Impact of Pre-Neoadjuvant Radioactive Iodine Seed Marking on Pathological Complete Response and Survival in Breast Cancer Patients

Yihao Geng, MM[1]; Qi Zhang, PhD[1]; Zhiqiang Shi, PhD[1]; Zhao Bi, PhD[1]; Yongsheng Wang, PhD[1]; PengFei Qiu, PhD[1]*

[1]Breast Cancer Center, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, 250117, Jinan, Shandong, China

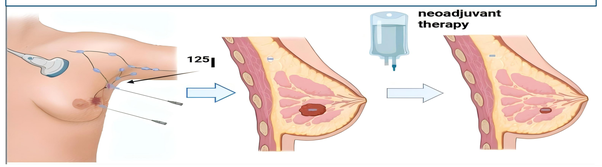
SAN ANTONIO BREAST CANCER SYMPOSIUM
DECEMBER 10–13, 2024
SABCS.ORG

Abstract

Pre-neoadjuvant marking of the primary tumor and biopsy-confirmed metastatic axillary lymph nodes is critical for enabling de-escalation of surgery, facilitating the retrieval of the lesion and assessing treatment response. ^{125}I seeds are commonly used for marking. However, potential radiobiological effects from ^{125}I seeds could confound pathological assessment of treatment response, possibly leading to suboptimal adjuvant therapy decisions and compromised long-term prognosis. In our study, we evaluated the pathological and prognostic impact of ^{125}I seed marking before Neoadjuvant therapy (NAT) and employed peripheral blood profiling to explore immune-related mechanisms.

Introduction

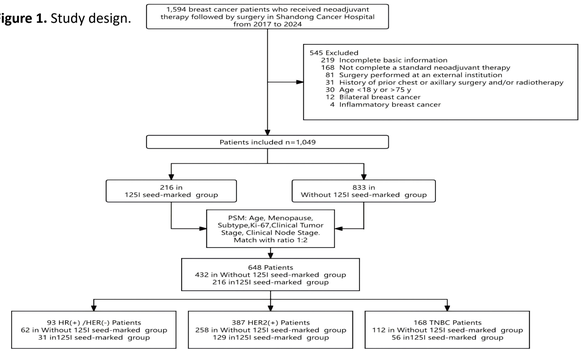
NAT has become the standard treatment for patients with locally advanced breast cancer and stage II–III HER2-positive (HER2+) or triple-negative breast cancer (TNBC)(1, 2). It is critical to accurately mark the primary breast tumor and positive axillary lymph nodes (ALN) prior to NAT, as it not only ensures precise surgical excision but also guides axillary downstaging and guarantees reliable lesion retrieval for pathological evaluation(3). However, there is a lack of consensus regarding the optimal methods and materials for accurate marking(4). Traditional marking techniques are associated with a localization failure rate of approximately 10%, In contrast, the use of ^{125}I seeds (with a radiation dose for ^{125}I seed application of 0.1–0.3 mCi) has significantly improved localization accuracy(5). Nevertheless, owing to its radioactive properties, concerns have been raised regarding the potential impact of ^{125}I seed marking on the assessment of the pathological complete response (pCR) after NAT(6),Moreover, whether this influence on pCR could lead to suboptimal adjuvant treatment decisions and potentially compromise long-term oncological outcomes remains unclear.



Methods and Materials

We conducted a retrospective analysis of 1,594 $cT_{1-4}N_{1-3}M0$ breast cancer patients who received NAT treatment at Shandong Cancer Hospital and Institute during 2017 to 2024. 216 patients with and 432 without 125I seed marking were included after a 1:2 propensity score match. The primary endpoint was pCR; the secondary was invasive disease-free survival (iDFS). To investigate immune modulation, peripheral blood samples from TNBC patients were collected at baseline as well as after second NAT cycle for flow cytometry ($CD3^+/CD4^+/CD8^+/CD16^+/CD19^+$)

Figure 1. Study design.



