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ASCO SPECIAL ARTICLE

Stereotactic Body Radiotherapy for Early-Stage Non–Small-Cell Lung Cancer: American Society of Clinical Oncology Endorsement of the American Society for Radiation Oncology Evidence-Based Guideline

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Editor's note: This American Society of Clinical Oncology Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a Data Supplement with additional evidence tables, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/thoracic-cancer-guidelines and www.asco.org/guidelineswiki.

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ABSTRACT

Purpose
The American Society for Radiation Oncology (ASTRO) produced an evidence-based guideline on treatment with stereotactic body radiotherapy (SBRT) for patients with early-stage non–small-cell lung cancer. ASCO has a policy and set of procedures for endorsing and/or adapting clinical practice guidelines that have been developed by other professional organizations.

Methods
The ASTRO Evidence-Based Guideline for Stereotactic Body Radiotherapy for Early-Stage Non–Small-Cell Lung Cancer was reviewed for developmental rigor by methodologists. An ASCO Expert Panel updated the literature search and reviewed the guideline content and recommendations.

Results
The ASCO Expert Panel determined that the recommendations from the ASTRO guideline, published in 2017, are clear, thorough, and based on the most relevant scientific evidence. ASCO statements and minor modifications were added to enhance the applicability of the ASTRO guideline for the broader ASCO audience.

Recommendations
For standard operative risk patients with stage I NSCLC, SBRT is not recommended outside of a clinical trial. Lobectomy with systematic lymph node evaluation remains the recommended treatment, although a sublobar resection may be considered in select clinical scenarios. Recommendations are provided regarding the use of SBRT in high operative risk patients and for inoperative patients, including in challenging scenarios where tumors are: centrally located, > 5 cm in diameter, lacking tissue diagnosis, synchronous primary or multifocal, second primary after pneumonectomy, proximal to or involved with mediastinal structures, abutting the chest wall, or recurring after previous treatment. Qualifying statements are included to provide further guidance for implementation, and the importance of a discussion of treatment options among members of the multidisciplinary cancer care team is emphasized. Additional information is available at: www.asco.org/thoracic-cancer-guidelines and www.asco.org/guidelineswiki.

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INTRODUCTION

More than 155,000 estimated deaths will be attributable to non–small-cell lung cancer (NSCLC) in the United States in 2017, making it the leading cause of cancer death for both men and women.[1] Approximately 16% of new cases will be early-stage localized tumors.[2,3] According to the 7th edition of the American Joint Committee on Cancer staging system, these are T1 or T2 tumors with no regional lymph node or distant metastases.[4]

Early-stage NSCLC has historically been treated with lobectomy[5] and mediastinal/hilar lymph node sampling,[3] while sublobar resection may be an option for patients with low pulmonary reserve and early-stage lung cancer.[6] In cases where patients are not fit or healthy enough to be candidates for surgery, or where surgery is declined, alternative effective treatment options are desirable. Historical attempts to use conventionally fractionated radiation therapy in this scenario have met with limited success in terms of local control due to difficulties with delivering an effective dose and

ASSOCIATED CONTENT

Appendix
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Data Supplement
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THE BOTTOM LINE

Stereotactic Body Radiotherapy for Early-Stage Non–Small-Cell Lung Cancer: American Society of Clinical Oncology Endorsement of the American Society for Radiation Oncology Evidence-Based Guideline

Guideline Questions

For patients with early-stage (T1-2, N0) NSCLC:

- When is SBRT appropriate for operable or inoperable patients?
- For medically inoperable patients, how can SBRT techniques be individually tailored in high-risk clinical scenarios?
- For medically inoperable patients, what is the role of SBRT as salvage therapy for early-stage lung cancer that recurs?

Target Population

Operable and inoperable patients with early-stage NSCLC.

Target Audience

Members of the multidisciplinary team, including surgical oncologists, radiation oncologists, medical oncologists, pulmonologists, and other health care providers.

ASCO Key Recommendations for SBRT for Early-Stage NSCLC

The recommendation statements outlined below include ASTRO's ratings of evidence quality and strength of recommendations. The ASCO Expert Panel's modifications and qualifying statements to ASTRO's recommendations appear in bold. A list of the original ASTRO recommendations can be found in Appendix Table A1 (online only). References to staging in this document are based on the 7th edition of the American Joint Committee on Cancer staging system.

Part 1. Recommendations for SBRT for patients with T1-2, N0 NSCLC who are medically operable.

- Recommendation 1A. **Patients with stage I NSCLC should be evaluated by a thoracic surgeon, preferably within a multidisciplinary cancer care team, to determine operability. The decision to undergo an operation should be made by the surgeon and patient, in collaboration with family members. Some criteria that have been used to define operative risk are listed in the qualifying statements below** (Strength of recommendation: strong; Quality of evidence: moderate).
- Recommendation 1B. For patients with standard operative risk and stage I NSCLC, SBRT is not recommended as an alternative to surgery outside of a clinical trial. Discussions about SBRT **among members of the multidisciplinary cancer care team may be appropriate.** For this population, lobectomy with systematic mediastinal/hilar lymph node evaluation remains the recommended treatment, though a sublobar resection may be considered in select clinical scenarios (Strength of recommendation: strong; Quality of evidence: high).
- Recommendation 1C. For patients with high operative risk stage I NSCLC, discussions about SBRT as a potential alternative to surgery are encouraged **within the multidisciplinary cancer care team. In cases where SBRT is offered,** patients should be informed that while SBRT may have decreased risks from treatment in the short term, the longer-term outcomes $>$ 3 years are not well established (Strength of recommendation: conditional; Quality of evidence: moderate).
  - ASCO qualifying statement: Where multidisciplinary consultation and patient preference result in a decision to perform resection in high operative risk patients, limited resection (segmentectomy or wedge resection), rather than lobectomy, is more commonly selected. At this time, there have been no prospective randomized trials completed that directly compare limited resection with SBRT.
  - ASCO qualifying statement: Longer-term data from the RTOG 0236 phase II trial of inoperable T1-T2N0M0 tumors $\leq$ 5 cm showed that rates of 5-year primary tumor, in-lobe, and locoregional failure were 7%, 20%, and 38%, respectively. Overall survival at 5 years was 40%. Treatment-related grade 3, grade 4, and grade 5 adverse events were reported in 27%, 4%, and 0% of patients, respectively.[3]
  - ASTRO qualifying statement: While there is no universally accepted definition, high operative risk has been defined by various studies as "$FEV_1 < 50\%$ predicted, diffusing capacity of the lungs for carbon monoxide $< 50\%$ predicted, or a combination of advanced age, impaired pulmonary function, pulmonary hypertension, and poor left ventricular function. A thoracic surgeon who specializes in lung resections remains the best person to assess operative risk."[3(p9)]

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THE BOTTOM LINE (CONTINUED)

Part 2. Recommendations for SRBT for medically inoperable patients with T1-2, N0 NSCLC.
With centrally located tumors:

- Recommendation 2A. SBRT directed toward centrally located lung tumors carries unique and significant risks when compared with treatment directed at peripherally located tumors. The use of 3 fraction regimens **is not recommended** in this setting (Strength of recommendation: strong; Quality of evidence: high).

ASCO qualifying statement: There is a significant rate of nodal disease in this population; therefore, pretreatment staging with positron emission tomography (PET)/computed tomography (CT) and invasive mediastinal/hilar staging with endobronchial ultrasound (EBUS)/mediastinoscopy is recommended.

- Recommendation 2B. **Providers should use caution when considering SBRT for central tumors. Delivery of SBRT** in **more than 3 (ie,** 4 or 5) fractions **may reduce the risk of severe toxicity.** Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment. For central tumors for which SBRT is deemed too high-risk **(eg, tumors directly abutting or invading the esophagus or proximal bronchial tree)**, hypofractionated radiotherapy utilizing 6-15 fractions **or conventionally fractionated radiotherapy may** be considered (Strength of recommendation: conditional; Quality of evidence: moderate).

ASTRO qualifying statement: Caution is recommended due to the potential for serious toxicity to normal centrally located tissues**.** "In this setting, adequate informed consent to patients—including a discussion of patient risk tolerance and goals of care—is a necessary part of communication between radiation oncologists and patients."[3(p12)]
ASCO qualifying statement: The RTOG 0813 phase I/II study aimed to evaluate escalating radiation doses ranging from 50 to 60 Gy in five fractions delivered every other day to central tumors $\leq$ 5 cm (including tumors within 2 cm of the tracheobronchial tree, and abutting the pericardium, mediastinum, or spine). Four patients, including one treated to 10.5 Gy $\times$ 5, two treated to 11.5 Gy $\times$ 5, and one treated to 12 Gy $\times$ 5, experienced grade 5 or fatal adverse events, while those treated at the lowest dose level did not experience any grade $\geq$ 3 events. We are currently awaiting mature, long-term efficacy results presented in full manuscript form from this trial. These results will be used to determine whether there is a dose that results in an acceptable balance of tumor control and toxicity.
For patients with tumors $>$ 5 cm in diameter:

- Recommendation 2C. SBRT **may be an** appropriate option for **select** tumors $>$ 5 cm in diameter with an acceptable therapeutic ratio. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment (Strength of recommendation: conditional; Quality of evidence: low).

