Synchrotron Biomedical Imaging –
Some Neuroscience Applications

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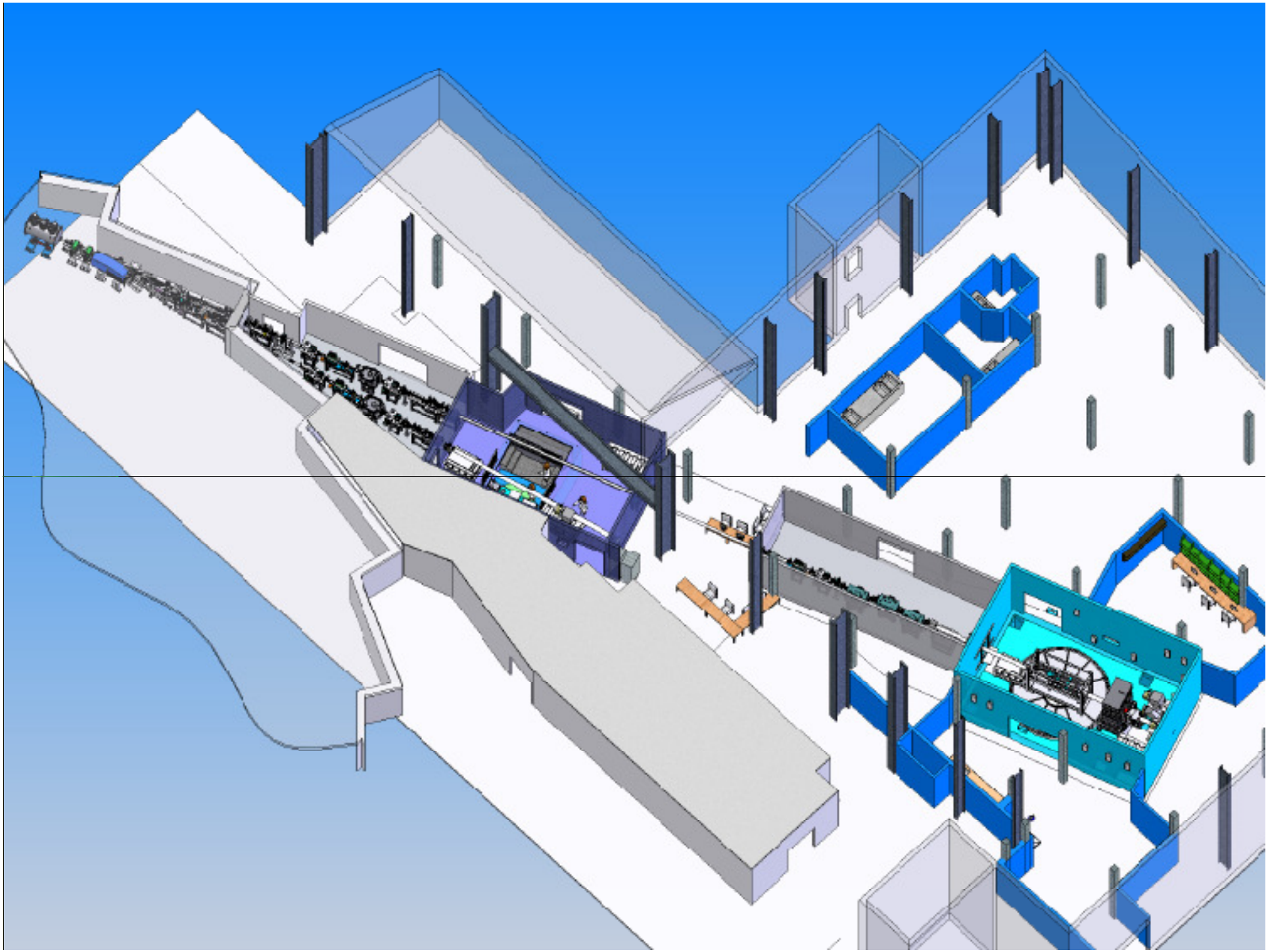
Anatomy & Cell Biology, University of Saskatchewan

University of Missouri

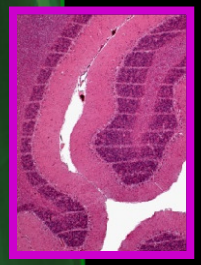
Life Sciences Summit

8-9 March 2010

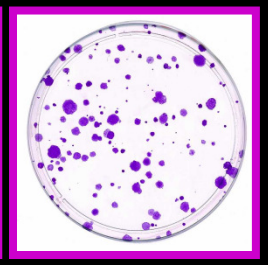
BioMedical Imaging & Therapy Facility



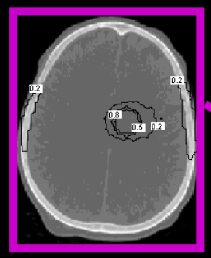
BioMedical Research Programs



MRT



PAT

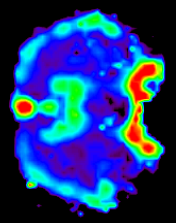


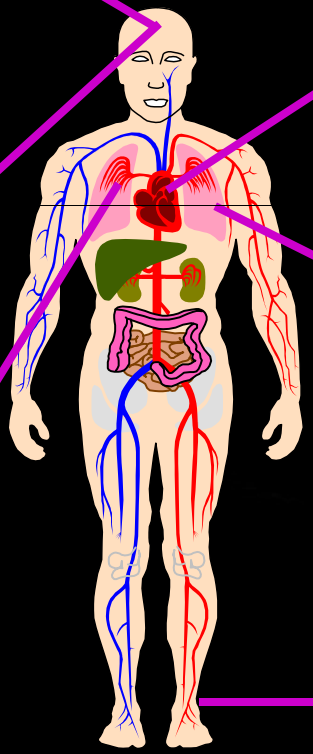
Tomo

RADIATION THERAPY

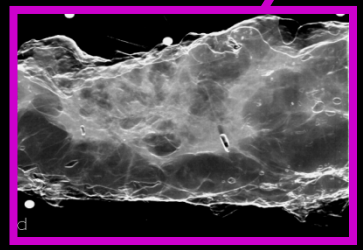
ANGIOGRAPHY

COMPUTED TOMOGRAPHY

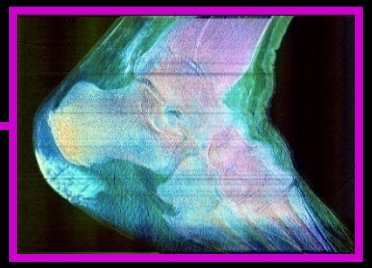




FUNCTIONAL LUNG IMAGING



MAMMOGRAPHY



CARTILAGE

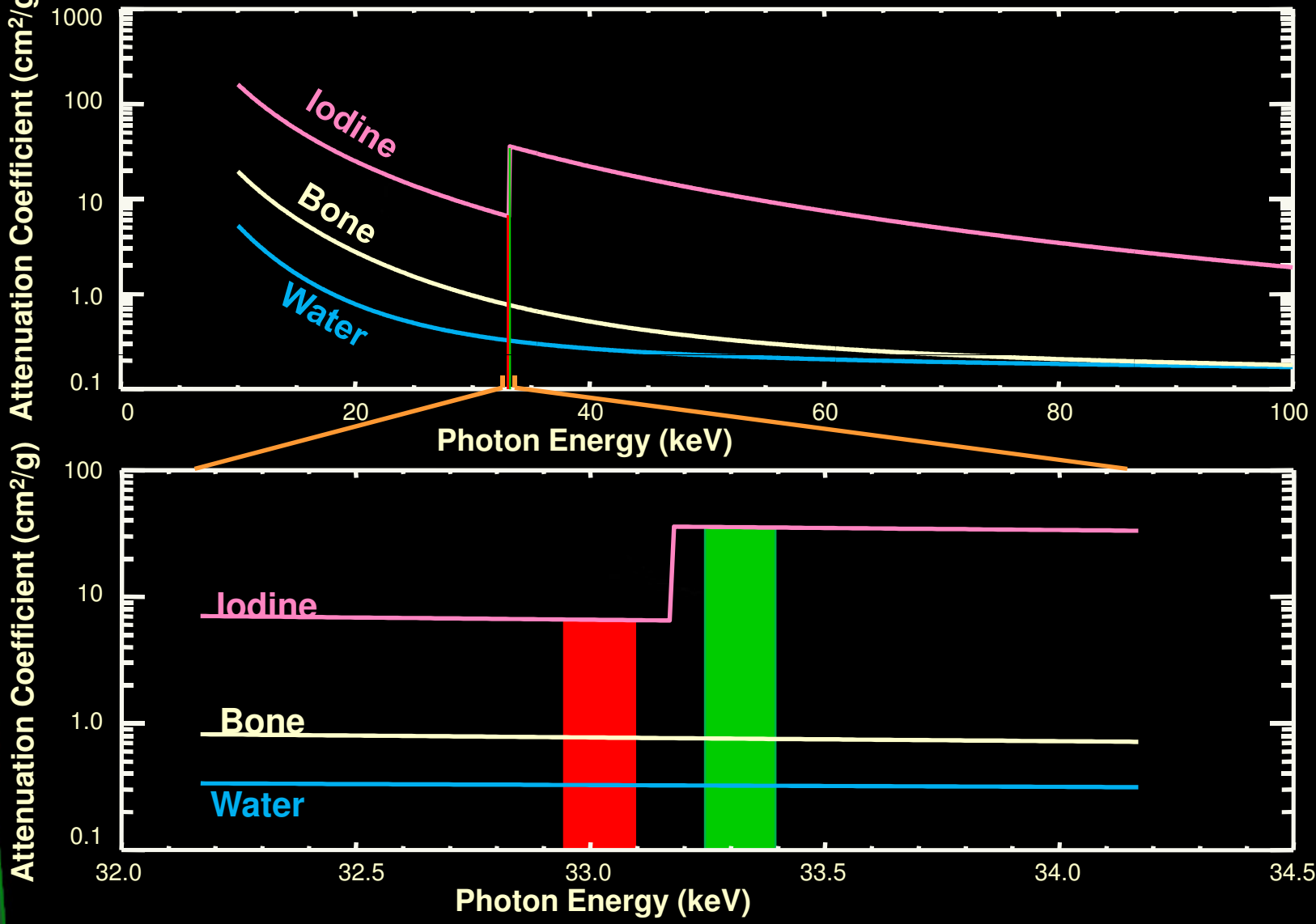
Technology – Synchrotron Biomedical Imaging Methods

Projection and CT

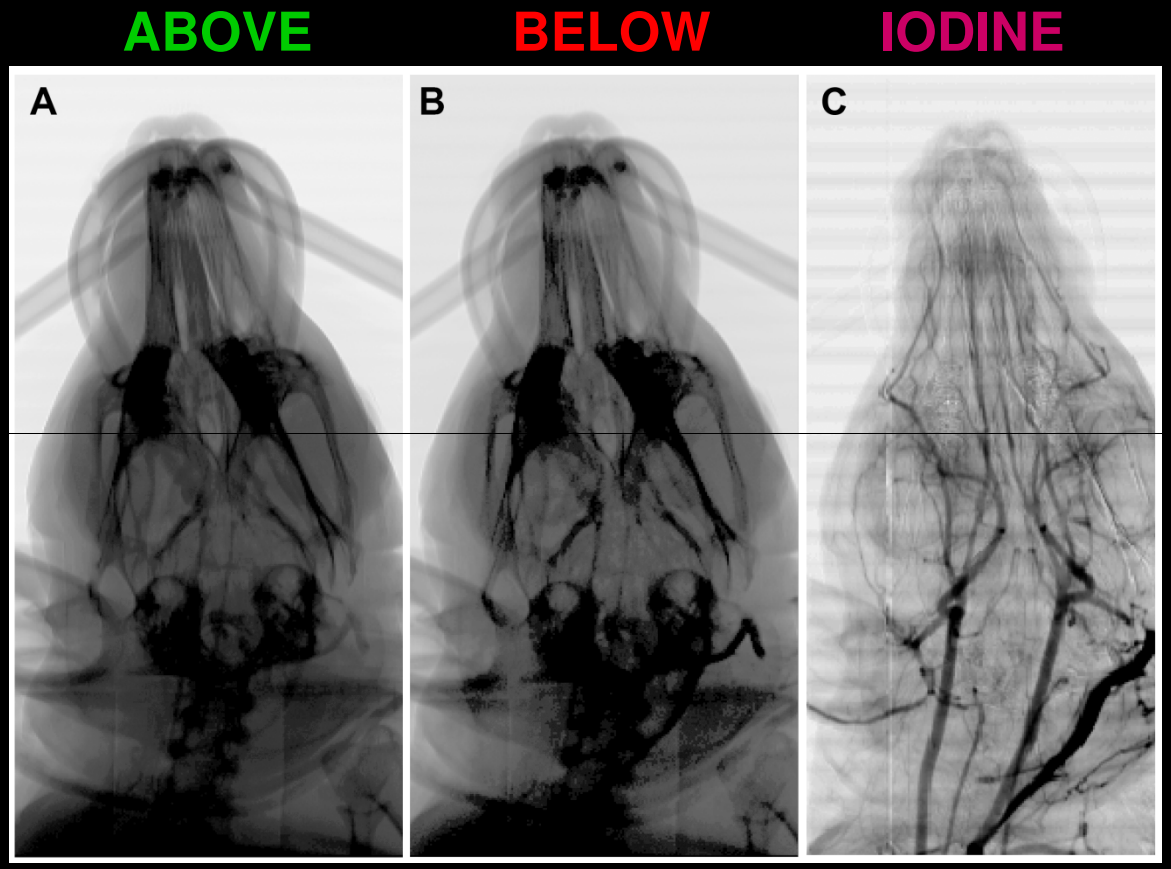
in vivo tissues

- Absorption Imaging
  - Uses tunability
- K-edge Subtraction
  - Uses tunability
- Fluorescence Imaging
  - Uses tunability and brightness
- Phase Contrast Imaging
  - Uses high source brightness (small source size)
- Analyzer Based Imaging / Diffraction Enhanced Imaging / Multiple Image Radiography
  - Uses high source brightness (high intensity)
- High Resolution Imaging / Microtomography
  - Uses high source brightness (intensity & source size)
  - Can apply most of above imaging methods

K-Edge Subtraction – Iodine Absorption



K-Edge Subtraction Images



Images acquired below (a) and above (b) the K-edge of iodine, both without easily discernible contrast in the cerebral arteries. The subtracted image (c), however, shows very good contrast in the cerebral arteries.

Courtesy Michael Kelly, MD

K-Edge Subtraction
Best Views - ID17 Imaging Facility ESRF

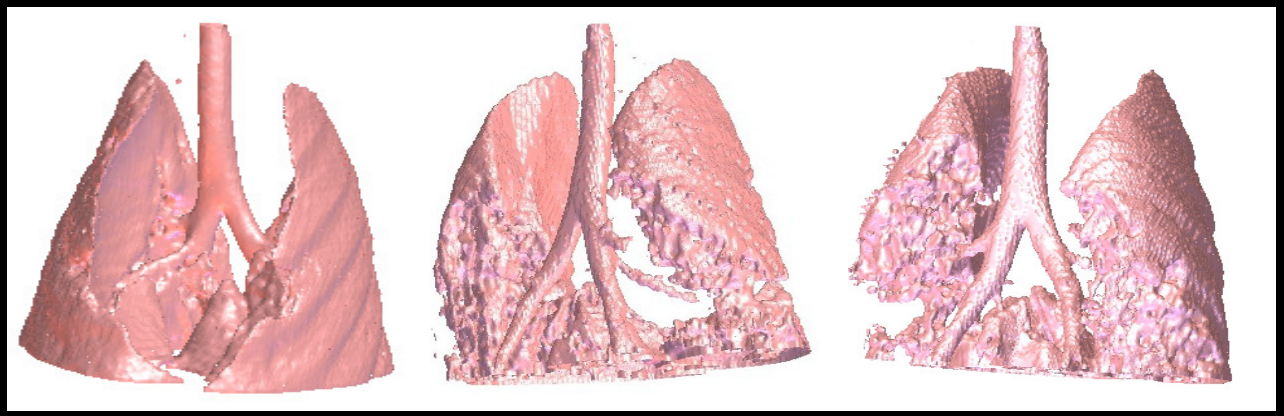
Courtesy W. Thomlinson

K-Edge Subtraction – Cardiopulmonary Physiology and Perfusion Studies

Xe perfusion studies of rabbit model system under influence of histamine

Post-Histamine

Normal Lung | 8 min | 30 min



Spiral CT Xe KES

Bayat et al. 2003; ESRF ID17

Conventional Digital Subtraction and Synchrotron K-Edge Subtraction

Conventional
Digital Subtraction Angiography
-adult rabbit

Synchrotron
K-Edge Subtraction Angiography
- rat

Angiogram of the Circle of Willis in antero-posterior projection after intra-arterial injection of iodinated contrast agent into the left carotid artery

Digital subtraction image in antero-posterior projection after intravenous injection of iodinated contrast agent

K-Edge Subtraction images of intracerebral arteries in antero-posterior projection (a): early filling phase (b): late filling phase.

