L-03

REAL-TIME MICRORADIOLOGY USING SYNCHROTRON X-RAYS

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Ever since the discovery by Wilhelm Conrad Röntgen in 1895 [1], medical radiology has been by far the most important application of x-rays. In most cases, the contrast in radiological images is mostly based on the different x-ray absorption by different parts of the specimen. Absorption is, however, very limited for x-rays: this is the basis of the success of radiology but also of its limitations.

In particular, weak absorption means small absorption differences between different materials and therefore limited contrast. This requires long exposures and a relatively high x-ray dose in some cases. Even though the contrast can be increased by injecting high - contrast fluid, the injection procedure is often complicated and may involve non-negligible risks for the patient.

On the other hand, phase contrast from using synchrotron coherent x-rays is very effective for low refractive index materials [2]. In this study, the coherence-based mechanisms that enhance contrast in radiological images using unmonochromatic synchrotron x-rays will be discussed. The competition between the refraction-based edge enhancement and the diffraction-based edge enhancement will be also illustrated. High time resolution (~1 msec) is able to demonstrate the successful application of the phase contrast method to microradiology, which includes sub-micron resolution in-situ or in-vivo imaging of microvessels in live specimen, electrodeposition, atomic diffusion through grain boundaries, *etc*.

The contrast mechanism prevailing in this study is largely based on the refraction of x-rays at the edge between two areas with different refractive indices [3]. The different deviations of the x-ray beams by the two sides create typical white-dark 'fringes' that enhance the edge visibility. In these tests, we succeeded in using unmonochromatic synchrotron beams and a simple detector system to implement live animals - including blood vessels - and their natural movement together with inorganic, non-biological, samples.

Figure 1 shows a typical example of our microangiography image in a mouse leg which was taken *in-vivo* with no contrast agent using unmonochromatic synchrotron x-rays. Microvessels down to 20 μm are clearly visible, their walls being enhanced by refraction-based contrast. The walls are in fact more visible without contrast agent than with contrast agent. Absorption, in fact, makes the edge enhancement less visible - whereas a large refractive-index difference washes out the edge-enhancing refraction pseudo-fringes [3-5].

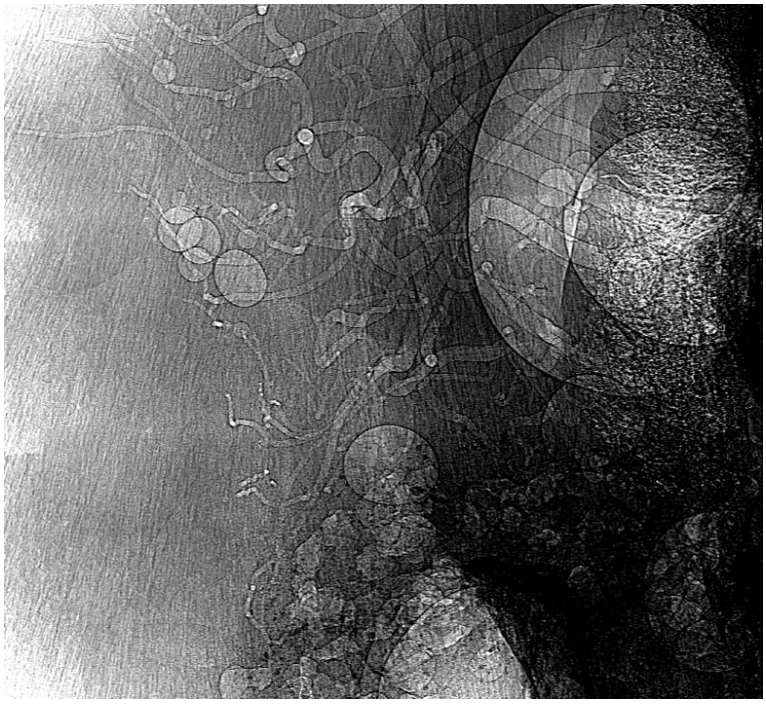

Figure 1.

Microangiographic image of blood microvessels taken *in-vivo* in a mouse leg using unmonochrotromatic synchrotron x-rays. (Field of view: 4×4 mm^2.)

This result, representative of a much larger body of experiments, demonstrates that high-resolution microangiography can be implemented without the complications and risks of contrast dye injection. A comparison with other techniques is quite interesting. In vitro studies with computed tomography or magnetic resonance imaging of phantoms and bone and breast-tissue specimens detect details not smaller than several tens of micrometres [6]. Angiography with monochromatic synchrotron x-rays and an iodine dye reveals details down to approximately 20 μm in live animals [7-10]. With the present technique, we can already detect much smaller details in-vivo.

The importance of dye-less microangiography need not be emphasized. Morphological vessel changes are frequently related to common vascular diseases. For example, the luminal narrowing of the heart coronary arteries and the brain small arteries causes heart and cerebral stroke due to arteriosclerosis. However, the conventional radiological detection of such features is complicated by the need for a contrast dye, whose injection may be a major cause of mortality and morbidity. Dyeless angiography would thus be a significant diagnostic improvement.

Also note the importance of detecting micro-vessels in tumors: tumor tissues need much nutrition and oxygen for growth and metastasis, supplied by newly developed fine vessels. Therefore their results could have a positive impact on diverse domains, such as fundamental studies of angiogenesis (vessel formation) and oncogenesis (tumor development), the early and accurate detection of tumors and vascular problems and of abnormal changes in the natural movements of vital organs.

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