Stereotactic body radiation therapy for ≥ 5 cm node-negative non-small cell lung cancer: Survey of U.S. academic thoracic radiation oncologists

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Abstract

Purpose: Large (≥ 5 cm) node-negative non-small cell lung cancer (NSCLC) is relatively uncommon; efficacy and toxicities of stereotactic body radiation therapy (SBRT) in this unique population have been under-evaluated.

Methods and Materials: We surveyed U.S. academic thoracic radiation oncologists regarding SBRT practice patterns in node-negative ≥ 5 cm NSCLC and assessed factors necessitating changes in SBRT management. A 25-question survey of demographics and practice patterns, including 5 clinical cases, was sent to 107 radiation oncologists who self-identified as thoracic/lung cancer specialists.

Results: Response rate was 34% (36/107). Among respondents, two-thirds had at least 6 years of work experience following residency; 67% and 67% annually treated > 60 lung cancer and > 25 lung SBRT cases, respectively. Nearly all (97%) routinely offered SBRT for ≥ 5 cm NSCLC, and 55% used a SBRT treatment of 50-60 Gy in 5 fractions, with fractions delivered every other day in 60%. Dosing/fractionation were most commonly altered for central disease (77%). Sixty percent would offer additional chemotherapy; chemotherapy was strongly considered for patients with good performance status (74%), younger age (69%), and larger tumor size (68%). The 5 clinical cases revealed significant practice variability in dose, fractionation, treatment timing, and chemotherapy use.

Conclusions: Practice patterns of SBRT for ≥ 5 cm NSCLC display substantial heterogeneity. Five-fraction regimens with biologically effective dose ≥100 Gy were most commonly performed, with common endorsement of every other day delivery and chemotherapy.

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Non-small cell lung cancer (NSCLC) is the most common cause of cancer death in the world.[1,2] Early stage NSCLC is commonly treated with lobectomy, with stereotactic body radiation therapy (SBRT) being the standard of care for inoperable early stage NSCLC.[2-12] Initial studies of SBRT have demonstrated excellent local control rates of ≥ 90%, but these large cohort studies have consisted primarily of small (≤ 4 cm) primary tumors, with node-negative NSCLC tumors ≥ 5 cm being vastly under-represented.[12] Owing to the uncommon nature of these large node-negative NSCLC tumors, data-driven recommendations regarding this patient population are largely lacking.[12-15] Hence, the National Comprehensive Cancer Network (NCCN) does not offer concrete guidelines on treatment of node-negative ≥ 5 cm NSCLC.[3]

Because of this limited data and lack of consensus, there is great heterogeneity in how these cases are treated in clinical practice, and many questions remain regarding practicality of several SBRT schemes in this population. Hence, we

Table 1. Demographics of the Surveyed Population (n = 36 Respondents)

Parameter	Respondents (Percent*)
Gender	
Male	30 (83.3%)
Female	6 (16.7%)
Median (range) age, years	46 (31-64)
Postresidency experience*	
0-5 years	12 (33.3%)
6-10 years	7 (19.4%)
11-20 years	10 (27.8%)
21-30 years	7 (19.4%)
>30 years	0 (0.0%)
Location of practice*	
Urban	28 (77.8%)
Suburban	6 (16.7%)
Rural	2 (5.6%)
Geographic region*	
Northeast	12 (33.3%)
Midwest	10 (27.8%)
South	7 (19.4%)
West	7 (19.4%)
Number of co-radiation oncologists in practice*	
1	0 (0%)
2-9	12 (33.3%)
10-25	17 (47.2%)
>25	7 (19.4%)
Percent of practice involving lung cancer	
0-25%	8 (22.2%)
26-50%	11 (30.6%)
>50%	17 (47.2%)
Total lung cancer cases seen per year	
0-30	4 (11.1%)
31-60	8 (22.2%)
61-90	6 (16.7%)
>90	18 (50.0%)
Total cases treated with lung SBRT per year	
0-10	4 (11.1%)
11-25	8 (22.2%)
26-50	11 (30.6%)
51-75	4 (11.1%)
>75	9 (25.0%)
Total ≥ 5 cm NSCLC cases treated with SBRT per year*	
0	5 (13.9%)
1-2	10 (27.8%)
3-5	10 (27.8%)
6-10	5 (13.9%)
>10	6 (16.7%)
Participation in lung cancer cooperative group trials	
Yes	34 (94.4%)
No	2 (5.6%)