Courtesy Michael Kelly, MD

K-Edge Subtraction Computed Tomography

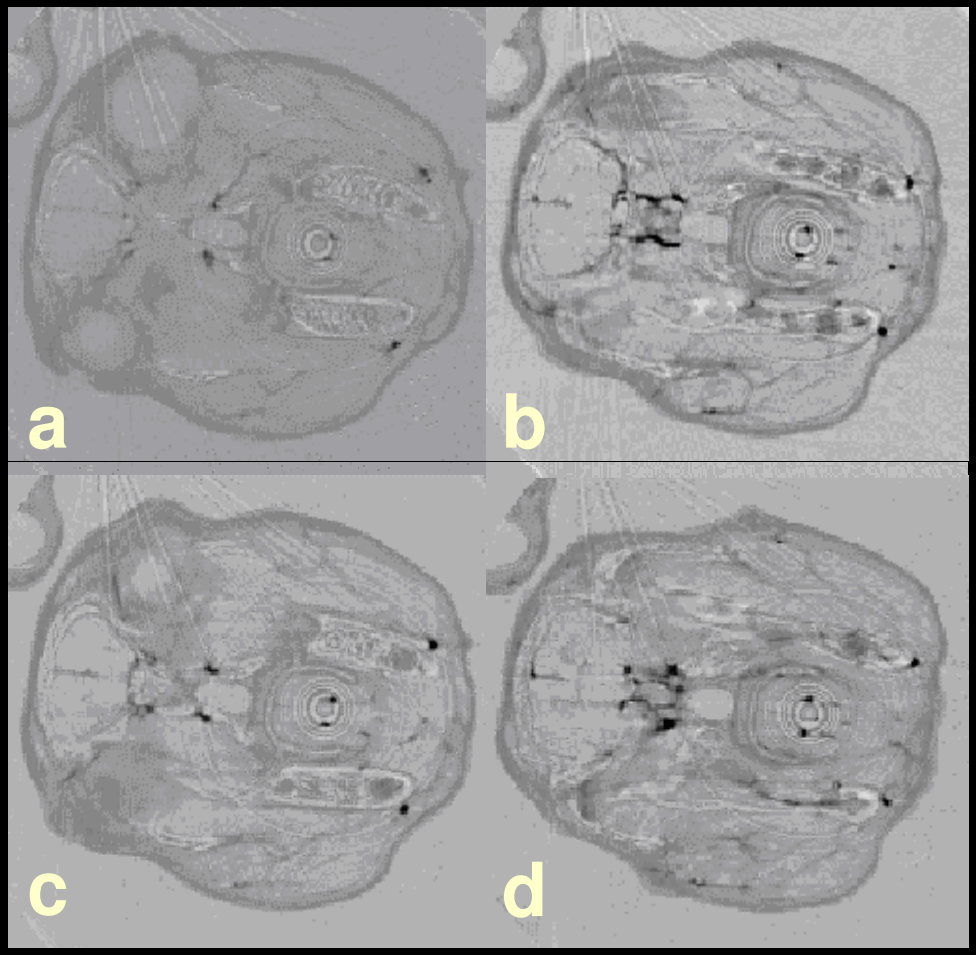
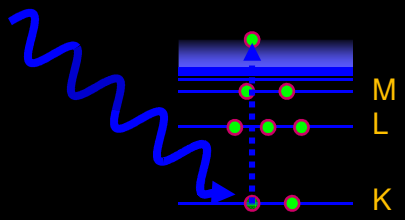


Image series acquired with Ge detector in tomography mode; helical CT scan; pixel size 350 x 350 µm; Iomeprol® 1 mL /sec for 3 seconds (total volume of 3 mL). Images were acquired 3 sec (a), 4 sec (b), 5 sec (c) and 6 sec (d) after injection.

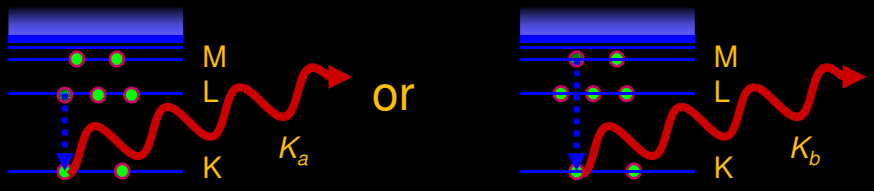
Courtesy Michael Kelly, MD

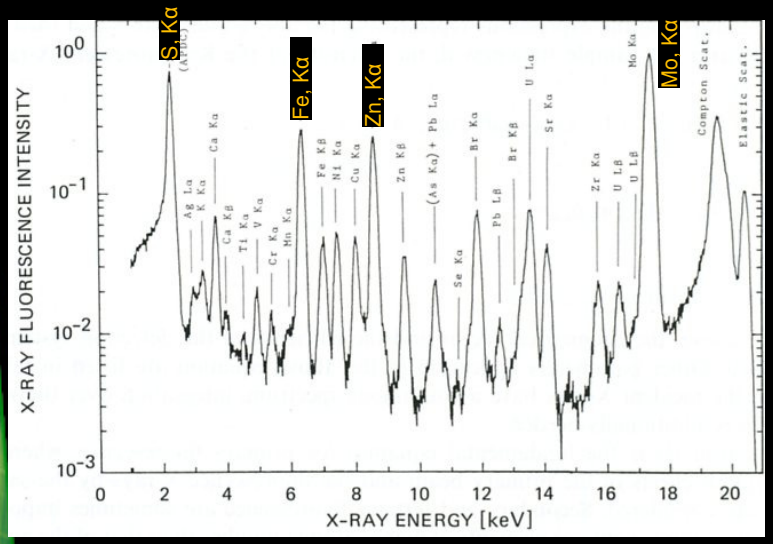
Fluorescence Imaging

Photoelectric Absorption



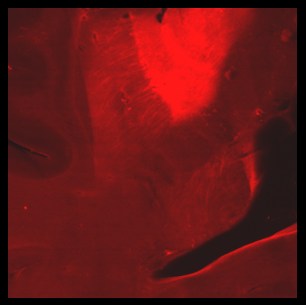
Fluorescent X-ray emission



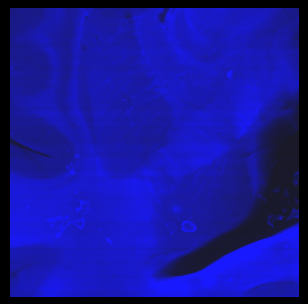


Courtesy M. Ishikawa

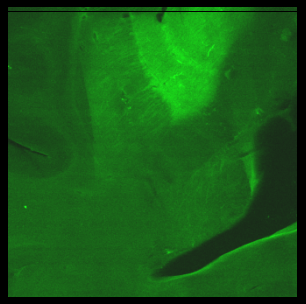
X-ray Fluorescence spectrum of preconcentrated sea water



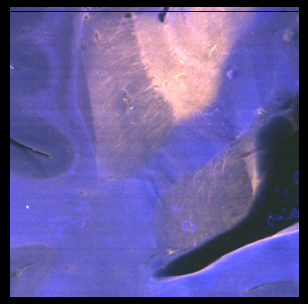
Iron



Zinc



Copper

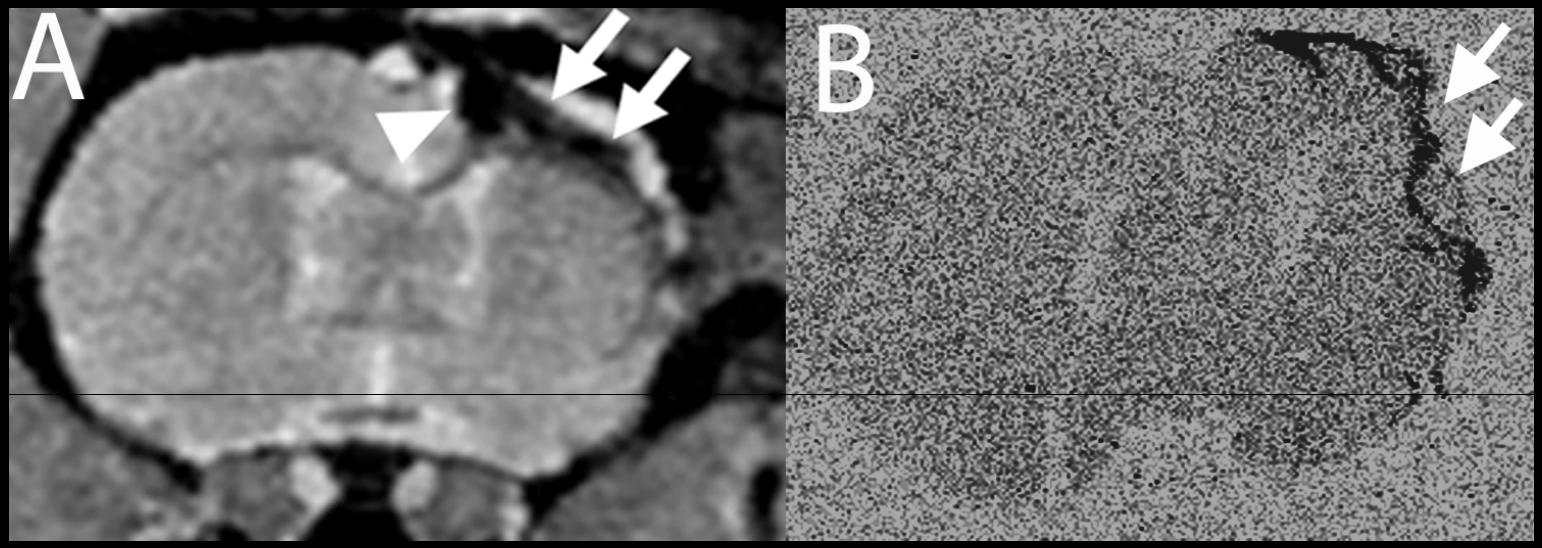


Fused color image

Fluorescence images of a human brain with Parkinsons disease

Courtesy Helen Nichol

Synchrotron Rapid Scanning X-ray Fluorescence Imaging and MRI



A. ex vivo whole brain Coronal T2 weighted spin echo MRI performed 5 weeks after implantation of SPIO labeled hCNS-SCns in a stroked rat brain. The site of implantation is denoted by the arrowhead. The arrows depict the SPIO that represents the migration of the stem cells to the site of prior infarction. B. RS-XFS performed in the same animal after sacrifice and coronal sectioning. The arrowheads denote the detection of iron. This is noted to correlate to the same location as seen in the MRI in A. Although the image is more pixilated better localization of the SPIO is observed.

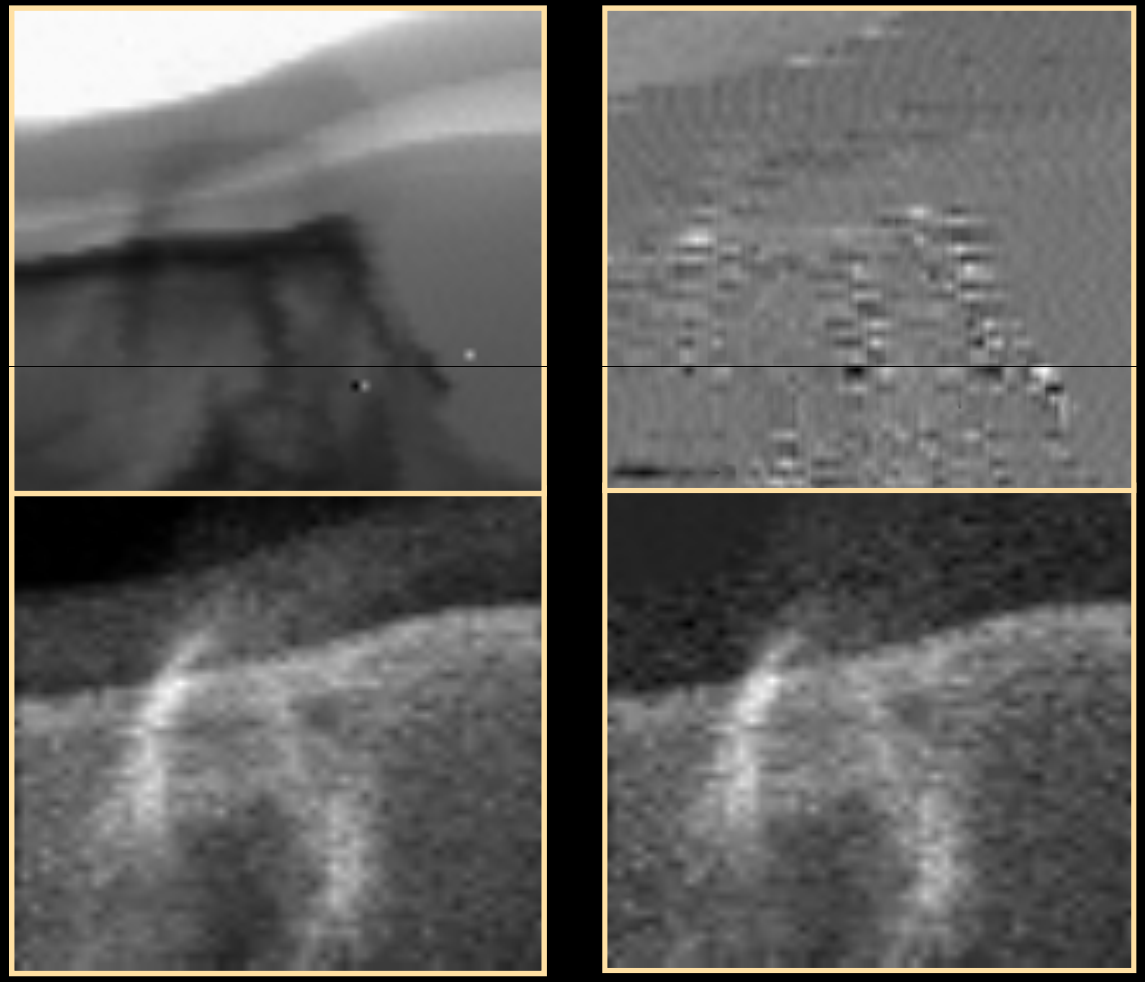
Courtesy Michael Kelly, MD

K-Edge Subtraction & Fluorescence Subtraction Imaging – Gene Expression Imaging

Rat 2, Lateral View, no flattener

KES

FSI



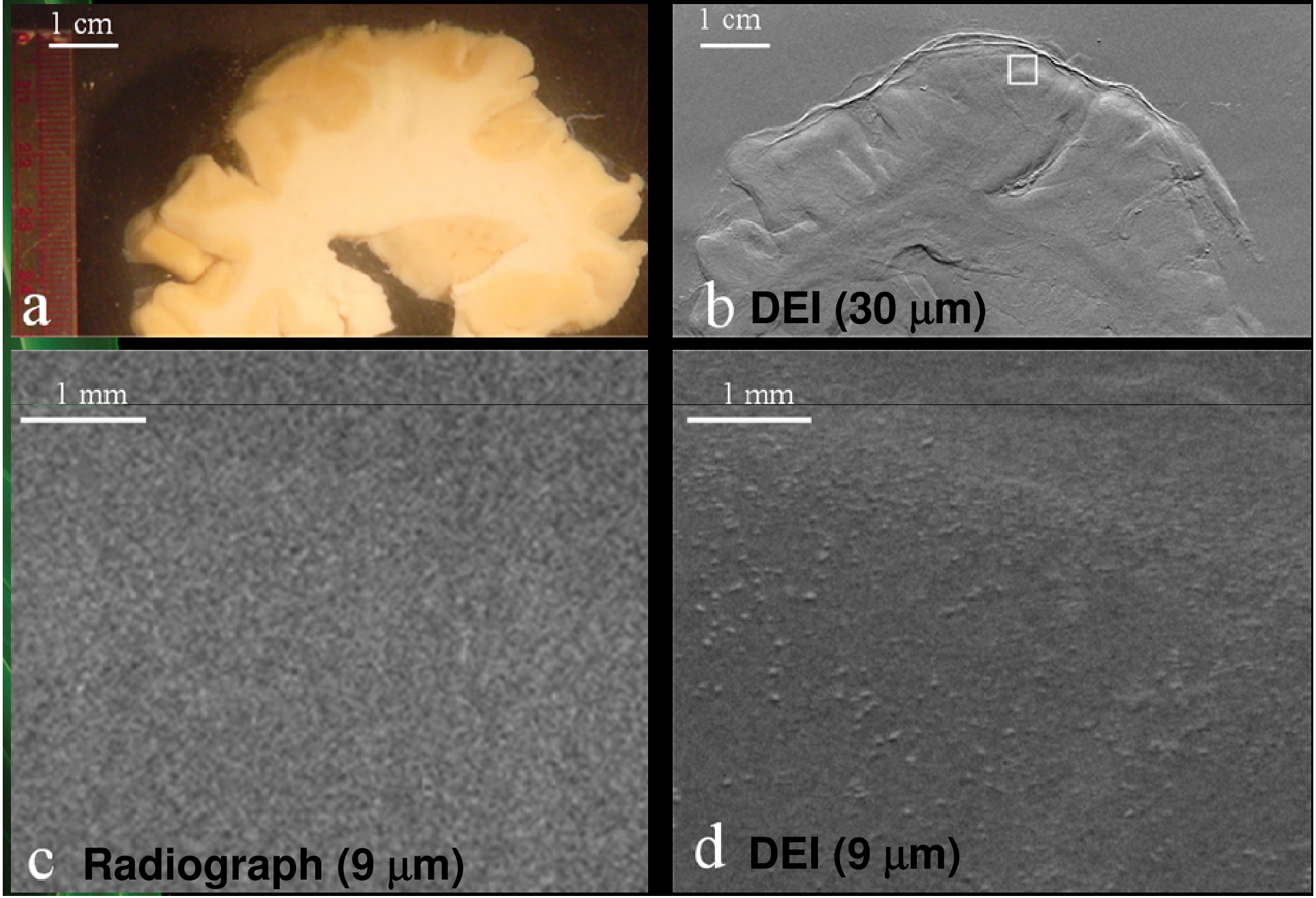
High energy image (hraw)

