4 Years of X-ray Imaging at 05B1-1 Beamline at BMIT

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Abstract — **The BioMedical Imaging and Therapy (BMIT) facility located at the Canadian Light Source, provides synchrotron-specific imaging and radiation therapy capabilities [1-5]. There are two separate endstations used for experiments: the Bending Magnet (BM) beamline described here and the Insertion Device (ID) beamline that started general user program in 2015.**

The bending magnet beamline 05B1-1 was used to acquire first images in December 2008 and was officially opened for general user program in 2011. This endstation is designed for imaging and therapy research primarily in animals ranging in size from insects to mice to small dogs and cats, as well as tissue specimens including plants.

Core research programs include human and animal reproduction, cancer imaging and therapy, spinal cord injury and repair, cardiovascular and lung imaging and disease, bone and cartilage growth and deterioration, mammography, developmental biology, gene expression research as well as the introduction of new imaging methods.

The monochromatic spectral range spans 15–40 keV, and the beam is more than 200 mm wide in the experimental hutch. Several different X-ray detectors are available with resolutions ranging from 2 µm to 200 µm.

Keywords— **05B1-1, 05ID-2, BMIT, Biomedical Imaging, Synchrotron Radiation**

I. Introduction

BMIT is the only synchrotron based dedicated Biomedical Imaging and Therapy facility in North America. BMIT design implements many lessons learned at other synchrotron institutions (SSRL, NSLS, DESY, SPRING-8 and ESRF). It provides unique synchrotron-specific X-ray imaging and therapy capabilities and it is used to address unsolved problems in medicine (human and animal), agriculture, and other biomedical sciences.

The Bending Magnet (BM) beamline provides research capabilities for absorption, phase contrast and Diffraction Enhanced Imaging (DEI, also known as ABI) in both planar and Computed Tomography (CT) mode for smaller sized samples that do not require very high X-ray energies and/or high X-ray flux. This end station is also intended to be used for developing, testing and validation of new ideas in X-ray imaging and therapy. Additionally, the endstation hosts new imaging methods, such as imaging based on structural aspects of tissues by diffraction, absorption spectroscopy imaging, fluorescence imaging, and others. Such tissue characterization methods and new imaging and therapy techniques may form the basis of programs that will translate to the Insertion Device (ID) beamline, to imaging facilities that use conventional X-ray sources, or even lead to clinical practice.

II. User program

The BM beamline has attracted significant user interest from the moment it became operational. The beamline has been oversubscribed from the start, and we are able to accept only about 50-60% of the general user proposals. Around 51 experiments, utilizing ~440 experimental shifts (1 shift = 8 hours) are supported per year. The average number of users coming to the beamline is ~100 per year. The majority of the user experiments, 70-80%, perform biomedical research in various fields like human and animal reproduction, cancer imaging and therapy, spinal cord injury and repair, cardiovascular and lung imaging and disease, bone and cartilage growth and deterioration, mammography, comparative biology, dental imaging, developmental biology, gene expression research, and others.

About 10-15% of the time is used by experiments aiming at the development of novel instrumentation and techniques for imaging research. The remaining few percent of the time goes to material science, fuel cell research, oil recovery, soil science, archeology, etc. The signature areas of research are development of novel imaging instrumentation, and bone and scaffold imaging.

The research conducted on the beamline over the last 4 years has been described in 44 journal publications, 8 conference proceedings papers and contributed to 13 theses.

III. Beamline

A. Beamline and Experimental Endstation

05B1-1 beamline design is described in detail in [3]. The BM beamline utilizes 10 mrad of the horizontal photon

D.A. Jaffray (ed.), *World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada*,
IFMBE Proceedings 51, DOI: 10.1007/978-3-319-19387-8_39

beam angle prepared by the source with critical energy of 7.57 keV. The design of the beamline provides access to the monochromatic X-ray beam with energy tunable in the range 15-40 keV or to pink beam. The maximum beam size in the experimental hutch POE-2 is 220 mm (h) x 5 mm (v).

