Radiotherapy Patterns of Care in Patients with Nodal Micrometastases: A Secondary Subgroup Analysis of SWOG 1007

Jose G. Bazan, MD MS[1]; Allison Meisner PhD[2]; Kevin Kalinsky, MD, MS[3]; Eileen Connolly, MD PhD[4]; William E. Barlow, PhD[5]; Wendy Woodward, MD PhD[6]; Alastair Thompson, MD[7]; Danika Lew, MA[2]; Priyanka Sharma, MD[8]; Lajos Pusztai, MD Dphil[9]; Reshma Jagsi, MD DPhil[3]

[1]City of Hope Comprehensive Cancer Center; [2]Fred Hutchinson Cancer Center; [3]Emory University; [4]Columbia University; [5]University of Washington; [6]MD Anderson Cancer Center; [7]Baylor College of Medicine, [8]University of Kansas; [9]Yale University

Abstract

Background: Little is known about regional nodal irradiation patterns of care or cancer control outcomes in patients with pN1mi disease. Here, we report patterns of care of RT use in patients with pN1mi disease that enrolled on SWOG 1007 (RxPonder).

Materials and Methods: We used prospectively collected RT forms to classify patients into 1 of 4 groups: 1) no RT, 2) Breast/Chestwall + Axillary RT; 3) Breast/Chestwall RT alone; 4) RNI

Results: We identified 573 patients with pN1mi disease and RT forms. Overall RNI use was 15%, 29% no RT (75% of patients treated with mastectomy), 10% breast/Chestwall+Axillary RT, 47% breast/Chestwall only.

Conclusion: Significant de-escalation of RT occurred in patients treated with pN1mi disease with only 15% receiving RNI and 75% of mastectomy patients not receiving any radiation. The impact of this de-escalation on cancer control outcomes is ongoing.

Introduction

- Comprehensive regional nodal irradiation (RNI) after either breast conserving surgery or mastectomy remains a standard of care for the majority of patients with breast cancer and axillary nodal ***macrometastases***
- For patients with nodal ***micrometastases (pN1mi)***, the benefit of RNI is less clear since these patients were not included on the historical randomized trials
- The Southwest Oncology Group 1007 (S1007) trial included hormone receptor-positive /human epidermal growth factor receptor 2 negative (HR+/HER2-) patients with pN1mi disease
- While RT use was not directed by the protocol, data on radiation therapy (RT) use and targets was prospectively collected
- Here, we report the patterns of care of RT use in patients with pN1mi disease on S1007

Figure 1. CONSORT Diagram

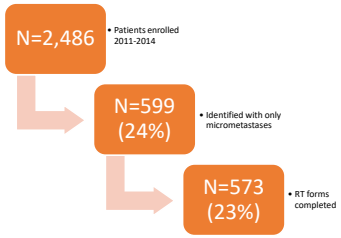


Table 1: Pt Characteristics	
Type of Surgery	
Lumpectomy	371 (65%)
Mastectomy	202 (35%)
Menopausal Status	
Premenopausal	192 (34%)
Postmenopausal	381 (66%)
Number of Positive Nodes	
1	500 (87%)
2-3	73 (13%)
Tumor Size, median (IQR)	1.7 cm (1.2-2.4 cm)
Lymphovascular Invasion	118 (21%)
Multifocal/Multicentric	104 (18%)
Grade	
1	152 (27%)
2	353 (62%)
3	54 (9%)
Unknown	14 (2%)
Histology	
ILC	72 (13%)
Mixed IDC/ILC	18 (3%)
IDC	483 (84%)
Received Chemotherapy	226 (39%)
Oncotype RS, median (IQR)	15 (11-19)

Methods and Materials

- We reviewed the pathology repots of all patients enrolled on S1007 from 2011-2014, prior to an amendment that excluded enrollment of patients with pN1mi disease
- We identified patients with only pN1mi disease
- We used the RT forms captured during the study to classify patients into 1 of 4 groups:
  - 1) No RT delivered
  - 2) Breast/Chestwall + Axillary RT
  - 3) Breast/Chestwall only RT
  - 4) RNI
- RNI was defined as inclusion of at least a supraclavicular (SCL) field
- Axillary RT was deinfed as directed irradiation to level I and/or level II axilla without treatment of the SCL region
- The analysis is primarily descriptive with use of chi-square test or t-test to compare groups
- We also fit a multivariate logistic regression model to estimate the odds ratio (OR) for the associations of individual factors with RNI vs. other or no RT

