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LIVE ANIMAL IMAGING PROGRAM AT BIO-MEDICAL IMAGING AND THERAPY FACILITY AT THE CANADIAN LIGHT SOURCE

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Abstract
The live animal imaging program at the Bio-Medical Imaging and Therapy (BMIT) facility at the Canadian Light Source has been developing for the last 5 years and continues to grow. It is expected to become a large portion of the user activity as numerous groups work towards the goal of live animal studies. Synchrotron-based imaging of live animals is an opportunity for great science that also brings challenges and specific requirements for the experimental end-station. The beamline currently provides basic support and has been improving the facilities available. For example, there have been changes to the lab to allow for longer rodent housing and improved housing during measurements. Remote control of heat lamps and of flow rate for gas anaesthesia allow a veterinarian or animal care worker to make adjustments without interrupting the imaging. Integration of user equipment such as heart/breathing monitoring and ultrasound equipment with the beamline systems can be used for gating control of imaging. Future improvements will be done with consultation with university veterinarians and the user groups.

INTRODUCTION

The Bio-Medical Imaging and Therapy (BMIT) facility at the Canadian Light Source (CLS) provides a world class facility with unique synchrotron specific imaging and therapy capabilities [1 – 3]. BMIT is used to study diverse problems in human medicine, veterinary medicine, micro-beam radiation therapy, dosimetry, agriculture, and other biomedical areas. The facility is comprised of 05ID-2 and 05B1-1 beamlines and supporting laboratories. This paper will first look at the background and requirements involved with working with live animals and then describe some of the engineering solutions which were developed in a collaboration of all those involved.

LIVE ANIMAL PROGRAM AT THE CLS

The live animal imaging program at the BMIT facility at the Canadian Light Source has been developing for several years and continues to grow. It is expected to become a large portion of the user activity as numerous groups work towards the goal of live animal studies. Key goals of the beamline include assuring best practices in animal anaesthesia monitoring and producing the best images and scientific results possible with minimal dose delivered. Figure 1 shows statistics for live animals brought to BMIT. Usage varies considerably depending on the research groups. Note that recent groups have begun to image larger animals such as rabbits and dogs.

There are a number of considerations for the design of the end-station for the imaging of live animals and university veterinarians are consulted closely. The key requirement centres on animal care. In brief, animals arrive at the facility and are under the care of a veterinarian or other animal care personnel. When ready, an animal is placed under anaesthesia and taken into the hutch to be imaged and/or treated. Treatments may include radiation or medical procedures. Imaging may be used to evaluate results. The animal is monitored throughout the process. Once the measurements are finished the animal is removed from the hutch for recovery in the lab. Other requirements are from external bodies. The CLS is regulated by the Public Health Agency and follows the Canadian Biosafety Standards and Guidelines[4, 5]. The CLS is also a member of the Canadian Council on Animal Care (CCAC) [6, 7] and a participant of the University Animal Care Committee [8].

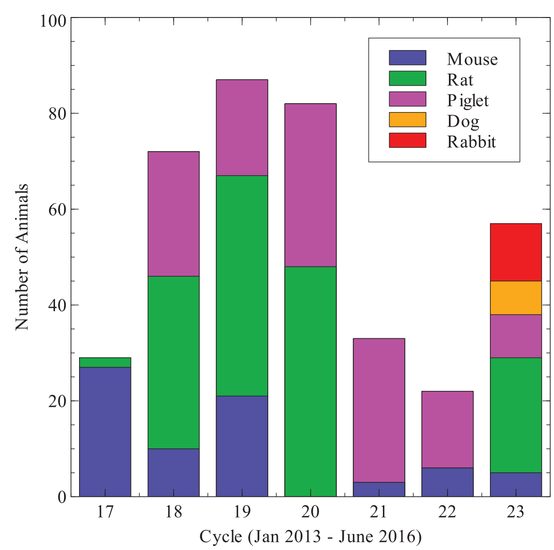

Figure 1: Animal usage statistics. Cycles correspond to 6 month periods.

LABORATORY FACILITIES

The CLS provides basic laboratory facilities and a change-room. There are two labs adjacent to the end-stations, as well as a life science lab nearby. These labs provide equipment for the users and areas for sample preparation. The labs include biosafety level 2 areas.

