ORIGINAL ARTICLE

Long-Term Survival and Failure Outcomes of Single-Fraction Stereotactic Body Radiation Therapy in Early Stage NSCLC

Austin J. Iovoli, MD,[a] Sharan Prasad, BSc,[b] Sung Jun Ma, MD,[a] Fatemeh Fekrmandi, MD, MSc,[a] Nadia K. Malik, MD,[a] Simon Fung-Kee-Fung, MD,[a] Mark K. Farrugia, MD, PhD,[a] Anurag K. Singh, MD[a,*]

[a]*Department of Radiation Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, New York*
[b]*Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York*

Received 5 June 2023; revised 12 October 2023; accepted 30 October 2023
Available online - 2 November 2023

ABSTRACT

Introduction: This study aims to report our 13-year institutional experience with single-fraction stereotactic body radiation therapy (SF-SBRT) for early stage NSCLC.

Methods: A single-institutional retrospective review of patients with biopsy-proven peripheral cT1-2N0M0 NSCLC undergoing definitive SF-SBRT between September 2008 and May 2022 was performed. All patients were treated to 27 Gy with heterogeneity corrections or 30 Gy without. Primary outcomes were overall survival and progression-free survival. Secondary outcomes included local failure, nodal failure, distant failure, and second primary lung cancer.

Results: Among 263 eligible patients, the median age was 76 years (interquartile range [IQR]: 70–81 y) and median follow-up time was 27.2 months (IQR: 14.25–44.9 mo). Median tumor size was 1.9 cm (IQR: 1.4–2.6 cm), and 224 (85%) tumors were T1. There were 92 patients (35%) alive at the time of analysis with a median follow-up of 34.0 months (IQR: 16.6–50.0 mo). Two- and five-year overall survival was 65% and 26%, respectively. A total of 74 patients (28%) developed disease progression. Rates of five-year local failure, nodal failure, distant failure, and second primary lung cancer were 12.7%, 14.7%, 23.5%, and 12.0%, respectively.

Conclusions: Consistent with multiple prospective randomized trials, in a large real-world retrospective cohort, SF-SBRT for peripheral early stage NSCLC was an effective treatment approach.

Keywords: Lung cancer; NSCLC; SBRT; Radiation; Radiosurgery

Introduction

NSCLC is the leading cause of cancer-related deaths in the United States, killing more than 120,000 people each year.[1,2] With increasing utilization of lung cancer screening, the proportion of patients diagnosed with early stage disease is rising.[3] Current standard-of-care treatment for early stage NSCLC includes surgical resection or radiation therapy depending on candidacy for surgery and patient preference.[4] Among both operable and inoperable patients, stereotactic body radiation therapy (SBRT) has been found to have high overall survival (OS) and local control with low toxicity rates.[5–10] Multiple studies have found SBRT to have comparable outcomes with surgical resection in early stage NSCLC, with the added benefit of noninvasiveness and stable quality of life.[5,11–14]

*Corresponding author.

Dr. Iovoli and Mr. Prasad are co-first authors.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Anurag K. Singh, MD, Department of Radiation Medicine, Roswell Park Comprehensive Cancer Center, 665 Elm Street, Buffalo, NY 14203. E-mail: Anurag.Singh@RoswellPark.org

Cite this article as: Iovoli AJ, Prasad S, Ma SJ, et al. Long-term survival and failure outcomes of single-fraction stereotactic body radiation therapy in early stage NSCLC. *JTO Clin Res Rep*. 2023;4:100598.

