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Recent Time Trends and Predictors of Heart Dose From Breast Radiation Therapy in a Large Quality Consortium of Radiation Oncology Practices

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Summary

With the recent focus on minimizing the radiation dose to the heart with adjuvant therapy for breast cancer, it is important to understand the current state of cardiac sparing and predictors of the heart dose. In a large US state-wide registry, we evaluated recent time

Purpose: Limited data exist regarding the range of heart doses received in routine practice with radiation therapy (RT) for breast cancer in the United States today and the potential effect of the continual assessment of the cardiac dose on practice patterns.
Methods and Materials: From 2012 to 2015, 4688 patients with breast cancer treated with whole breast RT at 20 sites participating in a state-wide consortium were enrolled into a registry. The importance of limiting the cardiac dose has been emphasized in the consortium since 2012, and the mean heart dose (MHD) has been reported by each institution since 2014. The effects on the MHD were estimated for both conventional and accelerated fractionation using regression models, with technique (intensity modulated RT [IMRT] vs 3-dimensional conformal RT), deep inspiration breath hold use, patient position (supine vs prone), nodal RT (if delivered), and boost (yes vs no) as covariates.

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trends in the mean heart dose, adjusting for the planned target dose and treatment technique. Our findings indicate that the mean heart dose decreased significantly for left-sided breast cancer during a 4-year period using ongoing monitoring of the cardiac dose by institution.

Results: For left-sided breast cancer treated with conventional fractionation, the median MHD in 2012 was 2.19 Gy versus 1.65 Gy in 2015 ($P<.001$). The factors that significantly increased the MHD for conventional fractionation were increased separation relative to 22 cm (1.5%/1 cm), supraclavicular or infraclavicular nodal RT (17.1%), internal mammary nodal RT (40.7%), use of a boost (20.9%), treatment year before 2015 (7.7%), and use of IMRT (20.8%). For left-sided BC treated with accelerated fractionation, the median MHD in 2012 was 1.70 Gy versus 1.22 Gy in 2015 ($P<.001$). The factors that significantly increased the MHD for accelerated fractionation were separation (1.7%/1 cm), use of a boost (20.0%), year before 2015 (8.5%), and use of IMRT (19.2%). The factors for both conventional fractionation and accelerated fractionation that significantly reduced the MHD were the use of deep inspiration breath hold and prone positioning.

Conclusions: The MHD for left-sided breast cancer decreased during a recent 4-year period, coincident with an increased focus on cardiac sparing in the radiation oncology community in general and a state-wide consortium specifically. These data suggest a positive effect of systematically monitoring the heart dose delivered.

Introduction

Adjuvant whole breast radiation therapy (RT), with or without regional irradiation, results in improvements in locoregional control, reductions in distant metastatic spread, and increases in breast cancer—specific survival (1-3). These benefits, however, must be balanced against potential toxicities, including cardiac injury leading to cardiac events. Early observational studies suggested that the cardiac dose from breast RT can be substantial and that the risk of cardiac toxicity increases with an increasing radiation dose to the heart (4, 5).

A recent review of the heart doses with delivery of breast RT in reported series worldwide from 2003 through 2013 found a mean heart dose (MHD) of 5.4 Gy (range <0.1-28.6) among patients treated for left-sided breast cancer (6). Less is known about the range of heart doses delivered in routine practice in the United States today and the potential effect of ongoing systematic monitoring of cardiac doses on treatment planning techniques. The goals of the present study were to assess the extent of cardiac sparing in a large prospective observational cohort during a recent 4-year period and to determine the variation in cardiac dose with contemporary treatment techniques and patient characteristics.

Methods and Materials

Patients

From 2012 to 2015, 5579 patients with breast cancer who underwent lumpectomy and whole breast RT at 20 sites participating in an ongoing state-wide consortium were entered into a registry, with web-based transmission of the clinical and treatment details (7). The consortium, the Michigan Radiation Oncology Quality Consortium (MROQC), was established to identify the treatment practices that decrease radiation-related complications in the treatment of breast and lung cancer in the state of Michigan. The MROQC is supported by Blue Cross Blue Shield of Michigan and Blue Care Network as a part of the Blue Cross Blue Shield of Michigan Value Partnerships Program. The MROQC includes urban, suburban, and rural centers, hospital-based and stand-alone centers, and large and small radiation oncology centers. The smallest number of cases per institution was 22; the largest was 486.

