Tumor Locations Impact on Cardiac Toxicity in Women that Received Partial Breast Irradiation

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Introduction

Background:

- Cardiac toxicity is one of the known side-effects of breast radiation therapy.[1]
- Radiation related cardiac morbidity may include atherosclerotic coronary heart disease, myocardial infarctions, coronary revascularization, heart failure, valvular disease, arrythmia, unstable angina, or other major cardiovascular events that result in hospitalization.[1]
- Potential toxic effects to the heart and other normal tissues must be weighed against the benefit in cancer control conferred by radiation therapy.[2]
- Breast conservation therapy (BCT) is a widely accepted treatment approach for the management of early stage breast cancer.[3]
- BCT involves a resection of the breast tumor (lumpectomy, segmental mastectomy, or wide local excision) followed by either whole breast or partial breast irradiation.[3]
- Research has found that the long-term survival rate of patients that undergo BCT is equivalent to those that undergo radical mastectomy for select patients.[4]
- Additionally, BCT is well tolerated, has minimal long-term complications, favorable cosmetic outcomes, and reduced psychological trauma.[3]
- All of the patients in the study received a special form of radiation therapy called accelerated partial breast irradiation (APBI).
- APBI delivers a high dose of radiation to a small portion of the breast most at-risk for harboring residual, microscopic disease, rather than irradiating the entire breast.[3,5]

Aims & Objectives:

- To determine if tumor location correlates with the risk of cardiac toxicity.

Methods

Data Collection:

IDENTIFY PATIENTS

OBTAIN CANCER INFORMATION

UNDERLYING CONDTIONS

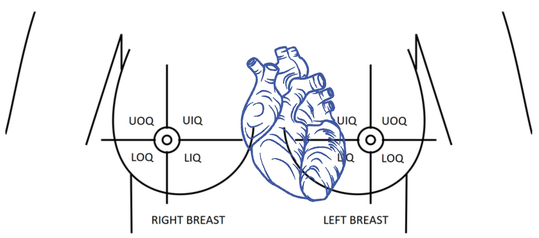
CARDIAC EVENTS

COMPARE

This study was a retrospective chart review using data gathered by the Beaumont Radiation Oncology Department between 1993 and February 2017. Women that were excluded from the study included those that received external beam irradiation before or after receiving APBI therapy, had multiple forms of cancer, or recurrent breast cancer.

Information regarding patient age, the TNM stage of the breast cancer, hormone receptor status of the tumor, location of the tumor, the amount of radiation received, whether or not the patient received chemotherapy, smoking history, and underlying medical conditions (including lung disease, kidney disease, hypertension, hyperlipidemia, and diabetes) were recorded.

The ICD-9 and ICD-10 codes used to indicate one or more of the cardiac events were gathered. Based on the identified patients we were able to compare which ones had suffered a cardiac event following their APBI therapy.



Statistical Analysis:

Both univariate and multivariate analysis were used to determine if tumor location and therapy had a direct impact on future cardiac events.

Results

Patient Demographics:

341 patients were included in the study, ages 59-72. 51 patients had left inner central breast cancer and 100 had right outer breast cancer. These two locations were picked specifically because they confer the closest and furthest proximity to the heart, respectively. Most patients were Hormone receptor positive (90%), HER2 negative (93%) and had T1 stage of cancer (53%). A Deyo-Charson Comorbidity Index score (DCCI) was calculated based on the multiplicity of the patient's comorbidities.

Table 1: Baseline Table

Characteristic	N=341		
Age at dx	65 (59, 72)	**N Stage**	
Unknown	1	pN0	216 (63%)
		pN1	6 (1.8%)
Quadrant Compare		Unknown	119 (35%)
Left Inner Central	51(15%)		
Left Outer	95 (28%)	**DCCI**	
Other	70 (21%)	0	91 (27%)
Right Inner Central	25 (7.3%)	1	125 (37%)
Right Outer	100 (29%)	2+	123 (36%)
		Unknown	2
Hormone Receptor			
Negative	29 (8.5%)	**Smoking**	
Positive	307 (90%)	Current/Former Smoker	163 (47%)
Unknown	5 (1.5%)	Never Smoker	159 (47%)
		Unknown	19 (6%)
HER2 Receptor			
Negative	317 (93%)	**Chemotherapy**	
Positive	13 (3.8%)	0 (None)	287 (84%)
Unknown	11 (3.2%)	1 (Received)	46 (14%)
		Unknown	8 (2%)
T Stage			
pT1	181 (53%)	**Endocrine Therapy**	
pT2	16 (4.7%)	0 (None)	142 (42%)
pTis	26 (7.6%)	1 (Received)	199 (58%)
Unknown	118 (35%)		

