



STEREOTACTIC BODY RADIATION THERAPY FOR THE TREATMENT OF EARLY STAGE NON SMALL CELL LUNG CANCER

A Technology Assessment

INTRODUCTION

The California Technology Assessment Forum was requested to review the scientific evidence for the use of Stereotactic Body Radiation Therapy (SBRT) for the treatment of early stage non small cell lung cancer (NSCLC) in medically inoperable patients. Given that the major treatment goal for non small cell lung cancer is to obtain local control, is SBRT a viable therapeutic option for patients who are medically inoperable? Secondly, given its potentially less invasive approach, is it a viable option for patients who are potentially operable as an alternative to surgery?

At this time, most of the available evidence focuses on the use of radiosurgery for treatment of medically inoperable patients who have few treatment options and thus that will be the focus of the review.

BACKGROUND

Lung Cancer is the number one cause of cancer mortality in both men and women. In the U.S. in 2008, there will be an estimated 215,020 new cases of lung cancer and an estimated 161,840 deaths from lung cancer¹.

The therapeutic approach to lung cancer depends on whether it is small cell or non small cell lung cancer and on the extent of disease. Staging is based on whether or not there is involvement of nodes and or evidence of metastatic disease.

For non small cell lung cancer, the TNM (tumor, lymph nodes, metastasis) staging criteria is used. Stage 1 disease is local disease without regional lymph node or metastatic involvement. Stage 1 disease is divided into Stage 1A and Stage 1B, based on the size of the primary tumor. Stage 1 A is defined as a tumor of 3 cm or less in



diameter, and Stage 1 B (T2NoMO) includes tumors >3 cm in diameter, and tumors of any size that are growing into the mainstem bronchus and or involving the pleura or causing atelectasis or obstructive pneumonia that involves less than an entire lung.

The primary treatment for patients with early non small cell lung cancer is surgery. Lobectomy and pneumonectomy are associated with three to five year survival rates of 60% to 80%. Lesser surgical therapies such as wedge resection are options, but result in less local control².

Many patients are “medically inoperable,” with severe medical diseases and early stage tumors (e.g. T 1 and T 2 tumors) and are not operative candidates. There is no standard approach for these individuals. Treatment options include conventional fractionated radiotherapy (XRT), which is typically given in small doses over many sessions. Historically, survival with conventional radiotherapy which has three year survival of 15% to 45%³⁻⁵, is much lower than that seen with surgery. However, comparison of the patients who receive XRT with those who undergo surgery is difficult. Radiotherapy treated patients are more likely to have many co-existing medical problems, such as heart disease, chronic obstructive pulmonary disease (COPD), diabetes and vascular disease that make them less likely to survive.

Since survival in NSCLC is highly correlated with local control, local control is often used as a surrogate measure for survival. There are three ways to improve local control with XRT- 1) increase the total dose, 2) increase the radiosensitivity, and 3) increase the dose per fraction. Any of these strategies typically include some type of image guidance to target the tumor cells, while minimizing toxicity to healthy tissue.

To date, strategies that involve increasing the total dose of XRT have not resulted in improved local control. Improving radiosensitivity with chemotherapy is used in Stage III tumors, although this may be associated with more damage to normal tissues, such as the esophagus. Increasing the dose per fraction appears to be the potentially most promising approach.

Radiosurgery is the application of very high doses of ionizing radiation in larger than traditional fractionation to much smaller than traditional radiotherapy fields, often with the integration of advanced modalities for tumor imaging and devices for tumor immobilization. The concept of radiosurgery was developed by Dr. Lars Laskell in the 1950's and was initially used in the brain and spine for brain tumors and metastatic disease.



With the hypofractionated approach, more radiotherapy is given less often. A daily dose of 2.5-3.4 GY is given with <6-7 GY per fraction. The current indications for stereotactic radiosurgery are a tumor <5 CM NOMO. Since the goal

is to target tumor and avoid normal tissue, body and respiratory movements must be minimized. Body fixation is obtained by placing the patient in a special stereotactic body frame to minimize body movement. The patient must be able to stay in the full body frame for at least 30 minutes.

