Longitudinal Generalized Q-Sampling MRI Evaluation in Rabbit Brain after Cerebral Hemisphere Radiation Exposure

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Introduction

Radiation therapy is widely used for the treatment of both primary and metastatic brain tumors and can lead to cellular, vascular and axonal injury and further behavioral deficits. Imaging assessment of the brain damage caused by radiation therapy is very important for determining patient prognoses. Previously we used diffusion tensor imaging (DTI) and T2-weighted imaging (T2WI) to evaluate post-irradiation brain injury [1]. To improve evaluation of the neuro-toxic adverse effects of irradiation treatment in both gray and white matter structures, in this study we longitudinally evaluated the changes in various brain compartments on a clinical MR scanner by using generalized q-sampling imaging (GQI) [2] indices mappings, generalized fractional anisotropy (GFA), quantitative anisotropy (QA) and isotropic value (ISO) of the orientation distribution function (ODF), for single sub-lethal high dose (30 Gy) cerebral hemisphere exposure radiation-induced brain injury on adult rabbit model.

Materials and Methods

Five male New Zealand rabbits of one year of age received irradiation of 30 Gy (collimations = 4 cm x 5 cm) to the right hemi-brain with a single highly collimated 6MV photon beam from a Varian CL21EX linear accelerator (Varian, Palo Alto, CA, USA) under anesthesia. Brain MRI examinations were performed before irradiation and at 1st to 48th week post-irradiation (totally 12 time points) on a 1.5T MR scanner (Sonata, Siemens, Erlangen, Germany) with double loop array coils. Whole brain coronal multiple shells diffusion data were acquired using a multi-slice, single-shot spin echo EPI sequence with TR/TE=2900/128 ms, resolution = 0.78 x 0.78 x 2 mm^3, number of slices = 12 (contiguously from the genu of the corpus callosum to the end of the cerebrum). They were obtained using 12 diffusion-encoding directions with b values changing from 0 to 2,000 s/mm^2.

In data analysis, denoise was performed using MATLAB first [3]. After denoise, GQI indices mappings, including GFA, QA and ISO were calculated from multiple shells diffusion data using DSI studio (NTU, Taiwan) (Fig. 1). Using imageJ (NIH, USA), ROIs were drawn manually on three consecutive slices of the GQI indices mappings in 4 different compartments, bilateral cerebral cortex, external capsules, hippocampi and thalami. All the results were expressed as mean ± standard error (SE), and the ratios of right (injury) / left (control) were calculated for statistical analysis. Paired t-test was used to detect statistical differences between the pre- and the post-irradiation time points. A p-value of <0.05 was considered to indicate statistical significance (Fig. 2).

Results and Discussions

Three rabbits died at 26th, 32nd and 33rd weeks after the irradiation. These deaths were possibly due to poor eating and drinking. Therefore, the MRI data from the baseline to the 24th week were used for further statistical analysis. One of the remaining rabbits was sacrificed for histological evaluation after the 48th week of MRI scans. In cortex: there was no clear trend in the GFA R/L ratio. The QA and R/L ratio showed a decrease at the 1st week and rapid increased at the 2nd week, follow by reaching a plateau, and the differences reached statistical significance at the 2nd week (p-value = 0.031) in the ISO R/L ratio. In external capsule: there was no clear trend in the GFA R/L ratio. The QA and ISO ratio showed a rapid increased during the initial 2 weeks, follow by reaching a plateau and gradually decrease. The differences reached statistical significance at the 2nd week (p-value = 0.038) in the ISO R/L ratio. In hippocampus: there was no clear trend in the GFA R/L ratio. The QA and ISO R/L ratio showed a decrease at the 1st week and rapid increased at the 2nd week, follow by gradually decrease after 12th week post-irradiation, and the differences reached statistical significance at the 12th week (p-value =0.016) and the 16th week (p-value =0.007) in the QA R/L ratio. In thalamus: there was no clear trend in the GFA R/L ratio. The QA and ISO R/L ratio showed a decrease at the 1st week and rapid increased at the 2nd week, follow by gradually decrease, and the differences reached statistical significance at the 16th week (p-value = 0.047) in the ISO R/L ratio.

