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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INTRODUCTION

We previously evaluated late-onset cardiac disease in the Childhood Cancer Survivor Study (CCSS) with patients diagnosed 1970-1999[1]. Since most individuals in CCSS were treated prior to 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 model, H_{Atlas} (Figure 1a).

Recently, we enhanced our phantom with an anatomically more realistic heart model, H_{Hybrid} (Figure 1a).[2]

The H_{Hybrid} model was developed:

- by combining the age-scalable capability of our computational phantom with anatomical accuracy of the University of Florida (UF)/National Cancer Institute (NCI) reference phantom series (adopted by the International Commission on Radiation Protection)[3]
- from the 5-year-old UF/NCI reference phantom heart model because it was the closest age match to the median age at diagnosis (7 years) of the CCSS cohort

We also created alternate heart models (Figure 1b) using the other aged UF/NCI phantoms (0.1, 1, 10, and 15 years with separate male and female models for age 15 years).

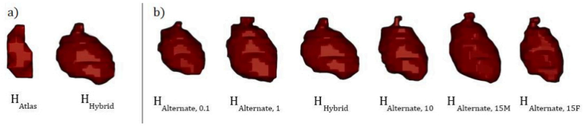

Figure 1: Volume renderings of (a) H_{Atlas} and H_{Hybrid} and (b) $H_{Alternate}$ models

PURPOSE

The main purpose of this study was to examine the impact of using an enhanced heart model to estimate cardiac risk in survivors of childhood cancer.

Additionally, we examined the impact of using a single heart model for the entire cohort compared to models that more closely matched an individuals' age/sex

METHODS

The CCSS includes 24,214 individuals diagnosed 1970-1999, median age at diagnosis of 7.0 (range 0–20.9) years and a follow-up of 27.5 (range 5.6–58.9) years. For those treated with RT (n=11,667), RT fields were reconstructed on an in-house phantom scaled to their age at RT.[4] Note that when the phantom was scaled to different ages, separate scaling functions were applied to each of the body regions to account for the non-uniform growth in the lateral, superior-inferior, and anterior-posterior directions of the different regions.[5]

- For each individual we calculated mean heart dose for two different heart models
  (1)H_{Hybrid} and
  (2) $H_{Altenate}$ model that most closely matched the individual's age/sex

The heart models within each age-scaled phantom were also scaled to age at RT by applying trunk-specific scaling functions.[5]

The selection process for the $H_{Alternate}$ model is illustrated in Figure 2.

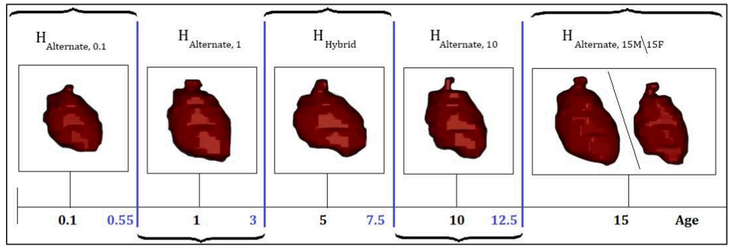

Figure 2: Illustration of age/sex-matched heart selection process. Example: For an individual that was 11.3 years at RT, the $H_{Alternate,10}$ model was selected, which was then scaled to age 11.3 years.

We evaluated RT dose-response relationships using piecewise-exponential models, adjusting for attained age at evaluation, sex, diagnosis age, race, smoking history, diagnosis year, and chemotherapy exposure. Relationships were examined using mean heart doses calculated for H_{Hybrid} and $H_{Altenate}$ models.

RESULTS

- When comparing RT dose-response relationships established using mean heart doses for H_{Hybrid} and H_{Atlas} models, relative rates of cardiac disease for all outcomes:
  - Increased monotonically with mean heart dose ≥10 Gy (P<0.001)
  - Are higher than previously estimated for dose between 20 and 29.9 Gy

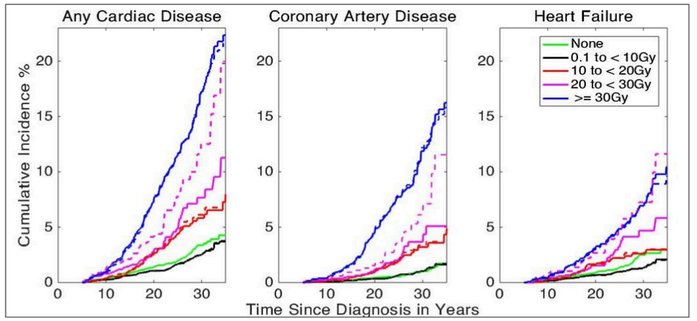

Figure 3: Cumulative incidence of cardiac outcomes for H_{Hybrid} (dashed lines) and H_{Atlas} (Solid Lines).

RESULTS

- RT dose-response relationships established using mean heart doses for H_{Hybrid} and the $H_{Alternate}$ models were within 10 % for all outcomes and all dose ranges.

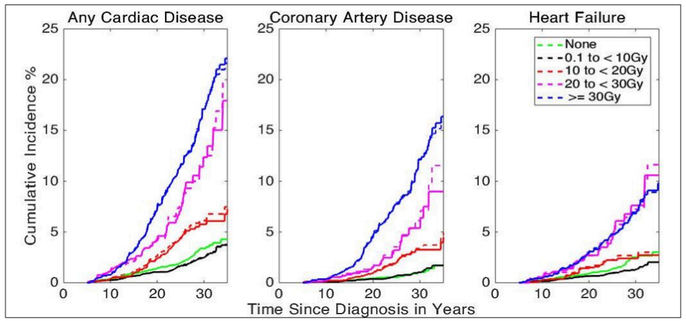

Figure 4: Cumulative incidence of cardiac outcomes for H_{Hybrid}(dashed lines) and $H_{Alternate}$ (Solid Lines).

CONCLUSIONS

This study confirms the findings of our prior study[1] that established a linear relationship between mean heart dose and risk for late cardiac disease. However, with an anatomically more realistic heart model, relative rates of cardiac disease are higher than previously estimated for doses between 20 and 29.9 Gy. It is important to note that the shift in the dose and results are due to use of an updated cardiac model and not a change in the way patients were treated. Also, the data suggest that the results are robust to subtle differences in heart anatomy.

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