Minimizing the motion associated with respiration is also important. Respiratory motion control is achieved in three ways: 1) Tracking: a tumor motion surrogate is correlated with all phases of the respiratory cycle. This surrogate such as a point on the chest wall or a breathing flow detector drives the position of the respiration beam; 2) Respiratory gating is also important to ensure that radiation is delivered only at certain phases of the respiratory cycle (typically end expiration which is longer and more stable) and special software is typically required.; and 3) Respiratory inhibition: the tumor is targeted and as much normal tissue as possible is spared. Methods to achieve this include forced breath hold and external abdominal compression that limits diaphragmatic breathing.

TECHNOLOGY ASSESSMENT (TA)

TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies.

The device used for SBRT is a linear accelerator. There are many manufacturers who have received FDA 510(k) clearance for their devices. Those devices with FDA clearance to treat extracranial lesions are:

CyberKnife (Accuray, Inc, Sunnyvale, CA), XKnife-4 (Radionics, Burlington, MA), Synergy (Elekta, Stockholm, Sweden), Hi-ART System (TomoTherapy, Madison, WI), Novalis (BrainLAB AG, Germany).

Trilogy System with RapidArc (Varian, Palo Alto, CA.), Primatom (Siemens Medical Systems, Concord, CA)

Many of these devices have additional planning capabilities such as the Primatom from Seimens Medical Systems which includes the Primus linear accelerator and a Somatom CT scanner.

TA Criterion 1 is met.

TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

Search Methods:

We searched Medline, the Cochrane clinical trials database, Cochrane reviews, database and the Database of Abstracts of Reviews of Effects (DARE) using the search terms of stereotactic body radiation therapy cross referenced with lung cancer. In addition, we searched the bibliographies of the identified articles and other reviews to identify primary data sources and search strategies to ensure a complete review of the relevant literature. The abstracts of citations were reviewed for relevance and all potentially relevant articles were reviewed in full. Studies were included if they included medically inoperable patients being treated for early stage NSCLC. Studies were excluded if they only focused on metastatic lung lesions. Additional studies were excluded if they only involved treatment with a single dose of radiotherapy. We identified relevant published series: 14 were case series⁶⁻¹⁹ and are described in Table 1. The remainder were prospective studies. Among the five completed studies, two were Phase II studies, one was a Phase I/II study and two were Phase I dose escalation studies²⁰⁻²⁴. The outcomes evaluated included survival, cause specific survival, percentage achieving local control and percent with local failure. Most publications measured more than one outcome. We did not find any completed trials comparing SBRT to an alternative treatment. There are five ongoing Phase 2 studies- the three in the U.S. are sponsored by Radiation Therapy Oncology Group (RTOG) and are multi-institutional and the two others are taking place in Japan and Scandinavia. Two of the ongoing phase II studies are comparing SBRT to another treatment, either surgery or conventional XRT. The study comparing SBRT to conventional XRT is being conducted in Europe.

While abstract data are referenced in the text of this document, data cannot be considered as scientific evidence by CTAF or this reviewer until published in a peer-reviewed professional journal.

TABLE 1: Stereotactic Body Radiation Therapy for Early Non-Small Cell Lung Cancer: Results of Retrospective Studies

STUDY	STUDY SITE	N	INTERVENTION	INCLUSION	DURATION OF FOLLOW UP	OUTCOMES FOR THOSE WITH NSCLC
Onishi, 2004 ⁶	Multi-institutional in Japan	245 (158 medically inoperable)	18-75 Gy in 1-2 fractions	Stage 1 T1N0M0	24 months	3 year overall survival 56%; 3 year overall survival for medically operable 88% with BED >100 and 69% with BED <100
Pennathur, 2007 ²⁵	University of Pittsburgh	32 (5 had mets)	20 Gy single fraction	Primary, recurrent or metastatic lung cancer; all stages; medically inoperable, failure of prior therapies or refusal to have surgery	15 months	78% overall survival at 1 year 01% overall survival for Stage 1 Patients with primary lung cancer not analyzed separately
Uematsu, 2001 ⁸	National Defense Medical College, Japan	50	50-60 Gy 5-10 FX	T1-2N0Mo Medically inoperable or refused surgery	36 months	3 year survival 66%; 88% cause specific survival 86% in medically operable 94% local control
Arimoto, 1998 ⁹	Case Series	24				
Wulf, 2004 ¹⁰	U of Wuerzburg, Germany	20	3 x 10 G or 3 x 12-12.5 Gy	T1-T3N0M0 Medically inoperable	11 months	52% 1 year and 32% 2 year survival
Lee, 2003 ¹¹	U of Ulsan, South Korea	28 (9 primary lung cancers)	3-4 x 10 Gy	Primary lung cancer	18 months	39% showing complete response; 43% showed partial response; primary and metastatic disease not reported separately
Ricardi, 2007 U of Turin ¹²	University of Turin	54 (43 available for analysis)	15 Gy x 3	Stage 1 NSCLC	14.7 months	44.2% complete response; 32.5% partial response



