



A heart atlas for breast radiation therapy and the influence of delineation education on both intra and interobserver variability

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Abstract

Purpose We developed a heart atlas for breast radiation therapy and evaluated the influence of education on intra and inter-observer similarity, and cardiac dose reporting.

Materials and methods The data of 16 left breast cancer patients were analyzed. Eight observers delineated heart and cardiac subunits [left (LCA) and right (RCA) coronary arteries, left anterior descending artery (LAD), bilateral atrium and ventricles] before the education. A radiologist and radiation oncologist developed the atlas and delineated the gold standard (GS) volumes. Observers repeated the delineation after education. RT plans were made for pre/post-atlas contours. The similarity was assessed by Dice (DSC) and Jaccard (JSC) similarity coefficient indices. The absolute difference rate was calculated for the dose analysis.

Results The inter-observer similarity increased in heart and all subunits. The intra-observer similarity showed a heterogeneous distribution. The absolute difference rate in dose reporting was statistically significant for the bilateral atrium, right ventricle, LAD, LCA + LAD, RCA's maximum doses ($p < 0.05$). The maximum dose reporting differences from the GS decreased from 16.9 to 8.9% for LAD ($p = 0.011$); from 14.8 to 9.3% for LCA + LAD ($p = 0.010$).

Conclusion The cardiac atlas reduces the intra-interobserver differences and improves dose reporting consistency. The first intra-observer similarity analysis was made in our study and revealed the need for repeated education to increase the consistency.

Keywords Breast radiotherapy · Heart atlas · Cardiac subunit delineation

Introduction

Breast cancer is the most common cancer in women [1]. Successful local (surgery, RT) and systemic therapies (chemotherapy, hormonotherapy, targeted therapies) improve the survival rates, and prolong the survival time for breast cancer. The place of RT in the adjuvant treatment of breast cancer is essential because of the local control and survival advantage it provides [2–4]. Therefore, RT has a vital role in the treatment of breast cancer, and it constitutes the main component of the adjuvant treatment in BCS (breast-conserving surgery) cases and most of the mastectomy cases [5–11].

Radiation oncologists aim to delineate the target volumes (breast, chest wall, nodal regions, tumor bed), and give a homogenous dose to these volumes and protect the organs at risk (OAR) in breast RT to limit the early and late side effects [12]. The heart should receive the lowest dose as possible in left breast RT [13]. Heart and all its subunits are sensitive to radiation. The long-term follow-up of

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survivors from the atomic bomb showed that cardiac mortality increased by 14% with 1 Gy increase in the mean heart dose [14]. As a result of the radiation-induced cardiac damage; pericarditis, pericardial effusion, adhesions and fibrosis, endocarditis, congestive heart failure, cardiomyopathy, valve insufficiency and stenosis, branch blocks, coronary artery disease, and myocardial infarction may occur [15–17].

In the three-dimensional conformal radiotherapy, the heart dose has been recorded with OAR drawing, and the cardiac toxicity has been studied in a number of research [18–20]. Numerous large-sampled retrospective studies with breast cancer patients indicate a relationship between the cardiac mortality and the dose-volume histograms [18, 19, 21, 22]. Darby et al. reported a total of 963 women with major cardiac events (myocardial infarction, coronary revascularization, death due to ischemic heart disease) from 2168 breast cancer patients. The mean heart dose in this population was 4.9 Gy, and the major coronary events increased linearly by 7.4% per Gy without a significant threshold [22]. Duma et al. stated that the mean cardiac dose may not be a useful marker for LAD and left ventricular doses, and stated that cardiac subunits must be delineated to assess specific late side effects [23]. Today, cardiac subunits are not routinely drawn. Therefore, tolerance doses for these structures are not yet clearly defined and can only be calculated by consistent delineation of the OAR and reporting the reliable doses [13]. So, we developed an atlas for heart delineation and evaluated the influence of delineation education on the reduction of intrainterobserver differences and cardiac dose reporting.

Materials and methods

Patient selection

Patients with early-stage left breast cancer who were between the ages of 18–70, who did not receive RT previously and who had RT to the left breast with no nodal irradiation were included in the study. The patients included in the study had no previously known heart disease or cardiac risk factors. Additionally big breasted patients (chest wall separation ≥ 25 cm) or the patients who have any thoracic anatomical disorders (pectus excavatum, pectus carinatum etc.) were excluded from the study.

Simulation, delineation, and radiotherapy planning

CT simulation was performed using a breast board, with both arms up and head turned to the opposite breast position, by holding a deep breath according to our clinical protocol for early-stage left breast cancer. In all cases, Clinical Target Volume-breast (CTV-breast), Planning Target Volume-breast

(PTV), and non-cardiac OAR (lungs, esophagus, spinal cord, right breast) were delineated by an independent radiation oncologist. The reference source of the RTOG was used for the CTV-breast delineation [24]. A 5 mm PTV margin was given to the CTV. Following that, the structure sets that including heart and cardiac subunits (LCA, RCA, LAD, bilateral atrium and ventricles) were created for the observers. Eight radiation oncologists contoured these sets.