ISSN: 2666-3643
https://doi.org/10.1016/j.jtocrr.2023.100598

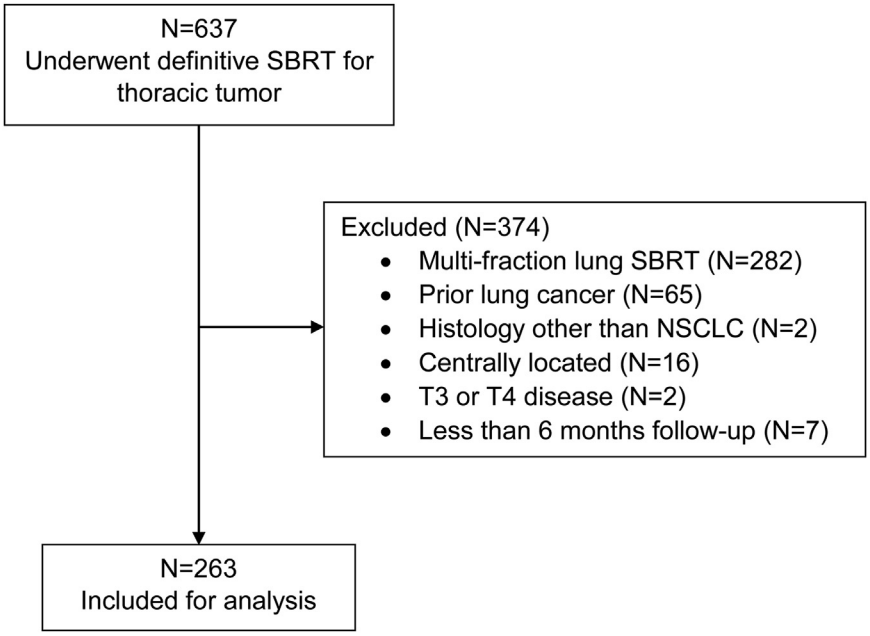

Figure 1. Patient selection CONSORT diagram. SBRT, stereotactic body radiation therapy.

SBRT for early stage NSCLC is frequently delivered in multiple days or weeks in three to eight fractions, with insurance companies often billing per fraction delivered.[15] Two prospective randomized studies have evaluated SBRT delivered in a single-fraction (SF-SBRT) and found similar outcomes and toxicity to multifractionated regimens.[16,17] In contrast, no randomized data exist to support five-fraction SBRT.[9] In the United States, Medicare reimbursement for single-fraction SBRT is approximately half that of five-fraction SBRT.[18]

Despite excellent outcomes and decreased cost, lack of familiarity among institutions remains a barrier to the widespread adoption of SF-SBRT in routine practice.[8,18–22] Increased utilization of SF-SBRT during the coronavirus disease 2019 pandemic has proven to be a cost-effective and practical solution to increase treatment compliance in patients with lung cancer.[21,23,24] Data regarding long-term outcomes with SF-SBRT in real-world clinical practice are limited. To support the growing literature on SF-SBRT, this study aims to report our 13-year single-institutional experience with SF-SBRT for peripheral early stage NSCLC.

Materials and Methods

Study Population

The patient cohort was derived from 637 patients who received thoracic SBRT at a single institution between September 2008 and May 2022. To be included in this study, patients had to meet the following criteria: (1) biopsy-proven peripheral cT1-2N0M0 NSCLC, (2) definitive treatment with SF-SBRT, and (3) minimum follow-up time of 6 months. Patients were excluded if (1) SF-SBRT was given for recurrence, salvage, or oligometastases; (2) SBRT was delivered as a second radiation course; or (3) the patient received treatment for prior lung cancer. Patients who died within 6 months of SF-SBRT but otherwise met the inclusion criteria were included. A total of 263 patients met the inclusion criteria (Fig. 1). Data were collected under a protocol (EDR 171710) approved by the Institutional Review Board at Roswell Park Comprehensive Cancer Center, which included a waiver of informed consent. The Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline was followed.

Clinical Evaluation and Follow-Up

Clinical evaluation and workup to determine eligibility for thoracic SBRT were previously described.[25] SBRT was considered for patients who were medically inoperable or declined surgery. Complex cases were discussed at a multidisciplinary tumor board, and consensus recommendations were formulated. Candidacy for surgical resection was determined at the discretion of the thoracic surgeon as those medically fit to undergo a wedge resection or greater. All patients were cN0 as determined by positron emission tomography with diagnostic computed tomography (PET-CT) imaging and/or endoscopic nodal sampling. Patients were followed up three months after SBRT completion with a diagnostic chest CT and repeat chest imaging every 3 to 6 months up to a year, after which imaging was taken every 6 months. Suspicious imaging findings

were further worked up with PET-CT imaging or biopsies as clinically indicated.

