In-vivo Fluorescent X-ray CT Imaging of Mouse Brain

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Abstract. Using a non-radioactive iodine-127 labeled cerebral perfusion agent (I-127 IMP), fluorescent X-ray computed tomography (FXCT) clearly revealed the cross-sectional distribution of I-127 IMP in normal mouse brain in-vivo. Cerebral perfusion of cortex and basal ganglion was depicted with 1 mm in-plane spatial resolution and 0.1 mm slice thickness. Degree of cerebral perfusion in basal ganglion was about 2-fold higher than that in cortical regions. This result suggests that in-vivo cerebral perfusion imaging is realized quantitatively by FXCT at high volumetric resolution.

Keywords: In-vivo imaging, Cerebral perfusion, Fluorescent X-ray CT, Functional imaging, Molecular imaging, Small animal, Experimental study
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INTRODUCTION

In biomedical field, functional evaluation is quite useful to understand the process, diagnosis and treatment of various diseases [1]. Micro positron emission tomography (micro-PET) [1-3] and micro single photon emission computed tomography (micro-SPECT) [4, 5] are recently used to visualize in-vivo biochemical processes in small animal. However, the use of radionuclide agent is indispensable in PET and SPECT study, and the volumetric resolution of these techniques is limited to about 1 mm^3 and 0.5 - 0.1 mm^3, respectively.

Fluorescent X-ray technique using synchrotron X-ray, which is usually used to observe the surface of the object, can detect very low contents of medium or heavy trace elements with concentrations in the order of picograms [6]. To depict the distribution of specific elements inside the object without slicing procedure, fluorescent X-ray computed tomography (FXCT) with synchrotron radiation is being developed [7-10]. The FXCT could depict iodine within a phantom, and the endogenous iodine of an excised human thyroid [11-13]. Furthermore, the FXCT was applied to assess the functional information of ex-vivo brain and heart of small animals similar to autoradiogram, and we successfully observed the cerebral blood flow [14] and myocardial fatty acid metabolism [15, 16] after injecting various types of non-radioactive iodine labeled agent. Since the significant results were obtained by ex-vivo studies, in-vivo FXCT imaging was performed by using a germanium detector with high count rate capability and energy resolution [17]. Here, the experimental results of in-vivo cerebral blood flow imaging of mouse brain obtained by FXCT is described.

METHODS AND MATERIALS

The experiment was carried out at the bending-magnet beam line BLNE-5A of the Tristan accumulation ring (6.5 GeV) in Tsukuba, Japan. The photon flux rate in front of the object was approximately 9.3 x 10^7 photons/mm^2/s for

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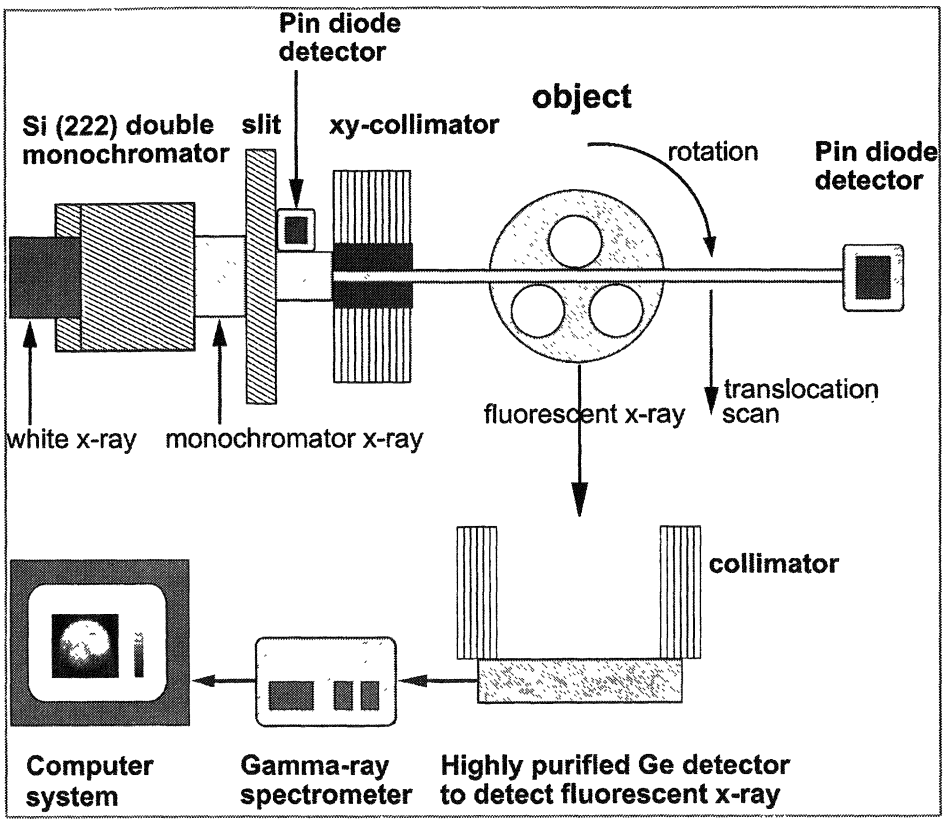

FIGURE 1. Schematic diagram of fluorescent X-ray computed tomography system.

beam current of 40 mA. FXCT system consists of a silicon (220) double crystal monochromator, an X-ray slit system, a scanning table for subject positioning, a fluorescent X-ray detector, and two pin-diode detectors for incident X-ray and transmission X-ray data (Fig. 1). The white X-ray beam was monochromatized to 37 keV X-ray energy. The monochromatic X-ray was collimated into a pencil beam (1 x 0.1 or 0.2 mm^2: horizontal and vertical direction). Fluorescent X-rays induced by incident X-ray beam were detected in a high purity germanium (HPGe) detector operating in the photon-counting mode, and the HPGe detector was oriented perpendicular to the incident monochromatic X-ray beam. The data acquisition time of the HPGe detector for each scanning step was set 5-s.