In 297 cases, the dose-volume histogram (DVH), Digital Imaging and Communications in Medicine, and/or other physics data were not adequately provided, and these cases were excluded from the analyses. In 588 cases, DVH data were not submitted, either because it was not required at the time (n=574) or the data were missing (n=14). These cases were also excluded. In 2012 and 2013, DVH data were not required for right-sided cases when the heart was >2 cm from the edge of the treatment field; thus, DVH data were not submitted for 574 right-sided breast cancer cases. Beginning in 2014, our policy changed, and a heart DVH was required for all cases, independent of the laterality and the heart proximity to the edge of the treatment field. Finally, 6 additional cases treated with accelerated fractionation with nodal fields to the supraclavicular (SCV) nodes, infraclavicular (ICV) nodes, or internal mammary nodes (IMNs) were excluded owing to our inability to adjust for the potential influence of nodal RT on the heart dose, given the extremely small sample size (0.4% of eligible accelerated cases). With these exclusions, the final sample size was 4688, with 2657 left-sided breast cancer cases (1785 treated with conventional fractionation and 872 with accelerated fractionation to the whole breast) and 2031 right-sided breast cancer cases (1247 treated with conventional fractionation and 784 with accelerated fractionation).

Statistical analysis

Linear regression models were used to estimate the effect of patient, treatment, and institutional characteristics on the MHD and the observed trend over time. Because the MHD exhibited a right-skewed, non-normal distribution, the natural logarithm (log) of the MHD was modeled as the dependent variable, and the models satisfied the normality assumption for error residuals. The level of detailed Digital Imaging and Communications in Medicine data needed to generate biologically equivalent doses between accelerated whole breast irradiation (AWBI) and conventional whole breast irradiation (CWBI) was not available to the MROQC; thus, the data were modeled separately by laterality and fractionation. For conventionally treated cases, the log MHD was modeled using the following covariates: use of intensity modulated RT (IMRT; defined as $\geq$5 segments per any unique gantry angle for the primary breast plan) versus 3-dimensional conformal RT (3D-CRT); use of deep inspiration breath hold (DIBH; yes vs no); position (supine vs prone); boost (yes vs no); nodal treatment (SCV/ICV lymph nodes treated vs IMNs treated with or without SCV/ICV or axillary nodes); year (centered at 2015); breast volume; and separation distance. For AWBI cases, the log MHD was modeled using the same covariates used for CWBI, with the exception of the covariate nodal treatment, because those cases were excluded. An unadjusted comparison of the median MHD from early (2012) to late (2015) cases in our series was conducted using the rank-sum test statistic. The regression models for conventional fractionation were based on whole breast doses of approximately 45 to 50.4 Gy. The dose most commonly used for the accelerated fractionation analyses was 42.56 Gy. All statistical tests throughout were 2-sided, and P values $\leq$5% were considered statistically significant.

Results

Treatment

Treatment was delivered by physician preference at each institution using either 3D-CRT or IMRT techniques, with or without motion management techniques (Table 1). Of the 4688 patients, 60.2% underwent 3D-CRT and 39.8%, IMRT. Of the patients in the overall series, 13.7% were treated with DIBH (24.1% of patients with left-sided cancer), 35.3% with AWBI, and 4.3% with prone positioning. Most patients (83.7%) received a boost to the lumpectomy cavity. A few patients received nodal irradiation to the SCV nodes, ICV nodes, or IMNs (17.1% with conventional fractionation [11.2% SCV/ICV nodes alone and 5.9% IMN with or without SCV/ICV nodes] and none with accelerated fractionation). At the consortium meetings, which were held 3 times each year, the use of cardiac contours in accordance with the University of Michigan cardiac atlas were emphasized (8). The atlas was posted on the Internet for access to all consortium members (the Knowledge Base, a resource of terminology definitions and frequently asked questions).

