

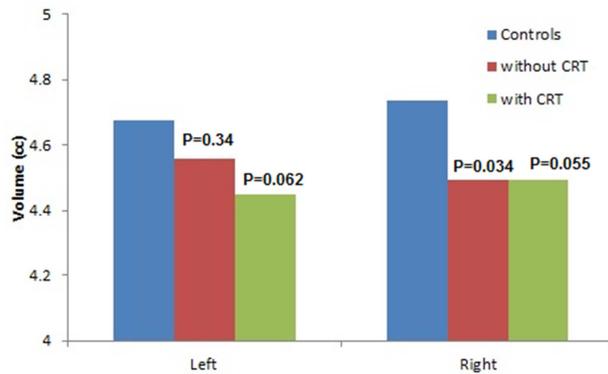
# Hippocampal Shape Analysis in Adult Survivors of Childhood Acute Lymphoblastic Leukemia: The Effect of Cranial Radiotherapy

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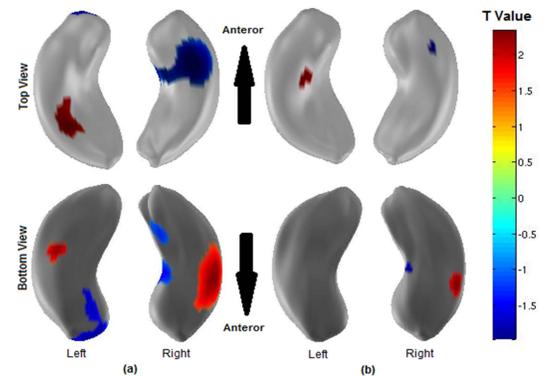
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**INTRODUCTION:** The hippocampi, located in the medial temporal lobes, are important sub-cortical structures that coordinate memory function and are vulnerable to radiation and chemotherapy. In this study, the shapes of hippocampi of adult survivors treated for childhood acute lymphoblastic leukemia (ALL) were investigated: survivors treated with both cranial radiotherapy (CRT) and chemotherapy and survivors treated with chemotherapy only. The hippocampal shapes of the two groups were compared with healthy controls. It was hypothesized that hippocampal shape would be different between survivors and controls, with the survivors treated with CRT demonstrating a larger discrepancy.

**METHOD AND MATERIAL:** The MR scans of 73 adult childhood ALL survivors and 22 adult healthy controls (age  $23.03 \pm 2.65$ ) were used for retrospective study. The MR images of ALL survivors were taken at least 15 years after diagnosis. Among the ALL survivors, 39 (age  $26.70 \pm 3.44$ ) received both CRT and chemotherapy and the remaining 34 (age  $25.17 \pm 3.53$ ) received chemotherapy only. The delineation of left and right hippocampal volume was performed on T<sub>1</sub> weighted 3D MR image of each subject using the FreeSurfer<sup>1</sup> software package and then manually corrected according to the general guideline<sup>2</sup>. The 3D hippocampal shape analysis was performed using the MATLAB based software package SPHARM\_MAT<sup>3</sup> on the segmented hippocampal volume of each subject. SPHARM\_MAT uses the spherical harmonic (SPHARM) basis functions to represent a closed surface. In the SPHARM method, the hippocampal surface was first mapped to a unit spherical surface and then the SPHARM coefficients up to 12 degrees were fitted as the shape descriptor. Each individual SPHARM model can be placed in a common space by aligning the first-order ellipsoids across all subjects. With aligned SPHARM models, the hippocampal shape can be sampled back into the common subject space as a triangular mesh by icosahedron division of the spherical surface. In this study, each subject was sampled by the 4<sup>th</sup> icosahedron level which is a triangular mesh with 2562 vertexes. Since the correspondences on each vertex across the subjects have been established, a two-sample t-test can be performed on each vertex. The calculated T values and associated p-values were saved on an average shape model.



**Figure 1:** Mean volumes of left and right hippocampus for the controls (blue), adult ALL survivors without CRT (Red) and with CRT (green). The p values for each group of survivors compared to controls were also shown on the graph.



**Figure 2:** Hippocampal shape differences between normal controls and ALL survivors with CRT (a) and without CRT (b). The T value color map on the right displays positive and negative T values representing the outward and inward shape deformation.

**RESULTS:** The results of hippocampal volume analysis were shown in Figure 1. Mean left and right hippocampal volume for the two groups of ALL survivors are lower than that of normal controls, but did not reach statistical significance or was only weakly significant. The results of shape analysis are shown in Figure 2. The metric for statistical analysis was the deformation on the surface normal direction. The positive and negative T values represent the outward and inward deformation respectively. Only those vertexes with  $p < 0.05$  were mapped in Figure 2. The shape deformation patterns of the two survivor groups can be visually observed. Regardless of cancer treatment, there was more significant deformation on the right than on the left. The survivors treated with CRT had more significant deformation on both hippocampal surfaces than those survivors treated with chemotherapy only. For survivors treated with chemotherapy only, 0.8% of the left and 1.8% of the right hippocampal surfaces were found significantly different from that of controls. For survivors treated with CRT, 7.1% of the left and 14.9% of the right were different from controls. Interestingly, the regions in the right hippocampus that were significantly deformed in the chemotherapy only group and the CRT group were similar, suggesting some specific hippocampal regions are more susceptible to damage from cancer treatment.

**DISCUSSION/CONCLUSION:** A trend of hippocampal volume atrophy in both survivor groups was observed. The results of shape analysis suggest that treatment including CRT can cause more permanent hippocampal shape abnormality than chemotherapy alone. However, both treatment regimens damaged some specific hippocampal regions which may be more susceptible to cancer treatment.

**REFERENCES:** [1] Fishl B. et al, Cereb. Cortex, 2004 [2] Duvernoy H. et al, Springer 2013 [3] Styler M. et al, MICCAI, 2006