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Axillary Lymph Node Coverage in Breast Cancer Patients Treated with Adjuvant Radiation Using High Tangent Fields Technique: A Single Institution's Experience

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ABSTRACT

Background: The high tangent field (HTF) technique is used to provide radiation coverage of the inferior axillary nodal levels for breast cancer patients when the lower axilla is at risk for micrometastatic disease. Despite its use in clinical practice, there is concern about whether HTF provide sufficient coverage of level I and II axillary nodal regions. The purpose of this study is to quantify and evaluate the coverage of HTF at our institution.

Methods: Patients diagnosed with early invasive breast carcinoma (pT1-2 pN0-1a) who received HTF radiation between January 1st, 2012, and December 31st, 2016 were retrospectively reviewed. Level I and II axillary nodal regions were contoured on each patient's simulation CT. Dosimetric parameters were re-calculated to evaluate coverage. Statistical analysis was conducted using Mann-Whitney-U method.

Results: Thirty-seven patients with low-risk breast adenocarcinoma were included. For level I and II, the mean V90% was 94.63% ± 7.60% and 73.33% ± 21.83% respectively. Twenty-nine patients received adequate V90% coverage of level I and had a mean level II V90% of 76% ± 18.71% while eight patients who did not receive adequate V90% level I coverage had a mean level II V90% of 63.64% ± 30.22%. The median level II V90% of patients receiving adequate and inadequate level I V90% was 77.74% and 71.11% respectively; the difference was not statistically significant ($P = 0.33$).

Conclusion: HTF provides adequate coverage for level I nodes, but inadequate coverage for level II. Contouring nodal volumes may assist field placement and improve nodal volume coverage.

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INTRODUCTION

Breast cancer remains the most common cancer diagnosed in women, accounting for 25% of new cases in Canada and a 13% mortality-rate.[1] Research in the last three decades has undoubtedly contributed to early detection, improved clinical outcomes, and decreased morbidity for patients. Locoregional management of early invasive disease has typically involved breast-conserving surgery followed by postoperative radiotherapy (RT) as a mainstay of treatment; however, management of the axilla has

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undergone considerable change in recent years. Regional lymph node management has evolved significantly since the integration of sentinel lymph-node biopsy (SLNB) into standard practice for investigating clinically negative axillae: this has resulted in fewer unnecessary surgeries with axillary lymph-node dissection (ALND) and consequently decreased treatment-related morbidity.[2] The Z0011 trial demonstrated that SLNB alone compared to ALND did not result in decreased survival in patients with limited nodal disease.[3-5] The AMAROS trial compared ALND to adjuvant axillary RT following a positive SLNB and confirmed that both provided equal and excellent axillary control and RT resulted in lower treatment-associated morbidity.[6] Thus, adjuvant regional nodal irradiation (RNI) is often employed to treat patients with limited nodal involvement after SLNB. Comprehensive adjuvant RNI conventionally employed a 4-field technique, which includes the standard pair of tangential fields and opposing anterior and posterior supraclavicular fields, in order to cover axillary lymph node levels, I, II, and III, internal mammary nodes, as well as the supraclavicular lymph node region. Newer techniques include intensity modulated radiation therapy (IMRT) or volumetric arc radiation therapy (VMAT).

Despite the decreased morbidity of RNI when compared to axillary lymph node dissection, radiation oncologists have aimed to reduce the potential of treatment-associated toxicities, and some use the high tangent technique in clinical scenarios where there is potential risk of nodal involvement. Currently, guidelines for the treatment of early-stage breast cancer report the inclusion of full RNI is often at the discretion of the treating radiation oncologist.[7] Compared to the 2-field standard tangential fields (STF), high tangent fields (HTF) have the superior border raised within 2 cm of the humeral head.[8-10] The HTF technique was developed with adjustments to the posterior borders using 3D planning, resulting in what is now referred to as modified-high tangent fields (mHTF).[9-12] The aim of HTF and mHTF is to limit radiation toxicity compared to comprehensive RNI whilst simultaneously providing coverage of the inferior axillary nodal levels (levels I and II). Studies have found that while mHTF increases incidental doses to the ipsilateral lung, the risk of treatment-associated morbidity, such as radiation pneumonitis, remains low.[12] Recent surveys still suggest significant practice variation in terms of radiation field design for breast cancer patients with a clinically node-negative axilla and 1-3 positive sentinel lymph nodes (SLNs) and no ALND.[13,14.]