Heart dose for patients with left-sided breast cancer

As shown in Figure 1 and Table 2, the median MHD for all patients with left-sided breast cancer treated with conventional fractionation decreased from 2012 through 2015, from 2.19 Gy to 1.99 Gy, 1.60 Gy, and 1.65 Gy, respectively ($P<.001$). When the cases of breast-only treatment were analyzed, the median MHD decreased from 2.09 Gy to 1.54 Gy during the 4-year period ($P<.001$). Similarly, for cases with breast and nodal fields treated, the median MHD decreased from 2.64 Gy to 1.85 Gy ($P<.001$). When the median MHD was analyzed by the type of nodal field treated, the median MHD decreased from 2.72 Gy in 2012 to 1.69 Gy in 2015 for treatment to the SCV/ICV nodes without IMN RT ($P<.001$). The corresponding values were 2.62 Gy and 1.99 Gy when both the SCV/ICV nodes and IMNs were treated ($P=.192$). For patients undergoing AWBI to the breast only, the median MHD decreased from 1.70 Gy in 2012 to 1.22 Gy in 2015 ($P<.001$).

Heart dose for patients with right-sided breast cancer

As expected, patients with right-sided breast cancer received lower cardiac doses than did their counterparts with left breast cancer. The median MHD for all right-sided breast cancer cases from 2012 through 2015 treated with conventional fractionation are provided in Figure 1 and Table 3. The median MHD, in general, decreased during the 4-year period ($P=.053$; 2012 vs 2015). However, for right-sided cases only, the DVH estimates were only provided for 2012 and 2013 when the heart border was within 2 cm of the RT field edge. As of 2014, DVH estimates were required for all right-sided cases. Given the selection of right-sided breast cancer patients in 2012 and 2013 for whom DVH data were provided, inclusion of these estimates in the analyses would have exaggerated the decrease in MHD observed during the study period. Therefore, all subsequent right-sided analyses included the 2014 and 2015 cases only. When considering only the cases from 2014 to 2015, the difference in the median MHD for all right-sided cancer cases significantly increased from 0.67 Gy to 0.74 Gy ($P=.001$). The absolute magnitude of the difference (ie, 0.07 Gy), however, was small. Similarly, for breast-only RT cases, a significant increase was found in the median MHD from 2014 to 2015 from 0.64 Gy to 0.70 Gy ($P=.007$). However, the absolute difference, 0.06 Gy, was again minimal. The median MHD for patients treated to the breast and regional nodal fields in 2014 and 2015 was 0.83 Gy and 0.92 Gy, respectively ($P=.075$). When the median MHD was analyzed by the type of nodal fields treated, the median MHD from 2014 to 2015 did not

Table 1 Treatment and clinical characteristics of the combined patient cohort

		Left-sided		Right-sided	
Variable	Total	CWBI	AWBI	CWBI	AWBI
Treatment planning					
3D-CRT	2822 (60.2)	1108 (62.1)	512 (58.7)	755 (60.6)	447 (57.0)
IMRT	1866 (39.8)	677 (39.9)	360 (41.3)	492 (39.5)	337 (43.0)
Use of DIBH					
No	4045 (86.3)	1327 (74.3)	689 (79.0)	1245 (99.8)	784 (100)
Yes	643 (13.7)	458 (25.7)	183 (21.0)	2 (0.2)	-
AWBI	-	NA	NA	NA	NA
No	3032 (64.7)	-	-	-	-
Yes	1656 (35.3)	-	-	-	-
Position					
Supine	4488 (95.7)	1709 (95.7)	818 (93.8)	1205 (96.6)	756 (96.4)
Prone	200 (4.3)	76 (4.3)	54 (6.2)	42 (3.4)	28 (3.6)
Use of boost					
No	765 (16.3)	108 (6.1)	310 (35.6)	93 (7.5)	254 (32.4)
Yes	3923 (83.7)	1677 (94.0)	562 (64.5)	1154 (92. 5)	530 (67.6)
Nodal treatment					
None	4169 (88.9)	1483 (83.1)	872 (100)	1030 (82.6)	784 (100)
SCV/ICV	339 (7.2)	203 (11.4)	-	136 (10.9)	-
IMN ± SCV/ICV	180 (3.8)	99 (5.6)	-	81 (6.5)	-
Year of MROQC start					
2012	408 (8.7)	278 (15.6)	73 (8.6)	43 (3.5)	12 (1.5)
2013	863 (18.4)	435 (24.4)	136 (15.6)	227 (18.2)	65 (8.3)
2014	1611 (34.4)	567 (31.8)	269 (30.9)	499 (40.0)	276 (35.2)
2015	1806 (38.5)	505 (28.3)	392 (45.0)	478 (38.3)	431 (55.0)
Breast volume (cm^3)	1143.8 ± 698.6	1215.1 ± 801.9	1030.4 ± 554.0	1205.3 ± 692.7	1009.9 ± 548.5
Separation (cm)	22.6 ± 3.9	22.7 ± 4.0	21.9 ± 3.5	23.1 ± 4.0	22.3 ± 3.7

