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Clinical Investigation: Breast Cancer

Radiation Field Design and Patterns of Locoregional Recurrence Following Definitive Radiotherapy for Breast Cancer

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Summary

Radiotherapy promotes locoregional control and improves survival in breast cancer patients. To determine the relationship between locoregional recurrence and radiotherapy field design and dose, we fused radiotherapy planning computed tomography (CT) images and dose delivered to the initial primary breast cancer with positron emission tomography (PET)-CT images identifying subsequent locoregional recurrence. In our study, most locoregional recurrences occurred in areas not adequately covered by the prescribed radiation dose for the primary breast cancer.

Purpose: Locoregional control is associated with breast cancer-specific and overall survival in select women with breast cancer. Although several patient, tumor, and treatment characteristics have been shown to contribute to locoregional recurrence (LRR), studies evaluating factors related to radiotherapy (XRT) technique have been limited. We investigated the relationship between LRR location and XRT fields and dose delivered to the primary breast cancer in women experiencing subsequent locoregional relapse.

Methods and Materials: We identified 21 women who were previously treated definitively with surgery and XRT for breast cancer. All patients developed biopsy-result proven LRR and presented to Emory University Hospital between 2004 and 2010 for treatment. Computed tomography (CT) simulation scans with XRT dose files for the initial breast cancer were fused with ^{18}F-labeled fluorodeoxyglucose positron emission tomography (FDG PET)/CT images in DICOM (Digital Imaging and Communications in Medicine) format identifying the LRR. Each LRR was categorized as in-field, defined as $\geq$95% of the LRR volume receiving $\geq$95% of the prescribed whole-breast dose; marginal, defined as LRR at the field edge and/or not receiving $\geq$95% of the prescribed dose to $\geq$95% of the volume; or out-of-field, that is, LRR intentionally not treated with the original XRT plan.

Results: Of the 24 identified LRRs (3 patients experienced two LRRs), 3 were in-field, 9 were marginal, and 12 were out-of-field. Two of the 3 in-field LRRs were marginal misses of the additional boost XRT dose. Out-of-field LRRs consisted of six supraclavicular and six internal mammary nodal recurrences.

Conclusions: Most LRRs in our study occurred in areas not fully covered by the prescribed XRT dose or were purposely excluded from the original XRT fields. Our data suggest that XRT technique, field design, and dose play a critical role in preventing LRR in women with breast cancer.

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Introduction

Advances in systemic therapy have led to significantly lower rates of distant metastasis and improved overall survival (OS) in women with breast cancer. Due to the relatively lower risk of distant recurrence seen in patients treated with modern therapies, locoregional recurrence (LRR) has emerged as an important predictor of breast cancer-specific and OS even in the setting of early stage, node-negative disease (1).

Various tumor, patient, and treatment factors are known to predict for LRR. Tumor characteristics associated with higher rates of LRR include high-grade histology results, angiolymphatic invasion, and triple-negative or HER2-positive receptor status (2, 3). Positive nodes and extranodal extension have also been predictive of LRR following mastectomy (4). Examples of patient characteristics contributing to LRR include young age and African American race (5). Treatment factors associated with higher rates of local control include surgical margins greater than 1 or 2 mm (3, 6) and systemic treatment with chemotherapy, trastuzumab, and endocrine therapy, when indicated (7). Several studies have also alluded to the importance of radiation therapy (XRT) technique in preventing LRR, but research thoroughly evaluating the influence of XRT field design and dose on LRR is limited. In fact, previous publications have focused more on total dose delivered (eg, boost dose) rather than actual field design (8).

In the modern era, computed tomography (CT)-based planning has been used to individualize treatment and tailor XRT treatment fields to encompass the breast and draining lymphatics while minimizing dose to the heart, lungs, and spinal cord. Three-dimensional planning has also enabled more accurate demarcation of the lumpectomy cavity at depth rather than relying solely on the surgical scar at the skin's surface (9). Furthermore, the Radiation Therapy Oncology Group (RTOG) breast contouring atlas has assisted radiation oncologists by establishing guidelines for contouring nodal volumes at risk and normal tissue structures that should be avoided during XRT (10). Collectively, these advances in technology have the potential to improve local control rates by optimizing dose coverage of the breast and draining lymph nodes. Moreover, while the importance of XRT technique in preventing LRR has previously been established in other malignancies such as cervical and head and neck cancers (11, 12), no study has systematically examined the importance of XRT field design with modern imaging modalities and treatment planning in preventing LRR in breast cancer patients.

We examined a group of breast cancer patients who received definitive postoperative radiation therapy and subsequently developed LRR, treated at Emory University. We systematically evaluated the influence of XRT treatment technique, both field design and dose, on local control by superimposing the ^{18}F-labeled fluorodeoxyglucose positron emission tomography (FDG PET)/CT-detected local recurrence on the original XRT treatment plan for the initial breast cancer diagnosis. Our goal was to determine whether XRT technique might play a role in preventing LRR.

Methods and Materials

After obtaining institutional review board approval, we reviewed the records of 791 breast cancer patients and identified 35 women with LRR treated at Emory University between 2004 and 2010. Of these 35 patients, 21 had CT simulation scans with dose files available from their initial treatment as well as [^{18}F]FDG PET/CT scans confirming subsequent LRR in DICOM (Digital Imaging and Communications in Medicine) format. Alignment of these images was needed to clearly depict the relationship between LRR location and planned XRT dose. Patient, tumor, and treatment characteristics were obtained from the medical records of each patient.

Evaluation and treatment of the original breast cancer

Patient median age at initial breast cancer diagnosis was 52 years (range, 29-76 years). Twelve women were postmenopausal; 61% of patients were African American. Other tumor and treatment characteristics are listed in Table 1. All women were initially evaluated with mammograms and ultrasonograms to determine primary tumor location and axillary lymph node status. All patients received definitive surgery (lumpectomy [n = 10] or mastectomy [n = 11]) with lymph node assessment (sentinel lymph node biopsy or axillary lymph node dissection) and definitive XRT with or without systemic therapy, as determined by the treating medical oncologist. Among the 21 patients who

Table 1 Tumor characteristics at initial diagnosis

Characteristic	No. (%)
Tumor laterality	
Right	6 (29%)
Left	15 (71%)
T stage	
DCIS	2 (10%)
T1	2 (10%)
T2	7 (33%)
T3	7 (33%)
T4	3 (14%)
N stage	
N0	8 (38%)
N1	9 (43%)
N2	3 (14%)
N3	1 (5%)
Tumor location	
Central	1 (5%)
Upper inner	8 (38%)
Lower inner	3 (14%)
Upper outer	4 (29%)
Lower outer	1 (5%)
Not recorded	2 (9%)
Lymphovascular space invasion	
Yes	4 (19%)
No	17 (81%)
Extracapsular extension	
Yes	1 (5%)
No	21 (95%)
Biologic subtype	
ER/PR$^+$, HER2$^-$	6 (29%)
ER/PR/HER2$^+$	2 (9%)
ER/PR/HER$^-$	11 (52%)
ER/PR$^-$, HER2$^+$	2 (9%)

Abbreviations: DCIS = ductal carcinoma in situ; ER = Estrogen Receptor; PR = Progesterone Receptor.