Breast Cancer: Biology or Stage?

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A 44-year-old woman was found to have 2 groups of calcifications within the left breast on routine screening mammogram: one at 2 o’clock measuring 28 mm and a second at 3 o’clock measuring 40 mm. Follow-up diagnostic mammogram confirmed multiple groups of pleomorphic calcifications spanning >7 cm in the upper outer quadrant. Stereotactic core needle biopsy noted invasive carcinoma, predominantly lobular type, grade 2, estrogen receptor positive (Allred 8), progesterone receptor positive (Allred 8), HER2 negative (0) at the 2 o’clock site; and ductal carcinoma in situ without invasion at 3 o’clock. Mastectomy with sentinel lymph node biopsy revealed 2 sites of invasive disease. The first was a

Fig. 1. (A) Left breast mammogram. (B) Invasive ductal carcinoma, 20× magnification. (C) Classic-type invasive lobular carcinoma, 20× magnification.

Conflict of interest: none.
14 mm, grade 3, pleomorphic invasive lobular carcinoma at 2 o’clock; the second was a morphologically distinct 19 mm, grade 3, invasive ductal carcinoma, estrogen receptor positive (Allred 7), progesterone receptor positive (Allred 7), HER2 negative (2+, fluorescence in situ hybridization negative) at 3 o’clock. There was no lymphovascular invasion, and negative margins were obtained. Sentinel lymph node biopsy noted isolated tumor cells (approximately 15) in 1 of 2 sentinel lymph nodes examined. Five additional negative nonsentinel nodes were noted in the mastectomy specimen. OncotypeDx score for the 2 invasive lesions returned at 11 and 45, respectively. Given the high OncotypeDx score for the invasive ductal carcinoma, TAC chemotherapy was recommended. The patient completed a total of 6 cycles.

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This patient (1) meets none of the classic criteria for postmastectomy radiation therapy as her disease burden is relatively low. In a similar early-stage patient cohort, retrospective series have suggested a risk of locoregional recurrence <5% (2).

However, it is increasingly clear that tumor biology plays a significant role in the risk of locoregional recurrence, and randomized data suggest that patients with biologically aggressive disease may derive greater benefit from postmastectomy and regional nodal irradiation. In a node-negative, estrogen receptor–positive patient, the Oncotype (Genomic Health, Redwood City, CA, US) score has similarly been linked to risk of recurrence (3). Though event rates are small and confidence intervals wide, patients undergoing mastectomy with a high-risk Oncotype had a 16.8% risk of locoregional recurrence at 10 years, with the highest risk estimates noted in women aged <50 years.

Although the data are not robust enough for a strong recommendation and patient preferences will be critical, the risk of recurrence may be higher than stage alone would suggest and a course of postmastectomy radiation therapy for risk reduction could be considered. The same rationale could be applied to consideration of regional nodal treatment, but in this patient with upper outer quadrant tumors, the unclear benefit must be weighed against the increased risk of lymphedema. In contrast, provided the mean heart dose is <2 Gy, the long-term risk from chest wall treatment in a patient without reconstruction should be minimal. I would target the chest wall alone and, with no nodal radiation therapy planned, would deliver a hypofractionated schedule of 40 Gy in 15 fractions (4).

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References


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PMRT: Please Mind Randomized Trials

A 44-year-old woman with 2 synchronous left upper—outer quadrant high-grade estrogen receptor (ER)–positive, progesterone receptor–positive, HER2-negative pT1c pN0(i+)(sn) breast cancers undergoes mastectomy and sentinel lymph biopsy, followed by adjuvant chemotherapy for an OncotypeDx (Genomic Health, Redwood City, CA) Recurrence Score (RS) of 45 (1). We estimate her 10-year risk of locoregional relapse (LRR) without postmastectomy radiation therapy (PMRT) to be <6%. In a secondary analysis of National Surgical Adjuvant Breast and Bowel Project B-28, women with ER-positive pN1 breast cancer treated with mastectomy, anthracycline-based chemotherapy, and tamoxifen without PMRT had low rates of mastectomy and sentinel lymph biopsy, followed by adjuvant chemotherapy for an OncotypeDx (Genomic Health, Redwood City, CA) Recurrence Score (RS) of 45 (1). We estimate her 10-year risk of locoregional relapse (LRR) without postmastectomy radiation therapy (PMRT) to be <6%. In a secondary analysis of National Surgical Adjuvant Breast and Bowel Project B-28, women with ER-positive pN1 breast cancer treated with mastectomy, anthracycline-based chemotherapy, and tamoxifen without PMRT had low rates of LRR, regardless of the OncotypeDx RS (2). The 10-year LRR risks for low (RS < 18), intermediate (RS of 18-30), and high (RS > 30) scores were 2.4%, 4.1%, and 6%, respectively, and the OncotypeDx RS was not significantly associated with LRR for these patients (P = .64). Age and tumor grade were not significant predictors of LRR in multivariate analysis.
Despite our patient’s high OncotypeDx RS, her long-term clinically detectable LRR risk without PMRT will not exceed the 6% rate observed in the postmastectomy, pN1, high RS cohort of B-28.

PMRT is not routinely indicated for node-negative patients, as evidenced by the landmark Early Breast Cancer Trialists’ Collaborative Group meta-analysis demonstrating no disease control or survival improvement in this population (3). More recent prospective trial data have suggested certain subsets of pN0 patients may benefit. In European Organisation for Research and Treatment of Cancer 22922, women with node-positive and those with node-negative medial or central breast tumors had a similar disease-free survival advantage from regional nodal irradiation (4). PMRT may also improve outcomes in triple-negative pN0 breast cancer (5). These data, however, do not apply to our patient with upper—outer quadrant ER-positive disease. Our patient does have sentinel lymph node isolated tumor cells (ITCs), but the distinction between pN0(i+ and pN0(i− is clinically insignificant when one is making adjuvant radiation therapy decisions. The MIRROR (Micrometastases and Isolated Tumor Cells: Relevant and Robust or Rubbish?) study showed no difference in breast cancer events for women with ITCs who did not receive axillary irradiation or lymph node dissection (6), and a Harvard retrospective study reported comparably low LRR rates in postmastectomy patients who did and did not have sentinel lymph node ITCs (10-year LRR rates of 2.8% and 3%, respectively) (7).

In summary, our patient has a low risk of LRR despite her high OncotypeDx RS and other disease features. In Europe, she could have been enrolled in the Medical Research Council SUPREMO (Selective Use of Postoperative Radiotherapy After Mastectomy) trial investigating PMRT for pT1N1, pT2N1, and pT2N0 (or multifocal tumor spanning >2 cm) with high-grade or lymphovascular space invasion-positive disease (8). We do not recommend PMRT off of a clinical trial because, to our knowledge, there are no published prospective or randomized data indicating the described patient would benefit.

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References


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