Treatment Planning

All patients underwent SF-SBRT per RTOG 0915 or RCPI-124407, with a small group of patients enrolled on each.[17,26] Patients underwent CT simulation in the supine position with arms above their head using a thoracic Medical Intelligence BodyFIX immobilization system (Elekta, Stockholm, Sweden). Tumor motion management included either abdominal compression or respiratory gating, as previously described.[17,27] Dose-delivery techniques used included noncoplanar three-dimensional conformal fields or volumetric-modulated arc therapy. Heterogeneity corrections were used only for patients treated with intensity-modulated radiation therapy. Normal tissue dose constraints from RTOG 0915 were used.[26] Eclipse (Varian Medical Systems, Palo Alto, CA) was used for the generation and evaluation of radiation treatment plans. Most patients treated with SF-SBRT at our institution were given 27 or 30 Gy, with the former reflecting heterogeneity corrections made with a new dose calculation algorithm introduced in 2017. Given this fact, both treatments are felt to be equivalent as they deliver a similar biologically effective dose.[28]

Patient Data

Pertinent clinicopathologic data were abstracted from the medical records and stored in a secure REDCap database.[29,30] Clinically relevant variables investigated included sex, race, performance status, medical history, smoking status, peripheral blood markers, histology, size, staging, tumor standard uptake value, SBRT dose, and operability status. Performance status was defined by Karnofsky performance status (KPS).

Primary outcomes were OS and progression-free survival (PFS). OS was defined as the time between treatment start date and death or last known follow-up. PFS was defined as the time between treatment start date and death, any tumor recurrence, or last known follow-up. Secondary outcomes evaluated were local failure (LF), nodal failure (NF), distant failure (DF), and second primary lung cancer (SPLC). LF was based on RTOG 0236 as meeting both criteria of (1) local enlargement defined as at least a 20% increase in the longest diameter of the gross tumor volume per CT scan and (2) evidence of tumor viability.[31] Tumor viability could be affirmed either by finding PET imaging with uptake of a similar intensity as the pretreatment staging PET or by repeat biopsy-confirming carcinoma. NF was defined as tumor recurrence in any thoracic nodal station and DF as any extrathoracic or contralateral lung recurrence. SPLC was defined based on the Martini and Melamed criteria as a new biopsy-proven intrathoracic malignancy with different histology or with the same histology and at least one of the following: (1) cancer-free interval of at least 2 years, (2) associated carcinoma in situ, or (3) be located in a separate lung or lobe without common lymphatics and without distant metastases.[32] Ipsilateral lung failures not meeting the definition of LF, NF, DF, or SPLC were coded separately. All disease failures were evaluated in a multidisciplinary setting based on radiographic findings and, if available, biopsy results of metastatic sites. Toxicity data were not available for analysis.

Statistical Analysis

Estimates for OS and PFS were conducted using the Kaplan-Meier method. Cox univariate analysis was performed to identify variables associated with OS and PFS. Cox multivariate analysis (MVA) was then performed for the same survival outcomes adjusting for variables with p values less than 0.10 on univariate analysis. Fine-Gray competing risk MVA controlling for the same factors in the OS model was used to evaluate LF, NF, and DF with death as a competing event. All p values were two sided, and variables with p less than 0.05 were considered statistically significant. Statistical analysis was conducted using R (version 4.2.0, R Project for Statistical Computing, Vienna, Austria).

Results

Baseline patient characteristics and treatment details are described in Table 1. For the total cohort of 263 patients, median age was 76 (interquartile range [IQR]: 70–81) years and median follow-up time was 27.2 (IQR: 14.3–44.9) months. There were 92 patients (35%) alive at the time of analysis with a median follow-up of 34.0 (IQR: 16.6–50.0) months. Most patients were female (57%) and had a KPS of greater than or equal to 80 (60%). Most patients were former (66%) or current (25%) smokers. Median tumor size and standard uptake value were 1.9 cm (IQR: 1.4–2.6) and 5.9 (IQR: 3.4–9.2), respectively. Only 58 patients (22%) underwent workup with endobronchial ultrasound before the treatment. For patients with pulmonary function testing data available (n = 108), the median forced expiratory volume at 1 second was 58% (range, 19–163). Primary reasons for inoperability included inadequate pulmonary function in 20%, cardiac comorbidities in 8%, and multifactorial or poor KPS in the remaining patients. There were 60 patients (23%) included who were medically operable but declined surgery due to patient preference. Of the 60 medically operable patients, 22 (37%) were candidates for a lobectomy and the remaining were candidates for sublobar resections.

