

## **X-ray Imaging Session Chair: Alberto Bravin**

Alberto Bravin received his PhD in Physics at the University of Trieste (Italy) on the development of X-ray phase contrast imaging. In 1999, he joined the European Synchrotron Radiation Facility (ESRF) in Grenoble (France) and since 2003 he has been in charge of the Bio-medical beamline ID17. At the ESRF, he is leading the preclinical phase contrast imaging programs applied to mammography and cartilage studies and the in-house research program on Microbeam Radiation Therapy applied to brain tumors. Dr. Bravin has co-authored more than 60 peer-reviewed papers.

## **SR Biomedical Imaging 2004-2007: Opening New Doors**

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Biomedical imaging with synchrotron radiation has shown a rapid development in the past years. Thanks to technical developments, both in the instrumentation and in the image processing, but also to the growing interest of the medical communities, new research subjects have appeared beside the more traditional in-vitro (mammography, cartilage) and in-vivo (brain and coronary imaging) applications.

Computed tomography and tomosynthesis applied to phase contrast imaging, submicron imaging, in-vivo cells and in-situ nanoparticles visualization are just examples of the emerging fields and applications. This paper will give an overview of the most exciting latest developments which are of potential interest for the medical community.

## **A Comparison of Tissue Phase-Retrieval Approaches for Medical X-ray Imaging**

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Retrieval of the tissue phase-maps has great potential for improving tissue contrast and achieving quantitative imaging for tissue characterization. The robustness of a phase-retrieval approach is of critical importance for clinical imaging applications. On the one hand, the limits on permissible organ radiation doses make acquired images much noisier than that encountered in other non-clinical applications. On the other hand, the phase changes of pathological tissues are small and the diagnosis accuracy would be very much vulnerable to the phase-retrieval errors. For example, while a 4cm-thick breast tissue generates about 700 radians, phase-shift difference between a 5mm-size invasive ductal carcinoma in breast and surrounding parenchyma is of only about 5 radians for 60 keV x-rays. In this work the robustness of phase-retrieval from a single image based on the phase-attenuation duality is compared to its performance with that with the popular TIE-based phase-retrieval approaches for 60-keV x-rays by means of computer simulations. The imaged object is a hypothetical breast of 4 cm thick with very low tissue attenuation contrasts 0.83% for 60 keV x-ray, this attenuation contrast corresponds to that between a 5mm-size invasive ductal carcinoma and surrounding normal breast parenchyma. We assumed a quantum noise 5% associated for low dose imaging. With a single phase-contrast image and our duality-based approach a breast phase-map was retrieved with an average relative phase-error of 0.11%. For the TIE-based phase retrieval approach, an additional image acquired at the contact mode with an anti-scatter grid was simulated. With these two images (one attenuation image and one phase-contrast image) the breast phase-map was retrieved by the TIE-based approach. Since TIE-based phase-retrieval suffers from intrinsic instability, the Tikhonov regularization was employed. In spite of increased radiation dose to breast (due to two acquired images needed), phase-error with the TIE-retrieved breast phase-map is 0.91%, and the tissue-contrast distortion in TIE-retrieved breast phase map is prominent. Hence the phase-attenuation duality-based approach is superior to TIE-based approaches for tissue phase retrieval with hard x-rays. Finally, the phase-contrast tomography with these approaches will be compared.

**KEYWORDS:** Phase contrast; phase retrieval

## **Dual Image Analyser-Based Phase Contrast X-Ray Imaging of Small Animals.**

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Analyser-based phase contrast X-ray imaging can provide high contrast images of biological tissues with exquisite sensitivity to boundaries between tissues. The phase and absorption information can be extracted by processing multiple images acquired at different analyser orientations. Recording both the transmitted and diffracted beams from a thin Laue analyser crystal can make possible phase retrieval for dynamic systems by allowing full field imaging. The thorax of a mechanically ventilated newborn rabbit pup was imaged using this technique using a 26 keV beam from the SPring-8 synchrotron radiation facility. The diffracted image was produced from the (111) planes of a 50mm x 40mm, 95 micron thick Si(220) surface-cut analyser crystal. The beam and analyser were sufficiently large to encompass the thorax of the rabbit pup, making it possible to observe changes in anatomy with high contrast and spatial resolution.

KEYWORDS: Phase Contrast Imaging Small Animals

## **Imaging of Lung Function Using Synchrotron Radiation Computed Tomography: What's New?**

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There is a growing interest in imaging techniques as non-invasive means of quantitatively measuring regional lung structure and function. Abnormalities in lung ventilation due to alterations in airway function such as those observed in Asthma and COPD are highly heterogeneous, and experimental methods to study this heterogeneity are crucial for better understanding of disease mechanisms and drug targeting strategies. In severe obstructive diseases requiring mechanical ventilation, the optimal ventilatory strategy to achieve recruitment of poorly ventilated lung zones remains a matter of considerable debate. We have used Synchrotron Radiation Computed Tomography (SRCT) for the in vivo study of regional lung ventilation and airway function. This imaging technique allows direct quantification of stable Xenon (Xe) gas used as an inhaled contrast agent based on K-edge subtraction imaging. Dynamics of Xe wash-in can be used to calculate quantitative maps of regional specific lung ventilation. More recently, the development of Spiral-CT has allowed the acquisition of 3D images of the pulmonary bronchial tree and airspaces. This technique gives access to quantitative measurements of regional lung volume, ventilation, and mechanical properties. Examples of application in an experimental model of allergic asthma and in imaging lung recruitment as a function of mechanical ventilation parameters will be presented. Future orientations of this project as well as applications of other SRCT lung imaging techniques such as Diffraction-Enhanced Imaging will be discussed.