During the planning, the tangential breast fields were constructed based on the dose limits in the clinical protocol. A total dose of 50 Gy (2 Gy/fraction/day) was prescribed to the PTV-breast using 6 MV-X energy with the irregular surface compensator technique in the Varian Eclipse™v11 treatment planning system. First, the angles of the beams were chosen to obtain the maximal protection of LAD and the left lung without entering the opposite breast. Multileaf collimator (MLC) fall-off was given to the skin surface. Dynamic MLC fields were obtained by sliding window technique. The weight of the beams was equal and the dose normalization was adjusted to ensure that the mean dose of PTV would be 50 Gy. After the first dose calculation, fields with less than 95% and more than 105% of the dose were detected in the patient, and the dose-flux was regulated in these regions. This calculation technique was continued until 95% of the dose covered the PTV and the field covered by the 105% dose within the target remained below 10%.

The cardiac atlas of our clinic was created by an experienced radiologist and a radiation oncologist on an independent patient who had the same CT protocol (Figs. 1, 2). In our study, a new atlas that reflects all CT slices was created hence the previously created cardiac atlases did not reflect all the CT slices. Also, all cardiac subunits were aimed to be delineated, including bilateral atriums, which had not been examined in previous delineation studies. The anatomical margins of the structures that were delineated in our atlas were accepted as in the study of Feng et al. [25]. After the education, the observers repeated the delineation. The radiologist and the radiation oncologist who made the atlas, drew the heart and subunits of each patient, separately. These volumes were defined as the gold standard (GS). At the end of the delineation, the doses were recalculated. Plans for GS volumes were also generated.

