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DTI/DKI of Treatment-Induced Microstructural Brain Changes in Childhood Cancer Survivors

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Treatment outcome of pediatric malignancies have improved significantly over the past decades but survivors face long term morbidity including neurocognitive impairment. The use of cranial irradiation is well-recognised to be a major contributor to the multifactorial causes.

We have evaluated several cohorts of childhood cancer survivors who have undergone whole brain irradiation; namely medulloblastoma, acute lymphoblastic leukemia (ALL) and germ cell tumour (GCT) survivors, using Diffusion tensor MRI (DTI) or Diffusion kurtosis MRI (DKI). We evaluated its novel role as a marker for treatment-induced neurotoxicity, and then performed translational studies using a rat model of radiation-induced white matter injury to elucidate the histological correlates of the diffusion indices. We found diffusion indices to be associated with known neurotoxicity risk factors (dose intensity of radiation, younger age at treatment, time period after treatment) and neurocognitive and functional scores in children.

Hence, our results support the use of DTI/DKI to probe microstructural brain changes, and as a biomarker to monitor radiation-induced neurotoxicity.

However, whilst quantitative metrics of diffusion are promising as biomarkers, it's routine use in daily clinical practice is limited by high variability and lack of protocol standardization. To bridge the translational gap and to impact clinical practice, further work to improve accuracy, evaluate reproducibility, promote standardization and implementation into the clinical workflow are necessary.

Keywords: Diffusion tensor Imaging, Biomarker, Childhood cancer survivor, neurotoxicity