Definition: Therapeutic ratio refers to a treatment schedule that balances maximizing tumor cell kill while minimizing radiation-induced acute and late morbidity to surrounding critical structures.
ASCO qualifying statement: There is a significant rate of nodal disease in this population; therefore, accurate pretreatment invasive mediastinal/hilar staging with EBUS/mediastinoscopy is recommended.
ASCO qualifying statement: Chemotherapy is currently recommended as the standard treatment of tumors $>$ 4 cm after surgical resection. Adjuvant therapy may also be considered after SBRT; however, limited data are available to support its use.
For patients lacking tissue confirmation (diagnosis):

- Recommendation 2D. Whenever possible, obtain a biopsy prior to treatment with SBRT to confirm a histologic diagnosis of a malignant lung nodule (Strength of recommendation: strong; Quality of evidence: high).
- Recommendation 2E. SBRT **may** be delivered in patients who refuse a biopsy, have undergone nondiagnostic biopsy, or who are thought to be at prohibitive risks of biopsy. Prior to SBRT in patients lacking tissue confirmation of malignancy, **treatment options should** be discussed **with**in a multidisciplinary **cancer care team** with a consensus that the lesion is radiographically and clinically consistent with a malignant lung lesion based on tumor, patient, and environmental factors (Strength of recommendation: strong; Quality of evidence: moderate).

ASTRO qualifying statement: Tumor-specific factors to consider include lesion size, growth over time, presence of spiculations or lack of benign-appearing calcifications, PET avidity, and lesion location. Other patient-specific factors, such as smoking history or history of prior lung cancers, should also be considered. Regional environmental factors, such as the incidence of histoplasmosis, may affect the probability that a lesion is malignant and should also be considered in the calculation of obtaining histologic confirmation.[3]
ASCO qualifying statement: Patients should be staged with PET/CT and mediastinal/hilar nodal sampling when feasible.
ASCO qualifying statement: For patients deemed to be at prohibitive risk of biopsy, a multidisciplinary discussion should occur to ensure that safe means of obtaining tissue are not feasible (eg, transbronchial biopsy, etc). In addition, consideration should also be given as to whether SBRT would pose prohibitive risks. The goals, expectations, and potential increased risks of SBRT should be carefully weighed and discussed with the patient and family in the context of shared decision making.

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THE BOTTOM LINE (CONTINUED)

For patients with synchronous primary or multifocal tumors:

- Recommendation 2F. Multiple primary lung cancers (MPLC) can be difficult to differentiate from intrathoracic metastatic lung cancer and pose unique issues for parenchymal preservation; therefore, it is recommended that they are evaluated by a multidisciplinary **cancer care** team (Strength of recommendation: strong; Quality of evidence: moderate).
- Recommendation 2G. PET/CT and brain MRI are recommended in patients suspected of having MPLC to help differentiate from intrathoracic metastatic lung cancer. Invasive mediastinal**/hilar** staging **with EBUS/mediastinoscopy** should be **strongly considered** (Strength of recommendation: strong; Quality of evidence: moderate).
- Recommendation 2H. SBRT may be considered **by the multidisciplinary cancer care team** as a **potentially** curative treatment option for patients with synchronous MPLC. (Strength of recommendation: conditional; Quality of evidence: low)

ASTRO qualifying statement: SBRT for synchronous MPLC has equivalent rates of local control and may have comparable toxicity but decreased rates of overall survival compared with SBRT for single tumors.[3] The decision to treat multiple lesions with SBRT is an individualized process that should be discussed by a multidisciplinary cancer care team, as this approach may increase radiation doses to normal tissues and increase the risk of toxicity in some cases (Strength of recommendation: conditional; Quality of evidence: low).

- Recommendation 2I. SBRT **may be considered by the multidisciplinary cancer care team** as a **potentially** curative treatment option for patients with metachronous MPLC (Strength of recommendation: strong; Quality of evidence: moderate).

ASTRO qualifying statement: SBRT for metachronous MPLC has comparable rates of local control and toxicity and overall survival compared with single tumors.[3]

For patients who underwent pneumonectomy and now have a new primary tumor in their remaining lung:

- Recommendation 2J. SBRT may be considered **by the multidisciplinary cancer care team as a potentially** curative treatment option for patients with metachronous MPLC in a postpneumonectomy setting (Strength of recommendation: conditional; Quality of evidence: low).

ASTRO qualifying statement: "While SBRT for metachronous MPLC appears to have equivalent rates of local control and acceptable toxicity compared to single tumors, SBRT in the post-pneumonectomy setting might have a higher rate of toxicity than in patients with higher baseline lung capacity."[3(p22)] Delivery of SBRT would depend on tumor location, size, and patient comorbidities, and patients should be thoroughly evaluated by a multidisciplinary cancer care team.

ASTRO qualifying statement: "Generally, great caution should be taken to minimize the dose to the single lung, as high-grade radiation pneumonitis in a single lung may be a serious and potentially life-threatening toxicity."[3(p23)] The potential for radiation pneumonitis should be discussed with patients, and a pulmonary evaluation should be obtained, including pulmonary function tests and consideration of a pulmonary evaluation by a dedicated pulmonologist.

Part 3: Recommendations for patients with tumors with intimal proximity/involvement of mediastinal structures (bronchial tree, esophagus, heart, etc).

- Recommendation 3A. **Providers should use caution when considering SBRT for** tumors in close proximity to the proximal bronchial tree. **Delivery of SBRT in** 4-5 fractions **may reduce the risks of severe toxicity.** Physicians should endeavor to meet the constraints that have been used in prospective studies, given the severe toxicities that have been reported (Strength of recommendation: strong; Quality of evidence: low).

ASTRO qualifying statement: There are a limited number of retrospective studies that report the use of SBRT in patients with tumors abutting the proximal bronchial tree. Patients with tumors abutting the proximal airways should be counseled about the potential for fatal treatment complications, even when dose constraints and highly conformal SBRT techniques are used.[3]

ASCO qualifying statement: Appropriate staging, including PET/CT and invasive mediastinal/hilar staging with EBUS/mediastinoscopy, are recommended due to the high risk of nodal disease in this patient population.

- Recommendation 3B. **Where a discussion within the multidisciplinary cancer care team results in a recommendation for SBRT for** tumors in close proximity to the esophagus, physicians should endeavor to meet the constraints that have been used in prospective studies or otherwise reported in the literature, given the severe esophageal toxicities that have been reported (Strength of recommendation: strong; Quality of evidence: low).

ASTRO qualifying statement: Severe, life-threatening esophageal toxicity is possible after SBRT. Despite limited data to support firm recommendations, dose to the esophagus should be carefully assessed and minimized. Highly conformal techniques can be used to facilitate esophageal avoidance with central tumors.[3]

- Recommendation 3C. For tumors in close proximity to the heart and pericardium, SBRT should be delivered in 4-5 fractions with low incidence of serious toxicities to the heart, pericardium, and large vessels observed. Adherence to volumetric and maximum dose constraints used in prospective trials or reported in the literature may optimize the safety profile of this treatment (Strength of recommendation: strong; Quality of evidence: low).

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THE BOTTOM LINE (CONTINUED)

For tumors abutting or invading the chest wall:

- Recommendation 3D. SBRT is an appropriate option for treatment and **may** be offered for T1-2 tumors that abut the chest wall. Grade 1 and 2 chest wall toxicity**, presenting most commonly as pain due to rib fracture or irritation of the intercostal nerves,** is a common occurrence post SBRT that usually resolves with conservative management. Patients with peripheral tumors approximating the chest wall should be counseled on the possibility of this common toxicity (Strength of recommendation: strong; Quality of evidence: high).

ASTRO qualifying statement: The volume of chest wall receiving SBRT has been identified as a predictor of chest wall toxicity; however, the use of highly conformal techniques to reduce this volume may increase dose to the ipsilateral lung. Thus "compromising coverage of the planning target volume (PTV) or PTV trimming away from the chest wall are not favored as techniques to meet chest wall constraints."[3(p27)]

- Recommendation 3E. Until further evidence becomes available to inform the topic, the ASCO Expert Panel defers a decision for or against endorsement of the use of SBRT in patients with cT3 disease due to chest wall invasion.

