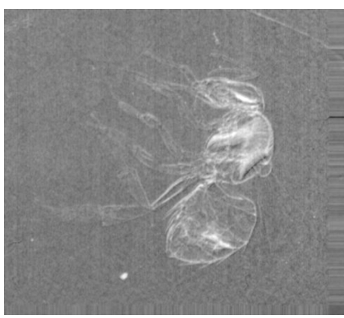
Linear approximation of rocking curve at half values (I_R and I_L)

$$I_L = I_R\left(R(\Theta_L) + \frac{\partial R}{\partial \Theta}(\Theta_L)\Delta\Theta_z\right)$$

$$I_H = I_R\left(R(\Theta_H) + \frac{\partial R}{\partial \Theta}(\Theta_H)\Delta\Theta_z\right)$$

Θ_Z = refraction Image

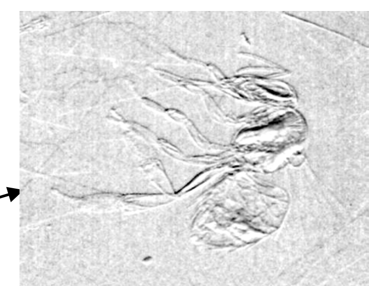
I_R = apparent absorption image (absorption +extinction)



Apparent Absorption Image

$$I_R = \frac{I_L \cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_H} - I_H \cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_L}}{R(\Theta_L)\cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_H} - R(\Theta_H)\cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_L}}$$

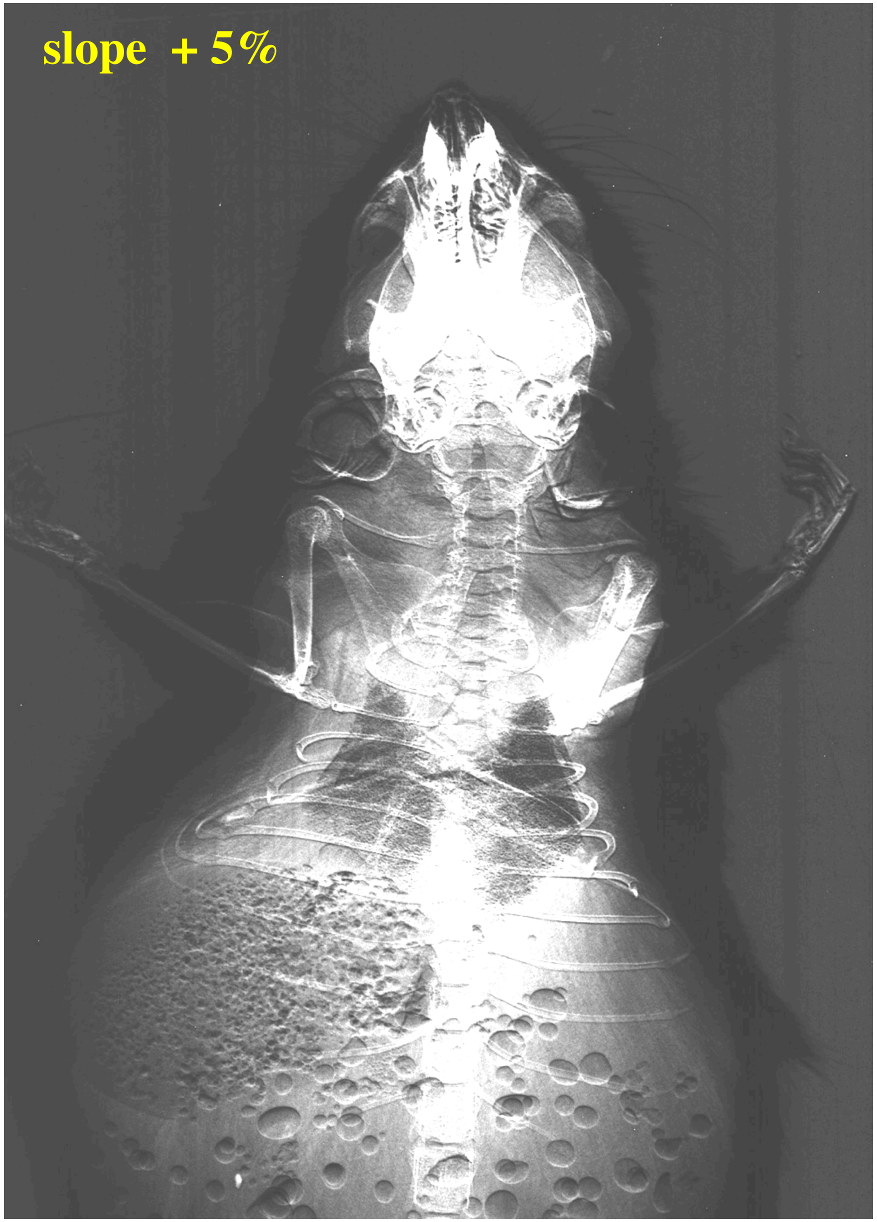
$$\Theta_Z = \frac{I_H \cdot R(\Theta_L) - I_L \cdot R(\Theta_H)}{I_L \cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_H} - I_H \cdot \left.\frac{dR}{d\Theta}\right|_{\Theta_L}}$$



Refraction Image

Ref: Chapman et al, Phys.Med.Biol, 42,1997

ABI images for different analyzer positions



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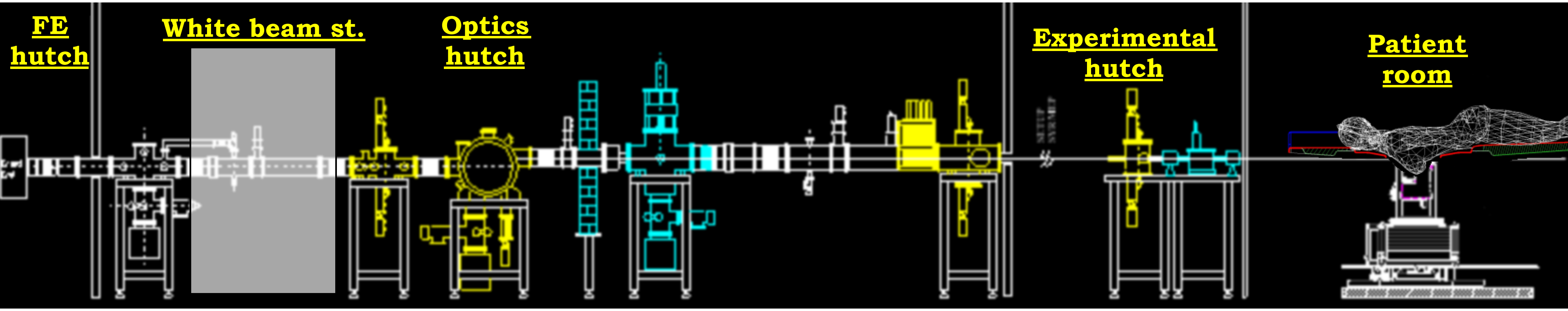
Apparent absorption and refraction images

Apparent absorption

Refraction image

SYRMEP layout



Not in scale!

- Front-end hor. acceptance: **7 mrad**
- Source-to-detector distance ≅ **15** m (white beam station), ≅ **25** m (exp. hutch), ≅ **32** m (patient room)
- Beam hor. size at sample ≅ **10** mm (white beam station), ≅ **160** mm (exp. hutch), ≅ **210** mm (patient room)
- Source size FWHM (h x v) ≅ 240 μm x 90 μm
- Energy range: **8.5 - 40 keV**, B.W. $\Delta E/E \cong 2 * 10^{-3}$

Techniques

- Absorption/Phase Contrast Imaging (free propagation)
- Dual energy imaging (K-edge subtraction)
- Analyzer Based Imaging (ABI)

Modes:
- *Planar*
- *Micro-CT*

EURO-BIOIMAGING

Node for Phase contrast imaging

Breast imaging – first protocol with patients at Elettra

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Agreement among the Public Hospital of Trieste, the University of Trieste and Elettra

Aim: Explore the potential of phase contrast imaging on selected cases

Target: Patients whose conventional diagnosis gave uncertain results.

Modality:
I) PHC radiography with film systems
II) PHC imaging with digital detectors
III) Tomo-mammography

} *Projection imaging*
X-ray energy: 17– 22 keV

(X-ray energy: 32-40 keV)

Outcomes from the first protocol (I, II)

SR exams have:
- higher specificity,
- better agreement with the golden standard (biopsy),
- improved image quality,
- strong reduction of delivered doses.

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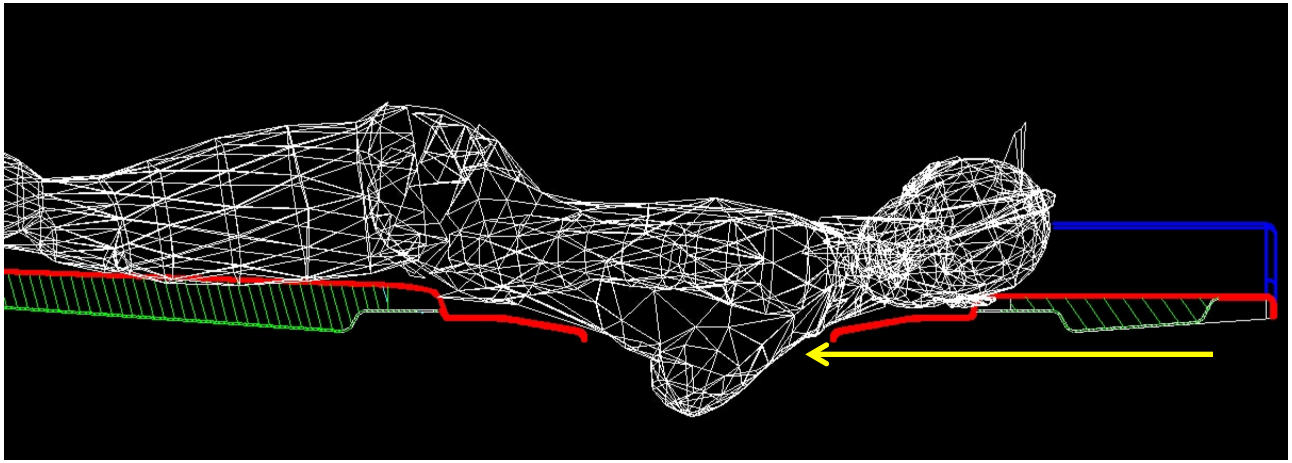
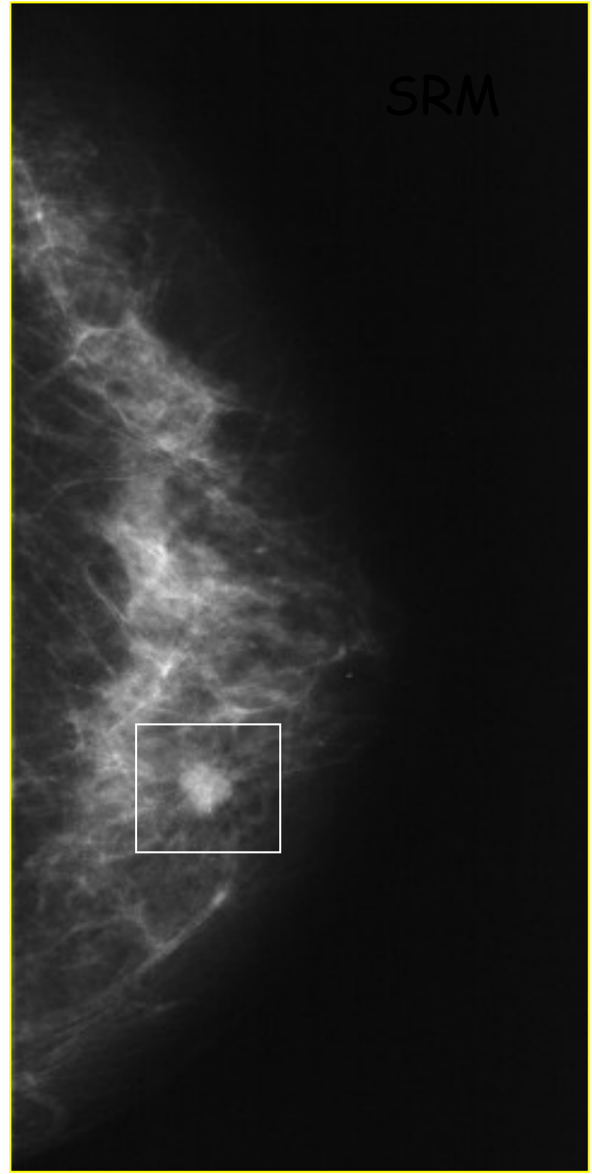
UNIVERSITÀ DEGLI STUDI DI TRIESTE
Fondazione
FONDAZIONE CRTRIESTE

E.Castelli et al.: Radiology, vol 259 (2011), R.Longo et al., Phil. Trans. R. Soc. A 372 (2014)

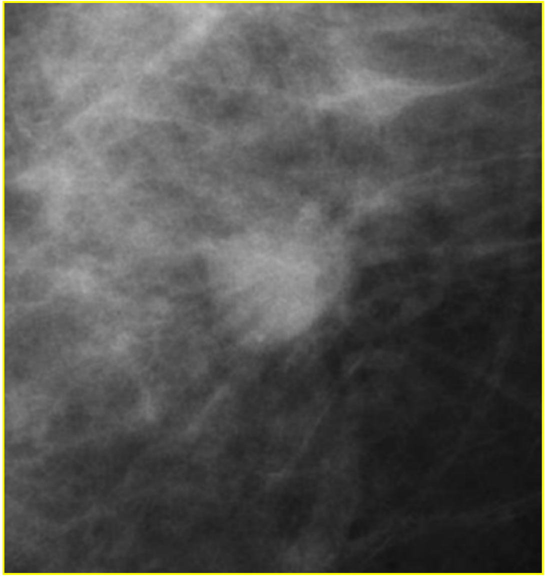
Patient support

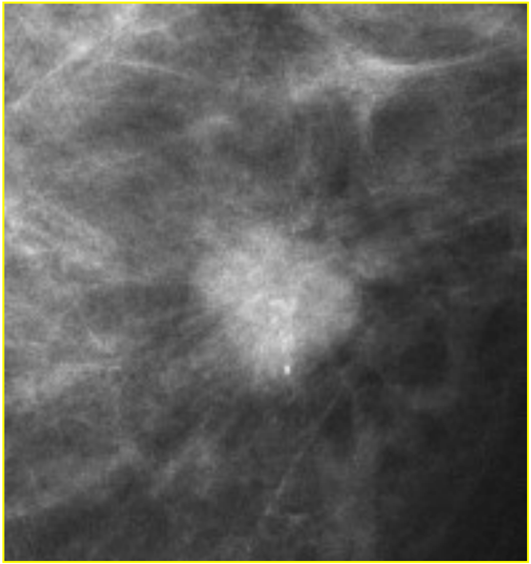


CONVENTIONAL unit



Synchrotron Radiation



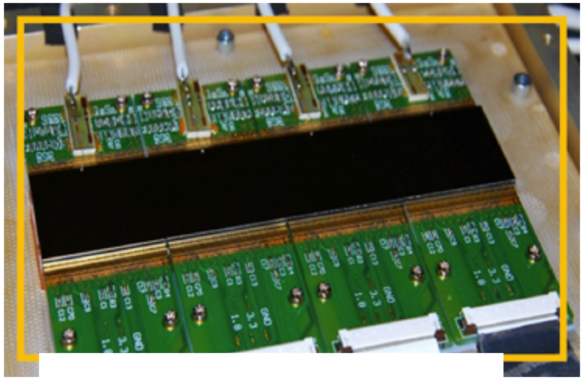


Next-step: Tomo-mammography project (SYRMA-CT)

Goal: Design a new clinical protocol combining **planar projection mammography** and a **CT scan** (inline PHC) on a limited breast portion

Diagnostic aim: contribute to solve the cases of lesions overlap, improve the lesions characterization and visualize better their infiltration in the healthy tissue