Results

The ^{125}I marked group achieved significantly higher pCR rates than the without ^{125}I seed marked group: total pCR (55% vs. 46%, P=0.030), breast pCR (63% vs. 53%, P=0.016), and axillary pCR (71% vs. 60%, P=0.009). Subgroup analyses highlighted the greatest benefits in TNBC (tpCR:59% vs. 39%, P=0.033) and hormone receptor-positive/HER2-negative (HR+/HER2−) subtypes (tpCR:26% vs. 8%, P=0.028). After a median follow-up of 36.7 months, 50 iDFS events were recorded.The ^{125}I marked group achieved significantly higher pCR rates than the without ^{125}I seed marked group: total pCR (55% vs. 46%, P=0.030), breast pCR (63% vs. 53%, P=0.016),axillary pCR (71% vs. 60%, P=0.009).

Subgroup analyses highlighted the greatest benefits in TNBC (tpCR:59% vs. 39%, P=0.033) and hormone receptor-positive/HER2-negative (HR+/HER2−) subtypes (tpCR:26% vs. 8%, P=0.028). After a median follow-up of 36.7 months, 50 iDFS events were recorded. the 3-year iDFS was significantly higher in the ^{125}I seed marked group (96% vs. 90%; P = 0.018). Kaplan-Meier survival analysis based on pCR achievement showed that patients achieved pCR in both groups had a lower risk of recurrence compared to non-pCR patients (^{125}I seed marked group: 99% vs. 83%, P = 0.003; without ^{125}I seed marked group: 96% vs. 85%, P = 0.021).Importantly, within the pCR patients, Both groups exhibited similarly favorable prognosis, regardless of ^{125}I seed marked (99% vs. 96%, P = 0.875).Flow cytometry showed increased $CD8^+$ T cells and $CD16^+$ NK cells, and reduced $CD4^+$ T cells in ^{125}I marked patients.

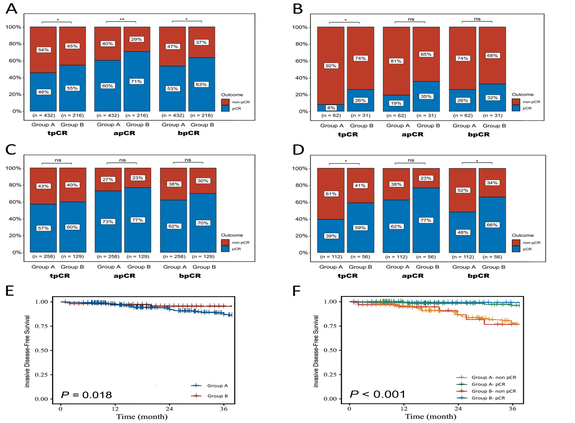


Figure 2: Impact of ^{125}I seed marking on neoadjuvant therapeutic efficacy and postoperative disease recurrence..
A: Intergroup differences in pCR rates among the overall population. B: HR+/HER2-subgroup. C: HER2+ subgroup. D: TNBC subgroup. E: The impact of ^{125}I seed marking on the 3-year iDFS in the overall population. F: Kaplan-Meier curves of 3-year iDFS stratified by ^{125}I seed marking status and pCR status.
Group A=without ^{125}I seed-marked group. Group B=^{125}I seed-marked group
*:p<0.05; **:p<0.01; ***:p<0.001; NS: No statistically significant difference

Figure 3 Flow cytometry.
A: Preliminary results of flow cytometry in different immune cell subsets. B: Baseline CD3+ flow cytometry results in the ^{125}I seed marking group. C: CD3+ flow cytometry results during treatment in the ^{125}I seed marking group. D: Baseline CD3+ flow cytometry results in the without ^{125}I seed marking group. E: CD3+ flow cytometry results during treatment in the without ^{125}I seed marking group.

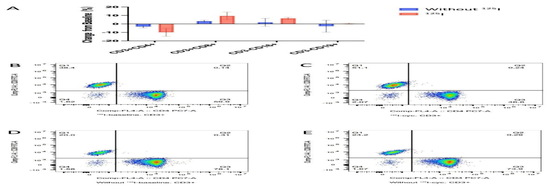


Table 1. Partial Results: Baseline Characteristics of Patients Before and After Propensity Score Matching (PSM)^{125}I seed marking group.