Part 4. Recommendations for the role of SBRT in medically inoperable patients, as salvage therapy for early-stage lung cancer that recurs. After conventionally fractionated radiotherapy, SBRT, or sublobar resection:

- Recommendation 4A. The use of salvage SBRT after primary conventionally fractionated radiation may be offered to selected patients **who are identified as appropriate candidates following a discussion among members of the multidisciplinary cancer care team** (Strength of recommendation: conditional; Quality of evidence: low).

ASTRO qualifying statement: Patients should be informed of the risk of significant (including fatal) toxicities associated with SBRT as salvage therapy after conventionally fractionated radiation.[3]

ASTRO qualifying statement: "For centrally located salvage SBRT after an in-field recurrence, … severe toxicities were more common than some other retrospective reports and included a 23% grade 3 pneumonitis risk, 6% grade 5 pneumonitis risk, and 6% grade 5 hemoptysis risk. The authors conclude that local control can be achieved but that the high-risk nature of these central in-field recurrences warrants caution due to significant risk of grade 5 fatal events."[3(p30)]

- Recommendation 4B. Patient selection for salvage SBRT after **prior treatment, including** primary conventionally fractionated radiation**, SBRT, or sublobar resection,** is a highly individualized process. Radiation oncologists should assess evidence-based patient, tumor, and treatment factors prior to treatment initiation (Strength of recommendation: strong; Quality of evidence: low).

ASTRO qualifying statement: "Salvage SBRT treatment plans should ideally be reviewed with medical physics and other radiation oncologists (in a peer review quality assurance setting) to ensure high-quality results to optimize patient selection, maximize local control and survival, and minimize treatment toxicities."[3(p30)]

ASTRO qualifying statement: Toxicities vary on an individual basis depending on patient's health, prior treatment, comorbidities, etc and should be discussed within the multidisciplinary cancer care team. "Predictors of toxicity for SBRT salvage include central tumor location, in-field recurrence, larger treatment volumes, bilateral mediastinal primary PTV targets, composite lung V20 (the percentage of the lung volume [with subtraction of the volume involved by lung cancer] that receives radiation doses of 20 Gy or more) $\geq$ 30%, $FEV_1 \leq 65\%$,[9] and poor baseline performance status."[3(p30)]

Patients' values, goals, and preferences.

ASCO qualifying statement: In written comments, the ASCO Expert Panel Patient Representative noted that there is a lack of strong evidence for many of the guideline recommendations. Thus, the Representative emphasized the importance of shared decision making between physicians, patients, and families in this context, because benefits and risks can have a different meaning for each patient, and patients and families will vary in their values, goals, and preferences, depending on factors such as overall health, comorbidities, and age (J. Feldman, personal communication, April 2017).

Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at www.asco.org/thoracic-cancer-guidelines and www.asco.org/guidelineswiki. Patient information is available at www.cancer.net

A link to the ASTRO guideline can be found at http://www.practicalradonc.org/article/S1879-8500(17)30121-2/fulltext

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

high rates of toxicity because of limited ability to define and constrain treatment volumes with this technique.[3] For these reasons, stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiation therapy or SABR, defined as "a strategy that employs very high (ie, ablative) doses of radiation delivered to the cancer target over 1-5 fractions with highly conformal techniques,"[3(p1)] emerged as a treatment option. In the Radiation Therapy Oncology Group (RTOG) 0236 phase II trial of SBRT in inoperable patients with peripheral tumors ≤ 5 cm, 5-year estimates of primary tumor, involved-lobe, and locoregional failure were 7%, 13%, and 38%, respectively, after a median follow-up of 4 years.[7] Due to difficulties with accrual, no phase III randomized controlled trials comparing SBRT to surgical resection have been completed to date; however, it is already widely used for early-stage peripherally located inoperable lung cancer[8] and has shown encouraging results in patients who are not fit or healthy enough to undergo surgery.[5]

The American Society of Radiation Oncology (ASTRO) has developed an evidence-based guideline for the use of SBRT in patients who are considered standard operative risk or high operative risk and those who present with more clinically challenging scenarios in terms of tumor size or location, as well as cases without tissue diagnosis or with tumors that are synchronous primary or multifocal, second primary after pneumonectomy, or recurrent after previous treatment.[3] The ASCO Expert Panel (Appendix Table A2, online only) critically appraised the ASTRO guideline on SBRT for early-stage NSCLC and added minor clarifications and qualifying statements to the ASTRO recommendations to enhance the applicability of the guideline for the broader ASCO audience. This endorsement reinforces the recommendations provided in the ASTRO guideline and acknowledges the effort put forth by ASTRO to produce an evidence-based guideline informing practitioners who care for patients with early-stage NSCLC. The ASTRO recommendations are listed in the Bottom Line Box, with qualifying statements from the ASCO Expert Panel. The full ASTRO guideline is available at http://www.practicalradonc.org/article/S1879-8500(17)30121-2/fulltext, with supplemental material available at http://www.practicalradonc.org/article/S1879-8500(17)30121-2/addons.

OVERVIEW OF THE ASCO GUIDELINE ENDORSEMENT PROCESS

ASCO has policies and procedures for endorsing and/or adapting practice guidelines that have been developed by other professional organizations, with the goal of increasing the number of high-quality, ASCO-vetted guidelines available to the ASCO membership. The process involves an assessment by ASCO staff of candidate guidelines for methodological quality using the Rigour of Development subscale of the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument (see Methodology Supplement for more detail). The ASTRO guideline for SBRT in early-stage lung cancer rated highly on the AGREE II instrument and was identified as a potential candidate for endorsement by ASCO. During the endorsement process, modifications and qualifying statements were made by the ASCO Expert Panel to improve the guideline's applicability to the broader ASCO guideline audience.

DISCLAIMER

The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. ("ASCO") to assist providers in clinical decision making. The information therein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis, and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

GUIDELINE AND CONFLICTS OF INTEREST

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

CLINICAL QUESTION(S) AND TARGET POPULATION

The ASTRO guideline addressed four key clinical questions regarding the treatment of early-stage NSCLC with SBRT: (1) When is SBRT appropriate for patients with T1-2, N0 NSCLC who are medically operable? (2) When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC who have (a) centrally located tumors, (b) tumors > 5 cm in diameter, (c) tissue

confirmation (diagnosis) lacking, (d) synchronous primary or multifocal tumors, (e) undergone pneumonectomy and now have a new primary tumor in their remaining lung. (3) For patients who have medically inoperable early-stage lung cancer, how can SBRT techniques be individually tailored to provide an adequate dose for tumor eradication with minimal risk to normal structures in the following high-risk clinical scenarios: (a) tumors with intimal proximity/involvement of mediastinal structures (bronchial tree, esophagus, heart, etc), (b) tumors abutting or invading the chest wall. (4) In medically inoperable patients, what is the role of SBRT as salvage therapy for early-stage lung cancer that recurs (a) after conventionally fractionated radiotherapy, (b) after SBRT, (c) after sublobar resection? The target population for the ASTRO guideline is patients with early-stage operable or inoperable NSCLC cancer.

SUMMARY OF THE ASTRO GUIDELINE DEVELOPMENT METHODOLOGY

The ASTRO Board of Directors approved the development of an evidence-based clinical practice guideline on SBRT for early-stage lung cancer in June 2015. A task force consisting of radiation oncologists with surgical and patient representation was formed to work together to develop the guideline. A manuscript was drafted, and, following review by five expert reviewers and a public comment period, the ASTRO Board of Directors approved the final guideline in March 2017. The ASTRO guideline provides guidance regarding the use of SBRT for patients in challenging, controversial, high-risk, and salvage clinical scenarios. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system and panel consensus were used by ASTRO to rate the quality of evidence and strength of recommendations. The literature search of PubMed MEDLINE spanned January 1995 to August 3, 2016. Details of the search strategies and the study inclusion criteria and outcomes of interest are available at http://www.practicalradonc.org/article/S1879-8500(17)30121-2/fulltext. The ASTRO searches identified 172 studies for inclusion in the qualitative literature synthesis.

RESULTS OF THE ASCO METHODOLOGY REVIEW

The methodology review of the ASTRO guideline was completed independently by two ASCO guideline staff members using the Rigour of Development subscale from the AGREE II instrument. Overall, the ASTRO guideline scored 80% (Methodology Supplement). Detailed results of the scoring for this guideline are available upon request to guidelines@asco.org.

RESULTS OF THE ASCO CONTENT REVIEW

The comments from a preliminary ASCO content review of the ASTRO guideline were forwarded to ASTRO for consideration during their public consultation process. The ASCO Expert Panel reviewed the ASTRO SBRT guideline and concurs that the recommendations are clear, thorough, based on the most relevant scientific evidence in this content area, and present options that will be acceptable to patients. Overall, the ASCO Expert Panel agrees with the recommendations as stated in the guideline, with minor modifications and qualifying statements.