Key element: CdTe single photon counting detector, 60 μm pixel size, 25×2.5 cm² active area by PiXirad



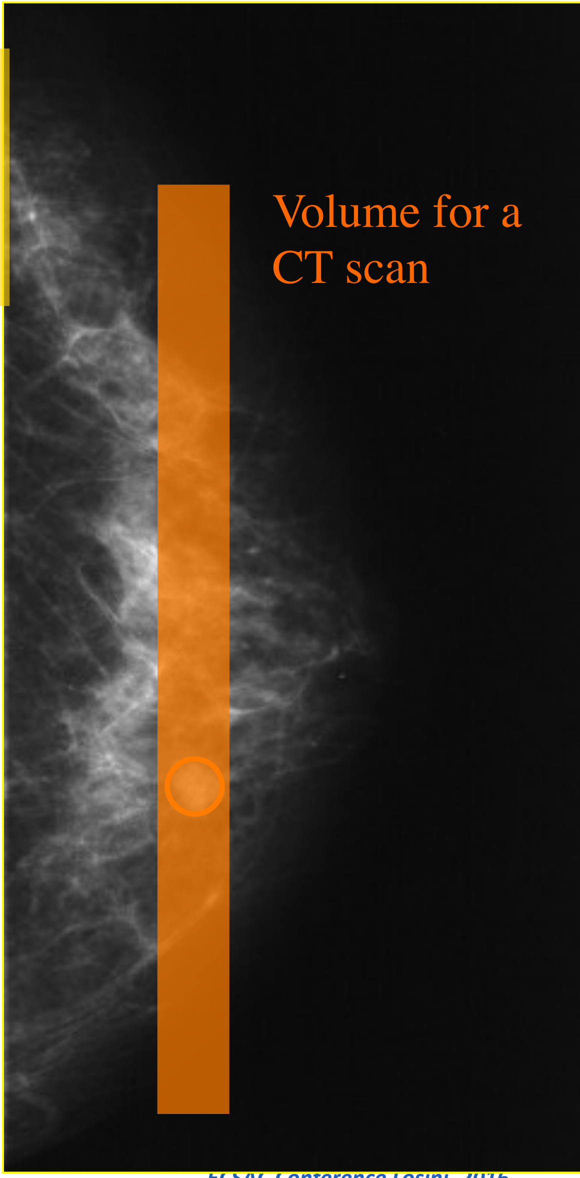
Project financed by **Istituto Nazionale di Fisica Nucleare** (INFN), Sections of: Trieste, Ferrara, Pisa, Napoli, Sassari

Approval by ethic committee is needed

Main issues to be addressed

Exam procedure

- Identification of the region for the CT scan
- Choice of imaging parameters (X-ray energy, n. of projections, exp. time, etc.)
- Optimization of pre-processing and recon algorithms
- Post-processing
- *Dosimetry issues* and safety system upgrade
- Protocol implementation in the exam supervisor



- CT scan (~600 projections) must be performend at the same dose of a conventional examination (~5-10 mGy): feasibile?
- Is *phase contrast* effective at high X-ray energy and with such low dose/ projection?

Phase retrieval algorithm [*]

- Phase and amplitude extraction from a single distance image of a homogeneous object
- Refractive index: $n = 1 - \delta + i\beta$ δ: phase shift term, β: absorption
- Transport of Intensity Equation (TIE) – Hom. phase retrieval algorithm
- Hom. Approx. : tissue as an homogeneus medium (δ/β=cost)

[*]Paganin, D., et al:, "Simultaneous phase and amplitude extraction from a single defocused image of a homogeneous object. Journal of microscopy, 206(1), 33-40 (2002).

Low dose phase contrast breast tomography: optimization of reconstruction workflow

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Combined experiments carried out at Elettra and at the Australian source with different detectors and energy ranges

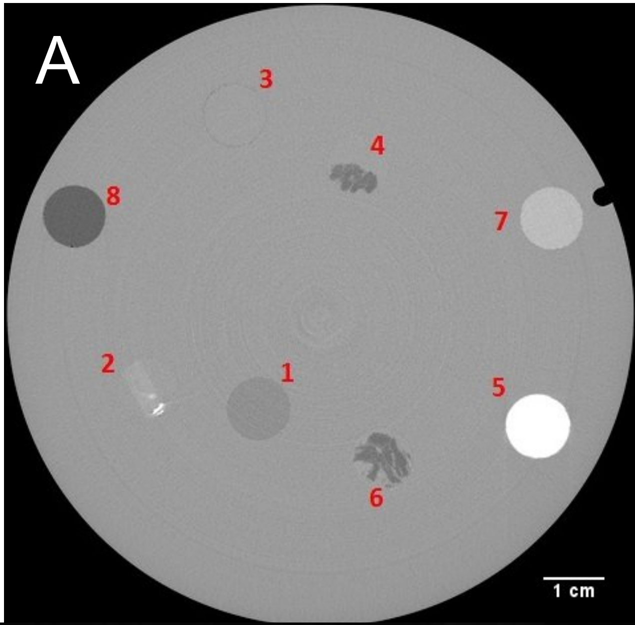
Geometrical test object and tissue specimens

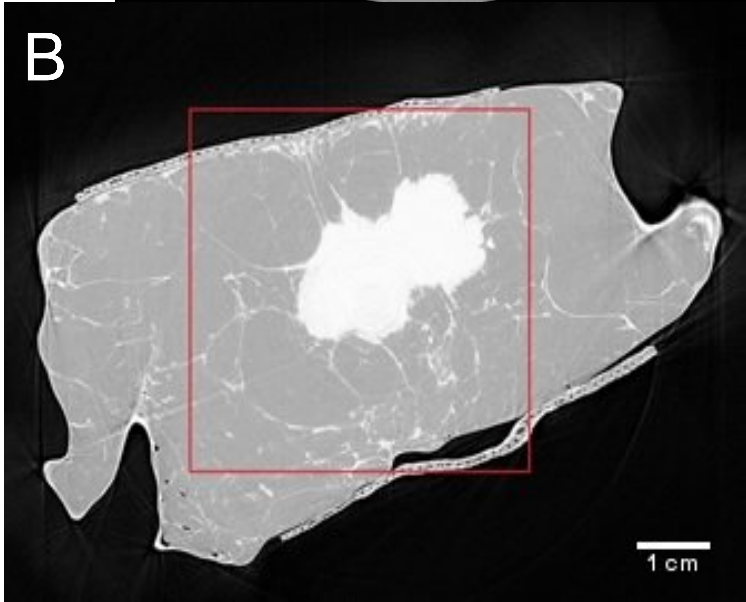
CT in PB mode @ diagnostic dose (2.5 mGy AGD)

Reconstruction workflows
Pre-processing, reconstruction, post-processing

Definition of image quality indexes & functions for comparison

Radiological Assessment





A) Polycarbonate phantom where 1 = Glycerol (C3H8O3), 2 = Unknown tissue (Malignant), 3 = Water (H2O), 4 = Fibrous tissue, 5 = Calcium Chloride (CaCl2), 6 = Adipose tissue, 7 = Paraffin wax, 8 = Ethanol (EtOH).

B) Reference image for the mastectomy sample reconstructed with FBP algorithm and considering 3600 high statistic projections. The red square indicates the region-of-interest used for the image quality assessment.

THE UNIVERSITY OF MELBOURNE — UNIVERSITÀ DEGLI STUDI DI TRIESTE — CSIRO — Elettra Sincrotrone Trieste — UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG — Australian Synchrotron

G. Tromba

S. Pacilè, et al: Biomed. Opt. Express 6 (2015)

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Reconstruction workflows

Abbreviation	Phase retrieval	Reconstruction	Post-proc.
FBP	no	FBP	
FBP-ITER	no	FBP-ITER	
SIRT	no	SIRT	
SART	no	SART	
CGLS	no	CGLS	
EST	no	EST	
phr FBP	yes	FBP	
phr FBP-ITER	yes	FBP-ITER	
phr FBP-ITER Epan17	yes	FBP-ITER	Epanechikov (w = 17)
phr FBP-ITER Susan5	yes	FBP-ITER	Susan (w = 5)
phr TV-MIN	yes	TV	
phr SIRT	yes	SIRT	
phr SART	yes	SART	
phr CGLS	yes	CGLS	
phr EST	yes	EST	

Image quality indexes & functions

Full-reference indexes

(require a ref. image)

MSE – Mean Squared Error
SNR – Signal-to-Noise Ratio
UQI – Universal Quality Index
NQM – Noise Quality Measure
SSIM – Structural Similarity Index

No-reference indexes

CNR – Contrast to Noise ratio
FWHM – Full width half maximum
Qs – Image quality characteristic(*)

$$CNR = A_{feature}^{1/2} \frac{|\langle \beta_{lesion} \rangle - \langle \beta_{adipose} \rangle|}{[(\sigma_{lesion}^2 + \sigma_{adipose}^2)/2]^{1/2}}$$

$$Q_s = \frac{SNR_{out}}{F_{in}^{1/2} \Delta x}$$

F_{in} = incident photon fluence
Δx = spatial resolution of the imaging system
SNRout = output signal-to-noise ration

(*) T. Gureyev et al, Opt. Express 22, (2014)

Radiological Assessment

From 0 (worst case) to 4 (best image)

No-diagnostic power (0 – 2)
Poor diagnostic power (2 – 3)
Full diagnostic power (> 3)

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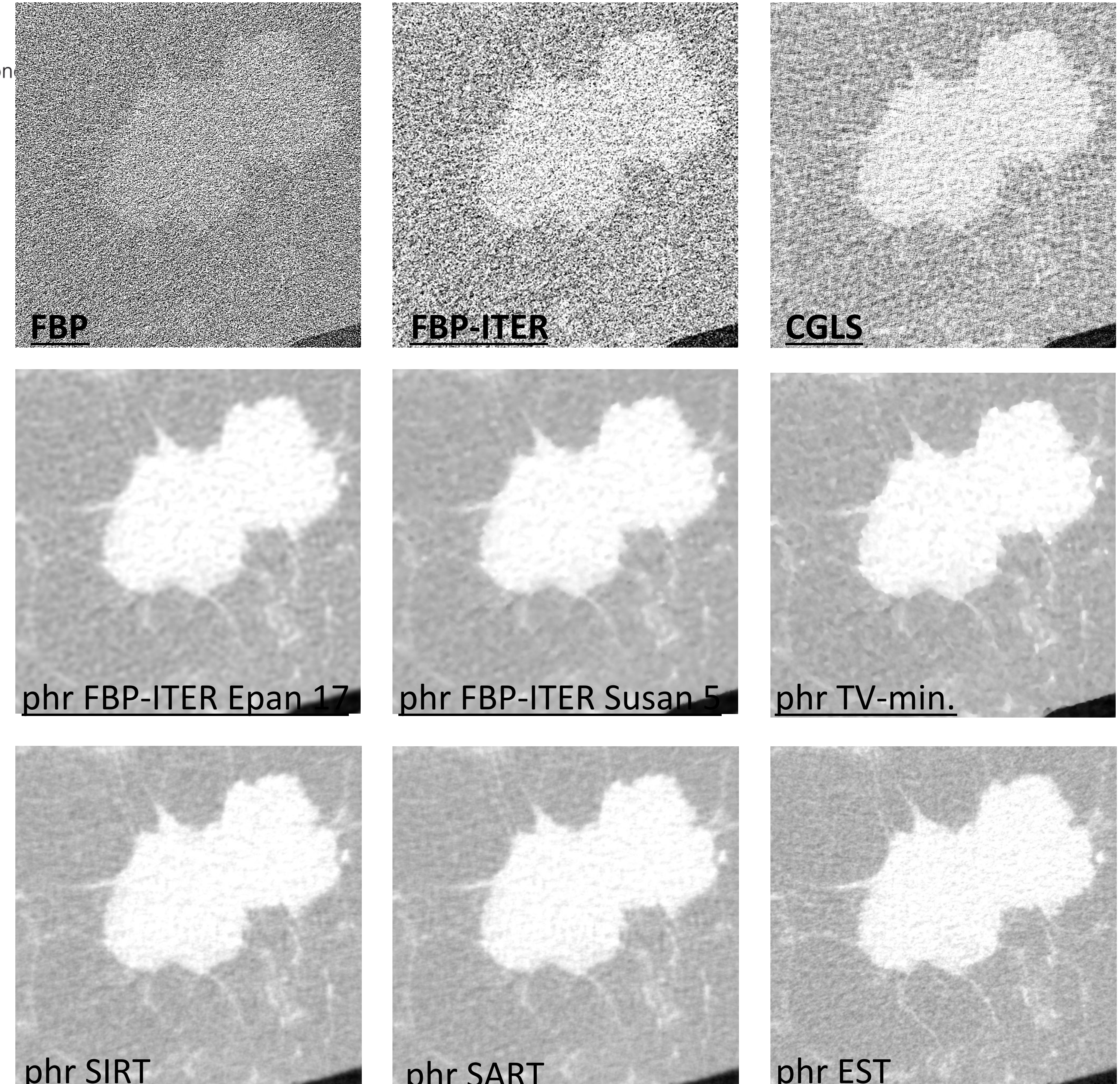
NO-DIAGNOSTIC POWER

