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Multi-institutional Results of Breast Proton Radiation Therapy: An Analysis of the PCG Registry

Carlos E. Vargas, M.D.
Mayo Clinic Arizona, Department of Radiation Oncology
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Overview

- Study Aim
- Methods
- Results
- Conclusions

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Study Aim

Determine disease-specific outcomes and toxicities associated with proton therapy for the treatment of breast cancer.

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Methods

- Records of 341 patients treated with proton radiotherapy for breast cancer between 2011 and 2016 were identified from a prospective multi-institutional database.
- Excluded patients with metastatic disease (N = 6).
- Final analysis included N = 52 patients with re-irradiation and N = 286 patients treated *de novo.*
- Acute toxicity was defined as any adverse event (AE) occurring within 6 months of the start of radiotherapy.
- Late toxicity was defined as any event beginning or persisting for 6 months or longer from the start of radiotherapy.
- All AEs were recorded using CTCAE V4.0.
- Cancer specific failures were measured from the completion date of radiation therapy.

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Results

- Median follow-up was 1.1 years (0.2-3.7 years)
  - 73% of patients were followed for longer than 6 months.
- Pathological nodal stage was pN1-3 in 68% and regional lymph nodes were treated in 226/335 cases (68%).
- N = 283 patients received radiotherapy for the first time
  - N = 40 patients received APBI (40Gy RBE).
- N = 243 patients were treated to the intact breast (44%) or chest wall (56%)
  - Median dose of 45 Gy RBE (range: 40Gy-70Gy RBE).

Results

- Deaths occurred in 4.4% of patients
  - Breast cancer related deaths in 3%
  - Loco-regional failures were seen in 2.4% of patients
  - Distant failures in 6.9%
- Excluding re-treatments, acute grade 2 or higher toxicity was seen in 76% of patients.
- Acute grade 3 toxicity was seen in 7.8%.
- Chronic grade 3 toxicities were seen in 0.1% (N = 1) of patients.
- N = 29 grade 3 events related to RT were recorded.
- N = 76 patients had pencil beam scanning and G3 AE were seen in 7.8% vs. 9.5% of double scatter patients.

Proton radiotherapy treatment

Total number of patients	**N = 335**
De novo radiation treatment	N = 283
Retreatments	N = 52

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Proton radiotherapy treatment

Proton Radiotherapy Type	**N = 335**
Re-irradiation	N = 52
APBI	N = 40
Chest Wall	N = 135
Whole Breast	N = 108

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Toxicities in re-irradiation vs. *de novo* treatment

Fisher's test	Grade 3 toxicity	≤ Grade 2 toxicity	Total # of patients	P-value
Re-irradiation	9	43	52	
***De novo* treatment**	20	263	283	
Total # of patients	29	306	335	P =0.028

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Clinical outcomes in re-irradiation vs. *de novo* treatment

	Failures	No Failures	Total # patients	P-value
Local Failure				
Re-treatment	3	49	52	
No retreatment	5	278	283	
	8	327	335	P = 0.11
Distant failures				
Re-treatment	7 (13.5%)	45	52	
No retreatment	16 (5.7%)	267	283	
	23	312	335	P = 0.06
Breast ca deaths				
Re-treatment	4 (7.7%)	48	52	
No retreatment	6 (2.1%)	277	283	
	10	325	335	P = 0.05
Deaths				
Re-treatment	6 (11.5%)	46	52	
No retreatment	9 (3.3%)	274	283	
	15	320	335	P = 0.017

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Toxicities: Accelerated partial breast vs. whole breast or chest wall RT

- 20 AEs out of 283 cases were noted (excluding retreatments)
- APBI had no G3 AEs, although borderline significant secondary to the small number of APBI cases

	Grade 3 toxicity	≤ Grade 2 toxicity	Total # patients	P-value
APBI	0	40	40	
WBRT or CW RT	20 (9.0%)	223	243	
Total # patients	20	263	283	P =0.08

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Toxicities: Lymph node involvement

- In patients with no LN involvement including API and breast/CW, there were no grade 3 AEs observed (reached statistical significance)

	Grade 3 toxicity	≤ Grade 2 toxicity	Total # patients	P-value
Lymph node involvement	20 (10.7%)	167	187	
No lymph node involvement	0	96	96	
Total # patients	20	263	283	P= 0.0003

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Toxicities: Radiation doses

- A dose relationship associated with greater toxicities emerged from our analysis.

	Grade 3 toxicity	≤ Grade 2 toxicity	Total # patients	P-value
Dose ≥ 61.34 Gy	6 (17.6%)	28	34	
Dose < 61.34 Gy	14 (5.6%)	235	249	P =0.02
Total # patients	20	263	283	

Toxicities: Location and type of proton RT

- No relationship between CW vs. WBRT or PBS vs. double scatter emerged in our analysis

	Grade 3 toxicity	≤ Grade 2 toxicity	Total # patients	P-value
WBRT	14	135	149	
CW	6	88	94	
Total # patients	20	221	243	P =0.49
PBS	3	37	40	
Passive scatter	17	226	243	
Total # patients	20	263	283	P =0.99

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Conclusions

- Our study is one of the largest experiences with proton therapy for the treatment of breast cancer.
- A statistically significant difference in AEs was observed in patients receiving re-treatment vs. *de novo* RT.
- A relationship between treatment volume and dose of RT with G3 AEs was seen.
- No grade 4 AEs were observed in any patient.
- Local control was excellent after re-irradiation and no different than patients treated *de novo*
- Distant metastases, and overall death were higher for re-irradiated patients suggesting that radiation improves local control but an overall benefit is unclear.

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Questions and Discussion

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