METHODS AND RESULTS OF THE ASCO UPDATED LITERATURE REVIEW

ASCO guidelines staff updated the ASTRO literature search. PubMed MEDLINE was searched from August 1, 2016 to April 1, 2017. The search was restricted to systematic reviews, meta-analyses, randomized controlled trials and observational studies published in English. The updated search for all questions yielded 319 records. Nine of these studies, including a systematic review and eight observational studies, met the inclusion criteria. The results of these studies, which are outlined briefly, were consistent with the ASTRO guideline recommendations. See Data Supplement 1 for detailed data tables and Data Supplement 3 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram outlining the results of the literature search update.

CHARACTERISTICS AND QUALITY ASSESSMENT OF INCLUDED STUDIES

One systematic review of SBRT that included 34 studies of outcomes in 4,570 patients with mostly inoperable SBRT met the inclusion criteria for the updated literature review.[12] Three studies using administrative data from large databases, including the Surveillance, Epidemiology, and End Results (SEER) database, and the National Cancer Database (NCDB) also met the inclusion criteria.[5,10,11] The NCDB includes data for approximately 70% of patients with NSCLC in the United States,[5] while SEER is a collection of registry data on cancer cases from various locations and sources throughout the United States (http://seer.cancer.gov/about). These large database studies included an analysis of 5,821 elderly patients $\geq$ 65 years of age,[10] a study of $>$ 15,000 patients who were free of the comorbid conditions that can frequently confound outcomes of comparisons between SBRT and surgery,[5] as well as a study that evaluated the efficacy of SBRT delivered to patients with larger tumors.[11]

Of the remaining five studies,[12-16] four were single-institution case series,[13-16] of which one was prospective[14] and the remaining three were retrospective.[13,15,16] One study included data from multiple institutions.[12] The sample sizes for these studies ranged from 59[14] to 201[11] patients. Each study focused on specific populations of interest, including patients undergoing SBRT in the recurrent setting,[14] patients with larger tumors,[11,12,15] patients who had been diagnosed with interstitial lung disease prior to SBRT,[13] and elderly patients.[10,16] There were no studies found in the update that addressed other subpopulations of patients undergoing SBRT that were highlighted in the ASTRO guideline, including those with centrally located tumors, lack of tissue confirmation of cancer diagnosis, and synchronous or metachronous MPLC.

No randomized controlled trials met the inclusion criteria for the literature review update. Due to the potential for bias that is associated with nonrandomized study designs, observational studies are usually considered low-quality evidence (ie, there is generally a low level of confidence in the estimate of the effects demonstrated in observational studies). This quality rating may be upgraded to moderate in cases where there is a very large effect, evidence of a dose-response gradient, or where potential confounding would be expected to reduce the effect.[17] As none of these moderating effects were observed across the small number of studies that met the update inclusion criteria, this body of evidence is rated low quality.

A common method of analysis across a number of the included studies was propensity matching analysis (PMA), which is intended to reduce "bias due to confounding factors by matching patients on numerous baseline variables using a multivariable logistic regression model."[16(p2)] This type of analysis can help reduce the bias arising from the tendency for less-healthy patients to receive SBRT. Where available, results within studies from PMAs are reported in the outcomes section rather than results from unmatched analyses.

This is the most recent information as of the publication date. For updates, the most recent information, and to submit new evidence, please visit www.asco.org/thoracic-cancer-guidelines and the ASCO Guidelines Wiki (www.asco.org/guidelineswiki).

OUTCOMES OF INCLUDED STUDIES

Systematic Reviews. Murray et al[8] reported results for 4- to 5-year overall survival and local control with SBRT to be 39.6% (95% CI, 17% to 83%; based on results from eight studies) and 89.6% (95% CI, 83% to 95%, based on results from five studies), respectively. The authors reported that grade 3 and 4 adverse events ranged from 2.7% to 27% across studies. The most common adverse events reported by patients were pneumonitis, dyspnea, chest pain, and pneumonia. Grade 1 and 2 adverse events were common, especially fatigue.

Large administrative database studies (SEER and NCCB). Three retrospective studies from large administrative databases were included.[5,10,11] Paul et al[10] used the SEER database to explore outcomes for elderly patients (≥ 65 years of age) who underwent SBRT or thoracoscopic resection (sublobar resection in the case of tumors ≤ 2 cm). The results of their primary analysis comparing patients with tumors ≤ 5 cm using PMA methods found a significantly improved rate of overall survival with video-assisted thoracoscopic resection versus SBRT (hazard ratio [HR], 1.92; 95% CI, 1.62 to 2.26; $P < .001$). In a second large database study, Rosen et al[5] focused on healthy patients only in their analysis of the NCDB to reduce the potential for bias associated with unhealthy patients being more likely to receive SBRT and also more likely to have worse outcomes. For clinical stage T1 patients, the difference in overall survival was not significant up to 7.5 months after diagnosis; however, after 7.5 months of follow-up, the HR showed a significant difference in favor of patients treated with lobectomy versus SBRT (HR, 0.38; 95% CI, 0.33 to 0.43).[5] PMA results demonstrated a median survival of 59% (lobectomy) versus 29% (SBRT; $P < .001$).[5] Another recently published NCDB study included 201 patients who underwent SBRT with tumors ≥ 5 cm, 15% of whom had also received chemotherapy.[11] In this study, the median overall survival was 25.1 months.

Single-institution studies. **Patients with larger (≥ 5 cm) tumors.** Tekatli et al[15] retrospectively explored the use of SBRT in a study of 63 patients who received doses of five fractions delivered in 2 weeks (every other day) or eight fractions delivered in 2.5 weeks at 7.5 Gy per fraction (three or four fractions per week). Patients were followed for a median of 54.7 months, and the local control rate was 95.8% at 2 years, while overall survival was 81% at 2 years and 31.5% at 4 years, and disease-free survival was 82.1% at 2 years. The grade ≥ 3 toxicity rate was 30%, with radiation pneumonitis the most frequently reported adverse event, affecting 19% of study participants. Fatal toxicity occurred in five of the eight patients (63%) who initially presented with interstitial lung disease (ILD).

Patients with pre-existing ILD. Bahig et al[13] focused specifically on the subset of patients with preexisting ILD who received SBRT.[13] The SBRT doses in this group were according to the STARS (Stereotactic Ablative Radiotherapy in Stage I Non-Small Cell Lung Cancer Patients Who Can Undergo Lobectomy), RTOG 0236, and RTOG 0813 RTCs. The authors found that the ILD-positive patients experienced a significantly greater rate of grade ≥ 3 radiation pneumonitis compared with the ILD-negative patients (32% *v* 4%; $P < .001$).

SBRT in the recurrent setting. In the only prospective study included in the updated evidence base, Sun et al[14] explored the use of SBRT in the recurrent setting, delivered at a dose of 50 Gy in four fractions. After salvage radiation therapy, the rate of local failure calculated using the competing risks method was 3.5% (95% CI, 0.6% to 13.5%) at 1 year and 5.2% (95% CI, 1.7% to 15.7%) at 5 years. The rates of any failure were 15.4% (95% CI, 8.5 to 28.1) at 1 year and 32.8% (95% CI, 22.7 to 47.5) at 5 years. Median overall survival was 63.8 months (95% CI, 46.8 to 80.9 months) from time of salvage radiation therapy. There was an overall rate of grade 2 adverse events of 31%, the most common of which was radiation pneumonitis. Grade 3 adverse events were experienced by three patients (5%), including one instance of dermatitis and two cases of radiation pneumonitis.[14]

SBRT in an elderly patient population. Another retrospective study[16] used propensity matching analysis to compare 35 older (≥ 60 years) matched pairs who underwent either surgery or SBRT. Local recurrence was significantly higher with SBRT compared with surgery (1-, 3-, and 5-year local control rates with surgery: 91.3%, 84.6%, 80.7%, respectively, and 1-, 3-, and 5-year local control rates with SBRT: 78.7%, 71.0%, 53.6%, respectively). Results for overall survival did not differ significantly. This study did not report adverse events.

Multi-institution studies. **Patients with larger (≥ 5 cm) tumors.** Verma et al[12] analyzed 92 patients from 12 institutions who underwent SBRT for tumors ≥ 5 cm (median, 5.4 cm; range, 5.0 to 7.5 cm). Median overall survival was 21.4 months, and 2-year survival was 46%. The rate of local control was 95.7% at 1 year and 73.2% at 2 years. The rate of grade ≥ 3 toxicity was 6.5%. Five grade 3 toxicities were experienced, including one case of dermatitis and four cases of radiation pneumonitis. In addition, one case of grade 5 radiation pneumonitis occurred.