Abbreviations: 3D-CRT = 3-dimensional conformal radiation therapy; AWBI = accelerated whole breast irradiation; CWBI = conventional whole breast irradiation; DIBH = deep inspiration breath hold; ICV = infraclavicular (nodes); IMNs = internal mammary nodes; IMRT = intensity modulated radiation therapy; MROQC = Michigan Radiation Oncology Quality Consortium; NA = not applicable; SCV = supraclavicular (nodes).
Data presented as n (%) or mean ± standard deviation.

decrease with treatment to the SCV/ICV nodes without IMN RT (ie, 0.83 Gy and 0.91 Gy, respectively; $P=.078$). The corresponding values were 1.02 Gy and 0.94 Gy from 2014 to 2015 when the SCV/ICV nodes and IMN were treated ($P=.782$). For breast-only AWBI, the MHDs for 2012 and 2015 were 0.70 Gy and 0.56 Gy, respectively ($P=.168$); however, the corresponding values for 2014 and 2015 were essentially the same at 0.55 Gy and 0.56 Gy, respectively.

Regression models for mean dose to the heart

The effect of treatment planning and patient variables on the MHD for left- and right-sided breast cancer is shown in Table 4. For left-sided breast cancer, the models estimated the baseline MHD in 2015 for an average-size patient treated at 1 of the consortium institutions with a breast volume of 1000 cm^3 and 22 cm separation would be 1.32 Gy for conventional fractionation and 1.14 Gy for accelerated fractionation. The baseline estimate further assumed use of 3D-CRT without DIBH, with supine positioning, and with no boost or nodal RT. For left-sided breast cancer, increasing separation, treatment year before 2015, nodal treatment, and the use of a boost significantly increased the MHD. The use of IMRT also significantly increased the MHD. In contrast, the use of DIBH and prone positioning significantly reduced the MHD.

For right-sided breast cancer, the models estimated the baseline MHD in 2015 for a patient with a breast volume of 1000 cm^3 and 22-cm separation to be 0.60 Gy for conventional fractionation and 0.47 Gy for accelerated fractionation. For left-sided breast cancer, the baseline estimates assumed 3D-CRT, supine positioning, and treatment without a boost or regional fields. The same variables as in the left breast analysis positively and negatively affected MHD, with 3 exceptions. First, DIBH was not included in the model because breath-hold techniques are generally used for left-sided breast cancer. Second, a nonsignificant effect in the MHD was observed with the use of IMRT. Finally, the period modeled was only 2014 and 2015 owing to differential requirements for data submission for right-sided breast cases in 2012 and 2013.