The BMIT labs also provide a place for the temporary housing of animals, medical procedures and for recovery after experiments. For example rodents may be kept in micro-environment cages up to 72 hours. The lab has red film on the windows and red lights to simulate a day/night

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cycle for rodents. Other animals may be kept, if properly housed, for up to 24 hours. The hutches have a separate air intake from the rest of the experimental hall and can have up to 10 air exchanges per hour. There is a controllable air pressure differential with the hall and limited temperature control. Records of hutch conditions including temperature, humidity, and air flow data are available for audit purpose when requested.

END-STATION EQUIPMENT

The end-station is where the measurements are made and so is the nexus of all experiments. All the equipment is arranged around the holder where the animal will be placed for imaging or therapy. The goal is to be able to do as much as possible from outside the hutch as during the measurement no one can be inside. It is important to have coordination between the safe operation of the equipment which may not always be able to stop quickly and the animal care worker who may need rapid access to the animal to administer care. To facilitate this quick access and fast exit, a Zone Bypass Button (ZBB) feature has been implemented as an extension to the Access Security and Interlock System (ACIS)[9] used at the CLS.

Figure 2 and Figure 3 show experimental set-up at BMIT on the two currently used end-stations. These are meant as illustrative examples as there are many possibilities. Cameras are (security, web-cam) are arranged such that various aspects of the experiment can be monitored from outside (Figure 4). The breathing of the animal can be closely monitored as well as vital signs and temperature. The heat lamp is controlled from outside. A prototype has been made to control the anaesthesia gas levels. In Figure 2, the equipment is placed around the table. The animal (not shown) is on a motorized stage which is controlled remotely.

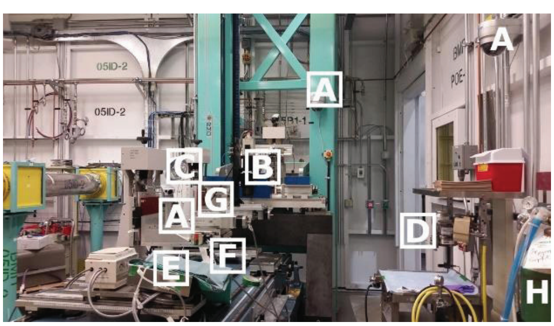

Figure 2: Experimental setup on 05B1-1 showing some of the equipment needed for an imaging session. A. cameras, B. detector, C. heat lamp, D. anaesthesia machine, E. heating pad, F. vital signs monitor, G. Sample location on stage, H. Oxygen tank.

Figure 3 shows a somewhat different configuration using a micro-beam therapy (MRT) lift. In this case, the animal (not shown) is on a medium size positioning device. Some of the equipment is arranged on the stage with the animal. This means that during a CT scan all of the equipment will rotate in addition to the animal. Consequently, all tubes, cables, wires, etc. need to be able to rotate without becoming entangled or pulled off. Wireless communication is necessary in order to record vital signs or to control equipment such as a ventilator, remotely.

The synchrotron beam is a stationary beam unlike in conventional imaging equipment. This means that it is the sample that must rotate and move in order to image which introduces a dimension of difficulty in the design. The sample must be held in place while preventing any motions that would distort the images. Naturally this includes the animal and the support apparatus. Samples may also have to be held vertically rather than in the more natural horizontal position used in clinical devices. The users and the facility have designed and built a plethora of mounting plates, adaptors, simple and complex animal holders, a universal sample holder and more in order to address this deceptively simple issue.

