Radiation induced injury of the lens and retina in rat eyes: Assessment with diffusion tensor imaging

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Introduction

An unknown risk for astronauts during exposure to galactic cosmic particle (GCP) irradiation in space flight is tissue damage of the eye. Undefined are the tissue effects produced by the high Z, high energy (HZE) particles that are found in space and the dose response of these tissues. In addition, the normal tissue of retina can be involved while undergoing cancer radiation therapy. The major goal of this study was to identify and quantify the evolution and dose response of radiation changes produced in the retina using MRI. We report a preliminary finding that diffusion tensor imaging is able to document altered lens and retinal tissue response to irradiation.

Materials and Methods

Irradiation

Five Sprague Dawley rats underwent 1 GeV/n iron beam irradiation in a single fraction at a dose rate of approximately 1.5 Gy/min for total doses of 4 Gy. Five controls were treated identically but without irradiation. Dose calibration was performed with three parallel plate ion chambers (IC1, IC2, IC3) positioned upstream of the target and a NIST traceable Far West thimble chamber was placed at target. The values of the thimble chamber were compared with the upstream ion chambers to determine the actual dose delivered to the animals. Rats were examined 9 months following irradiation in this study. The animals were anesthetized with a mixture of ketamine and xylazine. Following perfusion, the eyes were carefully excised from the cranial cavity and were post-fixed for one hour in 4% paraformaldehyde in 0.12 M Millonig's phosphate buffer. The eyes were then placed in buffer till the imaging time point.

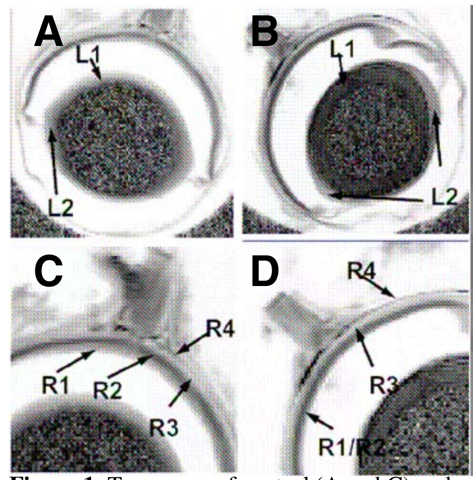

Figure 1. Trace map of control (A and C) and irradiated (B and D) eyes. Distinct structures of the lens are labeled as L1 (capsule) and L2 (cortex). The retina can also be divided into layers in the trace map: R1/R2 (photoreceptors), R3 (choroids), and R4 (sclera) layers.

Diffusion Tensor Microimaging

MR experiments were performed at 25°C on Varian Inova 600 spectrometer (Varian Associates, Palo Alto, CA). The magnet was equipped with a Venus 10-mm microimaging probe (Venus Inc., Livermore CA) capable of delivering 60G/cm per axis. Diffusion tensor imaging data were acquired with TR 1.0 sec, TE 35 msec, Δ 12.9 msec, δ 4.8 msec and slice thickness 1.0 mm, 256 × 256 data matrix, field-of-view 1.32 × 1.32 cm^2. Six diffusion encoding directions: [Gx,Gy,Gz] = [1,1,0], [1,0,1], [0,1,1], [-1,1,0], [0,-1,1], and [1,0,-1] and two b-values of 186 and 2989 s/mm^2 were used to calculate for Trace and relative anisotropy (RA).

Results and Discussion

The layering structure of both lens and retina is seen in the DTI map for both the control (Fig. 1A and C) and the irradiated (Fig. 1B and D) eye. The distinct layers of the lens are marked as L1, the capsule, and L2, the cortex. The retina is also divided according to the DTI parameter map (Fig. 1) as R1/R2 (the photoreceptors layers) R3 (choroids layer), and R4 (sclera layers).

In the irradiated eye, there was a 50% decrease in RA of the L2 (cortex) layer without changes in Trace (Fig. 2A and B) when compared to the normal lens tissue. Although there was not a significant change in trace or RA in the L1 (capsule) layer, a two-fold increase in the volume of this layer was observed (data not shown). These may suggest that the HZE irradiation alters the lens structure. The increased volume in L1 layer herein may be of pathological significance. There was no significant change in RA in the retinal layer (R1/R2) in the irradiated eye when comparing with the R2 of the control (Fig. 2C and D). However, a ~40% reduction of Trace in R1/R2 was clearly observed in the irradiated eye compared to that of R1 or R2 of the control. Of particular importance, the inner and outer retina layers were further distinguished in the control (Fig. 1C). The reduced Trace is suggestive of retinal injury in the photoreceptors layers. The injury to these layers was also apparent in the loss of the boundary of R1 and R2 in the control eye. Histological characterization supports these findings.

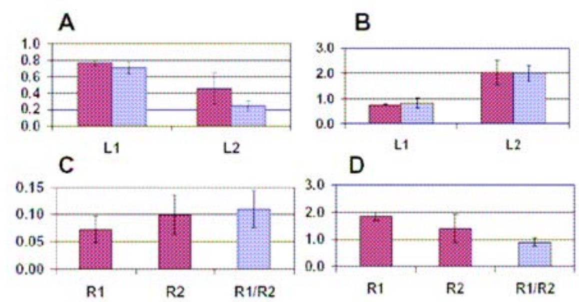

Figure 2. Relative anisotropy (A and C) and trace (B and D) for the lens (A and B) and retina (C and D) from both control (purple bars) and HZE irradiated (blue bars) rat eyes.

Conclusion

Our results suggest that diffusion tensor imaging can be used evaluate changes caused by radiation within the eye. Significant changes were demonstrated in both lens and retina 9 month after irradiation. Both capsule and cortex regions of the lens are damaged due to HZE irradiation. These are consistent with pathogenesis of cataract formation relating to these two layers. Degenerative retina layers were also observed by DTI on the injured rat eyes suggesting the sensitive of the photoreceptors layers to the HZE irradiation.