In the era of 3D CT-based radiotherapy planning, concerns have been raised about the adequacy of axillary lymph node level I and II coverage using HTF. Some studies have found that HTF provides sufficient coverage of level I and II axillary nodal regions, while others have found it to be inadequate.[8,10,12,15] Despite the lack of consensus in the literature, the mHTF technique has been informally integrated into clinical practice at our institution. Currently, the mHTF technique is utilized when only the lower axilla is likely to be at the greatest risk of harboring microscopic disease, and when the comprehensive RNI is thought to result in overtreatment. This judgement is made at the discretion of the treating oncologist; for example, a commonly considered clinical scenario is micrometastatic nodal involvement. There may be situations where the risk of nodal involvement is present but lower than cases with definite indications such as clinically node positive disease. Given the uncertainty of mHTF axillary coverage, this study aims to quantify and evaluate the coverage of the HTF technique at our institution.

METHODS

Patient Recruitment

In this case-series study, women diagnosed with early invasive breast carcinoma between January 1st, 2012, and December 31st, 2016 at our institution were identified through a Data Access Request. Patients with staging pT1-2 N0(i+), pT1-2N1(mic) or pT1-2N1a and pT1-2NX who received adjuvant radiation therapy using a high tangent technique, who had no evidence of distant metastasis, and were 18 years of age at diagnosis were included. Cases were confirmed to be treated with the high tangent technique by confirming they were planned to use a 2-field technique with the superior anatomic boundary up to the level of the humeral head.

Contouring and Dose Assessment

Radiation CT simulation scans of patients who met the inclusion criteria for the study were retrospectively reviewed. Level I and level II axillary nodal regions were then contoured on CT stimulation scans by a single radiation oncologist; nodal volumes were contoured as per RTOG contouring guideline using Eclipse (Varian Medical Systems) software. The radiation oncologist responsible for contouring the nodal volumes was blinded to the treating oncologist, patient identifiers, and the field borders previously used for treatment. Contoured volumes were then reviewed by a separate radiation oncologist.

Dosimetric parameters were evaluated using the original treatment fields by the mHTF technique, including the minimum, maximum, and doses to axillary levels I and II based on the retrospective nodal contours, as well as the incidental doses to the heart and ipsilateral lung. Adequate coverage of an axillary level was defined as 90% or more of the volume of the said level receiving 90% or more of the prescribed radiation dose (V90 ≥ 90%). An adequate dose was defined as receiving at least 90% (D90) and 95% (D95) of the prescribed radiation dose. Patients were stratified based on having received adequate coverage of an axillary nodal region, which we defined as V90% > 90% or V95% > 95%.

Statistical Analyses

Data analysis was conducted using Excel. Descriptive statistics were performed. A Mann-Whitney-U test was used to compare differences in coverage of axillary level II for patients receiving adequate coverage of level; alpha was set at 0.05.

For Descriptive statistics we used frequency and percent to report qualitative variables and to report quantitative one we used mean and standard deviation or median with inter-quartile range

RESULTS

Patient Demographics

A total of 37 patients with low-risk breast adenocarcinoma were identified as receiving radiotherapy with the high tangent technique. Twenty-eight patients received 42.5 Gray (Gy) in 16 fractions, five patients received 40.0 Gy in 16 fractions, while two patients received 50.0 Gy in 25 fractions and two patients received 50.4 Gy in 28 fractions. Patient characteristics are summarized in Table 1, with the majority (62.2%) being pT1. Figure 1 demonstrates axillary nodal volume contouring.

