Biomedical Imaging and Therapy Beamlines: an Introduction and Highlights

The Biomedical Imaging and Therapy (BMIT) beamlines at Canadian Light Source provide unique opportunities for biomedical and preclinical X-ray imaging and Computed micro-Tomography (μCT)

BMIT offers high-spatial resolution X-ray imaging and Computed Tomography (CT) through a variety of contrast mechanisms including absorption, refraction, and dark-field (scatter). The last two can provide an unprecedented contrast that conventional absorption imaging cannot, enabling detection of soft tissues. Contrary to conventional X-ray sources which produce broadband cone beam, X-rays at BMIT are monochromatic, nearly parallel, partially coherent, and the photon flux is many orders of magnitude higher. In many cases these distinctive properties of synchrotron radiation allow researchers to considerably reduce the radiation dose compared to lab-based μCT scanners.

The world-class research capabilities of BMIT are available for use by researchers from across Canada. Research time on BMIT is awarded based on the scientific merit of submitted proposals (visit https://www.lightsource.ca/apply_for_beamtime.html or https://bmit.lightsource.ca to find how to apply for beam time). Scientists can utilize BMIT techniques to:

- Perform **ultrafast** scans. CT scans can be performed up to 100 times faster than with lab scanners (Figure 1)
- Achieve **very high spatial resolution**. Sample features with characteristic dimensions down to two microns can be resolved, approaching the typical resolution of histology (Figures 1, 2, 4).
- Perform **low-dose** temporal *in-vivo* imaging of animal models. The dose deposited in specimens is up to 10 times smaller than with lab scanners (Figs. 3, 6).
- Differentiate between **soft tissues** which do not normally exhibit contrast when imaged with conventional laboratory and clinical X-ray scanners (Figures 3, 5, 6).
- Exploit outstanding **3D elemental sensitivity** to medical contrast agents including Sr, Ag, I, Xe, Ba, Gd, Au (Figure 4). Very low concentrations of an agent can be detected.

Instruments and techniques available at BMIT have been successfully applied to numerous biomedical and preclinical studies using both excised tissue specimens and animal models ranging in size from zebra fish and mice to piglets. Several examples are shown below. BMIT's powerful imaging capabilities are also routinely utilized by experts for research of alloys and composite materials, renewable energy, environmental science, and many other applications.

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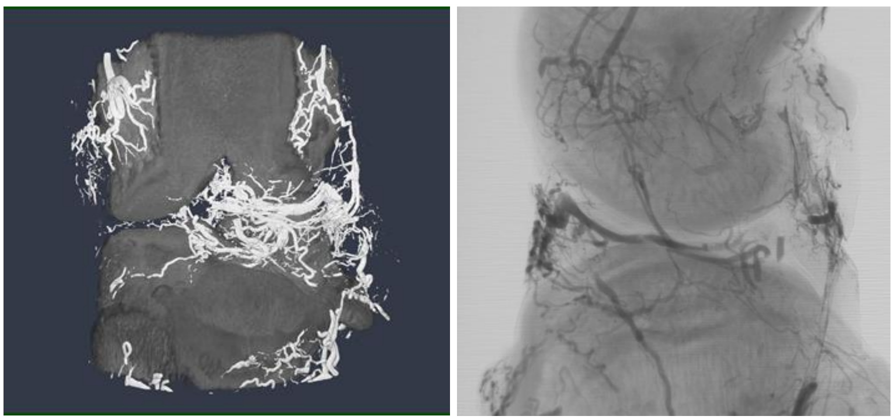
Biomedical Imaging and Therapy Beamlines Imaging Highlights

Micro-Angiography in a Rat Model of Osteoarthritis

These images represent *ex vivo* micro-angiography, after infusion of barium/gelatine mixture, in an osteoarthritic rat 6 weeks post-surgery. Vasculature down to two voxel size in diameter can be observed.



