Beamline 10: Imaging and medical therapy

10

Potential Research Fields

Life sciences

- Biological research – small animal imaging
- Biomedical and medical imaging
- Medical therapy
- Plants and crops

Physical sciences

- Forensics
- Advanced materials
  - Functional polymers
  - Ceramics
  - Nanomaterials and composites
  - Metals and alloys
  - Micro-electronic and magnetic materials
  - Biomaterials
- Engineering
- Mineral exploration and beneficiation
- Oil and gas production and distribution
- Agricultural technology

Advanced manufacturing

- Production of micro-devices

Introduction

It is proposed to construct a world class beamline for developing the technology for high resolution x-ray imaging of objects of the size of small animals, and a wide range of materials science samples in the first stage. Full human and large object imaging will be possible in a later stage. The technology for the beamline will build on the pioneering work of Australian scientists based largely in Melbourne[1].

One aspect of this work relates to the development of phase-contrast imaging techniques that transcend the conventional reliance on absorption to produce contrast. A second aspect relates to the development of theory to make these imaging techniques quantitative. These developments provide the basis for major advances in x-ray imaging science that are not only relevant for synchrotron-based imaging but also for radiography with conventional sources.

The beamline will be capable not only of satisfying the demand in Australia for synchrotron-based imaging using hard x-rays, but will also have sufficient flexibility and novel features to permit the development of new techniques and take advantage of the world standing that Australian scientists have in this area. It is intended that this beamline be a facility that will attract overseas researchers and which will be a flagship for the Australian synchrotron.

User Community

Potential users of this beamline include groups from at least fifteen biomedical research institutes (linked to pharmaceutical drug developments), five Cooperative Research Centres and a number of small to medium enterprises. Also, major manufacturing companies including automotive component suppliers and a number of major aerospace companies as well as the defence industry are expected to be interested in direct or collaborative research. Most of the biomedical and medical users will be new, because this is an area that cannot practically be addressed by current overseas synchrotron access arrangements as they involve live animal or patient studies.

Research Applications

The use of a synchrotron for imaging offers some remarkable improvements over the use of conventional radiographic equipment, greatly facilitating new x-ray imaging techniques as illustrated in the images in chapter 3. The combination of fine-tunable monochromatic x-rays with high intensity and collimation makes possible enormous improvements in contrast and resolution. Moreover, the use of new contrast mechanisms based on phase measurements, coupled with being able to choose the optimal monochromatic energy for the particular situation, results in very significantly lower tissue doses than the wider-spectrum x-rays of conventional x-ray sets. A very significant added advantage is that the beam energy can be tuned to energies that correspond to

1 S.W. Wilkins, T.E. Gureyev, D. Gao, A. Pogany, and A. Stevenson, Nature (1996) 384, 335–8, K.A. Nugent, D. Cookson, D. Paganin & Z. Barnea, Phys. Rev. Letts. 77, (1996) 66, 2961–4; Lewis R. Medical applications of synchrotron radiation X-rays. Phys. Med. Biol. 42 (7): 1213–43, 1997.

absorption by individual elements. As a result it is possible to image specific chemical elements with high sensitivity and micron, or even sub-micron, scale resolution.

The power of these imaging techniques is particularly suited to the study of living processes, as well as in situ materials processes such as solidification and precipitation phenomena in alloys[2]. The proximity between the Australian Synchrotron, Monash University, CSIRO, The University of Melbourne and the Monash Medical Centre will bring together a set of expertise and facilities that will enable this to be only the third beamline in the world especially configured for work on a wide range of live animals. The study of live animals for medical research is an area that is impractical under overseas access programs, and so relates to an essentially new and numerous Australian Synchrotron user class that has not been served in the past.

The properties of the proposed beamline, in particular the high energy capability, will also enable the study of novel methods of radiation therapy that cannot be achieved with any other type of x-ray source. Some of these methods show great promise for the treatment of cancer.

There are numerous applications for a facility such as this and the following represents just a small sample to illustrate the possibilities.