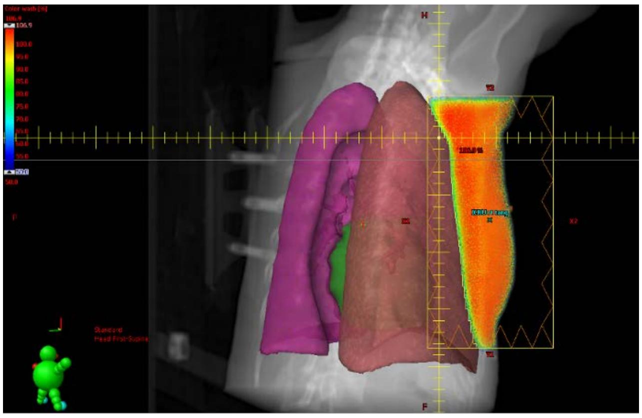

Figure 1. Example of axillary nodal volume contouring using the high tangent technique. Nodal volumes were contoured as per RTOG contouring guideline using Eclipse (Varian Medical Systems) software.

Table 1. Demographic and pathologic characteristics

Age (years)		Regional lymph nodes (N)	
Mean	65.1 (SD ± 10.3)	pN0	8 (21.6%)
Median	67 (IQR 12.7)	i+	6 (16.2%)
Range	44 - 85	pN1	27 (73.0%)
Mean BMI (kg/m^2)	28.4	mic	21 (56.8%)
Menopausal status		a	6 (16.2%)
Pre-	3 (8.1%)	pNX	2 (5.4%)
Peri-	2 (5.4%)	Distant metastasis	0
Post-	32 (86.5%)	Extranodal extension	
Focality		No	29 (78.4%)
Single	34 (91.9%)	Yes	6 (16.2%)
Multifocal	3 (8.1%)	Not assessed	2 (5.4%)
Primary histology		Lymphovascular invasion	
Ductal	31 (83.8%)	No	22 (59.5%)
Lobular	3 (8.1%)	Yes	13 (35.1%)
Mucinous	2 (5.4%)	Not assessed	2 (5.4%)
Ductal + Papillary	1 (2.7%)	Estrogen receptor status	
Tumour differentiation grade		Positive	31 (83.8%)
Grade 1	5 (13.5%)	Negative	6 (16.2%)
Grade 2	21 (56.8%)	Progesterone receptor status	
Grade 3	11 (29.7%)	Positive	29 (78.4%)
Margins		Negative	8 (21.6%)
Negative (>2 mm)	24 (64.9%)	HER-2 receptor status	
Close (≤2 mm)	9 (24.3%)	Positive	6 (16.2%)
Positive	4 (10.8%)	Equivocal	1 (2.7%)
		Negative	30 (81.1%)

Dosimetric Analysis

For Level I, the D95 was 3451 ± 1092 cGy and the D90 was 3873 ± 720 cGy which were both higher than the D95 and the D90 for Level II were 2258 ± 1505 cGy and 2596 ± 1484 cGy, respectively (Table 2). This was also seen in the mean dose delivered to Level I axilla which was 4145 ± 309 cGy, higher than the mean dose of 3687 ± 578 cGy delivered to Level II axilla (Table 2).

Volumetric Analysis

The mean V95% for Level I was 86.93% ± 13.82% and the mean V90 was 94.63% ± 7.60% which were both considerably greater than the V95% and V90% measured for Level 2 at 55.11% ± 25.85% and 73.33% ± 21.83% respectively. Similar volumetric measures were also conducted for the two main organs at risk: the ipsilateral lung and heart. For all patients, the mean V20 to the ipsilateral lung was 16.65% ± 4.68%. Of note, twenty-one of the thirty-seven patients evaluated had left-sided breast cancer and received incidental radiation to the heart with a mean V25% of 5.16% ± 3.77%. Table 2 describes the dosimetric parameters of axillary coverage for Level II. Ten patients had adequate V90% coverage of Level II with a mean V90% of 97.06% ± 3.57% while twenty-seven patients did not, with a mean V90% of 64.54% ± 18.93%. When stratifying patients based on Level II V95%, only one patient had sufficient coverage with a mean V95% of 99.57% and the remaining thirty-six patients who had inadequate coverage of Level II V95% had a mean V95% of 53.88% ± 25.09%.