In general, the regression models demonstrated an increase in the MHD with the use of IMRT compared with 3D-CRT, in particular, for left-sided breast cancer. In an attempt to understand whether the findings varied by the

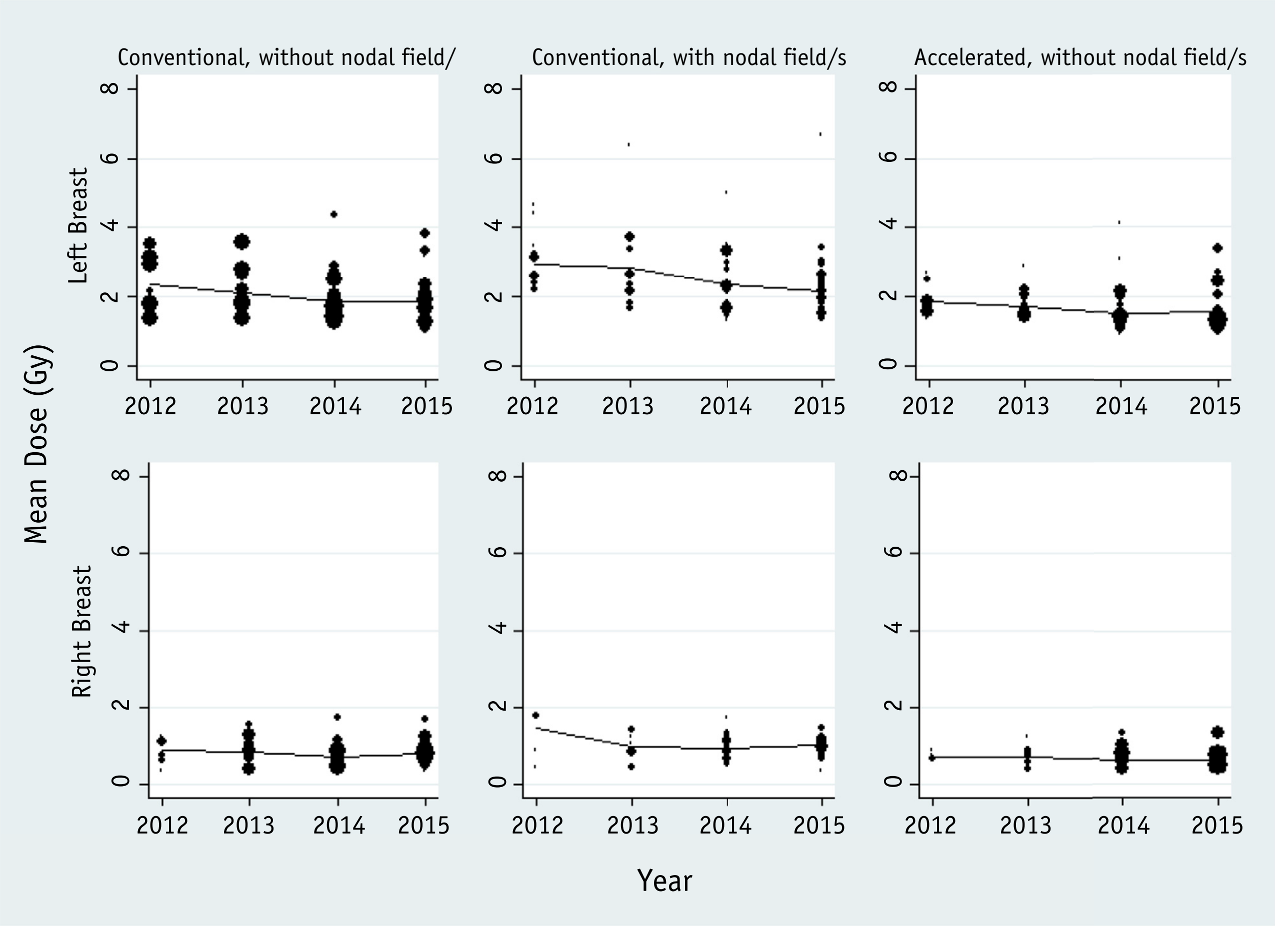

Fig. 1. The observed mean dose to the heart for the consortium (line) and the institutions (dots; proportional to the number of cases) stratified by fractionation schedule, laterality, and whether nodal fields were treated. The axes have been standardized for comparison between graphs.

type of IMRT technique used, additional analyses were performed. Within the subgroup defined as having received IMRT (using the definition of ≥5 segments per any unique gantry angle for the primary breast plan), we observed that those treated with inverse planning for right-sided breast cancer had a significantly higher MHD than those treated with forward planning, independently of fractionation (Table 5).

