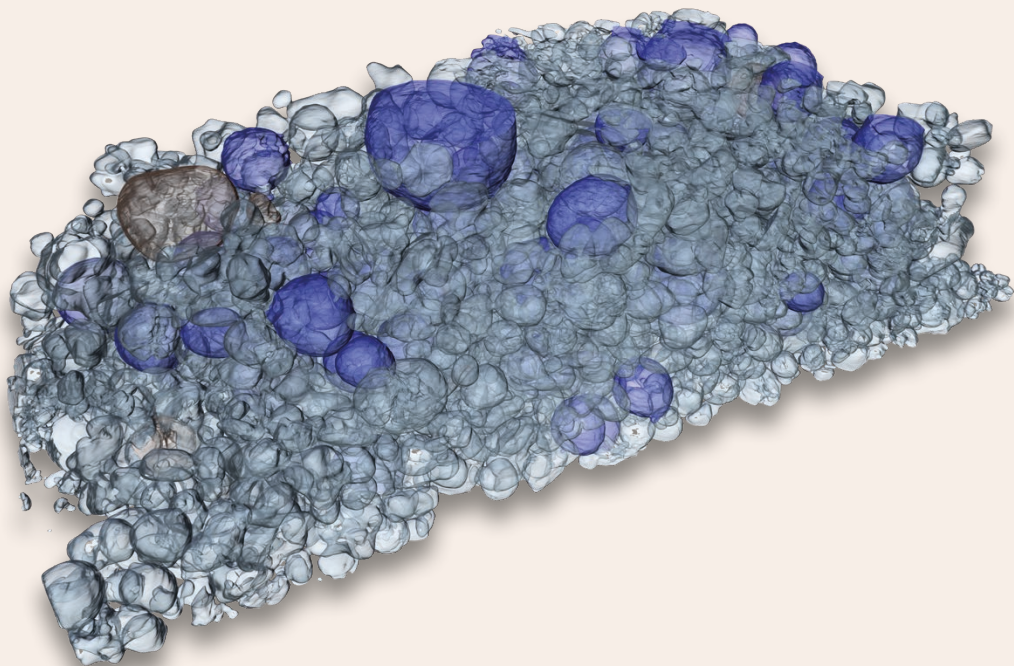


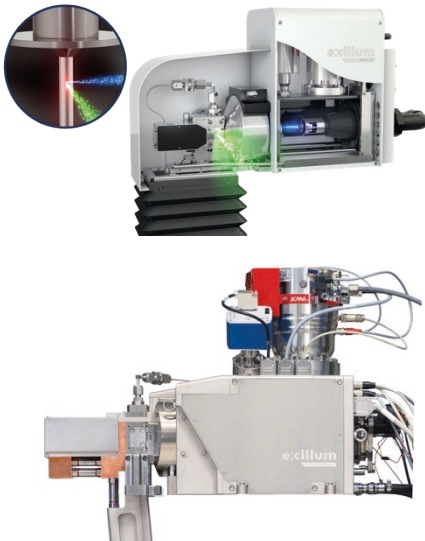
MetalJet and NanoTube for X-ray imaging applications



X-ray imaging

Imaging is the first historic application using X-rays, as demonstrated already by W. C. Röntgen. Even though most imaging done today uses the same method as Röntgen did, the image quality has become far better thanks to the improved sources and detectors. Medical imaging is the most common X-ray application, however, X-ray imaging is also widely used in various fields, from industrial inspection metrology to academic research.

The improved equipment has also opened up the possibility of new methods for X-ray imaging. They all differ in imaging performance and in their requirements on the equipment. Below we give a brief overview of popular imaging methods together with application examples using the Excillum MetalJet and NanoTube X-ray sources.



MetalJet series

The Excillum MetalJet series consist of the MetalJet E1+, and the MetalJet D2+ and the C2. The MetalJet features Excillum's unique metal-jet anode technology and advanced electron optics. Achieving significantly higher brightness and smaller spot sizes than any other available microfocus X-ray source, the MetalJet can create very brilliant and small beams enabling the closest possible performance to synchrotron capabilities in the home lab.

