Impact of Enhanced CT-based Heart Model on Estimating Radiation Therapy Related Late-Onset Cardiac Disease in the Childhood Cancer Survivor Study

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Purpose:

We previously evaluated late-onset cardiac disease in the Childhood Cancer Survivor Study (CCSS). Since individuals in CCSS were mostly treated without computed tomography (CT)-based planning, heart doses were estimated by reconstructing each individual's radiation therapy (RT)-treatment on an age-scaled phantom with a simple atlas-based heart. We recently enhanced our phantom by adding six CT-based heart models from international reference phantoms; one model was identified ("new base-heart") as anatomically most representative across the CCSS age-range (infant-adolescent). The purpose of this study was to examine the impact of using this enhanced heart model on estimating cardiac risk.

Methods:

The CCSS includes 24,214 individuals diagnosed 1970-1999, median age at diagnosis 7.0 (range 0–20.9) years and at last follow-up 27.5 (range 5.6–58.9) years. For those treated with RT (n=11,667), mean heart dose (D_m), V_5, and V_{20} were calculated for six heart models. We evaluated dose-response relationships using piecewise-exponential models, adjusting for attained age at evaluation, sex, diagnosis age, race, smoking history, diagnosis year, and chemotherapy exposure. Each individual's D_m, V_5, and V_{20} were assigned using: [1] the new base-heart and [2] a heart model matched to closest age/sex.

Results:

For new base-heart, relative rates (RR) of any cardiac disease increased linearly with $D_m \geq 10$Gy ($P<0.001$), and both $V_{5,V20=0\%} \geq 50\%$ and $V_{20}<30\%$ were associated with elevated risks (RR=1.4; 95% CI=1.0-2.1) and (RR=1.6; 95% CI=0.9-2.8), respectively; risks captured by RRs from new base-heart, when compared to atlas-based heart, were larger for D_m, similar for V_5, and smaller for V_{20}. The RRs calculated using the new base-heart and age/sex-matched hearts agreed on average within 10%, suggesting robustness.

Conclusion:

With an anatomically realistic heart, cardiac disease risk increased linearly with D_m, V_5, and V_{20}. However, further investigation of substructure dose response is warranted because of the complex nature of the changes with D_m, V_5, and V_{20} compared to previous atlas-based heart.