**Cancer-Specific Outcomes of Hypofractionated Locoregional Radiation Therapy for Patients with Stage I-III Breast Cancer**

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**Purpose/Objective(s):** Hypofractionated (HypoF) radiotherapy (RT) is well established following breast conserving surgery for breast cancer but many centers continue to use conventional fractionation (CF; ≤ 2Gy/day) if regional lymph nodes are included in the target volume. At our institution, HypoF regional nodal RT (15-16 fractions of >2Gy/day) has been used for over 30 years, with published data reporting no additional toxicity. This study evaluated long-term, population-based cancer-specific outcomes of HypoF vs CF for breast/chest wall plus regional nodal RT for patients with breast cancer.

**Materials/Methods:** A prospective provincial database was used to identify 6,247 newly diagnosed patients with Stage I-III breast cancer treated with curative intent breast/chest wall + regional nodal RT from 1998 to 2010. Loco-regional relapse free survival (LRRFS) and distant relapse free survival (DRFS) were compared using Kaplan Meier (KM) analyses of HypoF vs CF, for the entire cohort and for high-risk subgroups: grade 3, ER-negative, HER2+, and ≥4 positive nodes. Multivariable Cox regression analysis (MVA) was performed to assess the effect of RT fractionation on LRRFS.

**Results:** Overall, 70% (4384) received HypoF and 30% (1863) received CF. Median follow up was 12.2 years and was similar between the two groups (HypoF: 12.8 yrs vs CF: 11.2yrs). Patients treated with HypoF were significantly older, more likely to be post-menopausal, HER2+, not receive chemotherapy, and less likely to have Stage III disease. Ten-year outcomes in the HypoF vs CF cohorts were: LRRFS 94.5% vs 94.1% (p=0.91), and DRFS 73.5% vs 74.4%, p=0.31). On subgroup analysis, LRRFS and DRFS were not different between HypoF and CF cohorts with grade 3, ER- , or ≥4 positive nodes (all p>0.05). On MVA, HypoF was not associated with inferior LRRFS compared to CF (HR 1.0, 95% CI 0.9 – 1.1, p=0.996).

**Conclusion:** This large, population-based analysis with long-term follow-up demonstrates that modest hypofractionation provides similar local and distant control outcomes compared to conventional fractionation when the RT volume included the breast/chest wall plus regional lymph nodes. Hypofractionation is an effective alternative for patients with stage I-III breast cancer receiving nodal RT.