Iodine image ($\rho_c t_c$)

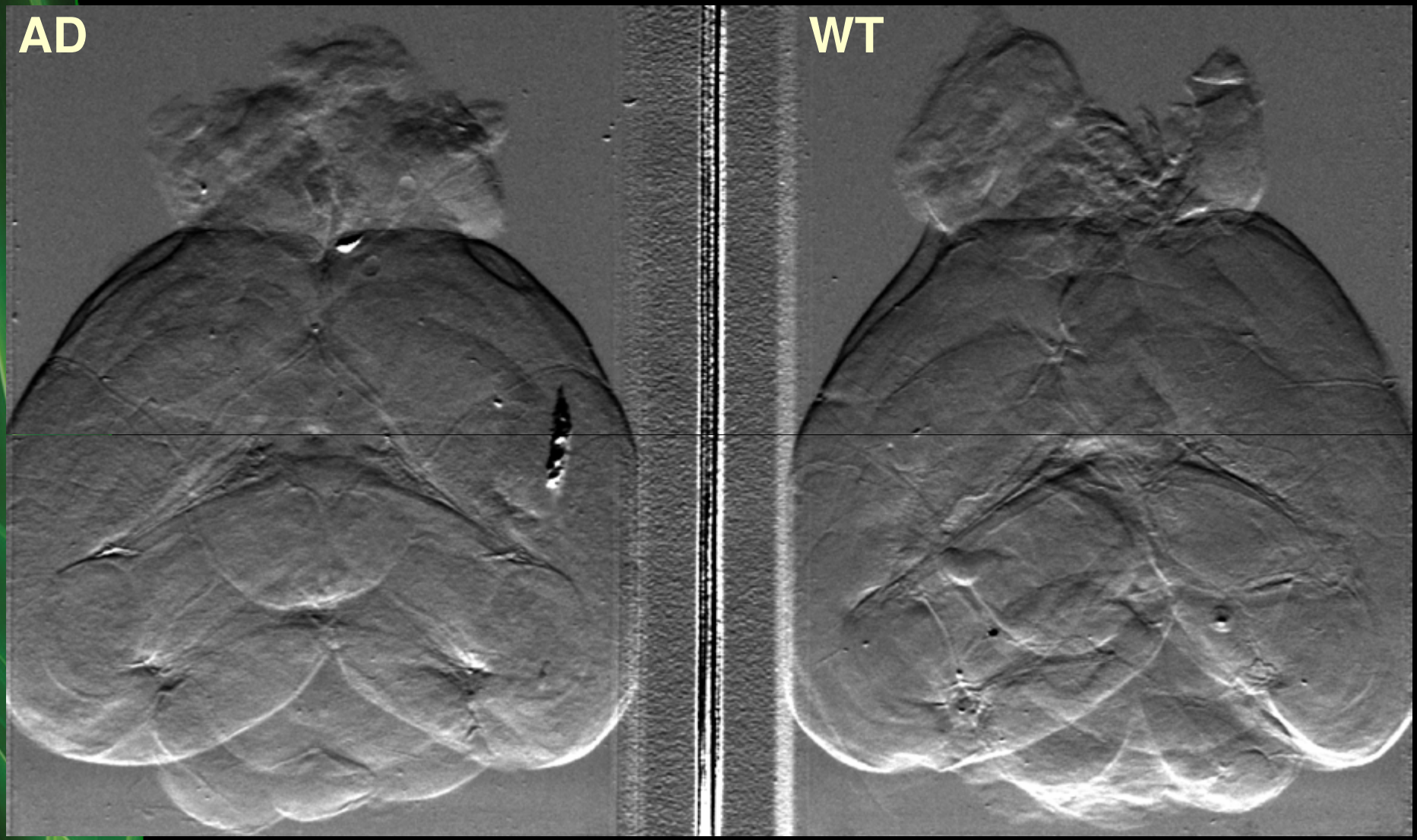
1630hrs, Mar 7th,
Above edge:
scalars070,
scalarDataVariable070,
fluorescence: animal09
Below edge:
scalars071,
scalarDataVariable071,
fluorescence: animal10

Data from HXMA Beamline Canadian Light Source

Alzheimer's Plaques in Human Brain

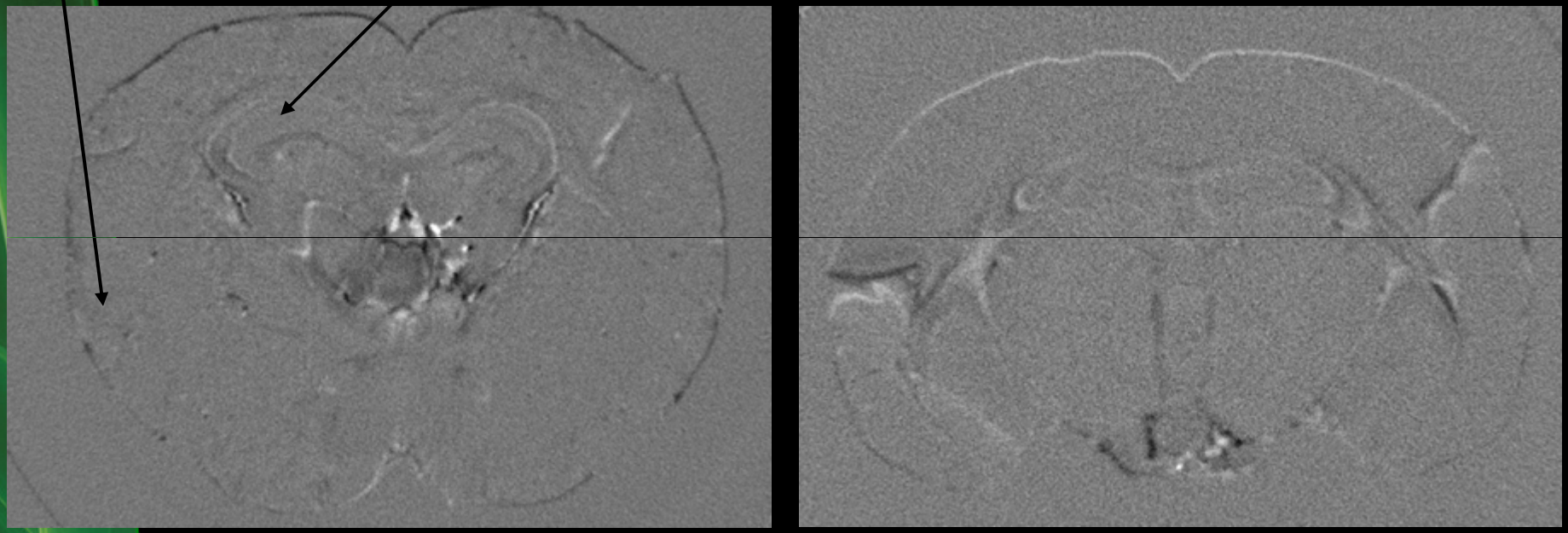


Planar in Mouse Models

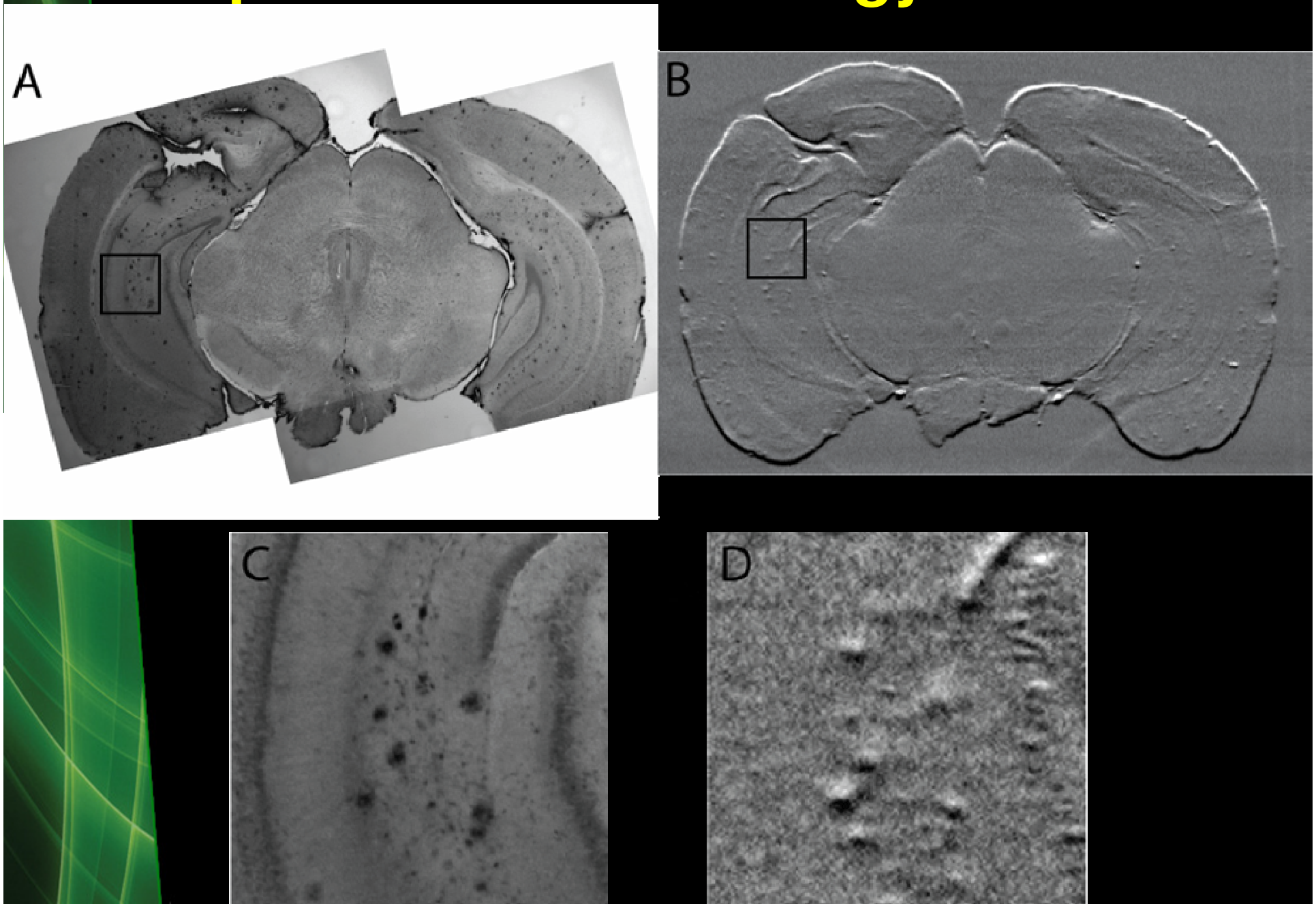


Brai
matc

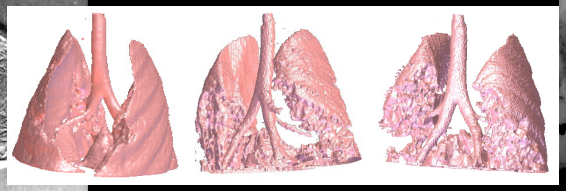
CT imaging of AD model mouse brains

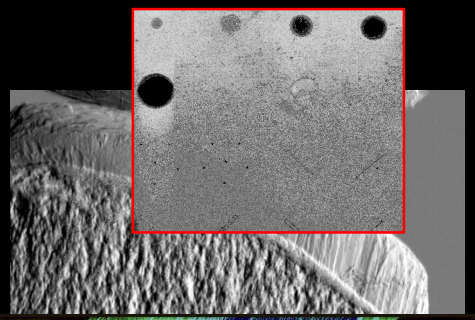


Comparison with Histology



THE END – Questions?



You can contact us at
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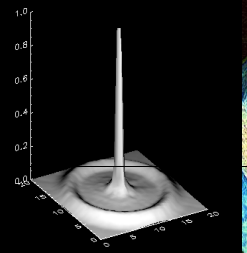
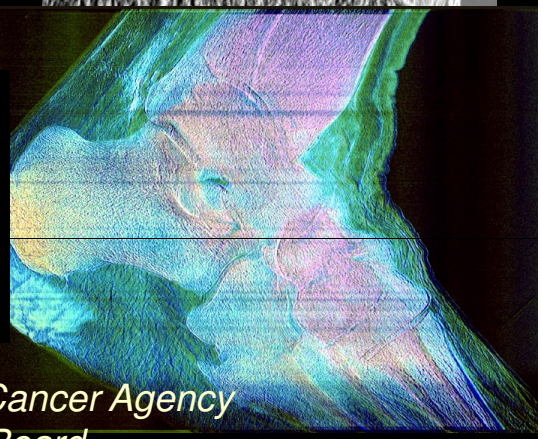
tomasz.wysokinski@lightsource.ca

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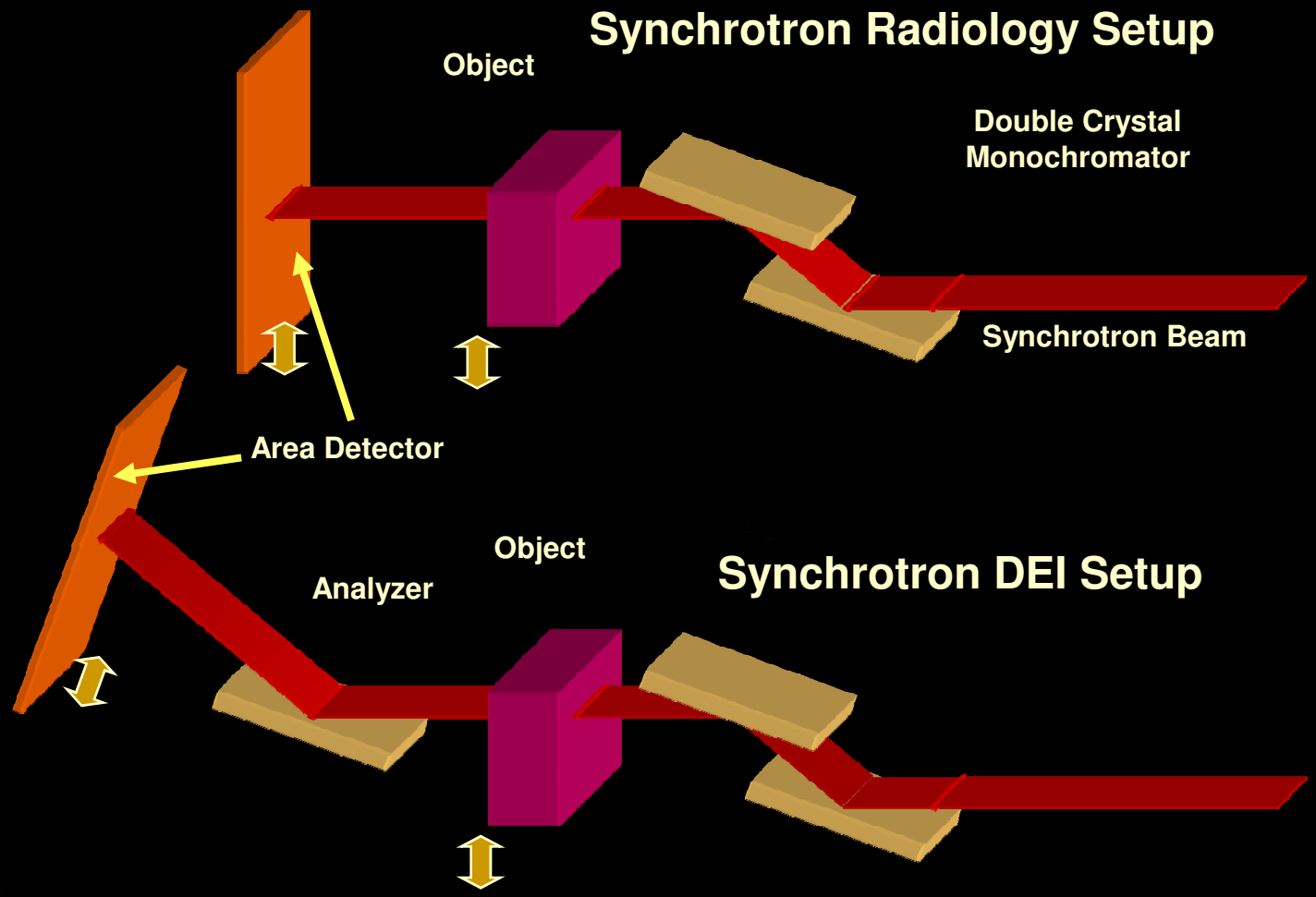
SK Health Research Foundation
Saskatoon Health Region
Royal Univ. Hospital Foundation
City Hospital Foundation
Regina Qu'Apelle Health Region
Hospitals of Regina Foundation
Canadian Cancer Society - SK
Saskatchewan Cancer Agency
Alberta Cancer Board
Breast Cancer Society of Canada
University of Saskatchewan -
College of Medicine
Western College of Veterinary Medicine
College of Kinesiology
Department of Psychology
College of Nursing
College of Dentistry
College of Agriculture