Table 1. Baseline Patient Characteristics

Characteristic	n	% or IQR
No. of patients	263	100
Sex		
Male	112	42.6
Female	151	57.4
Median age, y	75.9	70.4-81.1
Race		
White	237	90.1
Black	14	5.3
Other/unknown	13	4.9
Treatment on protocol		
Yes	20	7.6
No	243	92.4
KPS		
100	6	2.3
90	48	18.3
80	103	39.2
70	55	20.9
60	37	14.1
50	11	4.2
40	3	1.1
Smoking status		
Never	20	7.6
Former	174	66.2
Current	69	26.2
Median pack-years	48.5	30-60
EBUS done		
Yes	58	22.1
No	205	77.9
Histology		
Adenocarcinoma	137	52.1
Squamous cell carcinoma	103	39.2
NSCLC (NOS)	23	8.7
Site		
Left upper lobe	75	28.5
Left lower lobe	49	18.6
Right upper lobe	80	30.4
Right middle lobe	12	4.6
Right lower lobe	47	17.9
Median tumor size, cm	1.9	1.4-2.6
Median SUV	5.9	3.4-9.2
Synchronous tumors		
No	254	96.
Yes	9	3.4
SBRT dose		
2700 cGy	147	55.9
3000 cGy	113	43.0
3400 cGy	3	1.1
Reason for SBRT		
Medically inoperable	203	77.2
Declined surgery	60	22.8
Overall stage		
IA1	17	6.5
IA2	128	48.7
IA3	79	30.0
IB	27	10.3
IIA	12	4.6

IQR, interquartile range; KPS, Karnofsky performance status; EBUS, endobronchial ultrasound; NOS, not otherwise specified; SUV, standard uptake value; SBRT, stereotactic body radiation therapy.

Treatment outcomes for the cohort are described in Table 2, and OS is presented in Figure 2. Median OS was 33.7 months (95% confidence interval [CI]: 30.5–43.2). On MVA, factors associated with worse OS included greater age at treatment (hazard ratio [HR] = 1.02, 95% CI: 1.00–1.04, $p = 0.046$), male sex (HR = 1.40, 95% CI: 1.03–1.89, $p = 0.031$), and KPS less than 80 (HR = 1.75, 95% CI: 1.26–2.42, $p < 0.001$; Supplementary Table 1). No associations with OS were found for histology or operability status. The only factor associated with PFS was male sex (HR = 1.38, 95% CI: 1.03–1.85, $p = 0.031$; Supplementary Table 2).

A total of 74 of 263 patients (28%) developed disease progression. The numbers of patients who developed LF, NF, DF, and SPLC were 19, 24, 41, and 12, respectively. Of 171 patients who passed away, only 59 (35%) developed disease progression before death. Cumulative incidence plot of LF is found in Figure 3. Among the 19 LFs, 13 (68%) were biopsy-proven and the remaining had PET-CT evidence of tumor viability. On MVA, the only clinical factor associated with LF was tumor size (HR = 1.49, 95% CI: 1.00–2.20, $p = 0.046$). MVA factors associated with NF included younger age (HR = 0.95, 95% CI: 0.91–0.99, $p = 0.010$) and NSCLC not otherwise specified (NOS) histology (HR = 2.86, 95% CI: 1.06–7.74, $p = 0.039$). MVA factors associated with DF included adenocarcinoma histology (HR = 2.55, 95% CI: 1.18–5.49, $p = 0.017$) and medical inoperability (HR = 2.56, 95% CI: 1.02–6.43, $p = 0.046$).