*Percentages may not add up to 100% due to rounding. Abbreviations: SBRT, stereotactic body radiation therapy; NSCLC, non-small cell lung cancer.

surveyed U.S. academic thoracic radiation oncologists to assess current practice patterns, and to determine which clinical parameters significantly altered their therapeutic decision-making for the treatment of large, node-negative NSCLC.

Methods and Materials

We asked 107 thoracic radiation oncologists from 71 U.S. academic institutions to participate in a 25-question survey. All invited participants self-identified as specializing in thoracic and/or lung radiation oncology. A single thoracic/lung radiation oncologist was invited per institution in most cases; however, multiple radiation oncologists were invited for select larger institutions in which multiple providers specifically focus their clinical practice on lung cancer. The invitation contained instructions for participation and information regarding the study. The first invitation was sent on June 29, 2016. Participants who requested not to be contacted in the future were immediately removed from the database. The remaining respondents were contacted with a reminder email on July 12, 2016, to maximize response rate. No further communication with participants ensued.

Responses were anonymous and were recorded with Google (N = 34) or Word documents (N = 2). The complete survey **(Supplemental Figure 1)** was divided into demographic questions, clinical scenarios in which respondents commented on typical treatment preferences, and 5 clinical cases to assess dose/fractionation of SBRT and chemotherapy administration. Demographic questions addressed clinical experience, the nature of the clinician's practice, and patient volume. Next, preferences on mediastinal staging modalities, chemotherapy use and timing, and practical/technical aspects of SBRT were recorded. Subsequently, various clinical scenarios were presented to assess whether each respondent would change management. Respondents selected from a list of several potential reasons for adding chemotherapy in addition

Table 2. Practice Patterns of the Surveyed Population (n = 35 Respondents)*

Parameter	Respondents (Percent)
Mediastinal staging modality used in patients with ≥ 5 cm NSCLC and negative mediastinal nodes on CT	
PET scan only	4 (11.4%)
EBUS and/or mediastinoscopy plus PET scan	31 (88.6%)
SBRT dose (in Gy)/fractionation (number of fractions) used most routinely for ≥ 5 cm NSCLC**	
50-60/5	21 (55.3%)
54-60/3	7 (18.4%)
48-50/4	3 (7.9%)
60/8	3 (7.9%)
70/10	3 (7.9%)
Other	1 (2.6%)
SBRT timing scheme of ≥ 5 cm NSCLC	
Daily	14 (40.0%)
Every other day	21 (60.0%)
SBRT delivery preference	
Fixed-beam 3D (forward planning)	1 (2.9%)
Fixed-beam IMRT (inverse planning)	4 (11.4%)
Dynamic arc therapy (forward planning)	4 (11.4%)
VMAT (inverse planning)	22 (62.9%)
No preference	4 (11.4%)
Increased patient age factoring into changing dose/fractionation scheme	
Yes	2 (5.7%)
No	33 (94.3%)
Poor performance status factoring into changing dose/fractionation scheme	
Yes	8 (22.9%)
No	27 (77.1%)
Central tumor location factoring into changing dose/fractionation scheme	
Yes	25 (71.4%)
No	10 (28.6%)
Administration of chemotherapy for patients with ≥ 5 cm NSCLC being definitively treated with SBRT	
Yes	21 (60.0%)
No	14 (40.0%)
Preferred timing of chemotherapy***	
Prior to SBRT	4 (19.0%)
After SBRT	17 (81.0%)
Concurrent with SBRT	0 (0%)
Concurrent with SBRT with additional chemotherapy before or after SBRT	0 (0%)
Factors in ≥ 5 cm NSCLC considered to administer chemotherapy	
Good performance status	26 (74.3%)
Younger age	24 (68.6%)
Larger size of tumor	24 (68.6%)
Chest wall invasion	15 (42.9%)
Central tumor location	12 (34.3%)
Poor tumor differentiation on biopsy	12 (34.3%)
No pathologic mediastinal staging performed	9 (25.7%)
Adenocarcinoma histology	7 (20.0%)
Visceral pleural involvement	7 (20.0%)
Not consider chemotherapy with these factors	5 (14.3%)