DISCUSSION

ASCO endorses the ASTRO Stereotactic Body Radiation Therapy for Early-Stage Non–Small-Cell Lung Cancer Evidence-Based Clinical Practice Guideline with qualifying statements and minor modifications to the ASTRO guideline recommendations. The ASTRO guideline recommendations confirm that surgery remains the standard of care for standard operative risk patients with early-stage NSCLC and provides guidance on the use of SBRT for inoperable patients in more challenging clinical scenarios. The ASCO Expert Panel added minor modifications to several of the recommendations to emphasize the importance of discussing treatment options within the multidisciplinary cancer care team wherever possible. In addition, the Expert Panel emphasized the importance of adequate staging, including PET/CT and invasive staging of mediastinal and hilar nodes with mediastinoscopy or EBUS, in subpopulations with higher rates of nodal metastases, such as patients with tumors ≥ 5 cm. They also chose to include some qualifying statements and key evidence from the ASTRO guideline narrative to provide context for the recommendations and assist practitioners in implementation of the guideline.

In addition, when reviewing the ASTRO guidelines, the Expert Panel discussed the recommendations for SBRT for tumors abutting or invading the chest wall (Recommendations 3D, 3E). The Panel agreed that while SBRT may be an option for tumors abutting the chest wall, chest wall pain due to rib fracture or irritation of the intercostal nerves due to treatment with SBRT is a common occurrence. The Panel also agreed with the ASTRO guidelines indicating that chest wall pain can be alleviated with conservative management and that prevalence of this toxicity should be discussed with patients with peripheral tumors approximating the chest wall. Few patients with tumors invading the chest wall have been enrolled in prospective trials of SBRT; therefore, the ASCO Expert Panel concluded that a recommendation for or against SBRT could not be endorsed at this time due to the lack of a sufficient body of evidence on outcomes in the population with cT3 tumors < 5 cm.[3]

At this time, there is a lack of strong evidence for use of SBRT in many of the subpopulations addressed in the guideline. As a result, the patient representative on the ASCO Expert Panel highlighted the importance of shared decision making between physicians, patients, and families. She emphasized that benefits and risks can have a different meaning for each patient, and patients and families will vary in their values, goals, and preferences, depending on factors such as overall health, existing comorbidities, and age (J. Feldman, personal communication, April 2017).

The ASCO literature search update resulted in nine new studies added to the evidence base. These additional studies did not present evidence that resulted in any modifications to the ASTRO recommendations. One study demonstrated that patients with preexisting

interstitial lung disease had a significantly higher rate of grade ≥ 3 radiation pneumonitis, and the authors of that study advised that care be taken when weighing the risks and benefits of treatment in that subgroup.

Some patient-matched comparisons of surgery compared with SBRT in our updated literature search, such as an NCDB study of patients without comorbidities, demonstrated significantly better results for patients who underwent surgery. These retrospective, nonrandomized studies have an inherent risk of confounding due their study design; therefore, to improve the evidence base for clinical decision making, adequately powered randomized controlled trials are needed to accurately compared SBRT with surgery.[8] Several prospective studies are currently underway, such as the VALOR (Veterans Affairs Lung cancer surgery Or stereotactic Radiotherapy) study in operable patients (ClinicalTrials.gov identifier: NCT02984761), and the Stablemates trial comparing SBRT to sublobar resection in high-risk patients (ClinicalTrials.gov identifier: NCT02468024). The most relevant comparison may be SBRT versus minimally invasive surgery rather than thoracotomy, which is associated with higher rates of morbidity.[10]

These guidelines, although currently providing the best possible guidance on SBRT in early-stage NSCLC, will be updated as more and better information is published, including new data from ongoing randomized trials.

ADDITIONAL RESOURCES

More information, including a Data Supplement with the updated search strategy and PRISMA flow diagram, a Methodology Supplement, slide sets, and clinical tools and resources, is available at www.asco.org/thoracic-cancer-guidelines and www.asco.org/guidelineswiki. Patient information is available at www.cancer.net. Visit www.asco.org/guidelineswiki to provide comments on the guideline or to submit new evidence.

Related ASCO Guidelines

- Integration of Palliative Care Into Standard Oncology Care[18] (http://ascopubs.org/doi/full/10.1200/JCO.2016.70.1474)
- Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I to IIIA Completely Resected Non–Small-Cell Lung Cancers[19] (http://ascopubs.org/doi/full/10.1200/JCO.2017.72.4401)
- Management of Chronic Pain in Survivors of Adult Cancers[20] (http://ascopubs.org/doi/full/10.1200/JCO.2016.68.5206)
- Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers[21] (http://ascopubs.org/doi/full/10.1200/JCO.2016.70.5400)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. American Cancer Society: Cancer Facts & Figures 2016. Atlanta, GA, 2016. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2016/cancer-facts-and-figures-2016.pdf
2. Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, April 2015.
3. Videtic GMM, Donington J, Giuliani M, et al: Stereotactic body radiation therapy for early-stage non–small cell lung cancer: An ASTRO Evidence-Based Guideline [Supplementary Material: http://www.practicalradonc.org/cms/attachment/2106516698/2081656719/mmc1.pdf]. Pract Radiat Oncol 7:295-301, 2017
4. Edge SB, Byrd DR, Compton CC, et al (eds): AJCC Cancer Staging Manual, 7th Ed. Paris, France, Springer, 2010
5. Rosen JE, Salazar MC, Wang Z, et al: Lobectomy versus stereotactic body radiotherapy in healthy patients with stage I lung cancer. J Thorac Cardiovasc Surg 152: 44-54.e9, 2016
6. Asamura H: Role of limited sublobar resection for early-stage lung cancer: Steady progress. J Clin Oncol 32:2403-2404, 2014
7. Timmerman RD, Hu C, Michalski J, et al: Long-term results of RTOG 0236: A phase II trial of stereotactic body radiation therapy (SBRT) in the treatment of patients with medically inoperable stage I non–small cell lung cancer. Int J Radiat Oncol Biol Phys 90:S30, 2014
8. Murray P, Franks K, Hanna GG: A systematic review of outcomes following stereotactic ablative radiotherapy in the treatment of early-stage primary lung cancer. Br J Radiol 90:20160732, 2017
9. Liu H, Zhang X, Vinogradskiy YY, et al: Predicting radiation pneumonitis after stereotactic ablative radiation therapy in patients previously treated with conventional thoracic radiation therapy. Int J Radiat Oncol Biol Phys 84:1017-1023, 2012
10. Paul S, Lee PC, Mao J, et al: Long term survival with stereotactic ablative radiotherapy (SABR) versus thoracoscopic sublobar lung resection in elderly people: National population based study with propensity matched comparative analysis. BMJ 354: i3570, 2016
11. Verma V, McMillan MT, Grover S, et al: Stereotactic body radiation therapy and the influence of chemotherapy on overall survival for large (≥ 5 centimeter) non–small cell lung cancer. Int J Radiat Oncol Biol Phys 97:146-154, 2017
12. Verma V, Shostrom VK, Kumar SS, et al: Multi-institutional experience of stereotactic body radiotherapy for large (≥ 5 centimeters) non–small cell lung tumors. Cancer 123:688-696, 2017
13. Bahig H, Filion E, Vu T, et al: Severe radiation pneumonitis after lung stereotactic ablative radiation therapy in patients with interstitial lung disease. Pract Radiat Oncol 6:367-374, 2016
14. Sun B, Brooks ED, Komaki R, et al: Long-term outcomes of salvage stereotactic ablative radiotherapy for isolated lung recurrence of non–small cell lung cancer: A phase II clinical trial. J Thorac Oncol 12: 983-992, 2017
15. Tekatli H, van 't Hof S, Nossent EJ, et al: Use of stereotactic ablative radiotherapy (SABR) in non–small cell lung cancer measuring more than 5 cm. J Thorac Oncol 12:974-982, 2017
16. Wang P, Zhang D, Guo XG, et al: A propensity-matched analysis of surgery and stereotactic body radiotherapy for early stage non–small cell lung cancer in the elderly. Medicine (Baltimore) 95:e5723, 2016
17. The Cochrane Collaboration: Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0, in Higgins JPT, Green S (eds), March 2011. Part 12.2 Assessing the quality of a body of evidence. URL: http://handbook-5-1.cochrane.org/

18. Ferrell BR, Temel JS, Temin S, et al: Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 35:96-112, 2017

19. Kris MG, Gaspar LE, Chaft JE, et al: Adjuvant systemic therapy and adjuvant radiation therapy for stage I to IIIA completely resected non–small-cell lung cancers: American Society of Clinical Oncology/Cancer Care Ontario Clinical Practice Guideline Update. J Clin Oncol 35:2960-2974, 2017

20. Paice JA, Portenoy R, Lacchetti C, et al: Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 34: 3325-3345, 2016

21. Armenian SH, Lacchetti C, Barac A, et al: Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 35: 893-911, 2017

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Appendix

Table A1. Original ASTRO and ASCO Endorsed Research Questions, Recommendations, and Qualifying Statements