At 1000 watts, the Excillum MetalJet E1+ delivers 17 times more X-ray flux across a broad spectral range compared to a 30 W conventional tungsten-solid-anode microfocus source with the same 30 μm spot size. In the spectral range of 24-29 keV where the indium and tin characteristic emission lines are present, the flux advantage is as high as 100 times. The MetalJet E1 is built for 24/7 continuous performance, and it has sub- μm positional stability and an unprecedented 24 keV indium $K\alpha$ emission.

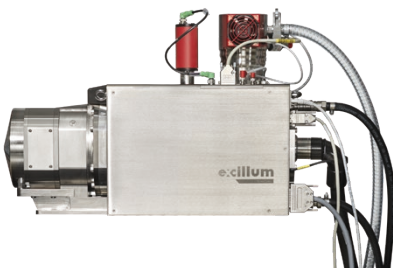
NanoTube N3

The Excillum NanoTube N3 enables industry-leading 150 nm resolution in geometric-magnification X-ray imaging systems up to 160 kV depending on source model. High flux and exceptional spot stability make the source ideal for demanding 3D computed tomography applications as well as 2D imaging in both industrial and research environments.

The NanoTube N3 is based on advanced electron optics and the latest tungsten-diamond transmission target technology. Automatic e-beam focusing and astigmatism

correction ensures that the smallest possible, truly round spot is consistently achieved during day to day operation.

The NanoTube N3 also has the unique feature of internally measuring and reporting the current spot size. In addition, advanced cooling and thermal design results in extreme stability over long exposures. This enables an unprecedented true resolution of 150 nm lines and spaces.



Attenuation-contrast imaging

Attenuation-contrast imaging is the conventional way of obtaining X-ray images.

In recent decades, the technology development towards fast high-resolution imaging has been driven by the needs in scientific research, industrial R&D, and production quality control. To visualize fine details of the microstructure in the object, the imaging can be done either by using X-ray radiation coming from a small emission spot, or by using X-ray optics to build a microscope setup.

An X-ray tube with extremely small emission spot size can give high resolution imaging without optics. The advantages of this

approach without optics, is the efficiency across the full energy spectrum as well as the ease in getting a large field of view.

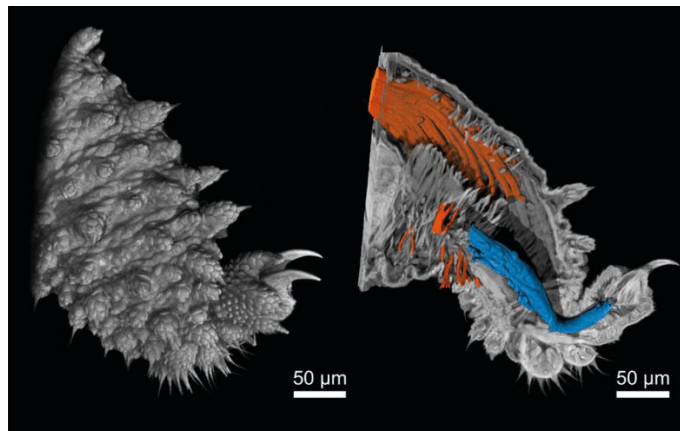
With a minimal spot size below 400 nm, the Excillum NanoTube enables lensless sub-micron X-ray microscopy and NanoCT in the laboratory. For the applications where a 5-20 μm spot is enough, the MetalJet offers up to 10 times more brightness than any other microfocus tube. Moreover, the high stability of the source emission spot over long time also guarantees minimal impact of drift during long acquisitions, which is important for high resolution imaging.

Application examples

A NanoCT instrument comprising of a NanoTube and a photon counting detector provides the ability to do tomography with very high resolution. At the Technical University of Munich (Germany) such an instrument has achieved state-of-art ~ 100 nm spatial resolution and capability of investigating phase-contrast imaging.

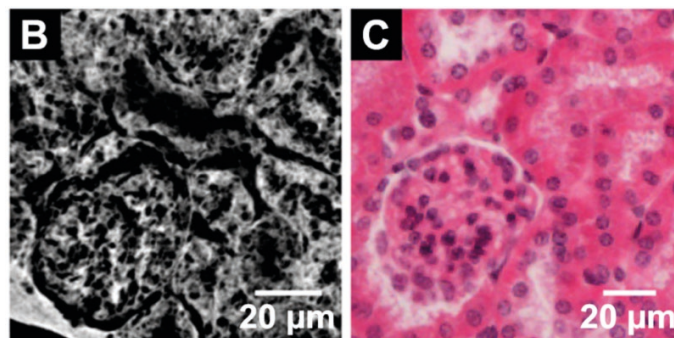
Nano-CT images of the limb of Onychophora (0.4 mm long). The surface morphology (left) can be visualized with an image quality similar to scanning electron microscopy, and simultaneously the visualization of internal musculature (right) at a resolution higher than confocal laser scanning microscopy.