Biomedical imaging

Despite being by far the most popular medical imaging modality, lack of soft tissue contrast is a significant problem in both medical and biomedical conventional x-ray imaging. The relatively small variations in density and composition of soft tissues means that their x-ray attenuation characteristics are very similar. Conventional radiography produces images through the differential absorption of x-rays, and so provides very little soft tissue contrast unless high doses are employed as in computed tomography. Synchrotron-based imaging techniques, however, can also produce high resolution images using differences in the refraction and scatter of x-rays as they pass through tissue. Genuine soft tissue contrast with micrometre-scale resolution is possible with synchrotron x-ray imaging.

The collimation and monochromaticity of the imaging and medical therapy beamline will allow high resolution images to be recorded at a far lower dose than required by conventional equipment. This then will allow longitudinal studies (serial imaging) to be performed for investigations where the dose required by conventional imaging would confound the experiment. A large area of application for the beamline is in the area of small-animal imaging in relation to medical research and the development of new pharmaceuticals.

One of the problems at present is that animals are often sacrificed in order to obtain anatomical information at high resolution. The present beamline will allow in vivo imaging of small animals and so provide the major advantage of allowing longitudinal studies to be carried out. This has the significant advantage of following the same animal through the process and also dramatically reducing the number of animals sacrificed in a study.

Imaging of advanced materials and manufactured products

The high contrast, high speed, high coherence and microtomography capabilities can be exploited to enormous effect in the areas of materials science, non-destructive testing and mineralogy.

Examples include:

- in situ studies of precipitation and voids in industrially important light metal alloys
- minerals studies, including sedimentation of slurries, especially relating to compressibility and permeability; Also studies of reactivity of small particles at temperature
- the study of membranes for use in advanced fuels cells
- studies of fracture in ceramics
- the use of high resolution computed tomography (CT) for the study of porosity in oil bearing rocks. By tuning to different energies it will also be possible to image the amount of residual oil left in the rock following extraction
- investigation of micro/nano structured devices by micro-CT, e.g. for use in automotive applications
- the study of advanced materials following and during various stresses, both mechanical and environmental. Many advanced materials, for example those in aerospace applications, are composed of materials that cannot be imaged with conventional x-ray techniques due to lack of contrast.

Imaging of plants

The same contrast mechanisms used to visualise soft tissues in animals can also render visible many of the structures inside plants. An enormous range of studies are envisaged but of particular interest is the study of drought- and salt-tolerant species with a view to developing more efficient crops for Australia. Phase-contrast CT techniques will be employed to study the development of root structures without removing the plant from the soil, while K edge and micro-fluorescence imaging will be used to study protein hormone flow dynamics.

Radiotherapy

In the biology of cancer, imaging and therapy are inextricably linked. The capabilities of beamline 10 are designed for excellent imaging and are also ideally suited for the study and development of novel radiotherapy techniques.

2 R.H. Mathiesen, L. Arnberg, K. Ramsøskar, T. Weitkamp, C. Raur, A. Snigirev. Time resolved x-ray imaging of aluminium alloy solidification processes. Metallurgical and Materials Transactions B, v. 33B, 2002 pp. 613–623; and Mathiesen, R. H. Arnberg, L. F. Mo, Weitkamp, C. Snigirev, A. Time resolved x-ray imaging of dendritic growth in binary alloys. Phys. Rev. Letts. v. 83, No 24, p 5062, 13 Dec. 1999 (full text PDF available through CSIRO e-journals; movies available at http://www.phys.ntnu.no/~ragmat/index.html)

As described in chapter 3, the major problems with radiotherapy lie in determining the extent of the spread of the disease and delivering sufficient radiation to the tumour without damaging surrounding healthy tissues. These problems are particularly acute in brain tumours where the surrounding tissue is extremely sensitive. Synchrotron radiation is able to deliver a high dose to the targeted area only, with an accuracy that is significantly better than current clinical techniques. Research will focus on three possible techniques: photon activation therapy (PAT), CT therapy, and microbeam radiation therapy.

