Diffusion Tensor Imaging Reveals White and Gray Matter Modifications after Low Dose ^{56}Fe Irradiation

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Introduction

Radiation of high-energy charged particles (HZE) poses a significant health hazard for astronauts during space travel and work. Magnetic resonance imaging (MRI) has proved to be a sensitive method for detection of tissue modifications within hippocampus exposed to ^{56}Fe irradiation, in which the alterations in T2 relaxation time and apparent diffusion coefficient (ADC) corresponded to hippocampal related cognitive impairment[1]. It is known that white matter is vulnerable to radiation. In the current study, the integrity of white matter tracts were evaluated and compared to that of gray matter regions in rats exposed to brain-only ^{56}Fe radiation using diffusion tensor imaging (DTI).

Methods and Materials

Male Sprague Dawley rats were exposed to brain-only ^{56}Fe irradiation (0, 1, 2 and 4 Gy, n=4 per group). ^{56}Fe beams (600 MeV/n) were collimated to irradiate only the brain. At 18 mo post-irradiation, *ex vivo* DTI was performed on a Bruker Advance 11.7T MRI (8.9 cm bore, 3.0 cm ID volume quadrate coil) with the following parameters: TR 2.5 s, TE 29 ms, Δ 20 ms, δ 3 ms, NEX 4, slice thickness 0.6 mm, field-of-view (FOV) 2 cm and data matrix 256×256. Diffusion sensitizing gradients were applied along six directions with b-values of 0 and 1 ms/μm^2. DTI were processed using an in-house Matlab routine and multiple measures including trace (Tr), relative anisotropy (RA), axial diffusivity and radial diffusivity were quantified. The regions of interest (ROIs) were selected in corpus callosum (CC), hippocampus, substantial nigra and cortex. ANOVA was performed to compare the quantitative measurements among dose groups. Statistical significance was accepted at $p < 0.05$.

Results

Tr significantly decreased at all doses within the hippocampus, but increased in a dose dependent manner within the CC (Fig. 1A). Similarly, there was a significant increase in RA within the CC but RA exhibited a dose-dependent decrease in the cortex (Fig. 1B) with no change in the hippocampus. While the axial diffusivity increased in a dose dependent (1-4 Gy) manner within the CC, radial diffusivity increased at 1 and 2 Gy but decreased at 4 Gy (Fig.1B). Axial and radial diffusivity were significantly increased at 2 and 4 Gy within the substantia nigra. Correlative histopathology revealed increased glial staining at 4 Gy without overt neuronal loss in all of the ROIs. Immunohistochemical staining is being undertaken to further correlate with DTI findings.

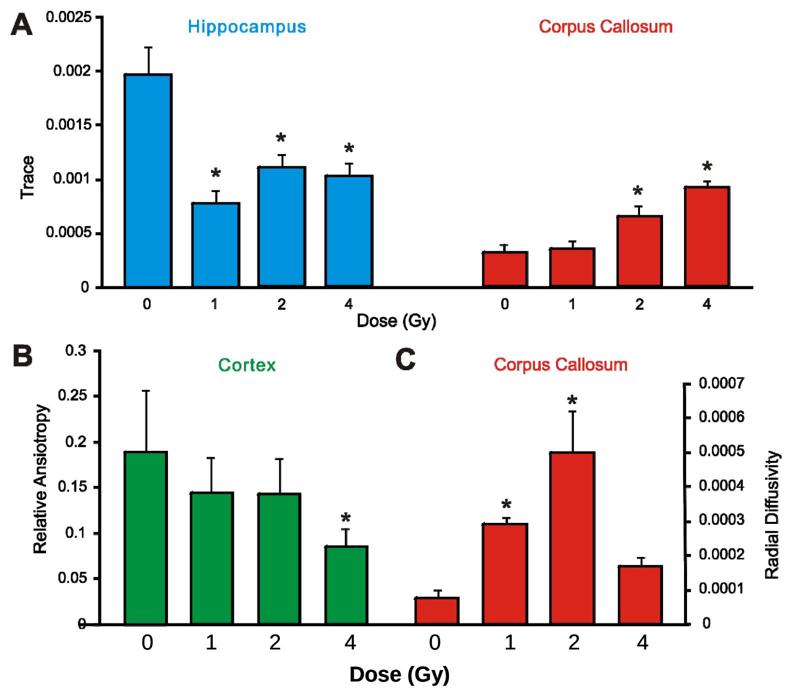

Fig. 1. DTI analysis reveals differential changes in different brain regions after ^{56}Fe exposure. * p<0.05 vs 0 Gy

Conclusions

In a rat model of brain-only ^{56}Fe radiation, which simulates the space environment, DTI measures are able to assess altered microstructure and cellular organization within both white and gray matter, providing a sensitive method in delineation of radiation effects. The differential profiles of DTI-derived parameters in white matter tracts and gray matter regions suggest disturbances in the integrity of white matter and cellular compositions of gray matter may both contribute to the progressive neuro-degeneration following brain irradiation.

References

1) Obenaus, A., Huang, L., Smith, A., Favre, C, Nelson, G. Kendall, E. (2008) Magnetic resonance imaging and spectroscopy of the rat hippocampus 1 month after 56Fe Radiation. Rad Res. Feb; 169:149-61