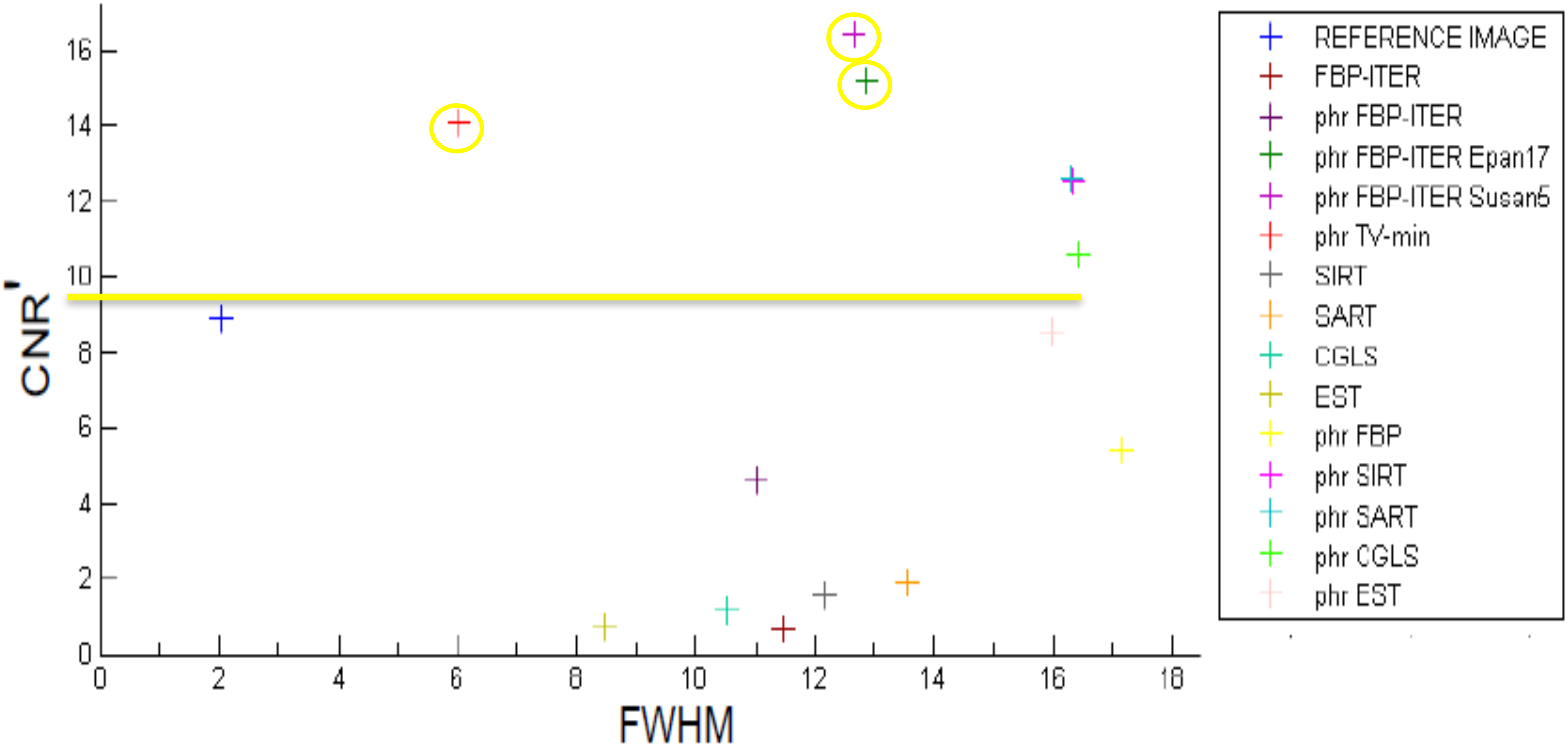
POOR-DIAGNOSTIC POWER

FULL-DIAGNOSTIC POWER



S. Pacilè, et al: Biomed. Opt. Express 6 (2015)

Contrast-to-noise ratio and image *blurring*

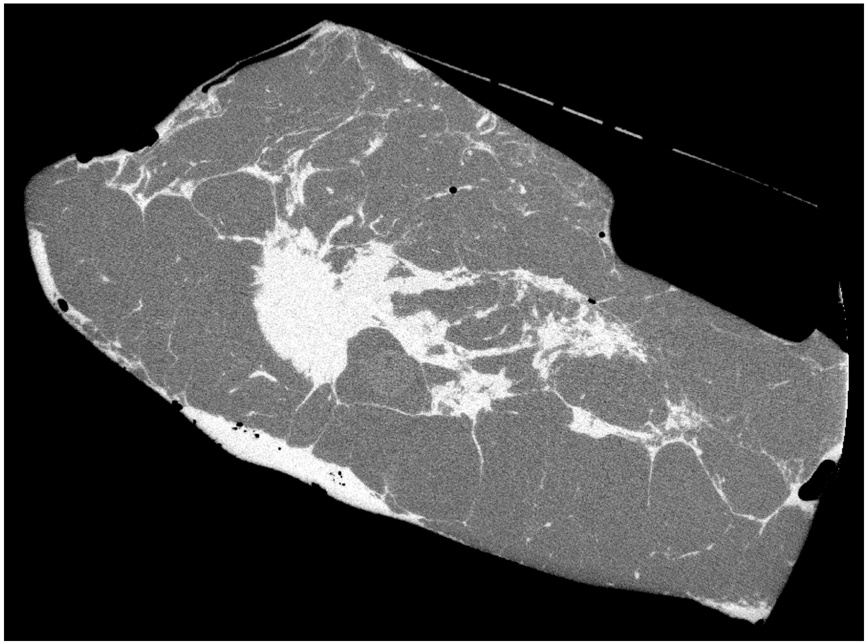


Full statistics ref image recontructed with phase retrieval and FBP: CNR' = 30.5, FWHM = 5.8

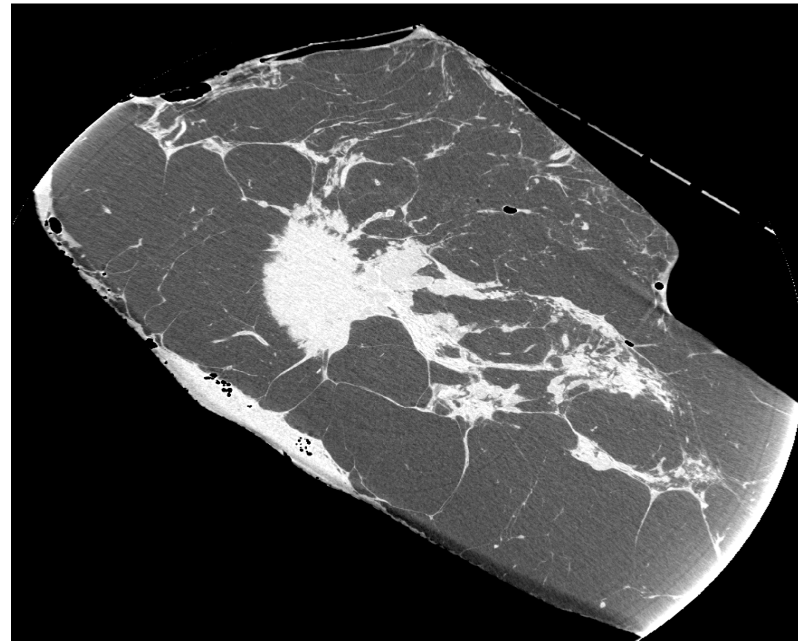
FWHM expressing image blurring is evaluated on the phantom images)

S. Pacilè, et al: Biomed. Opt. Express 6 (2015)

Experiment at SYRMEP, Nov. 2015 – large propagation distance (9m)



Slice reconstructed from high-dose CT (~20 mGy) scan at 0 m propagation distance Hamamatsu detector



Same slice reconstructed from low-dose (5 mGy mGD) PCT scan at 9 m propagation distance Hamamatsu detector

E = 38 keV
Absorption and PB CT slice of a mastectomy sample with a tumour
Detector: Hamamatzu Flat Panel, pixel size = 100 μm

Courtesy of T.Gureyev

Potentials of ABI

- Studies of cartilages and bones interfaces

- Imaging of finger joints

ABI studies of Cartilage and bone interface

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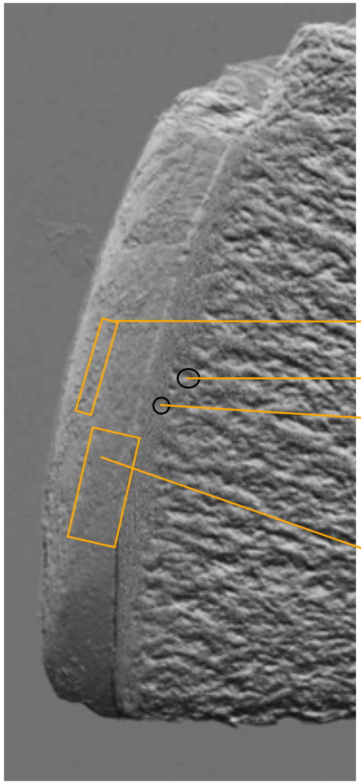
Osteoarthrosis (OA) is a disease characterized by the progressive degeneration of articular cartilage and the development of altered joint congruency. It has a high incidence in the adult population. Affecting mainly the elderly population, it is one of the main causes of disability worldwide. Conventional radiography detects only **important osseous changes**, at advanced OA stage, when therapeutic strategies are less effective. **Early changes** in the **cartilage** and other **articular tissues** are **not** directly visible. MRI imaging works better but the maximum achievable spatial resolution is not always adequate.



Need to study:

- cartilage
- cartilage-bone interfaces
- changes in the bone structure

Superficial Layer (Zone of horizontal collagen fibers with flat cells)

Subchondral Bone Plate (**Important for diagnostic purposes in OA**)

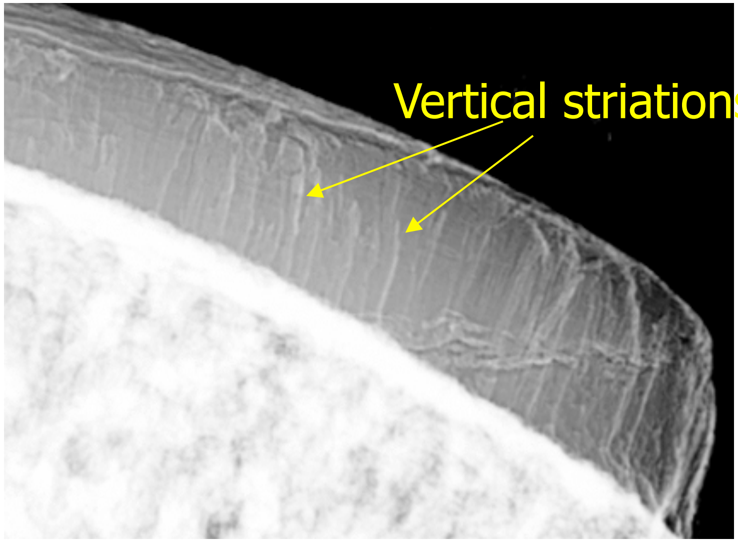
Tidemark (Border between normal and mineralized cartilage)

Transitional and Deep Layer (round cells, collagen fiber switches from horizontal to vertical orientation, increasing stiffness and material density)

Aim: detect the architectural arrangement of collagen within cartilage and evaluate how the cartilage degeneration affects the underlying subchondral and trabecular bone.

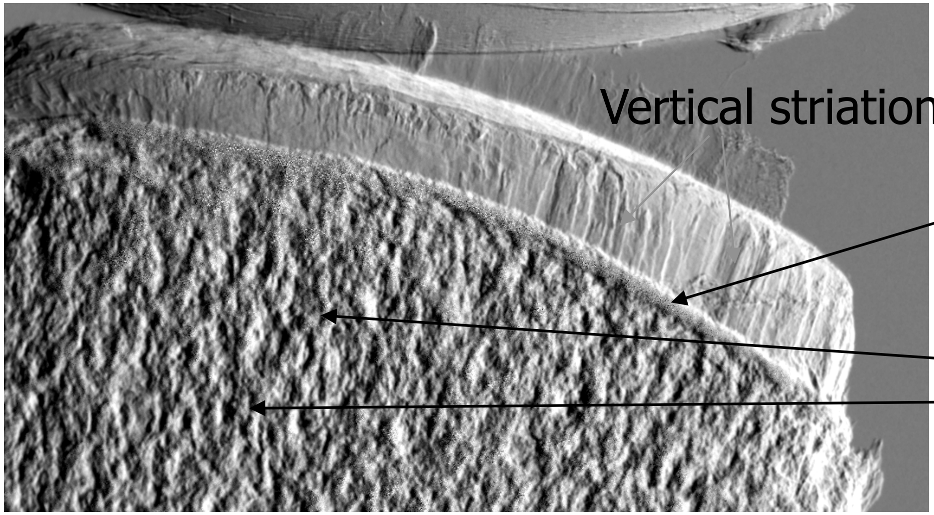
Femur head core cuts: collagen arcades structure

- The ABI technique allows to visualize the discontinuities in the sample and the inner structures invisibles by means of conventional X-Ray imaging.
- The transition bone-cartilage is emphasized.
- The articular cartilage striations are well visible due to X-ray diffraction at edges of fibers



Apparent absorption image

Refraction image



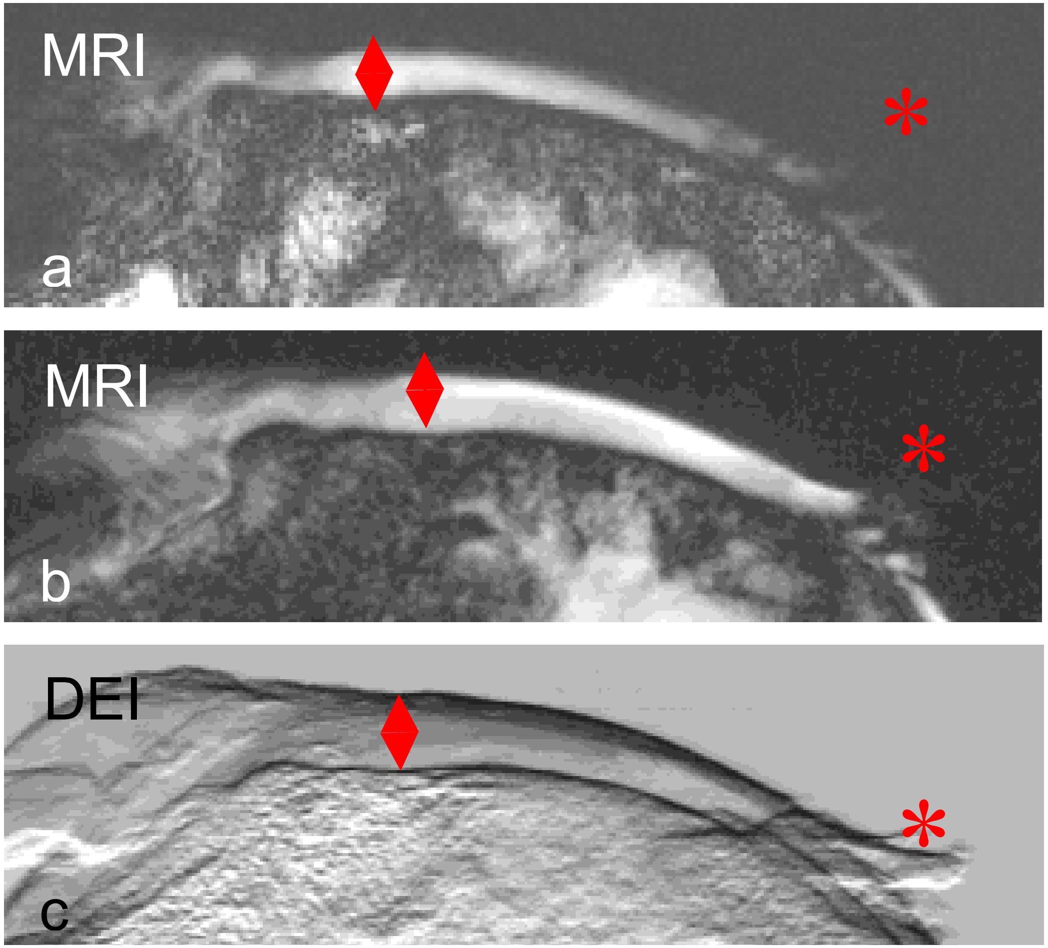
Subchondral bone

Trabecular bone

Elettra
25 keV

Muehleman C, et el., Osteoarthritis and Cartilage 12 (2): 97-105 FEB 2004

Femur head core cuts: comparison with MRI



5 sec

150 sec

A Wagner, et al., Nucl. Instr. and Meth. in Phys. Res. Section A, 548(1), 47-53 (2005).

