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Is Tangential Beam Breast Radiotherapy Sufficient for Adequate Dosimetric Coverage of Axillary Lymph Node Level I, II and III in Indian Scenario? A Single Institutional Study

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Abstract

Breast cancer is a globally prevalent malignancy, with an annual incidence of approximately 579,100 cases and causing around 270,000 deaths. In India, the Indian Council of Medical Research (ICMR) reports an annual diagnosis rate of 13.5% for Carcinoma Breast cases. Managing breast carcinoma involves surgery, radiotherapy, chemotherapy, endocrine therapy, or a combination of these interventions, influenced by various prognostic factors. Axillary surgery plays a pivotal role in breast cancer prognosis, with the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial impacting surgical approaches. The After Mapping of the Axilla: Radiotherapy or Surgery (AMAROS) trial explored alternatives, revealing non-inferiority of axillary radiation with reduced morbidity.

In modern radiotherapy, tangential beam breast radiotherapy offers enhanced target structure coverage, including axillary lymph nodes, while minimizing exposure to critical organs. This study assesses dose distribution and coverage of axillary lymph nodes (level I, II, and III) and organs at risk through tangential field breast/chest wall radiotherapy. Utilizing the Radiation Therapy Oncology Group (RTOG) guidelines and CT-based treatment planning, the study provides a comprehensive evaluation of clinical target volumes. The outcomes are discussed in the context of patient somatotype and radiotherapy techniques, emphasizing the potential benefits of tangential beam breast radiotherapy in optimizing treatment outcomes.

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Introduction

Breast cancer stands as one of the globally prevalent malignancies, witnessing an annual incidence of approximately 579,100 cases and causing approximately 270,000 deaths each year [1]. In India, the Indian Council of Medical Research (ICMR) reports that around 13.5% of Carcinoma Breast cases are diagnosed annually [2]. The multifaceted management of breast carcinoma poses a significant challenge encompassing surgery, radiotherapy, chemotherapy, endocrine therapy or a combination of these interventions. The selection of localized or systematic therapies hinges upon several prognostic and predictive factors including tumor pathology, breast carcinoma histology, axillary lymphatic nodal status, ER/PR status, Her2 scoring, multi-gene testing, presence of metastatic disease, patient comorbidities, age, and menstrual status [3].

Axillary surgery plays a pivotal role in breast cancer prognosis, with randomized trials revealing its significance in reducing local recurrence and potentially enhancing survival rates [4]. Sentinel lymph node biopsy has emerged as an advancement, prompting debate regarding the role of axillary dissection, especially in cases of micrometastatic involvement where systemic therapy and whole breast irradiation may obviate the need for systematic axillary lymph node dissection [5]. However, comprehensive axillary lymph node coverage through radiotherapy techniques is imperative to avoid such dissection. Sentinel lymph node biopsy has become the standard surgical evaluation for the axilla in clinically node-negative breast cancer cases, and subsequent management decisions are made based on pathological reports [6].

The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial has significantly influenced the surgical approach to the axilla in early breast cancer patients, proving comparable locoregional control and survival between patients undergoing Axillary Lymph Node Dissection

(ALND) and those treated with Sentinel Lymph Node Dissection (SLND) alone [7]. The After Mapping of the Axilla: Radiotherapy or Surgery (AMAROS) trial explored an alternative approach, randomizing patients with positive sentinel lymph nodes to ALND or axillary radiation therapy, revealing non-inferiority of axillary radiation with reduced morbidity [8].

In the context of modern radiotherapy techniques, tangential beam breast radiotherapy has appeared as a promising approach, providing enhanced coverage of target structures, including axillary lymph nodes, while minimizing exposure to critical organs such as the lungs, heart, and contralateral breast [9]. Studies have explored the coverage and dose distribution for axillary lymph nodes using standard or high tangential fields, with outcomes indicating dependence on patient somatotype and radiotherapy techniques [10].

