Temporal Alterations in Brain Water Diffusivity in Acute Radiation Injury

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Introduction: With increasing use of nuclear technologies in power production, medical and industrial applications, and in a scenario of nuclear terrorism/war, there is an enhanced likelihood of accidental radiation exposure to occupational workers, patients and public. Studies from exposed human and animals indicate that radiation from cobalt can affect a wide variety of tissues particularly those with greater levels of cellular turnover and divisions.¹ It has been argued that central nervous system (CNS) has a limited repertoire of responses to radiation injury. However, few animal studies have shown cognitive impairment, personality changes and gait disturbance after a mild dose of whole body irradiation. Radiation-induced brain injury can be divided into 3 phases: acute, early delayed and late delayed. The pathophysiology of CNS radiation injury shares many similar damage pathways with ischemic, inflammatory, and demyelinating insults.² Diffusion tensor imaging (DTI) has shown promise as a non-invasive marker of ischemia as well as inflammatory pathologies. The aim of our study was to follow up acute radiation induced changes in brain parenchyma of Strain A mice after a single sub-lethal dose irradiation by using DTI.

Materials and methods: Male A1 strain mice of 10-12 weeks of age (n = 8) were exposed to radiation dose of 8 Gy from 60Co source in a GC-220 AECL CANADA operating at a dose rate of 0.1916 Gy/min. Brain MRI experiments were performed at 0h, 6h, 1 day, 3 day and 5 days post irradiation. All MR imaging was performed in a Bruker Biospin 7.0 Tesla 30 cm horizontal bore magnet (Bruker Biospin Ettlingen, Germany). High-resolution anatomical RARE images were acquired. DTI images were acquired using a multi-slice, multiple-shot spin echo EPI sequence with the following parameters: repetition time (TR) / echo time (TE) = 5000 ms/34.46 ms, number of gradient encoding directions = 81, and b = 672 s mm⁻². The other parameters were: acquisition matrix = 128 × 128, field-of-view = 2 cm × 2 cm, slice thickness = 1 mm, and number of slices = 9 (contiguous). ParaVision 5.1 software was used for the generation of FA and MD maps. Regions of interest (ROIs) were placed on corpus callosum (CC), parietal cortex (Ctx), thalamus (Th), and hippocampus bilaterally. FA and MD values from right and left hemisphere were pooled together for statistical analysis.

One-way analysis of variance (ANOVA) with multiple comparisons using Bonferroni, Post Hoc test was performed to evaluate the differences in DTI measures among different timepoints. No abnormalities were observed on anatomical images at any timepoint. Mean±SD of FA and MD values were summarized in table. A decrease in MD values was observed in all regions at 3rd and 5th day compared to baseline study. Significantly decreased MD and FA values were observed in CC on 3rd and 5th day compared to baseline study. In CC and Ctx, initially an increasing trend in FA values was observed on moving from 0 hour to 1 day followed by a sharp decrease in FA on 3rd and 5th day.

Discussion: In our longitudinal study we observed decreased MD values at 3rd and 5th day after irradiation compared to baseline, along with an initial increase followed by a decrease in FA values. Our observations of MD and FA change in brain parenchyma after radiation injury can be explained by pathologic changes, like hypoxia, ischemic and inflammation. The mechanisms involved in the pathogenesis of CNS radiation injury are inflammation, ischemia and free radical activation. MD values are the most sensitive measure for detecting acute ischemia. The brain MD changes are a function of intracellular-extracellular water homeostasis.³ Influx of water from fast extracellular diffusion compartment to slow intracellular diffusion compartment results in a net decrease in regional MD values. Both reduced and normal-to-elevated FA values have been reported in acute infarcts less than 24 hours after the onset of symptoms.⁴,⁵ Some have proposed that increased diffusion anisotropy indicates continued structural integrity and tissue salvageability and that increased anisotropic diffusion occurs as a result of fluid shift from the extracellular space to the intracellular space without membrane rupture. Further decreased FA at 3rd and 5th day may signify the loss of cellular integrity with irreversible cellular injury. Our quantitative DTI results suggest the radiation induced hypoxic changes in brain parenchyma during acute phase even before conventional MRI.