

Diffusion tensor imaging for evaluation of radiation-induced developmental abnormalities in the white matter

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INTRODUCTION

Prenatal radiation exposure can induce various kinds of central nervous system (CNS) disorders, such as white matter alterations and microcephaly, depending on the dose, affected region and gestation period [1]. It is known that MR diffusion tensor imaging can detect white matter developmental abnormalities, including developmental delays [2] [3]. In this study, we evaluated the developmental white matter disorder induced by prenatal X-ray exposure using diffusion tensor imaging. Fractional anisotropy (FA) maps calculated from the diffusion tensor images were compared to a histological study of myelination staining (LFB, Luxol fast blue).

MATERIALS AND METHODS

Pregnant SD female rats (N = 6, 253 ± 35 g, Japan SLC, Hamamatsu, Japan) were exposed to a single whole-body x-ray irradiation at a dose of 1.5 Gy on day D15 of pregnancy. The X-ray irradiation conditions were 200 kVp, 20 mA, 0.5 mm Cu + 0.5 mm Al filter, 110 cm distance from focus to object and a 0.27–0.28 Gy/min dose rate [4]. After birth, we examined 12 neonatal male rats chosen at random, comprising 6 normal and 6 radiation-exposed rats. In the MRI study, coronal multi-slice T₁-weighted MR (multi-slice SE: 16 slices; TR/TE, 400/9.57 ms; slice thickness, 1.0 mm; matrix, 256×256 ; field of view, 25.6×25.6 mm; average, 4) diffusion tensor images were acquired using a 7.0 T-MRI system (Magnet: Kobelco +JASTEC Japan; Console: Bruker Biospin, Germany) in combination with a volume coil for transmission (Bruker) and 2ch phased array coil for reception (Rapid Biomedical, Germany). Diffusion tensor imaging was performed using spin-echo 4-shots echo planar imaging (slice thickness, 1 mm; field of view, 25.6×25.6 mm²; matrix, 128×128 ; number of repetitions, 1; TR, 3000 ms; TE, 33 ms; number of diffusion directions, 30; b = 0; 1000 s/mm²; δ = 3 ms; Δ = 23 ms). We measured the whole brain, covered by 16 slices, for volumetry and compared the one slice (bregma 0 mm in normal rats) to the histology of the corresponding slice. All rats were sacrificed for histology (LFB staining) after the MRI experiments. The region of interest (ROI) in the white matter (CC, corpus callosum; EC, external capsule) included tissue corresponding to a level of 0 mm posterior from the bregma. The area containing LFB-positive cells was identified in immunohistochemical staining of CC and EC tissue by converting blue-stained positive cells to a binary map using ImageJ software (Ver.1.40g, National Institutes of Health, USA). The total area of the positive regions was measured and the percentage of the LFB positive area was calculated. Statistical analysis was performed using an unpaired t-test and PRISM5 Graphpad software (P<0.001).

