



# Multi-Institutional Results of Breast Proton Radiation Therapy: An Analysis of the Pcg Registry

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## Purpose

This study aimed to determine disease-specific outcomes and toxicities associated with proton therapy for breast cancer treatment.

## Methods

Records of 335 breast cancer patients with localized disease treated with proton radiotherapy (RT) in a multi-institutional prospective registry between 2011 and 2016 were analyzed. Late toxicity is (CTCAE V4.0) any event beginning or persisting for 6 months or longer from the start of radiotherapy and acute Adverse Events (AE) before that. Cancer events were measured from the completion of RT.

## Results

Median follow-up was 1.1 years (0.2-3.7 years) and 73% for longer than 6 months. Nodal stage was pN1-3 in 68%. Re-irradiation was delivered to 52 (15.5%), chest wall RT 135 (40.3%), whole breast 108 (32.3%), and partial breast RT 40 (11.9%). Loco-regional failures were seen in 2.4%, distant failures in 6.9%, breast cancer deaths in 10 (3.0%), and deaths in 15 (4.5%). AEs  $\geq$ G3 or  $\geq$ G2 were different between retreatment (9, 17.3%; 43, 82.7%) and de novo (20, 7.1%; 191, 67.5%),  $p=0.028$  and  $p=0.032$ . Only one chronic G3 AE was seen. Retreatment was associated with similar loco-regional failure rates 3 (5.8%) vs 5 (1.8%),  $p=0.11$ . However, distant failures (7 and 13.5% vs 16 and 5.7%;  $p=0.06$ ), breast cancer deaths (4 and 7.7% vs 6 and 2.1%;  $p=0.05$ ), and overall deaths (6 and 11.5% vs 9 and 3.2%;  $p=0.017$ ), were higher. Volume treated was a predictor of G2 or G3 AEs; AEs  $\geq$ G3 or  $\geq$ G2 were different between patients treated to the regional lymph nodes (20, 10.7%; 165, 88.2%) vs local RT (0, 0.0%; 25, 26%),  $p=0.0003$  and  $p=0.0001$ . A relationship between dose and AEs was found; for  $\geq$ G3 the dose threshold was 61.3 Gy (6 and 17.5% vs 14 and 5.6%;  $p=0.02$ ) and for  $\geq$ G2 it was 45.5 Gy, (17 and 50.0% vs 173 69.4%;  $p=0.0319$ ).

## Table A

**Toxicity ( $\geq$ G2) outcomes for patients treated with proton therapy for localized breast cancer**

	$\geq$ G2	G0-G1	Total	Fisher's exact test
Retreatment	43 (82.7%)	9	52	
No retreatment	191 (67.5%)	92	283	
	234 (69.9%)	99	335	$P < 0.05$
APBI	6 (15.0%)	34	40	
WBRT or CWRT	183 (75.3%)	60	243	
	189 (66.8%)	94	283	$P < 0.01$
WBRT	69 (63.8%)	39	108	
CWRT	116 (85.9%)	19	135	
	185 (76.1%)	58	243	$P < 0.01$
PBS	36 (72%)	14	50	
Passive scatter	155 (63.8%)	88	243	
	191 (67.5%)	102	293	$P = 0.328$
LN	165 (88.2%)	22	187	
No LN	25 (26.0%)	71	96	
	190 (67.1%)	93	283	$P < 0.01$
$\geq 45.5$ Gy	17 (50.0%)	17	34	
$< 45.5$ Gy	173 (69.4%)	76	249	
	190 (67.1%)	93	283	$P < 0.05$

## Table B

**Toxicity (G3) outcomes for patients treated with proton therapy for localized breast cancer**

	G3	G0-G2	Total	Fisher's exact test
Retreatment	9 (17.3%)	43	52	
No retreatment	20 (7.1%)	263	283	
	29 (8.7%)	306	335	$P < 0.05$
APBI	0 (0.0%)	40	40	
WBRT or CWRT	20 (8.2%)	223	243	
	20 (7.1%)	263	283	$P = 0.08$
PBS	3 (7.5%)	37	40	
Passive scatter	17 (7.0%)	226	243	
	20 (7.1%)	263	283	$P = 0.99$
LN	20 (10.7%)	167	187	
No LN	0 (0.0%)	96	96	
	20 (7.1%)	263	283	$P < 0.01$
$\geq 61.34$ Gy	6 (17.6%)	28	34	
$< 61.34$ Gy	14 (5.6%)	235	249	
	20 (7.1%)	263	283	$P = 0.02$

## Table C

**Treatment failure and death outcomes for patients treated with proton therapy for localized breast cancer**

Local failures	Failure	No Failure	Total	Fisher's exact test
Retreatment	3 (5.8%)	49	52	
No retreatment	5 (1.8%)	278	283	
	8 (2.4%)	327	335	$P = 0.11$
Distant failures	Failure	No Failure		
Retreatment	7 (13.5%)	45	52	
No retreatment	16 (5.7%)	267	283	
	23 (6.9%)	312	335	$P = 0.06$
Breast Ca Deaths	Death	No death		
Retreatment	4 (7.7%)	48	52	
No retreatment	6 (2.1%)	277	283	
	10 (3.0%)	325	335	$P = 0.05$
All Deaths	Death	No death		
Retreatment	6 (11.5%)	46	52	
No retreatment	9 (3.2%)	274	283	
	15 (4.5%)	320	335	$P = 0.02$
	20 (7.1%)	263	283	$P = 0.02$

## Conclusion

Proton beam radiation was associated with low chronic G3 AEs including re-treatment cases. Volume and dose thresholds were found.