Dose Distribution of Microplanar Beam Array for Microbeam Radiation Therapy

An array of planar synchrotron-generated X-ray beams collimated in a micrometer scale (microplanar beams) has the potential to create a new modality of radiotherapy, as reported by a group of NSLS of Brookheven National Laboratory (BNL), NY, USA in 1992 [1]. In 1995, the BNL group reported the experimental results that necrosis was not observed when irradiating brain tissue with microplanar beams at 312 - 5000 Gy, and no brain damage was observed microscopically when irradiating at 312 - 625 Gy [2]. Furthermore, they found that irradiation with microplanar beams caused growth delay or cell ablation in 9L gliosarcoma implanted in rats with less damage to the contiguous normal tissues [3]. These properties of the microplanar beams are summarized as follows: (a) microplanar beams spare normal tissues such as skin and the central nervous system (CNS), and (b) preferentially damage tumors. However, the mechanism of how normal tissues are spared is still unknown and under discussion.

The techniques of X-ray microplanar beam irradiation were first developed at BNL in the 1990s, and X-ray microplanar beam irradiation has been studied at the European Synchrotron Radiation Facility, Grenoble, France since the mid-1990s. A feasibility study of MRT at SPring-8 was initiated under the collaboration of JASRI, the National Institute of Radiological Sciences and Kitasato University in 2005. The experiments have been carried out at beamline **BL28B2**. We developed multi-slit collimators (MSCs) and evaluated them before beginning the experiments. The final MSC has thirty slits with dimensions of 25 μm height × 30 mm width × 5 mm length in the direction of the beam, which are interspersed with a spacing of 200 μm as shown in Fig. 1. The MSC was assembled by Mitaya Manufacturing Co., Ltd., Kawagoe, Japan. It is composed of an alternate stack of 175-μm-thick tungsten plates and 25-μm-thick polyimide sheets. Less than 0.01% of the photon flux penetrates through the tungsten plate and about 50% of the photon flux penetrates through the polyimide sheets. The polyimide sheets and tungsten plates are in tight contact with each other because they are pressed together with top and bottom brass plates without the use of any materials such as adhesives. The MSC was placed about 44 m downstream from the light source, and biological samples were set at about 1 m downstream from the MSC.

We carried out experiments to reproduce and confirm the sparing effects of microplanar beams on rat's CNS first. In the experiments, a ten-microplanar-beam array with a field size of 2 × 2 mm was irradiated onto rats' heads to penetrate through the cerebellum. The rats were placed prone across the beam direction and exposed to the microplanar beams at 500 - 10,000 Gy. Figure 2 shows a sliced cerebellum extracted from a rat that was irradiated with an

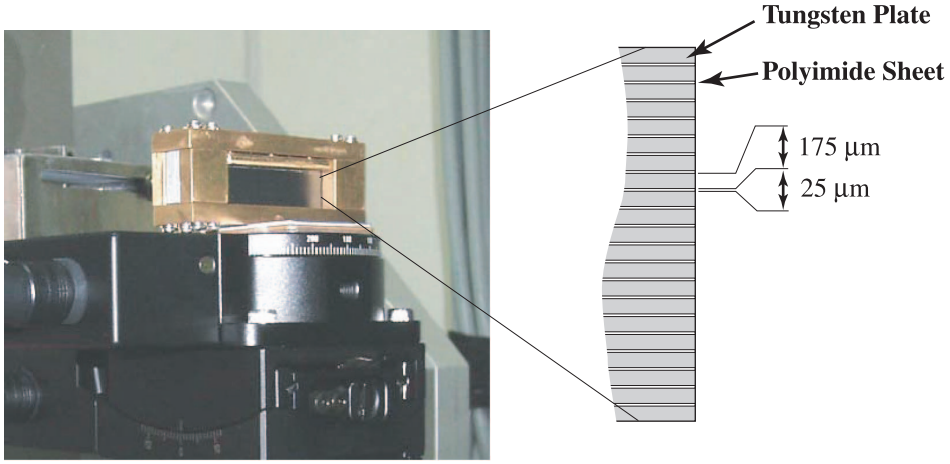

Fig. 1. Multislit collimator (MSC). It is composed of a stack of alternating tungsten plates and polyimide sheets. There are thirty slits 25 μm high, 30 mm wide and 5 mm deep (in beam direction).

entrance dose of about 300 Gy, and euthanized three days after the irradiation. The linear tracks are clearly visible. We also carried out *in vivo* experiments to confirm the tumoricidal effect and the sparing effect for skin as well as *in vitro* experiments to investigate the sparing mechanism from the viewpoint of by-stander effects. In the former experiments, we implanted fibrosarcoma NFs-a into the legs of young mice and irradiated them with microplanar beams at 200 - 1500 Gy. The mice were reared for about one month to observe the tumor growth. The measurement of the subcutaneous tumor sizes showed growth delay in tumors irradiated at various doses.

From a physical point of view, the dose distribution of the microplanar beam array is the most important. The array of microplanar beams has a spatial dose distribution with alternating high-dose areas (peak) and low-dose areas (valley). The valley dose is required to be lower than the tissue tolerance level for a broad beam, otherwise the advantageous response to the microplanar beams is presumably lost. We measured the relative dose distribution of the microplanar beam array physically and biologically. Figure 3 shows a sliced sample from the biological measurements. The valley dose was also measured physically and was preliminarily 0.2 - 0.3% of the peak dose.

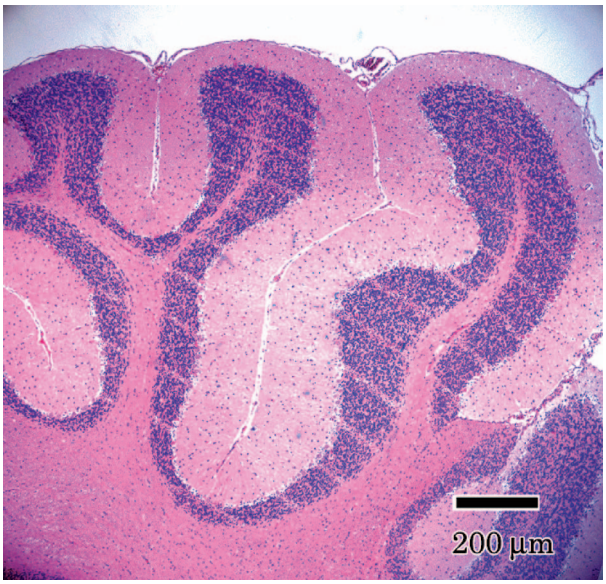

Fig. 2. Linear tracks of apoptotic granular cells developed in X-ray-irradiated stratum granulosum of cerebellum. No obvious changes were seen in the stratum moleculare, (hematoxylin-eosin staining).

Fig. 3. The distribution of DNA lesions induced by irradiation with microplanar beams in a tumor implanted in a leg of a mouse is shown with the relative dose distribution of the microplanar beam, which was measured using a CCD camera. Subcutaneously implanted fibrosarcoma NFs-a in the legs of mice were irradiated at 50 - 500 Gy. The mice were euthanized 0.5 or 5 hours after the irradiation to extract the tumors. The extracted tumors were fixed in ethanol over night, and embedded in paraffin to prepare 10-µm-thick sliced samples. Finally, under a microscope, we observed DNA lesions colorized by the γH2AX antibody, which reacts selectively with double-strand-breaks in DNA. The DNA lesions, which were colored brown, aligned along the beam path. This method enables us to biologically measure not only the width of the microplanar beam that penetrated through the tissue, but also the valley dose relatively.

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References

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