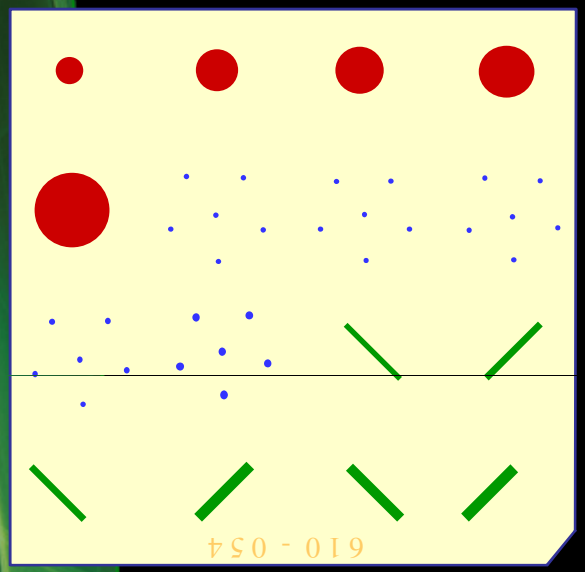
Synchrotron Radiography and Setup for Diffraction Enhanced Imaging (DEI) or Analyzer Based Imaging (ABI) or Multiple Image Radiography (MIR)



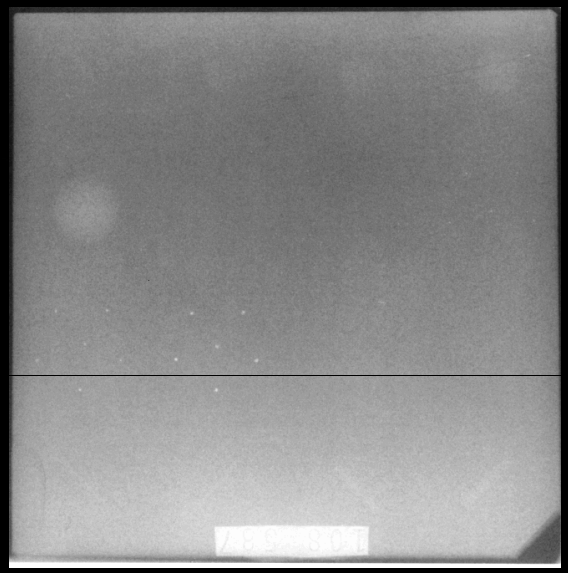
BMIT Lives!!

Mouse @ 41keV ~2mGy exposure 17 December 2008

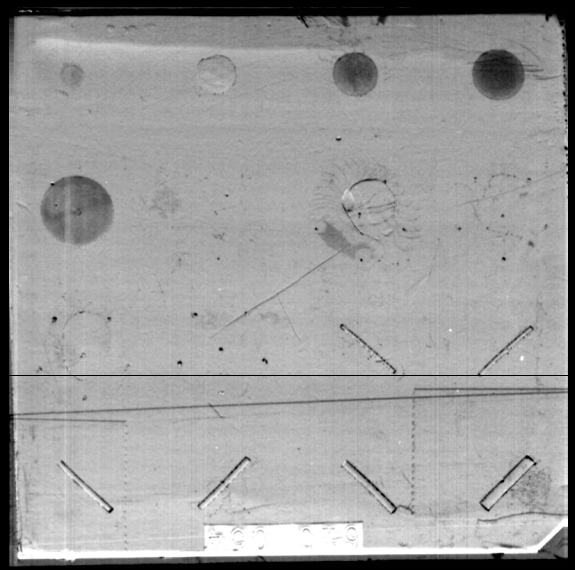
Comparison - Conventional and Diffraction Enhanced X-ray Imaging



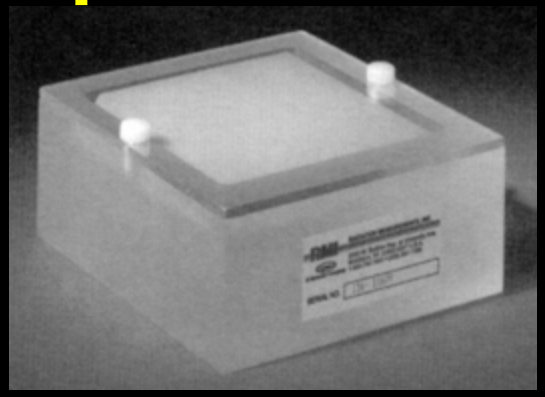
Map



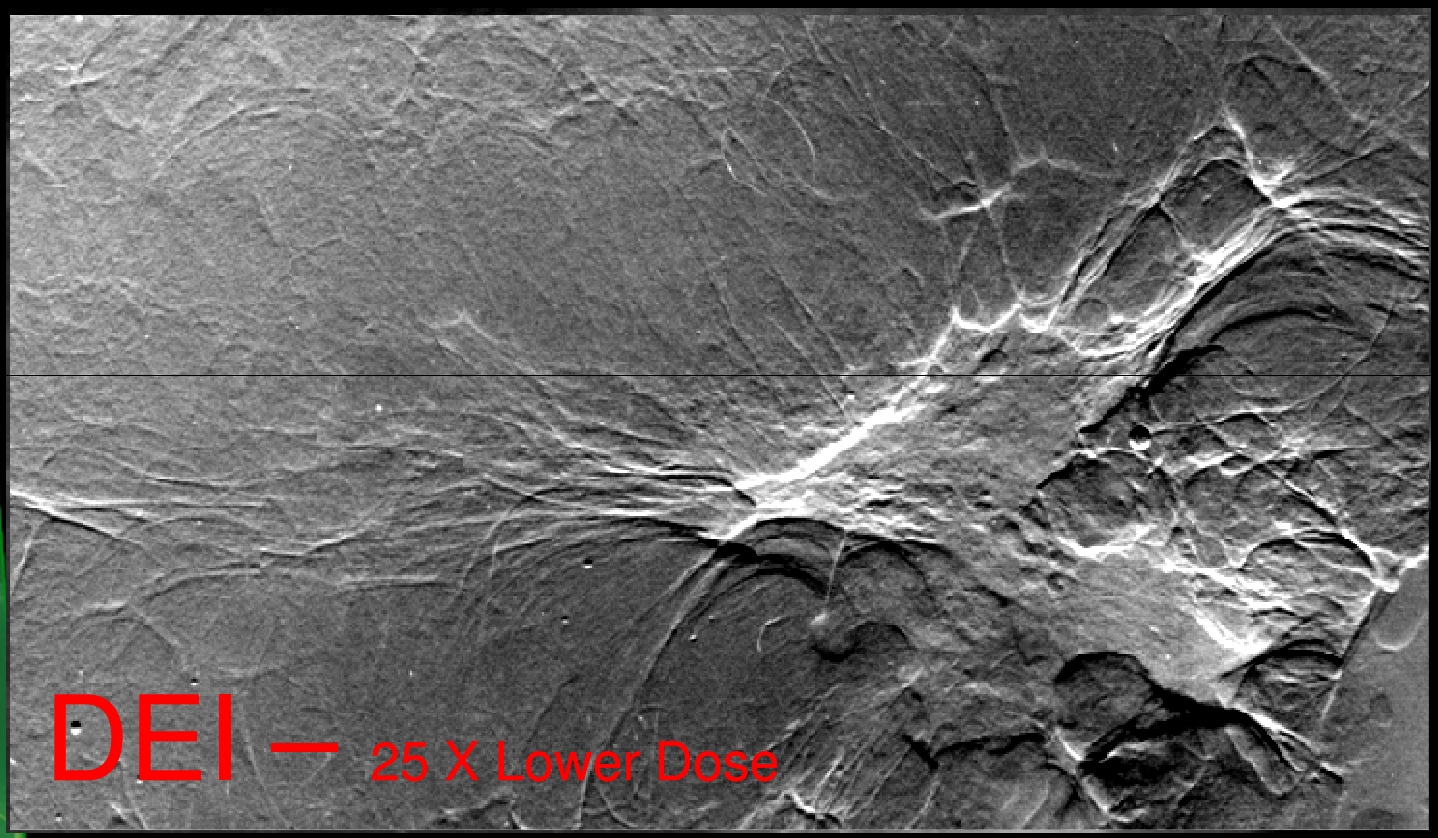
Conventional



DEI



Diffraction Enhanced Imaging – Mammography – mastectomy specimen

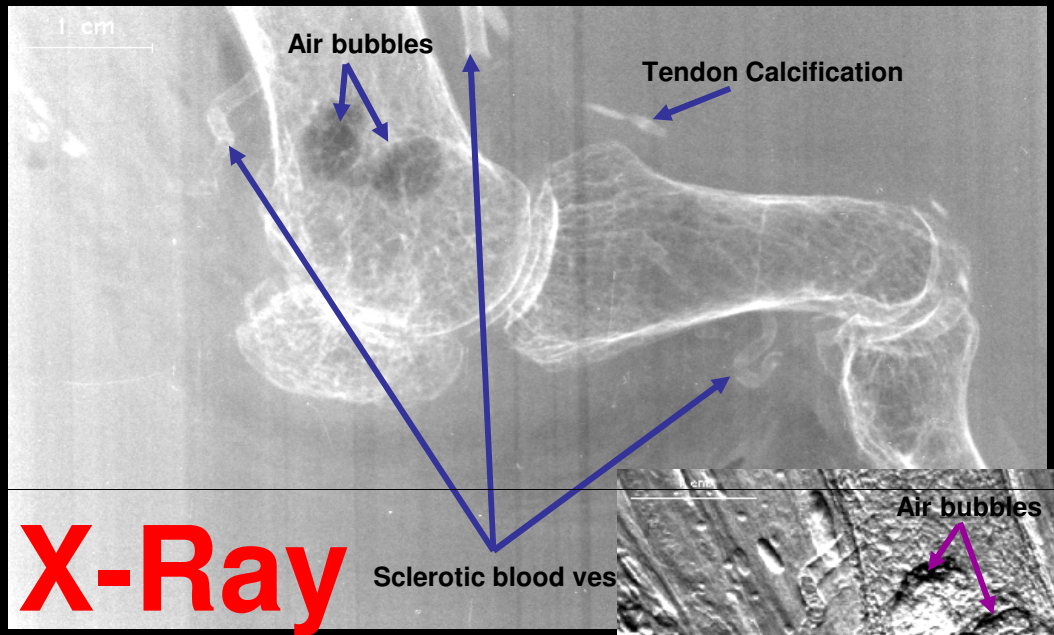


Multiple Image Radiography-
projection image of a foot

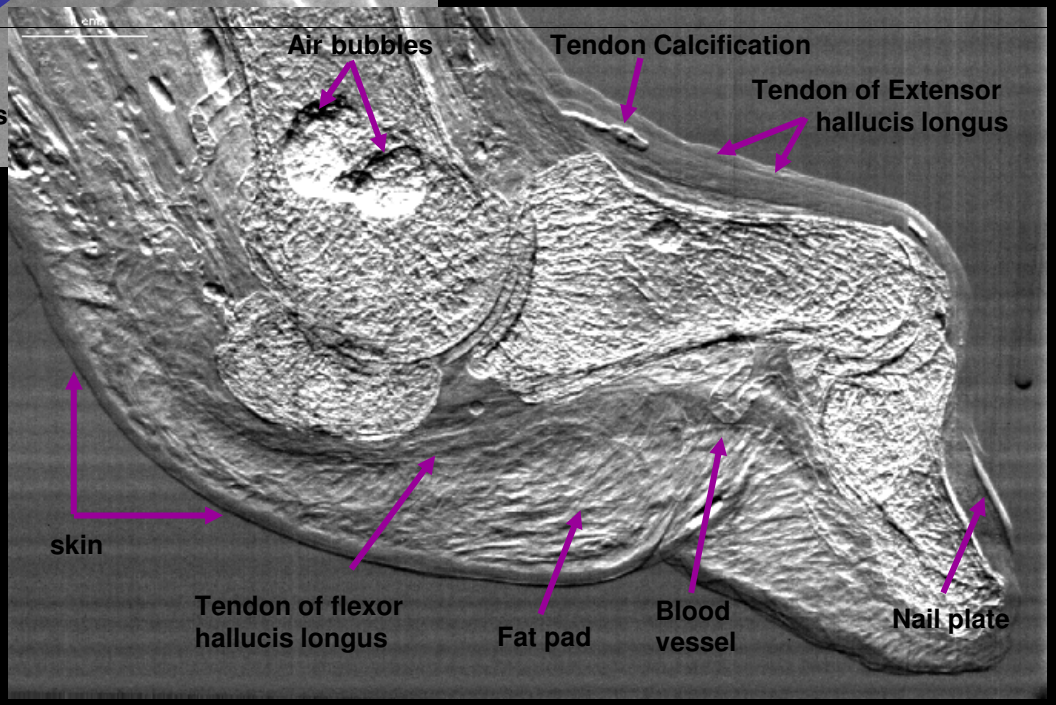
Muehleman, Jun (Rush), Brankov, Wernick, Chapman(IIT);
Zhong(BNL)