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Scorsetti, 2007 Italy ¹³	Instituto Clinico Humanitas, Italy	43	30.5 Gy in 1-4 fractions	T1-2, N0, MO	14 months	53% 2 year survival
Brown, 2007 ¹⁴	CyberKnife Center in Miami	59	15-67.5 Gy in 1-5 fractions	Stage iA or 1 B	1-33 months Median not reported	86% alive at 1-33 month follow up
Baumann, 2006 ¹⁵	Karolinska Hospital, Sweden	138	30-48 Gy in 2-4 fractions	Stage I	33 months	3 year survival 52% 5 year survival 26%
Zimmerman, 2005 ¹⁶	Technical University, Germany	30	24-37.5 GY in 3-5 doses	Stage I	18 months	80% 12 month survival 75% 24 month survival
Onimaru, 2003 ¹⁷	Hokkaido University Japan	46 (26 with primary lung cancer)	48-60 GY in 8 doses	Stage 1	17 months	47% 2 year survival 60% 2 year cause specific survival
Hara, 2006 ¹⁸	International Medical Center of Japan	59 (11 with primary lung cancer)	20-34 Gy single dose	Stage 1	12 months	76.5% 1 year survival 41% 2 year survival Primary lung cancer not analyzed separately
Fritz, 2006 ¹⁹	Germany	58 (33 primary lung cancer)	30 Gy single dose	Stage 1	18 months	1 year survival 83% 3 year survival 53%

BED Biologically Effective Dose

Table 2: Prospective Studies of Stereotactic Body Radiation Therapy for Early Stage Non Small Cell Lung Cancer

STUDY	TYPE	LOCATION	N	INTERVENTION	INCLUSION	OUTCOMES
COMPLETED						
Timmerman, 2006 ²⁰	Phase II	U of Indiana, US	70	60-66 Gy in 3 fractions	Stage 1 Medically inoperable	Survival Local Control
Koto, 2007 ²¹	Phase II	Japan	31	45 Gy in 3 fractions	T1-2, N0Mo	Survival
Nagata, 2005 ²²	Phase I/II	Japan	45	48 Gy in 4 fractions	Stage 1 A or 1B lung cancer	Survival Local Control



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Le, 2006 ²³	Phase I Dose Escalation	Stanford, CA	32 (21 with NSCLC)	60-66 Gy in 20-22 Gy fracs 15-30 Gy single	Stage 1	Survival
Timmerman, 2003 ²⁴	Phase 1 Dose Escalation	U of Indiana, US	37	24-60 Gy in 3 fractions	T1 or T2 NoMo	Local Control
ONGOING						
RTG 0236	Phase 2	U.S. Multi-institutional	52	3 fractions 20 Gy each=60 Gy	Medically inoperable T1-3 tumors <5 cm ; no lymph nodes, peripheral (excludes tumors of proximal bronchial tree)	Local control and toxicity
RTOG 0618	Phase 2 multi-institutional	U.S. Multi-institutional		20 Gy x 3 vs. surgery;	Tumor <5 Cm ; operable disease	Local control and toxicity
RTOG 0633	Phase 2 Multi-institutional	U.S. Multi-institutional		More gentle fractionation	Centrally situated tumors; medically inoperable	Local control and toxicity
JCOG 0403	Single arm Phase 2	Japan	Accrual plans 100 inoperable and 65 operable patients	48 Gy in 4 fractions over 4-8 days	Operable patients with clinical stage 1A	3 year survival
SPACE	Phase II two arms	Scandinavia	100	66 GY in 3 fractions vs. Conventional treatment 70 Gy with 2 GY per fraction in 35 fractions	Stage I medically inoperable Peripheral tumors	3 year survival

GY Gray

SPACE Stereotactic Precision And Conventional radiotherapy Evaluation

NSCLC Non-small cell lung cancer

JCOG Japan Clinical Oncology Group

RTOG Radiation Therapy Oncology Group

Table 3: Results of Phase I and II Studies of Stereotactic Body Radiation Therapy for Early Stage Non Small Cell Lung Cancer