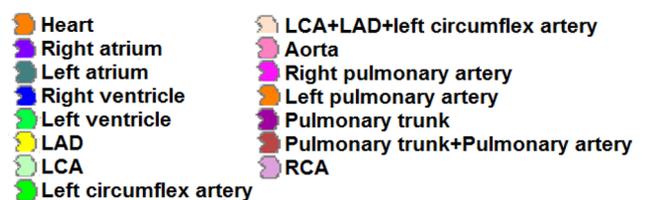


Fig. 1 Heart atlas key

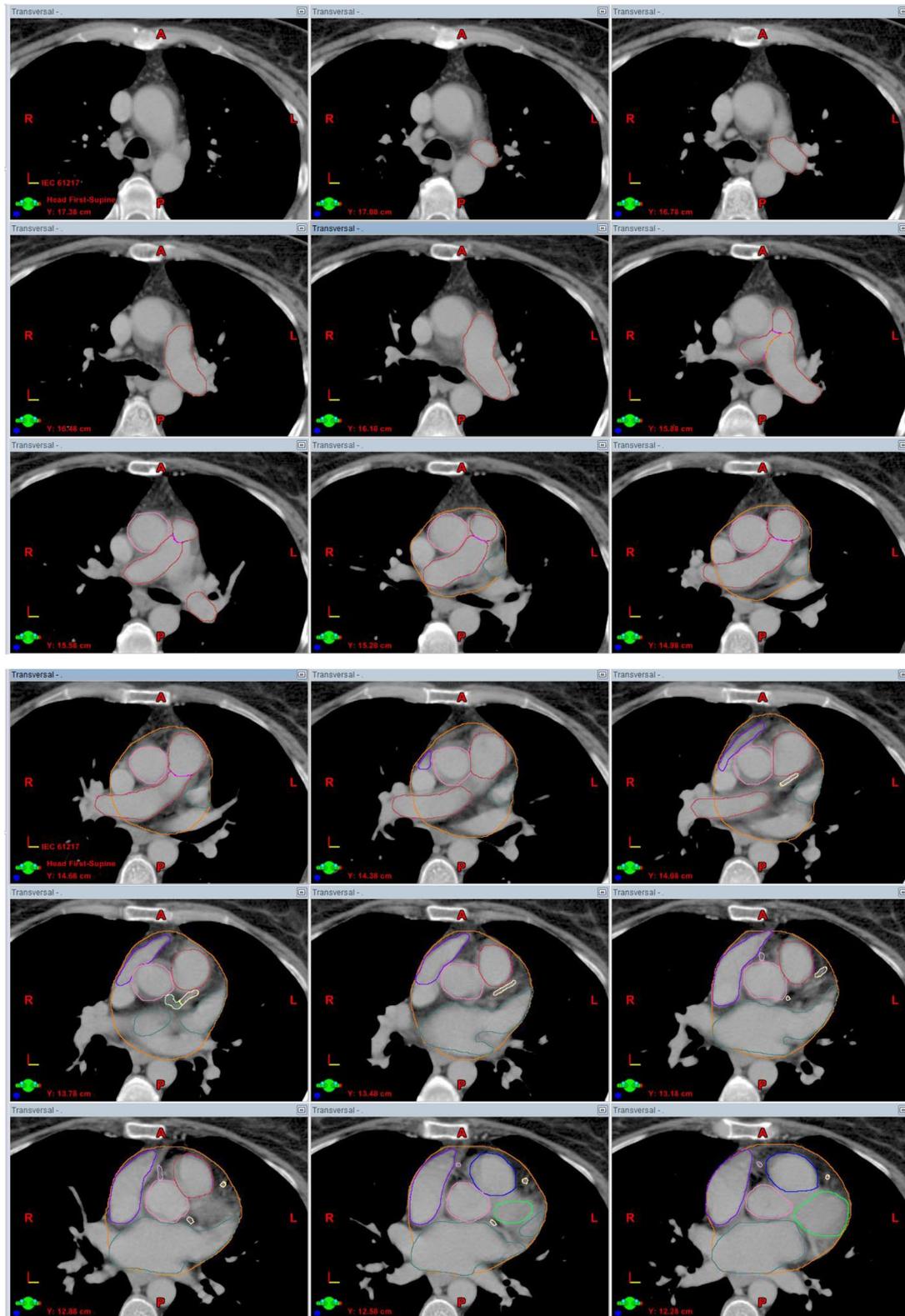


Fig. 2 Heart atlas (slice thickness of 3 mm)

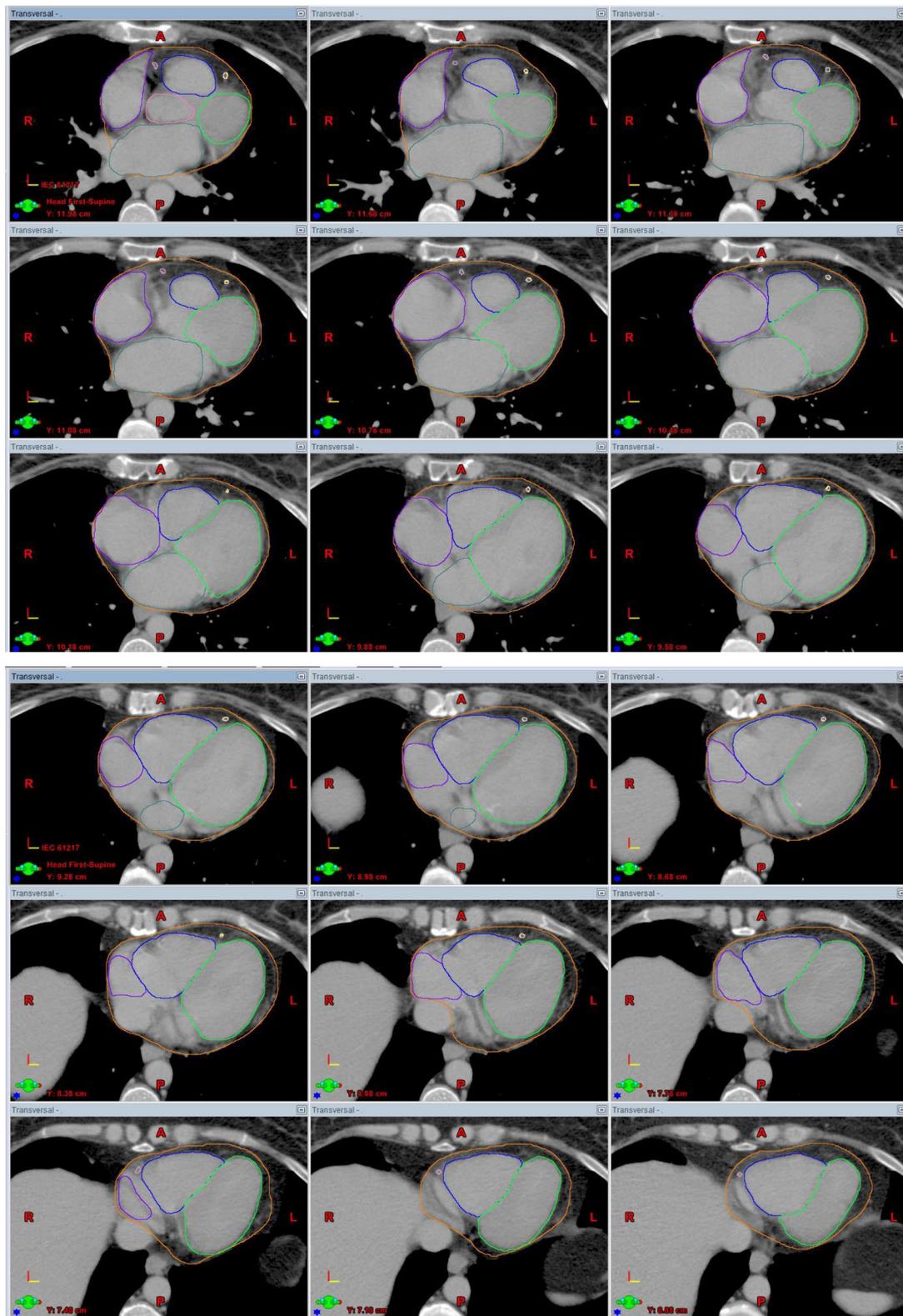


Fig. 2 (continued)

