

Utilizing a Novel Calculator to Evaluate the Risk of Acute Cardiac Events After Breast Conserving Surgery or Mastectomy for Patients Receiving Supine Radiation Therapy Without Breath Hold Techniques

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ABSTRACT

Radiation therapy remains an important component of curative treatment for patients with breast cancer (BC). Wide variability remains in acceptable dose tolerances to cardiac substructures when treatment planning. The University of Texas MD Anderson Cancer Center (MDACC) recently developed a cardiac risk calculator incorporating a patient's baseline health and the volume of the left ventricle receiving 5 Gy (LV-V5) to predict the 9-year cumulative incidence (CI-9yr) and the 9-year cumulative excess risk (CER-9yr) of an acute cardiac event (ACE). We applied this model at Baptist MD Anderson Cancer Center (BMDACC) on patients previously treated without breath hold during radiation.

Twenty patients with left sided and 20 with right sided BC were selected from our Breast Registry and were subdivided into treatment to the breast only or to the breast/chest wall with regional nodal irradiation (RNI). Age, hypertension, diabetes, and ischemic heart event history were gathered from electronic chart records. The left ventricle was contoured and the LV-V5 dose was calculated retrospectively. The cardiac risk was analyzed after entering data into the MDACC Calculator.

Our cohort represented a mean age of 58 with 72.5% having at least one cardiac risk factor. The mean LV-V5 was 4.35% for left breast, 0% for right breast, 27.85% for left side with RNI, and 1.43% for right side with RNI. The CI-9yr for patients with left sided BC is twice the risk than that of right sided patients as follows: 7.8% for left breast only and 5.4% RNI compared to 3% and 2.1% for the right breast or RNI patients respectively. While the CER-9yr for right-sided patients was little or none, the CER-9yr was 0.51% and 1.6% for left breast only and RNI respectively. The MDACC calculator highlights that traditional treatment planning techniques for BC radiotherapy are acceptable for treatment to the right breast, but patients with left sided disease may benefit from treatment technique modifications.

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PURPOSE

The purpose of this study is to evaluate the cardiac risk of 40 breast cancer (BC) patients treated supine with free-breathing technique radiotherapy based on their cardiac risk factors and radiation exposure to the left ventricle using the MDACC Acute Cardiac Event Risk Calculator.

INTRODUCTION

Comprising of 12.5% of all new cancer cases and approximately 2.3 million new diagnoses in 2020 globally, BC remains to be the most common cancer in females and second most common of all cancers worldwide.¹ Radiation therapy (RT) is a central component of BC treatment after breast-conserving surgery or mastectomy in conjunction with chemotherapeutic agents with advances in local regional control.² As overall survival improves, more attention is being turned to late effects from all treatment modalities. Research shows a correlation with late cardiac effects and increasing incident radiation exposure to the heart.³ Common to all evaluations is an understanding of the patient's clinical history, cardiac risk factors, and systemic therapies that may influence their cardiac health. Current research is taking a more refined approach to cardiac substructures in conjunction with patient factors. This study may help determine if improvements to treatment planning guidelines should be made to reduce the patients' cardiac risk to acceptable tolerances.

METHODS AND MATERIALS

- This research was exempt from review by the Baptist Health Institutional Review Board.

- Our cohort consists of 40 patients randomly selected.

Patient Inclusion Criteria

- Female
- 18 years or older
- Positioned supine
- Enrolled in BMDACC Breast Registry
- Treated from October 2017 to October 2020
- Received EBRT

Patient Exclusion Criteria

- Positioned prone
- Received bilateral breast or chest-wall EBRT
- Received only non-radiological treatment

Subgroups Based on Treatment Site

- 10 left breast alone
- 10 left breast or chest-wall with RNI
- 10 right breast alone
- 10 right breast or chest-wall with RNI