STUDY	TYPE	LOCATION	N	INTERVENTION	INCLUSION	DURATION OF FOLLOW UP	OUTCOMES
Timmerman, 2006 ²⁰	Phase 2	U of Indiana, US	70	60-66 Gy in 3 fractions	Stage 1 Medically inoperable	17.5 months	2 year survival 54.7% 95% 2 year local control
Koto, 2007 ²¹	Phase 2	Japan	31	45 Gy in 3 fractions	T1-2, N0Mo	32 months	3 year survival 71.7% 3 year cause specific survival 88.5%
Nagata, 2005 ²²	Phase 1/2	Japan	45	48 Gy in 4 fractions	Stage 1 A or 1B lung cancer	30 months	98% local control survival for Stage 1 A:92% 1 year and 83% 3 year Survival for Stage 1B:1 year 82% and 3 year 72%
Le, 2006 ²³	Phase I Dose Escalation	Stanford, CA	32 (21 with NSCLC)	60-66 Gy in 20-22 Gy fracs 15-30 Gy single	Stage 1	12 months	91% survival >20G 54% survival <20 Gy
Timmerman, 2003 ²⁴	Phase 1 Dose Escalation	U of Indiana, US	37	24-60 Gy in 3 fractions	T1 or T2 NoMo	15.2 months	6/37 local failure

Level of Evidence: 4, 5

TA Criterion 2 is not met



TA Criterion 3: The technology must improve net health outcomes.

Retrospective Studies: The ideal therapy for early NSCLC is surgery, which typically results in three to five year survival of 60% to 80%. Lesser surgical therapies are typically associated with lower survival rates. For patients who are medically inoperable, standard radiation therapy results in much lower three to five year survival, on the order of 15% to 45%.

A total of 14 case series of hypofractionated SBRT in the treatment of NSCLC have been reported (Table 1). Each study included between 20 and 245 patients. The majority of participants were either medically inoperable or refused surgical intervention. Five of these studies were conducted in Japan. The remainder of the studies were conducted in the U.S, Europe and Korea. The total radiation dose received ranged from 18-75 Gy and was given in 1-8 doses. Median length of follow up ranged from 11 to 36 months.

Among those retrospective studies reporting one year survival, 52% to 86% were alive at one year. Among those retrospective studies reporting 3 year survival, 52% to 88% of individuals were alive at three years.

The largest retrospective study was a multi-institutional study from Japan⁶. This study included 245 patients from 13 institutions, 158 of whom were medically inoperable. All had tumors that were Stage 1- T1, N0M0. Median length of follow up was 24 months. Three year survival overall was 56% and five year survival was 47%. The cause specific three and five year survival rates were both 78%. In the medically operable patients, the overall survival was much higher- it was 88% with a BED of >100 Gy and 69% with a BED of <100 Gy.

The results of these studies suggest that SBRT is associated with improved survival compared with what has historically been seen in other studies with conventional radiotherapy. In addition, the very high survival seen in medically operable patients seems particularly promising. Local control appears to be dramatically better with SBRT compared with that typically achieved with conventional radiotherapy. However, since none of the retrospective studies compared individuals treated with SBRT to individuals treated with conventional radiotherapy, direct comparisons cannot be made.

Completed Phase I and II Studies: To date five Phase 1 and 2 studies of SBRT for the treatment of NSCLC have been completed. The Phase I studies focused on local control and toxicity. The Phase II studies included a total of 146 patients and assessed survival and local control. In the U.S., Timmerman and colleagues conducted a Phase II

study at the University of Indiana. A total of 70 patients with stage 1, medically inoperable lung cancers were treated with 60-66 GY in three fractions. Mean follow-up was 17.5 months. Two year survival was 54.7%²⁰. The other two Phase II studies were conducted in Japan and included 76 patients with Stage 1 lung cancer. All received 45-48 GY in 3-4 fractions and were followed form 30-32 months. Three year survival ranged from 71.7% to 83%^{21, 22}.

An important toxicity was seen in the University of Indiana Study. Patients who were treated for tumors in the regions around the proximal bronchial tree or chest were more likely to have Grade 3 toxicities than those with peripheral tumors²⁰. Because of this, the ongoing Radiation Therapy Oncology Group trial, RTOG 0236, includes only individuals with peripheral tumors.