*One of the 36 respondents stated that they do not treat ≥ 5 cm NSCLC. The responses in this table, therefore, are based on the 35 respondents who completed these questions. **Three respondents gave 2 answers each. ***Chemotherapy timing question is out of 21 respondents who stated they would administer chemotherapy for patients with ≥ 5 cm NSCLC being definitively treated with SBRT.
Abbreviations: SBRT, stereotactic body radiation therapy; NSCLC, non-small cell lung cancer; PET, positron emission tomography; EBUS, endobronchial ultrasonography; IMRT, intensity-modulated radiation therapy; VMAT, volumetric-modulated arc therapy

Table 3. Dose/Fractionation Schemes in Respondents Opting to Change Such with Central Lesions (n = 25)

SBRT dose (in Gy)/ fractionation scheme (number of fractions) used for central tumors	
50-60/5	9 (36.0%)
60/15	8 (32.0%)
60/8	3 (12.0%)
70/10	2 (8.0%)
Other	3 (12.0%)

to SBRT. Lastly, 5 clinical cases were presented that holistically addressed the previously mentioned parameters; respondents were asked to comment on their chosen dose, fractionation, and timing, as well as adjuvant chemotherapy usage. At the end of the survey period, responses were collated and tabulated.

Results

Demographics

The overall response rate was 34% (36/107). **Table 1** illustrates respondent demographics. Thirty-three percent had 0-5 years of work experience after residency, 19% had 6 to 10 years, 28% had 11 to 20 years, and 19% had > 20 years. Most respondents practiced in an urban location (78%), and they most commonly worked in the Northeast (33%) and Midwest (28%). Forty-seven percent were partners in a radiation oncology practice of 10 to 25 radiation oncologists, whereas 33% were in a practice of 2 to 9 physicians.

Lung cancer patients comprised over half of the practitioner's patient volume for approximately half (47%) of respondents, with lung cancer patients constituting 26% to 50% of the practice in an additional 31% of respondents. Half of the surveyed population saw > 90 lung cancer cases per year. Two-thirds of respondents (67%) delivered SBRT to at least 26 patients annually, with high volume providers (> 75 cases per year) accounting for 25% of total respondents. Most respondents (86.1%) had significant experience delivering SBRT to NSCLC tumors ≥ 5 cm, with 28% treating 1 to 2 cases per year, 28% treating 3 to 5 cases per year, 14% treating 6 to 10 cases per year, and 17% treating >10 cases per year. Of those surveyed, 94% participated in lung cancer cooperative group trials.

Practice Patterns

Table 2 highlights the collective responses to the survey's practice pattern questions. Eighty-nine percent used endobronchial ultrasound (EBUS) and/or mediastinoscopy in addition to positron emission tomography (PET) scanning as part of the initial staging workup. One respondent did not treat any NSCLC ≥ 5 cm with SBRT. Among respondents, 55% most typically treated ≥ 5 cm NSCLC with 50 to 60 Gy in 5 fractions, with 18% using 48 to 54 Gy in 3 fractions, and 8% each preferring 48 to 50 Gy in 4 fractions, 60 Gy in 8 fractions, and 70 Gy in 10 fractions. Sixty percent of respondents would deliver fractions every other day, whereas 40% would deliver fractions daily.