M. Müller, et al., "Myoanatomy of the velvet worm leg revealed by laboratory-based nano-focus X-ray source tomography", PNAS (2017).

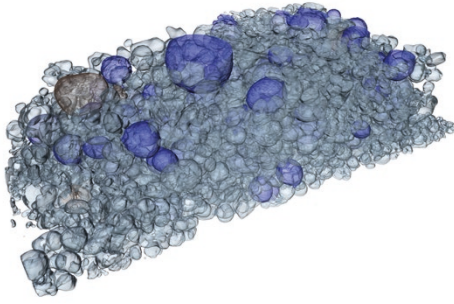


As another example from the same NanoCT system, the anatomical structures in the cortex of a mouse kidney sample was studied with a new staining method. The minimum intensity projection slice (left) of its Nano-CT image gains a good comparison to histological data (right).

M. Busse, et al., "Three-dimensional virtual histology enabled through cytoplasm-specific X-ray stain for microscopic and nanoscopic computed tomography", PNAS (2018).



X-ray microscopy



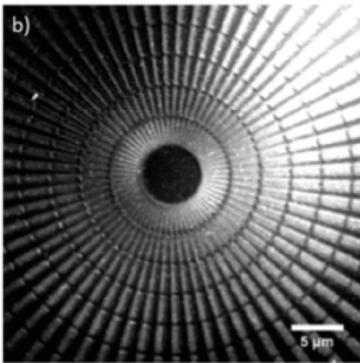
The other well-established way to obtain the ultimate resolution is to use X-ray optics and this optics-based X-ray microscopy technology has been successfully transferred from the synchrotron to the laboratory.

However, the X-ray optics limits the bandwidth of the spectrum, thus a high brightness and relatively monochromatic X-ray source is needed. The conventional laboratory-based X-ray microscopes often use high-power rotating-anode sources. The drawback of this setup is the high loss of flux, since the acceptance angle of the optics will strictly limit what radiation that can become useful. A MetalJet source offers a sharp, high-intensity K α line

from Gallium emitted from a small focal spot, making a considerably larger fraction of the flux useful in the optics setup. This higher brightness makes broad applications possible also on compact sources.

A similar NanoCT system with the new Excillum NanoTube N2 has been designed, developed and commissioned at Fraunhofer IIS, Würzburg, Germany. Together with an EIGER2 CdTe detector, the system has been optimized for materials characterization and NDT applications.

3D rendering of the NanoCT of a lithium ion battery cathode (NCA/LCO-E), showing particles of different sizes. Voxel sampling 140 nm.



Application examples

The periodic line patterns at the inner of a Siemens star, with 150 nm lines and spaces, can be resolved with the X-ray microscope based on the MetalJet D2 source. The image was taken with a Fresnel zone plate as imaging optics.

The volumetric rendering of the CT on a bent $\sim 4 \mu$ m tip of the bend tip of a damaged injection cannula with X-ray microscope based on Excillum's MetalJet source. The voxel size was 147 nm.

C. Fella, et al., "Hybrid setup for micro- and nano-computed tomography in the hard X-ray range", Rev. Sci. Instrum. (2017).



X-ray phase-contrast imaging

Phase-contrast imaging has developed rapidly and is known to give high contrast to the weakly absorbing materials, such as soft biological matter, polymers and many other organic compounds.

Compared to absorption-contrast imaging, the requirements on the equipment are in general higher for phase-contrast imaging. To be able to obtain contrast, an X-ray source with high transverse coherence is needed. This means that the source either needs to have a small emission spot or needs to be moved far away

from the object. Both options require the compromise of lower flux, which leads to very long exposure time. To keep the exposure times short, an X-ray source with a small emission spot that can still maintain a high flux is very beneficial.