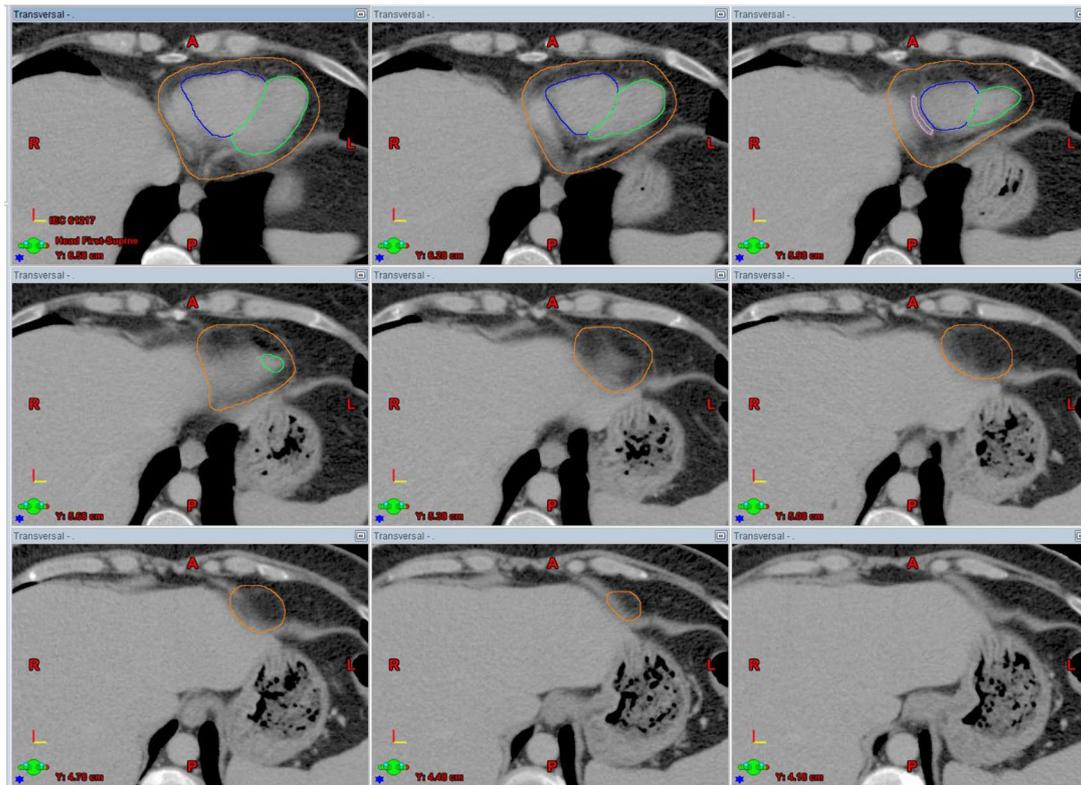


Fig. 2 (continued)

Evaluation of the data

Similarity analysis

Structure sets were exported to Matlab[®] version 7.11 R2010b for similarity analysis. The delineated volumes were compared by the DSC [26] and JSC [27] on a homemade Matlab[®] code. They were defined as follows:

$$DSC = 2 |A \cap B| / |A| + |B|,$$

$$JSC = |A \cap B| / |A \cup B|.$$

DSC and JSC are used to determine the spatial intersection between the segments that can take values between 0 and 1. The value of zero means there is no overlap between sets; the value of 1 means the sets being compared are exactly the same [28]. In our study, to make it easier to understand and compare with the similarity ratios in other studies, the similarity indexes are expressed by the percentage value that is obtained by multiplying by 100.

Volume and dose analysis

The volume data of all structures were calculated. The maximum and mean doses (D_{\max} , D_{mean}) received by the heart, LAD, LCA, and left ventricle were used for the dose

analysis. Also, the dosereporting consistency was calculated by the absolute difference ratio formula [25] which is:

$$\left| \frac{\text{The dose of the observer} - \text{dose of the GS}}{\text{dose of the GS}} \right| \times 100\%$$

This formula gives the information on the percentage changes in dose reporting and allows to make the dose comparisons independently from the patient-specific thoracic wall anatomy and breast shape. The closer the percentage value to zero is, the more consistently the dose is reported.

Statistical analysis

All of the data were evaluated via SPSS 18.0. The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to test normal distribution. Since the groups did not have a normal distribution, they were compared with the Wilcoxon Signed-Rank test. The p value less than 0.05 was considered to be statistically significant.