ASTRO Recommendation	ASCO Endorsed Recommendation	ASTRO Evidence Rating and Strength of Recommendations
Key Question 1: When is SBRT appropriate for patients with T1-2, N0 NSCLC who are medically operable?		
Recommendation 1A: Any patient with operable stage I NSCLC being considered for SBRT should be evaluated by a thoracic surgeon, preferably in a multidisciplinary setting, to reduce specialty bias.	Recommendation 1A: **Patients with stage I NSCLC should be evaluated by a thoracic surgeon, preferably within a multidisciplinary cancer care team, to determine operability. The decision to undergo an operation should be made by the surgeon and patient, in collaboration with family members. Some criteria that have been used to define operative risk are listed in the qualifying statements under Recommendation 1C.**	Strength of recommendation: strong; Quality of evidence: moderate
Recommendation 1B: For patients with standard operative risk (ie., with anticipated operative mortality of $< 1.5\%$) and stage I NSCLC, SBRT is not recommended as an alternative to surgery outside of a clinical trial. Discussions about SBRT are appropriate, with the disclosure that long-term outcomes with SBRT > 3 years are not well-established. For this population, lobectomy with systematic mediastinal lymph node evaluation remains the recommended treatment, though a sublobar resection may be considered in select clinical scenarios.	Recommendation 1B: For patients with standard operative risk and stage I NSCLC, SBRT is not recommended as an alternative to surgery outside of a clinical trial. Discussions about SBRT **among members of the multidisciplinary cancer care team may be appropriate**. For this population, lobectomy with systematic mediastinal/hilar lymph node evaluation remains the recommended treatment, though a sublobar resection may be considered in select clinical scenarios.	Strength of recommendation: strong; Quality of evidence: high
Recommendation 1C: For patients with high operative risk (ie., those who cannot tolerate lobectomy, but are candidates for sublobar resection) stage I NSCLC, discussions about SBRT as a potential alternative to surgery are encouraged. Patients should be informed that while SBRT may have decreased risks from treatment in the short term, the longer-term outcomes > 3 years are not well-established.	Recommendation 1C: For patients with high operative risk stage I NSCLC, discussions about SBRT as a potential alternative to surgery are encouraged **within the multidisciplinary cancer care team. In cases where SBRT is offered,** patients should be informed that while SBRT may have decreased risks from treatment in the short term, the longer-term outcomes > 3 years are not well-established. ASCO qualifying statement: Where multidisciplinary consultation and patient preference result in a decision to perform resection in high operative risk patients, limited resection (segmentectomy or wedge resection), rather than lobectomy, is more commonly selected. At this time, there have been no prospective randomized trials completed that directly compare limited resection with SBRT or lobectomy. ASCO qualifying statement: Longer-term data from the RTOG 0236 phase II trial of inoperable T1-T2N0M0 tumors ≤ 5 cm showed that rates of 5-year primary tumor, in-lobe, and locoregional failure were 7%, 20%, and 38%, respectively. Overall survival at 5 years was 40%. Treatment-related grade 3, grade 4, and grade 5 adverse events were reported in 27%, 4%, and 0% of patients, respectively. ASTRO qualifying statement: **While there is no universally accepted definition, high operative risk has been defined by various studies as** "$FEV_1 < 50\%$ predicted, $D_{LCO} < 50\%$ predicted, or a combination of advanced age, impaired pulmonary function, pulmonary hypertension, and poor left ventricular function. Operative risk should be assessed by a thoracic surgeon who specializes in lung resections."[3]	Strength of recommendation: conditional; Quality of evidence: moderate
Key Question 2 (part 1): When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC: for patients with centrally located tumors:		
Recommendation 2A: SBRT directed toward centrally located lung tumors carries unique and significant risks when compared with treatment directed at peripherally located tumors. The use of 3 fraction regimens should be avoided in this setting.	Recommendation 2A: SBRT directed toward centrally located lung tumors carries unique and significant risks when compared with treatment directed at peripherally located tumors. The use of 3 fraction regimens **is not recommended** in this setting. ASCO qualifying statement: There is a significant rate of nodal disease in this population; therefore, pretreatment staging with PET/CT and invasive mediastinal/hilar staging with EBUS/mediastinoscopy is recommended.	Strength of recommendation: strong; Quality of evidence: high

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Table A1. Original ASTRO and ASCO Endorsed Research Questions, Recommendations, and Qualifying Statements (continued)

ASTRO Recommendation	ASCO Endorsed Recommendation	ASTRO Evidence Rating and Strength of Recommendations
Recommendation 2B: SBRT directed at central lung tumors should be delivered in 4 or 5 fractions. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment. For central tumors for which SBRT is deemed too high-risk, hypofractionated radiotherapy utilizing 6-15 fractions can be considered.	Recommendation 2B: **Providers should use caution when considering SBRT for central tumors. Delivery of SBRT in more than 3 (ie,** 4 or 5**)** fractions **may reduce the risk of severe toxicity**. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment. For central tumors for which SBRT is deemed too high-risk **(eg, tumors directly abutting or invading the esophagus or proximal bronchial tree)**, hypofractionated radiotherapy utilizing 6-15 fractions **or conventionally fractionated radiotherapy may** be considered. ASTRO qualifying statement: **Caution is recommended due to the potential for serious toxicity to normal centrally located tissues.** "In this setting, adequate informed consent to patients—including a discussion of patient risk tolerance and goals of care—is a necessary part of communication between radiation oncologists and patients"[3] ASCO qualifying statement: The RTOG 0813 phase I/II study aimed to evaluate escalating radiation doses ranging from 50 to 60 Gy in five fractions delivered every other day to central tumors ≤ 5 cm (including tumors within 2 cm of the tracheobronchial tree, and abutting the pericardium, mediastinum, or spine). Four patients, including one treated to 10.5 Gy × 5, two treated to 11.5 Gy × 5, and one treated to 12 Gy × 5, experienced grade 5 or fatal adverse events, while those treated at the lowest dose level did not experience any grade ≥ 3 events. We are currently awaiting mature, long-term efficacy results presented in full manuscript form from this trial. These results will be used to determine whether there is a dose that results in an acceptable balance of tumor control and toxicity.	Strength of recommendation: conditional; Quality of evidence: moderate
Key Question 2 (part 2): When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC: for patients with tumors > 5 cm in diameter:		
Recommendation 2C: SBRT is an appropriate option for tumors > 5 cm in diameter with an acceptable therapeutic ratio. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment.	Recommendation 2C: SBRT **may be an** appropriate option for **select** tumors > 5 cm in diameter with an acceptable therapeutic ratio. Adherence to volumetric and maximum dose constraints may optimize the safety profile of this treatment. Definition: Therapeutic ratio refers to a treatment schedule that balances maximizing tumor cell kill while minimizing radiation-induced acute and late morbidity to surrounding critical structures. ASCO qualifying statement: There is a significant rate of nodal disease (locate reference) in this population; therefore, accurate pretreatment invasive mediastinal/hilar staging with EBUS/mediastinoscopy is recommended. ASCO qualifying statement: Chemotherapy is currently recommended as the standard treatment of tumors > 4 cm after surgical resection. Adjuvant therapy may also be considered after SBRT; however, limited data are available to support its use.	Strength of recommendation: conditional; Quality of evidence: low
Key Question 2 (part 3): When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC: for patients lacking tissue confirmation (diagnosis):		
Recommendation 2D: Whenever possible, obtain a biopsy prior to treatment with SBRT to confirm a histologic diagnosis of a malignant lung nodule.	Recommendation 2D: Whenever possible, obtain a biopsy prior to treatment with SBRT to confirm a histologic diagnosis of a malignant lung nodule.	Strength of recommendation: strong; Quality of evidence: high
Recommendation 2E: SBRT can be delivered in patients who refuse a biopsy, have undergone nondiagnostic biopsy, or who are thought to be at prohibitive risks of biopsy. Prior to SBRT in patients lacking tissue confirmation of malignancy, patients are recommended to be discussed in a multidisciplinary manner with a consensus that the lesion is radiographically and clinically consistent with a malignant lung lesion based on tumor, patient, and environmental factors.	Recommendation 2E: SBRT **may** be delivered in patients who refuse a biopsy, have undergone nondiagnostic biopsy, or who are thought to be at prohibitive risks of biopsy. Prior to SBRT in patients lacking tissue confirmation of malignancy, **treatment options should be discussed within a multidisciplinary cancer care team** with a consensus that the lesion is radiographically and clinically consistent with a malignant lung lesion based on tumor, patient, and environmental factors. ASTRO Qualifying statement: Tumor-specific factors to consider include lesion size, growth over time, presence of spiculations or lack of benign-appearing calcifications, PET avidity, and lesion location. Other patient-specific factors, such as smoking history or history of prior lung cancers, should also be considered. Regional environmental factors, such as the incidence of histoplasmosis, may affect the probability that a lesion is a malignant and should also be considered in the calculation of obtaining histologic confirmation.[3] ASCO qualifying statement: Patients should be staged with PET/CT and mediastinal/hilar nodal sampling when feasible. ASCO qualifying statement: For patients deemed to be at prohibitive risk of biopsy, a multidisciplinary discussion should occur to ensure that safe means of obtaining tissue are not feasible (eg, transbronchial biopsy, etc). In addition, consideration should also be given as to whether treatment would pose prohibitive risks. The goals, expectations, and potential increased risks of SBRT should be carefully weighed and discussed with the patient and family in the context of shared decision making.	Strength of recommendation: strong; Quality of evidence: moderate

