

Mapping radiation dose distribution on the Fractional Anisotropy Map: Applications in the assessment of treatment-induced white matter injury.

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Introduction:

Medulloblastoma (MED) survivors commonly suffer from neurocognitive deficits which impact significantly on their quality of life (1). Treatment using whole brain radiotherapy is considered to be the major contributory factor that insults white matter and causes these deficits. There is emerging evidence that diffusion tensor MR imaging (DTI), using fractional anisotropy (FA), is sensitive in detecting and monitoring white matter injury in these patients (2,3). Knowledge of regional susceptibility to radiation and dose-effect relationship are important in the understanding of pathophysiology of radiation injury and in radiotherapy planning. In this study we describe a method to map whole brain radiation dose distribution onto FA images and illustrate its applications for studying dose-effect relationships and regional differences in the brain of two medulloblastoma survivors.

Method:

Two newly diagnosed MED patients (A: female, aged 10.7 years and B: male, aged 9.4 years) were recruited for the study. Patient A and B received 23.4Gy and 36Gy of cranio-spinal irradiation respectively, both followed by a boost to the posterior fossa to give a total dose of 56Gy. Both patients also had prior surgical excision of the tumour and subsequent chemotherapy. They underwent DTI scans at baseline (before radiotherapy) and 3 follow-ups approximately 3 months, 6 months and 1 year after radiotherapy. Two normal control subjects (both male; aged 23 years and 33 years respectively) were also recruited for the validation of the method and underwent DTI scans at two different time points respectively. DTI scan was performed using a 1.5T imager with a standard head coil. Diffusion weighted images were acquired in 25 gradient encoding directions using single-shot echo-planar imaging (TR=10000ms, TE=100ms, acquisition matrix=128 x 128, field of view =28cm, slice thickness of 5mm with 1.5mm gap, b factor=1200s/mm²). Radiotherapy plan was carried out for patients based on CT image; and for control subjects, similar but pseudo radiotherapy plan based on MR images was carried out and dose distribution was calculated accordingly. The follow-up FA maps were coregistered to baseline FA maps by applying the transformation parameters derived from non-diffusion weighted (b0) images and automatic segmentation for white matter was carried out on b0 images. Δ FA maps representing relative FA change in white matter were hence generated for visual inspection and subsequently quantitative analysis. The dose distribution was also coregistered to baseline FA images by applying the parameter derived from CT-b0 coregistration so as to study the dose-FA change relationship. A 5Gy dose window was used to study the effect of dose on FA. Δ FA of different dose regions were calculated using Δ FA = (follow up FA - baseline FA) / baseline FA. Similar analyses were performed on control subjects to assess the noise level of our method. Standard deviation (SD) of Δ FA in each dose region was also calculated to reflect the spatial heterogeneity and 95% confidence interval (CI) of mean Δ FA was calculated to reflect the reliability of each mean Δ FA value. Based on findings on visual inspection of the Δ FA maps, frontal lobe, parietal lobe and brainstem masks were created, in conjunction with white matter mask, to compare the white matter FA changes in these regions so as to determine regional susceptibility.

Result:

Fig. 1 shows a Δ FA map with radiation iso-dose contours superimposed where black indicates more severe FA reduction and white indicates less severe reduction. The severity of FA drop in relation to the dose received can thus be appreciated voxel-by-voxel for the whole brain. The DTI imaging and processing noise was small with root mean square value of 1.49% for FA. In both patients reduction in FA increased with increasing radiation dose up to 45Gy after which reduction in FA became less severe and approached normal (Fig. 2). Although spatial heterogeneity, due to inherent FA heterogeneity and the heterogeneous effect of radiation on FA was quite high within each dose region (Fig. 3), the 95% confidence intervals of mean Δ FA were relatively small as shown in Fig. 2, indicating that the reliability of our calculation was at an acceptable level. On visual inspection of the Δ FA maps, we found more severe FA reduction in the frontal lobes compared to the parietal lobes despite the same irradiation dose exposure, suggesting regional susceptibility in the frontal lobe, and FA increase in the brainstem after radiation in both patients (Fig. 4).

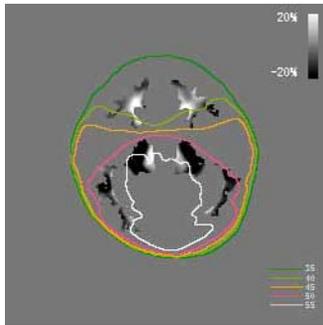


Fig. 1:

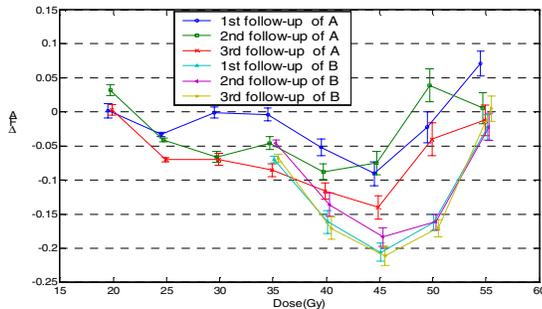


Fig. 2:

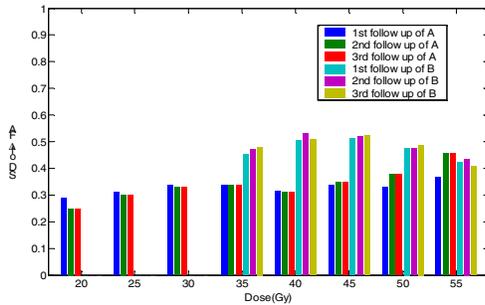


Fig. 3:

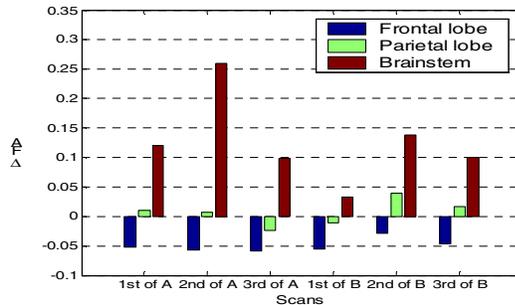


Fig. 4:

Discussion:

We have successfully mapped radiation dose distribution onto Δ FA images. This tool is potentially useful for the study of radiation-induced brain injury, including the evaluation of dose-effect on mean FA change and regional susceptibility in individual subjects. The preliminary findings of regional susceptibility in the frontal lobe compared to parietal lobe and increased FA in the brainstem after radiation require further verification by large scale studies.

References:

1. Mulhern RK, et al, 2004. *Lancet Oncol.* 5: 399-408. 2. Khong PL, et al, 2003. *AJNR.* 24: 734-740. 3. Leung LH, et al, 2004. *Neuroimage.* 21: 261-268.