

# Prospective Evaluation of SBRT for Definitive Management of Medically-Inoperable Lung Cancer



Arica Hirsch, MD<sup>1</sup>; Majid Mohiuddin, MD<sup>1</sup>; James Ruffer, MD<sup>1</sup>; Angelica Green, AS<sup>1</sup>; Revidiasa Semanjaku, BS<sup>2</sup>

<sup>1</sup>Department of Radiation Oncology; <sup>2</sup>Russell Institute for Research & Innovation; Advocate Lutheran General Hospital



## Abstract

**INTRODUCTION:** In patients with clinical stage I NSCLC, surgical resection is the recommended therapy. However, in those patients deemed medically inoperable, Stereotactic Body Radiation Therapy (SBRT) provides an effective non-invasive alternative. We prospectively evaluated treatment outcomes of SBRT in early stage, medically inoperable NSCLC patients treated between 2011 and 2014.

**METHODS:** 67 patients with medically-inoperable, primary NSCLC were evaluated in this study with a prospectively maintained database between 12/27/2011 and 4/29/2014. 25 males and 42 females were included, between 60 to 90 years of age. Histologies are as follows: adenocarcinoma (37), non-small cell carcinoma, NOS (5), squamous cell carcinoma (21), and other (4). 25 patients underwent fiducial placement. Patients received a total dose of 45-60Gy in 3-5 fractions. The prescription isodose line ranged between 58% -80% and the tumor volumes measured between 3.86cm<sup>3</sup> and 153.93cm<sup>3</sup>. Acute and late toxicities were graded with CTCAE Version 3.0. Study outcomes included: local control (LC), regional control (RC), distant control (DC), overall survival (OS), acute and late toxicities.

**RESULTS:** With a median follow-up of 18.3 months, LC, RC and DC rates were 97%, 80.6%, and 85% respectively, and overall survival, 75%. Grade 1 and 2 dyspnea was observed in 10% and 5% of patients, respectively, and grade 1 cough in 20% of patients. No clinically significant pneumonitis was experienced in this study. Local control was examined as a function of tumor size, tracking technique and dose-fractionation. Only dose-fractionation was found to correlate with local control rates (p=0.034).

**CONCLUSION:** Stereotactic Body Radiation Therapy (SBRT) is an effective mode of therapy for medically inoperable patients with early stage NSCLC. These results are comparable to those described in the literature for surgical resection in this patient population, suggesting that SBRT can be an equally effective non-invasive alternative for appropriately selected patients.

## Introduction

Medically inoperable early stage lung cancer can pose unique challenges in management, as even conservative surgical resection may result in significant morbidity in this population.

Stereotactic body radiation therapy (SBRT) with CyberKnife is a unique, non-invasive treatment approach, capable of delivering high-dose ablative treatment robotically to small tumors <5cm, with high accuracy and tumor tracking capability resulting in minimal exposure of surrounding normal tissue.

Prospective phase 1 and phase 2 studies examining outcomes of SBRT in the management of medically inoperable lung cancer demonstrate high rates of local control with minimal morbidity.

This study evaluated the treatment outcomes of CyberKnife SBRT at Illinois CyberKnife in early stage medically inoperable NSCLC patients.