**KEYWORDS:** Synchrotron Radiation, Computed Tomography, Asthma, Regional lung ventilation

## Refraction-Based 2D, 2.5D and 3D Medical Imaging: Stepping Forward to a Clinical Trial

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X-ray dark-field imaging (XDFI) [1] using a transmission angle analyzer with a theoretically predicted thickness such as 2.124 mm has been successfully developed. The FOV of 90 mm x 90 mm [2] with the spatial resolution of 50 microns is available. This can visualize articular cartilage [2] and micro-papillary carcinoma [3]. That the contrast of breast cancer is based on Ca concentration was confirmed by 2-D x-ray fluorescence imaging [4]. Thinning the analyzer down to 125 microns can achieve a higher spatial resolution of being able to observe isolated breast cancer cells and stroma of the same micro-papillary carcinoma [5]. Furthermore the algorithm for a 3-D reconstruction due to refraction was newly developed [6-9]. Image of ductal carcinoma has been successfully achieved [10], leading to a potential use as endoscope [11]. Quite recently XDFI-based tomosynthesis [12] has been successfully developed to visualize sliced information of soft tissue such as articular cartilage and breast cancer. This would make a path to a clinical trial much shorter. The system is under development by a collaborative team.

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## Refraction-Enhanced Tomosynthesis by X-Ray Dark-Field Imaging

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A tomogram of a finger joint based on X-ray Dark-Field Imaging (XDFI) was demonstrated using the shift-and-add tomosynthesis algorithm. The experiment was performed at beamline 14B of the Photon Factory in Tsukuba, Japan, using synchrotron X-ray from the vertical wiggler. Incident X-rays were monochromated to 36.0 keV by a Si(333) double crystal monochromator installed in the beamline. The X-ray optics for XDFI comprised two Si crystals: an asymmetric cut Si(220) monochromator-collimator and a 1.1 mm thick Si(220) Laue-case analyzer. The object was an intact cadaveric proximal interphalangeal joint fixed in formalin. Raw tomosynthesis image data were acquired by XDFI in a total of 41 views through an angle of 20 degrees in increments of 0.5 degrees; the object and detector were rotated synchronously such that the fulcrum plane in the object and detector plane remained parallel. The X-ray dosage for one raw image was set to approximately one-eleventh of that for one usual projection image by XDFI. All of the 41 appropriately shifted raw image data were added to produce any tomogram parallel to the fulcrum plane. We successfully obtained a clear tomogram of the finger joint, including articular cartilage, which is invisible to conventional tomosynthesis. The practical depiction ability was preserved even when the raw image data for tomosynthesis was diminished to 11 views through an angle of 10 degrees in increments of 1 degree; consequently, we can obtain any tomogram for the same X-ray dosage as that received for one usual projection image by XDFI. Intrinsically, a projection image by XDFI is composed of mixed contrast based both on X-ray absorption and refraction rather than that based on pure distribution of the X-ray refractive index; these contrasts are mixed in a tomogram obtained by the shift-and-add XDFI tomosynthesis algorithm. Nevertheless, it is significant to clinical medicine that an inner structure such as articular cartilage, invisible to conventional X-ray imaging methods, has been successfully visualized on a tomogram with the preservation of refraction-enhanced contrast.

**KEYWORDS:** tomosynthesis, shift-and-add, X-ray dark-field imaging, synchrotron radiation, Laue analyzer, articular cartilage

## **Synchrotron Based In-Vivo Tracking of Implanted Mammalian Cells**

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One of the great challenges in contemporary medical imaging is to visualise the position of small clusters of cells in 3-D, and in-vivo. The ability to track implanted targeted cells as they grow or metastasise in a natural environment will be invaluable for many areas of biomedical research. We have started to work on a protocol which will lead to this ability. Using glioma as a model we have embarked on developing imaging techniques at synchrotron facilities, which will potentially provide few cell sensitive CT imaging at the micron resolutions, and with low enough dose for small animal testing. This presentation will show the latest results from synchrotron CT encephalography on some animal models.

**KEYWORDS:** Glioma, cell tracking, synchrotron x-ray imaging

## **Imaging Gold-Loaded Tumor Cells Implanted into the Rat Spinal Cord using Computed Tomography**

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Therapeutic approaches using implantation of cells to stall or cure the disease in multiple sclerosis, Parkinson's disease or acute neurotrauma are still in the developmental stage. One of the major concerns is that implanted cells can form tumors in distant organs. We are in the process of developing a synchrotron-based imaging protocol that we hope will allow us to trace implanted cells in a live host organism.

**Material and Methods:** Our experiments were conducted at the SYRMEP beamline of the Elettra synchrotron (Italy). Phase contrast images were produced using a monochromatic x-ray beam in CT modes as well as a micro CT unit. C6 glioma cell cultures were exposed to colloidal gold in the growth medium and implanted in spinal cords of adult male Wistar rats. Animals were sacrificed at various time points after implantation and tissues stored in formalin until used.

**Results:** Gold-loaded cells were seen in the spinal cords after implantation and following tumor development. 3D reconstructions of the tumor cells revealed cell clusters penetrating the surrounding bone as well as larger intact tumors.

**Conclusion:** Synchrotron-based imaging proved a valuable tool for the detection of gold-marked cells in our animal model.

This project was supported by CIHR, SHRF, the University of Saskatchewan and the Brain Tumor Foundation of Canada (Canada); by the MRC of England and by the University of New England (Australia).

**KEYWORDS:** computed tomography, tumor, gold, spinal cord