Objects were 3 mice and an acrylic phantom with three sub-holes. Since radioactive I-123 labeled N-isopropyl-p-iodoamphetamine (I-123 IMP) is popularly used to evaluate cerebral blood flow in clinical SPECT study [18], we attempted to use a non-radioactive I-127 labeled IMP (I-127 IMP) for in-vivo FXCT imaging of mouse. In-vivo FXCT imaging of mouse started 5 min after intravenous injection of I-127 IMP under the anesthetized with pentobarbital. The 20-mm in diameter acrylic phantom filled with various concentration of iodine solution was also imaged to determine the absolute iodine content within brain. Object was scanned with 1-mm translation step over target range and 6 degree rotation step over a range of 180 degrees. FXCT images were reconstructed by the algebraic method with attenuation correction for the incident beam and the emitted fluorescent X-ray using the TXCT data [19]. The TXCT image was reconstructed by using the filtered back projection method with the Shepp and Logan filter.

Our present experiment was approved by the Medical Committee for the Use of Animals in Research of the University of Tsukuba, and it conformed to the guidelines of the American Physiological Society.

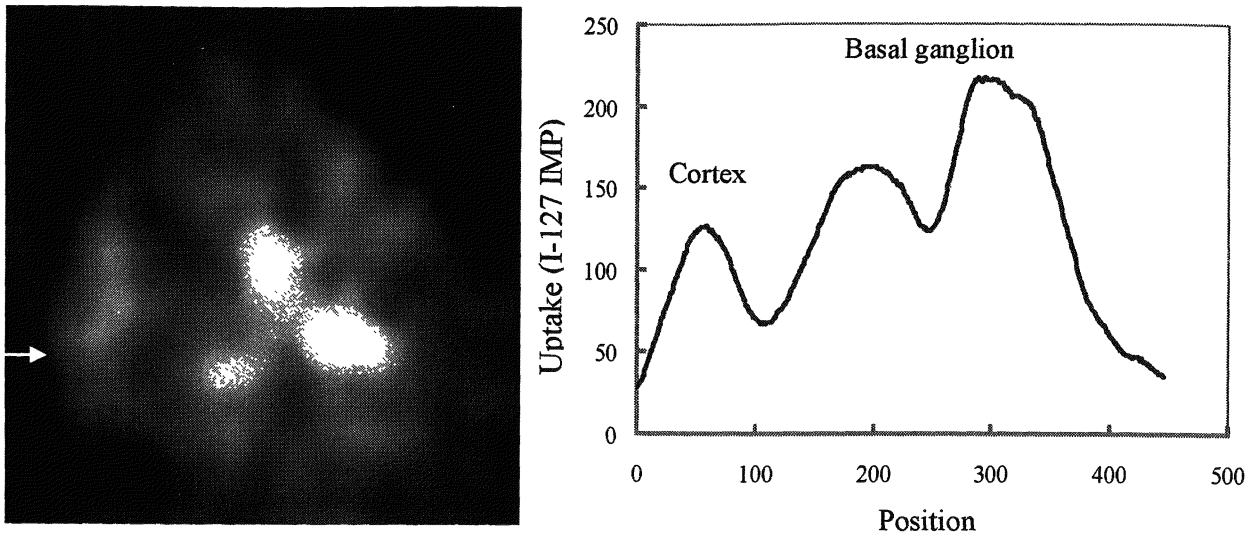

FIGURE 2. Cerebral perfusion image with I-127 IMP and its profile analysis of a mouse brain by fluorescent X-ray computed tomography.

RESULTS AND DISCUSSIONS

In-vivo cerebral perfusion of mouse was clearly imaged by FXCT at an 1 mm spatial resolution with a 0.1 or 0.2 mm slice thickness (Fig. 2). Cerebral cortex and basal ganglion were well visualized, and the cerebral perfusion in basal ganglion was about 2-fold higher than other cortical regions probably due to anesthesia. Reduced cerebral perfusion in left cerebral cortex might be caused by ischemia. In profile analysis, the degree of regional cerebral perfusion was assessed quantitatively as shown in Fig. 2. Using calibration data from the phantom, cerebral uptake of the iodine in mouse was estimated about 0.02-0.04 mg/g.

The volumetric resolution of this in-vivo FXCT image was 0.1 or 0.2 mm^3 (1-mm x 1-mm x 0.1 or 0.2-mm). This resolution was almost comparable to super micro-SPECT imaging as 0.1 mm^3 [5, 20]. Since the duration of anesthesia is limited, in this study, the spatial resolution had been restricted to 1 mm by scanning time. However, we can obtain much higher spatial resolution image of 0.5-mm with a 0.4-mm slice thickness by using the HPGe detector with much higher count rate capability. For this purpose, we are now developing high speed FXCT system. In addition, the use of non-radioactive agent is significantly suitable to perform the biomedical experiment because the preparation of drug and experiment are quite easy without radiation exposure for researchers.

Thus, in-vivo FXCT is a powerful tool to image the functional information with high spatial resolution and without the use of non radioactive labeling agents.

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