## Methods

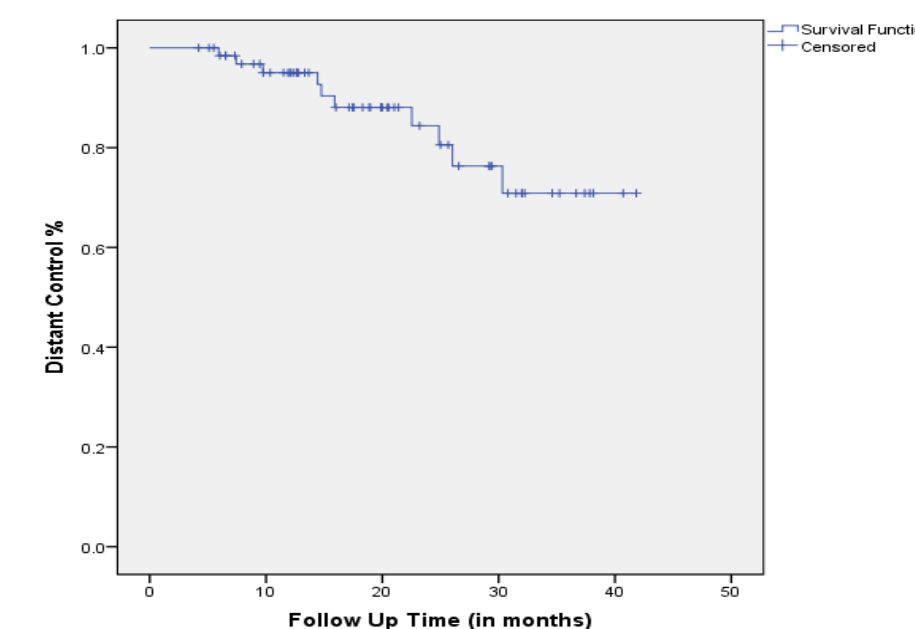
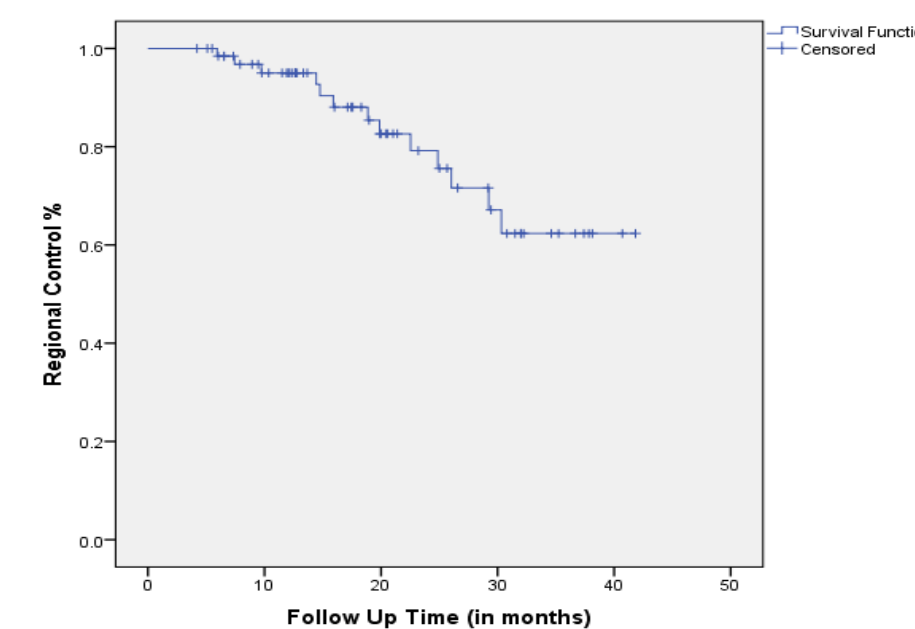
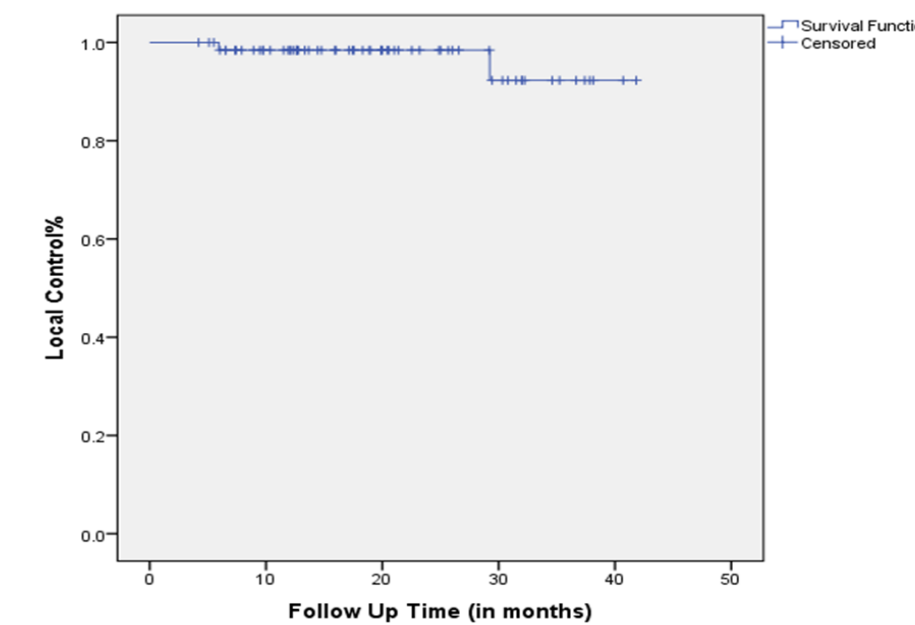
- This study collected data from 67 consecutive patients with medically inoperable stage 1 lung cancer, treated between 2011-2014.
- The patients, between the ages of 60 to 90 years, presented with stage I non-small cell lung cancer, with tumor size  $\leq$  5cm, and were deemed medically inoperable by either a pulmonologist or thoracic surgeon.
- The primary endpoints of this study include assessment of local, regional and distant tumor control, overall survival, and toxicity (Common Terminology Criteria for Adverse Effects: cough, dyspnea, and pneumonitis).
- This study also examined variables of tumor size, tracking technique, and dose-fractionation to correlate with local control.
- Statistical analysis (Kaplan Meyer curves with log rank) were performed using SPSS 22.0