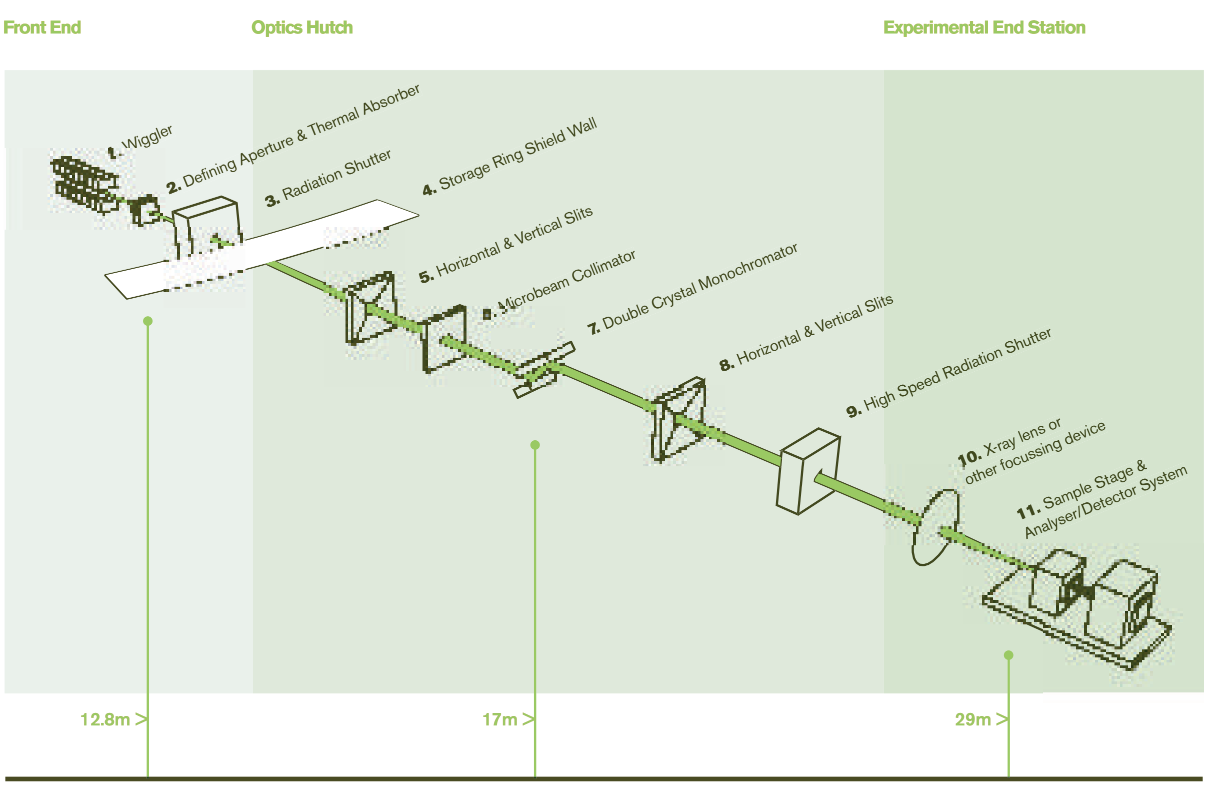
PAT and CT therapies both use specific x-ray energies that are preferentially absorbed by an element that has been delivered into the tumour. In PAT, a chemical agent (e.g. cis-platinum, which is also used for chemotherapy) is introduced and concentrates in the tumour. By choosing the correct energy, the x-ray beam interacts preferentially in the tumour and delivers a high localised dose. CT therapy also uses a contrast agent (e.g. iodine) that concentrates in the tumour, but takes advantage of beam spreading effects and stereotactic methods to spare normal tissues.

Perhaps the most exciting possibility is microbeam radiation therapy (MRT). Here extremely large radiation doses are applied to tissues in an array of micrometre-thick highly collimated x-ray beams. The extraordinary aspect of microbeam radiation is that it spares healthy tissue far better than large-area beams of the same dose and yet the tumour is still damaged. The reason for this effect is unknown, and is a fertile area for study. The method has been used with great effectiveness to deliver doses in excess of 1000 Gy to live animals. Note that 10 Gy delivered in a conventional treatment is lethal.