Phase-contrast imaging was originally developed for biomedical applications, where it is very beneficial for imaging of soft tissues. Recently, it has seen a growing interest also in materials science, engineering and industrial non-destructive testing.

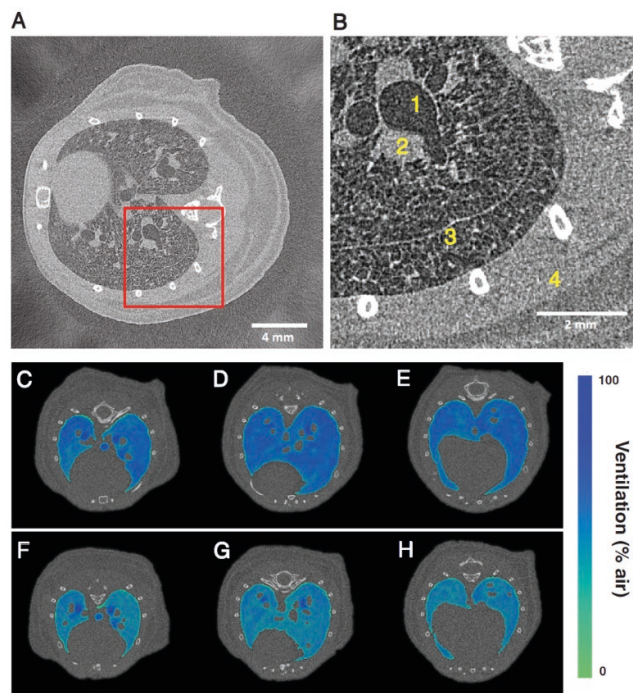
X-ray propagation-based phase-contrast imaging (PBI)

PBI has the simplest measurement geometry, similar to conventional attenuation-contrast imaging and requires no optical elements. However, implementing PBI in a compact laboratory-scale setup puts high requirements on the spatial coherence of the source, detector resolution and long distance between sample and the detector. Both the MetalJet and NanoTube sources meet the requirements for doing laboratory-based high-resolution PBI.

Application examples

High resolution propagation-based imaging system for in vivo dynamic computed tomography of lungs in small animals

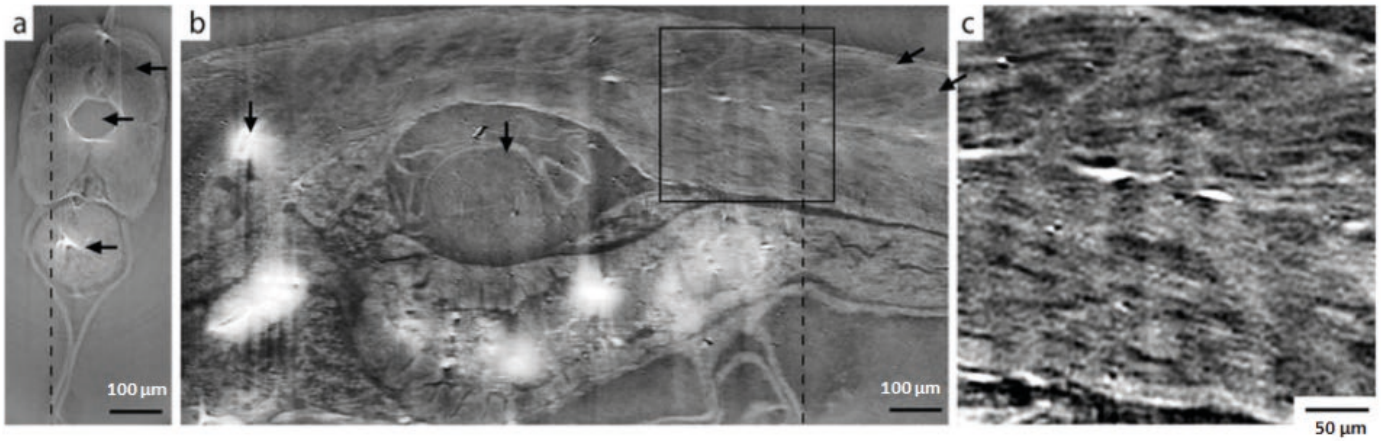
By operating a MetalJet D2+ at 250 W and 15 μm spot size, it has been shown that phase-contrast tomography can be used for dynamic imaging of live mice. In research work done in Australia, time-resolved computed tomography was performed to image the ventilation in the lungs of mice. A flat-panel detector acquired projections with only 18 ms exposure time, allowing a full tomography in 32 s. These very short exposure times and controlled breathing, allowed small airways down to 55-60 μm in diameter to be imaged dynamically. This high quality dynamic imaging of lungs enables determination of the lung function, even down on a regional level. Furthermore, high quality dynamic CT potentially has many other applications.