## Patient Demographics

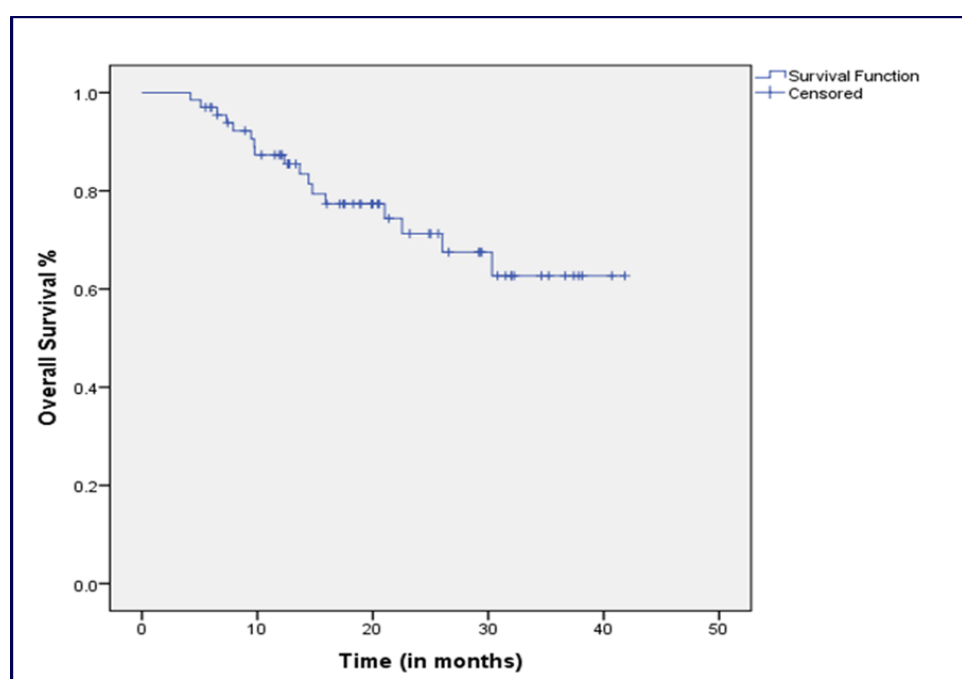
n (%)	n=67
Gender, female	42 (63)
<b>Histology</b>	
Adenocarcinoma	37 (55)
Squamous cell	21 (31)
Non-small cell	5 (8)
<b>Stage</b>	
IA	47 (70)
IB	20 (30)
<b>Tracking Technique</b>	
Fiducial markers	25 (37)
X-sight spine	13 (19)
X-sight lung	29 (43)
<b>Fractions</b>	
5	29 (43)
3-4	38 (57)
Median Follow-up, months	18.3
Mean Tumor Size, cm	2.41
Mean Isodose Line, %	63.7