This study evaluates the dose distribution and coverage of axillary lymph nodes (level I, II, and III) and organs at risk (ipsilateral lung and heart in left-sided breast cancer) through tangential field breast/ chest wall radiotherapy. The contours are based on the Radiation Therapy Oncology Group (RTOG) guidelines, using a CT-based treatment planning approach for precise delineation of clinical target volumes.

Material and Method

Patient characteristics

This prospective study was conducted over a one-year period at a single center. The study included 50 patients diagnosed with early-stage breast cancer, who had undergone either Breast Conservative Surgery or Modified Radical Mastectomy and were subsequently initiated on Adjuvant Radiotherapy from 2019 to 2021 as shown in Flow chart 1 and Figure 1. Participants were recruited from the Cancer Research Institute OPD after obtaining written informed consent and ethical clearance from the institution's ethics committee.

Inclusion criteria

Patients with early-stage breast cancer, ECOG PS 0 and I, aged 18 or older, histopathologically confirmed breast carcinoma, and indication for adjuvant radiotherapy post-surgery were considered for inclusion.

Exclusion criteria

Patients with a history of previous treatment for any other malignancy, locally advanced breast cancer, evidence of distant metastasis, concomitant morbid conditions preventing radiotherapy use, major medical or psychiatric illnesses interfering with radiotherapy completion or follow-up, blood urea and serum creatinine higher than twice the normal value, liver function tests more than twice the normal value, and active untreated infections were excluded.

CT Planning and Study Design

Patients underwent contrast-enhanced CT scans and radiotherapy treatment after providing informed written consent. The positioning for breast treatment involved indexing the breast board on the flat CT-simulator table. Patients were positioned supine, with the chest wall parallel to the table, immobilized using a thermoplastic cast, and arms positioned above the head as shown in Figure 2. During CT simulation, the breast and lumpectomy scar were outlined with a radio-opaque wire. CT data was transferred to the treatment planning system (Oncentra), and clinical target volumes and organs at risk were delineated following RTOG contouring guidelines.

Whole breast Radiation: Clinical Target Volume was remaining breast after surgery.

Chest Wall Radiation: The target volume includes the ipsilateral chest wall, mastectomy scar and drainage sites.

Delineation of organs at risk including lung, heart and contra lateral breast was done.

The prescribed dose of 50 Gy was delivered in 25 fractions.

Definition of Axillary Nodal Volumes

Axillary nodal volumes (Level I, II, and III) were contoured using CT data, with specific definitions for each level. Level I, lateral to the pectoralis minor muscle, extending superiorly to the axillary vein; Level II, between the medial and lateral borders of the pectoralis minor muscle, extending superiorly to the axillary vein; and Level III, the area between the fourth and fifth thoracic ribs. Contouring was performed by a radiation oncologist and reviewed by an expert

