Overall survival (OS) for both groups was similar; median OS for PET-only patients was 26.8 months compared with 22.4 months in PET-plus-invasive mediastinal staging ($P = .28$). Both groups had similar rates of local recurrence-free survival (82.5% vs 89.6%), regional recurrence-free survival (89.5% vs 81.9%), and distant recurrence-free survival (78.2% vs 85.6%).

Neither pretreatment staging method was predictive of OS or recurrence-free survival. Regression analysis showed that staging method type, prior cancer, age, and the presence of synchronous tumors were not significant predictors of OS or recurrence-free survival ($P > .05$). However, central location (HR, 1.46) and advanced tumor stage (HR, 1.49) were factors that predicted worse OS ($P < .05$).

The authors concluded that because of the similar clinical outcomes, more invasive mediastinal staging might be unnecessary for patients with early-stage NSCLC receiving SBRT.

Table 1. Late-Phase Adverse Events in the Radiation Therapy Oncology Group 0126 Study

Toxicity: Grade	Dose Group, %		HR (95% CI)	*P* Value
	High	Low		
GI				
2+	22	16	1.40 (1.10 to 1.77)	.0063
3+	5	4	NR	.035
GU				
2+	15	10	1.70 (1.23 to 2.33)	.001
3+	3	3	NR	.14

GI, gastrointestinal; GU, genitourinary; NR, not reported.

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High-Dose RT Does Not Improve OS in Prostate Cancer

Written by Mary Mosley

A phase 3 dose escalation study of radiation therapy (RT) in patients with localized prostate cancer was terminated early and did not find an improvement in the primary outcome of overall survival (OS). The Radiation Therapy Oncology Group 0126 study, presented by Jeff Michalski, MD, Washington University School of Medicine, St Louis, Missouri, USA, found significant improvements in the rates of local control, distant metastases, and biochemical disease-free survival.

The intermediate-risk patients were randomized to a high or low dose of RT (79.2 Gy in 44 fractions, n = 748; 70.2 Gy in 39 fractions, n = 751). They were stratified by Gleason score (GS; 6 vs 7), prostate-specific antigen level (PSA; between 10 and 20 ng/mL vs < 15 ng/mL), and treatment (3D conformal radiation therapy vs intensity-modulated radiotherapy). At baseline, the median age was 71 years, and the tumor stage was T1 and T2 in 57% and 43% of each group, respectively. Most patients (83% of low dose and 85% of high dose) had a GS of 7, and most (70%) had a PSA < 10 ng/mL. Of the low- and high-dose groups, 85% and 83% had a GS 7 and a PSA < 15 ng/mL. The median follow-up was 7.0 years in all patients.

The OS was 66.7% and 65.6% in the high- and low-dose groups, respectively (HR, 0.98; 95% CI, 0.79 to 1.21; log-rank $P = .87$). Death due to prostate cancer was uncommon, at 13%, while death from other cancer was 22% and other causes, 46%, based on a blinded review. Time to prostate cancer death was similar, at 3.5% and 5.6% in the high- and low-dose groups, respectively (HR, 0.61; 95% CI, 0.33 to 1.11; Gray test, $P = .11$).

An important and significant difference was seen in biochemical failure at 10 years. Based on the ASTRO consensus definition, it was 30% and 45% in the high- and low-dose groups, respectively (HR, 0.59; 95% CI, 0.49 to 0.70; Gray test, $P < .0001$), and based on the Phoenix definition, it was 26% and 43%, respectively (HR, 0.59; 95% CI, 0.48 to 0.72; Gray test, $P < .0001$).

A significant improvement in the rates of local progression and distant metastases was seen at 10 years. With high- versus low-dose RT, the local progression rates were 4% and 8% (HR, 0.42; 95% CI, 0.24 to 0.73; Gray test, $P = .0059$), and the distant metastasis rates were 5% and 8% (HR, 0.60; 95% CI, 0.37 to 0.98; Gray test, $P = .026$). Salvage therapy was more common in the low-dose group (20.6% vs 13.5% in the high-dose group; $P = .0002$).

