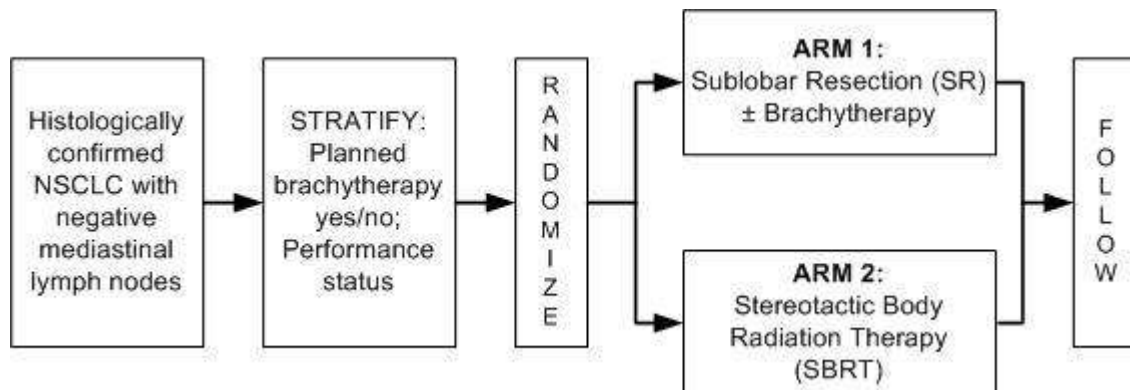


# Study: ACOSOG Z4099/ RTOG 1021 A Randomized Phase III Study of Sublobar Resection (+/- Brachytherapy) versus Stereotactic Body Radiation Therapy in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC)

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## 1.0 SCHEMA



Required sample size: 420

## 2.0 OBJECTIVES

### 2.1 Primary Objective

To ascertain whether patients treated by SBRT have a 3-year overall survival (OS) rate that is no more than 10% less than patients treated with SR.

### 2.2 Secondary Objectives

- To compare loco-regional recurrence-free survival between study arms. See Evaluation of Outcomes for recurrence definitions.
- To compare disease-free survival between study arms.
- To compare grade 3 or higher specific adverse event profiles between study arms; specific comparisons will include AEs at 1, 3, 6 and 12 months post therapy.
- To compare pulmonary function between patients treated with SBRT and patients treated with SR.
- To compare the adverse events and PFTs in each arm for patients with low or high Charlson comorbidity index scores, including a test interaction between Charlson comorbidity index scores (low vs. high) and treatment arm.

## 3.0 PATIENT SELECTION

1. Age > 18 years.
2. ECOG performance status (PS) 0, 1, or 2.
3. Biopsy-proven non-small cell lung cancer (NSCLC).

4. Tumor  $\leq 3$  cm maximum diameter, clinical stage Ia or selected Ib (i.e., with visceral pleural involvement) by PET/CT scan of the chest and upper abdomen performed within 60 days prior to registration.
5. All clinically suspicious mediastinal N1, N2, or N3 lymph nodes ( $> 1$  cm short-axis dimension on CT scan and/or positive on PET scan) confirmed negative for involvement with NSCLC by one of the following methods: mediastinoscopy, anterior mediastinotomy, EUS/EBUS guided needle aspiration, CT-guided, video-assisted thoracoscopic or open lymph node biopsy.
6. Tumor verified by a thoracic surgeon to be in a location that will permit sublobar resection.
7. Tumor located **peripherally** within the lung. NOTE: Peripheral is defined as not touching any surface within 2 cm of the proximal bronchial tree in all directions. See the diagram in Section 2.2. Patients with non-peripheral (central) tumors are NOT eligible.
8. No evidence of distant metastases.
9. PFTs with DLCO within 90 days prior to registration.
10. Patient at high-risk for surgery by meeting a minimum of one major criteria or two minor criteria as described below:

**Major Criteria**

- FEV1  $\leq 50\%$  predicted
- DLCO  $\leq 50\%$  predicted

**Minor Criteria**

- Age  $\geq 75$
- FEV1 51-60% predicted
- DLCO 51-60% predicted
- Pulmonary hypertension (defined as a pulmonary artery systolic pressure greater than 40mm Hg) as estimated by echocardiography or right heart catheterization
- Poor left ventricular function (defined as an ejection fraction of 40% or less)
- Resting or Exercise Arterial pO<sub>2</sub>  $\leq 55$  mm Hg or SpO<sub>2</sub>  $\leq 88\%$
- pCO<sub>2</sub>  $> 45$  mm Hg
- Modified Medical Research Council (MMRC) Dyspnea Scale  $\geq 3$ .

**Grade Description**

0	No breathlessness except with strenuous exercise
1	Breathlessness when hurrying on the level or walking up a slight hill
2	Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level
3	Stops for breath after walking about 100 yards or a few minutes on the level
4	Too breathless to leave the house or breathless when dressing or undressing

11. No prior intra-thoracic radiation therapy. NOTE: Previous radiotherapy as part of treatment for head and neck, breast, or other non-thoracic cancer is permitted. Previous chemotherapy or surgical resection for the lung cancer being treated on this protocol is NOT permitted.

12. Non-pregnant and non-lactating. Women of child-bearing potential must have a negative urine or serum pregnancy test within 60 days prior to registration. Peri-menopausal women must be amenorrheic  $> 12$  months prior to registration to be considered not of childbearing potential.

13. No prior invasive malignancy, unless disease-free for  $\geq 3$  years prior to registration (exceptions: non-melanoma skin cancer, in-situ cancers).