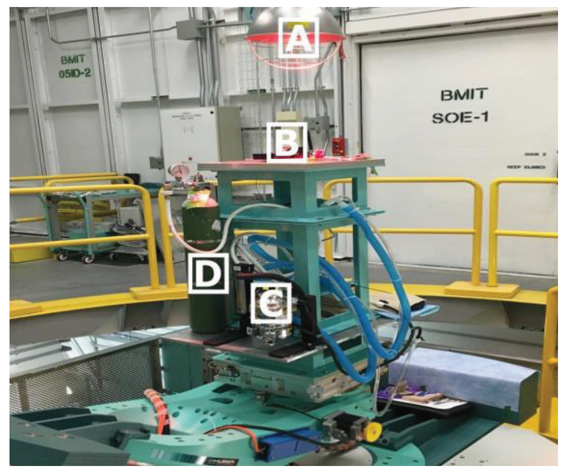

Figure 3: Experiment set-up for micro-beam therapy on 05ID-2 on MRT lift. A. heat lamp, B stage for sample, C. anaesthesia machine, D. oxygen tank.

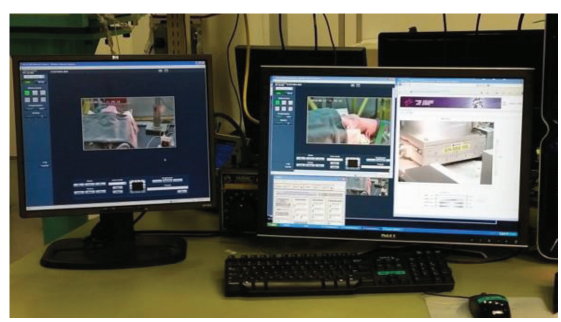

Figure 4: Conditions in the hutch are monitored from the control room. Multiple cameras, vital signs monitors and user equipment can be watched and controlled remotely.

A helpful tool for creating sample is the 3D printer. It can be time consuming and expensive to design, draw and machine a new sample holder or a part. The rapid drop in prices and ever expanding capabilities of 3D printers has meant that rapid prototyping and testing is quite affordable. One project went through multiple versions (~8) of a holder for a mouse for doing a CT of the lungs [10].

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Through the use of 3D printing they were able to design, test and determine problems quickly. 3D printing was used to create a plastic holder for cartilage samples that could be used for both phase-contrast computed tomography and magnetic resonance imaging [11]. Figure 5 shows a drawing for a cell irradiation holder that was 3D printed. This holder is intended for cells but relates to dosimetry and cell work which is needed for micro-beam radiation therapy, an area of interest at various synchrotron facilities. The simplicity of using 3D printing means that student projects can go from concept to design to a final project in a matter of days to weeks and if successful can then immediately be used in a research setting.

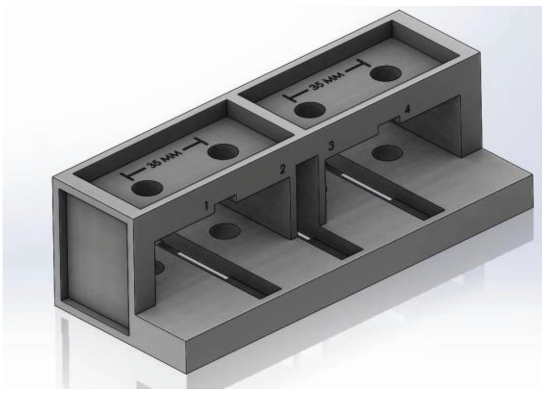

Figure 5: Drawing of cell irradiation holder. This holder has four holes for sample tubes and slots for tungsten plates for shielding between samples.

Software is an important component of beamline operation and it is important to be flexible as user needs can change rapidly. User groups are unlikely to have dedicated computer staff so it often falls to the beamline to provide technical assistance. A number of programs have been written using LabVIEW [12]. LabVIEW is an easy language for creating graphical interfaces. It is important to have fairly easy to use interfaces for users as they may little to no experience with the system. The main benefit for the staff is that rapid prototyping and custom programs are relatively easy to produce. This improves the ability of the beamline to alter measurements, match experimental requirements and to solve issues as they arise.

CONCLUSION

Live animal experiments are challenging but also present great opportunities for high-impact science. The engineering challenges include holding and remotely manipulating the animals in order to do the imaging. Each experiment can create specific engineering challenges. Multiple modalities must be supported and simultaneously it is necessary to ensure the health and safety of a living animal to the satisfaction of the attending veterinarian. It is the collaborative efforts of the users, animal care, and the beamline and engineering staff that allow for such rewarding work to progress and to advance the important science of a live animal imaging program.

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