**Table 1.** Patient demographics: majority of the patients were women; more than half of the patients presented with *Adenocarcinoma*; 70% of all cases were Stage IA; average tumor size was 2.41 cm; median follow-up time was 18.3 months

## Results



**Figures 1-3:** Survival Function for Local, Regional, and Distant Control (top, middle, bottom); all  $P < .05$



**Figure 4:** Overall Survival vs. Time

Advocate IRB #5967

	N	Number of Events	Censored (n, %)	P-value
<b>Tracking Technique</b>				
Fiducials w/ Synchrony	25	0	25 (100)	
X-Sight spine	13	1	12 (92.3)	
X-Sight lung	29	1	28 (96.6)	
Overall	67	2	65 (97.0)	0.505
<b>Tumor Size</b>				
$\leq$ 2cm	30	0	30 (100.0)	
>2cm	37	2	35 (94.6)	
Overall	67	2	65 (97.0)	0.183
<b>Dose Fraction Size</b>				
5000cGy/1000cGy	24	2	22 (91.7)	
Other	43	0	43 (100.0)	
Overall	67	2	65 (97.0)	0.034

**Table 2:** Local Control dependent on Tracking technique, Tumor Size and Dose Category

Type of Control	%
Local	97
Regional	80.6
Distant	85
<b>Overall Survival</b>	<b>75</b>

**Table 3.** Control and overall survival rates

## Conclusions

- Stereotactic Body Radiation Therapy (SBRT) is an effective mode of therapy for medically inoperable patients with early stage NSCLC.
- These results are comparable to those described in the literature for surgical resection in this patient population, suggesting that SBRT can be an equally effective non-invasive alternative, with diminished morbidity.
- Our data is comparable to other SBRT studies published in the literature. RTOG 0236 reported 3 year data on 59 patients with medically inoperable peripheral lung tumors, 54Gy in 3 fractions:
  - Local control: 97.6%
  - Distant control: 78%
  - Overall survival: 55.8%
  - Grade 3 toxicity: 12.7%
- This is a very well-tolerated treatment with only 15-20% grade 1 and 5% grade 2 toxicity.
- Possible correlation of outcome with total dose/fraction, with inferiority of 50Gy/10Gy (central tumors) relative to other fractionation schemes.
- Additional follow-up necessary to verify longer-term outcome.

## References

- Kelley, K.J., D.L. Benninghoff, R.I. Byrnes, and H.J. Zinkin. "Medically Inoperable Early-Stage Peripheral Versus Central Lung Cancer Treated With Stereotactic Body Radiation Therapy." *International Journal of Radiation Oncology\*Biophysics* 90.1 (2014): n. pag. Web. 22 Oct. 2015.
- Fakiris, Achilles J., Ronald C. McGarry, Constantin T. Yiannoutsos, Lech Papiez, Mark Williams, Mark A. Henderson, and Robert Timmerman. "Stereotactic Body Radiation Therapy for Early-Stage Non-Small-Cell Lung Carcinoma: Four-Year Results of a Prospective Phase II Study." *International Journal of Radiation Oncology\*Biophysics* 75.3 (2009): 677-82. Web. 22 Oct. 2015.
- Timmerman, Robert, Rebecca Paulus, James Gavin, Jeffrey Michalski, William Straube, Gregory Videtic, David Johnstone, Jack Fowler, Elizabeth Gore, and Hak Choy. "Result Filters." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 17 Mar. 2010. Web. 22 Oct. 2015.

## Authors Contact Information

Name	Phone	E-mail	Website
Arica Hirsch, M.D.	847-723-0100	ahirsch@chicagocancer.org	www.illinoisck.com
Majid Mohiuddin, M.D.	847-723-0100	mmohiuddin@chicagocancer.org	www.illinoisck.com
James Ruffer, M.D.	847-723-0100	jruffer@chicagocancer.org	www.illinoisck.com
Angelica Green, A.S.	847-723-0100	agreen39@ujic.edu	www.illinoisck.com
Revidiasa Semanjaku, B.S.	847-723-2243	revidiasa.semanjaku@advocatehealth.com	http://www.advocatehealth.com