It is possible that therapies utilising this effect may revolutionise the treatment of some kinds of cancers, which are currently untreatable. A strong program of research into the nature of this effect together with determining the most effective way of delivering the dose will be a significant activity on this beamline.

Fundamental physics of imaging

The field of x-ray phase-contrast imaging in Australia is a very active one with world leading groups at CSIRO, The University of Melbourne and Monash University, all near the Australian Synchrotron. The establishment of the imaging and medical therapy beamline will give an enormous stimulus to further extending this line of activity and to transferring much of the fundamental research into practice. A very strong collaborative effort is envisaged between these groups, spanning algorithm, software, detector and x-ray optics developments. This will result in a world leading centre for research and applications based around this beamline. The beamline will also provide a very valuable test-bed for new ideas in the area of x-ray imaging and holography, and in the development of new and improved x-ray optics.



BEAMLINE 10 Imaging & Medical Therapy (Stage 1)

Figure BL10.1. *Schematic of the short beamline for x-ray imaging and therapy (stage 1)*

Additional benefits

The very nature of the research on this beamline will also lead to advances in machine optics, precision electronic and hydraulic movement, support and restraint devices, image acquisition, detector technology data transfer and analysis, and information technology interfaces (for interrelating image data with biological and treatment data). This can have a very large spin-off effect in the whole field of medical, industrial and biomedical imaging, a $US4 billion/year industry at the present time. The beamline will give a major boost to Australia's medical physics, biophysics and materials science communities.

Beamline Design

The beamline will be the second insertion device beamline that we are aware of to be optimised for in-line phase-contrast imaging for in vivo small animal and clinical medical applications. The beamline will incorporate the capability of using both white and pink beam modes in order to facilitate short exposure times.

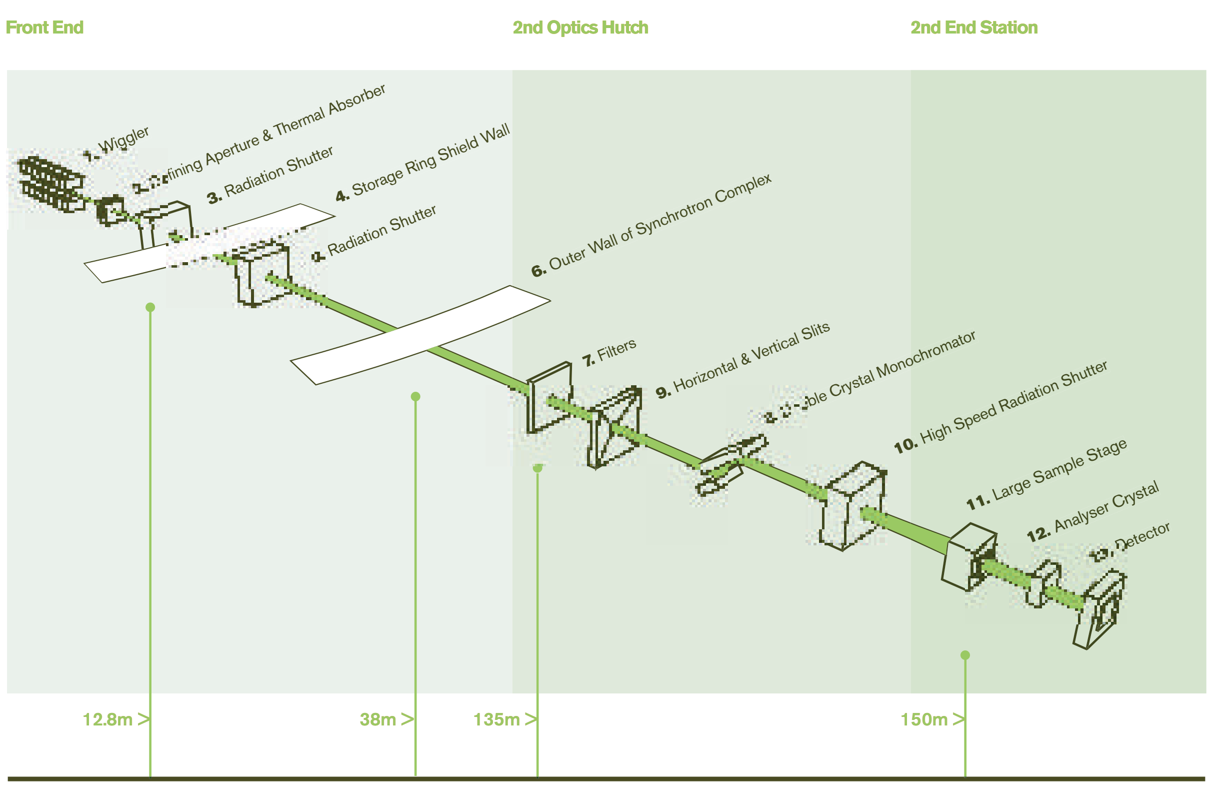
Two end stations are to be built. The first, as close as possible to the source, is to be built as part of the core initial suite of beamlines (category A, refer chapter 4). The second, a very long beamline with the sample station external to the main synchrotron building, at 150 m from the source, is a category B facility and will be built after the core suite of beamlines is established.