Data Collected from Electronic Chart Records

- Age at diagnosis
- Pre-existing cardiac risk factors (history of diabetes, hypertension, ischemic heart event)
- Pathological Stage
- Treatment Technique

Data Collected from RT Plan (Eclipse TPS v13.6)

- Prescription(s) (RX)
- LV-V5 (%) – volume of LV receiving 500 cGy
- Treatment Technique

Table 1. MDACC Cardiac Risk Calculation Model³

Weighted ACE Score	$= (0.8 \text{ DM}) + (1.4 \text{ HTN}) + (1.8 \text{ IHE})$
LP_{LV-V5}	$= (0.017 * B) + (0.063 * A) + (0.711 * C)$
CER-9yr	$= \text{CI-9yr} - \text{CI-9yr}_{0\text{Gy}}$ $= \text{CI-9yr} - [1 - \text{EXP}[-0.000223 * \text{EXP}(0.063 * A) + (0.711 * C)]]$

A=age, B=LV-V5, C=weighted ACE score, DM=diabetes, HTN=hypertension, IHE=ischemic heart event, LP_{LV-V5}=composite factor of risk for model, CI-9yr=cumulative 9-year incidence of ACE, CER-9yr=cumulative 9-year excess risk of ACE

RESULTS

Figure 1. No. of Pre-Existing Cardiac Risk Factors

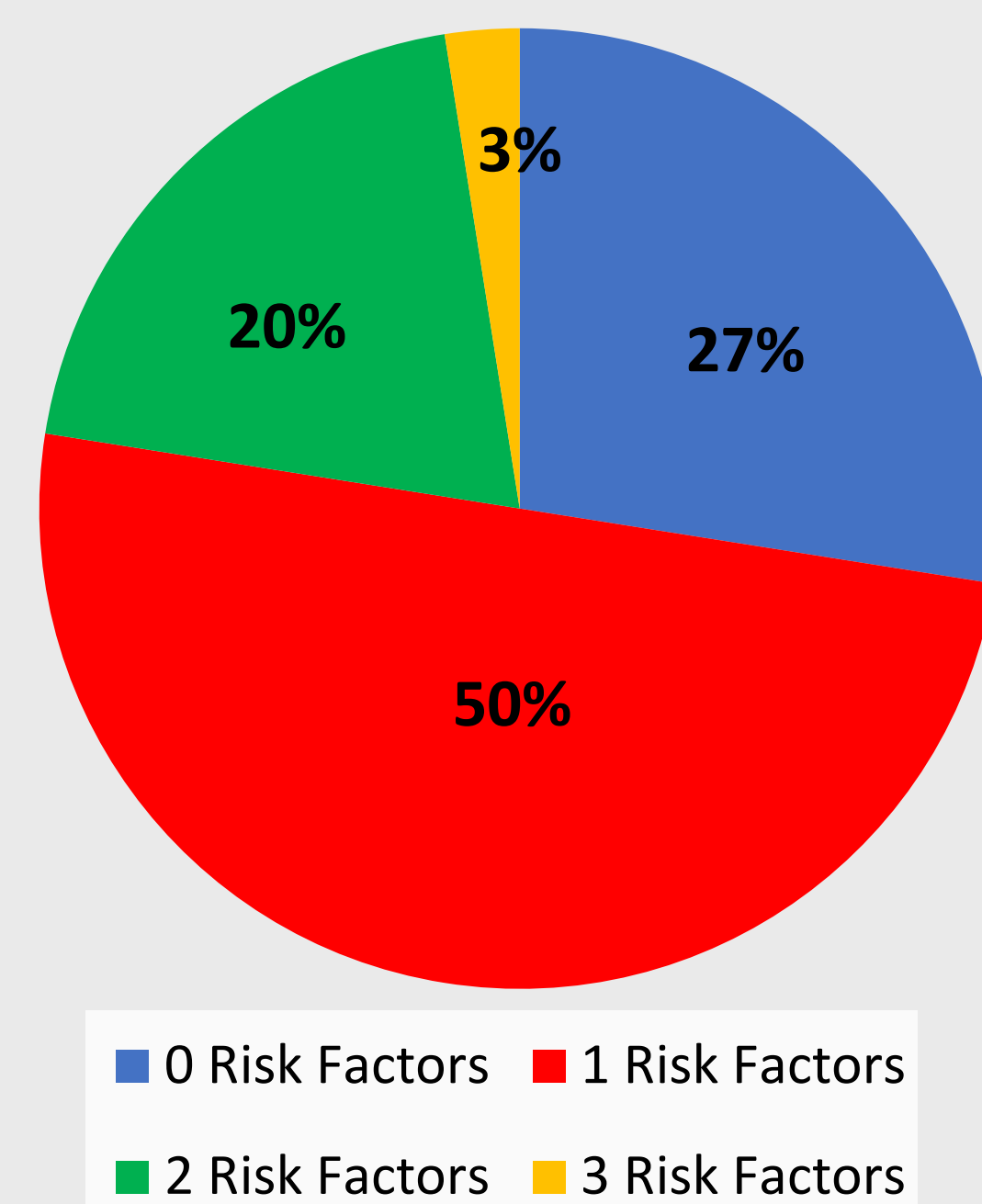


Table 4. Radiation Treatment Prescriptions

RX	Primary Dose			Boost Dose		
	4005 cGy	4272 cGy	5000 cGy	1000 cGy	1200 cGy	1400 cGy
Left-Sided Alone	8	2	0	4	2	2
Right-Sided Alone	10	0	0	9	0	0
Left-Sided + RNI	0	0	10	5	1	0
Right-Sided + RNI	0	0	10	4	1	0

Table 2. Radiation Treatment Technique

Treatment Technique	3D-CRT	VMAT
Left-Sided Alone	10	0
Right-Sided Alone	10	0
Left-Sided + RNI	1	9
Right-Sided + RNI	1	9

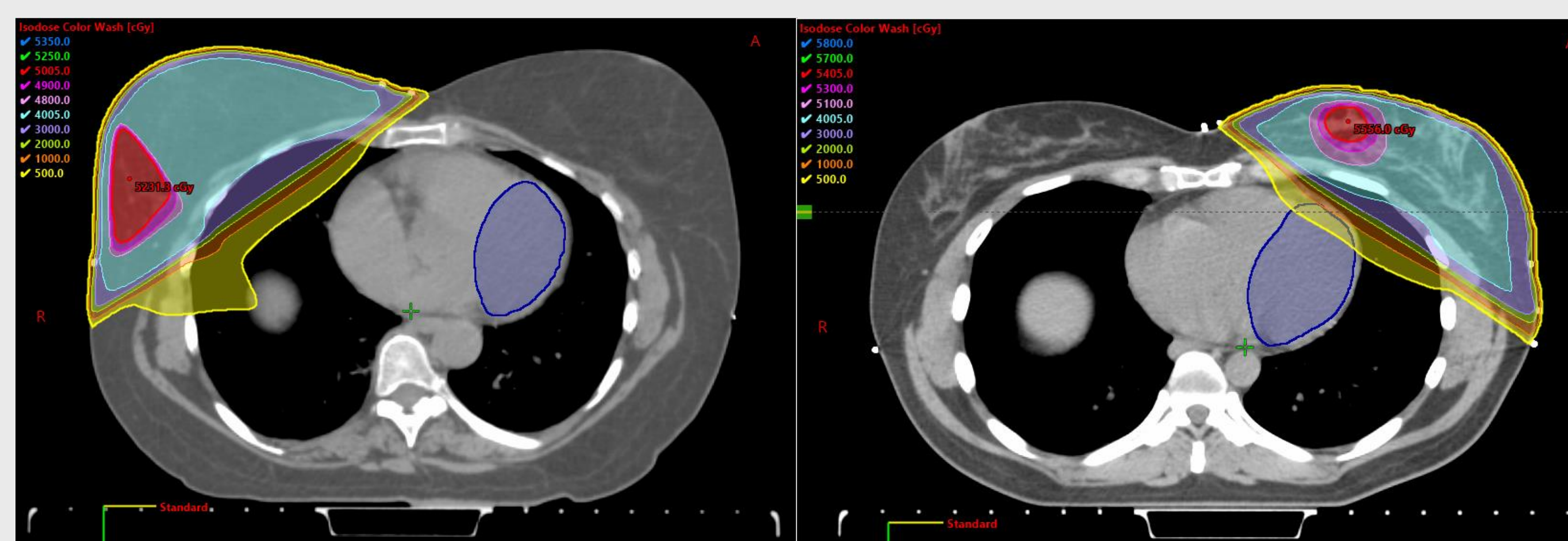
Table 3. No. of Patients with Different Weighted ACE Scores