Red – Absorption
Blue – Refraction
Green – Extinction

DEI of Toes

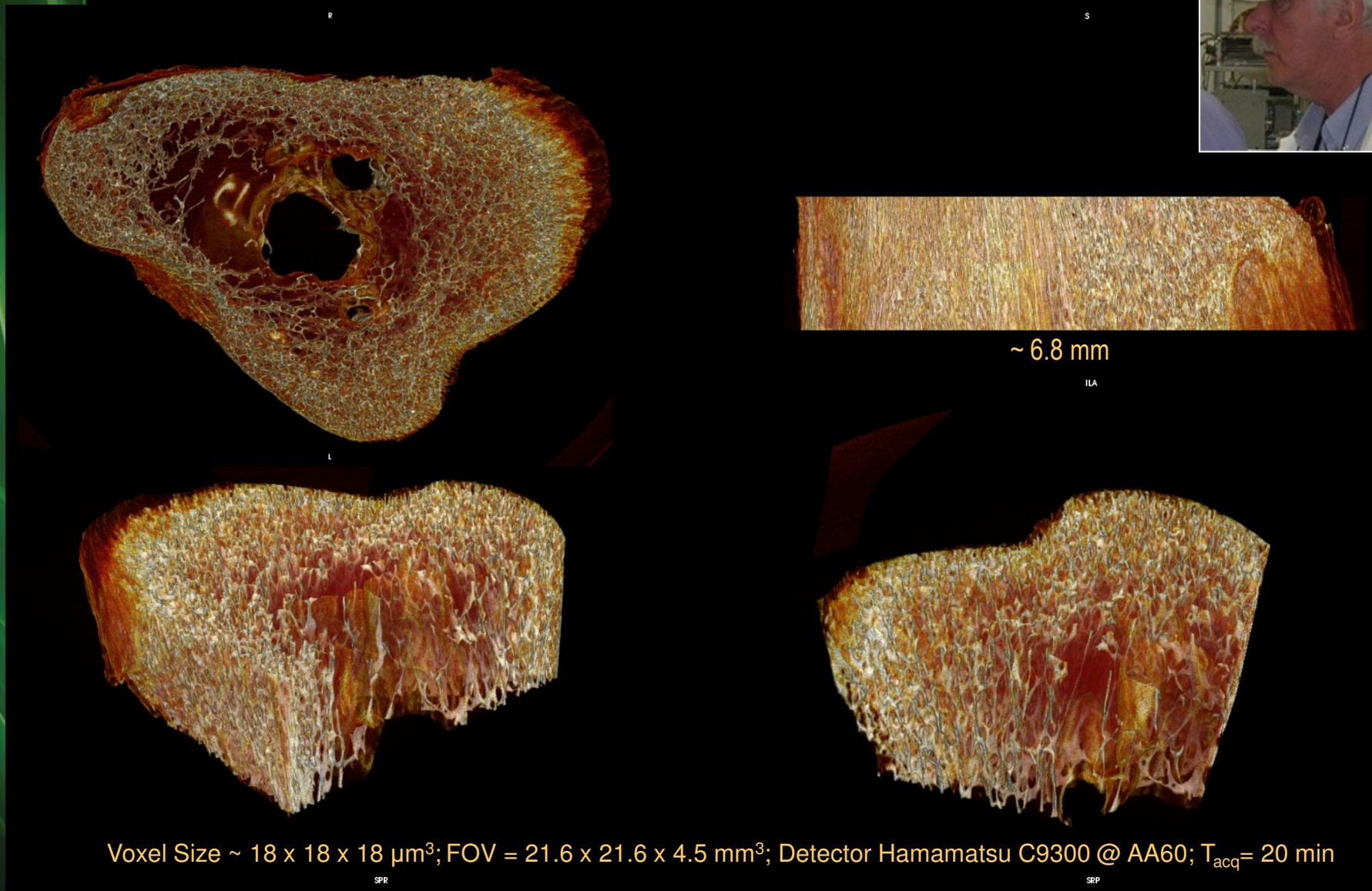


X-Ray



DEI

Absorption & Phase Contrast CT
- Broiler Chicken Bone



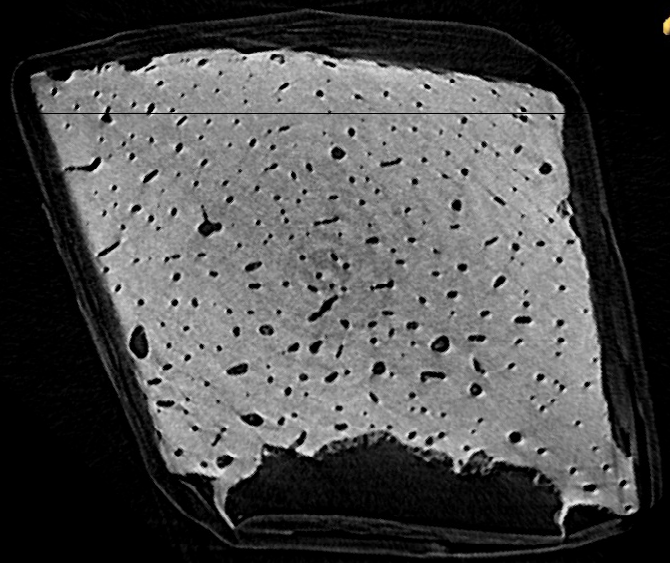
Voxel Size ~ 18 x 18 x 18 μm^3; FOV = 21.6 x 21.6 x 4.5 mm^3; Detector Hamamatsu C9300 @ AA60; T_{acq}= 20 min

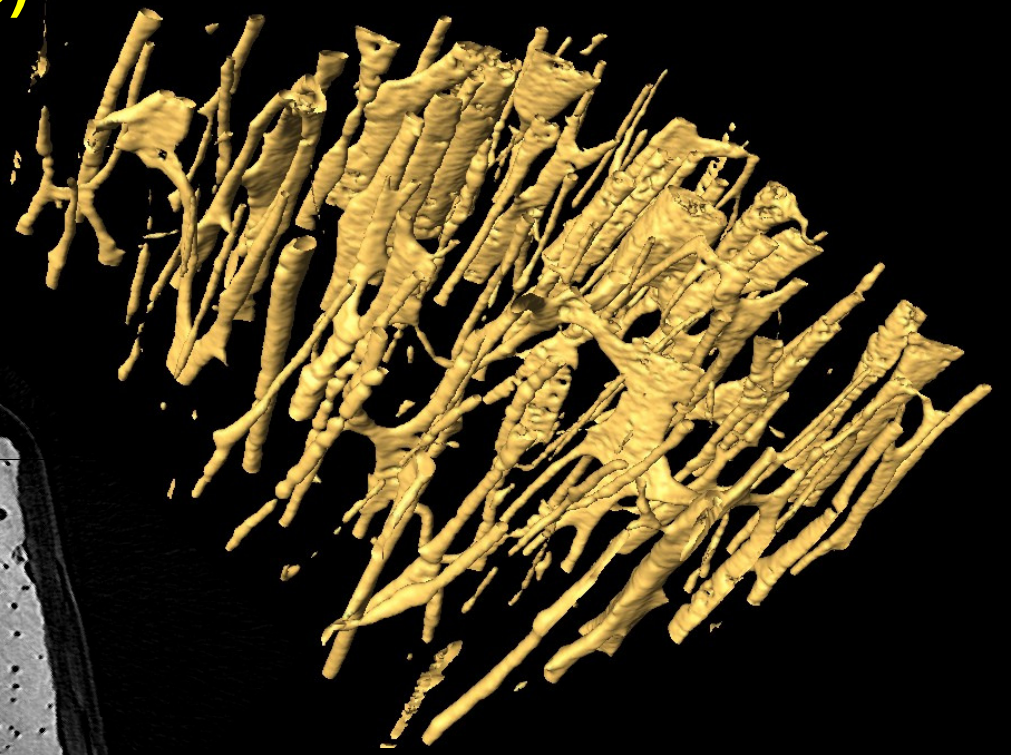
Thanks to Andrew Olkowski - proposal #9-2021

Absorption & Phase Contrast Micro-CT: Human bone

David Cooper (A & CB)

First BMIT micro-CT
of human cortical bone
10 um pixel size





Phase Contrast - Fly CT

Where we fit in world-wide

- BMIT is one of several biomedical facilities worldwide
  - ESRF ID17 Medical Beamline, Grenoble, France – much of BMIT was patterned after ID17 with significant upgrades
    - ID17 has very significant staffing and support
    - Now going through upgrades to pursue human therapy programs
  - Australian Synchrotron biomedical beamline, Melbourne – will come online soon
    - large group of scientists in support of research, both fundamental and applied
  - Trieste, Italy – the biomedical beamline at the synchrotron in Trieste
    - Human synchrotron mammography using phase contrast
    - active detector group (Much of our CT productivity in August was due to a visiting student from this group)
  - Spring-8, Japan – biomedical beamlines
    - Spectacular facility – used heavily by Japanese groups and Australian group
  - Photon Factory, Japan
    - some coronary angiography
    - Some analyzer based imaging
  - Shanghai Synchrotron, Shanghai, China – biomedical beamline
    - funded and is pursuing a broad based program that may include human research (lung?)

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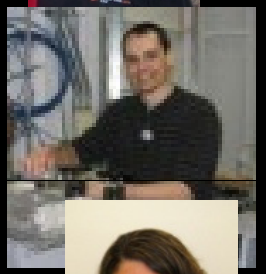
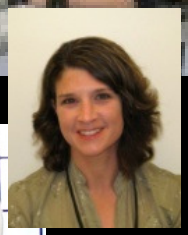
- Canadian Institutes of Health Research
- Canada Research Chairs
- Saskatchewan Health Research Foundation
- Canada Foundation for Innovation

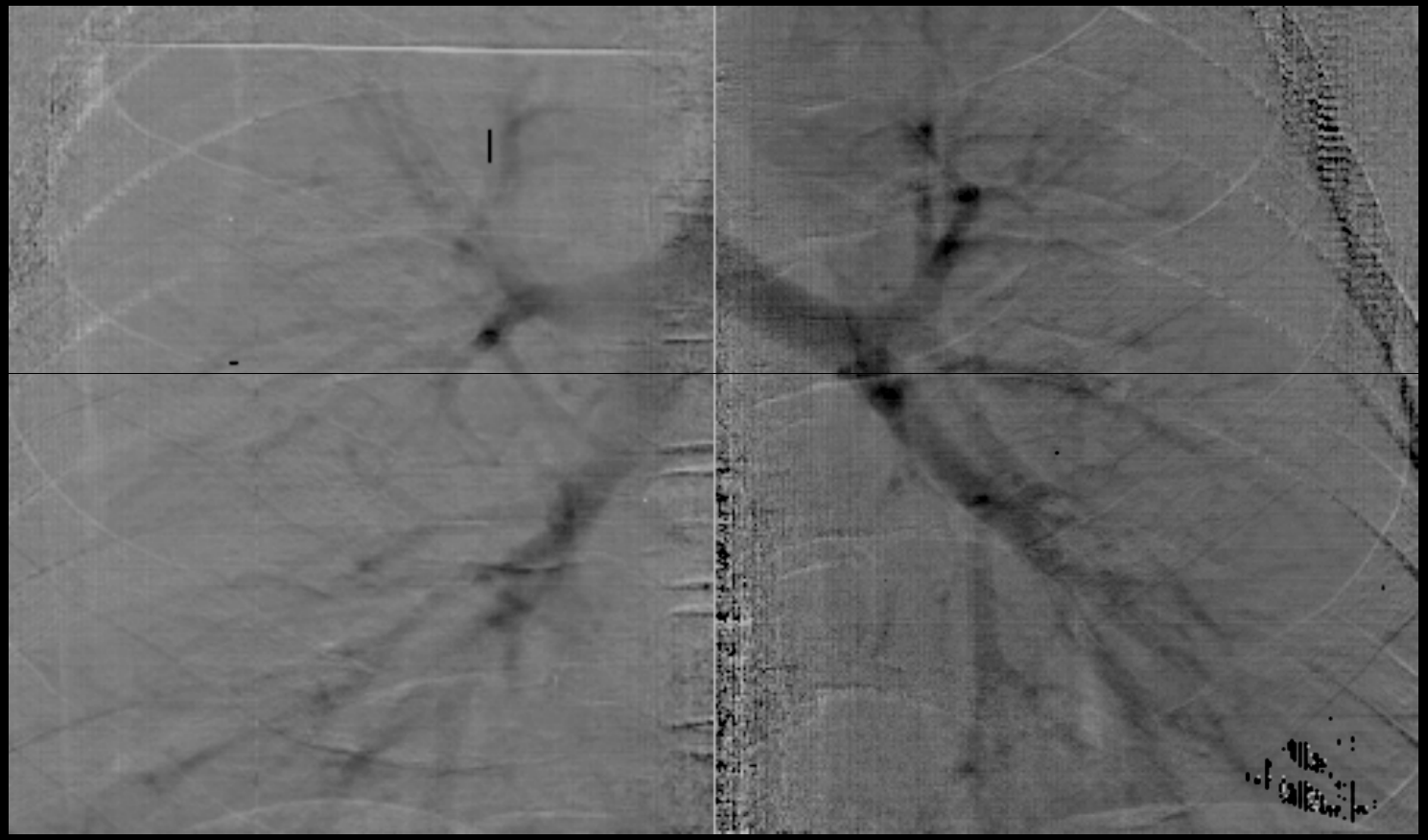
- CLS facility
- BMIT group
- Tomasz Wysokinski
  - Beamline Scientist
- George Belev
  - Beamline Associate
- Brian Bewer
  - PhD Candidate Physics
- Denise Miller
  - Software Developer
- Ying Zhu
  - PhD Candidate Biomedical Engr
- Honglin Zhang
  - PhD, 2009 Biomedical Engr

K-Edge Subtraction – Xe Human Bronchography

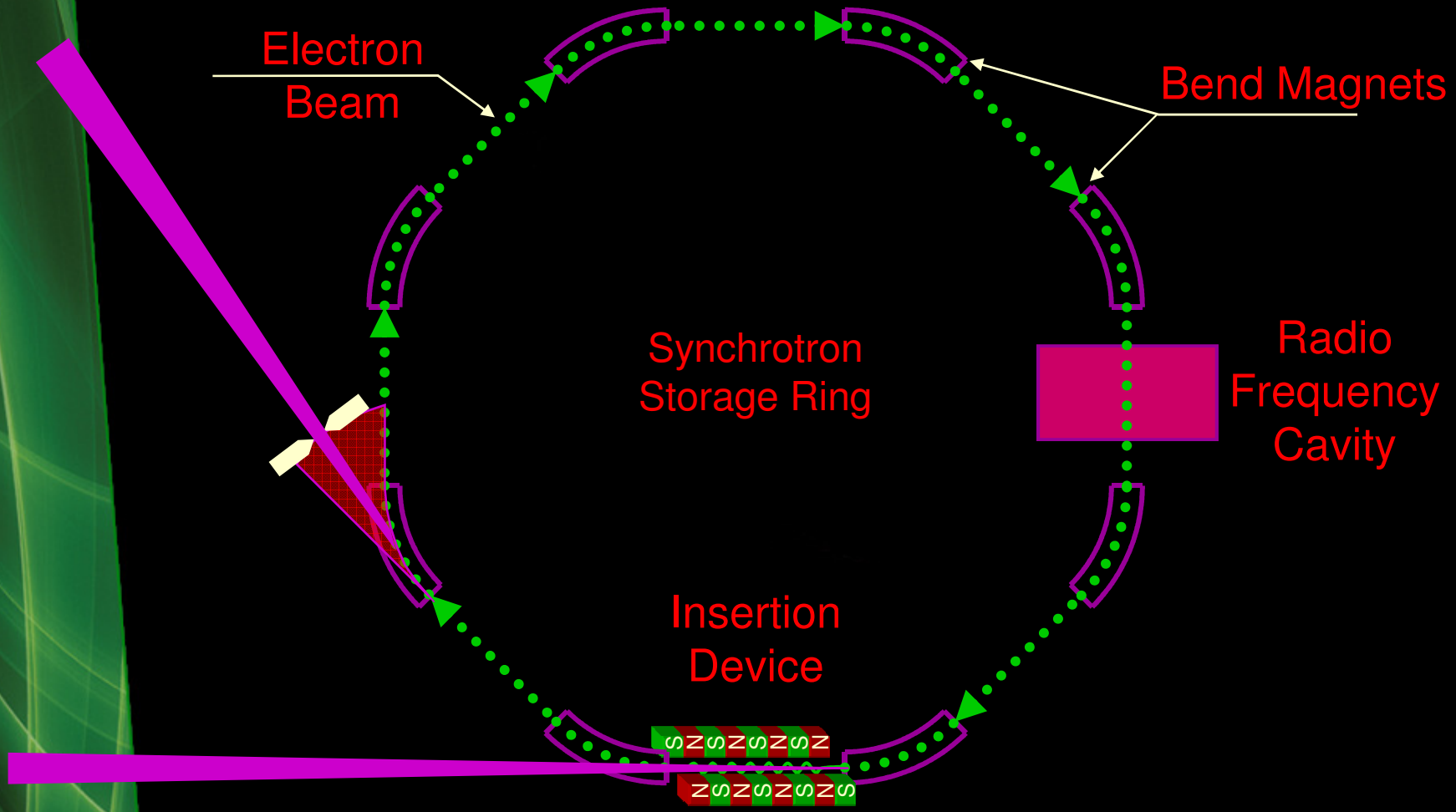
The Sample

Giacomini, Rubenstein Gordon, O'Neil, Van Kessel, Cason, Chapman, Lavender, Gmür, Menk, Thomlinson, Zhong



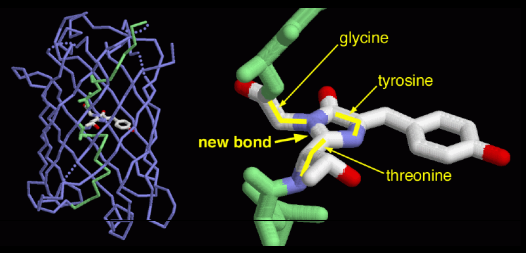
NSLS X17B2, 1996; *NIM A406:473-478 (1998)*

