**Comparison of 3-D Conformal and Intensity Modulated Radiation Therapy Outcomes for Locally Advanced Non-Small Cell Lung Cancer in NRG Oncology\_RTOG 0617**

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**Purpose/Objective(s):** Intensity modulated radiation therapy (IMRT) is being increasingly used for locally-advanced non-small cell lung cancer (NSCLC) as a measure to improve target coverage and spare toxicity. Outcomes of IMRT compared to 3D-conformal radiation therapy (3D-CRT) for NSCLC have not previously been assessed in a large prospective cooperative group clinical trial.

**Materials/Methods:** A secondary analysis was performed in patients with stage III NSCLC treated with radiation therapy (RT) in RTOG 0617, a randomized phase III comparison of standard-dose (60 Gy) versus high-dose (74 Gy) chemoradiotherapy +/- cetuximab. RT technique was one of three pre-specified stratification factors. Pre-treatment factors and dosimetric parameters were compared between RT techniques after adjusting for RT dose levels and cetuximab usage. The prognostic value of RT technique with respect to toxicity and efficacy was assessed through multivariate logistic regression and Cox proportional hazards model after controlling for RT dose level, cetuximab use and other prognostic factors.

**Results:** Among the 482 eligible patients treated with RT, 53% and 47% were treated with 3D-CRT and IMRT, respectively. The IMRT group had more stage IIIB (38.6 vs. 30.3%, P = 0.056), larger PTVs (mean, 486 vs. 427 mL, P = 0.005), and larger PTV:lung ratio (mean, 0.15 vs. 0.13, P = 0.013). For a given PTV volume, IMRT was associated with lower lung V20 (P = 0.08), and lower heart doses (V5, V20, and V40) than 3D-CRT. IMRT was associated with a 2-fold lower rate (3.5 versus 7.9%) of Grade 3+ pneumonitis (P = 0.0653). The relative reduction of lung V20 with IMRT was exchanged for significantly larger amounts of low dose (V5) delivered to the lung (62% versus 55%, P < 0.0001). The lung V20 was predictive of grade 3+ pneumonitis, while the lung V5 and mean lung doses were not. Larger heart V40 was associated with worse OS (HR = 1.013, P < 0.001), and the heart V40 was significantly lower in patients treated with IMRT. Patients treated with IMRT were also more likely (37 versus 29%) to receive full doses of consolidative chemotherapy (P = 0.05). OS and PFS were similar between IMRT and 3D-CRT.

**Conclusion:** Although IMRT was used to treat larger and less favorable tumors in RTOG 0617, it was associated with reduced risk of severe pneumonitis and an improved likelihood to receive full doses of consolidative chemotherapy. Lung V20, but not V5, was predictive of severe pneumonitis. The heart V40, shown to be highly prognostic for survival, can be substantially reduced with IMRT compared to 3D-CRT.