Original Article

Hypofractionated radiation therapy as palliative management for symptomatic and local control of advanced thoracic malignancies

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Background: Radiation therapy plays an important role for symptom palliation for intrathoracic malignancies ineligible for curative-intent therapy. Limited data exists regarding the role of stereotactic body radiation therapy (SBRT) versus conformal radiation in intrathoracic tumors for palliation. We report the efficacy of hypofractionated RT (or palliative SBRT) in the symptom management and durable control of lung and non-lung intrathoracic tumors.

Methods: We performed a retrospective review of ninety-two thoracic lesions across 76 patients who completed palliative SBRT with doses ranging 25–50 Gy in 5–10 fractions between 2009 and 2019. Symptoms (cough, chest pain, hemoptysis, shortness of breath) were assessed at consult and 1–6 months follow-up. Local control was evaluated using follow-up CT imaging via RECIST criteria. Descriptive statistics were used to evaluate symptom palliation and Kaplan-Meier method to analyze local control.

Results: Of primary lung (Cohort P) lesions, 40% showed stable symptoms, 30% never developed symptoms, and 19% showed symptom relief. CT imaging 1–6 months post-SBRT showed 91% with partial response (PR) or stable disease (SD) in Cohort P and 87% with PR or SD in metastatic (Cohort M) lesions. In patients with initial PR/SD, local control until death was achieved in 71% of Cohort P and 84% of Cohort M. Of our symptomatic patients (Cohort S), 98% showed no symptom progression post-radiotherapy. All patients with hemoptysis at presentation achieved hemostasis post-radiotherapy.

Conclusions: Palliative SBRT has the advantage of higher biologic dose without protracted course for patients with limited prognosis. Patients showed significant symptom palliation and long-term local control. Palliative SBRT represents a reasonable treatment modality for incurable thoracic malignancies.

Keywords: Palliative radiotherapy; radiation oncology; hypofractionated; stereotactic; thoracic cancers

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Introduction

Palliative radiation therapy is a mainstay of treatment in the setting of advanced, symptomatic cancers; however, the nature of palliative radiation treatment continues to be redefined. Historically, palliative radiotherapy has consisted of low dose conformal radiation courses which can improve a multitude of symptoms such as pain, bleeding, and obstruction. Stereotactic body radiation therapy (SBRT) is a form of

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short course radiotherapy that allows highly conformal and accurate delivery of high doses of radiation. Currently, there is minimal data regarding the role of SBRT versus conformal radiation for the palliation of symptoms due to malignancy. Additionally, a conflicting body of evidence surrounds the role of a higher biologic dose for an ideal palliative radiation dose for symptomatic thoracic malignancies.

Selecting the best modality of radiotherapeutic treatment for patients who have advanced thoracic disease not amenable to curative-intent therapies continues to be a challenge due to this conflicting body of evidence. In non-small cell lung cancers, some studies have shown improved palliation with higher radiation doses (1) while others have shown equal palliation of symptoms and survival regardless of dose (2,3). Most literature assessing the efficacy of SBRT has been in the curative or oligometastatic setting (4-12). In the realm of spinal and bone metastases, recent studies have assessed the role of SBRT in the palliative setting with overall mixed results in pain relief (13-17). However, no studies have yet explored the role of palliative SBRT in thoracic malignancies.

Symptomatic intrathoracic malignancies represent a site that is potentially well-suited for palliative SBRT, as some studies suggest a potential survival advantage to dose escalation. SBRT has the advantage of providing a higher biologic dose without a protracted treatment course which is more convenient for patients and limits delay to subsequent systemic therapies which are not recommended to be given concurrently in patients with metastatic disease (18,19). Additionally, SBRT allows for highly conformal treatments which spare adjacent normal tissues and have the potential to increase the therapeutic ratio in patients receiving treatment.

The aim of our study is to evaluate the efficacy of hypofractionated radiotherapy in the palliative management of advanced thoracic malignancies ineligible for curative-intent therapy for both symptom management and durable control of intrathoracic tumors. We report both the symptom palliation of advanced thoracic malignancies and durable local control for lung primaries (Cohort P) and metastatic lesions (Cohort M) following treatment. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1779).