Technology – Synchrotron Storage Ring



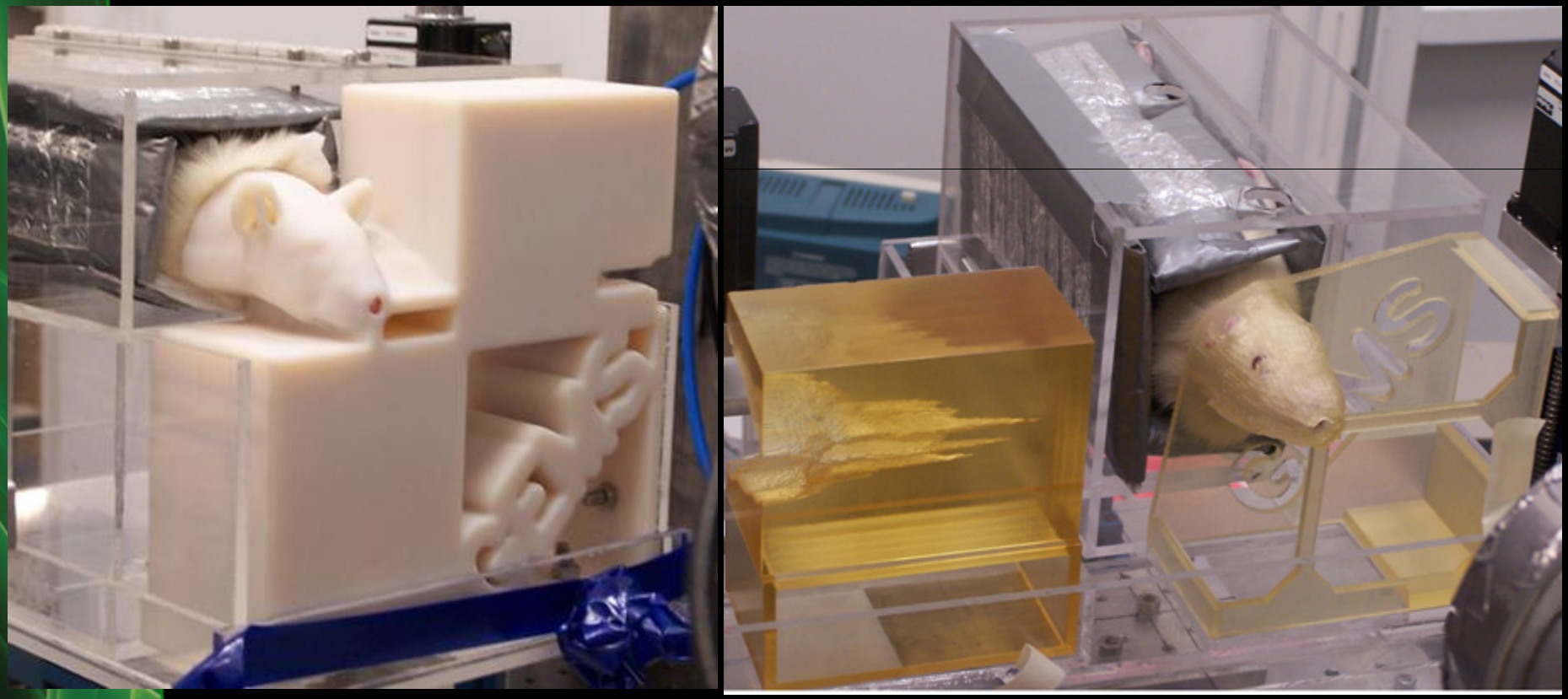
Gene Expression Imaging

- Genome known for many organisms
- Gene expression determines
  - development,
  - function, &
  - environmental reaction
- Imaging Methods
  - Green Fluorescent Protein (GFP) - optical
  - Radioactive Tracers
- Iodine accumulator
  - High concentration – K-edge subtraction (KES)
  - Low concentration – Fluorescence Subtraction Imaging (FSI)



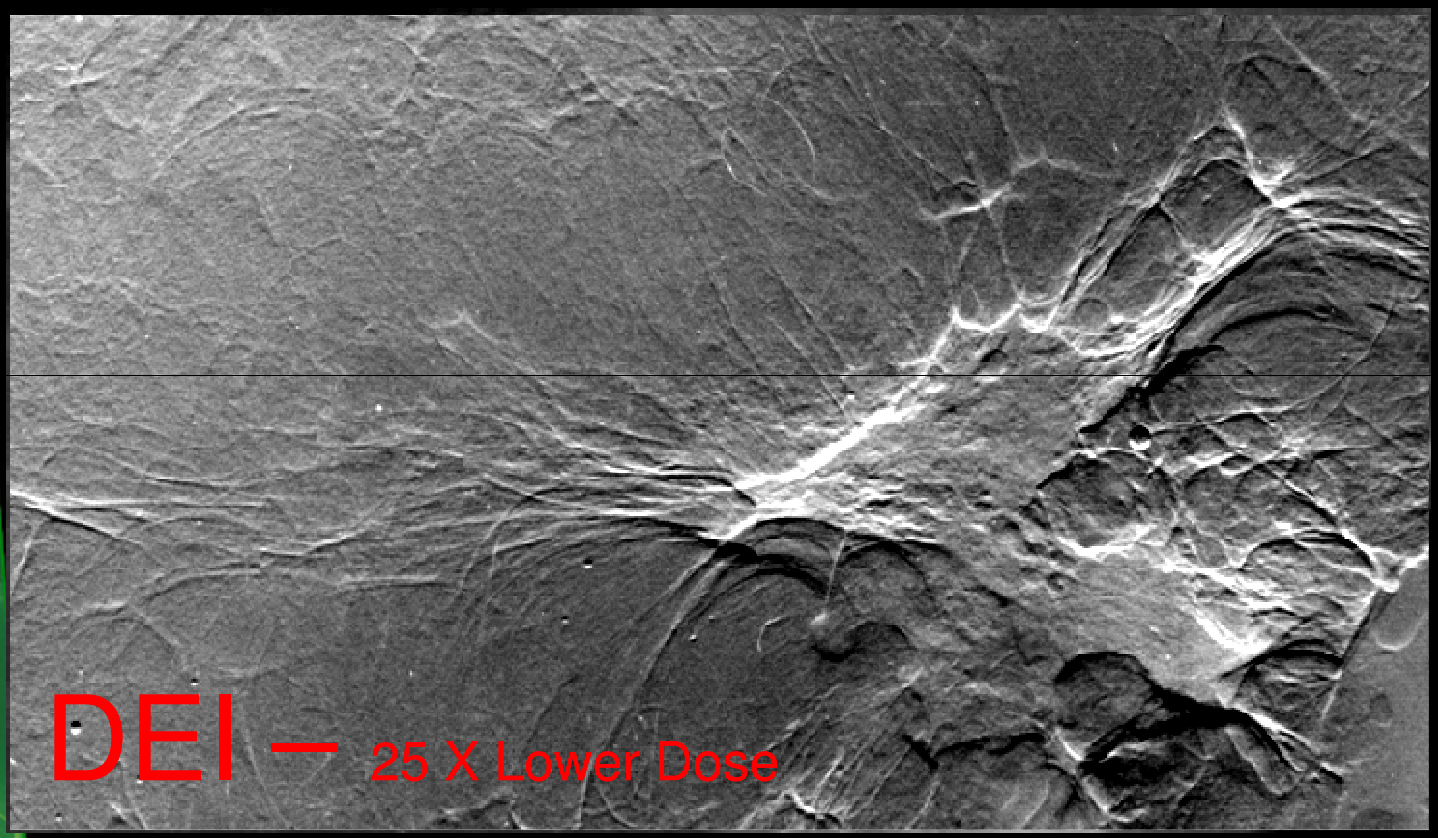
Fabrication Procedures - Experiments

- K-edge subtraction imaging experiments at the CLS HXMA beamline
- 0.25mm*28mm beam, 100eV above or below the iodine K edge
- line scan mode at 2mm/s vertical scan velocity

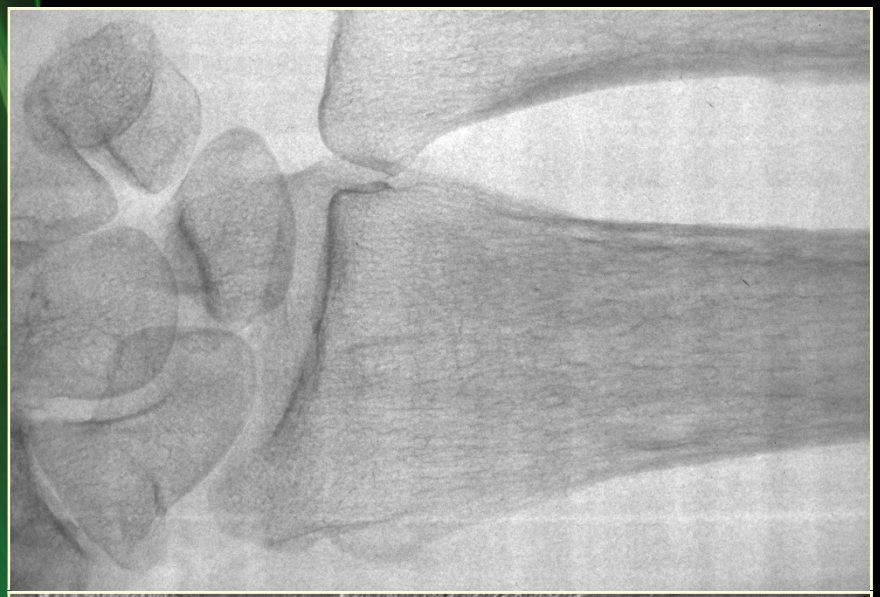


Courtesy Ying Zhu

Diffraction Enhanced Imaging – Mammography – mastectomy specimen



Cadaveric Wrist



Cadaveric Wrist -CLS BMIT

Radiograph

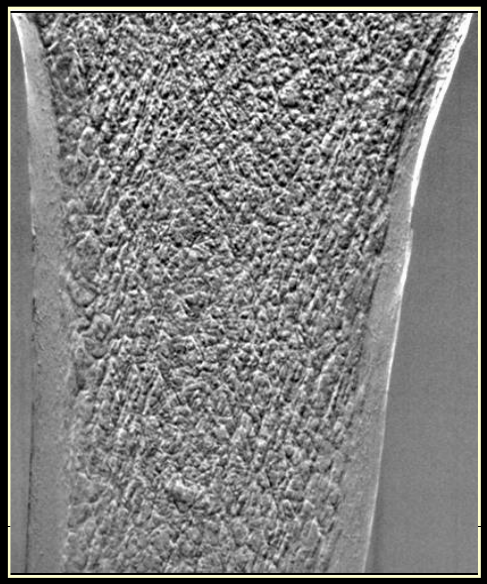
DEI 12 Feb 2009

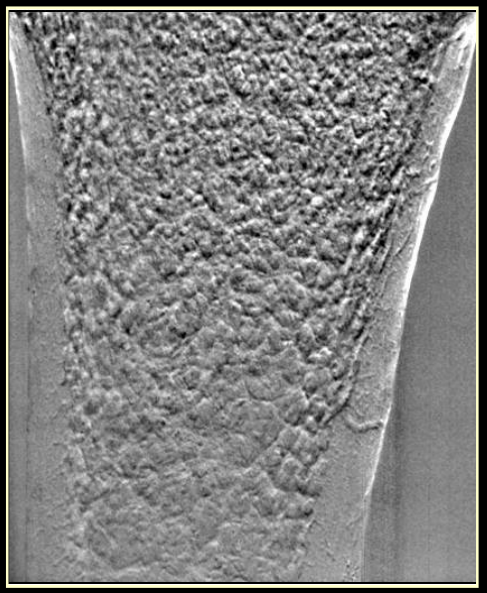
courtesy David Cooper, University of Saskatchewan

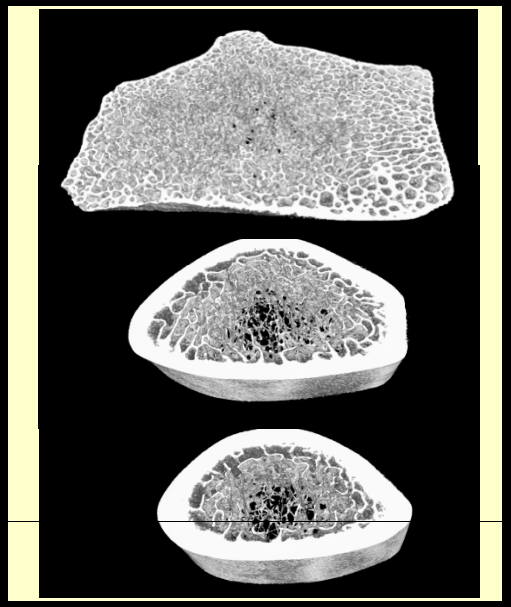
DEI: Correlative imaging
David Cooper (A & CB)

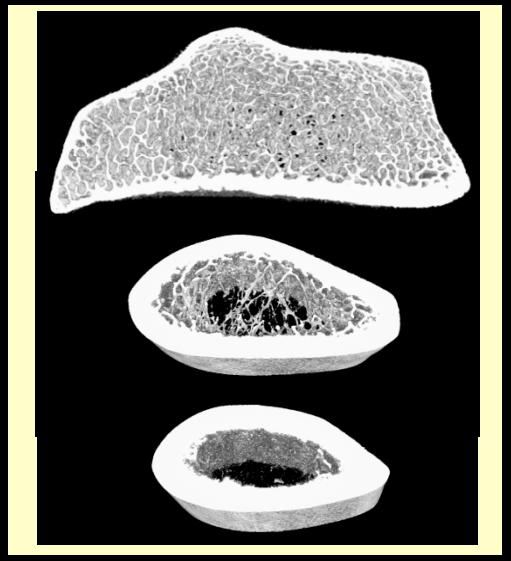
DEI vs.