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Table A1. Original ASTRO and ASCO Endorsed Research Questions, Recommendations, and Qualifying Statements (continued)

ASTRO Recommendation	ASCO Endorsed Recommendation	ASTRO Evidence Rating and Strength of Recommendations
Key Question 2 (part 4): When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC: for patients with synchronous primary or multifocal tumors:		
Recommendation 2F: Multiple primary lung cancers (MPLC) can be difficult to differentiate from intrathoracic metastatic lung cancer and pose unique issues for parenchymal preservation; therefore, it is recommended that they are evaluated by a multidisciplinary team.	Recommendation 2F: Multiple primary lung cancers (MPLC) can be difficult to differentiate from intrathoracic metastatic lung cancer and pose unique issues for parenchymal preservation; therefore, it is recommended that they are evaluated by a multidisciplinary **cancer care** team.	Strength of recommendation: strong; Quality of evidence: moderate
Recommendation 2G: PET/CT and brain MRI are recommended in patients suspected of having MPLC to help differentiate from intrathoracic metastatic lung cancer. Invasive mediastinal staging should be addressed on a case-by-case basis.	Recommendation 2G: PET/CT and brain MRI are recommended in patients suspected of having MPLC to help differentiate from intrathoracic metastatic lung cancer. Invasive mediastinal**/hilar** staging **with EBUS/ mediastinoscopy** should be **strongly considered.**	Strength of recommendation: strong; Quality of evidence: moderate
Recommendation 2H: SBRT may be considered as a curative treatment option for patients with synchronous MPLC. SBRT for synchronous MPLC has equivalent rates of local control and toxicity but decreased rates of overall survival compared with those with single tumors.	Recommendation 2H: SBRT may be considered **by the multidisciplinary cancer care team** as a **potentially** curative treatment option for patients with synchronous MPLC. ASTRO qualifying statement: SBRT for synchronous MPLC has equivalent rates of local control and **may have comparable** toxicity but decreased rates of overall survival compared with SBRT for single tumors.[3] **The decision to treat multiple lesions with SBRT is an individualized process that should be discussed by a multidisciplinary care team, as this approach may increase radiation doses to normal tissues and increase the risk of toxicity in some cases.**	Strength of recommendation: conditional; Quality of evidence: low
Recommendation 2I: SBRT is recommended as a curative treatment option for patients with metachronous MPLC. SBRT for metachronous MPLC has equivalent rates of local control and toxicity and overall survival compared with those with single tumors.	Recommendation 2I: SBRT **may be considered by the multidisciplinary cancer care team** as a **potentially** curative treatment option for patients with metachronous MPLC. ASTRO qualifying statement: SBRT for metachronous MPLC has comparable rates of local control and toxicity and overall survival compared with single tumors.[3]	Strength of recommendation: strong; Quality of evidence: moderate
Key Question 2 (part 5): When is SBRT appropriate for medically inoperable patients with T1-2, N0 NSCLC: for patients who underwent pneumonectomy and now have a new primary tumor in their remaining lung:		
Recommendation 2J: SBRT may be considered a curative treatment option for patients with metachronous MPLC in a post-pneumonectomy setting. While SBRT for metachronous MPLC appears to have equivalent rates of local control and acceptable toxicity compared with single tumors, SBRT in the post-pneumonectomy setting might have a higher rate of toxicity than in patients with higher baseline lung capacity.	Recommendation 2J: SBRT may be considered **by the multidisciplinary cancer care team as a potentially** curative treatment option for patients with metachronous MPLC in a post-pneumonectomy setting. ASTRO qualifying statement: "While SBRT for metachronous MPLC appears to have equivalent rates of local control and acceptable toxicity compared to single tumors, SBRT in the post-pneumonectomy setting might have a higher rate of toxicity than in patients with higher baseline lung capacity."[3] **Delivery of SBRT would depend on tumor location, size, and patient comorbidities and patients should be thoroughly evaluated by a multidisciplinary cancer care team**. ASTRO qualifying statement: "Generally, great caution should be taken to minimize the dose to the single lung, as high grade radiation pneumonitis in a single lung may be a serious and potentially life-threatening toxicity."[3] **The potential for radiation pneumonitis should be discussed with patients, and a pulmonary evaluation should be obtained, including pulmonary function tests and consideration of a pulmonary evaluation by a dedicated pulmonologist.**	Strength of recommendation: conditional; Quality of evidence: low
Key Question 3 (part 1): For patients with medically inoperable early-stage lung cancer, how can SBRT techniques be individually tailored to provide an adequate dose for tumor eradication with minimal risk to normal structures in high-risk clinical scenarios, including: for tumors with intimal proximity/involvement of mediastinal structures (bronchial tree, esophagus, heart, etc):		
Recommendation 3A: For tumors in close proximity to the proximal bronchial tree, SBRT should be delivered in 4-5 fractions. Physicians should endeavor to meet the constraints that have been used in prospective studies given the severe toxicities that have been reported.	Recommendation 3A: **Providers should use caution when considering SBRT for** tumors in close proximity to the proximal bronchial tree. **Delivery of SBRT in** 4-5 fractions **may reduce the risks of severe toxicity.** Physicians should endeavor to meet the constraints that have been used in prospective studies given the severe toxicities that have been reported. ASTRO qualifying statement: **There are a limited number of retrospective studies that report the use of SBRT in patients with tumors abutting the proximal bronchial tree**. Patients with tumors abutting the proximal airways should be counseled about the potential for fatal treatment complications, even when dose constraints and highly conformal SBRT techniques are used.[3] ASCO qualifying statement: Appropriate staging, including PET/CT and invasive mediastinal/hilar staging with EBUS/mediastinoscopy, are recommended due to the high risk of nodal disease in this patient population.	Strength of recommendation: strong; Quality of evidence: low

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Table A1. Original ASTRO and ASCO Endorsed Research Questions, Recommendations, and Qualifying Statements (continued)