Methods

Patient population and treatment

IRB approval (#190568) was obtained by the institution's Human Research Protections Program. This study consists of a retrospective chart review within a single academic medical center. We retrospectively identified all patients at UC San Diego Medical Center treated with palliative SBRT of both lung and non-lung primary malignancies with intra-thoracic disease requiring radiotherapy in our department between January 1st, 2009 and March 26th, 2019. All patients had thoracic tumors involving parenchymal, perihilar, and mediastinal lesions that were not candidates for curative intent radiation due to comorbidity, metastatic disease at presentation, inoperable advanced stage with poor performance status, and/or prior radiation treatment. This study set was defined by patients having undergone a radiation course with IMRT or VMAT and received at least 5 Gy per fraction. All patients underwent standard SBRT protocols as described below, though given that we allowed patients with up to 10 fractions this could also be defined as hypofractionated radiotherapy given the standard USA definition of SBRT representing 5 fractions or less. Within this group we identified 76 patients who received palliative radiation for stage IV or locally advanced, incurable lung disease. Most patients in the group had a follow-up 2 to 4 weeks post-treatment and another CT follow-up 3 to 6 months post-treatment. Patients receiving curative intent therapies (defined as a BED10 >100 Gy) were excluded. Patients missing data or follow-up visits or imaging were excluded for individual analyses.

Individual consent for this retrospective analysis was waived in accordance with HIPAA Privacy rule, 45 CFR 164 section 512(I) and satisfied criteria for waiver of individual authorization. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data collection

Baseline key patient characteristics including age, sex, stage, primary tumor histology, and any administration of chemotherapy prior to or following treatment were obtained from the electronic medical record. Additionally, key dates including date of diagnosis, date of follow-up CT scan, and date of death were recorded. The tumor size, as measured by the physician delineated gross tumor volume (GTV), for the initial and subsequent CT scan were recorded. Total radiotherapy dose and fractionation were recorded. Additionally, primary endpoints assessed included symptom response to treatment and local control. Symptom

Table 1 Patient baseline demographics and clinical variables

Variables	Total	Cohort P, n (%)	Cohort M, n (%)	P value
Number of lesions treated (n)	92	52 (57%)	40 (43%)	0.21
Average age (years)	69 (13.1)	73 (11.0)	65 (14.0)	0.01
Sex				0.75
Female	50 (54%)	27 (52%)	23 (57%)	
Male	42 (46%)	25 (48%)	17 (43%)	
ECOG				<0.01
0	21 (23%)	10 (19%)	11 (28%)	
1	29 (32%)	14 (27%)	15 (38%)	
2	7 (8%)	6 (12%)	1 (3%)	
3	1 (1%)	1 (2%)	0 (0%)	
Unspecified	34 (37%)	21(40%)	13 (33%)	
Stage (at time of RT)				–
I	2 (2%)	2 (4%)		
II	7 (8%)	6 (12%)		
IIIA	6 (7%)	6 (12%)		
IIIB	3 (3%)	3 (6%)		
IV	68 (74%)	31 (60%)	40 (100%)	
Unspecified	6 (8%)	4 (8%)		
Symptoms (prior to RT)				
Cough	32 (58%)	21 (62%)	11 (32%)	0.29
Pain	19 (35%)	12 (35%)	7 (20%)	0.69
Shortness of breath	40 (73%)	26 (76%)	14 (41%)	0.22
Hemoptysis	3 (5%)	2 (6%)	1 (3%)	1

Division of baseline characteristics of treated thoracic lesions based on primary cancer. Each instance (n) represents one lesion of interest. Difference in multi-category proportions evaluated with chi-square test, single category with 2-proportion Z test. Difference in means calculated using student's *t*-test. Categorical variables displayed as total number (percentage). Continuous variables displayed as mean (standard deviation). Cohort P, primary lung lesions; Cohort M, metastatic lesions to the thoracic region. ECOG, Eastern Cooperative Oncology Group. RT, radiation therapy.

response was determined by a 0-4 score based on 1 point for documented symptoms of hemoptysis, chest pain, shortness of breath, or cough at time of consult and whether these improved at the first follow-up between 1–6 months post-treatment based on the same 0-4 scoring system. Patients who had none of these symptoms at follow-up were considered to have a complete response and those with any improvement in symptoms were considered to have a partial response. Lastly, we reviewed follow-up CT imaging to evaluate for local control using RECIST criteria (20).

