

## The Evolution of Pediatric Hodgkin Lymphoma Therapy: Contemporary Protocols Significantly Reduce Radiation Exposure of Normal Tissues

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**Background:** Survivors of childhood Hodgkin Lymphoma (HL) are at an increased risk for radiation-related toxicity. However, most estimates of the magnitude of these risks are based on historical radiotherapy (RT) treatments that encompassed large volumes of normal tissue. We evaluated the normal tissue dose associated with two recent Children's Oncology Group (COG) trials and compared them with doses reconstructed from RT plans of HL survivors in the Childhood Cancer Survivors Study (CCCS).

**Methods:** Radiation doses to the female breast and heart were reconstructed from 50 HL survivors sampled from the CCSS cohort who received mediastinal RT (treatment dates 1970-86). These patients were matched based on gender, stage (I/II vs III/IV), patient size, and age at treatment (within 1 year) to HL patients with normal tissue dosimetry available treated with involved-field RT COG trials AHOD0031, open 2002-2009 (N=63) and AHOD0831, open 2009-2012 (N=96) to compare doses to normal organs.

**Results:** For patients with early stage disease, the average reduction in mean breast dose in the COG patients compared to CCSS was 83.5%, corresponding to an absolute reduction of 15.5Gy. For advanced stage disease, these dose reductions were 70.0% and 11.6Gy, respectively. The median volumes of breast tissue receiving  $\geq 5$ Gy decreased by 71.4% in early stage disease and 54.7% in late stage disease. Mean heart dose decreased by 68.6% in the early stage patients and 56.8% in the advanced stage patients, corresponding to absolute dose reductions of 22.9Gy and 17.6Gy, respectively. The volume of heart receiving  $\geq 5$ Gy decreased by 38.2% and 28.7% for early and advanced stage patients. All these comparisons were statistically significant ( $P < 0.05$ ).

**Conclusion:** These results are the first to compare normal tissue dosimetry for CCSS HL patients to that associated with contemporary IFRT treatment, demonstrating significant reductions in dose to breast and heart. These results illustrate the need to develop survivorship guidelines and modify contemporary treatments based on an updated understanding of the associated exposures.