RESULTS and DISCUSSION

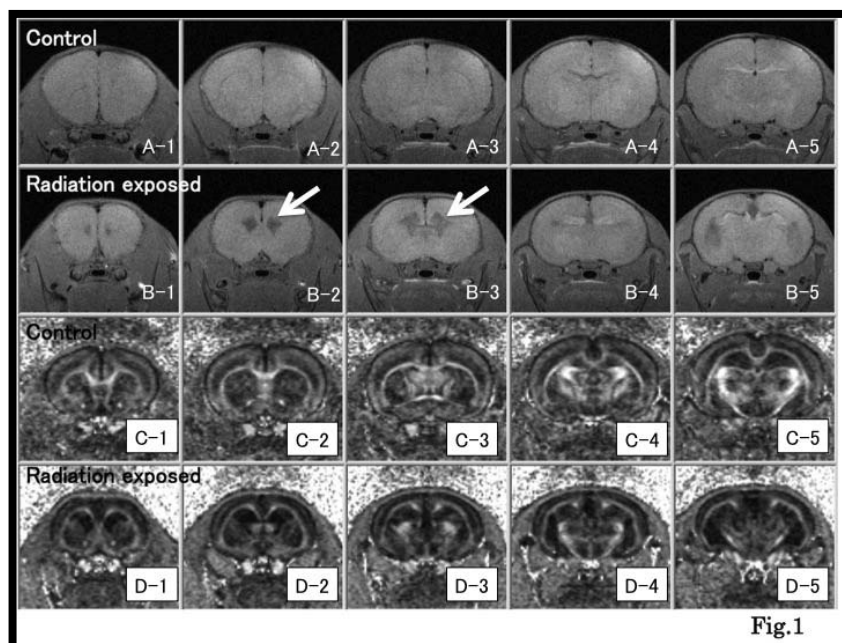


Fig.1

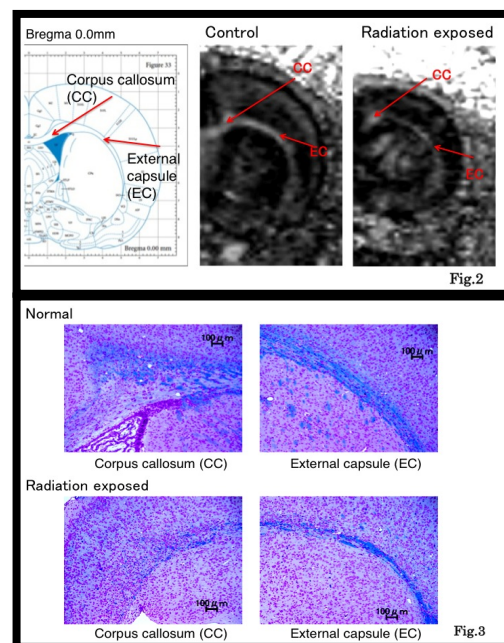


Fig.2

Fig.3

Figure 1: Typical T₁WI and FA map. Top row: T₁WI of control rat brain (A1-A5, 9th - 13th slices). Second row: T₁WI of radiation-exposed rat brain (B1-B5, 9th - 13th slices). Third row: FA maps of control rat brain (C1-C5, 9th -13th slices). Bottom row: FA maps of radiation-exposed rat brain (D1-D5, 9th -13th slices). The brain size of the X-ray exposed rats (51.4 ± 3.4 mm², $p < 0.001$) was clearly 45% smaller than that of normal rats (93.7 ± 2.3 mm²). All radiation-exposed rat brains showed a prominent dilatation of the cerebral ventricle (Figs. B2 and B3, white arrows).

Figure 2: Diffusion tensor imaging. Typical diffusion tensor images (FA maps) are shown for the control rats (middle) and radiation-exposed rats (right). The mean FA value in the CC of the radiation-exposed rats (0.49 ± 0.02) was significantly lower than that in the control rats (0.64 ± 0.01) ($p < 0.001$). The mean FA value in the EC of the radiation-exposed rats (0.41 ± 0.02) was significantly lower than that in the control rats (0.62 ± 0.03) ($p < 0.001$). The CC and EC in the white matter were identified using Paxino's brain atlas [4].

Figure 3: LFB histology. The top row presents LFB-stained histological slices of the cortex from a control rat. The bottom row shows LFB-stained histological slices of the cortex from a radiation-exposed rat. The percentage of LFB-positive cells in the radiation-exposed rat group was significantly lower (CC: $26.1 \pm 1.2\%$, EC: $34.5 \pm 2.4\%$) than that in the control rat group (CC: $48.8 \pm 1.4\%$, EC: $47.4 \pm 3.0\%$) ($p < 0.001$) (Magnification: $\times 400$, black bar = 100 μ m).

CONCLUSIONS

We found that FA maps from diffusion tensor imaging enabled noninvasive evaluation of the disturbance in myelination apparent in radiation-exposed rats. The distribution of LFB-positive cells agreed with the FA values in the CC and EC. This study provides useful information for biomedical assessment of radiation-induced developmental abnormalities in the white matter.

REFERENCES

- [1] Janeczko K, et. al. Brain Res 1997. [2] Ding, et.al. Eur Radiol 2009. [3] Yamada, et. al. Pediatrics. 2006 [4] Paxinos. Academic Press. 1998