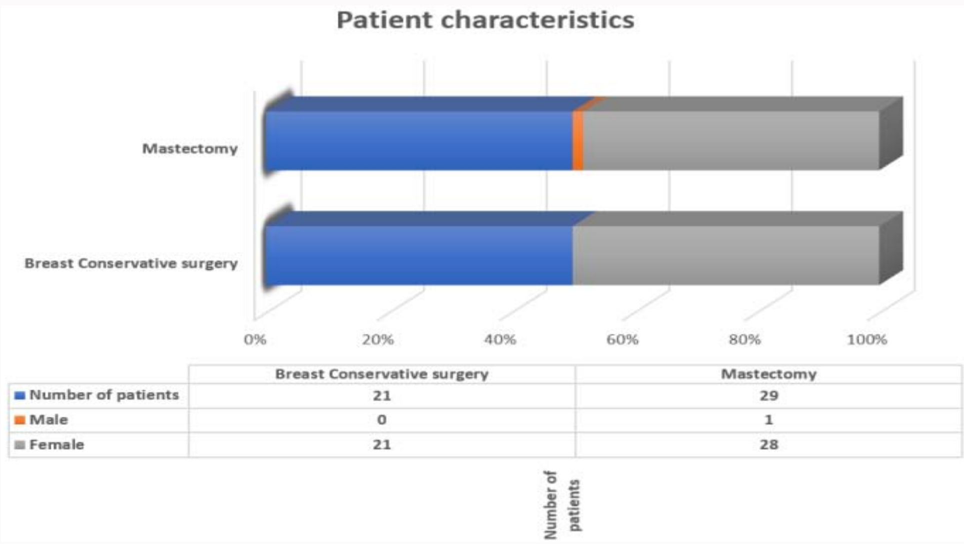
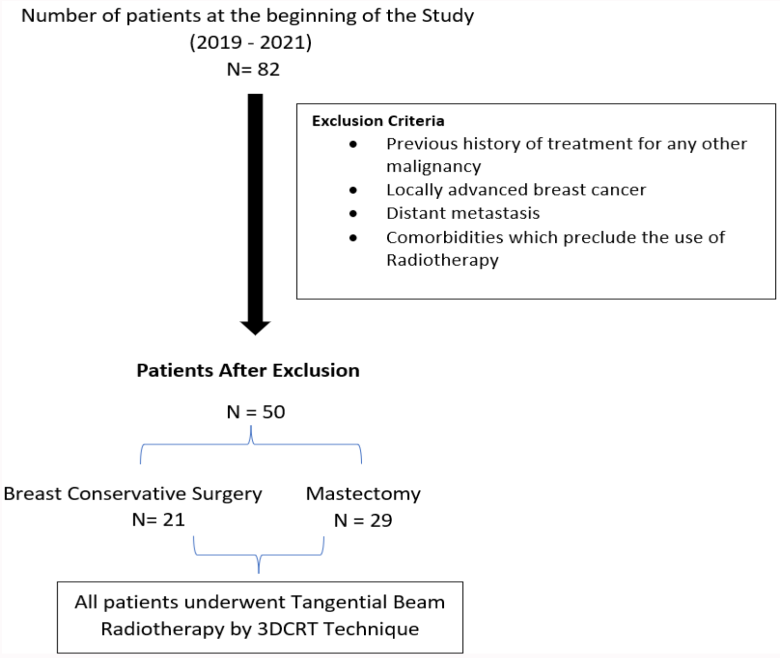


Figure 1: Representing characteristics of the patient in the study population (n=30).



Flow chart 1: Showing patient characteristics of the study.

radiologist.

- **6. Contouring the axillary Lymph Nodes According to RTOG Contouring Guidelines as shown in Figure 3Axillary lymph node level I**

Contouring axillary level, I is challenging as there are a paucity of vessels to follow. Identify where the pectoralis major muscle inserts onto the chest wall (usually around the fourth/fifth rib). Identify the $4^{th}/5^{th}$ rib as it exits off the thoracic vertebral body and follow it to the mid-axillary line in order to mark the caudal extent of level I. Include SLNB scarring and or clips. Contour this space as you scroll cranially including any medial vessels or nodes.

- **Axillary lymph node level II**

This nodal region essentially follows the axillary vessels where it first crosses the lateral edge of the pectoralis minor muscle to when it finally passes the medial edge of the pectoralis minor muscle. The pectoralis minor muscle should be included within the contour such that the contour extends to the inner surface of the pectoralis major muscle to include Rotter's nodes which are located between pectoralis major and pectoralis minor muscles.

- **Axillary lymph node level III**

Axillary level III essentially follows the superior part of the axillary vein as it passes the medial edge of pectoralis minor and then continues as the subclavian vein past the first rib. The medial limit is clavicle and the junction between the subclavian and internal jugular veins. Subclavian vein is located caudal to the artery. The cranial border includes the artery and connects to the caudal limit of the supraclavicular (sometimes called axillary level IV) CTV.