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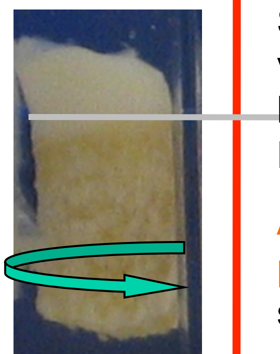
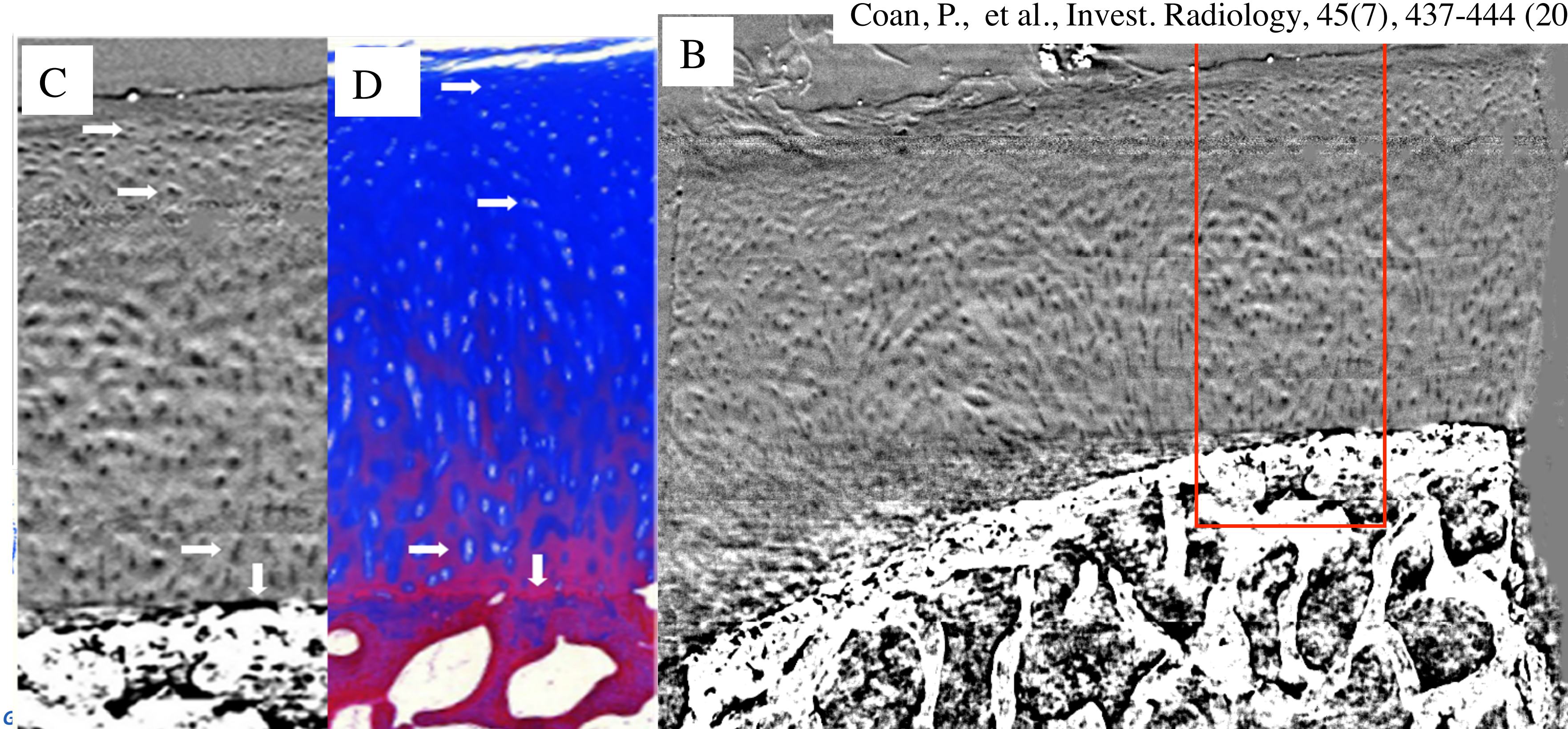
A



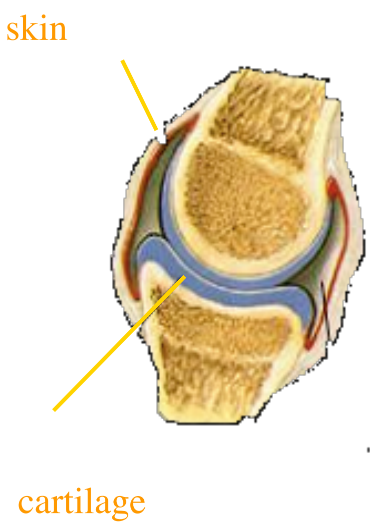
Specimen of normal cartilage (A), Coronal plane extracted from the reconstructed CT volume (B), Magnified portion identified by the ROI (C), Corresponding section from histologic preparation (D).
E = 26 keV, pixel size = 8 x 8 μm^2.

ABI in planar and tomographic modes was performed *in vivo* on articular joints of guinea pigs. Images showed the potential of technique in revealing initial lesions. Images with high spatial resolution and with an acceptable radiation dose.

Coan, P., et al., Invest. Radiology, 45(7), 437-444 (2010)



ABI studies of the finger joint

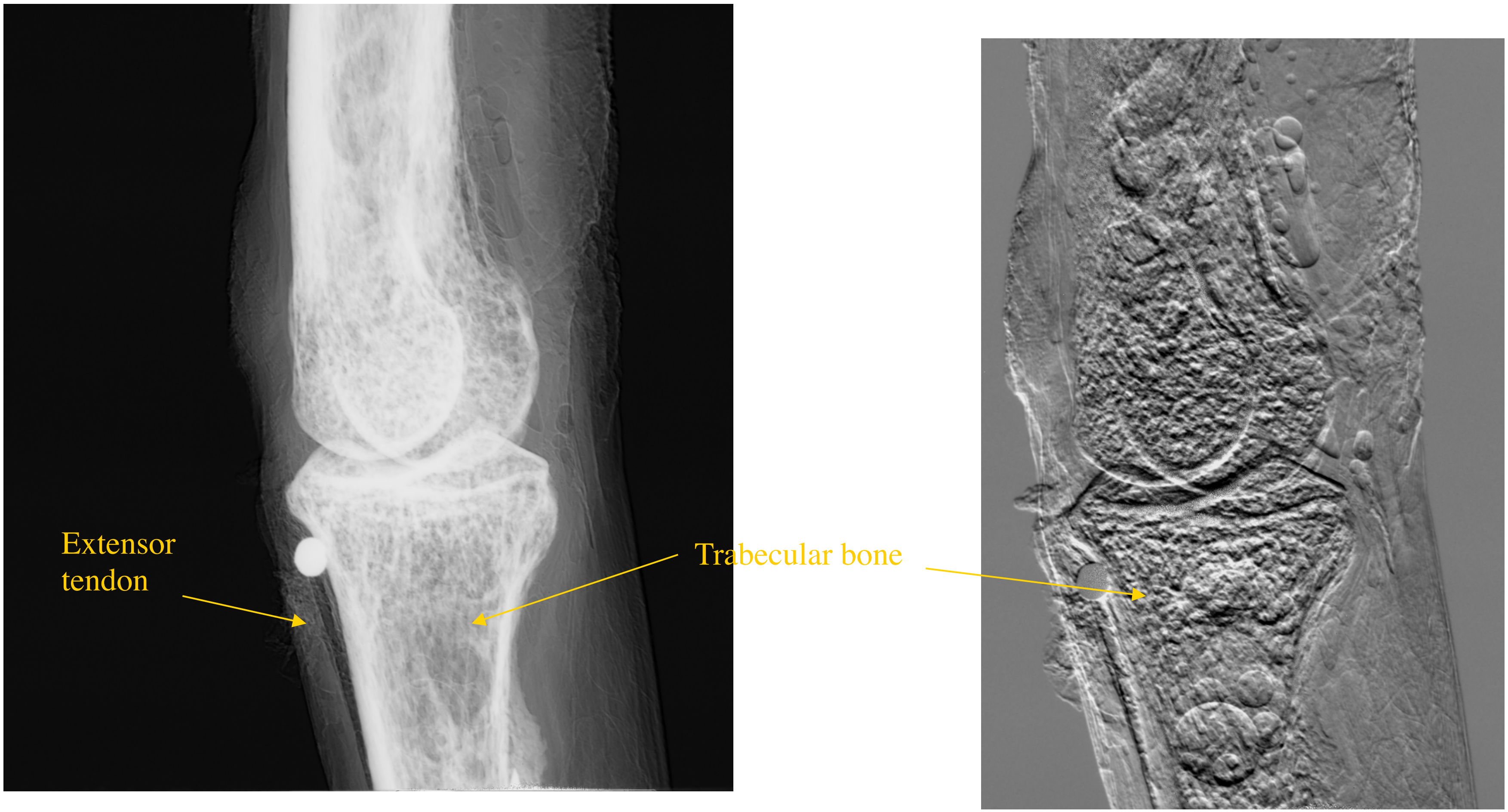


Conventional radiograph

Apparent absorption image @ 20 keV
at ELETTRA

Lewis, R. A., et al., British J. Rad., 76(905), 301-308 (2003)

Index finger proximal interphalangeal joint

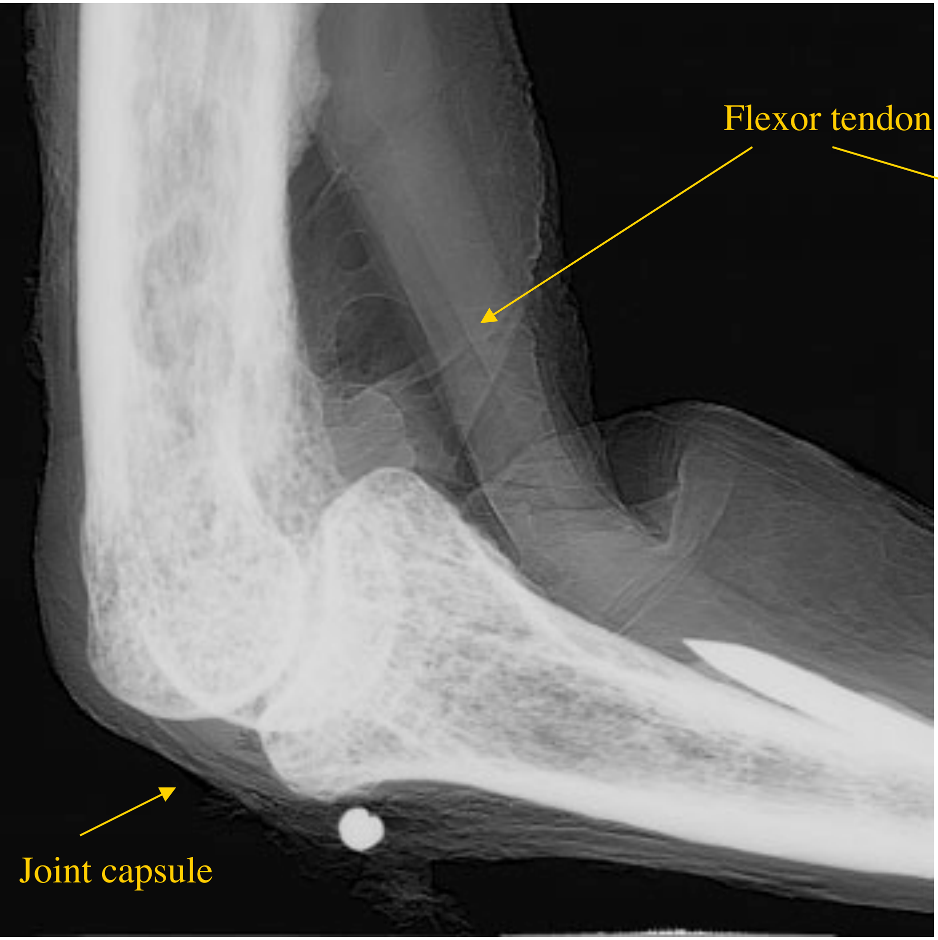


Apparent absorption Image

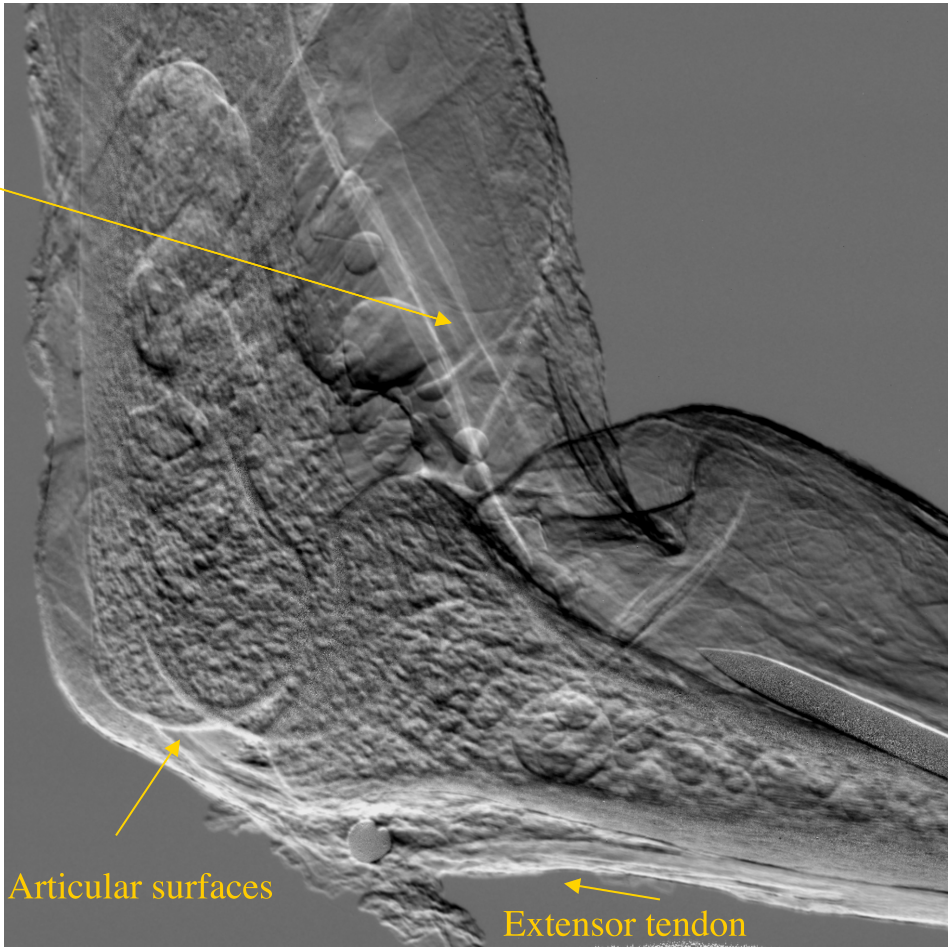
Refraction Image

Lewis, R. A., et al., British J. Rad., 76(905), 301-308 (2003)

Index finger proximal interphalangeal joint



Apparent absorption Image



Refraction Image

Lewis, R. A., et al., British J. Rad., 76(905), 301-308 (2003)

Lungs imaging

Techniques: Propagation based phase contrast

Modalities: planar for *in-vivo* images on rabbits

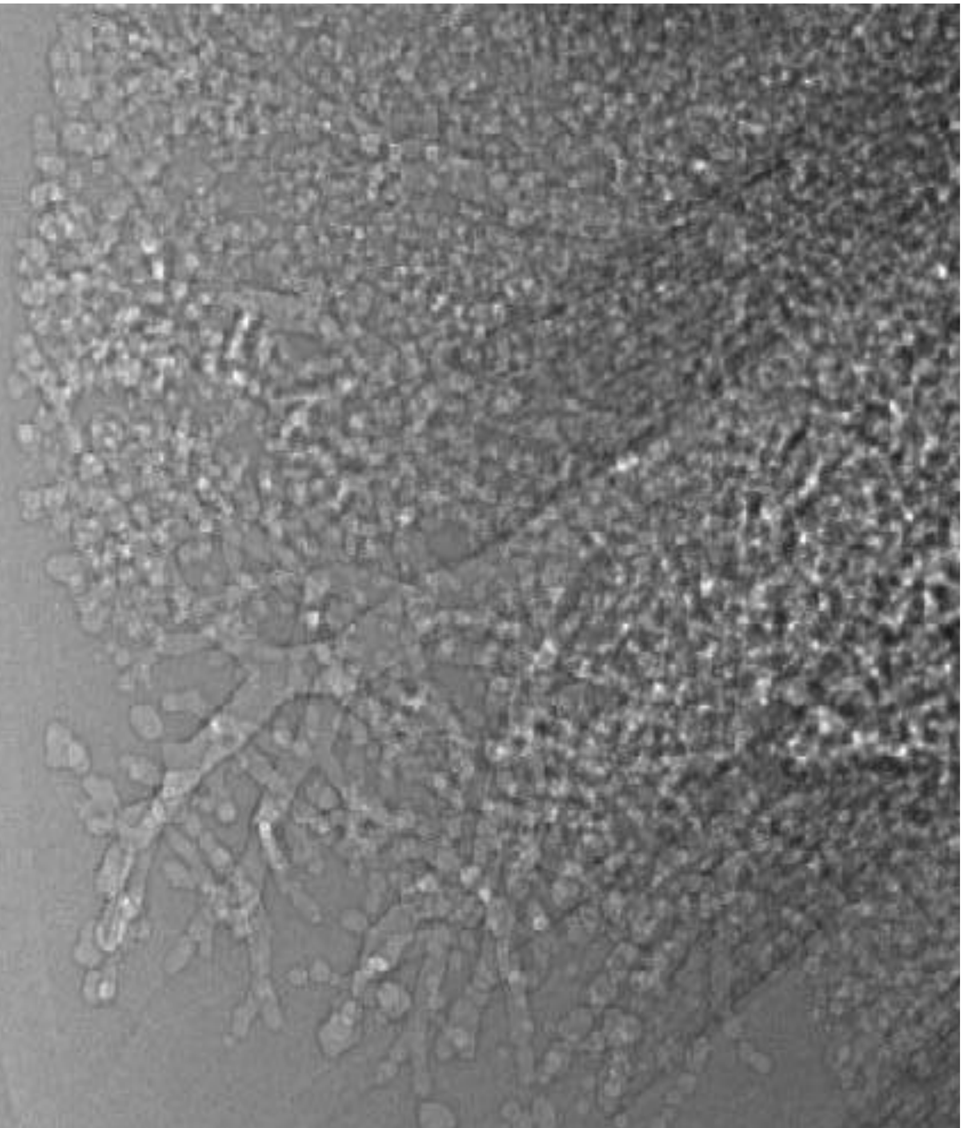
ex-vivo micro-CT for a high resolution functional and morphological imaging of asthmatic mice

In vivo studies at Spring 8 (Japan)

Effects of Ventilation on Lung Liquid Clearance at Birth

Elettra Sincrotrone Trieste

Aim: to observe lung aeration on a breath-by-breath basis.