ASTRO Recommendation	ASCO Endorsed Recommendation	ASTRO Evidence Rating and Strength of Recommendations
Recommendation 3B: For tumors in close proximity to the esophagus, physicians should endeavor to meet the constraints that have been used in prospective studies or otherwise reported in the literature given the severe esophageal toxicities that have been reported.	Recommendation 3B: **Where a discussion within the multidisciplinary cancer care team results in a recommendation for SBRT for** tumors in close proximity to the esophagus, physicians should endeavor to meet the constraints that have been used in prospective studies or otherwise reported in the literature given the severe esophageal toxicities that have been reported. ASTRO qualifying statement: "Severe, life-threatening esophageal toxicity is possible after SBRT. Despite limited data to support firm recommendations, dose to the esophagus should be carefully assessed and minimized. Highly conformal techniques can be used to facilitate esophageal avoidance with central tumors."[3]	Strength of recommendation: strong; Quality of evidence: low
Recommendation 3C: For tumors in close proximity to the heart and pericardium, SBRT should be delivered in 4-5 fractions with low incidence of serious toxicities to the heart, pericardium, and large vessels observed. Adherence to volumetric and maximum dose constraints used in prospective trials or reported in the literature may optimize the safety profile of this treatment.	Recommendation 3C: For tumors in close proximity to the heart and pericardium, SBRT should be delivered in 4-5 fractions with low incidence of serious toxicities to the heart, pericardium and large vessels observed. Adherence to volumetric and maximum dose constraints used in prospective trials or reported in the literature may optimize the safety profile of this treatment.	Strength of recommendation: strong; Quality of evidence: low
Key Question 3 (part 2): For patients with medically inoperable early-stage lung cancer, how can SBRT techniques be individually tailored to provide an adequate dose for tumor eradication with minimal risk to normal structures in high-risk clinical scenarios, including: for tumors abutting or invading the chest wall:		
Recommendation 3D: SBRT is an appropriate option for treatment and should be offered for T1-2 tumors that abut the chest wall. Grade 1 and 2 chest wall toxicity is a common occurrence post SBRT that usually resolves with conservative management. Patients with peripheral tumors approximating the chest wall should be counseled on the possibility of this common toxicity.	Recommendation 3D: SBRT is an appropriate option for treatment and **may** be offered for T1-2 tumors that abut the chest wall. Grade 1 and 2 chest wall toxicity**, presenting most commonly as pain due to rib fracture or irritation of the intercostal nerves,** is a common occurrence post SBRT that usually resolves with conservative management. Patients with peripheral tumors approximating the chest wall should be counseled on the possibility of this common toxicity. ASTRO qualifying statement: The volume of chest wall receiving SBRT has been identified as a predictor of chest wall toxicity; however, the use of highly conformal techniques to reduce this volume may increase dose to the ipsilateral lung. Thus "compromising coverage of the planning target volume (PTV) or PTV trimming away from the chest wall are not favored as a techniques to meet chest wall constraints."[3]	Strength of recommendation: strong; Quality of evidence: high
Recommendation 3E: SBRT may be used in patients with cT3 disease due to chest wall invasion without clear evidence of reduced efficacy or increased toxicity compared with tumors abutting the chest wall.	Recommendation 3E: Until further evidence becomes available to inform the topic, the ASCO Expert Panel defers a decision for or against endorsement of the use of SBRT in patients with cT3 disease due to chest wall invasion.	
Key Question 4 (part 1): In medically inoperable patients, what is the role of SBRT as salvage therapy for early-stage lung cancer that recurs? After conventionally fractionated radiotherapy:		
Recommendation 4A: The use of salvage SBRT after primary conventionally fractionated radiation may be offered to selected patients due to reported favorable local control and survival.	Recommendation 4A: The use of salvage SBRT after primary conventionally fractionated radiation may be offered to selected patients **who are identified as appropriate candidates following a discussion among members of the multidisciplinary cancer care team.** ASTRO qualifying statement: Patients should be informed of the risk of significant (including fatal) toxicities associated with SBRT as salvage therapy after conventionally fractionated radiation.[3] ASTRO qualifying statement: "For centrally located salvage SBRT after an in-field recurrence, … severe toxicities were more common than some other retrospective reports and included a 23% grade 3 pneumonitis risk, 6% grade 5 pneumonitis risk, and 6% grade 5 hemoptysis risk. The authors conclude that LC can be achieved but that the high-risk nature of these central in-field recurrences warrants caution due to significant risk of grade five fatal events."[3]	Strength of recommendation: conditional; Quality of evidence: low
Recommendation 4B: Patients treated with salvage SBRT after primary conventionally fractionated radiation should be informed of significant (including fatal) toxicities.	Recommendation 4B: See qualifying statements for recommendation 4A.	Strength of recommendation: strong; Quality of evidence: low

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Table A1. Original ASTRO and ASCO Endorsed Research Questions, Recommendations, and Qualifying Statements (continued)

ASTRO Recommendation	ASCO Endorsed Recommendation	ASTRO Evidence Rating and Strength of Recommendations
Recommendation 4C: Patient selection for salvage SBRT after primary conventionally fractionated radiation is a highly individualized process. Radiation oncologists should assess evidence-based patient, tumor, and treatment factors prior to treatment initiation.	Recommendation 4C: Patient selection for salvage SBRT after **prior treatment, including** primary conventionally fractionated radiation**, SBRT, or sublobar resection** is a highly individualized process. Radiation oncologists should assess evidence-based patient, tumor, and treatment factors prior to treatment initiation. ASTRO qualifying statement: "Salvage SBRT treatment plans should ideally be reviewed with medical physics and other radiation oncologists (in a peer review quality assurance setting) to ensure high-quality results to optimize patient selection, maximize local control and survival, and minimize treatment toxicities."[3] ASTRO qualifying statement: **Toxicities vary on an individual basis depending on patient's health, prior treatment, comorbidities, etc, and should be discussed within the multidisciplinary cancer care team.** "Predictors of toxicity for SBRT salvage include central tumor location, in-field recurrence, larger treatment volumes, bilateral mediastinal primary PTV targets, composite lung V20 $\geq$ 30%,[9] $FEV_1 \leq 65\%$,[9] and poor baseline performance status."[3]	Strength of recommendation: strong; Quality of evidence: low
Key Question 4 (part 2): In medically inoperable patients, what is the role of SBRT as salvage therapy for early-stage lung cancer that recurs? After SBRT:		
Recommendation 4D: Patient selection for salvage SBRT after previous SBRT is a highly individualized process. Radiation oncologists should assess evidence-based patient, tumor, and treatment factors prior to treatment initiation.	Recommendation 4D: See Recommendation 4C	Strength of recommendation: strong; Quality of evidence: low
Key Question 4 (part 3): In medically inoperable patients, what is the role of SBRT as salvage therapy for early-stage lung cancer that recurs? After sublobar resection:		
Recommendation 4E: Patient selection for salvage SBRT after prior sublobar resection is a highly individualized process. Radiation oncologists should assess evidence-based patient, tumor, and treatment factors prior to treatment initiation.	Recommendation 4E: See Recommendation 4C	Strength of recommendation: strong; Quality of evidence: low
Patients' values, goals and preferences:		
	ASCO qualifying statement: In written comments, the ASCO Expert Panel Patient Representative noted that there is a lack of strong evidence for many of the guideline recommendations. Thus, the Representative emphasized the importance of shared decision-making between physicians, patients and families in this context, because benefits and risks can have a different meaning for each patient, and patients and families will vary in their values, goals and preferences, depending on factors such as overall health, comorbidities and age (J. Feldman, personal communication, April 2017).	

NOTE. The ASCO Expert Panel's modifications and qualifying statements to ASTRO's recommendations appear in bold.
Abbreviations: ASTRO, American Society for Radiation Oncology; CT, computed tomography; D_{LCO}, diffusing capacity of the lungs for carbon monoxide; EBUS, endobronchial ultrasound; MPLC, multiple primary lung cancers; MRI, magnetic resonance imaging; NSCLC, non–small-cell lung cancer; PTV, planning target volume; RTOG, Radiation Therapy Oncology Group; SBRT, stereotactic body radiotherapy; V20, percentage of lung volume (with subtraction of the volume involved by lung cancer) that receives radiation doses of 20 Gy or more.

Table A2. ASCO Endorsement of the American Society for Radiation Oncology Guideline for Stereotactic Body Radiotherapy in Early-Stage Non–Small-Cell Lung Cancer Expert Panel Membership

Name	Affiliation
Bryan J. Schneider, MD, Co-Chair	University of Michigan, Ann Arbor, MI
Megan E. Daly, MD	University of California, Davis, CA
Mara B. Antonoff, MD	MD Anderson Cancer Center, Houston TX
Stephen Broderick, MD	Johns Hopkins Medicine, Baltimore, MD
Shruti Jolly, MD	University of Michigan, Ann Arbor, MI
Jill Feldman, Patient Representative	Lungevity Foundation, Chicago, IL
Bryan Meyers, MD	Washington University, St Louis, MO
Gaetano Rocco, MD	Istituto Nazionale Tumori, IRCCS, Naples, Italy
Chad Rusthoven, MD, Practice Guidelines Implementation Representative	University of Colorado Hospital, Aurora, CO
Ben J. Slotman, MD, PhD	Vrije Universiteit Medical Center, Amsterdam, Netherlands
Daniel H. Sterman, MD	NYU Langone Medical Center, New York, NY
Brendon Stiles, MD, Co-Chair	Weill Cornell Medical College, New-York Presbyterian Hospital, New York, NY

NOTE. ASCO Staff: Erin B. Kennedy, MHSc.

Stereotactic body radiotherapy (SBRT) is a definitive local treatment option for patients with stage I non-small cell lung cancer (NSCLC) who are not surgical candidates and patients who refuse surgery. The purpose of this study was to assess the impact of SBRT on T1â€“T2 NSCLC from a national registry, reflecting practices and outcomes in a real-world setting.Â Stereotactic body radiotherapy Lung cancer Non-small cell lung cancer Registry Radiosurgery. Introduction. The standard treatment for patients with stage I (IA and IB) non-small cell lung cancer (NSCLC) with no medical contraindication is surgery. Non-small cell lung cancer, version 5.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2017;15(4):504-535. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg.Â Stereotactic body radiotherapy for early-stage non-small-cell lung cancer: American Society of Clinical Oncology endorsement of the American Society for Radiation Oncology evidence-based guideline. J Clin Oncol. 2017:JCO2017749671. Videtic GM, Donington J, Giuliani M, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: executive summary of an ASTRO evidence-based guideline. Pract Radiat Oncol. The American Cancer Society medical and editorial content team. Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing. Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Ch. 69 - Cancer of the Lung: Non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. Abeloffâ€™s Clinical Oncology.Â NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. V.4.2019. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf on June 6, 2019.Â Radiation therapy for early stage lung cancer. Semin Intervent Radiol. 2013;30(2):185â€“190.