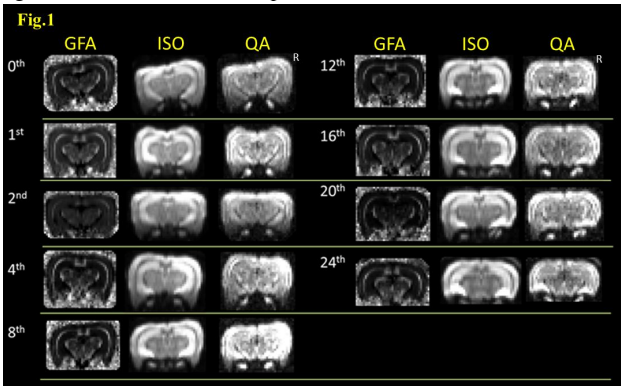

Fig. 1 GFA, ISO and QA mapping were calculated from the multiple shells diffusion data using GQI reconstruction at baseline and at the first to 24th week post-irradiation.

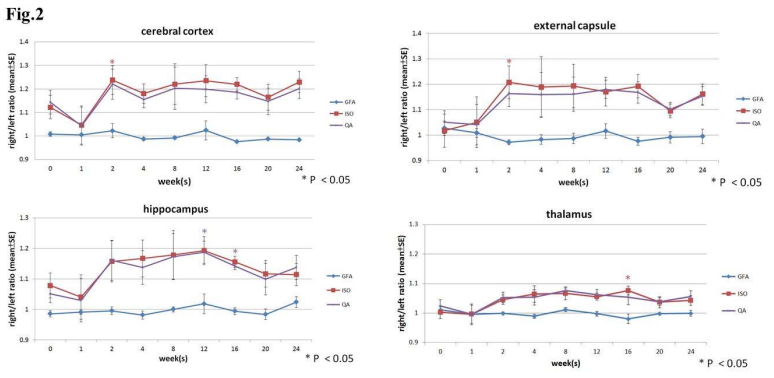

Fig. 2 Longitudinal R/L ratio changes of GQI indices in the cerebral cortex, external capsule, hippocampus and thalamus after irradiation.

GFA is calculated from an ODF and it has high correlation with fractional anisotropy (FA). The value of GFA deceases in fiber crossing or voxels with cerebral spinal fluid partial volume. The results of GFA R/L ratio changes in the 4 different compartments showed no clear trends, may be because that GFA is a voxel based evaluation and it cannot well reflect complex histopathological changes in the post-irradiation acute and early delayed phase, including reactive astrogliosis, vasogenic edema and demyelination [4, 5]. QA is calculated from the peak orientations on an ODF. It can be used to filter out false fibers in crossing fiber scenario and also showed less susceptible to partial volume effect, but consequently, QA is affected by T2 shine through effect, receiver gain, and B1 inhomogeneity [2]. Our results showed a decreased QA R/L ratio at the 1st week, that may be caused by an initially increase in reactive astrogliosis [5]. Increased QA R/L ratio after the 2nd week may result in T2 shine through effect which caused by vasogenic edema. ISO is the minimum distribution value of an ODF, and thus it represents background isotropic diffusion [2]. Our result showed decreased ISO R/L ratio at the 1st week, may be due to reactive astrogliosis, which decreases the free diffusion of water [5]. After the 2nd week, increased ISO indicate a result of mixed glial disruption and vasogenic edema.

Conclusions

With GQI indices, we can detect more complex pathophysiologic changes in both gray and white matter for the longitudinal evaluation of radiation-induced brain injury using a 1.5 T clinical MR scanner.

References

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