Birth: a major physiological challenge

- ✓ Clear the airways of liquid
- ✓ Entry of air generates surface tension
- ✓ 10 fold increase in pulmonary blood flow
- ✓ Large increase in blood oxygenation
- ✓ Animal model used to study respiratory problems affecting pre-term borns.

- ➢ Animal model: rabbit pups
- ➢ Imaged pups with phase contrast imaging (FPI), either before the first breath (fetus) and at fixed intervals after birth (up to 2h)

MONASH University Science

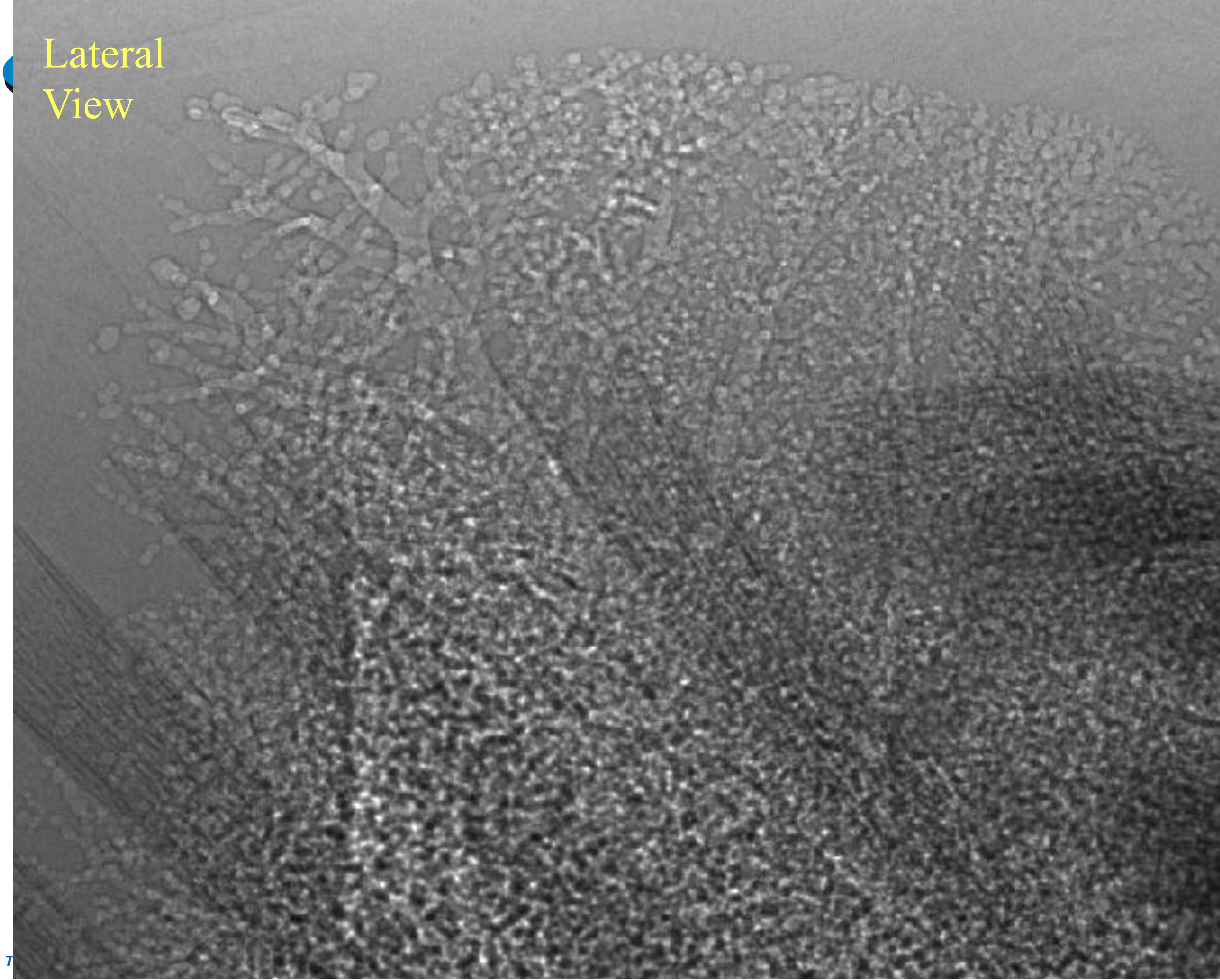
Courtesy of M. Kitchen, School of Physics

X-ray imaging of the lung

Absorption Contrast

Phase Contrast, 25 keV, z=2 m

Kitchen, M. J., et al., Phys. Med. Biol., 53(21), 6065-77 (2008).

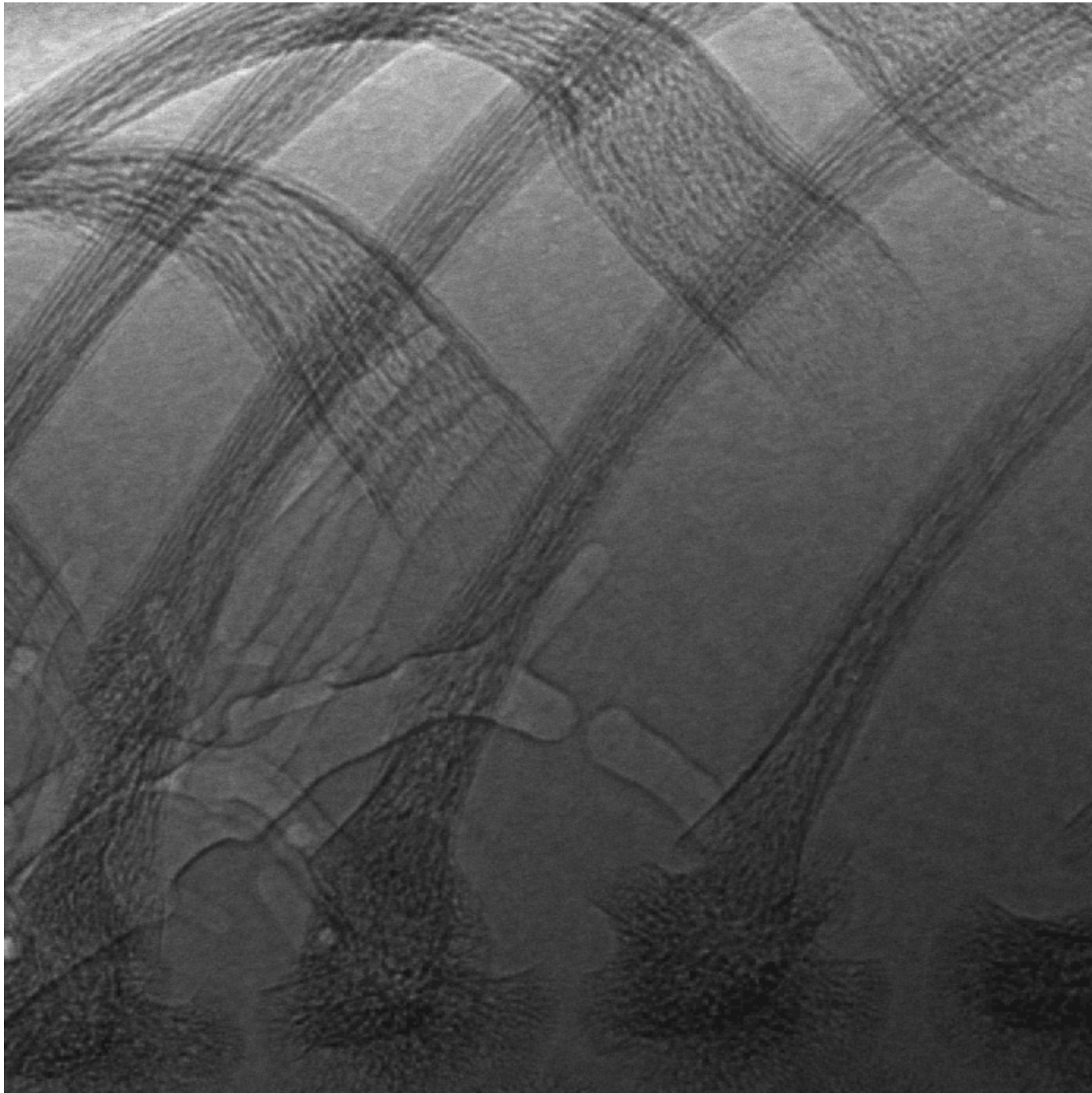

Lateral
View

Exp. time:
80 ms

Interval:
0.8 s

Skin Dose
~ 0.15
mGy
per frame

Pixel Size
22.5 µm



Imaging of inflammation in asthmatic mice: combining functional and structural information

Elettra Sincrotrone Trieste

- Model of allergic asthma induced by ovalbumin based on balb/c mice developed by CBM in collaboration with the University of Wien.
- Aim: evaluate the potential of SR-based technique for **functional** and **morphologic** imaging of mice lungs
- Available techniques: optical imaging and PHC micro-CT
- Imaging protocol: tracking macrophages distribution
- Perspective for in-vivo studies (planar protocol within 2017 at SYRMEP (coll Goettingen – Incoming Talent3 project)

cbm cluster in biomedicine

UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG

P³AGI Public Private Partnership for Asthma Imaging and Genomics

SEVENTH FRAMEWORK PROGRAMME

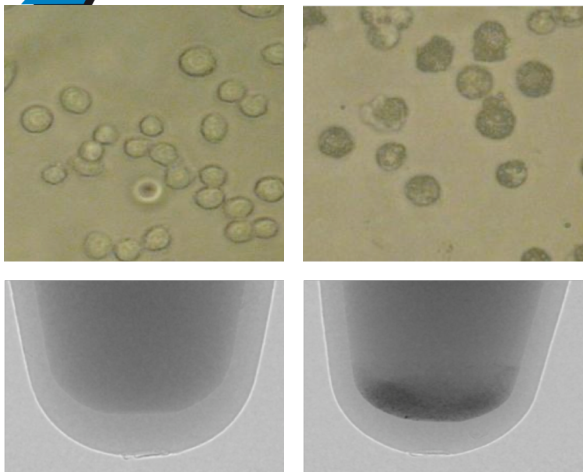
MEDIZINISCHE UNIVERSITÄT WIEN

Linköping University

Programme on Scientific and Technological Cooperation between Italy and Sweden financed by Ministero degli Esteri

Elettra Sincrotrone Trieste

Imaging protocol: use of macrophages with double staining



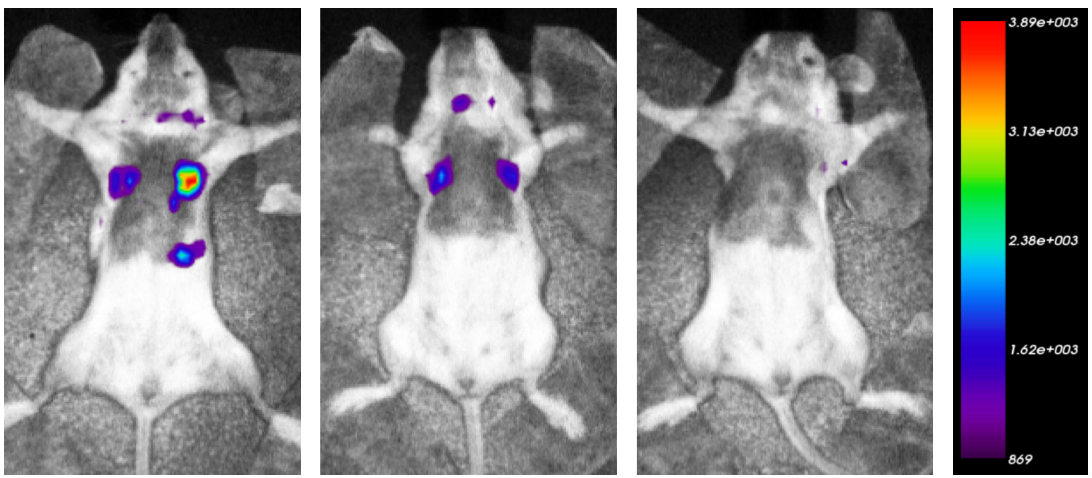
Unlabeled macrophages

Macrophages labeled with Ba

Use of immortalized Murine Alveolar Macrophage Cell line with double staining:

- **Barium sulfate** (clinical contrast agent Micropaque CT (Guerbet, F))
- **DiD fluorescent dye** to be used for cells localization inside the lungs using fluorescence microscopy.

