RADIATION THERAPY ONCOLOGY GROUP

RTOG 0236

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RADIATION THERAPY ONCOLOGY GROUP

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A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I/II Non-Small Cell Lung Cancer

SCHEMA

Patient Population: (See Section 3.0 for Eligibility)
Patients with T1, T2 (≤ 5 cm), T3 (≤ 5 cm), N0, M0 medically inoperable non-small cell lung cancer; patients with T3 tumors chest wall primary tumors only; no patients with tumors of any T-stage in the *zone of the proximal bronchial tree**. Patients with T3 tumors based on mediastinal invasion or < 2 cm toward carina invasion are not

RTOG Institution # _____

RTOG 0236 **ELIGIBILITY CHECKLIST (5/26/04) (6/14/05)**

Case # _____

_____(Y) 1. Non-small cell lung cancer histologically confirmed by biopsy or cytology?

_____ 2. TNM Stage:

_____

RTOG Institution # _____

1.0 INTRODUCTION

1.1 *Stage I Non-small Cell Lung Cancer*

systems allow even more dramatic reduction of treatment volumes facilitating hypofractionation with markedly in4reased daily doses and signifi

in one T1 patient. Additional patients were treated at

2.2.2 To observe patterns of failure (see definitions in Section 11.3), disease free survival, and overall survival.

The Facility Questionnaire requires the following:

Institutional and/or peer-reviewed documentation of accountability for internal organ motion including compensation for respiratory movement by one of the following methods:

- Inhibition of diaphragmatic movement by abdominal compression or equivalent;
- Active breath holding techniques synchronized to radiation delivery;
- Respiratory gating monitoring consistent breathing patterns synchronized to radiation

6.0 RADIATION THERAPY Note: Intensity Modulated RT (IMRT) Is Not Allowed

6.1 Dose Specifications

6.1.1 *Stereotactic Targeting and Treatment*

The term “stereotactic” for the purposes of this protocol implies the targeting, planning, and directing of therapy using beams of

tissue. The isocenter in stereotactic coordinates will be determined from system fiducials (or directly from the tumor) and22166Tslatd ftothe tureatmnte ectrdi. eTe tureatmnte dose planwill be dmade up

Organ	Volume	Dose (cGy)
Spinal Cord	Any point	18 Gy (6 Gy per fraction)
Esophagus	Any point	27 Gy (9 Gy per fraction)
Ipsilateral Brachial Plexus	Any point	24 Gy (8 Gy per fraction)
Heart	Any point	30 Gy (10 Gy per fraction)
Trachea and Ipsilateral		

Whole Lung

Both the right and left lungs should be contoured as one structure. Contouring should be carried out using pulmonary windows. All inflated and collapsed lung should be contoured; however, gross tumor (GTV) and trachea/ipsilateral bronchus as defined above should not d bincludin

ray. The infiltrate on chest x-ray should include the area treated to high dose, but may extend outside of these regions. The infiltrates may be

All deaths during and within 30 days of completion of protocol radiation therapy, regardless of attribution, must be reported by telephone within 24 hours of discovery to the RTOG Headquarters AE telephone line at (215) 717-2762. If the event is more than 30 days from completion of radiation treatment, but is felt to be definitely, possibly, or probably resulting from protocol radiation therapy, this event sh o u l d

Radiation therapy is the only modality in this protocol; therefore, serious adverse events are

same numbers as listed above.

6.10.3 *Documentation*

reported on the appropriate case repo
Primary Investigated s85

pulmonary windowing taken as part of scheduled protocol follow-up are preferred as the method of evaluation for response. When CT scans are not available, chest x-ray determination will be allowed as long as the target lesion is clearly visible. Changes in serum tumor markers will not be allowed for assessment of either local tumor progression or metastatic progression.

Local treatment effects in the vicinity of the tumor target may make determination of tumor dimensions difficult. For example, bronchial or bronchiolar damage may cause patchy consolidation around the tumor that over time may coalesce with the residual tumor. In cases where it is indeterminate whether consolidation represents residual tumor or treatment effect, it should be assumed that abnormalities are residual tumor. In order to make the assessment more objective, a central radiology review for CT response evaluation will be required for this protocol.

All other lesions (or sites of disease) that appear after treatment (e.g., regional lymph nodes and distant Tw[(Lses) should be identified as)]TJ/TT12 1 Tf23.3114 0 TD0.0003 Tc0.3087 Tw[(no

For network submission: The FTP account assigned to the submitting institution by the ITC shall be used, and e-mail identifying the data set(s) being submitted shall be sent to:

itc@castor.wustl.edu

For tape submission

12.3 Comorbidity Data Submission

Comorbidity data (Comorbidity Recording Sheet and Charlson Comorbidity Index) should be submitted within 2 weeks of study entry (the same time point as the initial assessment data) but will be submitted to: **Elizabeth Gore, M.D. Fax 414-805-4369.** Do not submit to RTOG Headquarters.

