# Automatic segmentation for the evaluation of cardiac substructure dose in support of epidemiological research on cardiovascular morbidity after breast radiotherapy

**M. M. Mille[1], J. W. Jung[2], B. Ky[3], W. Kenworthy[3], C. Lee[4], Y. Yeom[1], A. Kwag[5], W. Bosch[6], S. MacDonald[7], O. Cahlon[8], J. E. Bekelman[3], C. Lee[1]**

(1) National Institutes of Health, Rockville, MD, leechoonsik@mail.nih.gov ; (2) East Carolina University, Greenville, NC; (3) University of Pennsylvania, Philadelphia, PA

(4) University of Michigan, Ann Arbor, MI; (5) Vanderbilt University, Nashville, TN; (6) Washington University, St. Louis, MO; (7) Massachusetts General Hospital, Boston, MA

(8) Memorial Sloan Kettering Cancer Center, New York, NY

29th Annual Meeting
April 11-13, 2022

## INTRODUCTION

Evidence for an increased risk of ischemic heart disease and cardiac mortality has been reported for survivors who received radiotherapy for breast cancer, Hodgkin lymphoma, lung cancer, and childhood cancer [1]. However, it remains unclear how to best optimize the treatments because there are gaps in knowledge around which specific cardiac structures are at risk and the mechanism of damage [2]. Unfortunately, due to the tedious nature of the task, it is typical for only the whole heart, not heart substructures, to be contoured during treatment planning. As a result, most research on cardiac risk to date has used mean dose to the whole heart as a radiation exposure indicator. Studies which consider substructures tend to have a small number of patients and are not sufficiently powered. **The purpose of this work was to demonstrate an automatic segmentation algorithm which can be applied to large patient datasets.**

## AIM

We applied our previously published automatic segmentation method to contour heart substructures [3] on CT images of female patients selected from the RadComp Radiorepository who received external photon beam radiotherapy for breast cancer. The segmentation method uses a most-similar atlas selection and a structure-guided B-spline transformation.

## METHOD

**Patient Data From RadComp Clinical Trial**

- We collected non-contrast radiotherapy planning CT images for 100 breast cancer patients enrolled in the RadComp trial who received external photon beam radiotherapy
- The radiotherapy plans (prescribed doses ranged from 45 Gy to 50.4 Gy) represent current real-world practice in the United States for patients with a high risk of nodal recurrence in whom the internal mammary nodes are covered
- Two cardiologists generated a single consensus contouring of the whole heart, left atrium, right atrium, left ventricle, and right ventricle, and left anterior descending artery (LAD) on the images of all 100 patients
- We selected 30 of the patients to create a cardiac atlas library for the automatic segmentation, with remaining 70 patients used for testing performance (40 left breast RT, 30 right breast RT)

**Automatic Segmentation**

- The input to our automatic segmentation method is the contour of the whole heart which is assumed to be manually drawn on the CT images of the breast cancer patients at the time of treatment planning
- The 30 heart atlases in the library are then individually placed at the center of mass of each patient's whole heart and linearly scaled to match the whole heart volume. The scaled atlas (out of 30 possible choices) showing the greatest Dice similarity coefficient (DSC) (a volume overlap index between two volume objects ranging from zero to 100%) for the whole heart was selected
- Non-rigid transformation was applied between the selected atlas whole heart volume mask and the patient whole heart volume mask (not CT image) by a structure-guided B-spline 3D transformation

**Performance Evaluation**

- Geometric performance was quantified using the DSC and average surface distance (ASD) (the average of all distances between the surfaces of two objects) metrics to compare the manual and automatic structure contours
- Dosimetric performance was evaluated by applying the structure masks to the 3D dose matrix and comparing calculated dose for the cases of manual or automatic structure contours
- To assess sensitivity of the dose estimates, the substructure masks were shifted by 5 mm in a randomly selected 3D direction and then the dose was recalculated. A total of 100 realizations of this shift were performed and the maximal and minimal observed dose were recorded. A shift of this size (~5 pixels) reasonably simulates the variability in manual contouring, patient setup error, and/or motion of the heart