Weighted ACE Score	No. of Patients	% of Patients
0	11	27.5 %
0.8	2	5 %
1.4	18	45 %
2.2	8	20 %
4	1	2.5 %

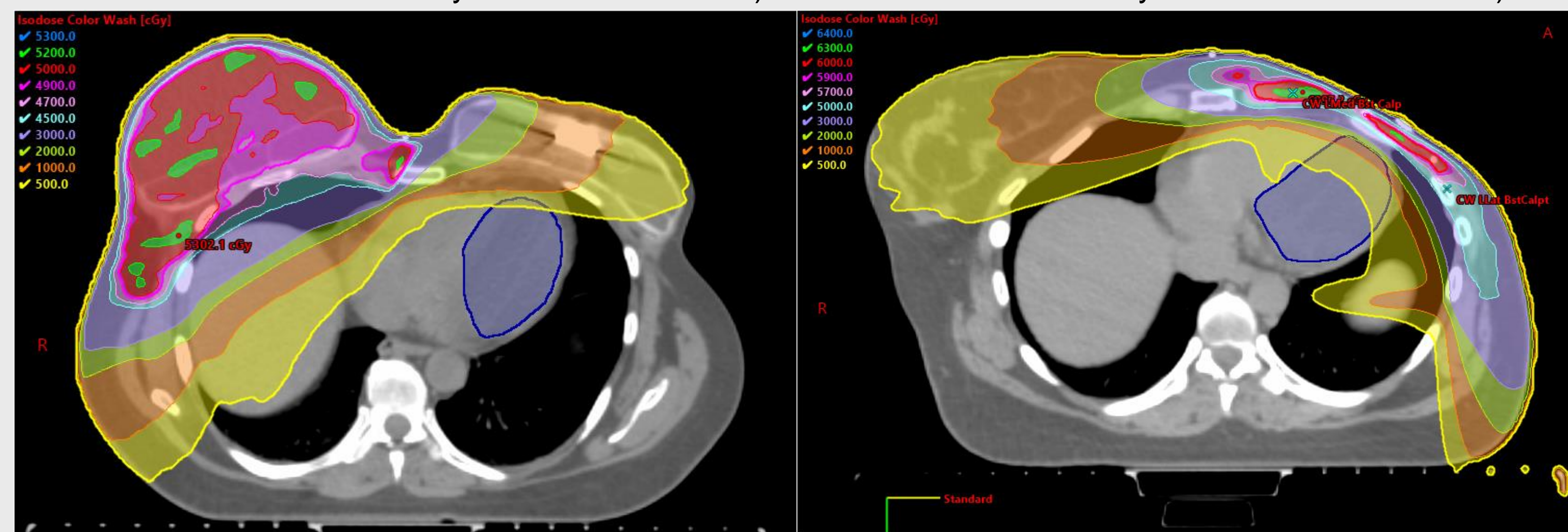
Table 5. Number of Patients with a History of Disease/Cardiac Risk Factor