Inverse planning with volumetric-modulated arc therapy (VMAT) was the preferred SBRT delivery technique for 63% of respondents, with the remainder generally split between inverse planning with fixed-beam intensity-modulated radiation therapy (IMRT), forward planning with dynamic arcs, and having no preference (11% each). Increasing patient age did not change dose and fractionation scheme for 94% of the surveyed population. Poor performance status, however, altered 23% of respondents' dosing and fractionation schemes. With poor performance status, 3 advocated 5-fraction regimens (45-50 Gy/5 fractions), 3 supported modestly hypofractionated schemes (60 Gy/20 fractions, 60 Gy/15 fractions, 50 Gy/10 fractions), and 2 supported palliative-type regimens (45 Gy/15 fractions, 30 Gy/10 fractions). Central tumor location altered treatment dosing/fractionation for 71% of respondents, with treatment modifications listed in **Table 3**.

Sixty percent of respondents recommended chemotherapy use in ≥ 5 cm NSCLC patients being definitively treated with SBRT, with 81% and 19% preferring chemotherapy administration following and prior to SBRT, respectively. The factors most commonly reported as leading to consideration of chemotherapy included good performance status (74%), larger tumor size (69%), and younger age (69%). The responses to several other pertinent clinical factors influencing chemotherapy use are recorded in **Table 2**. Twenty-six percent would consider chemotherapy if no pathologic mediastinal staging was performed, and 20% would consider chemotherapy if there was visceral pleural involvement or adenocarcinoma histology. Five respondents (14%) would not consider chemotherapy regardless of any of the above-mentioned factors.

Cases

The results of the surveyed clinicians' recommended dosing and fractionation schemes in 5 clinical cases are shown in **Table 4**. Respondents offered SBRT for all cases with the exception of 2 respondents who refrained from using SBRT in case 2, the case in which the largest tumor size (7.5 cm) was depicted.

Discussion

Although ≥ 5 cm NSCLC cases are relatively uncommon thoracic malignancies, there is no consensus recommendation for this patient population.[3] Additionally, in regard to the utility and efficacy of SBRT in large node-negative NSCLC, guidelines regarding dose and fractionation are lacking. As such, there is no consensus among providers regarding patient stratification and adjusting management accordingly based on various patient and tumor characteristics. Thus, our survey was designed to evaluate the diverse opinions of

Table 4. Clinical Cases (n = 35 Respondents)

Case	Respondents (Percent)
59 y/o patient, ECOG 1, with 5.0-cm poorly differentiated peripheral NSCLC, no nodes on PET, presenting for SBRT	
Dose (in Gy)/Fractionation Scheme (number of fractions)	
54-60/3	10 (28.6%)
48-50/4	7 (20.0%)
50-60/5	16 (45.7%)
60/8	0 (0.0%)
70/10	2 (5.7%)
60/15	0 (0.0%)
Conventional fractionation	0 (0.0%)
Other	0 (0.0%)
Frequency/Chemotherapy	
Fractions given daily WITH chemotherapy	4 (11.4%)
Fractions given every other day WITH chemotherapy	5 (14.3%)
Fractions given daily WITHOUT chemotherapy	11 (31.4%)
Fractions given every other day WITHOUT chemotherapy	15 (42.9%)
75 y/o patient, ECOG 0, with 7.5-cm well-differentiated peripheral NSCLC, no nodes on EBUS, presenting for SBRT	
Dose/Fractionation Scheme*	
54-60/3	1 (2.9%)
48-50/4	0 (0.0%)
50-60/5	16 (45.7%)
60/8	5 (14.3%)
70/10	1 (2.9%)
60/15	3 (8.6%)
Conventional fractionation	5 (14.3%)
Other (66/3, 60-72/4)	2 (5.7%)
No SBRT	2 (5.7%)
Frequency/Chemotherapy	
Fractions given daily WITH chemotherapy	9 (25.7%)
Fractions given every other day WITH chemotherapy	5 (14.3%)
Fractions given daily WITHOUT chemotherapy	8 (22.9%)
Fractions given every other day WITHOUT chemotherapy	13 (37.1%)
64 y/o patient, ECOG 1, with 5.6-cm poorly differentiated central NSCLC, no nodes on PET, presenting for SBRT	
Dose/Fractionation Scheme*	
54-60/3	0 (0.0%)
48-50/4	1 (2.9%)
50-60/5	22 (62.9%)
60/8	4 (11.4%)
70/10	1 (2.9%)
60/15	4 (11.4%)
Conventional fractionation	2 (5.7%)
Other (50/10)	1 (2.9%)
Frequency/Chemotherapy	
Fractions given daily WITH chemotherapy	5 (14.3%)
Fractions given every other day WITH chemotherapy	6 (17.1%)
Fractions given daily WITHOUT chemotherapy	15 (42.9%)
Fractions given every other day WITHOUT chemotherapy	9 (25.7%)