LabVIEW software & hardware from National Instruments is used to control the end-station components. This allows staff to rapidly create user-friendly interfaces and make custom programs for each experiment. Examples of such customizations include: measurement specified timing and triggering; incorporating dose information; 1Dimensional/2D/3D scanning and interfacing to user provided equipment.

The POE-2 hutch contains two optics tables. The upstream table has limited space and is used for in-line phase measurements requiring a long sample to detector distance (up to 6 m). It is also used for methods such as spectral K-edge subtraction as a single crystal monochromator can be placed deflecting the beam upwards. A rail system is in place to hold stages and the detector. The larger downstream table is used for most experiments and has space for several stages and user equipment. This table is typically used for projection or CT imaging and other measurements. This is also the location of the analyzer crystal and the detector positioner. The detector positioner has ~2 m vertical travel range for use both with the analyzer crystal or for other measurement geometries.

B. Controls and Human Factors

The majority of the operations software for permanent 05B1-1 beamline equipment (including filters, slits, monochromator, shutters etc.), as well as the software for monitoring beamline conditions, was developed using CLS' standard of EPICS (Experimental Physics and Industrial Control System) programs and either EPICS EDM or Qt / Python graphical user interfaces, with Pro-Dex MAXv / VME-based motor control. Wherever possible, high-level beamline software used by researchers provides an abstraction layer to hide the details of operation of the individual beamline components from the user. In addition, many ease-of-use features have been deployed, including an integrated main beamline operations screen. Beamline status screens feature a 3D beamline model showing the exact location of any problems with machine protection components on the beamline.

Human factors have been incorporated on BMIT wherever possible, including in the design of software and hardware, as well as ease-of-use features of beamline control stations and experiment hutches [6]. Software development on BMIT follows basic human factors principles: tasks are simplified as much as possible; standardization is used to reduce misinterpretation; memory dependence is reduced as much as possible. Feedback from our users continues to drive usability improvements to BMIT.

IV. Experimental Techniques

Several different imaging modalities can be used at the beamline. In addition to standard absorption X-ray imaging with both monochromatic and polychromatic X-rays, users have access to synchrotron imaging modalities such as K-edge subtraction imaging (KES), phase contrast imaging (PCI) and DEI both in projection and CT modes. This is mainly accomplished through having a number of detectors and utilizing a flexible set-up strategy. Experimental geometry can be varied as needed, including sample-to-detector distance up to 6 meters. A workshop is available for making simple sample holders or for attachment of user samples and equipment. Several cameras are available for monitoring and cables can be run to the outside for external control and measurement.

PCI and DEI are powerful tools for visualization of soft tissue (low Z materials) and allow for low dose imaging since the contrast is not based on the absorption of the X-rays. The DEI technique uses an analyzer crystal aligned with the second monochromator crystal, the analyzer is positioned between the sample and the detector. The angular position of the analyzer can be changed and images can be taken at different positions on the rocking curve for Multiple-Image Radiology (MIR). Mathematical processing of such images enables production of images with absorption, refraction and scatter contrast. The DEI technique was expanded to CT mode the key being to stabilize the position on the curve during the scans [7].

V. New instrumentation programs

X-ray optical instrumentation projects are being pursued at the BMIT beamlines to address the needs for various imaging programs. Two systems which are in the process of being implemented will be described here.

A. Spectral KES

A bent Laue silicon crystal has been used to micro-focus the X-ray beam to prepare a beam for small animal KES [8]. This system, which has a small focus size (80 μm) and very good angular energy dispersion, is called "spectral KES" because it allows the use of most of the vertical beam size with very few "edge crossing" energies [9]. In the spectral KES system only 5% of the vertical size of the beam is at edge crossing energies as compared to 33% on other sys-

tems that also typically block 50% of the flux. An analysis program was written which extracts contrast and material images in the same manner as KES, but accounts for the full energy dependence of the imaging beam. A schematic of the system is shown in Fig. 1a with an example of the use of the system for imaging iodine and xenon in Fig. 1b.