Time-resolved computed tomography of a live mouse (A). Close-up region (B) shows the anatomical features. The method demonstrates the differences in volume of air in the lungs after 0 hours mechanical ventilation (C)-(E), and after 2 hours (F)-(H). Image reprinted from M. Preissner, et al., "High resolution propagation-based imaging system for in vivo dynamic computed tomography of lungs in small animals", *Phys. Med. Biol.* (2018).

High-resolution zebrafish muscle imaging with X-ray PBI tomography

By using a MetalJet tube, PBI tomography of an unstained whole zebrafish was performed. This shows the capability of capturing the low contrast sub-5 μm details with sufficiently high contrast. The methodology paves the path for the non-invasive whole-body imaging at sub-cellular resolution for soft tissue research and small animal models, thus facilitate the deep understanding of muscular disease and assessing interventions.



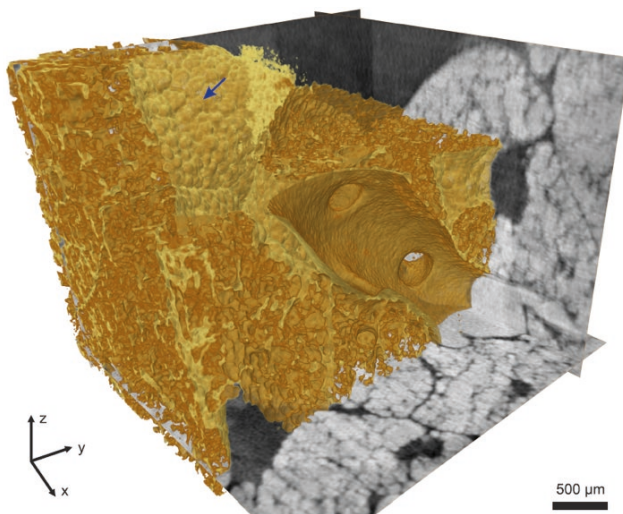
The PBI tomographic axial (a) and sagittal (b) slices and the zoom-in ROI (c) as the black box in (b).

- Exposure time = 115 s/projection
- Voxel size = 0.733 μm
- Tube voltage = 40 kV, tube power = 24 W
- FDI-VHR CCD camera with Gadox scintillator

W. Vågberg, et al., "X-ray phase-contrast tomography for high-spatial-resolution zebrafish muscle imaging", *Sci. Rep* (2015).

High resolution X-ray PBI lung tomography on whole mice at laboratory scale

The scientists at University of Göttingen demonstrated the high resolution PBI tomography on whole mice based on using a MetalJet source. With the optimized spectrum they demonstrated the applicability of PBI in local tomography for small animal imaging of lungs in the presence of highly absorbing surrounding tissue at μm -level resolution. The result indicated the application of this imaging method at cellular level for even larger biological samples.



3-D rendering of the PBI tomogram of the soft tissue in the thorax.

- Exposure time = 10 s/radiography
- Voxel size = 5 μm
- Tube voltage = 70 kV, tube power = 100 W
- Timepix Photon Counting detector

M. Krenkel, et al., "Propagation-based phase-contrast tomography for high-resolution lung imaging with laboratory sources", *AIP Adv.* (2016).