Technique:
Microtomography with absorption contrast

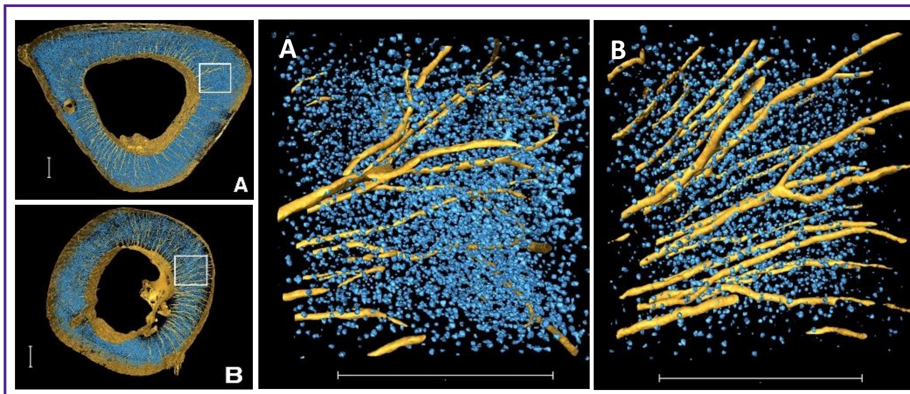
●	Photon Flux
●	Resolution
○	Low Dose
●	Energy Tunability
○	Phase/Dark-field

Courtesy of A. Panahifar
University of Saskatchewan

Figure 1. Contrast-Enhanced Imaging of Micro-Vasculature (Voxel size: 6.5 µm, X-ray energy: 37.6 keV, 2250 projections).
Panahifar, A., *et al.,* Synchrotron x-ray imaging applications in osteoarthritis. *Osteoarthritis and Cartilage,* 2018, 26:S472-S473.

Imaging the Effects of Prolonged Unloading on Osteocyte Lacunar Density in a Rat Model

The primary objective of this study was to test the hypothesis that unloading (sciatic neurectomy) during growth results in altered osteocyte lacunar density in the tibial diaphysis of the rat. Secondarily, a potential effect of unloading on mean lacunar volume was explored.



Technique:
Microtomography with phase contrast

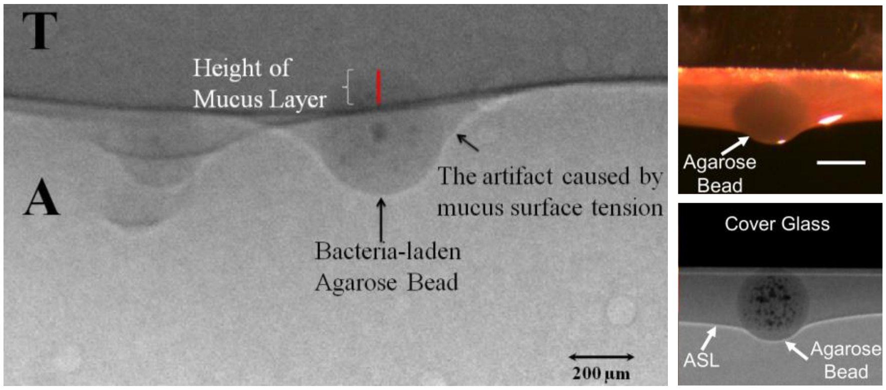
●	Photon Flux
●	Resolution
○	Low Dose
○	Energy Tunability
●	Phase/Dark-field

Courtesy of D. Cooper
University of Saskatchewan

Figure 2. Three-dimensional rendering of the vascular canals and osteocyte lacunae with enlarged subsections for a control rat (A) and an immobilized rat (B). Scale bar = 300 µm.
Britz HM., *et al.,* Prolonged unloading in growing rats reduces cortical osteocyte lacunar density and volume in the distal tibia. Bone. 2012, 51(5):913-9.

In vivo Imaging of Mucus Formation in a Piglet Model of Cystic Fibrosis

In this study the response of airway submucosal glands to inhaled bacteria and its connection to cystic fibrosis was investigated. Prior to using BMIT anatomical visualization of airway and mucus had been limited due to limitations of contrast and resolution available using conventional imaging techniques.