Results

Eight observers participated in the study, and 16 patients were included. The mean similarity indices between the observers and the GS are shown in Table 1. An increase

Table 1 The inter-observer similarity compared to GS delineation (%)

Structure	Mean percentage	Pre-atlas Median (range)	Post-atlas Median (range)	<i>p</i> *
Heart	DSC	94.2 (92.2–95.3)	94.4 (92.6–95.9)	0.215
	JSC	89.9 (82.7–91.7)	90.3 (87.9–92.4)	0.109
R. atrium	DSC	80.5 (73.1–83.4)	80.9 (76.8–84.8)	0.07
	JSC	69.9 (60.4–73.8)	70.7 (64.8–75.9)	0.03
L. atrium	DSC	79.1 (74.9–83.2)	81.6 (75.2–84.5)	0.001
	JSC	68.1 (62.5–72.6)	71.1 (63.9–74.3)	0.000
R. ventricle	DSC	79.9 (58.7–81.9)	82.3 (65.7–86.1)	0.000
	JSC	70.1 (45.8–73.6)	74.0 (52.2–78.0)	0.000
L. ventricle	DSC	86.2 (81.6–88.5)	88.9 (84.3–89.9)	0.001
	JSC	77.5 (71.2–86.4)	81.2 (74.0–82.9)	0.004
LAD	DSC	39.0 (14.9–52.8)	43.0 (17.9–50.9)	0.088
	JSC	28.6 (10.7–38.9)	31.3 (12.9–40.3)	0.079
LCA + LAD	DSC	39.3 (21.4–55.5)	44.8 (21.9–51.9)	0.02
	JSC	28.6 (15.1–41.3)	33.4 (16.2–41.0)	0.008
RCA	DSC	33.5 (0.0–68.2)	36.7 (17.2–69.8)	0.501
	JSC	24.0 (0.0–47.9)	27.8 (13.2–57.5)	0.034

Pre-atlas refers to the similarity rates before the atlas training and use

Post-atlas refers to the similarity rates after the atlas training and use

L. left, R. right, LAD left anterior descending artery, LCA left coronary artery, RCA right coronary artery, DSC Dice similarity coefficient, JSC Jaccard similarity coefficient

*Wilcoxon signed-rank test

in the similarity rate for the heart and all cardiac subunits was observed after the cardiac atlas education and use. This increase was statistically significant in the left atrium, bilateral ventricles, LCA + LAD structures for both similarity indices ($p < 0.05$). There was no significant increase in the heart similarity rate. A similarity rate of median 94% for the heart was obtained in both pre and post atlas delineations.

Table 2 summarizes how the atlas usage affected the intra-observer variation compared to the GS. The intra-observer

similarity for each structure was quite heterogeneous. The majority of the observers approached the GS. However, statistically significant deteriorations were observed in the heart drawing of the observers no. 2 and no. 6 ($p = 0.002$, $p = 0.011$), in the right ventricular drawing of the observer no. 8 ($p = 0.007$), and in the left ventricular drawing of the observer no. 5 ($p = 0.023$).

A statistically significant volume increase was observed in the heart, left atrium, bilateral ventricles and LAD

Table 2 The intra-observer similarity compared to GS delineation

Structure	Observer							
	1	2	3	4	5	6	7	8
Heart	↑, $p = 0.910$	↓, $p = 0.002$	↑, $p = \mathbf{0.000}$	↑, $p = 0.234$	↓, $p = 0.234$	↓, $p = 0.011$	↓, $p = 0.105$	↑, $p = \mathbf{0.005}$
R. atrium	↓, $p = 0.408$	↑, $p = 0.679$	↑, $p = 0.098$	↑, $p = \mathbf{0.003}$	↓, $p = 0.379$	↑, $p = 0.642$	↑, $p = 0.535$	↑, $p = 0.326$
L. atrium	↑, $p = 0.379$	↓, $p = 0.134$	↑, $p = \mathbf{0.001}$	↑, $p = 0.326$	↑, $p = 0.148$	↑, $p = 0.088$	↓, $p = 0.234$	↑, $p = 0.063$
R. ventricle	↑, $p = \mathbf{0.013}$	↑, $p = 0.301$	↑, $p = \mathbf{0.001}$	↑, $p = \mathbf{0.000}$	↓, $p = 0.408$	↑, $p = \mathbf{0.001}$	↑, $p = 0.352$	↓, $p = 0.007$
L. ventricle	↑, $p = \mathbf{0.030}$	↑, $p = \mathbf{0.004}$	↑, $p = \mathbf{0.005}$	↑, $p = \mathbf{0.001}$	↓, $p = 0.023$	↓, $p = 0.501$	↑, $p = \mathbf{0.023}$	↑, $p = \mathbf{0.003}$
LAD	↑, $p = 0.642$	↑, $p = 0.501$	↓, $p = 0.717$	↑, $p = 0.179$	↓, $p = 0.605$	↑, $p = 0.569$	↓, $p = 0.121$	↑, $p = \mathbf{0.010}$
LCA + LAD	↑, $p = \mathbf{0.001}$	↑, $p = \mathbf{0.002}$	↓, $p = 0.163$	↑, $p = 0.717$	↓, $p = 0.301$	↓, $p = 0.877$	↑, $p = \mathbf{0.010}$	↑, $p = \mathbf{0.008}$
RCA	↑, $p = 0.638$	↓, $p = 0.910$	↓, $p = 0.069$	↑, $p = \mathbf{0.041}$	↑, $p = 0.722$	↓, $p = 0.730$	↓, $p = 0.650$	↑, $p = \mathbf{0.036}$