Discussion

This is the largest cohort to date reporting long-term survival and failure outcomes for patients with peripheral early stage NSCLC treated with SF-SBRT. In this population of patients with predominantly medically inoperable lung cancer, long-term LF remains low but must be understood in the context of high competing risks of death and DF. The results from this study support previous findings from two randomized phase II trials that SF-SBRT for early stage NSCLC is a safe and effective treatment regimen, particularly in patients with competing comorbidities.[16,17,22]

Previous retrospective cohort studies reporting SF-SBRT outcomes for patients with peripheral early stage NSCLC found similar rates of 5-year LF (8.0%–12.2%) and 5-year OS (31.0%–36.9%) to the rates in the present study of 12.7% and 25.7%, respectively.[22,33] These real-world outcomes are comparable with those reported in the long-term results of RTOG 0915, which found 5-year LF and OS in the SF-SBRT arm to be 10.6% and 29.6%, respectively. The predominant pattern of failure in this population remains distant, with the Cleveland Clinic experience reporting a 2-year DF rate of 12.2% similar

Table 2. Select Treatment Outcomes for 263 Patients Treated With SF-SBRT for NSCLC

Outcome	n	2-y (%)	95% CI	5-y (%)	95% CI
Local failure	19	8.0	4.0-11.9	12.7	6.3-18.7
Nodal failure	24	8.6	4.6-12.4	14.7	8.2-20.7
Distant failure	41	13.4	8.8-17.9	23.5	16.0-30.2
Second primary lung cancer	12	2.8	0.3-5.2	12.0	7.2-19.2
Overall survival	-	65.1	59.3-74.4	25.7	19.8-33.3
Progression-free survival	-	54.7	48.7-61.4	22.0	16.6-29.2

CI, confidence interval; SF-SBRT, single-fraction stereotactic body radiation therapy.

to the rate of 13.4% in the current study, which we found further increased to 23.5% at 5 years.[22] Similar results between retrospective studies and patients enrolled on the trial reveal that trial outcomes can be achievable in routine practice with SF-SBRT. Although toxicity was unable to be assessed in this study, prior randomized trials comparing SF-SBRT with multifraction SBRT found no differences in toxicity or quality of life between arms.[16,17]

Only a third of patients in the present study who died had evidence of disease progression after treatment, highlighting the many competing risks for death in elderly patients with lung cancer. After multivariate analysis, factors associated with worse OS included older age, male sex, and poor KPS. No associations with OS were found for histology or operability status. The Cleveland Clinic experience similarly found OS to be associated with age and no association with histology.[22] Tumor size was the only factor identified that was associated with LF, which is consistent with studies evaluating LF after fractionated SBRT.[34–36] Increased risk of LF with increasing tumor size should be considered when treating with either fractionated or SF-SBRT for T2 or larger tumors. Histology having no impact on LF in our cohort is consistent with a prior SF-SBRT study[37]; however, this contrasts with previous reports evaluating patients treated with fractionated SBRT that revealed squamous cell carcinoma to be associated with worse LF and OS.[38,39] In regard to DF, adenocarcinoma histology and inoperable status were the only factors with a significant association ($p = 0.017$ and $p = 0.046$, respectively). The link between DF and inoperable status emphasizes the need for controlled randomized data in properly assessing differences in disease outcomes between SBRT and surgery in the management of early stage NSCLC.

Limitations

This study has several limitations owing to its retrospective nature, including lack of prospective collected toxicity data. Selection bias in the early years of the cohort cannot be excluded, but SF-SBRT did become our institutional standard by 2015.[25] Consistent

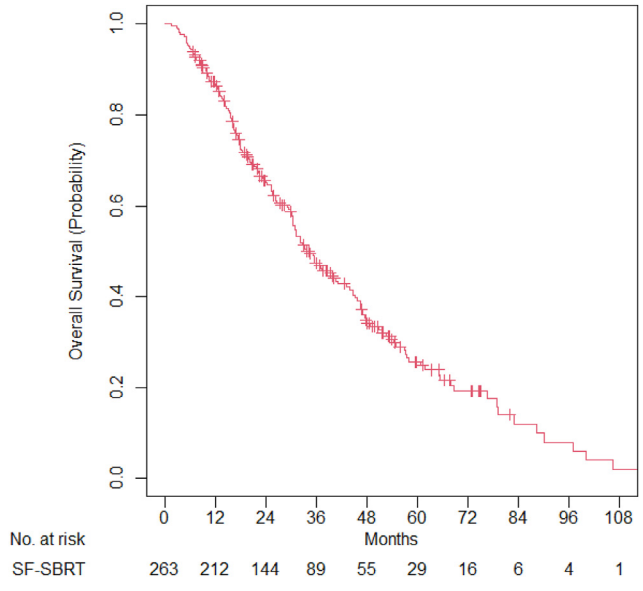

Figure 2. Overall survival for patients treated with SF-SBRT. SF-SBRT, single-fraction stereotactic body radiation therapy.

