Comparing Utilization and Survival Outcomes of Post-mastectomy Radiation Therapy (PMRT) in Invasive Lobular versus Ductal Carcinoma: A National Cancer Database Analysis

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BACKGROUND

- **Post-mastectomy Radiation Therapy (PMRT) improves locoregional control and overall survival in patients with** high-risk features such as ≥4 positive lymph nodes or T3–T4 tumors.[1]
- Guidelines recommend PMRT based on clinical risk but **do not differentiate by histologic subtype.**[2]
- However, **invasive lobular carcinoma (ILC) has distinct features compared to invasive ductal carcinoma (IDC).**
- **We hypothesized that (1) patients with ILC may be more likely to receive PMRT and (2) may derive greater relative survival benefit compared to those with IDC.**

METHODS

We used the National Cancer Database (NCDB) to address two questions:

1. Among patients with stage I-III breast cancer who underwent mastectomy, is PMRT more commonly used in ILC than IDC?

Analytic Dataset
N = 651,454

- Pathologic stage I-III
- 2010-2020
- Underwent mastectomy

➢ We used **chi-square test** to compare PMRT utilization.

2. Among patients with an indication for PMRT, is PMRT associated with greater survival benefit in ILC than IDC?

Survival Analysis Dataset
N = 199,228

Above inclusions + the following criteria as indications for PMRT:

- T3 tumor with age <50 years
- T3 tumor with lymphovascular invasion (LVI)
- ≥ N2 nodal involvement
- T1–2N2 with grade 3 or LVI
- Positive margins
- Grade 3 with LVI

➢ We calculated **absolute (ARR) and relative risk reductions (RRR) with PMRT, used multivariable Cox proportional hazards models** to evaluate the association between PMRT and overall survival (OS).
➢ We performed **an interaction test** to assess histology-specific associations of PMRT with OS.

PMRT use is significantly more common in patients with ILC, and is associated with greater survival benefit in those with ILC compared to those with IDC.

Table 1. Baseline patient characteristics

	Overall	ILC	IDC	p-value
All patients	651,454 (100%)	133,340 (20.47%)	518,114 (79.53%)	
Age at Diagnosis				<0.001
< 50	172,300 (26.45%)	26,134 (19.60%)	146,166 (28.21%)	
50-70	338,218 (51.92%)	73,688 (55.26%)	264,530 (51.06%)	
> 70	140,936 (21.63%)	33,518 (25.14%)	107,418 (20.73%)	
Pathologic Stage				<0.001
I	297,210 (45.62%)	46,072 (34.55%)	251,138 (48.47%)	
II	250,359 (38.43%)	56,539 (42.40%)	193,820 (37.41%)	
III	103,885 (15.95%)	30,729 (23.05%)	73,156 (14.12%)	
Tumor Grade				<0.001
I	79,453 (12.20%)	20,400 (15.30%)	59,053 (11.40%)	
II	211,620 (32.48%)	56,980 (42.73%)	154,640 (29.85%)	
III	155,710 (23.90%)	10,507 (7.88%)	145,203 (28.03%)	
Unknown*	204,671 (31.42%)	45,453 (34.09%)	159,218 (30.73%)	
Receptor subtype				<0.001
ER+PR+HER2-	280,829 (43.11%)	72,578 (54.43%)	208,251 (40.19%)	
ER+PR-HER2-	36,830 (5.65%)	9,765 (7.32%)	27,065 (5.22%)	
ER-PR-HER2-	53,719 (8.25%)	1,848 (1.39%)	51,871 (10.01%)	
HER2+	71,333 (10.95%)	5,570 (4.18%)	65,763 (12.69%)	
Unknown*	208,743 (32.04%)	43,579 (32.68%)	165,164 (31.88%)	
Pathologic T Stage				<0.001
T0	4,150 (0.64%)	307 (0.23%)	3,843 (0.74%)	
T1/T2	579,652 (89.36%)	106,738 (80.44%)	472,914 (91.65%)	
T3/T4	64,885 (10.00%)	25,644 (19.33%)	39,241 (7.60%)	
[Unknown]	[2,767]	[651]	[2116]	
Pathologic N Stage				<0.001
N0	393,961 (61.46%)	74,401 (56.73%)	319,560 (62.67%)	
N1	169,207 (26.40%)	35,524 (27.09%)	133,683 (26.22%)	
N2+	77,851 (12.14%)	21,221 (16.18%)	56,630 (11.11%)	
[Unknown]	[10,435]	[2,194]	[8,241]	

* Unknown category analyzed if > 5%

Figure 2. Kaplan-Meier analysis of 5-year overall survival among 199,228 patients with an indication for PMRT

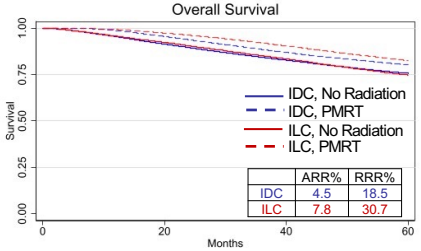
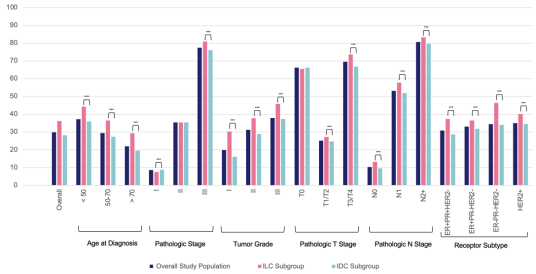


Figure 1. Proportion of patients receiving PMRT by histologic subtype and clinicopathologic features



- Overall, 30% patients received PMRT, with **significantly higher utilization rates in patients with ILC compared to IDC** (36% vs 28%, p < 0.001).
- In stratified analysis, ILC patients received more PMRT across receptor subtypes, tumor grade, pathologic T and N stage, and age groups, but only within the stage III cohort, **suggesting that higher stage is driving increased PMRT in ILC patients**.

Table 2. Adjusted hazard ratios for 5-year survival by histologic subtype

Subtype	aHR (95% CI)	p-value
All	0.73 (0.71–0.74)	<0.001
ILC	0.63 (0.60–0.67)	<0.001
IDC	0.75 (0.73–0.77)	<0.001

- Multivariate analysis adjusted for age, pathologic T and N stage, receptor subtype, grade, Charlson-Deyo score, and lymphovascular invasion.
- The effect of PMRT **differs significantly by histologic subtype (interaction p < 0.001)**.

Conclusions

- PMRT is more frequently utilized in patients with ILC than IDC, which is likely driven by higher overall stage.
- While PMRT is associated with improved overall survival in both ILC and IDC patients who have an indication for PMRT, **the relative survival benefit of PMRT appears greater in those with ILC.**
- These results could reflect **greater radiation sensitivity in those with ILC** or could be due to **greater prevalence of occult residual disease** after mastectomy in those with ILC.
- These results emphasize **the importance of considering histologic subtype when considering both use and omission of radiotherapy**.

ACKNOWLEDGEMENTS

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SCAN ME

[1] EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014.
[2] Jimenez RB, Abdou Y, Anderson P, et al. Postmastectomy Radiation Therapy: An ASTRO-ASCO-SSO Clinical Practice Guideline. J Clin Oncol. 2025.