Technique:
Radiography with phase contrast

○	Photon Flux
●	Resolution
●	Low Dose
○	Energy Tunability
●	Phase/Dark-field

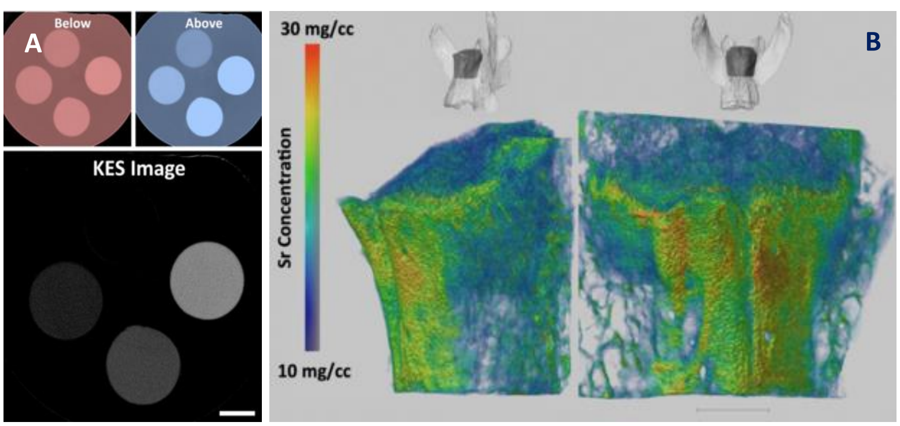
Courtesy of J. Ianowski
University of Saskatchewan

Figure 3. Phase-contrast visualization of the air/mucus interface and the bacteria-laden agarose bead. (T) indicates tissue; (A) indicates air space (*i.e.,* lumen of the trachea); (ASL) indicates airway surface liquid secretion.

Luan X., *et al.,* Cystic fibrosis swine fail to secrete airway surface liquid in response to inhalation of pathogens. *Nature Communication*, 2017, 5;8(1):786.

Mapping of Strontium Distribution in a Rat Model of Osteoporosis

K-edge subtraction (KES) imaging was used as a non-invasive imaging technique to track the 3D distribution of strontium within animal models of bone disease, and to determine the impact of strontium incorporation in mineralized bone upon mineral density and bone strength.



Technique:
Microtomography with K-edge contrast

○	Photon Flux
●	Resolution
○	Low Dose
●	Energy Tunability
○	Phase/Dark-field

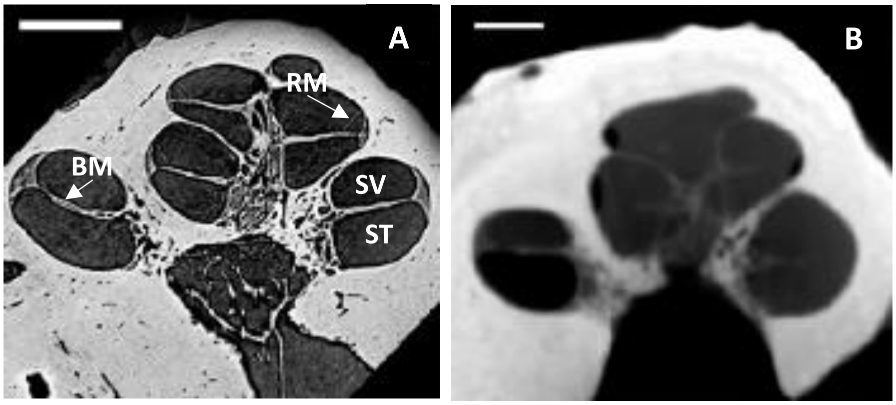
Courtesy of M. Doschak
University of Alberta

Figure 4. A) Tomographic images (top left) of the Sr solution phantom above and below the Sr K-edge, and the resulting difference image showing the location of Sr within the samples (bottom left). The highest concentration solution is located to the right and concentrations progressively diminish moving clockwise. B) Volumetric 3D SR KES renders of a rat vertebral sample. Periosteal formation as well as trabecular remodeling show uptake of Sr. The growth plate (superior) shows extensive labeling of newly formed cortical bone as well as trabecular remodeling events. Reference 3D renders are provided above for orientation (Scale bar = 1 mm).