History of Disease	No. of Patients	% of Patients
Diabetes	10	25 %
Hypertension	27	67.5 %
Ischemic Heart Event	1	2.5 %

Figure 2. Transverse Isodose Distribution of Breast Cancer RT Plans – (Tx Technique, Primary RX, Boost RX). Left Ventricle – dark blue, 500 cGy Isodose Line – yellow



A. Right-Sided Alone (3D-CRT, 4005 cGy to the whole breast and 1000 cGy boost to the tumor bed) B. Left-Sided Alone (3D-CRT, 4005 cGy to the whole breast and 1000 cGy boost to the tumor bed)



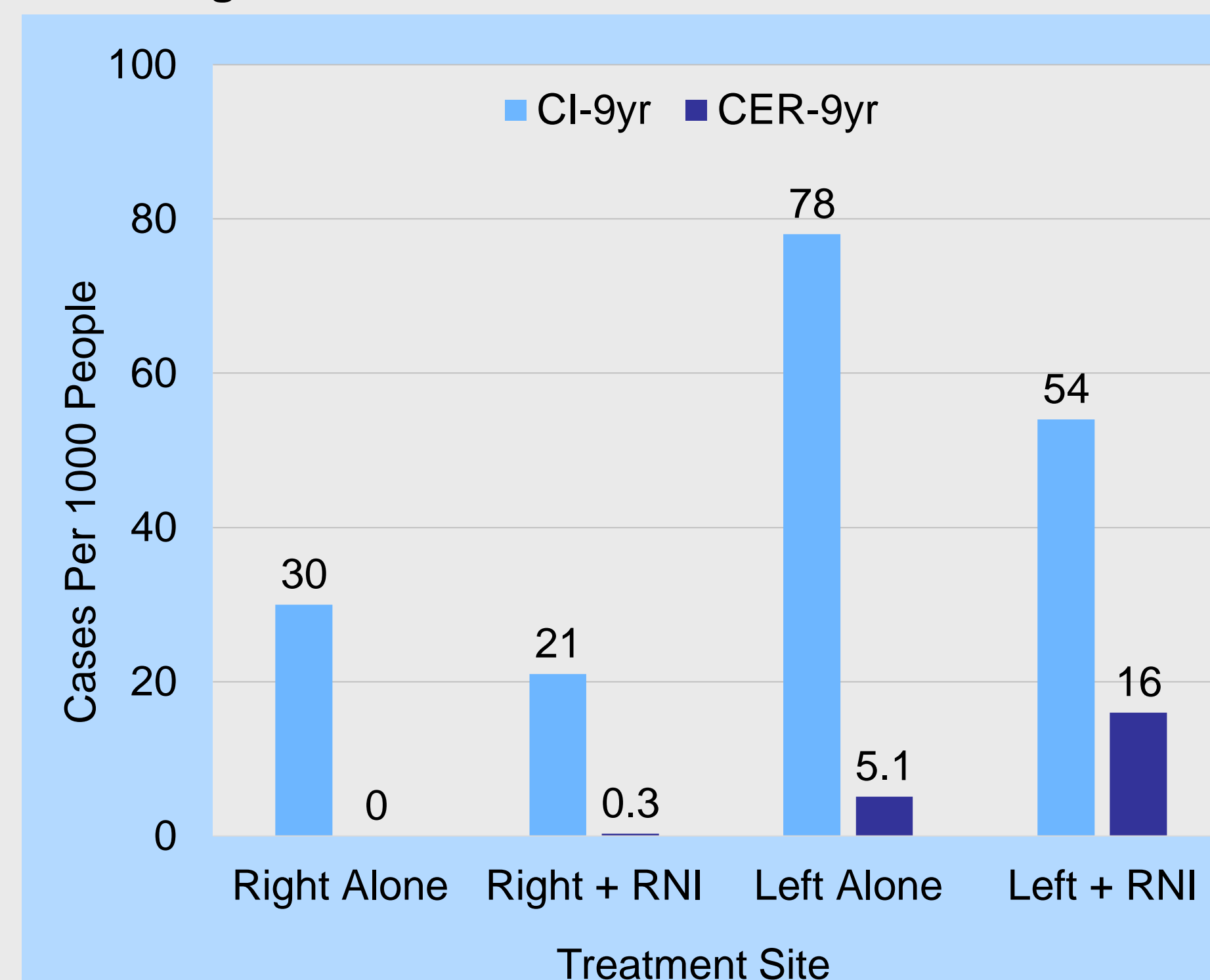
C. Right Chest-Wall + RNI (VMAT, 5000 cGy to the chest wall + RNI, and no boost to the scar) D. Left Chest-Wall + RNI (VMAT, 5000 cGy to the chest wall + RNI and 1000 cGy boost to the scar)