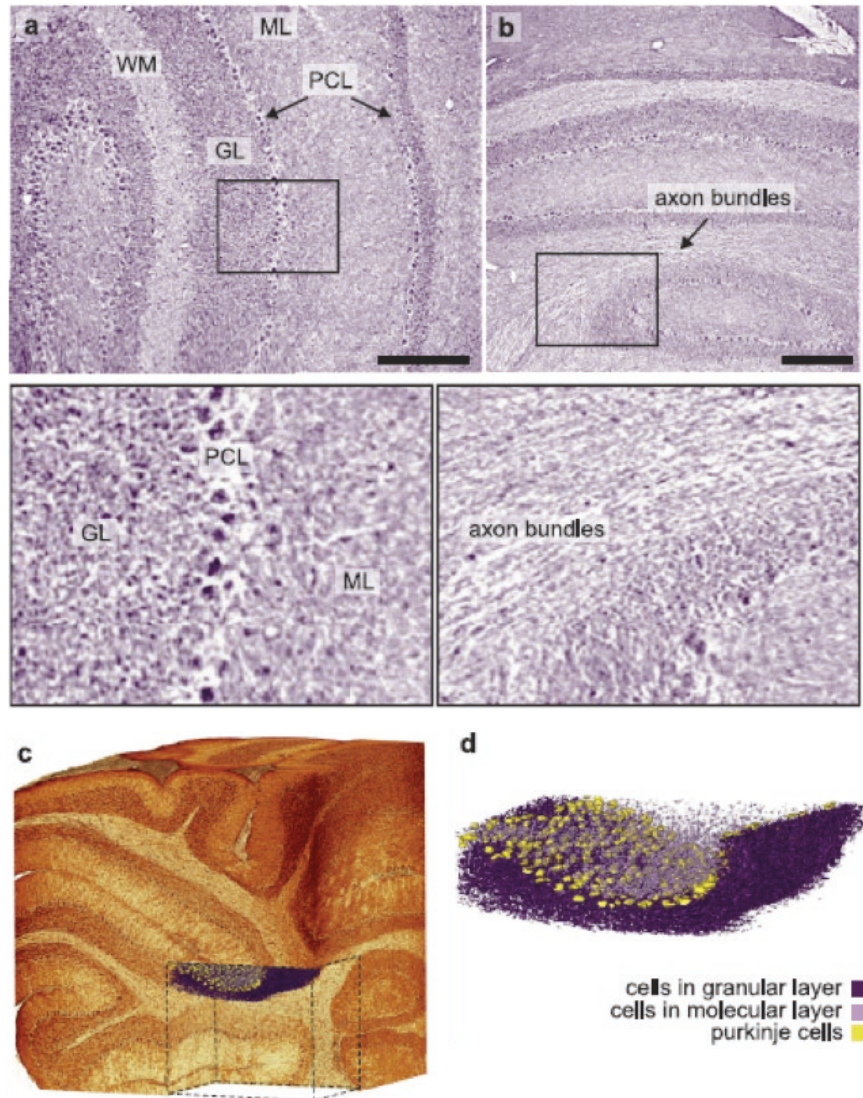
Cellular and sub-cellular resolution X-ray PBI tomography on mouse brain cytoarchitecture

More recently, another example from the research group in Göttingen investigated the mouse brain cytoarchitecture by PBI tomography at sub-cellular level resolution. Together with suitable phase-retrieval algorithm and novel tissue preparation, this study suggested a non-destructive imaging path in the studies of brain architecture in mammals.

PBI tomography slice along transverse (a) and another along longitudinal (b) directions; automatic volume rendering of the reconstructed volume (c) and the zoomed-in cellular segmentation (d). The molecular layer (ML), granular layer (GL), white matter (WM) and Purkinje cell layer (PCL) of the mouse cerebellar vermis at cellular resolution.

- Exposure time = 50 s/radiography
- Voxel size = 0.54 μm
- Tube voltage = 40 kV, tube power = 50 W
- Lens-coupled scintillator-based camera XSight

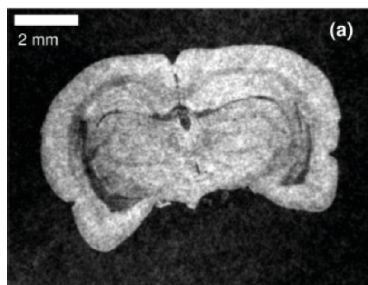
M. Töpperwien, et al., "Three-dimensional mouse brain cytoarchitecture revealed by laboratory-based x-ray phasecontrast tomography", Sci. Rep. (2017).



X-ray grating-based phase-contrast imaging (GBI)

GBI is another phase-contrast imaging technique that has been widely transferred to laboratory sources. It works with the conventional incoherent source by adding a grating made up of highly absorbing material. Naturally, this causes a loss in flux of more than 50%. A MetalJet X-ray source reaches the sufficient spatial coherence to enable GBI without the G0 grating, thus avoiding the loss of flux.