Statistical analysis

Summary statistics are reported for patient demographic and clinical variables as detailed in *Table 1*, where baseline continuous data are compared with student's *t*-test, single categorical data with 2-proportion Z test, and multi-group categorical data compared with Chi-square test. Patients were divided into primary thoracic (Cohort P) and metastatic other primary (Cohort M). Descriptive statistics, including mean and proportion, for age at consult, type of treatment

Table 2 Constraints in plan optimization for selected OAR

Organ at risk	Number of fractions		
	3	5	10
Great vessels	D_{max} ≤39 Gy	D_{10cc} ≤47 Gy	D_{max} <53 Gy (soft)
		D_{max} ≤52.5 Gy	V_{47Gy} <10 cc (soft)
Heart	D_{max} ≤30 Gy (soft)	D_{30cc} ≤30 Gy (soft)	D_{max} <51 Gy (soft)
		D_{max} ≤52.5 Gy (soft)	$V_{35\ Gy}$ <15 cc (soft)
Bronchus	D_{max} ≤30 Gy	D_{4cc} ≤18 Gy	D_{max} <51 Gy (soft)
		D_{max} ≤52.5 Gy	V_{39Gy} <5 cc (soft)
Esophagus	D_{max} ≤30 Gy	D_{max} ≤32 Gy	D_{max} <39 Gy (soft)
	D_{5cc} ≤17.7 Gy (soft)	D_{5cc} ≤27.5 Gy (soft)	V_{30Gy} <5 cc (soft)
Bilateral lung minus ITV	D_{mean} ≤8 Gy	D_{mean} ≤8 Gy	$MVS_{12.5Gy}$ >1,500 cc (soft)
	V_{20Gy} ≤15%	V_{20Gy} ≤15%	$MVS_{13.5Gy}$ >1,000 cc (soft)
Ribs	V_{30Gy} ≤30 cc (soft)	V_{30Gy} ≤30 cc (soft)	
Spinal canal	D_{max} <21.9 Gy	D_{max} ≤30 Gy	D_{max} ≤34 Gy

Constraints indicated as soft should not compromise plan quality or PTV coverage. If fulfilling a constraint cannot be achieved, for example in case of OAR/PTV overlap, the planning objective is decided by the treating physician. D_{max} is defined as $D_{0.03\ cc}$, and not as a maximum point dose. OAR, organs at risk; MVS, Minimum Volume Spared; PTV, planning target volume; ITV, internal target volume.

planning, radiation dose, fractionation scheme, previous chemotherapy, symptom response to SBRT, and radiologic response to SBRT. The Kaplan-Meier method was used for overall local control estimates with censoring performed for patients lost to follow-up. All statistical analyses were performed with statistical software R, version 3.5.1.

Radiation technique

Patients were immobilized with upper body vac-lok cushions in an arms-up position. 4D CT scans were acquired using the real-time positioning management (RPM) system (Varian Medical Systems, Palo Alto, CA, USA) to record the breathing trace. Depending on the amplitude of motion and regularity of breathing, a decision to gate treatment was made for each patient. Specifically, if tumor motion was larger than 5 mm, gated treatment centered around exhalation was typically recommended. The ITV (internal target volume) was delineated by a treating physician on the MIP (maximum intensity projection) and on scans of the respiration phases to ensure the ITV encompassed the full range of motion of the tumor within the selected gating window. Dose calculation was performed on a CT scan that averaged the corresponding respiration phases selected for treatment. Patients were treated with either 2–4 arc VMAT or 5–8 field IMRT. Plans were commonly normalized to deliver 100% prescribed dose to 95% of the PTV, or to at least 98% of GTV or ITV. An on-board imaging system was used for image guidance according to clinically used SBRT protocols. Orthogonal kV (kilovoltage) images were used to straighten and align patients, followed by a KV cone-beam computed tomography scan to align the tumor. For gated treatments, real-time fluoroscopy images were used to confirm the tumor motion during the selected gating window was encompassed by the ITV. Gated treatment using the real-time positioning management system was used in 74 of 92 treatments. Dose constraints used in plan optimization for selected organs at risk (OAR) are described in *Table 2*.