Macrophages were adminstered intra tracheally 48 hours after asthma induction



Asthmatic mouse treated with macrophages

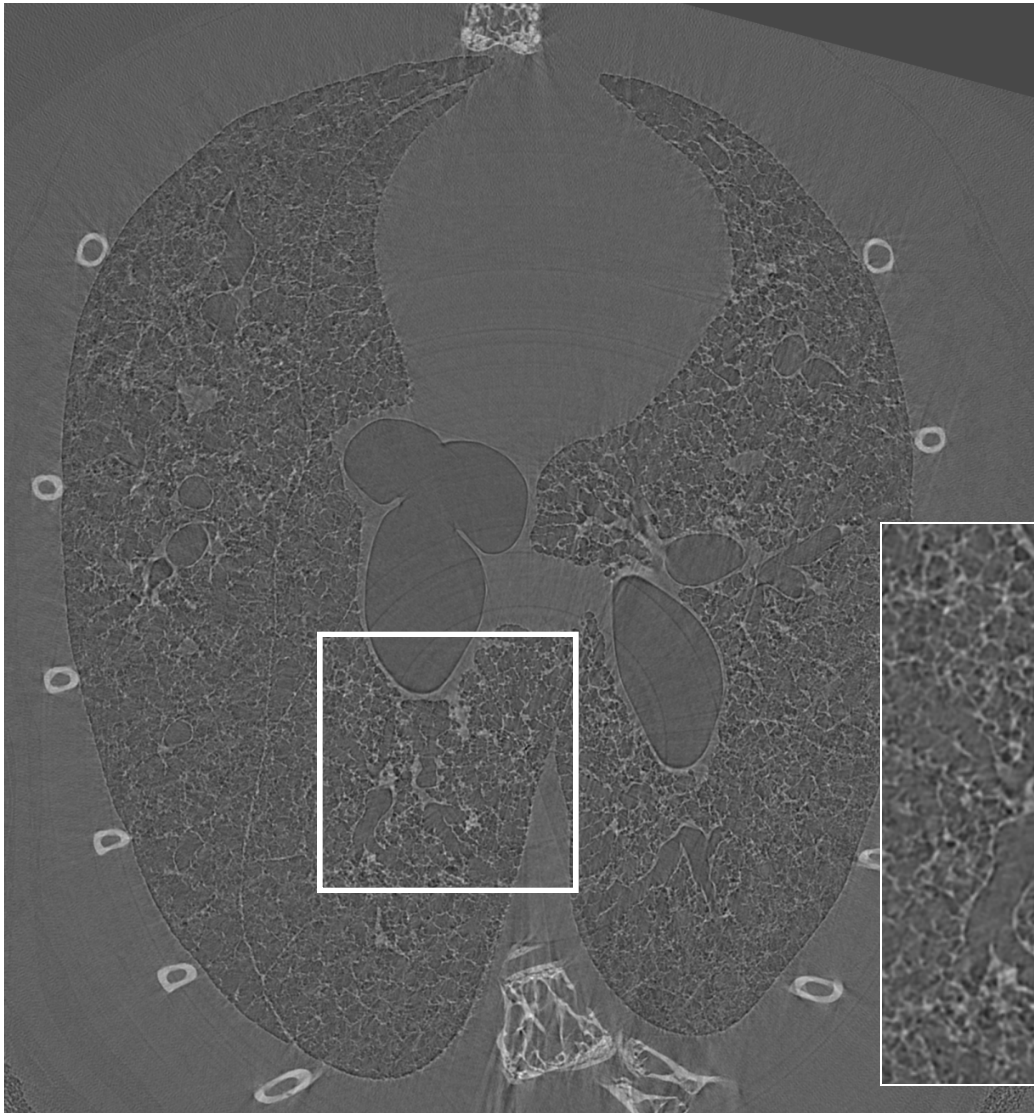
Normal mouse treated with macrophages

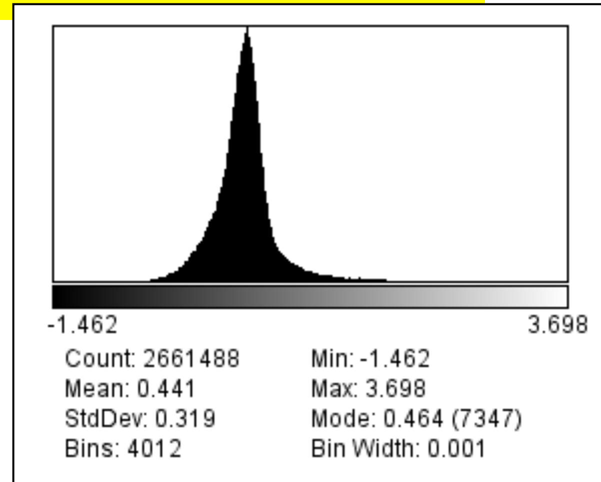
Native mouse untreated

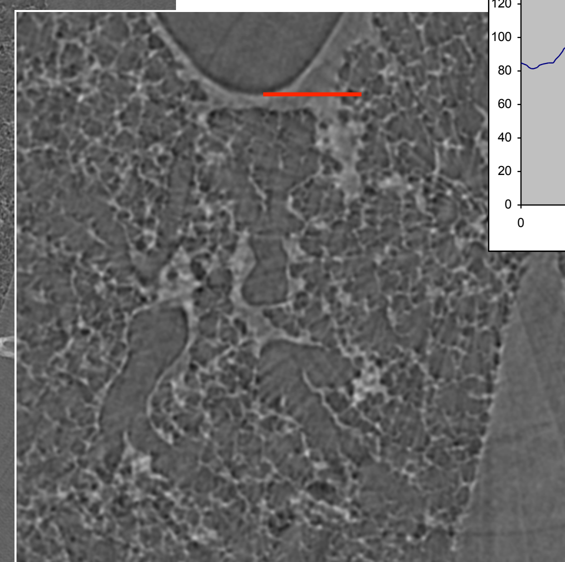
In vivo validation of homing of the macrophages to the inflammation sites.

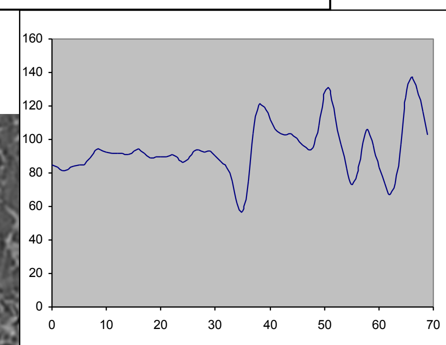
Images performed 24 hours after macrophages administration.

Reconstructed slice –
Filtered back projection standard reconstruction procedure









Typical edge enhancement effects due to phase contrast

Elettra Sincrotrone Trieste

Visualizing Barium brought by macrophages into the inflammation sites

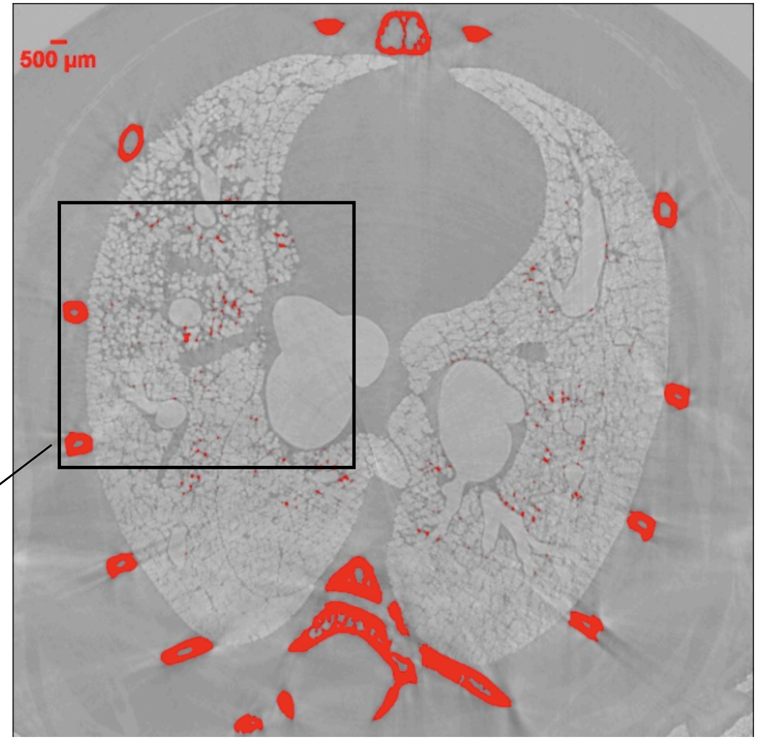
Sample: acute asthma mouse treated with macrophages labeled with Barium

Phase Retrieval pre-processing *algorithm* is applied to CT projections, (prior to the reconstruction) to enable the decoupling of *phase* from *absorption*

Assumptions (Paganin et al., 2002):

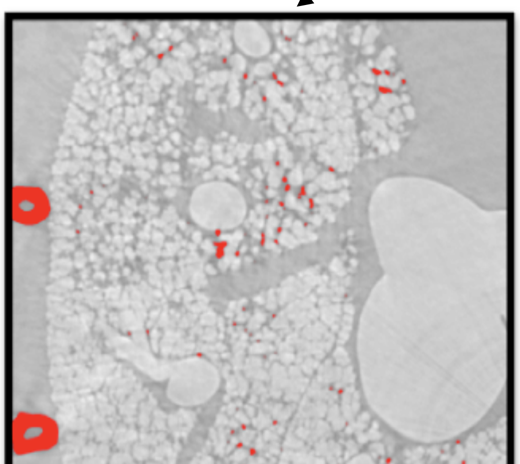
-near field phase contrast regime

- materials with δ/β = const



E=22 keV
PHC dist=30 cm

Bones
Barium

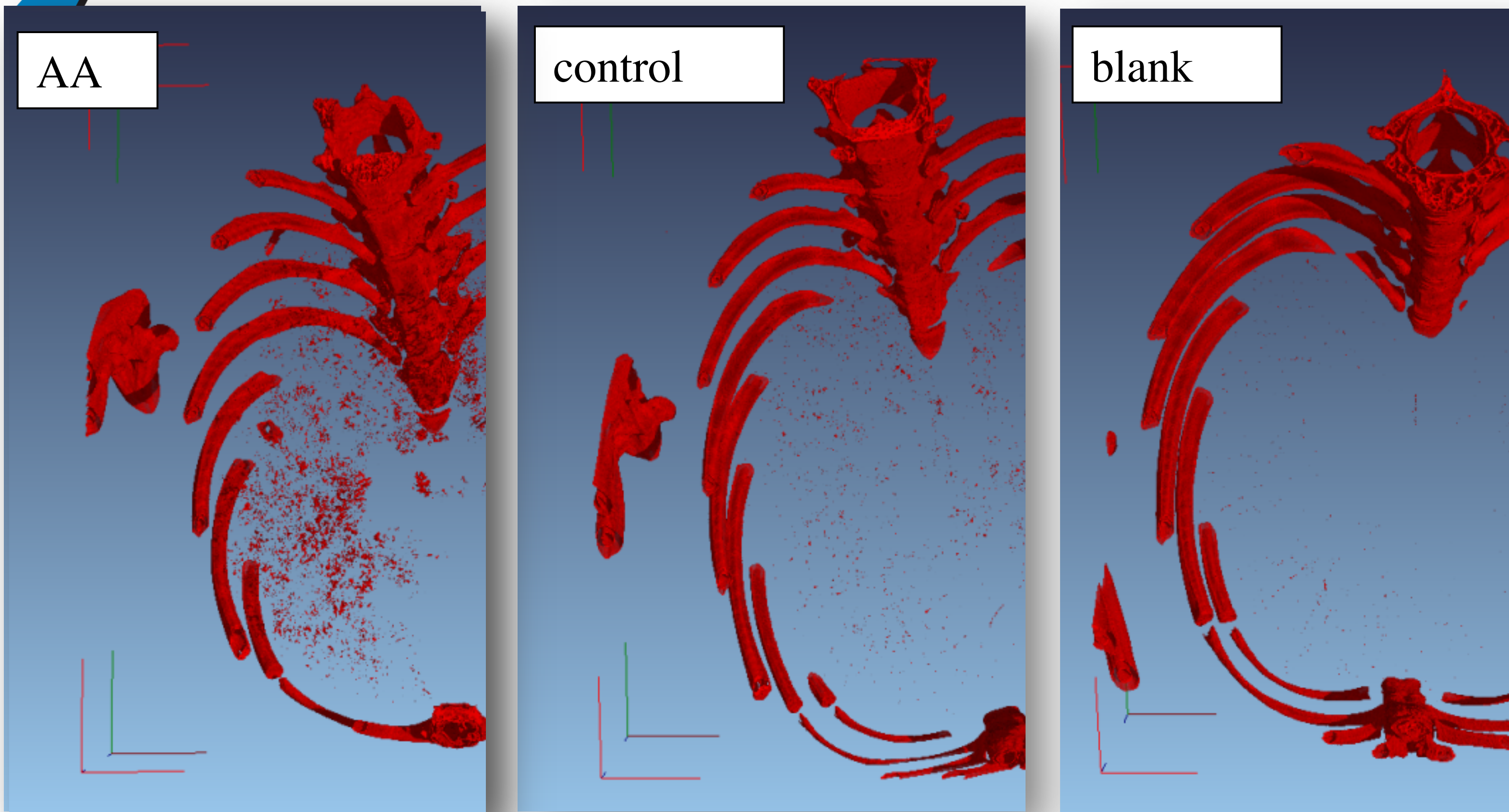


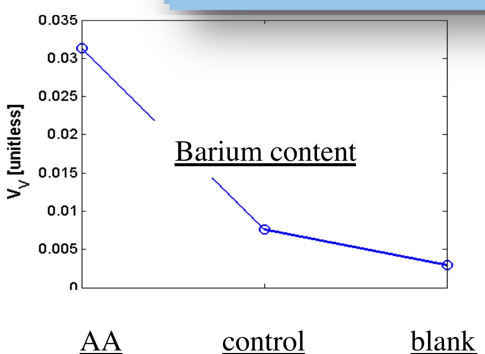
Application of Phase Retrieval for:

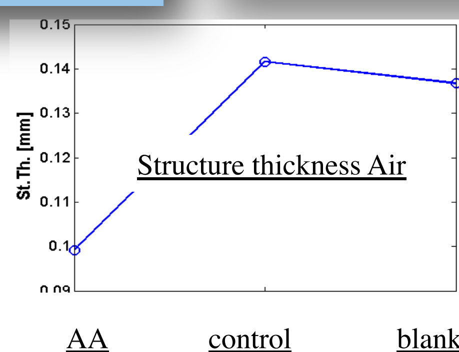
- Reducing the artefacts due to PHC effects around the tissue edges
- Reducing the noise
- Enhancing the phases separation

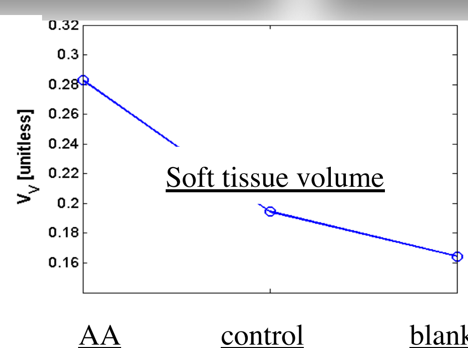
Visualization of labeled macrophages

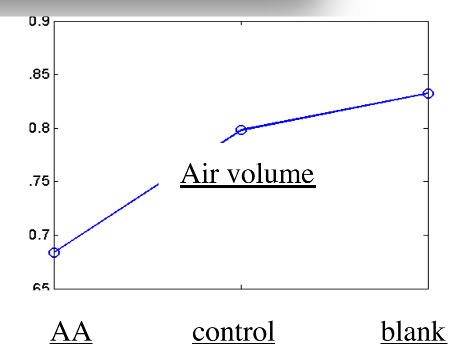
Elettra Sincrotrone Trieste











Quantification performed by Larsson E, using pore3D

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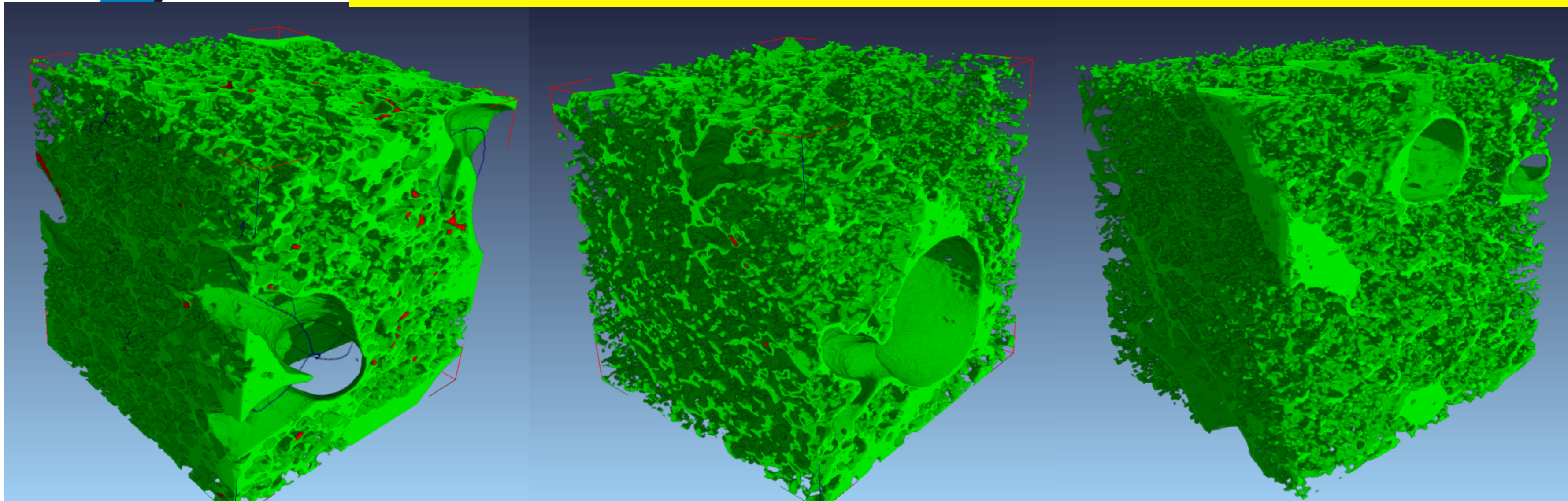
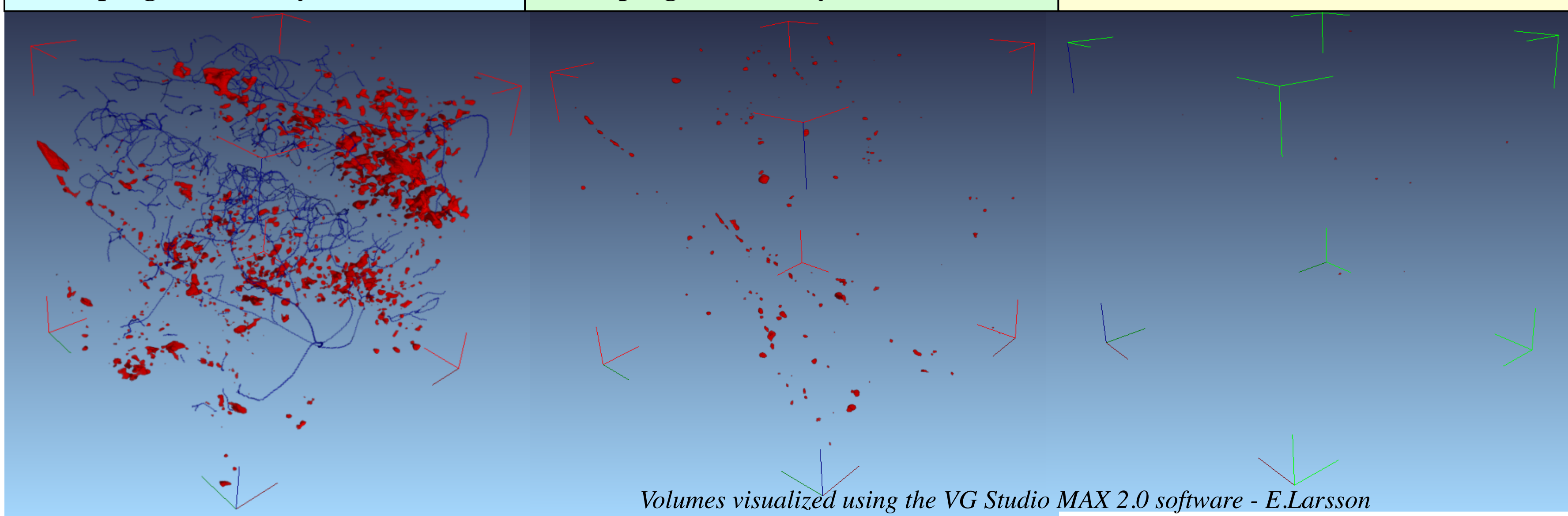
VOI of soft lung tissue