Axillary coverage was stratified by nodal level and V95% and V90% (Table 3). Of those who received adequate V90 coverage to Level I axilla, more than half also received adequate V95% coverage of the Level II axilla. Of those receiving adequate V95% coverage, the mean Level II V95% was 68.31% ± 19.90%, while the mean Level II V95% for the twenty-two patients who received inadequate coverage was 46.11% ± 25.93%. The median Level II V95% for patients receiving adequate and inadequate coverage of Level I was 73.93% and 43.13% respectively; the difference in median coverage was statistically significant ($P < 0.01$). Few patients (n=9) had adequate coverage of Level II axilla but conversely inadequate Level I coverage with a V90 of 71.11%, and the difference was not statistically significant ($P = 0.33$).

Table 3. V90% coverage of axillary level I stratified by level II coverage

V90% Coverage of Level I	Mean Level II V90%	SD
≥ 90% (n = 29)	76.00%	18.71%
< 90% (n = 8)	63.64%	30.22%
Mann-Whitney Statistic	U = 89.5	p = .33

DISCUSSION

Radiotherapy volumes must carefully be considered to reduce locoregional recurrence risk of breast cancer while balancing treatment-related toxicity. Comprehensive RNI uses a 4-field radiation technique, which includes two tangent fields as well as two opposing anterior and posterior supraclavicular fields. However, comprehensive RNI carries the risk of significant toxicity such as chronic lymphedema in the range of 7-15% for most patients.[16,17] For many patients with no or limited nodal disease, the highest risk of regional nodal recurrence would be around the adjacent level I and II axilla. Standard tangent radiotherapy fields partially cover the axilla, and HTF has been used to possibly improve this coverage. However, there is inconsistent literature on whether such techniques provide sufficient coverage of the region.

This study shows that in the era of field-based planning, the HTF provides adequate coverage for level I nodes, but inadequate coverage for Level II. A previous study evaluated nodal irradiation to axillary lymph node levels and similarly found Level I was adequately covered in most cases.[8] When nodal volumes are specifically contoured, it appears that coverage of both level I and II nodal regions do improve. In a more modern series where nodal volumes were specifically contoured; it was found that mHTF adequately covered axillary levels I and II.[12] This would be expected as field placement would then take into account the specific target delineation. However, there are multiple studies which report inadequate coverage specifically even when volumes are contoured. For example, one study evaluated the percentage prescribed radiation dose to the axillary region for normal tangential fields versus HTF and found that while HTF increased the doses achieved in the axillary region, the average doses were below 90% of the prescribed dose.[10] Another study found similarly that high tangent fields did not sufficiently cover Level I and II axillary levels.[15] Further, a study which utilized the same field design as the AMAROS trial to assess axillary lymph node coverage with HTF found that adequate coverage of level II was not achieved.[16] Thus, even when nodal volumes are contoured, differences in planning technique and contouring style lead to inconsistent coverage of Level II axillary nodes alone.

For level I nodes, the mean V90% was 94.6%, signifying acceptable baseline dose coverage, and this finding appears to be reproducible and consistent with existing literature that suggests mean V90% coverage of level I to range between 90 to 99% in multiple studies.[12,19] This result does exceed findings by studies which reported inadequate coverage.[10,15,18] However, these studies vary in their contouring of level I axilla and based conclusions on different metrics such as D90 and D95 coverage.

Our results do identify there is a modest drop in the mean V95% to 86.9%, and this may suggest

Table 2. Dosimetric parameters for level I and II axillary lymph nodes.

