



INTERVIEW

Jeffrey Bradley, MD

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Tracks 1-14

- Track 1** RTOG-0617: A randomized Phase III trial of high-dose or standard-dose RT and chemotherapy with or without cetuximab in newly diagnosed, unresectable Stage III NSCLC
- Track 2** Toxicities associated with high-dose versus standard-dose RT with concurrent chemotherapy/cetuximab
- Track 3** RTOG-1106: A Phase II trial of positron emission tomography/computed tomography (PET/CT) in guiding RT in patients with Stage III NSCLC
- Track 4** Proposed study of erlotinib or crizotinib followed by chemoradiation therapy versus chemoradiation therapy alone for Stage III EGFR mutation-positive or ALK fusion gene-positive NSCLC
- Track 5** RTOG-0618: A Phase II trial of stereotactic body RT for operable Stage I/II NSCLC
- Track 6** ACOSOG-Z4032: A randomized Phase III study of sublobar resection with or without brachytherapy in high-risk Stage I NSCLC
- Track 7** Initial results of the RTOG-0229 study: Neoadjuvant therapy with concurrent chemotherapy and high-dose RT followed by resection and consolidative therapy for Stage III NSCLC
- Track 8** **Case discussion:** A 71-year-old woman with a 40 pack-year smoking history and heavily pretreated squamous cell carcinoma of the lung received multiple courses of stereotactic RT
- Track 9** Benefits and challenges associated with lung cancer screening
- Track 10** **Case discussion:** A 58-year-old woman with a 40 pack-year smoking history and Stage IIIA NSCLC received chemoradiation therapy on the RTOG-1106 study
- Track 11** **Case discussion:** A 72-year-old smoker with Stage IIIA adenocarcinoma of the lung received preoperative chemoradiation therapy and panitumumab in combination with consolidation chemotherapy while enrolled on the RTOG-0839 trial
- Track 12** Indications for stereotactic body RT in early NSCLC
- Track 13** Ongoing and proposed clinical trials evaluating the role of proton-beam therapy in NSCLC
- Track 14** Comparative benefits of intensity-modulated RT and proton-beam therapy

Select Excerpts from the Interview

Track 7

- ▶ **DR LOVE:** Would you discuss the results of the RTOG-0229 study evaluating concurrent neoadjuvant chemotherapy and high-dose radiation therapy followed by resection and consolidation therapy for Stage III NSCLC?
- ▶ **DR BRADLEY:** The RTOG-0229 study evaluated patients with operable Stage III lung cancer who received chemotherapy and radiation therapy prior to surgery (Suntharal-

ingam 2012; [3.1]). The intent of the study was to clear the mediastinal lymph nodes using a radiation dose of 60 Gray with chemotherapy before surgery. The results demonstrated that mediastinal nodal clearance was achieved in 63% of the patients enrolled on the study. For patients who achieved mediastinal nodal clearance, the 2-year survival rate was 75%. For patients with residual nodal disease, the 2-year survival rate was 52%.

3.1

RTOG-0229: A Phase II Trial of Neoadjuvant Therapy with Concurrent Chemotherapy and Full-Dose Radiation Therapy Followed by Resection and Consolidative Therapy for Locally Advanced Non-Small Cell Lung Cancer

Response	N = 43
Mediastinal node clearance (MNC)	63%
Overall survival rate (2 y)	54%
Patients with MNC	75%
Patients with residual nodal disease	52%
Progression-free survival rate (2 y)	33%
Grade 3 and 4 toxicities	
Hematologic	35%
Gastrointestinal	14%
Pulmonary	23%

Median follow-up: 24 mo

Suntharalingam M et al. *Int J Radiat Oncol Biol Phys* 2012;84(2):456-63.

Track 9

▶ **DR LOVE:** What are your thoughts on the National Lung Screening Trial?

▶ **DR BRADLEY:** Our institution is strongly in favor of lung cancer screening, and we were instrumental in accruing patients to several screening trials, including the National Lung Cancer Screening Trial. A 20% reduction in mortality was observed among patients who had a smoking history of at least 30 pack-years and who were screened using low-dose computed tomography (CT) (3.2).

This is impressive, even with the limitation of only 3 rounds of screening. We have never observed a 20% drop in mortality from an intervention in lung cancer, so that's a huge advantage. I believe screening is probably *the* most important development in lung cancer in the past several years.

▶ **DR LOVE:** How significant is the issue of false-positive results?

▶ **DR BRADLEY:** False-positive results can be a problem in carrying out screening and determining which nodules are of concern. The question arises as to whose responsibility it is to follow up with patients who have nodules that are found to be positive by screening. We established a clinic for that patient population to determine how they should be cared for. The use of 3-dimensional software might be helpful in determining which nodules are of concern, but we have a lot more to learn before we implement something like that globally.

▶ **DR LOVE:** What criteria do you use to determine whether to biopsy a tumor?

► **DR BRADLEY:** If a tumor is growing and approaches a centimeter or so, I would recommend a biopsy and a PET scan to get some idea of the FDG activity. We typically recommend that these patients undergo scans approximately every 6 months to detect growth.

3.2

National Lung Screening Trial (NLST): Reduced Lung Cancer Mortality with Low-Dose CT Screening

	Low-dose CT group (n = 26,722)	Radiography group (n = 26,732)	Relative reduction in mortality
Rate of positive screening results	24.2%	6.9%	—
Incidence of lung cancer (cases per 100,000 person-years)	645	572	—
Deaths from lung cancer (no. per 100,000 person-years)	356 247	443 309	20.0% $p = 0.004$
Deaths from any cause	1,877	2,000	6.7% $p = 0.02$

“The cost-effectiveness of low-dose CT screening must also be considered in the context of competing interventions, particularly smoking cessation. NLST investigators are currently analyzing the quality-of-life effects, costs, and cost-effectiveness of screening in the NLST and are planning collaborations with the Cancer Intervention and Surveillance Modeling Network to investigate the potential effect of low-dose CT screening in a wide range of scenarios.”

National Lung Screening Trial Research Team et al. *N Engl J Med* 2011;365(5):395-409.

 **Track 12**

► **DR LOVE:** What are the indications for stereotactic radiation therapy in NSCLC?

► **DR BRADLEY:** The question of whether stereotactic radiation therapy is applicable arises in a number of different situations. The trials we have conducted have demonstrated that it is highly applicable for tumors that are in the periphery, not next to a major bronchus or a blood vessel like the aorta or pulmonary artery, where the risk may be higher. Results from a number of studies have also demonstrated that stereotactic radiation therapy is applicable for patients with Stage I lung tumors that are central and within 2 centimeters of a primary bronchus. However, the radiation dose must be lowered and 5 fractions must be administered instead of 3. We do not observe much toxicity in that setting.

Another setting in which the question of stereotactic radiation therapy arises is with a patient whose disease progresses on standard chemoradiation therapy for Stage III disease and who has a persistent lung nodule. Stereotactic radiation therapy in these situations is the subject of ongoing trials. ■

SELECT PUBLICATIONS

National Lung Screening Trial Research Team et al. **Reduced lung-cancer mortality with low-dose computed tomographic screening.** *N Engl J Med* 2011;365(5):395-409.

Suntharalingam M et al. **Radiation Therapy Oncology Group protocol 02-29: A phase II trial of neoadjuvant therapy with concurrent chemotherapy and full-dose radiation therapy followed by surgical resection and consolidative therapy for locally advanced non-small cell carcinoma of the lung.** *Int J Radiat Oncol Biol Phys* 2012;84(2):456-63.