Considering that GBI usually needs several images to step the G2 grating at every projection, making GBI tomography is often associated to very long exposure times. In this context, it is of deepest concern to keep the flux high!



Application examples

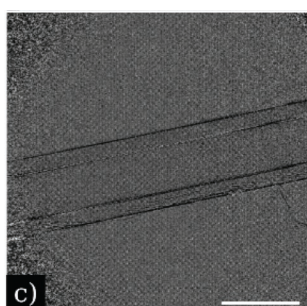
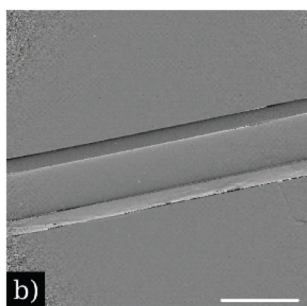
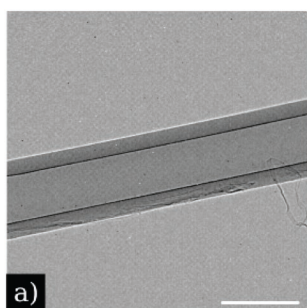
X-ray GBI microscope with MetalJet source

The joint research by scientists from KTH and ETH/PSI proved the advantage of using a MetalJet source in GBI, which significantly improved flux and visibility compared to a conventional microfocus tube. Moreover, a preliminary exploration of its biomedical application has been shown by tomography on a rat.

Comparison between phase-contrast (a) and attenuation-contrast (b) slices from GBI tomography based on a MetalJet source. The sample was a rat brain scanned in a liquid paraffin bath.

- Exposure time = 1 min/stepping image
- Voxel size = 20 μm
- Tube voltage = 50 kV, tube power = 40 W
- G1 is designed for π -phase shift at 25 keV, period = 4.12 μm
- CCD camera with Gadox scintillator

Reproduced from T. Thüring, et al., "X-ray grating interferometry with a liquid-metal-jet source", Appl. Phys. Lett. (2013).



X-ray grating interferometry at 9.25 keV with MetalJet tube

The research groups at Fraunhofer IIS (Würzburg, Germany) took the advantage of the high brightness Gallium's K α line of a MetalJet source together with a high resolution detector and applied it to GBI, as well as the possibility of single-grating setup. The high visibility confirmed the high spatial coherence of the MetalJet source. Its application in materials science was further exploited.

By using the Gallium K α line at 9.25 keV and high spatial coherence from a MetalJet source, researchers at the Fraunhofer IIS (Würzburg, Germany) show that grating interferometry is possible without the G0 grating. Furthermore, by employing a detector with very high resolution, the self-image from the G1 grating

can be resolved, which eliminates the need for a G2 grating and phase stepping. This results in that all three image modalities can be captured in a simpler experimental setting. Here, the source was operated at 70 kV and 50 W, a G1 grating a period of 2.4 μm and the detector had a pixel size of 0.67 μm .

Single grating imaging with MetalJet source and a high-resolution detector. A nylon fiber is imaged and a single image captures (a) attenuation (b) phase and (c) dark field. Scalebar is 260 μm .

A. Balles, et al., "X-ray grating interferometry for 9.25 keV design energy at a liquid-metal-jet source", AIP Conf. Proc. (2016).

X-ray speckle-based phase-contrast imaging (SBI)

In similarity to GBI, a MetalJet source contributes to SBI by providing high spatial coherence to resolve the μm -sized speckles and high brightness to reduce exposure time. More importantly, it will dramatically shorten the CT acquisition that uses speckle scanning technique, which consists of a 1D or 2D raster scan, but consequently needs longer acquisition time.