Ongoing Phase II Studies: There are five ongoing Phase II studies. Three are U.S. multi-institutional and are sponsored by the RTOG. One includes patients with medically inoperable peripheral tumors, the second will include patients with operable disease and the third will include patients with more centrally situated medically inoperable tumors and will use a gentler fractionation approach. The SPACE study is being conducted in Scandinavia and will compare SBRT with conventional radiotherapy. The final study is being conducted in Japan and will include patients who are both operable and inoperable. All will evaluate local control, toxicity and survival.

Toxicity results from the RTOG 0236 multi-institutional study were recently reported in abstract form at the American Society of Therapeutic and Radiation Oncology (ASTRO) meeting this year. A total of 55 patients with medically inoperable peripheral lesions were treated. The primary endpoint was local control and secondary endpoints included disease free survival, overall survival and toxicity. There were three interim analyses of toxicity. Individuals were followed for a mean of 12.6 months. There were no grade r toxicities (death), only one grade 4 toxicity (decrease in pulmonary function to <25% of predicted) and 5 grade 3 toxicities (including two patients who had a reduction in pulmonary function tests (PFTs). In this study, SBRT appeared to be safe in medically inoperable patients with peripheral lesions. Additional follow-up will be required to determine late toxicities and efficacy data are forthcoming, although at the time of abstract presentation, one patient had had a relapse.

At this time, it is unlikely that a phase II trial comparing SBRT to conventional radiotherapy will be performed in the U.S. When the idea was considered at the National Institutes of Health, it was deemed unethical to randomized patients to conventional radiotherapy. Therefore, any additional evidence for the efficacy of SBRT in the treatment of medically inoperable NSCLC will come from the completion and follow up of the ongoing Phase II trials.

Potential Benefits: Potential benefits include that SBRT is a non-invasive outpatient treatment; is more convenient than conventional radiotherapy, there is no surgical pain or risk of nosocomial infection, there is the potential to save inpatient and ICU costs, less lost time from work, less chronic pain and loss of respiratory capacity. It appears to lead to improved local control compared with historical controls and may lead to improved survival compared with conventional XRT, especially in medically inoperable patients.

Potential Negative Effects: Potential negative effects with SBRT include that increased toxicity has been seen when more centrally located tumors are treated. Complications include pulmonary complications, radiation pneumonitis and esophageal problems. The increased dose to the tumor can also lead to an increased dose to the lungs. Toxic late effects include devascularization, fibrosis and ulceration. Nerves and blood vessels are particularly prone to the toxic effects²⁰. Recent evidence reported in abstract form at the ASTRO meeting from RTOG 0236 showed that SBRT appeared to be safe in patients with peripheral lesions

Summary: Multiple case series and a few Phase I and II studies suggest that SBRT is beneficial for the treatment of NSCLC in medically inoperable patients. However, none of these studies directly compared SBRT to an alternative treatment and study follow-up is generally short. In addition, there are potential toxicities, especially for centrally located tumors, although the treatment of peripheral tumors appears to be safe... Local control appears to be improved with SBRT compared with conventional radiotherapy but evidence for the impact of SBRT on net health outcomes is not available. At this point, although SBRT for NSCLC in medically inoperable patients appears promising, however, there is no current evidence that it improves net health outcomes.

TA Criterion 3 is not met.

TA Criterion 4: The technology must be as beneficial as any established alternatives.

There are few treatment options for medically inoperable NSCLC. The usual treatment approach is conventional radiotherapy. Three year survival with conventional XRT is approximately 15% to 45%.³⁻⁵ Among the retrospective studies of SBRT reporting three year survival, survival rates ranged from 52% to 66%.^{6, 8, 13, 15} Among the Phase I and II studies of SBRT reporting three year survival, survival rates ranged from 71.7% to 83%.^{21, 22} However, none of the completed Phase II studies directly compared SBRT to a conventional radiotherapy or an alternative treatment. It is not possible to compare the survival in the retrospective studies or Phase I/II trials with the historical survival of patients treated with conventional radiotherapy in other studies.



There is the potential for significant toxicity with SBRT, especially with centrally located tumors, although treatment of peripheral lesions appears to be safer. In addition, the follow-up for most of the studies has been relatively short.

Both of the completed Phase I/II studies reporting three year survival were conducted in Japan. The medically inoperable patients in the U.S. seem to have worse survival than the medically inoperable patients in Japan which limits the generalizability from the Japanese studies.