Table 4 continues on the next page

Table 4. Clinical Cases (n = 35 Respondents)

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70 y/o patient, ECOG 2, with 5.4-cm poorly differentiated peripheral NSCLC with lymphovascular invasion, no nodes on mediastinoscopy, presenting for SBRT	
Dose/Fractionation Scheme*	
54-60/3	7 (20.0%)
48-50/4	5 (14.3%)
50-60/5	19 (54.3%)
60/8	0 (0.0%)
70/10	1 (2.9%)
60/15	2 (5.7%)
Conventional fractionation	0 (0.0%)
Other (34/1)	1 (2.9%)
Frequency/Chemotherapy	
Fractions given daily WITH chemotherapy	5 (14.3%)
Fractions given every other day WITH chemotherapy	2 (5.7%)
Fractions given daily WITHOUT chemotherapy	11 (31.4%)
Fractions given every other day WITHOUT chemotherapy	17 (48.6%)
62 y/o patient, ECOG 0, with 6.3-cm moderately differentiated central NSCLC, no nodes on EBUS, presenting for SBRT	
Dose/Fractionation Scheme*	
54-60/3	0 (0.0%)
48-50/4	1 (2.9%)
50-60/5	16 (45.7%)
60/8	5 (14.3%)
70/10	1 (2.9%)
60/15	5 (14.3%)
Conventional fractionation	4 (11.4%)
Other (70/2, 60/4, 70/10)	3 (8.6%)
Frequency/Chemotherapy	
Fractions given daily WITH chemotherapy	11 (31.4%)
Fractions given every other day WITH chemotherapy	4 (11.4%)
Fractions given daily WITHOUT chemotherapy	10 (28.6%)
Fractions given every other day WITHOUT chemotherapy	10 (28.6%)

*Percentages may not add to 100% due to rounding. Abbreviations: ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer; PET, positron emission tomography; SBRT, stereotactic body radiation therapy; EBUS, endobronchial ultrasonography.

U.S.-based academic practitioners. Furthermore, large-volume retrospective and prospective studies assessing optimal SBRT fractionation/timing, the role of chemotherapy, and the outcomes and toxicity of SBRT in this unique patient population did not exist when the survey was administered; however, a few recently published studies have begun to provide clinical data for this patient population.[16-20]

A vast majority (88%) of respondents preferred the addition of EBUS or mediastinoscopy in addition to PET scanning for staging, despite little evidence to support that lymph node sampling improves outcomes in stage I-IIIA NSCLC.[21,22] However, it must be recognized that large tumors, especially central ones, have notably higher risks of occult nodal involvement,[23] likely explaining why respondents preferred lymph node sampling in this higher risk patient population. Despite this increased risk, a recent multi-institutional retrospective analysis revealed no improvement in tumor control (local, regional and distant) or survival with the addition of mediastinal lymph node sampling.[24] Analysis to determine which subgroup(s) of patients with larger lesions that benefit the most from pathologic mediastinal evaluation is warranted.