Table 2 Heart dose and volume summary for left-sided breast cancer stratified by fractionation technique and year

Fractionation technique	Total left-side cancer: Cases (n)	Total left-side cancer: Median; mean ± SD (Gy)	Breast only: Cases (n)	Breast only: Median; mean ± SD (Gy)	Breast + nodal fields: Cases (n)	Breast + nodal fields: Median; mean ± SD (Gy)
Conventional						
2012	278	2.19; 2.42 ± 1.13	243	2.09; 2.37 ± 1.13	35	2.64; 2.79 ± 1.08
2013	435	1.99; 2.23 ± 1.18	373	1.91; 2.14 ± 1.16	62	2.56; 2.77 ± 1.17
2014	567	1.60; 1.97 ± 1.18	467	1.55; 1.89 ± 1.17	100	2.07; 2.35 ± 1.14
2015	505	1.65; 1.96 ± 1.06	400	1.54; 1.91 ± 1.07	105	1.85; 2.12 ± 1.00
Accelerated	NA	NA			NA	NA
2012			75	1.70; 1.85 ± 0.75		
2013			136	1.44; 1.67 ± 0.81		
2014			269	1.32; 1.53 ± 0.83		
2015			392	1.22; 1.55 ± 1.09		

Abbreviations: NA = not applicable; SD = standard deviation.

Table 3 Heart dose and volume summary for right-sided breast cancer stratified by fractionation and year

	Total right-side cancer		Breast only		Breast + nodal fields	
Fractionation technique	Cases (n)	Median; mean ± SD (Gy)	Cases (n)	Median; mean ± SD (Gy)	Cases (n)	Median; mean ± SD (Gy)
Conventional						
2012	43	0.89; 1.03 ± 0.61	33	0.88; 0.88 ± 0.47	10	1.58; 1.52 ± 0.77
2013	227	0.76; 0.87 ± 0.55	203	0.75; 0.85 ± 0.57	24	0.90; 0.97 ± 0.43
2014	499	0.67; 0.77 ± 0.48	410	0.64; 0.74 ± 0.46	89	0.83; 0.92 ± 0.45
2015	478	0.74; 0.84 ± 0.61	384	0.70; 0.80 ± 0.64	94	0.92; 1.02 ± 0.42
Accelerated	NA	NA			NA	NA
2012			12	0.70; 0.72 ± 0.28		
2013			65	0.66; 0.70 ± 0.37		
2014			276	0.55; 0.65 ± 0.57		
2015			431	0.56; 0.63 ± 0.35		

Abbreviations: NA = not applicable; SD = standard deviation.

Discussion

In the MROQC, a state-wide quality collaborative composed of a range of radiation centers in the state of Michigan, the MHDs were lower than those in historical studies (5, 6); they also decreased further within a recent 4-year period. Even the baseline MHDs in 2012 were, on average, consistently lower than those reported in the worldwide data, and these