Soft Tissue (green), Macrophages with barium (red), Medial axis/skeleton (blue)



a) asthmatic mouse treated with macrophages labeled by Barium	b) healthy mouse treated with macrophages labeled by Barium	c) control: healthy mouse untreated (no Barium)



Volumes visualized using the VG Studio MAX 2.0 software - E.Larsson

Cell tracking studies for imaging of brain tumors in rats

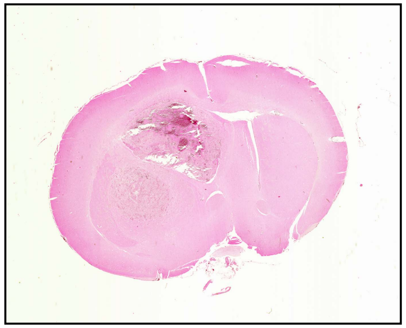
Glioblastoma multiforme (GBM) is the most common and most aggressive primary brain tumor in humans.

An animal model based on Wistar rats have been developed to study the behavior of the tumor and to monitor the effects of therapies.

Requirements for the cell tracking technique:

- to monitor the dynamic of tumour growth
- to follow the migration of tumour cells
- to understand the dynamic of metastasis spread

Section of healthy rat brain



Section of rat brain with C6 glioma 2 weeks after implantation

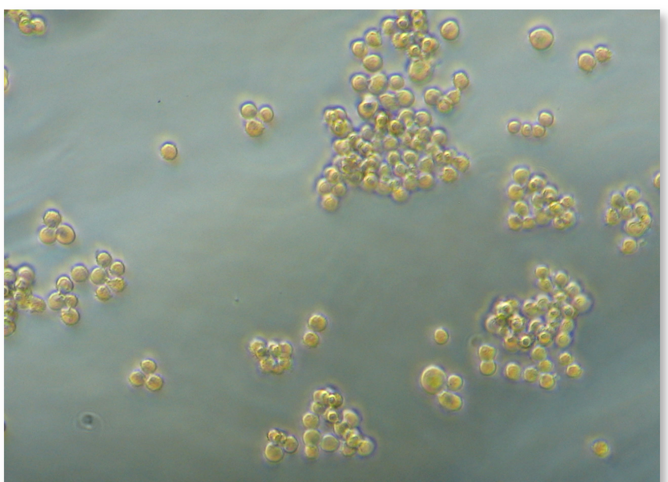
Canadian Light Source Centre canadien de rayonnement synchrotron · University of Saskatchewan · Università degli Studi di Trieste · Sir Charles Gairdner Hospital · MONASH University · elettra

Elettra Sincrotrone Trieste

C6 glioma cells were cultured and some of the cultures were exposed to colloidal Gold Nano Particles (GNP) for 22 hrs before harvest.

C6 glioma cells were implanted into the brain of adult male Wistar rats. The implantation was performed with the animals under general anesthesia. The animals were allowed to recover after the end of the implantation and were sacrificed two weeks later.

The detection of labeled cells is enhanced by the higher absorption of gold with respect to tissue and by PHC effects.



Gold Nano particles (GNP)

Our biological approach: Label tumor cells with sufficient Au nano particles (Ø ~ 50 nm)

Inert GNP bond to serum proteins

GNP are taken up by phagocytosis stored in lysosomes and are not released by exocytosis

Courtesy of E. Schultke, R.H.Menk et al.

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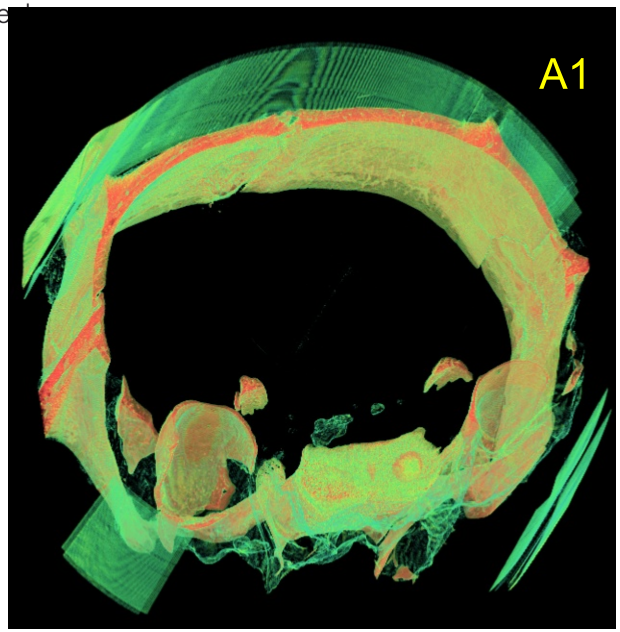
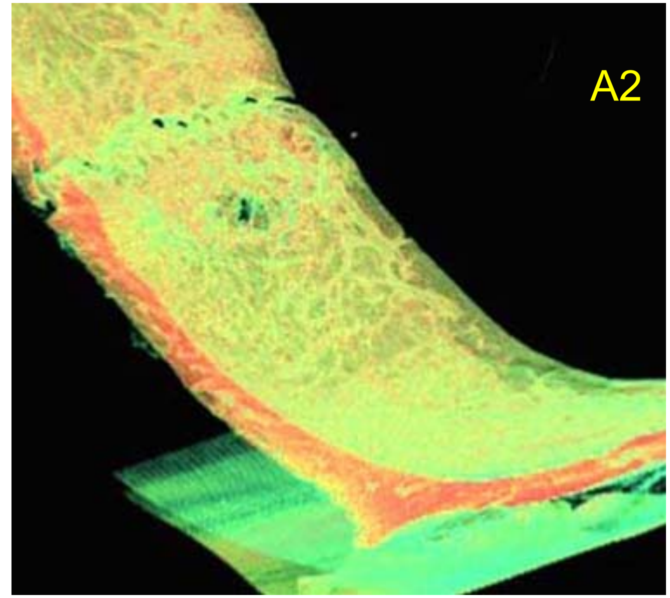
3D rendering of a 4 mm thick volume

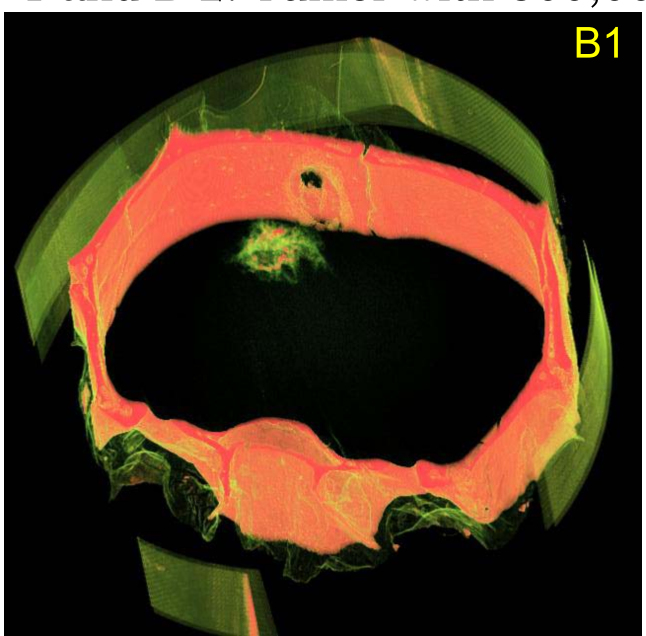
E = 24 keV
Num. proj. = 720
Pixel size =14μm

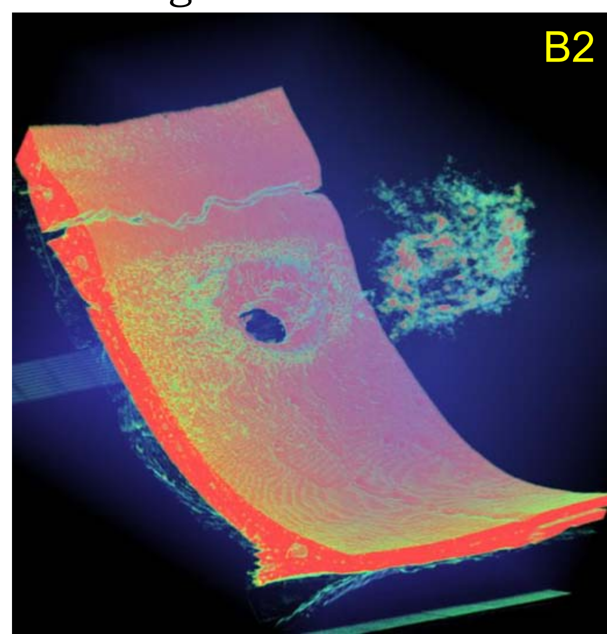
A 1 and A 2: Tumor without colloidal gold





B 1 and B 2: Tumor with 300,000 colloidal gold-loaded cells





Courtesy of E. Schultke, R.H.Menk et al.

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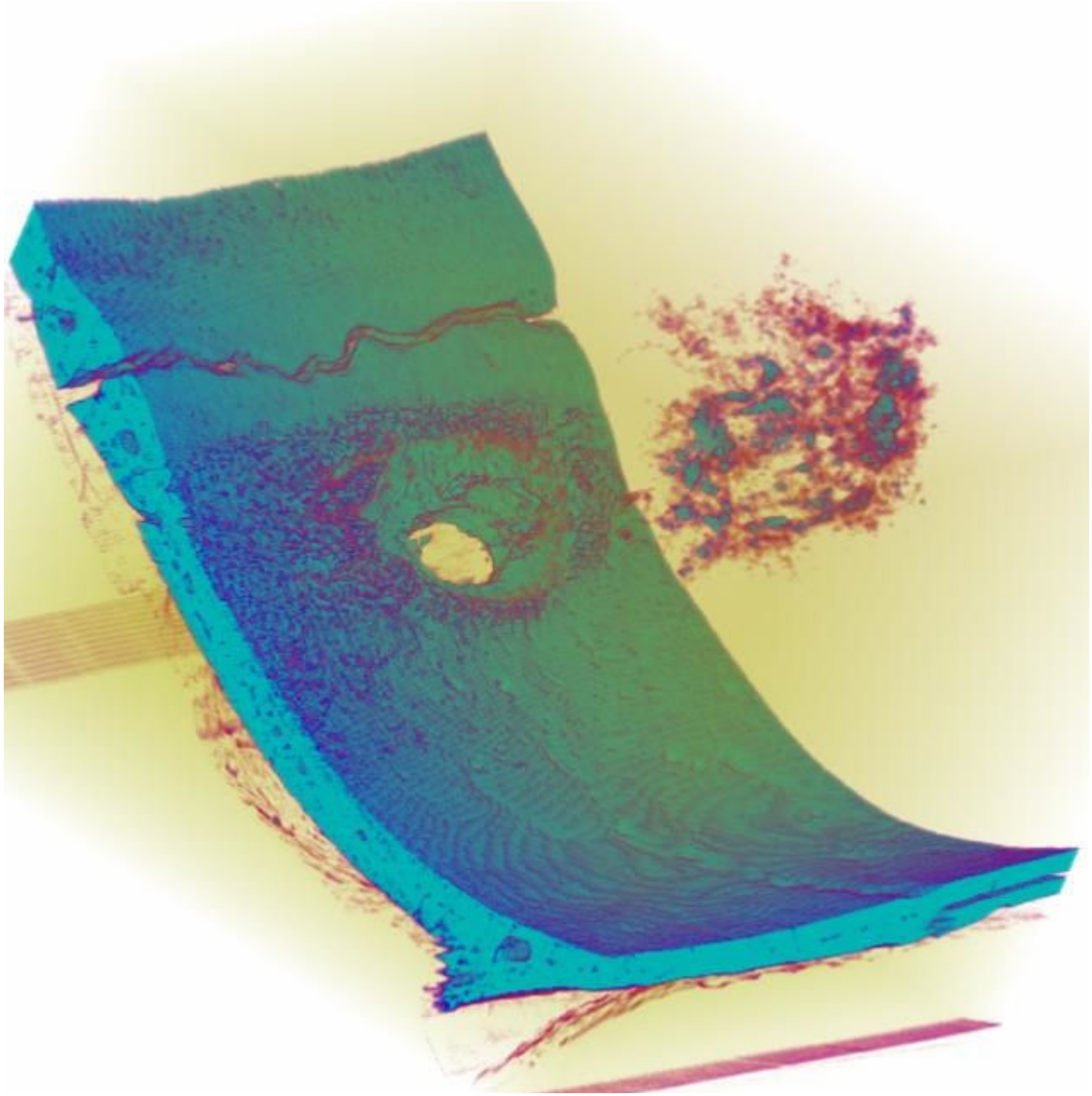
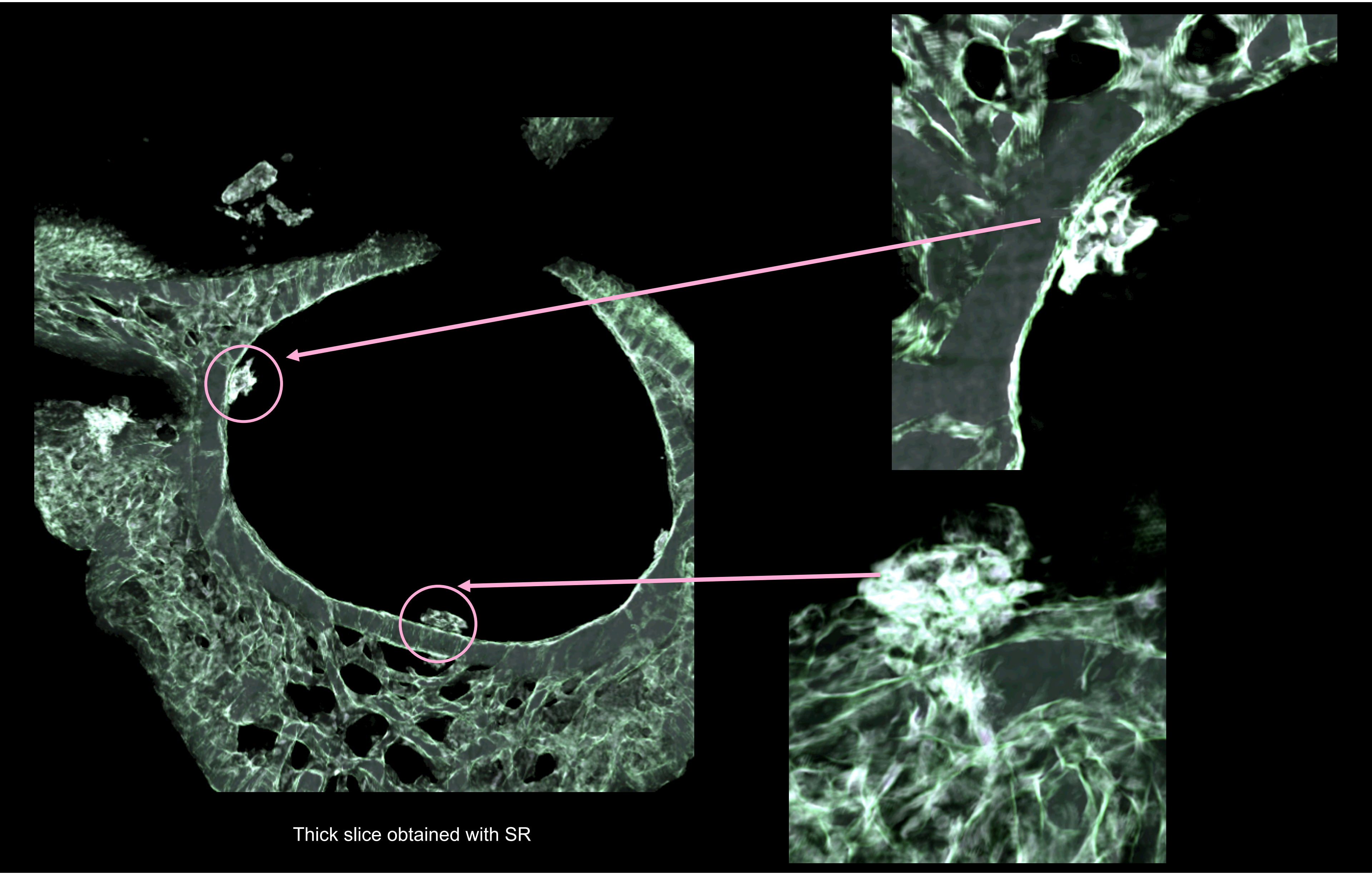