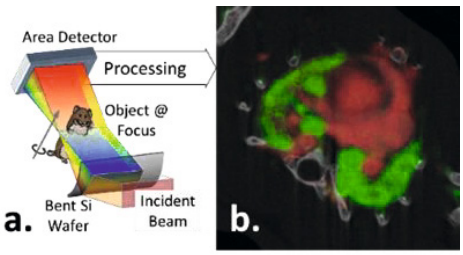

Fig. 1 Spectral KES system – schematic layout is shown in (a) and an example of use for computed tomography of iodine (red), xenon (green) and water (gray) imaging in a rat (b). The region shown is through the thorax of the animal (courtesy Nancy Ford, UBC, Vancouver, Canada).

B. Bent Laue Beam Expander

One of the emerging areas of synchrotron biomedical research is full field dynamic imaging that shows how a system behaves physiologically. The biomedical beamline at the CLS could not be built with sufficient length to allow the beam size to expand beyond about 5 mm on the BM beamline and 10 mm on the insertion device beamline.

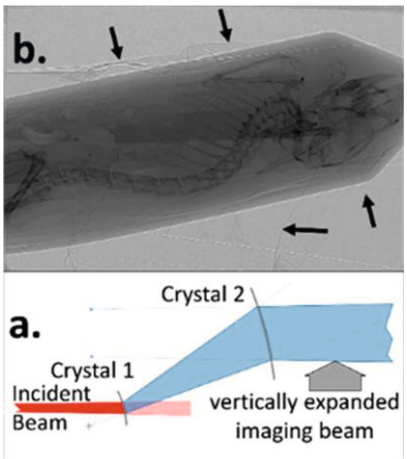

Fig. 2 Phase Preserving Beam Expander - the schematic of the system is shown in (a). The upper figure (b) shows a euthanized mouse in a tube. The arrows indicate phase contrast from masking tape.

We have developed a double crystal bent Laue monochromator that vertically expands the imaging beam (typically by a factor of 10). Initial implementation of this system is presented here [10]. A more advanced system with optical modifications also allows the preservation of phase contrast - see Fig. 2.

VI. Primary Research Areas

A. Bone Imaging

Imaging of skeletal structures has been an area of focus for BMIT right from the initial experiments performed on 05B1-1. A variety of techniques have been applied to the study of bone including KES imaging of strontium [11], DEI of trabecular structure [12] and phase contrast CT applied both *ex vivo* and *in vivo* [12-14]. A key pursuit over the past four years has been improving resolution, aiming for the scale of a single micron - a level capable of resolving cellular spaces (lacunae) within vertebrate bone.

Initial attempts utilizing a conventional beam monitor with a powder scintillator reached ~2 μm voxels and enabled detection of lacunae within rat bone specimens [15]. A system employing a microscope lens – based beam monitor with a single crystal scintillator was developed with Bruker Micro-CT. Operating at 1.4 μm voxels the system was successfully employed to study rat bone (manuscript under review) but this was only effective from a time perspective when utilizing filtered white beam due to flux limitations. Later experiments have yielded the first sub-micron voxel (0.7 μm) scan performed on 05ID-2 beamline (Fig. 3).

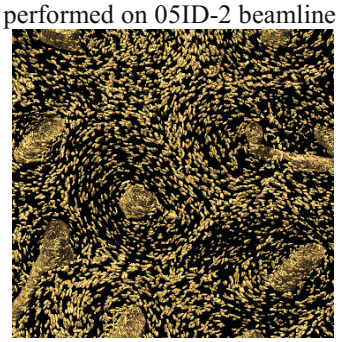

Fig. 3 3D rendering of human bone cellular spaces surrounding blood vessel canals. Data captured at 0.7 μm voxel size on 05ID-2 with monochromatic beam. Scan time was approximately 1.5 hours.

Future plans include the pursuit of a lateral beam focusing system utilizing the technology employed for the beam expander described above as well as modification to the Laue monochromator of the ID line to further improve flux and reduce scan times for energies in the range of 20-30 keV. The system thus holds the promise of scans at the micron scale in under an hour: a powerful capability with many applications extending beyond the study of bone.