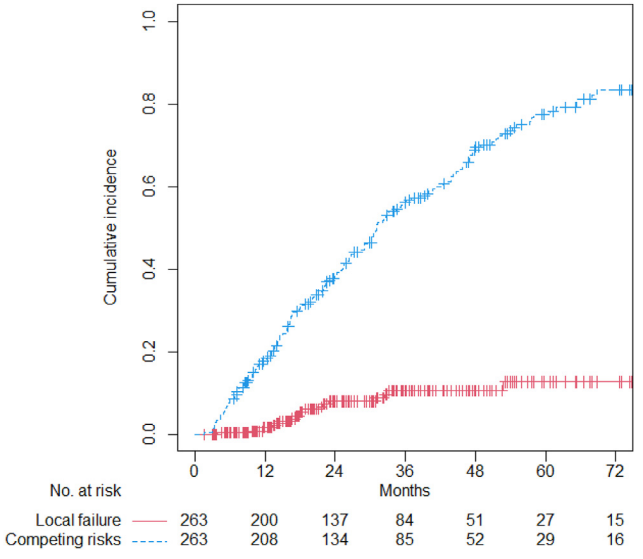

Figure 3. Cumulative incidence of local failure for patients treated with SF-SBRT. Competing risks were death and distant recurrence. SF-SBRT, single-fraction stereotactic body radiation therapy.

retrospective classification of operable status is difficult due to small variations in thoracic surgeon preferences. Of the 60 patients in this study considered operable, most (63%) were only candidates for sublobar or wedge resection.

Despite these limitations, this study is strengthened by histologic diagnosis for all patients, a consistent approach to treatment, and the largest SF-SBRT cohort reported to date. SF-SBRT has multiple advantages than multifraction SBRT, including patient convenience, accessibility, and cost-effectiveness while maintaining good oncologic outcomes.[21] Given these benefits, more widespread adoption of SF-SBRT in appropriately selected patients is supported. Particularly in patients with transportation difficulties, smaller tumors, substantial medical comorbidities, or traveling far distances, SF-SBRT is a reasonable safe and effective option to consider.

Conclusion

Consistent with multiple prospective randomized trials, in a large real-world retrospective cohort, SF-SBRT for peripheral early stage NSCLC was an effective treatment approach.

CRediT Authorship Contribution Statement

Austin J. Iovoli: Data curation, Investigation, Supervision, Formal analysis, Writing—original draft.

Sharan Prasad: Data curation, Investigation, Formal analysis, Writing—original draft.

Sung Jun Ma: Methodology, Supervision, Writing—review and editing.

Fatemeh Fekrmandi: Writing—review and editing.

Nadia K. Malik: Writing—review and editing.

Simon Fung-Kee-Fung: Writing—review and editing.

Mark K. Farrugia: Writing—review and editing.

Anurag K. Singh: Conceptualization, Validation, Supervision, Writing—review and editing.

Acknowledgments

This work was supported by the National Cancer Institute Cancer Center Support Grant (P30CA016056).

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at https://doi.org/10.1016/j.jtocrr.2023.100598.