The most common dosing and fractionation scheme among respondents was 50 to 60 Gy in 5 fractions (55%), which is consistent with the most commonly utilized regimens in recently published data.[16-18] Respondents also supported delivering treatments every other day (60%); however, there was considerable variation in this regard. Some studies have shown decreased toxicity with fractions delivered every other day, and that spacing out SBRT

treatments in other neoplasms can also reduce toxicities.[25,26] Decreased toxicity with every other day vs daily treatment has been reported for this patient population.[17] Moreover, inverse planning with VMAT was preferred (63%). This might reflect the recent increased use of VMAT and its advantage of reducing treatment times and potentially improving conformity of dose coverage. However, there are conflicting dosimetric data comparing IMRT and VMAT as means for SBRT delivery,[27-29] and the significance of dynamic motion effects during VMAT is currently not well defined for tumors ≥ 5 cm.[30]

Among age, performance status and central tumor location, the latter was most commonly associated (71%) with a change in management by the surveyed population. Of the 24 respondents who would change management, 11 (46%) switched from a classic SBRT scheme of ≤ 5 fractions to > 5 fractions. Given that prior reports of SBRT for lesions < 5 cm have demonstrated increased toxicity when treating centrally located lesions,[31] and that treating larger tumors presumably has higher risks of toxicities than smaller tumors, this finding of switching fractionation schemes for central tumors is not unanticipated. Higher rates of toxicities have been reported for central lesions;[16] however, more recent data suggest no toxicity differences based on tumor location.[18] Additional clinical outcomes data are needed to determine whether SBRT of larger tumors is associated with higher rates of toxicities than for < 5 cm tumors, and if toxicity rates are higher in central lesions despite more widespread adoption of modern SBRT techniques.

The addition of chemotherapy to SBRT was endorsed by 60% of respondents, of whom 81% preferred chemotherapy to be sequenced after SBRT. Despite this preference, only 2 studies have shown an overall survival (OS) improvement with the addition of adjuvant chemotherapy to SBRT.[32,33] In the current survey, chemotherapy was more commonly considered in patients with good performance status (74%), younger age (69%), and larger tumor size (69%). These characteristics highlight that the perceived ability to tolerate chemotherapy, rather than specific tumor characteristics, is a common guiding rationale behind recommending chemotherapy in this high-risk population. Interestingly, 74% and 57% of respondents chose not to offer chemotherapy in cases 1 and 5, which depicted younger patients with a good performance score. Regardless, with distant failure occurring in 19% to 33% of patients,[16-20] studies that assess the exact clinical benefit of adjuvant chemotherapy are greatly needed, and novel approaches of trialing SBRT and immunotherapy for this patient population may also prove beneficial.[34]

Responses to the 5 clinical cases further identified which clinical parameters altered SBRT treatment regimens and chemotherapy usage. SBRT regimens > 5 fractions were prescribed most commonly in case 5 (46%) and case 2 (40%), which presented a 6.2-cm central tumor and a 7.5-cm peripheral tumor, respectively. Regarding treatment timing, although 60% advocated this in the initial question, in no clinical case did > 60% of respondents endorse every other day fractionation. Administration of SBRT fractions every other day was highest in case 1 (57%), presenting a 5.0-cm peripheral tumor. In fact, the 2 cases with central disease showed the lowest proportion of respondents recommending every other day fractionation (43% and 40%), although these were least likely to receive 5-fraction regimens to begin with. Of note, a 3-fraction regimen was most common in case 1 (29%), a patient with a 5.0-cm peripheral tumor, and in case 4 (20%), a patient with a 5.4-cm peripheral tumor. Case 4 also displayed the lowest rate of chemotherapy administration (20%). In contrast, chemotherapy was recommended most commonly in case 5 (43%), which depicted a 62-year-old patient with good performance status and a 6.3-cm moderately differentiated central lesion. The responses to the cases differed from the generic practice patterns questions, clarifying that each treatment plan was indeed created on a case-by-case basis.