Statistical Analyses

Dose-Volume Histograms were utilized to calculate doses to various regions. Parameters such as mean dose, doses to specific volumes (e.g., *D*95% and *D*50%), and percentages of volumes receiving prescribed doses were calculated for breast, tumor bed, axillary levels, and organs at risk. Statistical comparisons between patients who underwent Modified Radical Mastectomy and Breast Conservative Surgery were performed, with a significance level set at $p<0.005$.

Results

Mean CLD was 1.89 cm (range 1.26–2.7 cm) and mean breast volume was 580 cm^3. All plans had adequate coverage to the breast and chest wall respectively, defined as 95% of the breast volume receiving at least 95% of the prescribed dose. As shown in Table 1 the doses received by 95% volume of the level I axillary lymph node was 46.6 Gy and 48.2 Gy in patients who had undergone breast conservative surgery and MRM respectively. Similarly, the dose received by 95% volume of axillary lymph node level II was 44.12 Gy and 46.21 Gy in patients who had undergone breast conservative surgery and MRM respectively and the dose received by 95% volume of axillary lymph node level III was 44.41 Gy and 46.21 Gy in patients who had undergone breast conservative surgery and MRM respectively. The dose and volume results are summarized in Table 1. There was no significant difference in axillary lymph node coverage between patients who had undergone breast conservative surgery or mastectomy. The mean dose received by ipsilateral lung was 9.10 Gy and 9.38 Gy respectively in patients who had undergone breast conservative surgery and mastectomy. Patients who had left sided breast cancer, mean dose to heart was analyzed. Mean dose to heart was 4.12 Gy and 5.81 Gy in patients who had undergone breast conservative surgery and mastectomy respectively. There was no significant statistical discrepancy in mean dose to OARs in patients who had undergone Breast conservative surgery and Mastectomy.

Discussion

Breast cancer is one of the most frequently diagnosed cancers globally and is the leading cause of cancer related death in women [11]. Breast carcinoma has been ranked number one cancer among Indian

Table 1: Shows dosimetric values for the tangential fields of axillary lymph nodes level I, II and III and OARs in patients undergoing breast conservative surgery and MRM respectively.

Structure	Parameter	3DCRT (BCS)	3DCRT (MRM)
Axillary Lymph node Level I	Mean Dose	48.68 ± 0.2	49.3 ± 1.2
	Dose received by 95% volume level I axillary Lymph node	46.6 ± 1.1	48.2 ± 1.4
Axillary Lymph node Level II	Mean Dose	46.23 ± 2.1	47.2 ± 1.32
	Dose received by 95% volume level II axillary Lymph node	44.12 ± 1.5	46.21 ± 1.5
Axillary Lymph node Level III	Mean Dose	45.23 + 1.6	46.12 + 2.1
	Dose received by 95% volume level III axillary Lymph node	44.41 + 1.2	46.21 + 1.6
Lung	Mean Dose	9.10 ± 1.31	9.38 ± 1.25
	V20	16.21 ± 1.29	18.21 ± 1.53
	V10	21 ± 1.56	23 ± 1.23
	V5	32 ± 1.76	33 ± 1.22
Heart (Left sided Breast Tumors)	Mean Dose	4.12 ± 1.43	4.81 ± 1.23
	V30	1.04 ± 1.32	1.07 ± 1.1

Figure 2: Representing patient position on CT Simulation with arms abducted and neck turned to opposite side. Breast Surgery scar is labelled by a radio opaque copper wire.

females with the age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women [2]. The choice of treatment modality depends on several prognostic and predictive factors which include tumor histology, clinical and pathological characteristics of the primary tumor, axillary lymph node status, tumor ER/PR status, HER2 status, comorbidities, patient's age and menopausal status [3].