desktop micro-CT

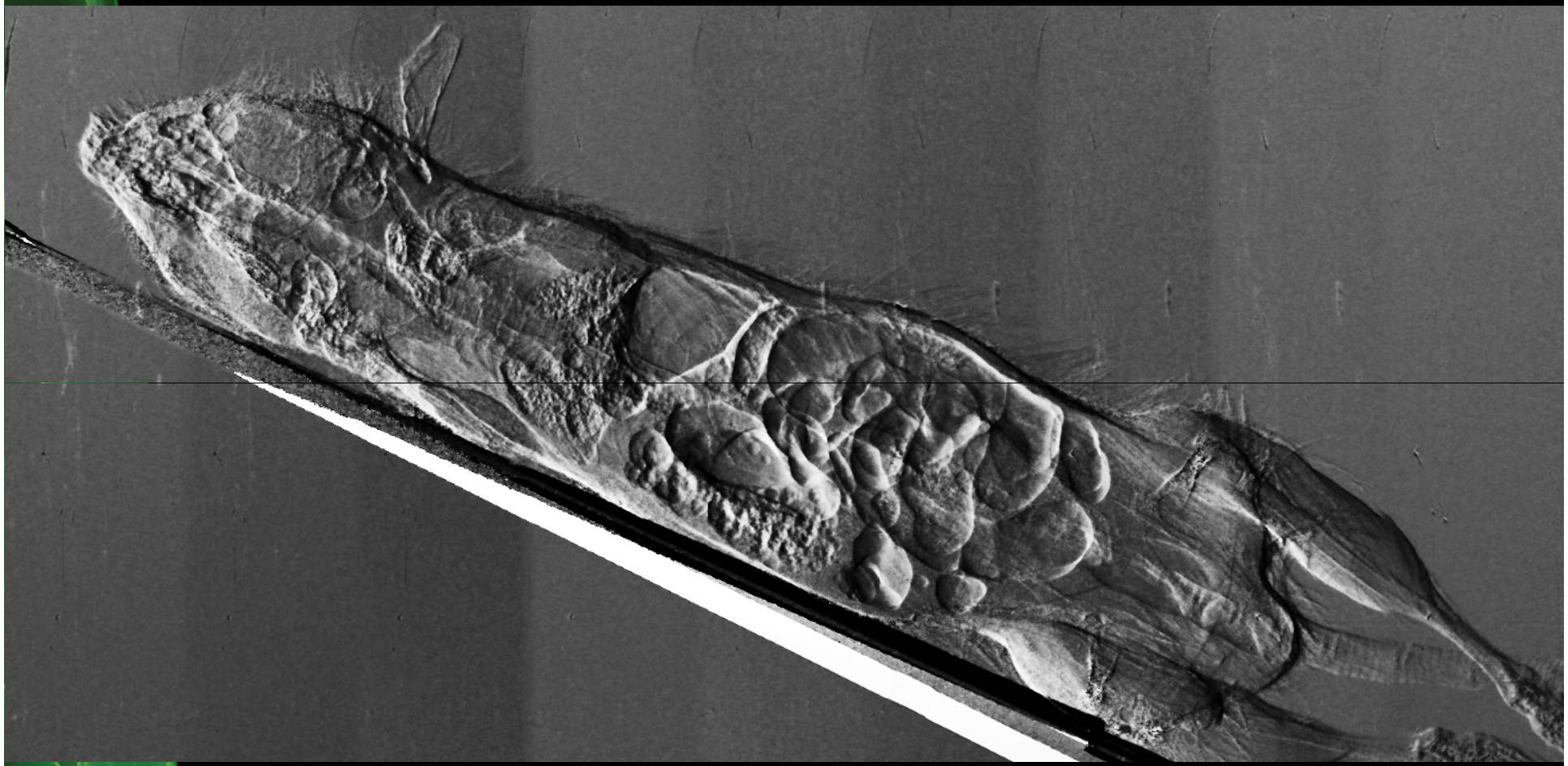








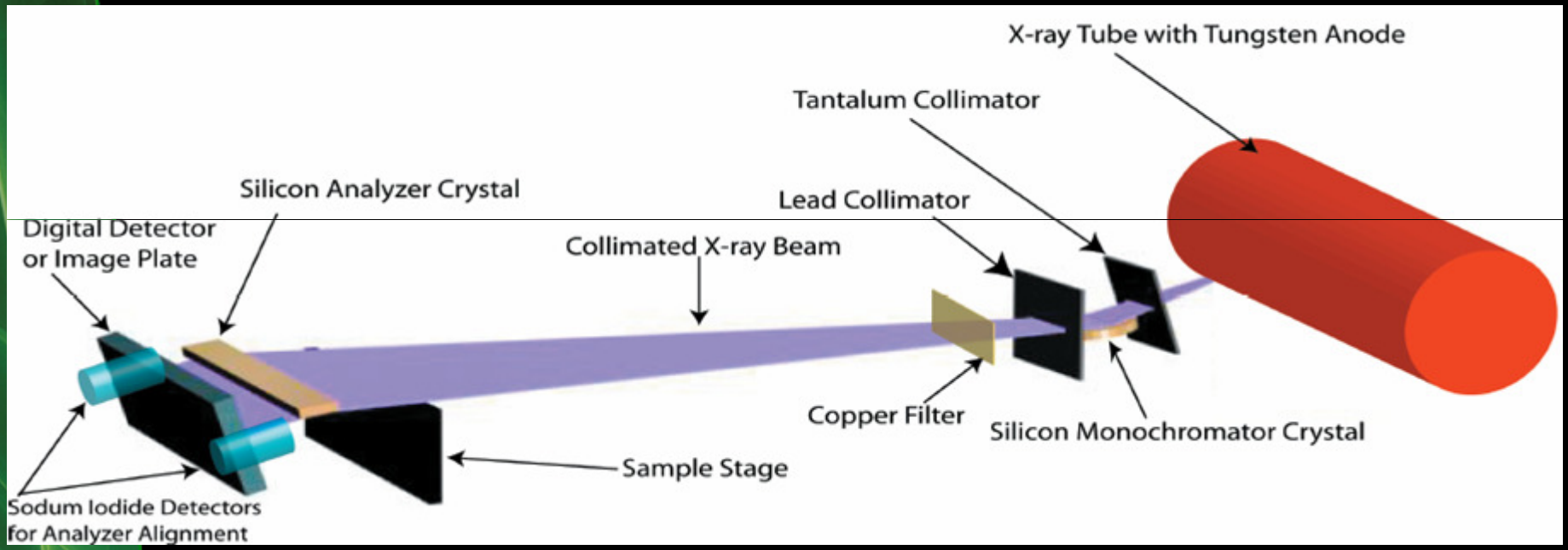
Nesch System Images



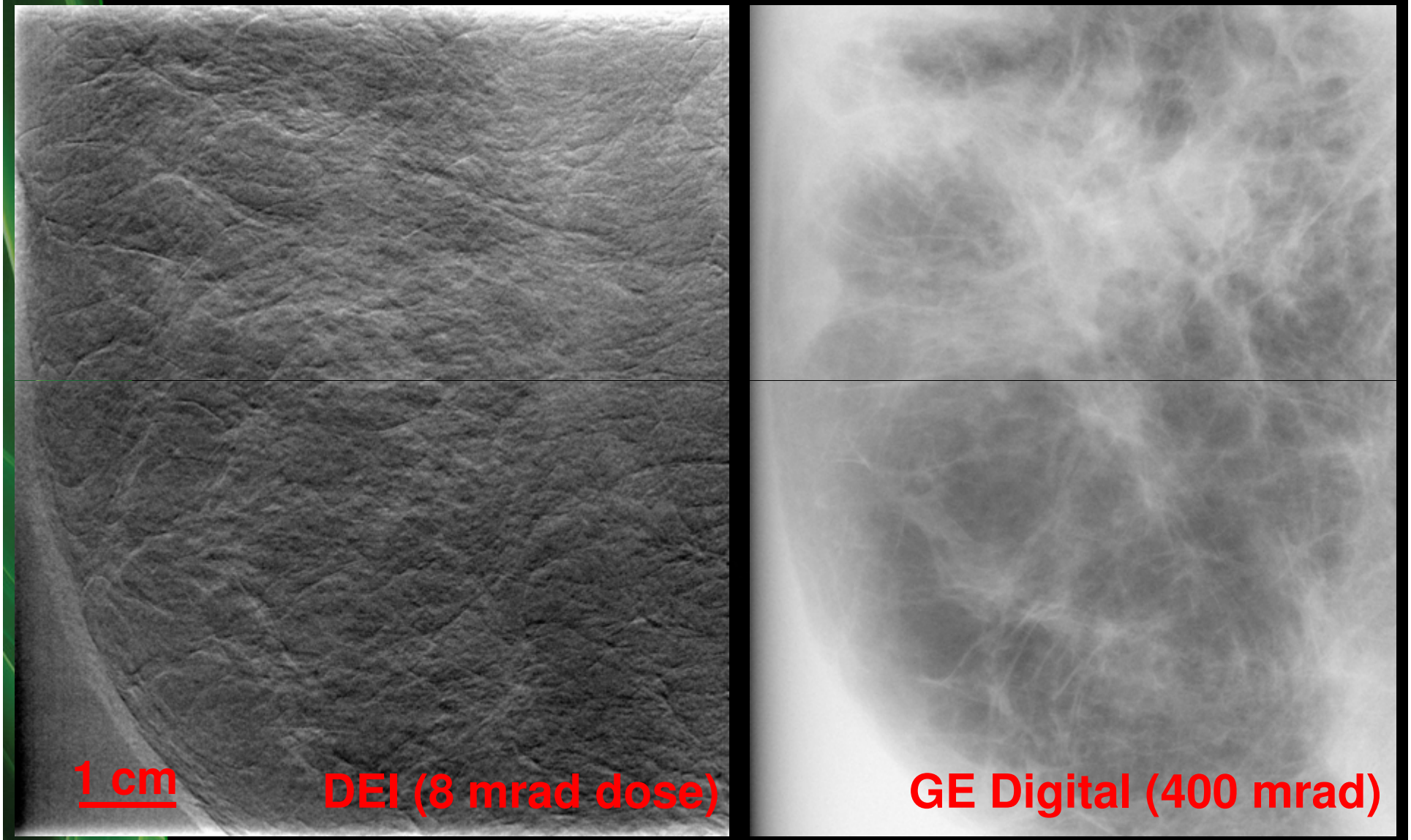
Refraction

www.neschllc.com

Conceptual Design –
Tungsten Anode Tube based DEI @ NSLS



Breast imaging –



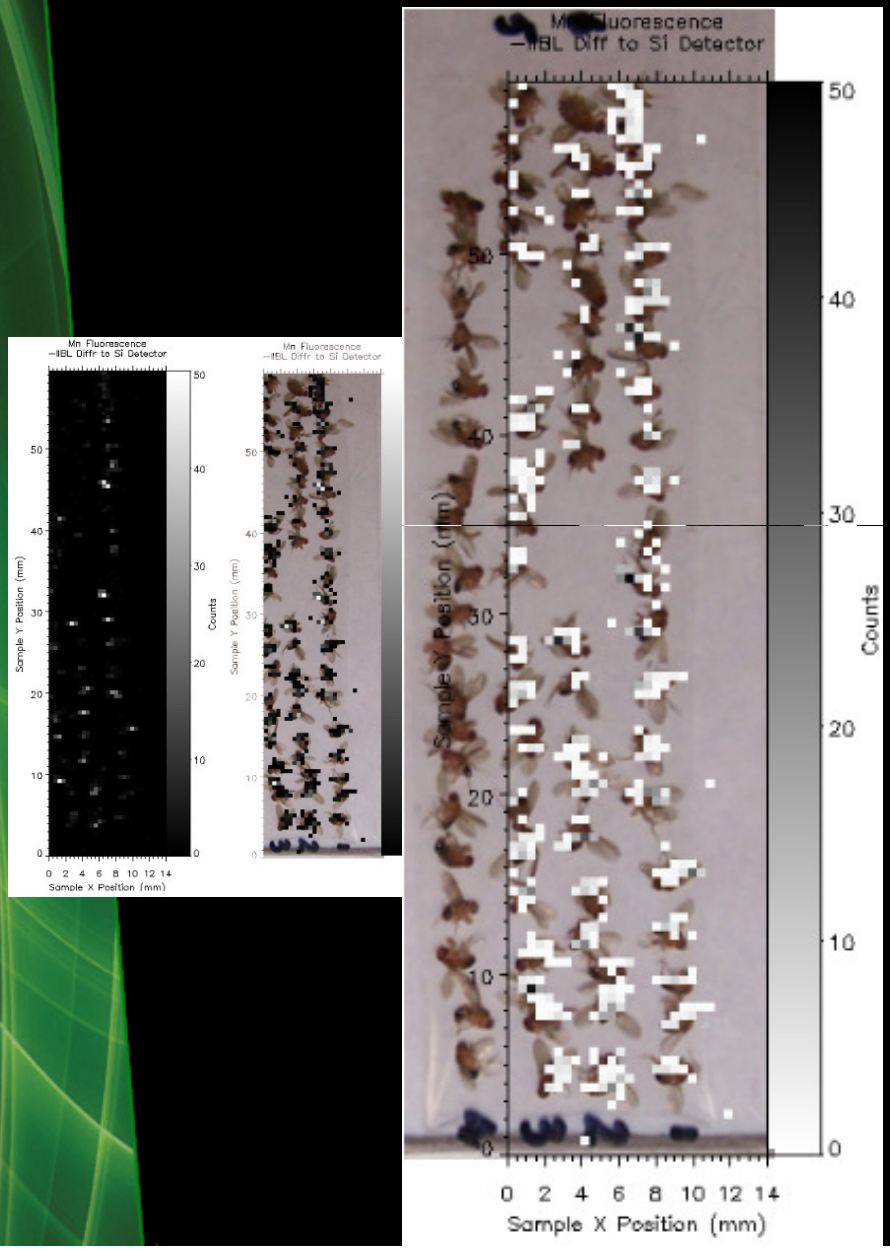
Element Specific Imaging / Fluorescence X-ray Absorption Spectroscopy Research

- Pushing the detectable fluorescence limit of an element, Mn while
- Eliminating adjacent (Fe) contamination that limits Mn detectability and prevents XAS

Biological XRF imaging – Diffraction data

fly_002.lvm

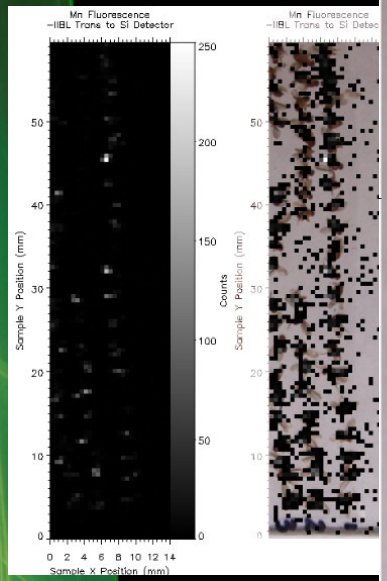
29X120
0.5s dwell

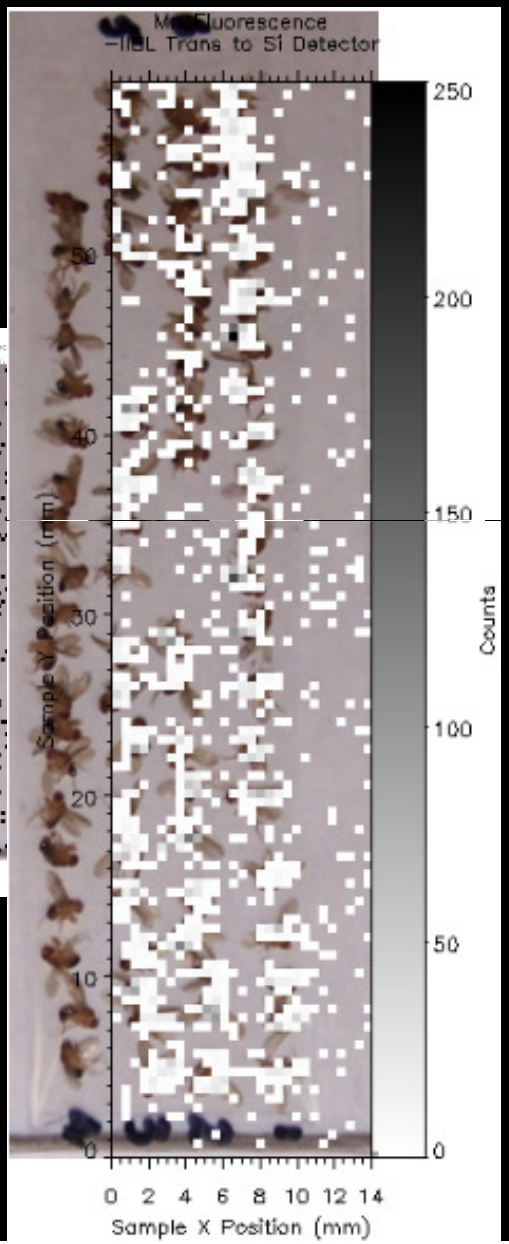


Biological XRF imaging – Transmission data

fly_002.lvm

29X120
0.5s dwell





Future

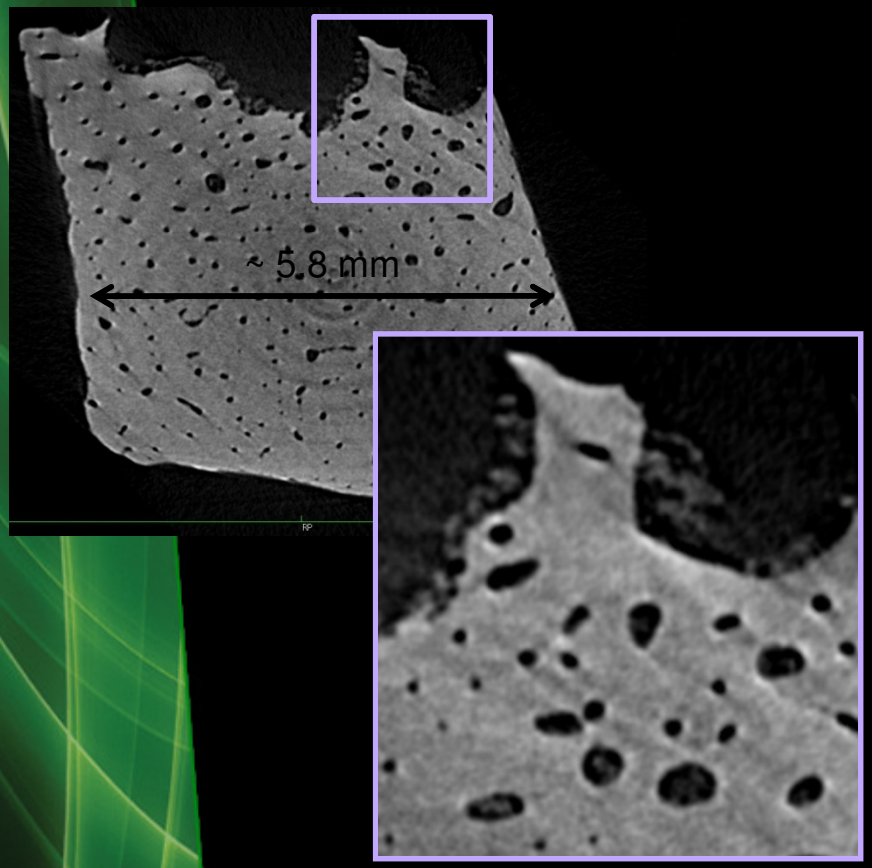
- BMIT is now being finished –
  - Transition from construction to commissioning and science
  - THE BEST IS YET TO COME!
- Functional imaging
  - Typically domain of fMRI, PET, & SPECT.
  - Gene expression, bronchrography and other contrast labeled x-ray methods
- Combined imaging methods
- Push detectable limits of contrast
- Understand and overcome imaging limitations
- Translate SR based methods to clinic or lab
  - Analyzer Based Imaging / Diffraction Enhanced Imaging
    - NextRay, LLC – looking at clinical applications
    - Nesch, LLC – small animal imaging
  - Now looking (again) at in-lab KES for gene expression

