**Survival Comparison of 3 Versus 4-5 Fractions for Stereotactic Body Radiation Therapy in Stage I Non-Small Cell Lung Cancer**

*H.S.M. Park, C.D. Corso, C.E. Rutter, A.W. Kim, J.B. Yu, Z.A. Husain, and R.H. Decker*

**Purpose/Objective(s):** The optimal dose-fractionation regimen for stereotactic body radiation therapy (SBRT) in the treatment of stage I non-small cell lung cancer (NSCLC) is controversial. RTOG 0236 initially established the standard-of-care as 60 Gy in 3 fractions (54 Gy in 3 fractions with heterogeneity corrections); however, alternative regimens of 48-50 Gy in 4-5 fractions are being used with increasing frequency, as they have been proposed to be safer and equally effective. This study aimed to compare overall survival (OS) between these two SBRT dose-fractionation regimens in a large national database.

**Materials/Methods:** Using the National Cancer Data Base, we identified clinical stage I NSCLC patients diagnosed in 2003-2011 who were treated with SBRT with 54-60 Gy in 3 fractions (“3fx”) or 48-50 Gy in 4-5 fractions (“4-5fx”). Patients who underwent definitive surgical resection or had any previous diagnoses of cancer were excluded. The chi-square test and multivariable logistic regression were used to identify predictors of 4-5fx utilization. Analysis of OS was planned using the log-rank test, Cox proportional hazards regression (or stratified analysis if the proportional hazards assumption is violated), and propensity score-matched analysis.

**Results:** A total of 5 600 patients were included in this analysis, of whom 2 756 (49.2%) received 3fx, and 2 844 (50.8%) received 4-5fx. The median biologically effective dose assuming a/b = 10 was 180 Gy for 3fx (range, 151.2-180.0 Gy) and 105.6 Gy for 4-5 fx (range, 100.0-112.5 Gy). The median age was 75 years, and T2 disease was present in 1 154 patients (20.6%). Compared to those receiving 3fx, patients receiving 4-5fx were significantly more likely to have T2 versus T1 disease (OR 1.76, 95% CI Z 1.53e2.01, P < .001) and be diagnosed in 2009-2011 versus 2003-2008 (OR 2.51, 95% CI = 2.22-2.85, P < .001). Patients receiving 4-5fx were observed to have lower OS than those receiving 3fx (median 35.1 vs 37.8 months, log-rank P = .003). Schoenfeld residuals showed that the proportional hazards assumption was violated, and therefore, Cox regression could not be performed. After stratification by tumor size and diagnosis year; however, dose-fractionation regimen was no longer associated with OS in any subset. Propensity score-matched analysis also showed no significant OS difference between 4-5fx and 3fx (median 37.9 vs 37.2 months, log-rank P = .090).

**Conclusion:** Based on a large national cohort, our adjusted analyses sug- gest that NSCLC SBRT patients receiving 48-50 Gy in 4-5 fractions achieve similar overall survival compared to those receiving 54-60 Gy in 3 fractions despite a lower biologically effective dose. Further research is needed to evaluate the impact of alternative dose-fractionation regimens on

SBRT outcomes, including local control, distant control, and toxicities.