**Oncotype Score and Benefit of Post-Mastectomy Radiotherapy in T1-2 N1 Breast Cancer**

C.R. Goodman,1 B.L.L. Seagle,2 S. Shahabi,2 and J.B. Strauss3;

*1Department of Radiation Oncology, Northwestern University Robert H. Lurie Comprehensive Cancer Center, Chicago, IL, 2Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Department of Radiation Oncology, Northwestern University Feinberg School of Medicine, Chicago, IL*

**Purpose/Objective(s):** Multiple randomized trials have shown that postmastectomy radiotherapy (PMRT) yields improvements in both locoregional control and overall survival for women with T1-2 N1 breast cancer. The value of PMRT in this patient population, however, has been questioned given advances in systemic therapy in the modern era. Additionally, no clinical or pathologic variables have been consistently identified as predictive markers for the benefit of radiotherapy in this population. In this study, Oncotype DX score was evaluated as a predictor of overall survival following PMRT in women with T1-2 N1 breast cancer.

**Materials/Methods:** An observational cohort study was performed on women with T1-2 N1 estrogen receptor (ER)-positive breast cancer identified from the 2004-2014 National Cancer Database who underwent total mastectomy and were evaluated for recurrence risk using the Oncotype DX multigene assay recurrence score (RS). Patients were excluded if they were treated with neoadjuvant chemotherapy or if they did not receive adjuvant endocrine therapy. Logistic regression was used to explore clinicopathological associations with recurrence risk. Kaplan-Meier and multivariable Cox proportional-hazards survival analyses were used to estimate associations of recurrence risk with overall survival using propensity score-adjusted and inverse probability-weighted matched cohorts. **Results:** Of the patients with a documented RS, 52.2% (2729/5224) were low-risk, while 25.4% (n = 1325) and 22.4% (n = 1170) were intermediate-risk and high-risk, respectively. Higher grade, absence of progesterone receptor expression, overexpression of Her2/neu, insurance through Medicare, and lower educational quartile were significantly associated with a high Oncotype score. Oncotype score was an effect modifier of the radiotherapy-survival association (P = 0.02). On matched cohort analysis, low-risk patients who did not receive PMRT had a 2.82- fold increased hazard of death compared to patients who did receive PMRT (CI = 1.65-4.83, P < 0.001). Intermediate-risk and high-risk patients did not derive a significant benefit from PMRT (HR = 0.98, CI Z 0.59-1.62, P = 0.93; HR Z 0.96, CI = 0.60-1.53, P = 0.85, respectively).

**Conclusion:** Improvement in overall survival following PMRT was limited to women with a low RS. Although counterintuitive, this finding harmonizes with subset analyses of seminal trials of PMRT in which women in the most favorable prognostic group derived the largest survival benefit from treatment. Underlying this finding may be the competing risk of distant metastatic disease seen in women with high RS. If prospectively validated, Oncotype RS may be valuable as a predictor of survival benefit of PMRT in women with limited nodal disease.