Table 4 Regression models by laterality and type of fractionation

	Left-sided breast cases (2012-2015)		Right-sided breast cases (2014-2015)	
Parameter	Conventional; *P* value	Accelerated; *P* value	Conventional; *P* value	Accelerated; *P* value
Baseline MHD	1.32Gy (1.20Gy-1.45Gy); <.0001	1.14Gy (1.06Gy-1.23Gy); .0003	0.60Gy (0.53Gy-0.67Gy); <.0001	0.47Gy (0.44Gy-0.51Gy); <.0001
IMRT (yes vs no)	20.8% (15.5%-26.4%); <.0001	19.2% (12.1%-26.7%); <.0001	−2.7% (−8.3% to 3.2%); .3654	3.3% (−3.8% to 11.0%); .3681
DIBH (yes vs no)	−17.6% (−21.7% to −13.4%); <.0001	−19.6% (−25.3% to −13.5%); <.0001	NA	NA
Position (prone vs supine)	−31.9% (−39.4% to −23.5%); <.0001	−19.5% (−29.7% to −7.9%); .0016	−33.6% (−43.6% to −21.8%); <.0001	−14.9% (−32.0% to 6.5%); .1577
Boost (yes vs no)	20.9% (10.5%-32.3%); <.0001	20.0% (12.7%-27.8%); <.0001	20.9% (8.2%-35.2%); .0009	24.3% (15.1%-34.3%); <.0001
Nodal treatment				
SCV or ICV vs none or axilla (level I and II)	17.1% (9.5%-25.2%); <.0001	NA	22.0% (11.6%-33.4%); <.0001	NA
IMNs ± SCV or ICV vs none or axilla (level I and II)	40.7% (28.0%-54.6%); <.0001	NA	41.1% (26.0%-58.1%); <.0001	NA
Year (centered at 2015)	−7.7% (−9.6% to −5.8%); <.0001	−8.5% (−11.3% to −5.7%); <.0001	7.7% (1.7%-14.0%); .0116	−1.7% (−8.6% to 5.6%); .6342
Breast volume (centered at 1000 cm^3)/every 100 cm^3	0.22% (−0.13% to 0.57%); .2280	0.3% (−0.5% to 1.1%); .4754	0.1% (−0.5% to 0.7%); .7320	−0.5% (−1.5% to 0.5%); .3187
Separation (cm) (centered at 22 cm)/every 1 cm	1.5% (0.8%-2.2%); <.0001	1.7% (0.4%-3.0%); .0130	0.9% (−0.1% to 1.9%); .0758	2.5% (1.0%-4.0%); .0013

Abbreviations: DIBH = deep inspiration breath hold; ICV = infraclavicular (nodes); IMNs = internal mammary nodes; IMRT = intensity modulated radiation therapy; MHD = mean heart dose; NA = not applicable; SCV = supraclavicular (nodes).
Data presented as mean (range).

Table 5 Forward- versus inverse-planned IMRT mean heart dose stratified by laterality and fractionation

Fractionation	Laterality	Forward-planned	Inverse-planned	*P* value*
Conventional	Right	297; 0.62; 0.70	159; 0.77; 0.93	<.001
Conventional	Left	303; 1.90; 2.30	182; 1.90; 2.20	.390
Accelerated	Right	150; 0.45; 0.52	176; 0.67; 0.75	<.001
Accelerated	Left	139; 1.30; 1.70	182; 1.35; 1.68	.364

Abbreviation: IMRT = intensity modulated radiation therapy.

Data presented as number of patients; median dose (in Gray); and mean dose (in Gray).

* Wilcoxon rank-sum *P* value comparing differences between median values.

decreased further over time. These reductions were coincident with an increased focus on cardiac toxicity secondary to RT in the academic community and media broadly and the emphasis placed on cardiac sparing in our collaborative quality consortium. The MHDs of patients treated at each institution were calculated and reported back to the institution, along with the consortium-wide average MHDs 3 times annually since 2014. Thus, the clinicians at each site can compare the results from their center relative to the others. The variability demonstrated across the centers in the consortium suggests that continued discussion regarding the clinical tradeoffs between whole breast coverage and cardiac sparing; the variables that affect the cardiac dose; and analyses of best practice in treatment setup, planning, and delivery could yield even greater consensus, uniformity, and improvement. We plan to continue to work with consortium members to better understand the variation in MHDs observed among the institutions. In addition, suggested limits for MHD by laterality are now being incorporated into routine treatment planning decisions by consortium members. This could further reduce heart doses going forward. Subsequent analyses will be performed to assess the effect of this additional treatment-planning initiative; however, the results obtained thus far suggest a favorable effect with ongoing monitoring of heart doses over time and comparing the institutional results against group norms. This practice could perhaps serve as a model for others, similar to collaborative quality improvement initiatives in other fields (9-11).

The cardiac dose is affected by clinical decisions about targets, prescribed dose and fractionation, and patient positioning and treatment planning choices. As expected, with higher doses delivered to the breast with the use of a boost to the lumpectomy cavity and/or incorporation of nodal basins into the target volume, the cardiac dose increased. This reinforces the importance of practices such as careful placement of electron boost fields to avoid exits over the heart, avoiding transmission through portions of the heart by photon boosts, and weighing the risk of breast cancer recurrence against the risk of radiation-induced cardiac disease, in particular, when considering regional irradiation.