## RESULTS

### Geometric Performance

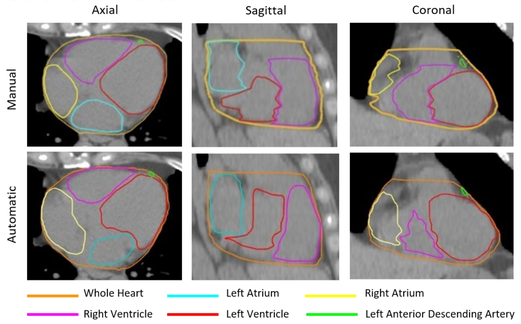
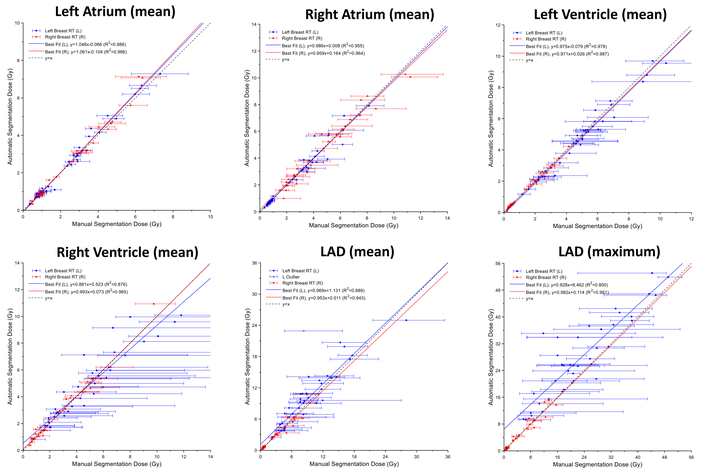



**Figure 1.** Comparison of manual (top row) and automatic (bottom row) heart contours in the axial (left), sagittal (middle), and coronal (right) views.

### Dosimetric Performance

**Figure 3.** Correlation plots and best fit lines showing the relationship between manual and automatic segmentation mean doses for left atrium, right atrium, left ventricle, right ventricle, and left anterior descending artery (LAD). The maximum dose to the LAD calculated by each method was also compared. Best fit lines were calculated separately for left- and right- sided treatment. Error bars represent the range of doses observed from the 5 mm shift sensitivity analysis.



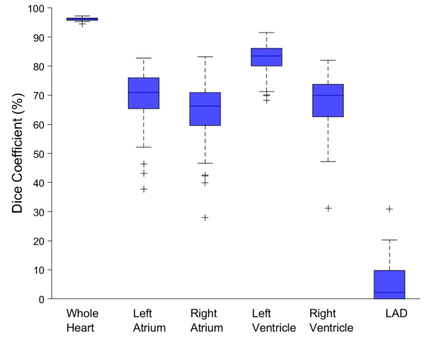




**Figure 2.** Box plots of the Dice similarity coefficient (DSC) for the whole heart and substructures for the 70 patients. Outliers are denoted by "+" and are defined as values located 1.5 interquartile ranges below the first quartile or above the third quartile.

**Table 1.** Comparison of the cardiac substructure doses between manual and automatic segmentations of a total of 70 breast cancer patients.

| Treatment Laterality | Cardiac Structures | Manual Dose (Gy) Median | Manual Dose (Gy) Range | Automatic Dose (Gy) Median | Automatic Dose (Gy) Range | Dose Difference (Gy)* Median | Dose Difference (Gy)* Range | Mean Dose Difference (%)* |
|---|---|---|---|---|---|---|---|---|
| Left (n=40) | WH | 4.6 | 1.0 – 10.5 | 4.5 | 1.0 – 10.5 | 0.06 | 0.00 – 0.41 | 1.7 |
| | LA | 2.4 | 0.4 – 7.3 | 2.4 | 0.3 – 7.3 | 0.14 | 0.01 – 0.74 | 9.1 |
| | RA | 2.3 | 0.3 – 8.1 | 2.3 | 0.3 – 7.9 | 0.08 | 0.00 – 1.58 | 8.7 |
| | LV | 5.0 | 1.2 – 10.4 | 4.7 | 1.2 – 9.7 | 0.19 | 0.00 – 0.97 | 5.9 |
| | RV | 4.6 | 0.8 – 11.8 | 4.5 | 0.8 – 10.1 | 0.48 | 0.04 – 2.57 | 14.4 |
| | LAD | 8.1 | 2.2 – 28.0 | 9.4 | 2.5 – 25.0 | 1.06 | 0.01 – 14.6 | 21.6 |
| | $LAD_{max}$ | 20.7 | 5.9 – 49.1 | 25.7 | 9.3 – 53.1 | 3.60 | 0.00 – 23.4 | 30.1 |
| Right (n=30) | WH | 2.0 | 0.6 – 7.2 | 2.1 | 0.7 – 7.1 | 0.02 | 0.00 – 0.09 | 1.0 |
| | LA | 1.6 | 0.4 – 6.4 | 1.7 | 0.3 – 7.1 | 0.09 | 0.00 – 0.97 | 8.5 |
| | RA | 4.2 | 1.5 – 11.2 | 4.3 | 1.0 – 10.3 | 0.28 | 0.01 – 1.18 | 9.5 |
| | LV | 1.0 | 0.2 – 4.1 | 1.1 | 0.1 – 4.2 | 0.06 | 0.00 – 0.46 | 9.2 |
| | RV | 2.3 | 0.5 – 9.8 | 2.6 | 0.4 – 10.9 | 0.25 | 0.01 – 1.30 | 14.4 |
| | LAD | 1.5 | 0.3 – 9.5 | 1.5 | 0.2 – 10.7 | 0.15 | 0.01 – 2.00 | 15.3 |
| | $LAD_{max}$ | 2.0 | 0.5 – 15.7 | 2.1 | 0.5 – 15.1 | 0.20 | 0.00 – 2.40 | 17.5 |