13.0 STATISTICAL CONSIDERATIONS

13.1 Study Endpoints

13.1.1 The primary endpoint of this trial is to estimate local control at two years.

13.1.2 To estimate itiarate of acute and late ireatment-re lated grade 3 or 4 toxicity (per CTCAE, v.3.0) related to specific symptoms, including:

- p Gastrointestinal: dysphagia, esophagitis, esophageal stricture, esophageal ulceration;
- p Cardiac: 98 icarditis, 98 icardial effusi on, cardiomyopathy, vent icular dysfunction;
- p Neurologic: myelitis, neuropathy — cranial and motor;
- p Hemorrhage: 9ulmonary or upper respiratory;
- p Pulmonary: decline in 9ulmonary function as measured by 9ulmonary function tests, pneumonitis, 9ulmonary fibrosis, hypoxemia, pleural effusion

Or any grade 4 or 5 toxicity attributed to itiaitirapy;

13.1.3 To estimate itiarates of local recurrence, regional recurrence, disseminated recurrence, disease-free and ovirall survival at two years.

13.2 Sample Size (8/6/04)

This phase II study aims to improvi itiaiwo-year local control rate from 60% to 80%. Local control is defined as itiaabsence of local pr ogression. Assuming at least an approximately exponential distribution of time to local progression,itiahazard rate for itiaexpected local control rate of 80% is 0.0093 per month, and itiahazard ra te for itiaunacceptable local control rate of 60% is 0.02128 per month. Using ttiaasymptotic properties of itia ratio of the logarithms of the observed and expected hazardfus18 cases of local progression ariarequired for a Typialaerror rate of 0.05 with 80% statistical power to detect a difference in local control rates at least this large. These figuresarequire 25 months of accrual to 49 patients and iwo years of follow up. Assuming that 5% of ttiapatients will be ineligible or inevaluable, **a total of 52 patients will be required for this trial.**

13.3 Interim Analyses for Early Stopping Due to Unacceptable Toxicity (11/21/05)

Early stopping of this trial will be based onaunacceptable toxicity, defined as acute (within 90 days of itiastart of treatment) or late (mori itan 90 days from itiastart of treatment) grade 3 or 4 toxicity (per CTCAE, v.3.0) related to specific symptoms as detailed in Section 13.1.2 or any grade 4 or 5 toxicity attributed to itiaitir apy. If a patient has mori itan oni unacceptable toxicity, itiy will only be counted as oni una cceptable toxicity for this analysis.

Three interim analyses of toxicity ari planned after 25%, 50%, and 75% of ttiaiotal number of evaluable patients to be accrued. Ttiainteri 98 TD0.06933(Size6ty mannn[(T[(Eipowe6(itin 90 daye)]TJ-19.5

toxicity data and make appropriate recommendations to the RTOG Executive Committee and Research Strategy Committee about the study. Additionally, the treatment-related unacceptable toxicity rate will continued to be monitored during the four year follow-up period. If the lower limit of a one-sided 95% normal approximation confidence interval for the unacceptable toxicity rate

Planned Gender and Minority Inclusion

Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	1	2	3
Not Hispanic or Latino	21	28	49
Ethnic Category: Total of all subjects	22	30	**52**
Racial Category			
American Indian or Alaskan Native	0	1	1
Asian	0	1	1
Black or African American	1	1	2
Native Hawaiian or other Pacific Islander	0	0	0
White	22	26	48
More than one race	0	0	0
Racial Category: Total of all subjects	23	29	**52**

40. Parmelee PA, Thuras PD, Katz IR, Lawton MP. Validation of the Cumulative Illness Rating Scale in a geriatric residential population. *J Am Geriatr Soc.* 43: 130-137, 1995.

41. Inouye SK, Peduzzi PN, Robison JT, Hughes JS, Horwitz RI, Concato J. Importance of functional measures in predicting mortality among olde1 hospitalized patients.*JAMA.* 279: 1187-1193, 1998.

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43. Kaplan E, Meier, H. Nonparametric Estimation From Incomplete Observations.

APPENDIX I

RTOG 0236

SAMPLE CONSENT FOR RESEARCH STUDY

STUDY TITLE

A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I/II Non-Small Cell Lung Cancer

This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take youa time to make youa decision. Discuss it with youa friends and family. The National Cancer Institute (NCI) booklet, "Taking Part in Clinical Trials: What Cancer Patients Need To Know," is available from youa doctor.

You are being asked to take part in this study because you have early stage lung cancer and cannot have surgery.

WHY IS THIS STUDY BEING DONE?

The usual treatment for early stage lung cancer is to remove the cancer with surgery. However, wheloesTheoancer 15.01

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

- A blood test to find out how much oxygen is delivered to the tissues

Á Difficulty breathingÁ FeverÁ Chest wall discomfort*Less Likely, But Serious*

_____Á Irritation of the lining around the heart, which can cause chest pain, shortness of breath, and ch

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be

including PDQ (Physician Data Query) visit
www.cancer.gov/cancerinfo/pdq

SIGNATURE

APPENDIX II

KARNOFSKY PERFORMANCE SCALE

100	Normal; no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some sign or symptoms of disease
70	Cares for self; unable to carry on normal activity or do active work
60	Requires occasional assistance, but is able to care for most personal needs
50	Requires con3iderable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated, although death not imminent
20	Very sick; hospitalization necessary; active support treatment is necessary
10	Moribund; fatal processes progressing rapidly
0	Dead

ZUBROD PERFORMANCE SCALE

0	Fully active, able to carry on all predisease activities without restriction (Karnofsky 90-100)-aei

APPENDIX IV

	Myocardial infarct	1