Cooper DM., *et al.,* Three dimensional mapping of strontium in bone by dual energy K-edge subtraction imaging. *Physics in Medicine and Biology*, 2012, 57(18):5777-86.

Visualizing 3D Cytoarchitecture of the Human Cochlea in an Intact Temporal Bone

This panel shows the ability of synchrotron X-ray absorption and phase contrast imaging to enable visualization of sensory cells and nerve fibers in the cochlea's sensory epithelium *in situ* (3D) in intact, non-decalcified, unstained human temporal bones.



Technique:
Microtomography with phase contrast

●	Photon Flux
●	Resolution
○	Low Dose
○	Energy Tunability
●	Phase/Dark-field

Courtesy of J. Iyer, Stanford; H. Ladak, Western University

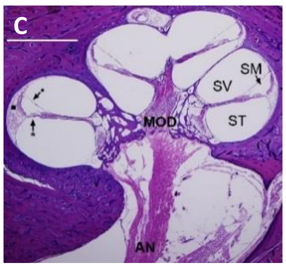
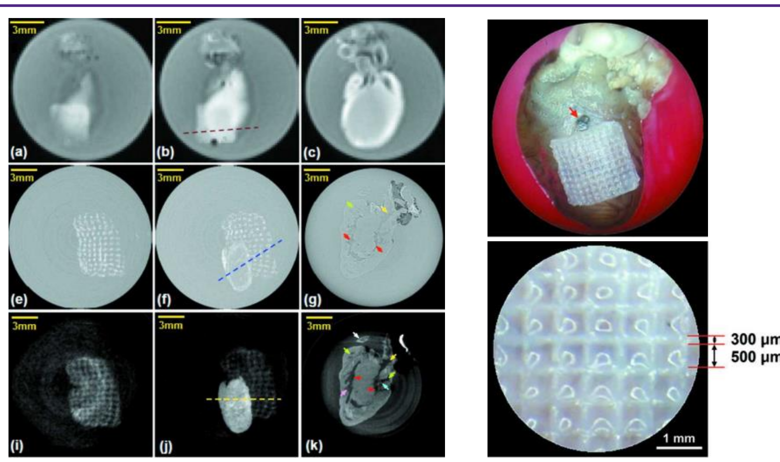


Figure 5. A) Synchrotron phase-contrast micro-CT; B) Conventional micro-CT; C) H&E stained histology. The basilar membrane (BM, *) and Reissner's membrane (RM, •) define the boundaries between the cochlea's three fluid-filled lumina: scala tympani (ST), scala media (SM), and scala vestibuli (SV). The lateral wall (■) attaches the basilar membrane to the cochlea's osseous shell, the otic capsule (Scale bar = 2mm).

Iyer JS, *et al.,* Visualizing the 3D cytoarchitecture of the human cochlea in an intact temporal bone using synchrotron radiation phase contrast imaging. *Biomed. Optics Express.* 2018, 9: 3757-67.

Imaging Low-Contrast Scaffolds for Cardiac Regenerative Therapy

The visualization of hydrogel-based cardiac scaffolds is essential for longitudinal studies of cardiac regenerative therapy. Synchrotron X-ray phase contrast imaging computed tomography provides significantly more information than clinical MRI (3T) to visualize the microstructural features of the hydrogel cardiac patch for scaffold-based myocardial tissue engineering.



Technique:
Microtomography with phase contrast and phase retrieval

●	Photon Flux
●	Resolution
●	Low Dose
●	Energy Tunability
●	Phase/Dark-field

Courtesy of M. Izadifar University of Toronto

Figure 6. A heart and the implanted patch: coronal slices from MRI images (a-c) and BMIT phase-contrast X-ray images with (e-g) and without (i-k) phase-retrieved applied. Low dose energy of 500mGy was achieved without compromising the signal-to-noise ratio. (Voxel size: 12.5µm, Propagation distance: 147cm, Energy: 25 keV).

Izadifar M., *et al.,* Potential of propagation-based synchrotron X-ray phase-contrast computed tomography for cardiac tissue engineering. *Journal of Synchrotron Radiation,* 2017, 24(Pt 4):842-853.