Parameter	All patients	Level I V95% coverage		Level I V90% coverage		Level II V95% coverage		Level II V90% coverage	
	(n=37)	≥95% (n=15)	<95% (n=22)	≥90% (n=29)	<90% (n=8)	≥95% (n=1)	<95% (n=36)	≥90% (n=29	<90% (n=8)
Level I									
Mean dose (cGy)	4145 ± 309	4206 ± 245	4103 ± 346	4228 ± 279	3841 ± 214	3871	4152 ± 310	4131 ± 125	4150 ± 356
V95%	86.93% ± 13.82%	98.00% ± 1.74%	79.38% ±13.35%	91.10% ± 11.61%	71.80% ± 10.45%	79.88%	87.12% ± 13.96%	93.32% ± 7.87%	84.56% ± 14.88%
V90%	94.63% ± 7.60%	99.66% ± 0.86%	91.20% ± 8.26%	97.74% ± 3.29%	83.35% ± 8.29%	86.92%	94.84% ± 7.60%	96.76% ± 4.95%	93.84% ± 8.32%
D95% (cGy)	3451 ± 1092	4077 ± 244	3025 ± 1239	3916 ±450	1767 ± 1091	1277	3512 ± 1043	3581 ± 901	3404 ± 1167
D90% (cGy)	3873 ± 720	4113 ± 244	3710 ± 883	4125 ± 266	2961 ± 1080	3437	3885 ± 726	3993 ± 226	3829 ± 832
Level II									
Mean dose (cGy)	3687 ± 578	3825 ± 411	3593 ± 662	3776 ± 453	3366 ± 866	4173	3673 ± 581	4131 ± 73	3522 ± 598
V95%	55.11% ± 25.85%	68.31% ± 19.90%	46.11% ± 25.93%	57.68% ± 24.07%	45.79% ± 31.25%	99.57%	53.88% ± 25.09%	85.18% ± 7.57%	43.97% ± 20.71%
V90%	73.33% ± 21.83%	83.49% ± 17.36%	66.40% ± 22.17%	76.00% ± 18.71%	63.64% ± 30.22%	100.00%	72.59% ± 21.66%	97.06% ± 3.57%	64.54% ± 18.93%
D95% (cGy)	2258 ± 1505	2676 ± 1563	1972 ± 1429	2330 ± 1491	1996 ± 1630	4094	2206 ± 1493	3851 ± 167	1667 ± 1337
D90% (cGy)	2596 ± 1484	2912 ± 1450	2380 ± 1501	2666 ± 1427	2340 ± 1759	4112	2553 ± 1483	3958 ± 98	2091 ± 1438

inconsistent dose coverage and variance depending on patient anatomy. Depending on institutional policies, axillary volumes may not be regularly contoured and this difference in coverage may pose a detriment towards treatment efficacy. Varying radiotherapy techniques also appear to affect the metrics of dose coverage. For example, the use of CT planning or MLC modulation can improve V95% coverage.[15] Field-in-field techniques also improve the dose homogeneity compared to simple 3D conformal technique (3DCRT) alone.[20] At our institution, we use a tangent technique with various dynamic MLC modulation techniques, and more recently, a forward planned intensity modulated radiotherapy technique. These techniques are newer and more advanced than those used in prior studies which identified poor axillary coverage, as their treatments likely used a 3DCRT technique alone.

Regardless of treatment modifying techniques, however, our study consistently shows inadequate coverage of the level II axilla, ultimately attributed to the anatomic limitations of a field based HTF in the absence of nodal contouring.

CONCLUSION

This study reports that HTF technique can provide reasonable coverage of level I axillary nodes and helps support its use in select breast cancer cases where there may be low risk of axillary nodal involvement and may benefit from treatment of the low axilla, but not to the entire regional nodes. HTF is also associated with relatively low doses to the lungs and heart organs at risk. The results of this study also emphasize that level II axilla is not adequately covered and is therefore not appropriate treatment for the mid to distal axilla. Axillary nodal coverage may be improved by contouring the nodal volumes to aid in the placement of high tangents to ensure adequate coverage. These results complement a growing body of literature which suggests adequate coverage of lower axillary nodal volumes when using HTF fields. Further research and prospective evidence would be required to ultimately define the role and indications for HTF.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL CONSIDERATIONS

None.

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