Homogeneity index, defined as the ratio of the maximum point dose to the prescribed dose, was (mean, standard deviation) 1.19±0.09. Conformity index, defined as the ratio of the volume receiving prescribed dose to the PTV volume was 1.02±0.08.

Results

Within our retrospective cohort, 92 total thoracic lesions were identified across 76 patients who completed SBRT in a palliative dose regimen between 2009 and 2019. 57%

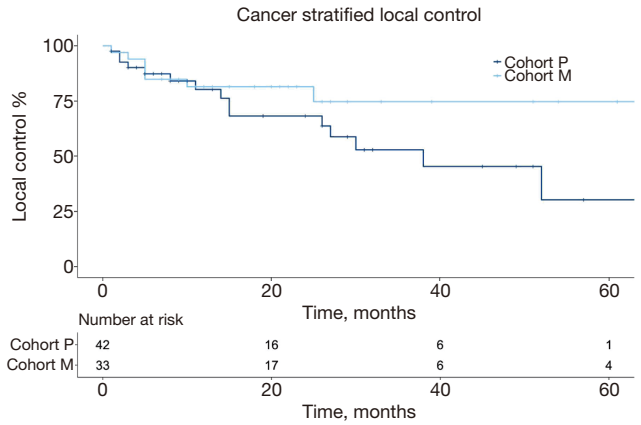

Figure 1 Kaplan-Meier plot showing local control of primary lung (Cohort P) versus metastatic (Cohort M) thoracic lesions following SBRT completion. SBRT, stereotactic body radiation therapy.

(n=52) of those thoracic lesions were of primary lung origin (Cohort P) while 43% (n=40) were metastatic from other sites (Cohort M) as described in *Table 1*. We then reviewed a smaller symptomatic cohort (Cohort S) to evaluate the effect of SBRT on symptomatic palliation which included patients that reported symptoms related to their disease at time of initial consult. Average age at time of consult was 69 years (range, 33–93 years) of which 46% (n=42) were male and 54% (n=50) were female. Among all patients, 88 of 92 lesions were in either the lung parenchyma or peri-hilar while 4 lesions were in the mediastinum. All patients received either IMRT (14%) or VMAT (86%) based treatment planning. Dose range was 25–50 Gy in 5–10 fractions with a minimum of 5 Gy per fraction. Common dose/fractionation schemes included 40 Gy in 5 fractions (26%), 30 Gy in 5 fractions (22%), 50 Gy in 10 fractions (18%), and 25 Gy in 5 fractions (17%). There were 37 patients with lesions which would be defined as "central" or "ultracentral." Among this cohort there was an even distribution of fractionations utilized which included 30 Gy in 5 fractions (32%), 40 Gy in 5 fractions (24%), 50 Gy in 10 fractions (24%), and 25 Gy in 5 fractions (19%).