Rat 7, 100000 gold loaded C6 cells, 14 days incubation

Rat 706: Metastasis spread in the spine



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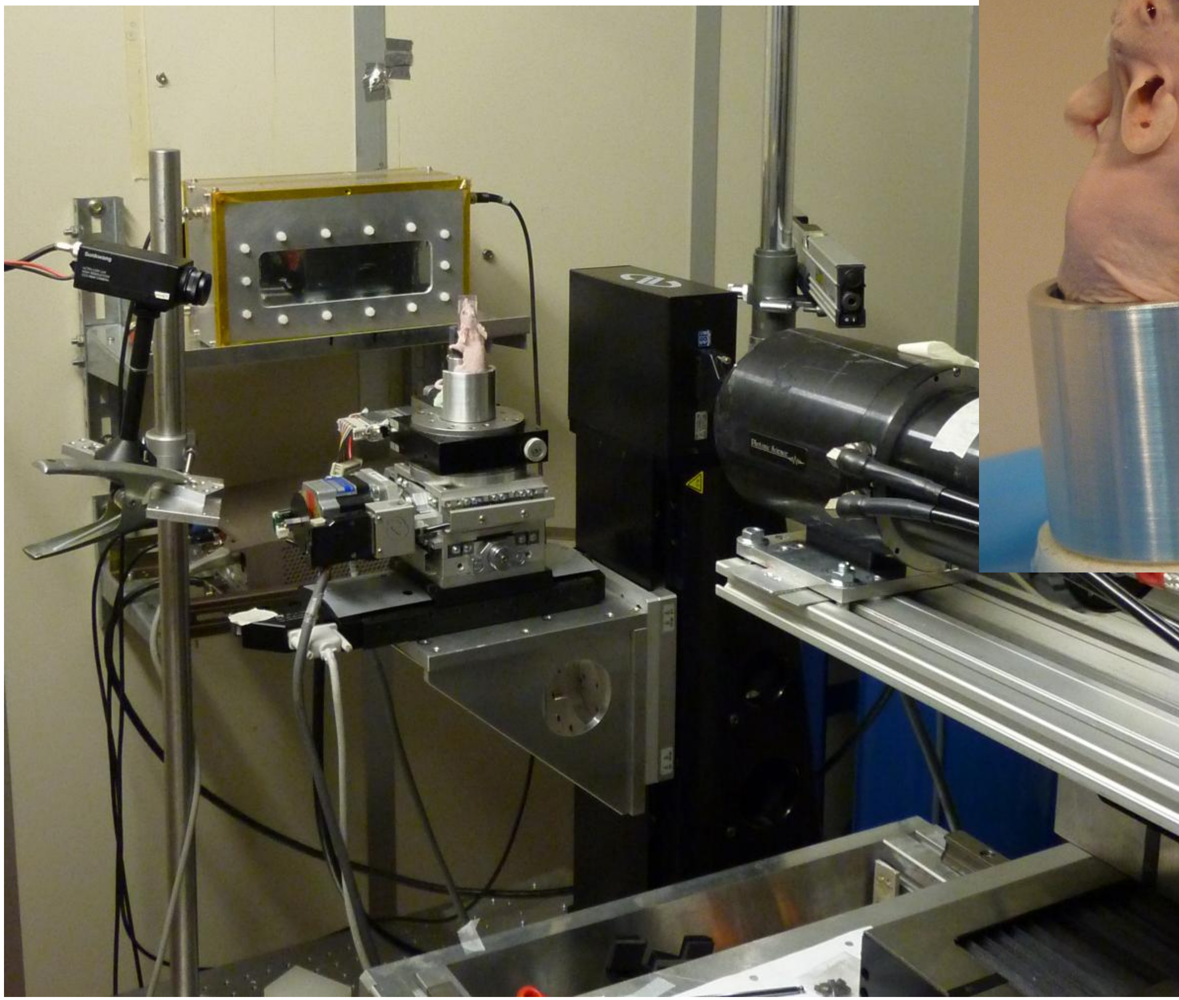
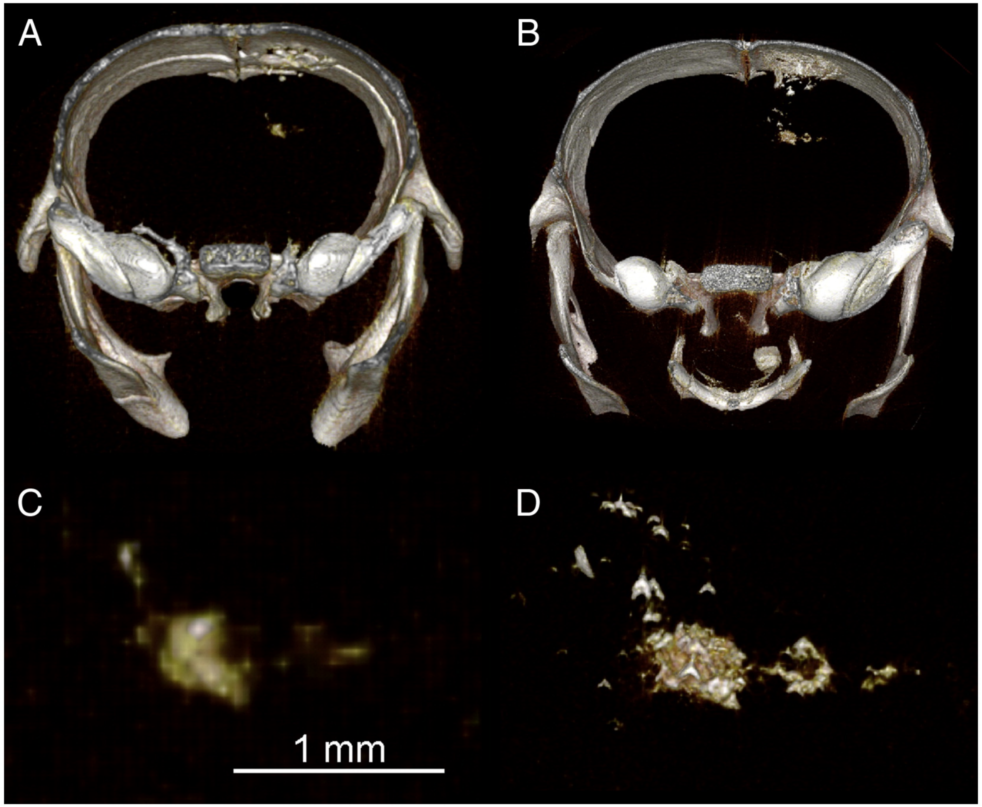


First experiment *in vivo* performed in Nov. 2010: lesions are visible also a low doses

Courtesy of A.Astolfo



- Comparison of two 3D renderings of a CT of a mouse injected with 100,000 GNP-loaded F98 cells depicts (A–C) the low x-ray dose in vivo data and (B–D) the high x-ray dose ex vivo data. The images in panels C and D are enlargements at full system resolution of the developed tumor depicted in panels A and B, respectively.

A. Astolfo et al., Nanomedicine: Nanotechnology, Biology and Medicine, Vol. 9, Issue,2013

Bone turnover in mice exposed to micro-gravity conditions

- 3 wild type (WT) mice and 3 pleiotrophin-transgenic (PTN-Tg) mice in a special payload (MDS - Mice Drawer System). The transgenic mouse strain over-expressing pleiotrophin (PTN) in bone was selected because of the PTN positive effects on bone turnover.
- **91 days in the International Space Station (ISS) by NASA: Aug. - Nov. 2009.**
- Controls:
  - mice on Earth in the same special payload MDS (*ground* mice)
  - mice in common cages (*vivarium* mice)
- SR μ-CT experiments were performed on femurs and spines
- Being non-destructive, μ-CT is very attractive for these rare specimens

University of Genova

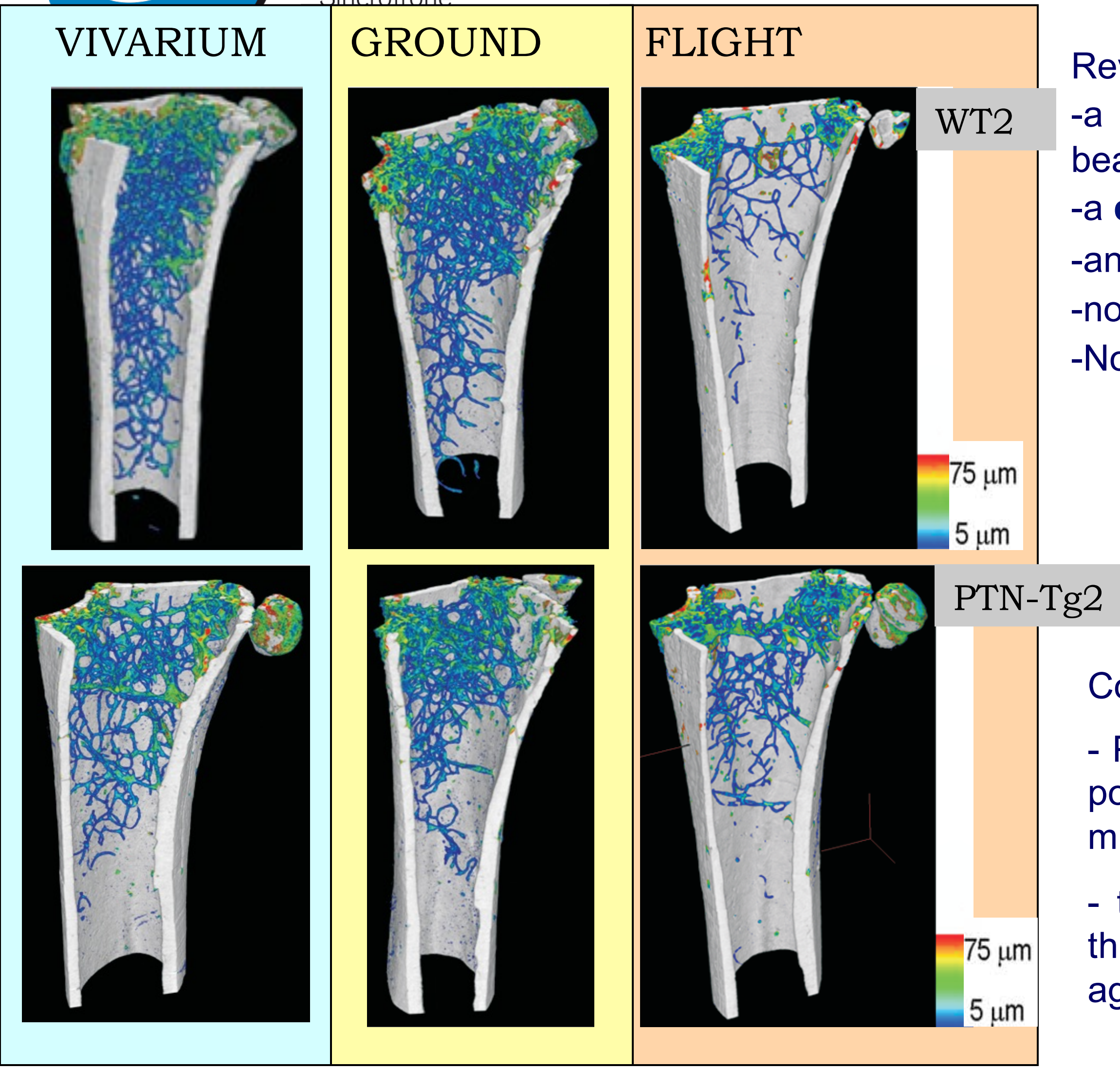
Università Politecnica delle Marche

University of Trieste – Dept. of Engineering

http://www.nasa.gov/mission_pages/station/research/experiments/MDS.html

Analysis of the microarchitecture of the trabecular bone in femurs

Elettra Sincrotrone



Revealed:

-a **bone loss** during spaceflight in the weight-bearing bones

-a **decrease** of the trabecular number

-an **increased** mean trabecular separation

-no significant change in trabecular thickness.

-No effects on not weight-bearing bones.

E = 19 keV
Pixel size = 9 mm
N. Proj = 900
Distance sample-ccd= 3 cm

Comparison WT vs.PTN-Tg2:

- PTN-Tg exposed to normal gravity has a poorer trabecular organization than WT mice

- the expression of the PTN gene during the flight resulted in some protection against microgravity's negative effects.

Color map represents bone trabecular thickness distribution in the femur (red = 75 µm, blue = 5 µm)

S. Tavella et al "*Bone Turnover in Wild Type and Pleiotrophin-Transgenic Mice Housed for Three Months in the International Space Station (ISS)*", PlosONE, March 2012.

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Final considerations

It is worldwide recognized phase contrast imaging represents a revolutionary tool in bio-medical imaging

Besides PBI and ABI, in the last years, other phase sensitive techniques, like:

- Crystal and grating based Interferometry;
- Coded aperture methods,

have been developed, offering new opportunities for soft tissues imaging

Many efforts are directed to export these techniques to laboratory and clinic environment, either developing innovative experimental setup, and new generation sources (μ-focus, compact synchrotrons, etc)

Veli Rat (Dugj Otok), view from the lighthouse (August 2016)

giuliana.tromba@elettra.eu

Thanks for your attention