Surgical dissection of the axilla is a vital procedure and is thought to be the most important prognostic tool in breast cancer [12]. The axillary surgery is important in decreasing local recurrence and potentially, improving survival [13]. Various randomized trials have shown that in clinically lymph node-negative patients who are treated with total mastectomy without axillary dissection or RT, experiences a 19% axillary failure rate. In contrast, those patients who are clinically lymph node-negative undergoing axillary dissection without axillary Radiotherapy experiences axillary recurrence rates of 2% [14]. With the recent advancement of Sentinel lymph node biopsy, role of axillary dissection has come to a point of debate, as it has been observed that in patients with micro metastatic involvement of the SLN, systematic ALND is not systematically recommended when patients receive systemic therapy and whole breast irradiation [15]. However, for the avoidance of axillary lymph node dissection in such cases, an absolute need of adequate coverage of axillary lymph nodes by radiotherapy techniques is required.

In the treatment planning of carcinoma breast, planning and implementation of radiotherapy must be optimal due to adjacent important structures such as lungs, heart and contra lateral breast. Hence, various contouring guidelines, such as RTOG, ESTRO etc., have been proposed for the accurate delineation of the target volumes and nodal clinical target volume including axillary levels I, II and III. Tony Mathew et al. conducted a study which compared the consistency of ESTRO and RTOG guidelines and concluded that with respect to axillary lymph node delineation, RTOG guidelines prove efficient in delineating axillary lymph node level I, II and III [16]. In our study all the axillary lymph nodes (level I, II and III) were contoured using the RTOG contouring guidelines which were well within the defined anatomical boundaries, which is in concordance with the study conducted by Tony Mathew et al.

Locoregional cancer control represents a crucial facet of breast cancer treatment and holds the potential to enhance survival outcomes in specific patient subgroups. However, the formidable challenge of uncontrolled axillary recurrence persists, presenting a dilemma as the removal of axillary nodes remains a primary contributor to locoregional morbidity. Striking a balance to minimize

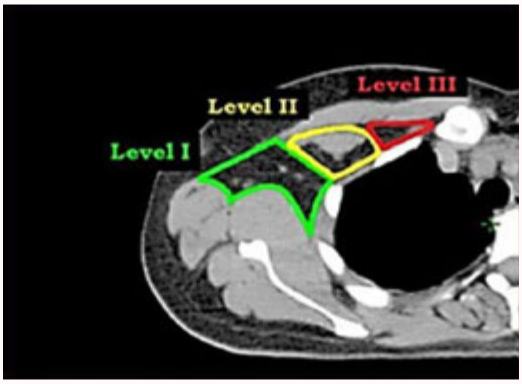


Figure 3: Showing contouring boundaries of axillary lymph node level I, II and III according to RTOG contouring guideline.

morbidity without compromising outcomes becomes paramount in the contemporary landscape of early-stage breast cancer therapy, where trimodality therapy (surgery, radiotherapy, chemotherapy and hormonal) is the norm, delivering excellent long-term results.

Amid efforts to decrease therapy-related morbidity while upholding the established efficacy of traditional treatments, a noticeable trend emerges in reducing the extent of surgical therapy for the axilla. This reduction corresponds with a positive decline in axillary morbidity, marking a progressive shift. Axillary surgery, a vital diagnostic procedure and considered the foremost prognostic tool in early-stage breast cancer, plays a pivotal role in predicting patient outcomes and guiding therapeutic decisions. The presence or absence, along with the number, of metastatic axillary lymph nodes becomes a critical determinant, influencing local recurrence rates and potentially improving overall survival outcomes.

The therapeutic significance of axillary lymph node dissection finds support in the National Surgical Adjuvant Breast Project (NSABP) B-04 study, revealing a substantial axillary failure rate of 19% in clinical lymph node-negative patients treated with total mastectomy without axillary dissection or radiotherapy [17]. In contrast, those undergoing axillary dissection without concurrent axillary radiotherapy experienced markedly lower axillary recurrence rates, reinforcing the therapeutic role of axillary lymph node dissection.

