

Late Effects of Cancer Treatment on Gray Matter Perfusion Assessed by Arterial Spin Labeling MRI and its Association with Neurocognitive Function

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Introduction: Cancer treatments have greatly improved over the last decades raising survival rates and curing more individuals. For example, survival rates for Acute Lymphoblastic Leukemia (ALL), the most prevalent childhood malignancy, has improved from 5-10% in the early 1960's to over 93% today [1]. Consequently, late effects of treatment with radiation and chemotherapy have become more apparent. Expanding our knowledge in this area is necessary to derive effective treatment options that simultaneously minimize late effects for future patients. It has been reported that children who receive prophylactic cranial radiation (CRT) for treatment of childhood leukemia are at significant risk of developing cognitive problems [2]. Inverse correlations have been reported between cerebral blood flow (CBF) and IQ in children with sickle cell anemia [3]. The purpose of our study was to explore the association between gray matter perfusion assessed by arterial spin labeling (ASL)-MRI and neurocognitive function in long-term adult survivors of ALL.

Methods: ASL-MRI was measured in long-term adult survivors of ALL who were treated about 20 years previously. Global cognitive skills were assessed using the Wechsler Abbreviated Scale of Intelligence [4]. ALL survivors were divided into two subgroups by CRT dose: 18Gy (F=9, M=9, age=25.6y ±3.8) or 24Gy (F=10, M=7, age=26.9y±3.1). ASL-MRI (Q2TIPS) measurement parameters were: TE/TR =23ms/2280ms, T1/TI2=700ms/1400ms, FOV=210x210mm², matrix=64x64, slice thickness=5mm, 11 slices. Quantitative CBF measures were calculated [5] and realigned by FLIRT (FSL-toolbox, FMRIB, Oxford, UK) to a 3D high-resolution T1w MPRAGE dataset. The 3D T1w images were automatically segmented by FAST creating a gray matter (GM) region of interest (ROI). Spearman correlations were used to test relationships between global cognitive skills (FSIQ) and GM perfusion values.

Results: Table 1 shows correlations between males and females by CRT dose. There was a significant inverse correlation (p=0.04) between FSIQ scores and GM perfusion for females who received 24Gy of CRT. This correlation was not observed in females who received less CRT or in males. Figure 1 displays the correlation of FSIQ scores and GM perfusion for females who received 18Gy (red) and 24Gy (blue) of CRT. Independent of sex or CRT dose, Wilcoxon rank-sum test determined those who demonstrated neurocognitive impairment (FSIQ < 85) had higher GM perfusion (p=0.034).

Discussion and Conclusion: Consistent with limited reports in other samples, e.g. the sickle cell cohort [3], increased GM perfusion was associated with neurocognitive impairment. Females have been identified as being at increased risk for neurocognitive impairment following CRT [3]. Our data might suggest a change in the vascular response of females who receive CRT of 24Gy and the observed globally increased CBF may be related to CNS complications. ASL may be a helpful tool to analyze this phenomenon further and, if used prospectively in a larger cohort, may provide insight into the evolution of this pattern.

References: [1] Pui C, et.al. NEJM. 2009;360:2730-41. [2] Nina K, et.al. J Natl Cancer Inst. 2010;102:881-893. [3] Strouse J. Blood. 2006;108:379-381. [4] Wechsler D. Wechsler Abbreviated Scale of Intelligence. Psychological Corporation; 1999. [5] Wang J, et.al. MRM. 2002;48:242-54.

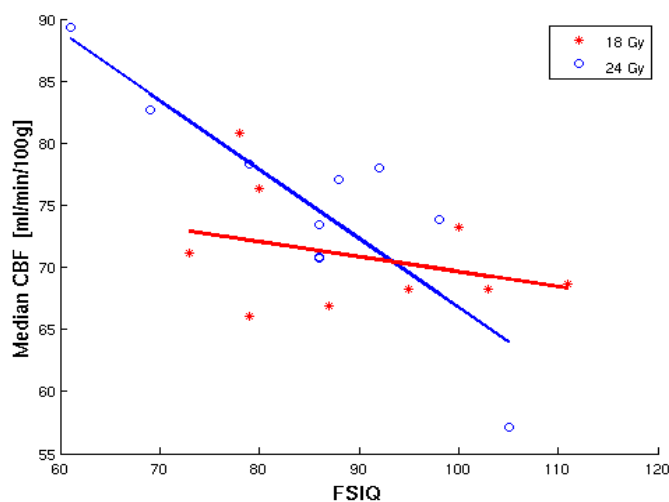


Figure 1: Scatter plot of FSIQ score versus median gray matter perfusion in female acute lymphoblastic leukemia survivors, who received 18Gy (red) or 24Gy (blue) of cranial radiation. There is a significant correlation (p=0.04) between FSIQ scores and gray matter perfusion for the females who received 24Gy.

	18 Gy	24 Gy
Female	R =-0.22	R=-0.64
	P=0.57	P=0.04
Male	R=0.00	R=0.00
	P=1.0	P=1.0
Male & Female	R=-0.10	R=-0.50
	P=0.68	P=0.04

Table 1: The Spearman correlation R and p-value are shown for FSIQ scores and gray matter (GM) perfusion values by gender and cranial radiation (CRT) dose. There was a significant inverse correlation (p=0.04) between GM perfusion and FSIQ score for females who received 24Gy of CRT.