Table 6. ACE Risk Calculator Results

Tx Site	Mean Age (Yrs)	Mean LV-V5 (%)	Mean Weighted ACE Score	Mean (Range)		
				Mean LP _{LV-V5}	Mean CI-9yr (%)	Mean CER-9yr (%)
Left-Sided Alone	61 (38-79)	4.35 (1.10-7.55)	1.62 (0-4)	5.04 (2.45-7.79)	7.8 (0.3-42)	0.51 (0.01-3)
Right-Sided Alone	62 (47-75)	0	1.20 (0-2.2)	4.73 (2.96-5.72)	3 (0.4-6.6)	0
Left-Sided + RNI	57 (38-78)	27.85 (6.24-55.80)	1.16 (0-2.2)	4.86 (2.91-6.91)	5.4 (0.4-20)	1.6 (0.2-8)
Right-Sided + RNI	52 (34-72)	1.43 (0-10.03)	0.86 (0-2.2)	3.89 (2.21-5.66)	2.1 (0.2-6)	0.03 (0-0.2)

RESULTS CONT'D

Figure 3. Risk of ACE Based on Treatment Site



Our cohort, with a mean age of 58 years (34-79), consisted of 27 intact breast patients (67.5%) and 13 chest-wall patients (32.5%). Out of 40 patients, 7 were diagnosed with stage 0, 15 with stage I, 11 with stage II, and 7 with stage III BC. At least 29 patients (72.5%) presented with at least one cardiac risk factor. More specifically, 50% had one risk factor, 20% with two, and 2.5% had three risk factors present (Figure 1).

The mean LV-V5 for both left and right-sided BC patients treated with RNI (27.85% and 1.43%) were higher by 6.4-fold and 1.4-fold than those treated to the breast alone (4.35% and 0%), respectively (Table 6). The volume of the left ventricle exposed to 500 cGy varies with the treatment technique used, patient anatomy, location of the target volumes, laterality of disease, and prescription doses (Figure 2). To no surprise, left-sided treatment with RNI shows the highest LV-V5 due to a combination of low dose scatter from arc therapy and the short distance of the left ventricle from the treatment field.

Compared to right-sided patients, the average CI-9yr for patients with left-sided radiotherapy increased by at least twice as much, as follows – 7.8% for left-sided only, 3% for right-sided only, 5.4% for left-sided with RNI, and 2.1% for right-sided with RNI. While the CER-9yr for right-sided patients was none to minimal, patients with treatment to the left breast only and left side with RNI had a mean 0.51% and 1.6% higher chance of an acute cardiac event 9 years after radiotherapy (Figure 3). The MDACC ACE Calculator shows little impact of RT to patient ACE risk for right-sided patients, but a significant increase in cardiac risk from left-sided RT.

CONCLUSIONS

Based on the MD Anderson Cancer Center Acute Cardiac Event Risk Calculator, current treatment planning guidelines are generally safe for radiotherapy to the right breast, but modifications in treatment techniques can be made for patients with left-sided disease to help lower their probability of an ACE occurring after RT.

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