SBRT for large node-negative NSCLC has many challenges, notably increased risks of toxicities and poorer tumor control, but its efficacy and toxicity have been reported in several recent studies. Significant (grade ≥ 3) toxicities have been reported in 5% to 30% of patients, and local control rates of 85% to 95% are nearly comparable to SBRT data for smaller lesions.[16-20] Despite the efficacy and safety of SBRT for large NSCLC, toxicity minimization is of the utmost importance in this population. The use of proton therapy could be a promising alternative to photon-based SBRT, wherein physical properties of the heavier proton particle that limits irradiation to normal adjacent tissues may translate into reduced toxicities to organs at risk, as well as potentially allow for dose escalation to improve local control. Intensity-modulated proton therapy, although in limited use, could further reduce toxicities.[35-37]

Respiratory gating, which propagates radiation delivery only at designated phases of the respiratory cycle, most commonly at the end of expiration, can further reduce dose to OARs. Inverse plan optimization of gating using patient specific data (ie, 4-dimensional computed tomography [4D-CT] and individual breathing patterns), as compared to traditional gating methods, has been shown to significantly reduce irradiation doses to the heart, esophagus and spinal cord.[38] Lastly, increased use of PET imaging for radiation treatment planning[39] and improvements in MRI-guided SBRT may allow for better delineation of the tumor from healthy tissue, leading to sharper planning treatment volumes.[40]

Although this is the first survey of its kind assessing practice patterns for patients with large, node-negative non-small

cell lung cancer, there are several limitations to this work. First, analysis is based on a limited number of respondents (n = 36). We limited the survey to academic thoracic radiation oncologists who self-identified as specialists in lung cancer to target a study population of providers who are most experienced in treating large node-negative NSCLC with SBRT. Fortunately, we do note a considerably high response rate among the total population surveyed (34%). Additionally, participation bias likely exists, as providers with more experience treating large tumors may have been more likely to complete the survey. As such, our results may not be representative of the practice patterns of SBRT in this unique patient population among the radiation oncology workforce outside of U.S. academia. Also, as in all surveys, wording of questions and limited space to offer a comprehensive clinical vignette or response options provided in the survey may have inappropriately simplified the complex nature of treatment planning in this challenging patient population. For instance, to simplify the wording of the survey, we did not acquire each respondent's dose/fractionation SBRT scheme simultaneously with dosing frequency, as we did for the clinical cases, and we instead used 2 separate questions to obtain this information. Lastly, when we assessed for chemotherapy usage in the cases, it was presented in a binary manner, which may have influenced respondents to not choose chemotherapy if they could not also dictate when it would be administered in relation to SBRT.

Conclusion

There are no current recommendations regarding SBRT for ≥ 5 cm node-negative NSCLC. Most commonly, respondents advocated treatment with 50 to 60 Gy in 5 fractions using VMAT, with fractions delivered every other day. However, substantial variability existed across treatment parameters. Central tumor location prompted most respondents to adjust their SBRT management, with roughly half adopting a > 5 fraction regimen. Chemotherapy was recommended more often in patients with good performance status, younger age and larger tumor size.

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Supplemental Figure 1. Complete Survey Sent to Academic Thoracic Radiation Oncologists

DEMOGRAPHICS

1. What is your gender?
   a. Male
   b. Female

2. What is your age?
   _____

3. Which one of the following best describes your clinical/work experience since completing residency training?
   a. 0-5 years
   b. 6-10 years
   c. 11-20 years
   d. 21-30 years
   e. > 30 years

4. Please describe your current practice location.
   a. Urban
   b. Suburban
   c. Rural

5. In which geographic region do you practice?
   a. Northeast
   b. Midwest
   c. South
   d. West

6. How many radiation oncologists are in your practice?
   a. 1
   b. 2-9
   c. 10-25
   d. > 25

7. What percentage of your practice involves lung cancer patients?
   a. 0-25%
   b. 26-50%
   c. > 50%

8. Which one of the following best describes the number of TOTAL lung cancer cases you see per year?
   a. 0-30 cases/year
   b. 31-60 cases/year
   c. 61-90 cases/year
   d. > 90 cases/year

9. Which one of the following best describes the number of patients with whom you treat lung SBRT per year?
   a. 0-10 patients/year
   b. 11-25 patients/year
   c. 26-50 patients/year
   d. 50-75 patients/year
   e. >75 patients/year

10. Which one of the following best describes the number of cases of ≥ 5 cm NSCLC you treat with SBRT per year?
    a. 0 cases/year
    b. 1-2 cases/year
    c. 3-5 cases/year
    d. 6-10 cases/year
    e. > 10 cases/year