Table 1. The baseline table highlights various important characteristics gathered about the patients.

Analysis:

Univariant and multivariable analyses showed that, when compared to patients with right outer breast cancer, women with left inner central breast cancer that received APBI therapy were at a more than two-fold risk of developing an adverse cardiac event with borderline significance (HR=2.06 [1-4.24], p = 0.05) (Table 2).

Table 2: Univariate & Multivariable Analyses

Covariate	N	Univariate			Multivariate		
		HR[1]	95% CI[1]	p-value	HR[1]	95% CI[1]	p-value
Quadrant Compare	341						
Right Outer		—	—		—	—	
Right Inner Central		1.03	0.39, 2.73	>0.9	1.12	0.42, 2.99	0.8
Left Outer		1.06	0.59, 1.92	0.8	1.04	0.56, 1.92	>0.9
Left Inner Central		1.64	0.86, 3.16	0.14	2.06	1.00, 4.24	0.05
Other		1.07	0.60, 1.89	0.8	1.01	0.56, 1.92	>0.9
Age at Dx	340	1.07	1.05, 1.10	<0.001	1.06	1.03, 1.09	<0.001
CDCI	339						
0		—	—		—	—	
1		1.54	0.64, 3.73	0.3	1.11	0.45, 2.75	0.8
2+		7.02	3.22, 15.3	<0.001	4.59	2.02, 10.4	<0.001

Table 2: Univariate and multivariable analyses done correlating selected variable with any cardiac events. [1] HR= Hazard Ratio, CI = Confidence Interval

Results (continued)

Figure 1: Cumulative Incidence of Any Cardiac Events by Quadrant Closest or Farthest From the Heart

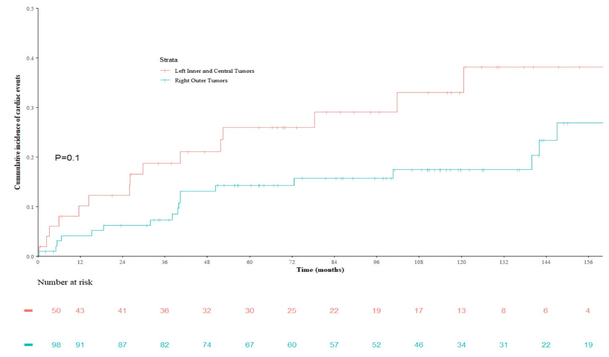


Figure 1. Cumulative Incidence of any cardiac event in tumors within the left inner and central breast compared to those in the right outer breast. These two locations were selected based on them being the closest and farthest from the heart, respectively.

Additionally, Kaplan Meier curves were used to compare the results of any cardiac events between those with left inner/central breast cancer and those with right outer breast cancer (Figure 1), suggesting a trend for increased cardiac events in those with left, inner quadrant tumor beds.

Conclusion

This study suggests that treatment of tumor beds located in the inner/central portion of the left breast is associated with a higher risk of developing cardiac toxicity. This supports routinely contouring and minimizing dose to the heart during APBI treatment planning.

Limitations

The major limitation of this study was the small sample size. Although 341 patients were identified as having received APBI, only 50-100 patients were included in our sub-groups.

The second limitation was that the dose of radiation received by the heart was never calculated or compared for the women in this study. This means that while we can assume that women that received APBI therapy for left inner/central breast cancer received a greater dose of radiation to the heart given its proximity, actual radiation doses were not calculated. Future studies comparing heart dose in patients receiving APBI versus whole breast irradiation are warranted.

References & Acknowledgements

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