Characteristic	Before PSM Group A# (N=833)	Group B# (N=216)	*P value*	After PSM Group A# (N = 4 3 2)	Group B# (N=216)	*P value*
Histopathologic type			*0.100*			*0.604*
Ductal	805(96.64)	214(99.07)		430(99.54)	214(99.07)	
Lobular or mixed	12(1.44)	2(0.93)		2(0.46)	2(0.93)	
Other	16(1.92)	0(0)		0(0)	0(0)	
Ki-67						
<20%	106(12.73)	11(5.09)	*0.001**	21(4.86)	11(5.09)	*0.999*
⩾20%	727(87.27)	205(94.91)		411(95.14)	205(94.91)	
Clinical T stage at presentation			*<0.001**			*0.906*
T1	117(14.05)	48(22.22)		86(19.91)	48(22.22)	
T2	532(63.87)	146(67.59)		298(68.98)	146(67.59)	
T3	95(11.40)	17(7.87)		38(8.80)	17(7.87)	
T4	89(10.68)	5(2.32)		10(2.32)	5(2.32)	
Clinical N stage at presentation			*0.007**			*0.616*
N0	75(9.00)	26(12.04)		47(10.88)	26(12.04)	
N1	550(66.03)	158(73.15)		303(70.14)	158(73.15)	
N2	135(16.21)	25(11.57)		63(14.58)	25(11.57)	
N3	73(8.76)	7(3.24)		19(4.40)	7(3.24)	
Subtype						
HR+/HER2−	316(37.94)	31(14.35)	*<0.001**	70(16.20)	31(14.35)	*0.086*
HER2+	339(40.70)	129(59.72)		219(50.69)	129(59.72)	
TNBC	178(21.36)	56(25.93)		143(33.10)	56(25.93)	
Breast Surgery						
Mastectomy	612(73.47)	164(75.93)	*0.463*	330 (76.39)	164(75.93)	*0.857*
Breast-conserving surgery (BCS)	221 (26.53)	52(24.07)		101 (23.61)	52(24.07)	
Axillary Surgery						
SLNB	330(39.62)	90(41.67)	*0.583*	173(40.05)	90(41.67)	*0.692*
ALND	503(60.38)	126(58.33)		259(59.95)	126(58.33)	
Radiotherapy						
Yes	347 (41.66)	79(36.57)	*0.175*	169 (39.12)	79(36.57)	*0.529*
No	486 (58.34)	137 (63.43)		263 (60.88)	137 (63.43)	

Conclusions

^{125}I seed marking before NAT improves pCR rates, especially in TNBC and HR+/HER2−subtypes. As pCR is strongly associated with improved iDFS, this increase in pCR likely translates into survival benefit. Flow cytometry suggests that localized radiation at the ^{125}I seed marking may promote $CD4^+$ T cell trafficking and Treg exhaustion, thereby enhancing effector and cytotoxic immune responses. These findings support the immunologic relevance of seed localization and provide a rationale for future immunotherapy combinations.

Contact

<Pengfei Qiu>
<Shandong cancer Hospital>
Email: qiu.pf@outlook.com
Website:
Phone: +053162626215

References

1. Tamirisa N, Hunt KK. Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline. Ann Surg Oncol. 2022;29(3):1489-92.
2. Leon-Ferre RA, Hieken TJ, Boughey JC. The Landmark Series: Neoadjuvant Chemotherapy for Triple-Negative and HER2-Positive Breast Cancer. Ann Surg Oncol. 2021;28(4):2111-9.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 3.2025. Plymouth Meeting (PA): National Comprehensive Cancer Network; 2025.
4. de Wild SR, Koppert LB, van Nijnatten TJA, Kooreman LFS, Vrancken Peeters M, Smidt ML, et al. Systematic review of targeted axillary dissection in node-positive breast cancer treated with neoadjuvant systemic therapy: variation in type of marker and timing of placement. Br J Surg. 2024;111(3).
5. Banys-Paluchowski M, Hartmann S, Ditsch N, de Boniface J, Gentilini OD, Stickeler E, et al. Comparison of marking techniques for target lymph nodes in 2,596 patients with node-positive breast cancer treated with neoadjuvant chemotherapy: Results from the prospective multicenter AXSANA/EUBREAST-03/AGO-B-053 study (NCT04373655). Journal of Clinical Oncology. 2025;43(16_suppl):503-.
6. Fan QD, Bi Z, Gong LG, Chen P, Cong BB, Qiu PF, et al. The feasibility of targeted axillary dissection for breast cancer axillary surgery de-escalation after neoadjuvant therapy: A prospective cohort study. Int J Surg. 2024.

This presentation is the intellectual property of the author/presenter. Contact them at <<qiu.pf@outlook.com>> for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com