11. Do you participate in lung cancer cooperative group trials?
    a. Yes
    b. No

QUESTIONNAIRE

1. As part of workup for a patient with ≥ 5 cm NSCLC with negative mediastinal nodes on CT scan, which of the following would you recommend for mediastinal staging (if tolerated)?
   a. PET scan only
   b. EBUS and/or mediastinoscopy plus PET scan

2. What is the SBRT dose and fractionation scheme that you most typically prescribe for ≥ 5 cm NSCLC?
   _____ Gy in _____ fractions

3. Which of the following best describes your SBRT timing scheme of ≥ 5 cm NSCLC?
   a. Daily
   b. Every other day
   c. Other

4. Which of the following is your preference, if any, regarding technique of SBRT delivery in these patients?
   a. Fixed-beam 3D (forward planning)
   b. Fixed-beam IMRT (inverse planning)
   c. Dynamic arc therapy (forward planning)
   d. VMAT (inverse planning)
   e. No preference

Supplemental Figure 1 continues on the next page

Supplemental Figure 1. Complete Survey Sent to Academic Thoracic Radiation Oncologists

Continued from the previous page

5. Would increasing patient age lead you to change the dose/fractionation scheme?
   a. Yes
   b. No

6. If yes, what would be your preferred dose and fractionation for elderly patients?
   _____ Gy in _____ fractions

7. Would poor performance status lead you to change the dose/fractionation scheme?
   a. Yes
   b. No

8. If yes, what would be your preferred dose and fractionation for patients with poor performance status?
   _____ Gy in _____ fractions

9. Would a central location of the tumor lead you to change the dose/fractionation scheme?
   a. Yes
   b. No

10. If yes, what would be your preferred dose and fractionation for centrally located tumors?
    _____ Gy in _____ fractions

11. Would you advocate administration of chemotherapy for patients with ≥5 cm NSCLC being definitively treated with SBRT?
    a. Yes
    b. No

12. If yes, what would be your preferred timing of chemotherapy?
    a. Prior to SBRT
    b. After SBRT
    c. Concurrent with SBRT
    d. Concurrent with SBRT with additional chemotherapy prior to, or after, SBRT

13. Which factor(s) in ≥ 5 cm NSCLC patients would lead you to consider chemotherapy? Please select all that apply.
    a. Younger age
    b. Good performance status
    c. No pathologic mediastinal staging performed
    d. Larger size of tumor
    e. Central tumor location
    f. Poor tumor differentiation on biopsy
    g. Visceral pleural involvement
    h. Chest wall invasion
    i. Adenocarcinoma histology
    j. I would not consider chemotherapy in any of these circumstances.

CASES

1. 59 yo patient, ECOG 1, with 5.0 cm poorly-differentiated peripheral NSCLC, no nodes on PET, presenting for SBRT.
   I would prescribe _____ Gy in _____ fractions given _____ and _____ chemotherapy.

2. 75 yo patient, ECOG 0, with 7.5 cm well-differentiated peripheral NSCLC, no nodes on EBUS, presenting for SBRT.
   I would prescribe _____ Gy in _____ fractions given _____ and _____ chemotherapy.

3. 64 yo patient, ECOG 1, with 5.6 cm poorly-differentiated central NSCLC, no nodes on PET, presenting for SBRT.
   I would prescribe _____ Gy in _____ fractions given _____ and _____ chemotherapy.

4. 70 yo patient, ECOG 2, with 5.4 cm poorly-differentiated peripheral NSCLC with lymphovascular invasion, no nodes on mediastinoscopy, presenting for SBRT.
   I would prescribe _____ Gy in _____ fractions given _____ and _____ chemotherapy.

5. 62 yo patient, ECOG 0, with 6.3 cm moderately-differentiated central NSCLC, no nodes on EBUS, presenting for SBRT.
   I would prescribe _____ Gy in _____ fractions given _____ and _____ chemotherapy.