The ongoing American College of Surgeons Oncology Group (ACSOG) trial Z-0011 represents a notable endeavor to discern the necessity of axillary dissection in patients with positive sentinel nodes undergoing breast-conserving therapy. The trial randomizes women with clinically axillary lymph node negative T1 or T2 breast cancer and positive sentinel lymph nodes to complete axillary dissection versus no further surgery [18]. All patients receive standard breast tangent radiotherapy, underlining the importance of regional lymph node considerations.

Despite the promise of innovative approaches such as sentinel lymph node mapping, concerns persist regarding the inadvertent irradiation of axillary lymph nodes in standard breast tangent fields. Clinical trials, including the ACSOG Z-0011 trial, necessitate careful interpretation, recognizing the potential impact of breast tangent radiotherapy on regional recurrence [18]. The quest for optimal treatment strategies continues, with a focus on reducing morbidity while preserving the efficacy of traditional therapies.

Recent advancements in treatment planning, including high tangential beam breast radiotherapy, aim to enhance coverage and minimize complications [19]. Studies evaluating the adequacy of standard breast tangent fields in covering axillary lymph nodes have uncovered disparities, emphasizing the importance of individualized treatment planning.

Beyond immediate concerns related to axillary surgery and radiotherapy, the broader landscape of breast cancer therapy demands a nuanced understanding of locoregional cancer control. Optimal locoregional cancer control has the potential to significantly improve survival outcomes in specific subgroups [20]. However, the challenge of uncontrolled axillary recurrence necessitates a delicate balance between therapeutic benefits and the morbidity associated with axillary node dissection.

Emphasizing the importance of trimodality therapy, which integrates surgery, radiotherapy, chemotherapy and hormonal interventions, the evolving landscape strives to achieve excellent long-term outcomes while minimizing morbidity. As surgical therapy for the axilla decreases, signaling a positive trend, the corresponding decline in axillary morbidity aligns with the overarching goal of improving patient well-being.

Therefore, in the present study, we evaluated the dose distribution and coverage of axillary lymph node levels I, II and III using the tangential beam radiotherapy. The doses received by 95% volume of the level I axillary lymph node was 46.6 Gy and 48.2 Gy in patients who had undergone breast conservative surgery and MRM respectively. Similarly, the dose received by 95% volume of axillary lymph node level II was 44.12 Gy and 46.21 Gy in patients who had undergone breast conservative surgery and MRM respectively and the dose received by 95% volume of axillary lymph node level III was 44.41 Gy and 46.21 Gy in patients who had undergone breast conservative surgery and MRM respectively. There was no significant difference in axillary lymph node coverage between patients who had undergone breast conservative surgery or mastectomy. The mean dose received by ipsilateral lung was 9.10 Gy and 9.38 Gy respectively in patients who had undergone breast conservative surgery and mastectomy. Patients who had left sided breast cancer, mean dose to heart was analyzed. Mean dose to heart was 4.12 Gy and 5.81 Gy in patients who had undergone breast conservative surgery and mastectomy respectively. There was no significant statistical discrepancy in mean dose to OARs in patients who had undergone breast conservative surgery and mastectomy.

Conclusion

This prospective study was conducted to analyze the adequacy of Tangential beam breast radiotherapy in terms of axillary lymph nodal coverage to level one, two and three, contoured using RTOG guidelines and to analyze the dosimetric coverage of organs at risk, with the intention to study if there is a need for high tangential beam radiotherapy in Indian population or if Tangential beam breast radiotherapy provides adequate coverage to the defined structures. Despite varied breast contour, chest wall convexity and axillary vein routes, dosimetric and volumetric coverage in Indian population, Tangential Beam Breast Radiotherapy showed adequate coverage of axillary lymph nodes level one and two using with minimal dose to organs at risk.

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