Table 2: RT Delivery	
No Radiation	**163 (29%)**
Lumpectomy	15 (4%)
Mastectomy	148 (73%)
Breast/CW+Low Axilla	**59 (10%)**
Lumpectomy	52 (14%)
Mastectomy	7 (4%)
Breast/CW Only	**267 (47%)**
Lumpectomy	252 (68%)
Mastectomy	15 (7)
RNI	**84 (15%)**
Lumpectomy	52 (14%)
Mastectomy	32 (16%)

Table 3: Logistic Regression for RNI	Odds Ratio (95% CI), p-value	Adjust OR (95% CI), p-value
Post-menopausal v Pre-menopausal	0.84 (0.52-1.36), p=0.48	
Mastectomy vs. Lumpectomy	1.16 (0.72-1.86), p=0.55	
2-3 nodes+ vs. 1 node+	**2.36 (1.31-4.22), p=0.004**	**2.34 (1.29-4.24), p=0.005**
Grade 3 vs. Grade 1-2/Unk	0.86 (0.37-1.96), p=0.71	
Lymphovascular Invasion (Y vs. N)	1.80 (1.07-3.03), p=0.03	1.63 (0.96-2.77), p=0.07
Multifocal/centric vs. Unifocal	0.80 (0.43-1.51), p=0.49	
Pure ILC vs. Other	1.06 (0.53-2.10), p=0.87	
T2-3 vs. T1	**1.98 (1.24-3.16), p=0.004**	**1.93 (1.20-3.11), p=0.007**
Chemotherapy (yes vs. no)	0.88 (0.55-1.42), p=0.61	
Oncotype RS (continuous)	0.98 (0.94-1.03), p=0.41	

Results

- Amongst 2,486 patients enrolled prior to the 2014 amendment, we identified 599 patients (24%) with only pN1mi disease
- Of these 599 patients, **573** patients had RT forms available for review (Figure 1)
- The majority of patients were postmenopausal (66%), most had undergone breast conserving surgery (65%) [**Table 1**]
- The median number of axillary nodes removed was 3 (IQR, 2-6) and 87% had disease limited to 1 node (**Table 1**)
- The median Oncotype DX score was 15 (IQR, 11-19) and <40% of patients received chemotherapy (**Table 1**)
- The overall distribution of RT use was **(Table 2):**
  - 1) No RT: 29%
  - 2) Breast/Chestwall+Axillary RT: 10%
  - 3) Breast/Chestwall RT alone: 47%
  - 4) **RNI: 15%**
- In particular, ***no patients received RT to the axilla alone without treatment of the breast/chestwall***
- Omission of RT was significantly more frequent in patients treated with mastectomy compared to breast conserving surgery: 73% (148/202) vs. 4% (15/371), p<0.001
- Rates of RNI use were similar between patients that had undergone mastectomy compared to breast conserving surgery: 15.8% vs. 14.0% (p=0.56)
- **Table 3** shows the results of the multivariate analysis of factors associated with the use of RNI versus other or no RT
  - **>1+ node vs. 1+ node**: OR=2.34 (95% CI, 1.29-4.24, p=0.005)
  - **T2-3 tumors vs. T1**: OR=1.93 (95% CI, 1.20-3.11, p=0.007)

Conclusions

- We characterized RT patterns of care in a large cohort of patients with pN1mi disease who were enrolled onS1007
- Nearly 75% of all patients that underwent mastectomy did not receive RT and only 15% of all patients received RNI suggesting significant de-escalation of RT in these patients
- These variations in practice patterns should encourage enrollment of patients with pN1mi disease onto the ongoing TAILOR RT trial
- Analysis of cancer control outcomes is ongoing

Contact

Jose G. Bazan, MD MS
Department of Radiation Oncology
City of Hope Comprehensive Cancer Center
Email: jbazan@coh.org
Phone: 614-517-0775

Funding

NIH/NCI/NCTN grants U10CA180888, U10CA180819

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