*Absolute difference between automatic and manual doses

**Table 2.** Comparison of sensitivity of cardiac substructure doses to a 5 mm shift in the manual contour. The maximal dose deviation is calculated as the largest deviation in dose observed for 100 realizations of a 5 mm contour shift relative to the dose from manual contouring.

| Treatment Laterality | Cardiac Structures | Absolute Maximal Dose Deviation (Gy) Median | Absolute Maximal Dose Deviation (Gy) Range | Relative Maximal Dose Deviation (%) Median | Relative Maximal Dose Deviation (%) Range |
|---|---|---|---|---|---|
| Left (n=40) | LA | 0.21 | 0.04 – 1.5 | 14 | 6 – 25 |
| | RA | 0.22 | 0.04 – 1.5 | 18 | 8 – 38 |
| | LV | 1.2 | 0.45 – 3.9 | 28 | 16 – 65 |
| | RV | 6.2 | 0.9 – 15.0 | 127 | 108 – 174 |
| | LAD | 4.3 | 1.3 – 15.1 | 45 | 10 – 160 |
| | $LAD_{max}$ | 11.4 | 2.0 – 29.5 | 56 | 8 – 234 |
| Right (n=30) | LA | 0.18 | 0.05 – 1.5 | 15 | 8 – 24 |
| | RA | 0.98 | 0.5 – 2.8 | 29 | 11 – 76 |
| | LV | 0.08 | 0.02 – 0.6 | 17 | 4 – 26 |
| | RV | 0.36 | 0.10 – 1.7 | 22 | 7 – 36 |
| | LAD | 0.15 | 0.04 – 2.5 | 18 | 7 – 51 |
| | $LAD_{max}$ | 0.39 | 0.06 – 3.2 | 16 | 8 – 98 |

## DISCUSSION

- The average DSC in the current study was 96% for the WH, 65 to 82% for the four chambers, and 6% for the LAD. We found that the ASDs for the WH, four chambers, and LAD were less than 2, 12, and 16 mm, respectively
- From the dosimetric performance evaluation, we found the doses to the cardiac structures based on our automatic segmentation agreed well with that of manual segmentation within expected variability of manual contouring. However, we found that our automatic segmentation method systematically overestimated the mean and maximum dose to the LAD for left breast treatments
- Nonetheless, it should be recognized that many studies report significant inter- and intra-observer variability in manual contouring, especially for small structures such as the LAD. Zhou et al. reported that the largest ASD for six patients among eight radiation oncologists was 35 mm for the LAD [4]. Our sensitivity analysis showed that even a 5 mm shift in the contours can result in substantial variation in dose, particularly for the RV and LAD for left breast radiotherapy and RA and LAD for right breast radiotherapy
- Even if the structures are perfectly contoured on the radiotherapy planning CT, the dose estimates would still be limited by patient setup error, patient breathing, and cardiac motion. Given these limitations, our results suggest that further geometric improvement in our automatic segmentation method is unlikely to significantly improve our structure dose estimates

## CONCLUSION

We found the dose to cardiac structures based on our automatic segmentation agrees well with the values from manual segmentation within expected variability of manual contouring. When applied to large patient datasets, our automatic segmentation method will facilitate the development of better prescriptive criteria that may be applied in effort to mitigate cardiovascular complications following breast radiotherapy.

## ACKNOWLEDGEMENTS

This research was funded by a Patient-Centered Outcomes Research Institute (PCORI) Award (PCS-1403-12804) and the intramural research program of the United States National Institutes of Health (NIH), National Cancer Institute, Division of Cancer Epidemiology and Genetics. The contents are solely the responsibility of the authors and do not necessarily represent the official views of the PCORI, its Board of Governors or Methodology Committee, or the NIH.

## REFERENCES

[1] Taylor CW, McGale P, Darby SC. Cardiac risks of breast-cancer radiotherapy: a contemporary view. Clin Oncol 2006; 18:236–46

[2] Darby SC, Cutter DJ, Boerma M, Constine LS, Fajardo LF, Kodama K, et al. Radiation-Related Heart Disease: Current Knowledge and Future Prospects. Int J Radiat Oncol Biol Phys 2010; 76:656–65.

[3] Jung JW, Lee C, Mosher EG, Mille MM, Yeom YS, Jones EC, et al. Automatic segmentation of cardiac structures for breast cancer radiotherapy. Physics and Imaging in Radiation Oncology 2019; 12:44–8.

[4] Zhou R, Liao Z, Pan T, Milgrom SA, Pinnix CC, Shi A, et al. Cardiac atlas development and validation for automatic segmentation of cardiac substructures. Radiother Oncol 2017:1–6.