References

1. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. *Mayo Clin Proc*. 2008;83:584–594.
2. Thandra KC, Barsouk A, Saginala K, Aluru JS, Barsouk A. Epidemiology of lung cancer. *Contemp Oncol (Pozn)*. 2021;25:45–52.
3. Potter AL, Rosenstein AL, Kiang MV, et al. Association of computed tomography screening with lung cancer stage shift and survival in the United States: quasi-experimental study. *BMJ*. 2022;376:e069008.
4. Tandberg DJ, Tong BC, Ackerson BG, Kelsey CR. Surgery versus stereotactic body radiation therapy for stage I non-small cell lung cancer: a comprehensive review. *Cancer*. 2018;124:667–678.
5. Chang JY, Mehran RJ, Feng L, et al. Stereotactic ablative radiotherapy for operable stage I non-small-cell lung cancer (revised STARS): long-term results of a single-arm, prospective trial with prespecified comparison to surgery. *Lancet Oncol*. 2021;22:1448–1457.
6. Chaudhuri AA, Tang C, Binkley MS, et al. Stereotactic ablative radiotherapy (SABR) for treatment of central and ultra-central lung tumors. *Lung Cancer*. 2015;89:50–56.
7. Crabtree T, Puri V, Timmerman R, et al. Treatment of stage I lung cancer in high-risk and inoperable patients: comparison of prospective clinical trials using stereotactic body radiotherapy (RTOG 0236), sublobar resection (ACOSOG Z4032), and radiofrequency ablation (ACOSOG Z4033). *J Thorac Cardiovasc Surg*. 2013;145:692–699.
8. Mou B, Hyde D, Araujo C, Bartha L, Bergman A, Liu M. Implementation of single-fraction lung stereotactic ablative radiotherapy in a multicenter provincial Cancer Program during the COVID-19 pandemic. *Cureus*. 2021;13:e15598.
9. Prezzano KM, Ma SJ, Hermann GM, Rivers CI, Gomez-Suescun JA, Singh AK. Stereotactic body radiation therapy for non-small cell lung cancer: a review. *World J Clin Oncol*. 2019;10:14–27.
10. Timmerman RD, Hu C, Michalski JM, et al. Long-term results of stereotactic body radiation therapy in medically inoperable Stage I non-small cell lung cancer. *JAMA Oncol*. 2018;4:1287–1288.
11. Timmerman RD, Paulus R, Pass HI, et al. Stereotactic body radiation therapy for operable early-stage lung cancer: findings from the NRG oncology RTOG 0618 trial. *JAMA Oncol*. 2018;4:1263–1266.
12. Tekatli H, Spoelstra FOB, Palacios M, van Sornsen de Koste J, Slotman BJ, Senan S. Stereotactic ablative radiotherapy (SABR) for early-stage central lung tumors: new insights and approaches. *Lung Cancer*. 2018;123:142–148.
13. Sebastian NT, Xu-Welliver M, Williams TM. Stereotactic body radiation therapy (SBRT) for early stage non-small cell lung cancer (NSCLC): contemporary insights and advances. *J Thorac Dis*. 2018;10(suppl 21):S2451–S2464.
14. Iovoli AJ, Yu B, Ma SJ, et al. Quality of life after stereotactic body radiation therapy or surgery for early-stage NSCLC: a systematic review. *JTO Clin Res Rep*. 2022;3:100417.
15. Lanni TB Jr, Grills IS, Kestin LL, Robertson JM. Stereotactic radiotherapy reduces treatment cost while improving overall survival and local control over