The rate of acute adverse events was similar in both groups. The incidence of genitourinary (GU) and gastrointestinal (GI) grade 2+ toxicity in the high- and low-dose groups was 2.4% and 2.8% ($P = .64$) and 11.1% and 12.8% ($P = .31$), respectively. The incidence of GU plus GI toxicity was 12.3% and 13.7% ($P = .42$). The rate of late-phase toxicity was higher at 10 years in the high- versus low-dose group (Table 1).

Dr Michalski stated that, compared with the other published trials of dose escalation of RT in patients

with prostate cancer, the present trial was the largest by about 2-fold. In all 6 trials, there was no improvement in OS, while there was an improvement in biochemical disease-free survival. The rates of grade 2+ GI toxicity were similar in the late phase in 6 trials, but the rate of GU toxicity was slightly higher in the present study.

ICORG 05-03 Results: Lower Dose of Radiation Noninferior in MSCC

Written by Mary Mosley

Malignant spinal cord compression (MSCC) is a common cancer-related complication for which the current standard of care is direct decompressive surgery plus postoperative radiation therapy (RT) [Patchell RA et al. *Lancet*. 2005]. The optimal modality and schedule for RT have not been determined. No significant difference between 3 different schedules of external beam radiation therapy (EBRT) was found in 2 different studies [Maranzano E et al. *J Clin Oncol*. 2005; *Radiother Oncol*. 2009]. The Spinal Cord Compression trial [ICORG 05-03, V6; NCT00968643] therefore tested 2 alternative schedules of RT in patients with MSCC treated with EBRT only. Of the 116 eligible patients, 76 patients (38 per group) were randomized to 20 Gy in 5 fractions (control arm, the commonly used dose in Ireland and the United Kingdom at trial initiation) or 10 Gy in 1 fraction (experimental arm). The trial was conducted from 2006 to 2014 in 5 centers, which showed the difficulty of conducting trials of emergency RT, stated Pierre Thirion, MD, St. Luke's Radiation Oncology Network, Dublin, Ireland. The patients in the treatment arms were similar at baseline. A low median Karnofsky Performance Status (KPS) score was found in the eligible vs evaluable patients.

The primary end point was change in mobility at 5 weeks using the modified 3-point Tomita scale. The overall response was similar in the control and experimental arms (68.4% and 78.9%, respectively). Only 10.5% of each arm had an improvement in mobility, whereas it remained the same in 57.9% of the control arm and 68.4% of the experimental arm. The mean score change was –0.29 and –0.08 in the control and experimental arms. The difference in the mean score change between the 2 arms was –0.21 (95% CI, –0.56 to –0.14), which fulfilled the noninferiority hypothesis. The only independent prognostic factor for the mobility status at 5 weeks was the baseline mobility status, stated Prof Thirion.

The secondary outcome of change in bladder control at 5 weeks, assessed by an in-house 3-point scale, was also similar in both groups, with an overall response of 75.7% and 86.8% in the control and experimental arms. The rates of improvement and stability in bladder control were 10.8% and 2.6% in the control arm and 64.9% and 84.2% in the experimental arms. The mean score change was –0.22 and –0.16 in the control and experimental arms.

Survival free of neurological deterioration was similar in both arms, with a median time to a neurological event of 1.4 months. Overall survival (OS) was also similar, with a median time of only 4 months. The independent prognostic factors for OS were young age, a primary cancer that was not lung cancer, high baseline KPS, and preserved baseline mobility.

Only 1 non-neurological event occurred acutely (in the experimental arm) and 2 occurred in the long term (1 in each arm). The rates of grade 0, 1, 2, and 3 toxicity were 47.6%, 31.1%, 20.3%, and 1% in the acute phase, and the long-term rates were 51%, 23.5%, 21.6%, and 3.9%, respectively.

EBRT alone provided only short-term stabilization of function in patients with MSCC, and their vital and functional prognosis remains poor. Similar outcomes were achieved with the 10-Gy and 20-Gy RT schedule. Prof Thirion stated that a 10-Gy single-fraction schedule represents a reasonable standard in clinical practice. Further clinical research is needed to improve outcomes in these patients.