The *p* values of this table are obtained with Wilcoxon signed-rank test

↑: The upward arrow indicates that the similarity rate compared to GS delineation increases with atlas training and use

↓: The downward arrow shows that the similarity rate compared to GS delineation decreases despite the atlas training and use

L. left, R. right, LAD left anterior descending artery, LCA left coronary artery, RCA right coronary artery

(Table 3). There was an increase of approximately 30 cm³ for the heart ($p=0.000$).

In our study, there was no significant difference in the average D_{\max} and D_{mean} for the heart and left ventricle ($p>0.05$). The average D_{\max} increased from median 19.4–22.9 Gy ($p=0.010$) for LAD and from 20.3 to 22.9 Gy ($p=0.044$) for LCA + LAD. The average D_{mean} increased from median 4.4 to 5.4 Gy ($p=0.001$) for LAD + LCA.

The absolute difference ratios for dose values of the pre- and post-atlas are given in Table 4. The differences for the maximum doses with the atlas use were decreased from median 16.9 to 8.9% for LAD ($p=0.011$); from 14.8 to 9.3% ($p=0.010$) for LCA + LAD. Differences for mean doses were decreased with the atlas use from median 34.9 to 22.3% for LAD ($p=0.07$); from 32.4% to 24.5% for LCA + LAD

($p=0.056$); from 36.3% to 31.9% for RCA ($p=0.006$). Also, the atlas use contributed to a more consistent reporting of the doses of the right ventricle and bilateral atrium, although they are located at the edge and/or outside of the region in the left breast RT ($p<0.05$).

Discussion

The heart should receive the lowest dose as possible in the left breast RT [13]. Despite the advanced techniques of RT, which mainly aims cardiac protection such as intensity-modulated RT, volumetric arc therapy, proton therapy, image-guided and respiratory-gated RT [29–32], there are no tolerance dose values, especially for cardiac subunits. This situation is due to the lack of detailed dosimetric studies that were made with consistent cardiac subunit delineation and the lack of practice for delineation of cardiac subunits in daily routine. Tolerance doses for these structures can only be calculated by a consistent delineation of the OAR and thus reliable dose reporting [13].

Studies for standardization of target and OAR delineations are limited in the literature for breast cancer. While most studies focus on target volume delineation, fewer studies focus on the heart and cardiac subunit delineations. According to these studies, inter-observer differences can be reduced, and this would lead to significant changes in dose reporting [13, 25, 33–36]. Patients with early left breast cancer were selected to generate standard RT plans and to perform standard dose evaluation in our study. Since the other atlases in the literature did not present all of the slices of the simulation CT, we developed our atlas to increase the image quality and make the drawing more accessible. We evaluated the effect of cardiac atlas education on observer

Table 3 The mean volume values of pre- and post-atlas (cm³)

Structure	Pre-atlas	Post-atlas	p^*
	Median (range)	Median (range)	
Heart	530.5 (467.3–798.0)	557.6 (472.8–829.6)	0.000
R. atrium	48.7 (30.4–70.9)	51.1 (26.9–72.2)	0.134
L. atrium	46.8 (29.8–78.4)	49.9 (31.1–49.6)	0.004
R. ventricle	96.1 (60.7–117.5)	100.5 (63.1–119.8)	0.044
L. ventricle	136.8 (102.5–228.1)	147.9 (111.4–238.8)	0.000
LAD	0.8 (0.6–1.2)	0.9 (0.7–1.3)	0.000
LCA + LAD	1.4 (0.8–1.9)	1.2 (0.8–1.7)	0.001
RCA	0.4 (0.2–1.3)	0.4 (0.2–4.3)	0.378

Pre-atlas refers to the volume values before the atlas training and use
Post-atlas refers to the volume values after the atlas training and use
L. left, R. right, LAD left anterior descending artery, LCA left coronary artery, RCA right coronary artery

*Wilcoxon signed-rank test

Table 4 The absolute difference ratios for dose values of pre- and post-atlas (%)

Structure	For D_{\max}			For D_{mean}		
	Pre-atlas	Post-atlas	p^*	Pre-atlas	Post-atlas	p^*
	Median (range)	Median (range)		Median (range)	Median (range)	
Heart	1.4 (0–30)	1.2 (0–30)	0.470	3.9 (1–9)	3.8 (1–10)	0.098
R. atrium	15.9 (6–37)	12.1 (2–38)	0.005	4.1 (2–12)	3.8 (1–7)	0.015
L. atrium	33.6 (22–75)	24.5 (11–64)	0.000	9.4 (5–25)	6.8 (3–15)	0.000
R. ventricle	14.5 (0–185)	6.8 (0–177)	0.035	10.3 (2–20)	7.6 (4–14)	0.039
L. ventricle	9.1 (0–57)	5.6 (0–35)	0.179	4.8 (2–12)	4.4 (2–126)	0.352
LAD	16.9 (0–80)	8.9 (0–95)	0.011	34.9 (6–90)	22.3 (6–85)	0.07
LCA + LAD	14.8 (0–129)	9.3 (0–95)	0.010	32.4 (9–89)	24.5 (7–79)	0.056
RCA	9.1 (2–23)	11.1 (1–114)	0.044	36.3 (13–83)	31.9 (13–71)	0.006