In conclusion, although SBRT for the treatment of medically inoperable lung cancer appears promising, there is currently not enough evidence to conclude that it is as beneficial as any of the established alternatives in improving net health outcomes. Evidence from ongoing Phase II trials should provide additional information.

TA Criterion 4 is not met.

TA Criterion 5: The improvement must be attainable outside of the investigational setting.

Because SBRT has not yet been established in clinical trials as improving net health outcomes for individuals with early stage NSCLC, we cannot evaluate whether any improvement is attainable outside investigational settings. However, if clinical trials are consistent with the results of the reported case series, which were performed in many large clinical settings, it would suggest that the results would be attainable outside of investigational institutions.

TA Criterion 5 is not met.

CONCLUSION

In summary, SBRT for the treatment of medically inoperable NSCLC is a promising new technology. These patients have few treatment options and conventional radiotherapy is associated with limited survival. Retrospective mostly single center studies have showed promise but have not directly compared SBRT with conventional radiotherapy. Early phase I and II trials also suggest improved survival, but have not included a comparison group. In addition, an increase in Grade 3 toxicity has been seen when treating centrally located tumors. However, recent analysis of the toxicity profile in RTOG 0236, a trial of SBRT in medically inoperable patients with peripheral lesions showed very low rates of toxicity at 12 month follow-up, suggesting that treatment of peripheral lesions is safe. Ongoing Phase II studies will provide additional information about survival and longer term toxicity and some will also compare SBRT with other treatment options.



The evidence is insufficient at this time to recommend SBRT as a treatment for medically inoperable early stage NSCLC. Additional follow-up of the ongoing Phase II trials will provide additional important information about long term toxicity and survival.

RECOMMENDATION

It is recommended that stereotactic body radiation therapy for the treatment of early stage lung cancer in medically inoperable patients does not meet CTAF TA criteria 2-5, for safety, effectiveness, and improvement in outcomes.

It is the opinion of the reviewer that criteria were not met as stated in the recommendation. However, after listening to the testimony of invited experts and further clarification of the data as the experts understand it, the CTAF panel voted six in favor and four opposed to the following alternate recommendation:

“In medically inoperable patients with early stage non-small cell lung cancer the evidence for SBRT is sufficient for peripheral lesions. These cases have few options and the current evidence suggests SBRT is better than conventional XRT.”

June 18, 2008

(This is a first review of this topic by CTAF)



RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association (BCBSA)

The BCBSA Technology Evaluation Center has not conducted a review of stereotactic body radiotherapy for any extracranial sites.

Centers for Medicare and Medicaid Services (CMS)

CMS is silent on the use of stereotactic body radiotherapy for the treatment of NSCLC.

California Radiological Society (CRS)

CRS recognized ASTRO participation at the meeting and deferred to their opinion.

American Society of Therapeutic and Radiation Oncology (ASTRO)

ASTRO representatives provided written opinion and testimony at the meeting.

California Thoracic Society (CTS)

CTS was invited to provide an opinion on the use of this technology and to provide testimony at the meeting.

American College of Chest Physicians (ACCP)

ACCP was invited to provide an opinion on the use of this technology and to provide testimony at the meeting.

Association of Northern California Oncologists (ANCO)

ANCO provided written opinion in support of the use of this technology. An ANCO representative was not available to attend.

Medical Oncology Association of Southern California (MOASC)

MOASC was invited to provide an opinion on the use of this technology and to provide testimony at the meeting.

National Comprehensive Cancer Network (NCCN)

The NCCN Clinical Practice Guidelines in Oncology™ for Non-Small Cell Lung Cancer v.2.2008 note support for the use of SBRT for NSCLC for patients with tumors 5 cm or less in maximal dimension that are not near a primary or secondary bronchus.(see pages 24 and 47)

ABBREVIATIONS USED IN THIS REVIEW

SBRT	Stereotactic Body Radiotherapy
NSCLC	Non small cell lung cancer
TNM	Tumor, lymph nodes, metastasis
XRT	External Radiation Therapy
COPD	Chronic obstructive pulmonary disorder
Gy	Gray
DARE	Database of Abstracts of Reviews of Effects
RTOG	Radiation Therapy Oncology Group
JCOG	Japan Clinical Oncology Group
BED	Biologically Effective Dose
SPACE	Stereotactic Precision And Conventional radiotherapy Evaluation
PFTs	Pulmonary function tests

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