The patient positioning choices were associated with significant reductions in cardiac dose, with an overall decrease of approximately 18% in our model for patients with left-sided breast cancer treated with conventional fractionation and DIBH and 32% for patients treated in the prone position. These positioning maneuvers are modifiable factors in a patient's treatment plan but are not commonly used (24% use of DIBH with left-sided breast cancer and 4.3% use of prone positioning in our consortium). However, many small studies have demonstrated that DIBH (12, 13) and prone positioning (14, 15) can reduce the cardiac dose. When we studied the data across the study period of 2012 to 2015 for changes in the use of DIBH and prone positioning within the consortium, the use of DIBH was relatively constant over time. The use of prone positioning did, however, significantly increase during the 4-year period for women with left-sided breast cancer, from 0.9% in 2012 to 6.0% in 2015, for an annual rate of change of 1.6% ($P<.0001$; data not shown). Thus, although the number of left-sided breast cancer cases in the consortium being treated with the prone position was still relatively low, an increase over time in the use of prone positioning was observed. However, personalized decisions about positioning should be made for each patient, because prone positioning has been shown to increase the heart dose in some individuals (16).

Somewhat counterintuitively, our data demonstrated that the use of IMRT compared with the use of 3D-CRT for left-sided breast cancer was associated with a 21% greater MHD with conventional fractionation (the largest fractionation cohort) and a 19% increase with accelerated fractionation. Further analysis suggested that, in general, a higher dose was delivered with inverse planning compared with that delivered with forward planning for right-sided breast cancer, although the median doses were not significantly different for left-sided breast cancer (Table 5). Inverse-planned IMRT often generates a more homogeneous dose distribution to a target volume than forward-planned IMRT. If dose homogeneity were the sole intent of IMRT planning, the heart dose could be increased. We hypothesized that this resulted in the significant increase observed using IMRT for left-sided breast cancer. A low-dose "bath" produced by an optimization algorithm over a larger anatomic extent to improve the dose homogeneity could increase the heart dose. This would be more easily detected in right-sided breast cancer in which the overall cardiac exposures are lower than those with left-sided breast cancer. This might explain our findings of a greater dose differential after inverse planning compared with forward planning in right-sided breast cancer compared with left-sided disease. These results underscore the importance of setting appropriate cardiac dose limits, in particular, with IMRT planning. If the cost function incorporates strict cardiac dose limits, which is possible with inverse planning, the heart doses will be constrained. However, even if cardiac dose constraints were incorporated into the cost function, if the dose goals were too permissive, the planning system would not further reduce the dose beyond those instructions. Thus, IMRT optimization is highly dependent on the exact cost function used in planning. Although no consensus has been reached regarding what the cost function value should be for the heart in clinical practice, cardiac dose constraints that limit the heart dose to as low a dose as possible yet allow therapeutic doses to the target volume are critically needed. This is especially true because Darby et al (5) have demonstrated a dose-response relationship between the heart dose and major coronary events. Thus, decisions to use IMRT should consider the need to limit the heart dose in the optimization schema when cardiac exposure is possible. Also, priorities for setting cost functions must be judiciously established and applied.

Although the information collected in the present large state-wide quality collaborative is quite detailed and included immobilization, simulation, planning, and delivery information, in addition to the DVHs, it was impractical to collect, analyze, and curate the full treatment plans for each patient or to review all heart contours. Thus, more specific information such as beam angle selection, customization of blocking, and cost function were not available for analysis. However, for a subset of patients, full treatment plans are currently being analyzed (reported separately). This information should provide additional insight into the best practices to minimize the heart dose.

Conclusions

Within a large, state-wide quality collaborative consortium, the cardiac dose was low overall compared with the published norms and has decreased further since 2012, coincident with the increased focus on cardiac sparing in consortium meetings and population-based research. Ongoing monitoring of the cardiac doses and comparisons of institutional averages against contemporary norms could further reduce cardiac radiation exposure by self-examination of treatment delivery techniques. Additional work by our group will focus on identifying the best practices to further minimize the cardiac dose, especially when IMRT is used.

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