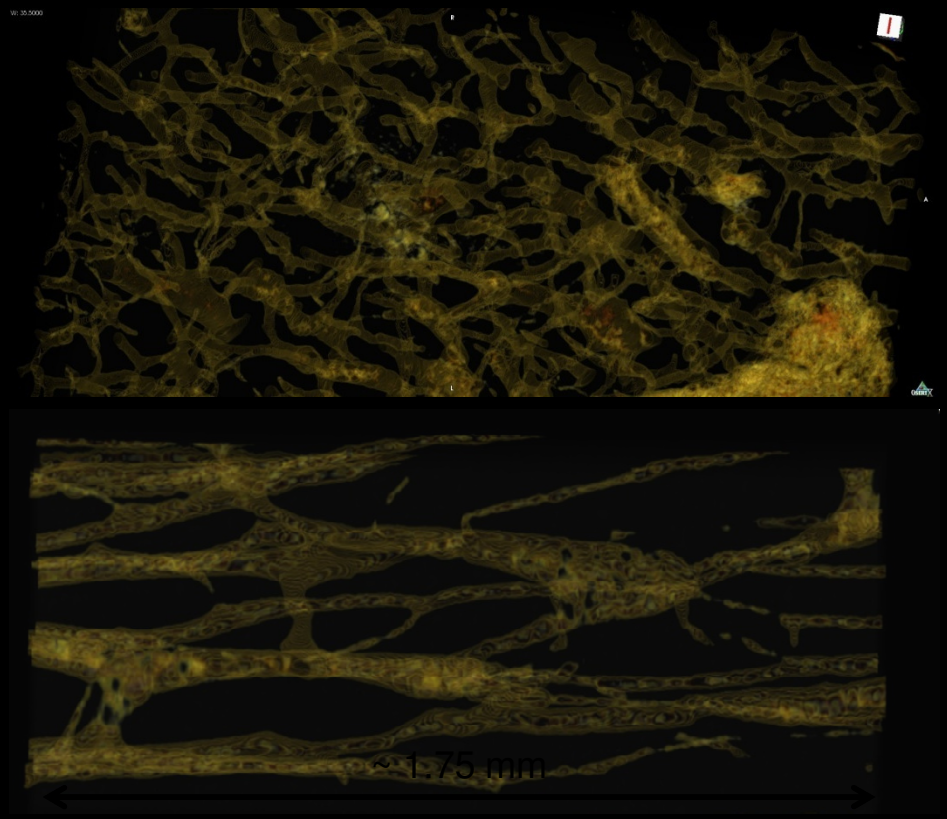
Phase Contrast CT - Results

Detector	Optics	Voxel size	Volume	Scan Time
C4742	*AA-40*	*10 x 10 x 10 µm³*	*6 x 6 x 4 mm³*	*~ 2 h*

Human Bone CT - Results

Human Bone Piece				
Detector	Optics	Voxel size	Volume	Scan Time
C4742	*AA-40*	*10 x 10 x 10 µm³*	*6 x 6 x 1.75 mm³*	*~ 1 h*

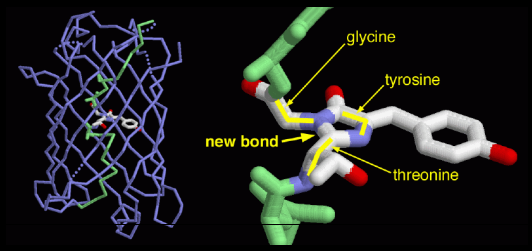




Thanks to David Cooper - proposal #8-1741

K-Edge Subtraction & Fluorescence - Gene Expression Imaging

- Genome known for many organisms
- Gene expression determines
  - development,
  - function, &
  - environmental reaction
- Imaging Methods
  - Green Fluorescent Protein (GFP) - optical
  - Radioactive Tracers
- Iodine accumulator
  - High concentration – K-edge subtraction (KES)
  - Low concentration – Fluorescence Subtraction Imaging (FSI)



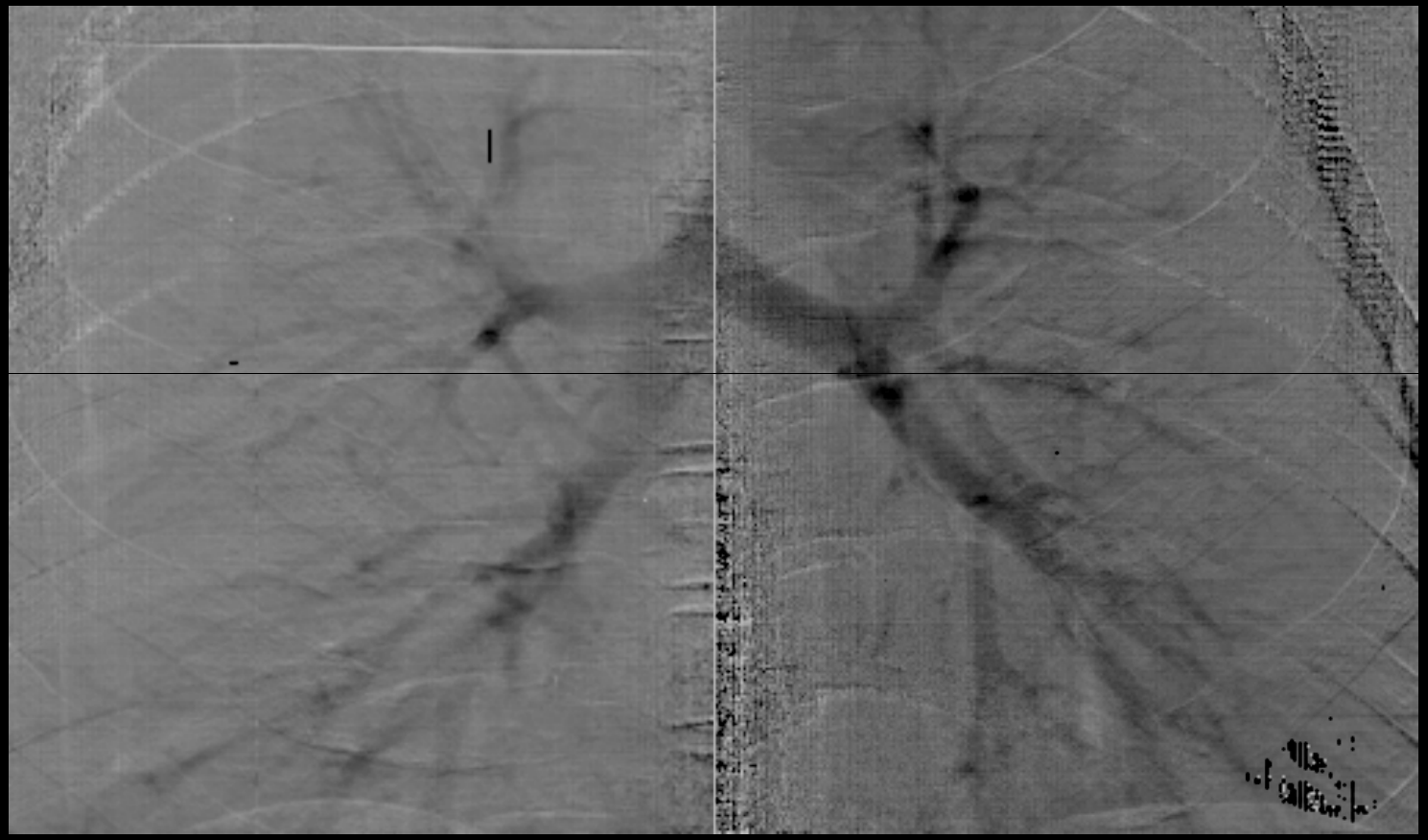
Limits for Human Use

- Research
  - Need program that requires SR to solve a research problem; i.e. previous examples:
    - K-Edge Subtraction Coronary angiography – looking at balloon angioplasty and stent vessel closure post-treatment (SSRL, NSLS, HasyLab, ESRF, PF)
    - Phase Contrast Mammography – looking at dense breast tissue with suspicious features (Trieste/ELETTRA)
  - Will require resources for safety system
  - Limited access to beam time
- Clinical
  - Cost – capital and operational

K-Edge Subtraction –
Xe Human Bronchography

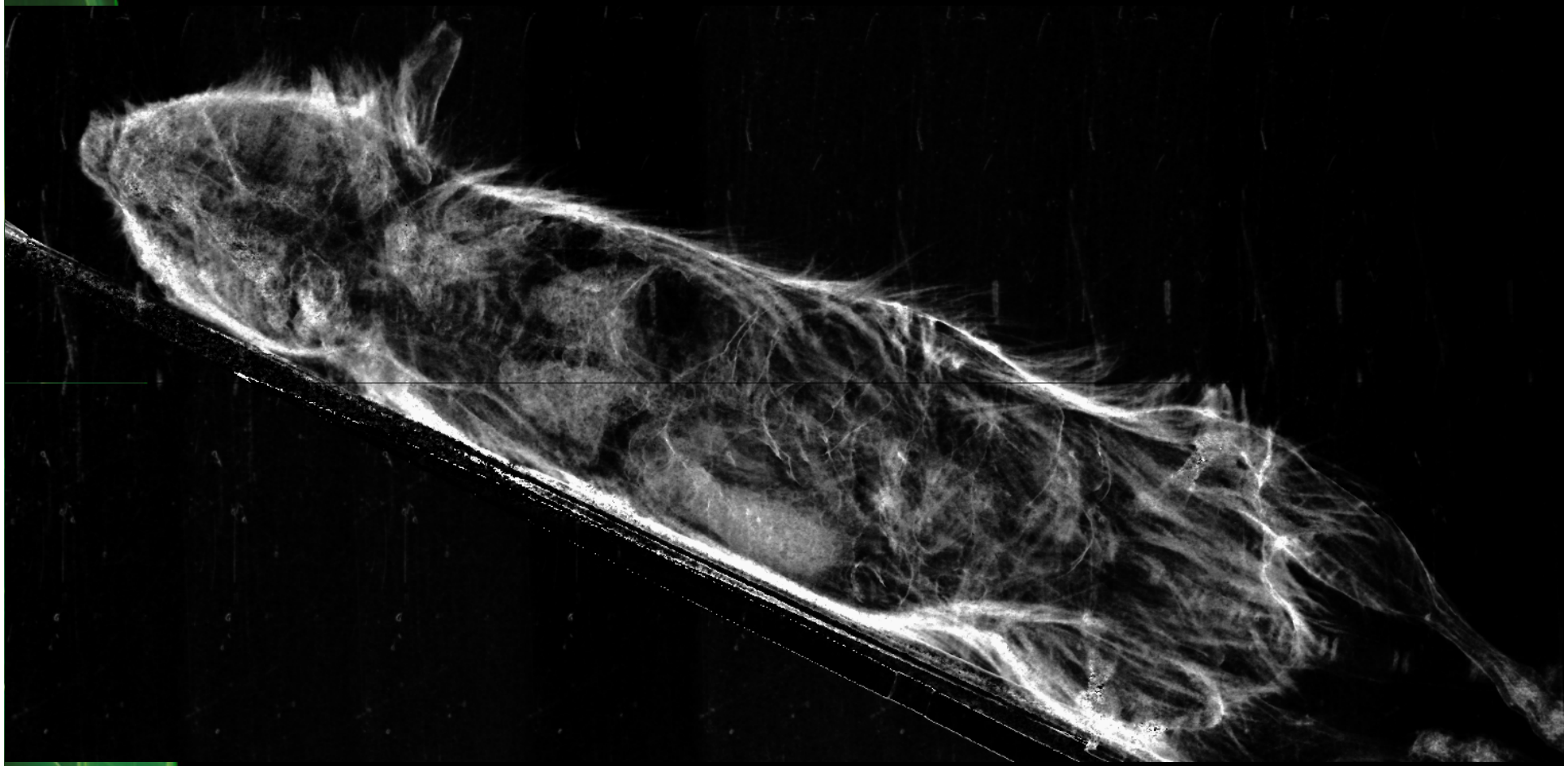
The Sample

Giacomini, Rubenstein Gordon, O'Neil, Van Kessel, Cason, Chapman, Lavender, Gmür, Menk, Thomlinson, Zhong



NSLS X17B2, 1996; *NIM A406:473-478 (1998)*

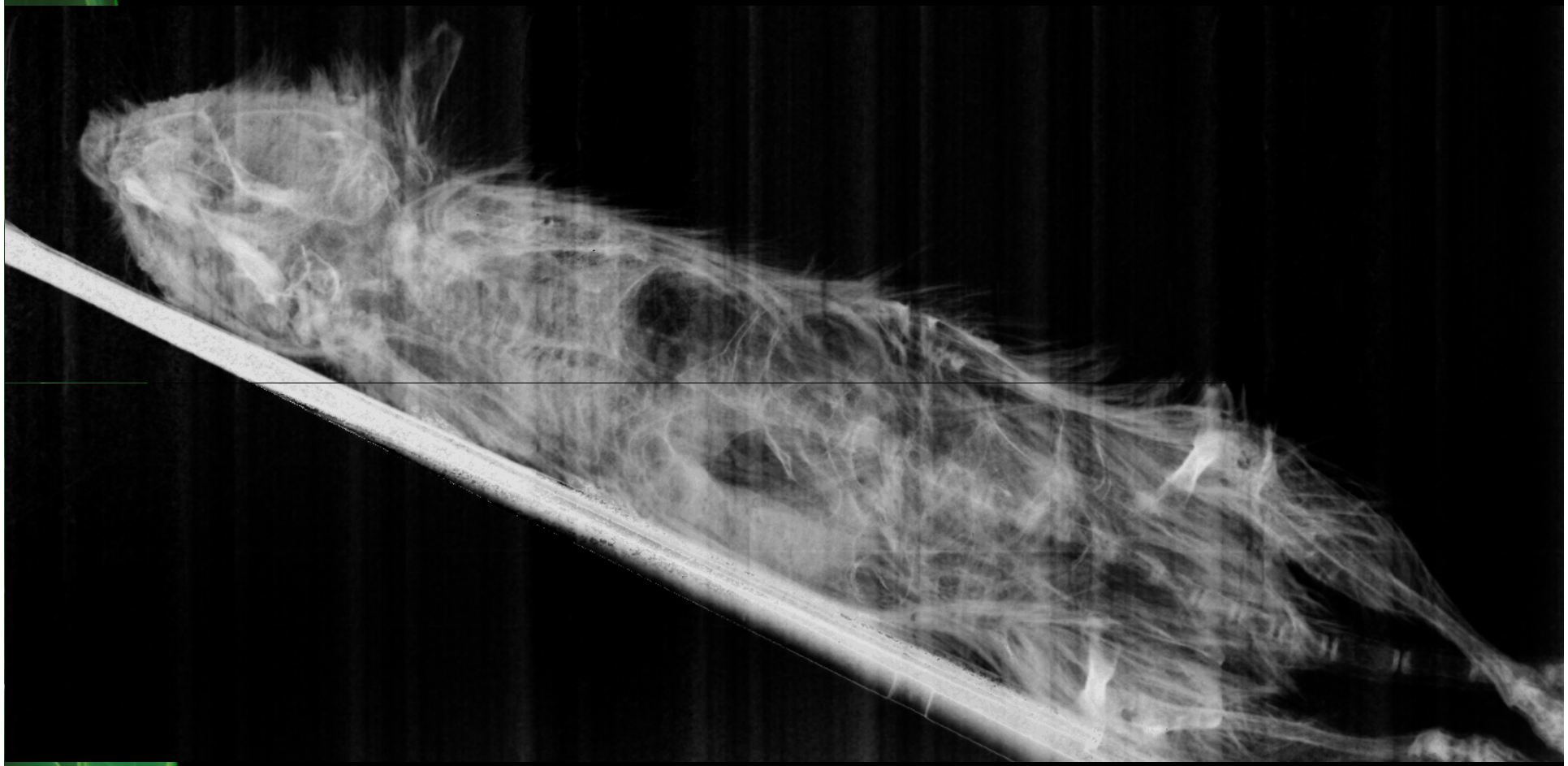
Nesch System Images



Absorption

www.neschllc.com

Nesch System Images



Extinction

www.neschllc.com