Pre-atlas refers to the absolute difference ratios for dose values before the atlas training and use

Post-atlas refers to the absolute difference ratios for dose values after the atlas training and use

L. left, R. right, LAD left anterior descending artery, LCA left coronary artery, RCA right coronary artery

*Wilcoxon signed-rank test

variabilities and dose reporting. The delineations were performed on 16 patients by eight observers, and the data were assessed through comparison.

Several studies in the literature examined the inter-observer similarities comparison to GS after the atlas education [25, 35]. Feng et al. developed a heart atlas and found statistically significant similarity improvements in the heart, LAD, LCA, RCA, and bilateral ventricles with the atlas usage ($p < 0.002$) [25]. In our study, the similarity indices increased in all structures with atlas education and use (Table 1). In the study of Feng et al., the similarity rate for the heart increased from 79 to 91% ($p < 0.001$) [25]. In our study, the similarity rate of the heart remained almost at the same level of 94% ($p = 0.256$). The similarity rates of the heart were higher in our study than the study of Feng et al., with this result, we concluded that in our clinical routine, the right principles were adopted for heart delineations. In the study of Feng et al., the similarity increased from 65 to 74% ($p = 0.003$) for the right and 87–92% ($p = 0.06$) for the left ventricle [25]. In our study, the DSC was found to be increased from 79.9 to 82.3% ($p = 0.000$) for the right; from 86.2 to 88.9% ($p = 0.001$) for the left ventricle. Additionally, we found a significant increase for the left ventricle in our research. Duane et al. developed a cardiac atlas including the anatomic segmentation of the left ventricle and coronary arteries. The delineations of these structures were made after atlas education. The mean DSC was 91% for the left ventricle and 73% for its segments [35]. Although it is not possible to determine the contribution of the education, the post-atlas ratios were similar to our study. There are no studies including atrium delineations in the literature. In our study for both atriums, a similarity rate of $> 80\%$ in DSC and $> 70\%$ in JSC were obtained by the use of atlas. In the study of Vennarini et al., where the LAD delineations made by a radiologist and radiation oncologist independently were compared in 25 breast cancer patients, there was no improvement in LAD delineations with the contrast agent administration. The researchers found that only proximal one-third of the artery was visible with the contrast agent [37]. Even if LAD is not visible, it is suggested to be drawn up to the apex of the heart [38]. Feng et al. found that the similarity rate in LCA and LAD doubled with the use of atlas, reaching up to 22%, 62% ($p < 0.001$), respectively [25]. The similarity increase in the LAD delineation was not significant in our study ($p > 0.05$). However, when LCA and LAD were evaluated together, the increase was found to be significant, reaching up to 44.8% ($p < 0.05$). Duane et al. reported DSC for coronary artery segments as 10–53% [35]. Since the coronary arteries were not delineated as segments in our study, it is not reasonable to compare the similarity rates of the coronary arteries to the rates of Duane et al.; however, a similarity rate of $< 50\%$ was

obtained in our study. The RCA similarity doubled up to 24% with the atlas in the research of Feng et al. ($p = 0.002$) [25]. In our study, only a significant increase to 27.8% ($p = 0.034$) was observed in the JSC for RCA in our study.

Among the differences between the statistical data of the coronary artery delineations in the studies; the arteries are small-volume structures, only a part of them are visible, and observers have to predict the rest of artery location anatomically; the unclear vessel boundaries due to the motion artifacts created by cardiac movements can be listed as the factors that affect the similarity index negatively.

This is the first study in the literature that analyzes intra-observer similarity. The intra-observer similarity for each of the structures was quite heterogeneous, but most of the observers made delineations similar to the GS delineation (Table 2). What is noteworthy here is that almost all of the observers drew at least one of the structures worse after the atlas education. Fortunately, this decrease in the similarity index reached to statistical significance only in a few of them. This result may be the underlying reason, why the similarity ratio in some structures do not increase, despite the education performed in the delineation studies that have not done intra-observer similarity analysis. Additionally, this finding reveals that repeated education may help increase the consistency in both the group and individuals.