B. Scaffolds Imaging

BMIT has become very attractive to Tissue Engineering (TE) researchers due to the advanced noninvasive 3D X-ray imaging techniques provided. In TE, biomedical imaging

techniques play an important role in the characterization of engineered tissue scaffolds [16-17]. Innovative imaging techniques are needed including advancements from 2D to 3D image analysis and quantification, from invasive/destructive methods to noninvasive, nondestructive and real-time methods. Izadifar et al. [18], working on cartilage TE, successfully visualized low density poly-ε-caprolactone scaffolds in pig joints in situ using the DEI-CT technique without contrast agents. The tomography results clearly show the 3D microstructure of the scaffolds and both pore size and strand size of the scaffolds are measurable from the images (Fig. 4).

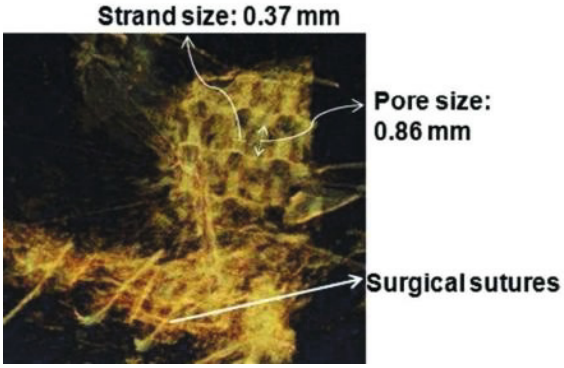

Fig. 4 The implantation site shows the grid structure of the scaffold with measureable strand and pore sizes and details including the sutures used in the surgery [18].

One of the advantages at BMIT compared to conventional CT is that the low density scaffolds and soft tissues can be directly visualized *in vivo*. There is a great need for the visualization of low density scaffolds and soft tissues in soft TE applications.

Phase contrast imaging techniques available at BMIT are well suited for soft tissue imaging. DEI has recently been shown to enable imaging of polymer scaffold structure which was embedded within muscle tissues by Zhu et al, who are conducting nerve tissue engineering studies at BMIT [19]. The structure of the muscle tissues can also be identified from the DEI images, while both the scaffold and tissue are invisible when using conventional X-ray imaging techniques (Fig. 5). Additionally, live animal imaging techniques are available at BMIT, which will be greatly useful for clinical studies in TE.

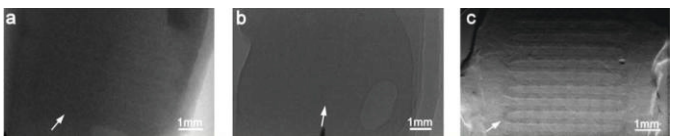

Fig. 5 X-ray images of the polymer scaffold embedded in rat muscle tissue: (a) laboratory-based radiograph at 60 kVp, (b) PCI image at 20 keV, and (c) DEI image at 20 keV. Arrows in (a), (b), and (c) indicate the location of the scaffold in the muscle tissues [19].

VII. Conclusions

The Canadian BMIT facility provides unique synchrotron-specific imaging capabilities that have proven to be powerful tools for visualization of soft tissue. The monochromatic spectral range spans 15–40 keV, and the beam is more than 200 mm wide in the experimental hutch. Several different X-ray detectors are available with resolutions ranging from 2 μm to 200 μm. With the opening of the ID beamline [4-5] program in 2015, the imaging program will extend to higher energies (up to 120 keV) and a higher capacity positioning system (up to 450 kg).

Acknowledgment

Research described in this paper was performed at the Canadian Light Source, which is funded by the Canada Foundation for Innovation, the Natural Sciences and Engineering Research Council of Canada, the National Research Council Canada, the Canadian Institutes of Health Research, the Government of Saskatchewan, Western Economic Diversification Canada, and the University of Saskatchewan.

Conflict of Interest

The authors declare that they have no conflict of interest.

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