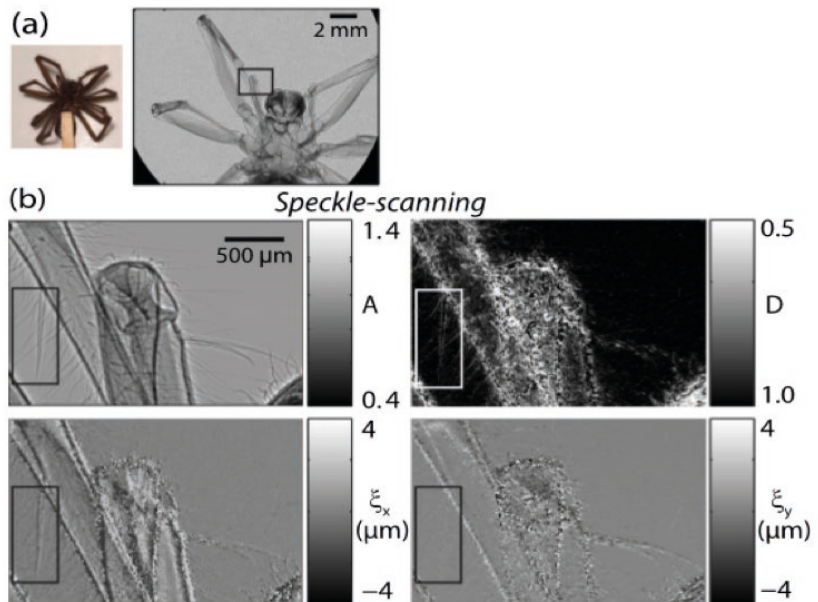
Application examples

Laboratory-scale SBI imaging based on MetalJet and scanning technique

Thanks to the high-brightness MetalJet source, the scanning technique was demonstrated the first time for a compact SBI setup by scanning a phantom and a dried spider. A $7\ \mu\text{m}$ fine hair was clearly visible on the retrieved images with a resolution higher than what can be achieved by the speckle-tracking method.

The radiographs on a dried spider in attenuation-contrast, dark-field contrast and phase-shift along transverse and longitudinal directions (b). (a) is the photo of the sample and one raw speckle image.

- Exposure time = 1 min/stepping image
- Effective pixel size = $4.5\ \mu\text{m}$
- Tube voltage = 50 kV, tube power = 30 W
- 32×32 2D raster scan with $1\ \mu\text{m}$ step size
- CCD camera FLI PL 9000



T. Zhou, et al., "Speckle-based x-ray phase-contrast imaging with a laboratory source and the scanning technique", *Opt. Lett.* (2015).

Laboratory-scale X-ray SBI microtomography for quantitative material characterization

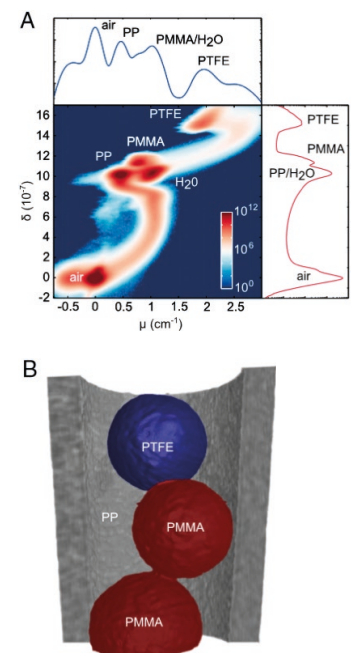
The collaboration between KTH and Diamond Light source showed the possibility of doing quantitative material characterization using the attenuation-contrast and phase-contrast 3D images acquired by SBI tomography based on a MetalJet source. The clear distinction among different material phases in the polymer colloidal suspension was demonstrated.

Quantitative analysis on the attenuation-contrast and phase-contrast tomograms on multi-material phantoms, which were acquired by the SBI tomography based on MetalJet source.

The 2D histogram of voxel value on those two tomogram (a) and the 3D rendering of the tomogram (b).

- Exposure time = 2 min/radiography
- voxel size = $4.7\ \mu\text{m}$
- Tube voltage = 50 kV, tube power = 30 W
- FDI-VHR CCD camera with Gadox scintillator

I. Zanette, et al., "X-ray microtomography using correlation of near-field speckles for material characterization", *PNAS* (2015).



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US 10 818 468, US 10 825 642, and Chinese Patents Nos. ZL 01816396.3, ZL 200780026317.0, ZL 200980155094.7, ZL 200980158566.4, ZL 201080070417.5, ZL 201280075230.3, ZL 201410213235.9, ZL 201510020687.X, ZL 201610033696.7, ZL 201780012946.1, and other corresponding national patents and patent applications pending.