When both end stations are completed, two distinct modes of in-line phase-contrast imaging will be available. The first will use projection imaging from a small secondary focus 'spherical wave case' to obtain high spatial resolution (~ 100 nm), for example in microelectronics inspection, mineral grains studies or study of biomedical samples, as well as in a large class of advanced materials and manufactured products. The second mode will use a large source to sample distance (of order of 150 m) 'plane wave case', to yield a large field of view for small animal, clinical medical and large materials science studies. Other modes of phase-contrast imaging, such as diffraction-enhanced imaging, will also be possible.

Some of the advantages of the long beam line are:

- high spatial coherence (and quasi plane wave)
- potentially very high spatial resolution (now detector limited)
- large field of view due to the wide horizontal beams, especially for biomedical and clinical medical imaging applications
- low background scatter in in-line imaging applications due to the very large 'air-gap effect'
- that it will be external to the main experimental hall, so will be well suited to the establishment of a clinical/human imaging suite.

The first station will also have the capability for research on various new cancer therapies, including microbeam radiation therapy. For this work high beam energies and very high intensities are required, so that exposure time can be very short (of the order of milliseconds).



BEAMLINE 10 Imaging & Medical Therapy (Stage 2)

Figure BL10.2. *Schematic for the long beamline for x-ray imaging and therapy (stage 2)*

Beam characteristics

The energy range will cover 4–120 keV (120 keV is required for radiotherapy) with $\Delta E/E \sim 10^{-3}$ as well as a white beam option. This will require a superconducting wiggler, variable from 2 to 4 T.

A beam with high (cross-sectional) uniformity is required and this may involve special (i.e. diamond) windows and apertures, mirrors and monochromators. The optics will need to be carefully manufactured to avoid unwanted phase-contrast effects.

The beam should be broad (Station 1: 50×3 mm²; Station 2: 250×15 mm²) at sample position for many imaging applications. This might be increased by beam expansion optics if necessary.

The positional stability of the source and the mechanical stability of the long beamline will be of importance in many experiments because of the large 'lever arm' effect.

Detectors

Various detectors are envisaged for use for imaging including large area imaging plates with inbuilt scanner. Particular attention will be directed towards acquiring high performance photon counting detectors (such as pixel arrays) and energy resolving detectors, in order to give low dose and a substantial increase in information (at no greater exposure).

Beamline 10 – Imaging and Medical Therapy	
Source	Wiggler (4 T)
Energy range	10–120 keV
Resolution $\Delta E/E$	$\sim 10^{-3}$
Beam size at sample (horizontal × vertical)	50×3 mm² (Station 1); 250×15 mm² (Station 2)