In the study of Lorenzen et al., volumetric information was given only for the heart. The heart volume increased from 668 to 751 cm³ with the atlas ($p < 0.0001$) [13]. A 30 cm³ increase in the heart volume was provided in our study ($p = 0.000$). Also, statistically significant volume increases were observed in the left atrium, bilateral ventricles, and LAD. It was detected that some observers included the circumflex artery to the LCA in the pre-atlas delineations which resulted in a decrease in the LCA + LAD volume from 1.4 to 1.2 cm³ with the use of the atlas ($p = 0.001$). Duane et al. reported an approximate 3 cm³ volume for the LCA+LAD with using constant 4 mm diameter for delineation [35]. However, coronary artery volumes were smaller in our research. Because in our study, the delineations were made independently from a constant diameter.

Lorenzen et al. reported higher doses in both heart and LCA + LAD with the atlas use. The average maximum and mean doses increased from 39 to 42 Gy, from 2 to 2.1 Gy for the heart and from 20 to 26 Gy, from 5.4 to 7 Gy for LCA+LAD, respectively ($p < 0.05$) [13]. In our study, there was no significant increase in the average D_{\max} and D_{mean} for the heart, since we could not achieve a significant improvement in the heart delineations. An increase about 3 Gy ($p < 0.05$) was found at the average D_{\max} for LAD and LCA + LAD volumes with the use of atlas because of being close to the high-dose region of the RT field. Although there was a significant improvement in the similarity for the left ventricle, this did not reflect the dose values.

To evaluate the effect of the similarity rate increase in the delineation to a more consistent dose reporting, it is necessary to interpret the changes concerning the GS doses. Feng et al. made the dosereporting comparison by taking the absolute difference of the observer and GS dose. The dose difference of the heart, LCA, LAD, RCA, and right ventricle decreased from 0.9 to 0.1 Gy; from 1.7 to 0.9 Gy; from 3.9 to 2.6 Gy; from 1.2 to 0.6 Gy and from 1.1 to 0.5 Gy ($p < 0.05$), respectively. The absence of the significant improvement in dose reporting for left ventricle was explained by the delineations made highly similar to the GS, even before the atlas [25]. In the study of Lorenzen et al., the inter-observer dose comparison was made with the coefficient of variation obtained by dividing the standard deviation to the mean value of the dose data. They reported that the maximum and mean heart doses were two times more consistent. For LCA + LAD, the atlas usage did not contribute to reducing the inter-observer coefficient of variation for the maximum and mean values [13]. We used the absolute difference rate for dose comparisons in our study. Statistically significant differences were obtained in bilateral atriums, right ventricle, LAD, LCA+LAD, RCA for the maximum doses; in bilateral atriums, right ventricle and RCA for the mean doses (Table 4). Although a significant increase in the similarity index was achieved for the left ventricle, dose reporting was not affected by the atlas usage. This result can be explained by the highly similar delineations even before the atlas, as in the study of Feng et al. The dose differences in our study decreased from 16.9 to 8.9% for LAD; from 14.8 to 9.3% for LCA + LAD for maximum doses and from 34.9 to 22.3% for LAD; from 32.4 to 24.5% for LCA+LAD for mean doses ($p < 0.05$). Atlas usage contributed to a more consistent reporting of maximum and mean doses of the right ventricle and bilateral atrium, although they are located at the edge and/or outside of the region in the left breast RT ($p < 0.05$). This finding may serve to provide a more consistent dose reporting on malignancies in which the heart enters into the RT field, such as lung cancer, lymphoma, thymoma, thereby providing better detection of the cardiac side effects. Currently, Dmax and Dmean for LAD are taken into consideration in the tolerance doses, and it is noteworthy that although the similarity indices are low compared to other cardiac units in our study, both LAD and LCA + LAD delineations have a significant contribution to the more consistent dose reporting. In our study, maximum dose reporting for RCA became inconsistently incompatible with the study of Feng et al. ($p = 0.044$), which could be explained by the lack of an increase in similarity ratios of RCA with the atlas use.

Our study has a number of strengths. Our atlas is the first atlas that reflects all CT slices with a high image quality. It is very convenient for daily use. The education was given by a radiologist with rich educational material including many cardiac-gated, contrasted images taken for diagnostic

purposes except for our atlas. Moreover, RT plans were made with the same dose targets to make a standard comparison. Atrial delineations were made in a delineation study for the first time. The comparisons in our study did not only provide insight for inter-observer similarity but also included the comparison of intra-observer similarity for the first time. Also, the volume and dosereporting evaluations provided an opportunity to show the contribution of the education in detail. Increased dosereporting consistency was obtained with the structures that located not only adjacent the breast RT field but also at the edge and/or outside of the RT field. Therefore, our atlas can be used in every malignancy in which the heart enters into the RT field, such as lung cancer, lymphoma, thymoma, besides breast cancer. The limitations of our study were that due to the limited the number of cases, standardization could not be achieved in the chest wall shape and the location of the primary tumor bed. For this reason, dose comparisons were only made with a dose of 50 Gy.

Conclusion

The education and use of the cardiac atlas contribute to the intra- and inter-observer differences to be reduced and increases the consistency in dose reporting. For the first time, an intra-observer similarity analysis was performed in a delineation study and this analysis revealed the need of repeated educations to increase the consistency of the group and the individuals.

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