standard fractionated radiation therapy for medically inoperable non-small-cell lung cancer. *Am J Clin Oncol*. 2011;34:494–498.
16. Videtic GM, Paulus R, Singh AK, et al. Long-term follow-up on NRG oncology RTOG 0915 (NCCTG N0927): a randomized Phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2019;103:1077–1084.
17. Singh AK, Gomez-Suescun JA, Stephans KL, et al. One versus Three fractions of stereotactic body radiation therapy for peripheral stage I to II non-small cell lung cancer: a randomized, multi-institution, Phase 2 trial. *Int J Radiat Oncol Biol Phys*. 2019;105:752–759.
18. Bartl AJ, Mahoney M, Hennon MW, et al. Systematic review of single-fraction stereotactic body radiation therapy for early stage non-small-cell lung cancer and lung oligometastases: how to stop worrying and love one and done. *Cancers (Basel)*. 2022;14:790.
19. Alongi F, Nicosia L, Figlia V, et al. A multi-institutional analysis of fractionated versus single-fraction stereotactic body radiotherapy (SBRT) in the treatment of primary lung tumors: a comparison between two antipodal fractionations. *Clin Transl Oncol*. 2021;23:2133–2140.
20. Fernandez C, Navarro-Martin A, Bobo A, et al. Single-fraction stereotactic ablative body radiation therapy for primary and metastasic lung tumor: a new paradigm? *World J Clin Oncol*. 2022;13:101–115.
21. Tjong MC, Louie AV, Singh AK, et al. Single-fraction stereotactic ablative body radiotherapy to the lung - the knockout punch. *Clin Oncol (R Coll Radiol)*. 2022;34:e183–e194.
22. Videtic GMM, Reddy CA, Woody NM, Stephans KL. Ten-year experience in implementing single-fraction lung SBRT for medically inoperable early-stage lung cancer. *Int J Radiat Oncol Biol Phys*. 2021;111:436–442.
23. Salama JK, Giuliani ME, Robinson CG, Daly ME. Single-fraction SBRT for early stage NSCLC-A viable option in "these uncertain times". *Int J Radiat Oncol Biol Phys*. 2021;109:1–4.
24. Ng SSW, Ning MS, Lee P, McMahon RA, Siva S, Chuong MD. Single-fraction stereotactic body radiation therapy: a paradigm during the coronavirus disease 2019 (COVID-19) pandemic and beyond? *Adv Radiat Oncol*. 2020;5:761–773.
25. Ma SJ, Serra LM, Syed YA, Hermann GM, Gomez-Suescun JA, Singh AK. Comparison of single- and three-fraction schedules of stereotactic body radiation therapy for peripheral early-stage non-small-cell lung cancer. *Clin Lung Cancer*. 2018;19:e235–e240.
26. Videtic GM, Hu C, Singh AK, et al. A randomized Phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with Stage I peripheral non-small cell lung cancer: NRG oncology RTOG 0915 (NCCTG N0927). *Int J Radiat Oncol Biol Phys*. 2015;93:757–764.
27. Videtic GM, Stephans K, Reddy C, et al. Intensity-modulated radiotherapy-based stereotactic body radiotherapy for medically inoperable early-stage lung cancer: excellent local control. *Int J Radiat Oncol Biol Phys*. 2010;77:344–349.
28. Xiao Y, Papiez L, Paulus R, et al. Dosimetric evaluation of heterogeneity corrections for RTOG 0236: stereotactic body radiotherapy of inoperable stage I-II non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2009;73:1235–1242.
29. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208.
30. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377–381.
31. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA*. 2010;303:1070–1076.
32. Martini N, Melamed MR. Multiple primary lung cancers. *J Thorac Cardiovasc Surg*. 1975;70:606–612.
33. Nicosia L, Reverberi C, Agolli L, et al. Long term results of single high dose Stereotactic Body Radiotherapy in the treatment of primary lung tumors. *Sci Rep*. 2019;9:15498.
34. Dunlap NE, Larner JM, Read PW, et al. Size matters: a comparison of T1 and T2 peripheral non-small-cell lung cancers treated with stereotactic body radiation therapy (SBRT). *J Thorac Cardiovasc Surg*. 2010;140:583–589.
35. Horner-Rieber J, Bernhardt D, Dern J, et al. Histology of non-small cell lung cancer predicts the response to stereotactic body radiotherapy. *Radiother Oncol*. 2017;125:317–324.
36. Verma V, Simone CB 2nd. Approaches to stereotactic body radiation therapy for large (>/=5 centimeter) non-small cell lung cancer. *Transl Lung Cancer Res*. 2019;8:70–77.
37. Videtic GMM, Reddy CA, Woody NM, Stephans KL. Local Control with Single-Fraction Lung Stereotactic Body Radiotherapy is not influenced by non-small Cell Lung Cancer Histologic Subtype. *Clin Lung Cancer*. 2022;23:e428–e434.
38. Baine MJ, Verma V, Schonewolf CA, Lin C, Simone CB 2nd. Histology significantly affects recurrence and survival following SBRT for early stage non-small cell lung cancer. *Lung Cancer*. 2018;118:20–26.
39. Abel S, Hasan S, White R, et al. Stereotactic ablative radiotherapy (SABR) in early stage non-small cell lung cancer: comparing survival outcomes in adenocarcinoma and squamous cell carcinoma. *Lung Cancer*. 2019;128:127–133.