Primary lung lesions

Of the total 76 patients who underwent SBRT seeking palliative symptomatic improvement and/or stability, 44 patients completing 49 total courses of SBRT to 52 primary lung lesions (Cohort P). The majority of Cohort P patients had stage IV (n=29, 66%) and stage III (n=9, 20%) non-small cell lung cancer. Among these 44 Cohort P patients, 46% (n=24) received chemotherapy prior to SBRT while 54% (n=28) did not. None of the patients in this study received concurrent chemotherapy. Among the 47 courses of treatment in Cohort P with follow-up within 3–6 months of SBRT completion, 30% (n=14) had no pulmonary symptoms at presentation and did not develop any new symptoms at initial follow-up, 19% (n=9) showed relief of at least 1 symptom at initial follow-up, and 40% (n=19) showed stable symptoms (did not worsen or improve). Only 11% (n=5) showed increase in symptoms following SBRT. There were only 2 patients with hemoptysis at presentation, and both achieved hemostasis following SBRT. Among the 45 treated lesions with available follow-up CT imaging 1–6 months after SBRT, 53% (n=24) showed partial response (PR), 38% (n=17) showed stable disease (SD), and 9% (n=4) showed progressive disease (PD) at initial follow-up. With further follow-up (median follow-up 20 months), 71% (n=29) of the 41 lesions with initial PR or SD demonstrated local control until death (*Figure 1*).

Metastatic lesions to thoracic cavity

Our analysis also included 32 patients completing 37 total courses of SBRT to 40 metastatic lesions (Cohort M). Of the 33 Cohort M patients with further follow-up, 79% (n=26) demonstrated local control until death while 21% of (n=7) patients had eventual local failure. Of the 40 Cohort M lesions, the most common primary sites were colorectal (n=11, 28%), genitourinary (n=7, 18%), and gynecologic (n=7, 18%). Genitourinary cancers included prostate and renal primaries while gynecologic included leiomyosarcoma, uterine, cervical primaries. Additional primary sites included melanoma, sarcoma, thymoma, breast, oropharyngeal and more. Of the 37 treated Cohort M lesions with follow-up CT imaging, 3 (8%) showed CR, 24 (65%) showed PR, 8 (22%) showed SD, and only 2 (5%) showed PD. With further follow-up, 84% (n=27) of the 32 lesions with initial PR or SD demonstrated local control until death (*Figure 1*).

Symptomatic palliation

Lastly, 45 patients reported symptoms at the time of initial consult and completed 50 courses of radiation to 55 different thoracic lesions (Cohort S). Cohort S included primarily stage IV (n=42, 76%) patients. The most common histology was NSCLC (n=34, 62%) while the most common primary site of patients from Cohort M was colorectal

Table 3 Lung dose-volume metrics for plan assessment for both physical dose and equivalent dose in 2 Gy fractions (EQD2)

Dose-volume metric (mean ± SD, range)	V_{5Gy}	V_{10Gy}	V_{20Gy}	Mean dose
Percent volume or physical dose	17.5±9.5 (2.3–41.3)	10.1±6.8 (0.8–34.1)	4.1±4.1 (0.2–25.5)	3.5±2.1 (0.6–12.5)
Fraction size adjusted, EQD2	–	–	7.2±5.6 (0.5–15.2)	4.1±2.8 (0.5–29.7)

The mean, standard deviation, and range of observed values are summarized. Mean radiation dose to the lungs was 3.5 Gy (range, 0.6–12.5 Gy, SD =2.1 Gy). EQD2, equivalent total dose in 2 Gy fractions; SD, standard deviation.

(n=6, 11%). Additional primary sites included breast, renal, sarcoma, and others (n=15, 27%). Of the 53 lesions treated with follow-up within 6 months, 21 (40%) showed relief of at least 1 symptom and 31 (58%) showed stable symptoms. Only 1 patient (2%) showed symptom progression. All patients with hemoptysis at presentation achieved hemostasis following SBRT. Of the 48 treated lesions with follow-up CT imaging, 1 (2%) showed CR, 28 (58%) showed PR, 15 (31%) showed SD, and 4 (8%) showed PD. With further follow-up (median 23 months), 57% (n=30) of the 53 lesions with initial PR or SD demonstrated local control until death.

Toxicity

Among our entire cohort of 76 patients, we found 9 patients had reported toxicities at follow-up. This included 4 patients with dysphagia (5%), 2 with dermatitis (3%), 2 with pneumonitis (3%), and 1 with chest wall pain related to prior RT.

Radiation dose metrics

Dose-volume metrics for plan assessment for both physical dose and equivalent dose in 2 Gy fractions (EQD2) are described in *Table 3*. The mean, standard deviation, and range of observed values are summarized. Mean radiation dose to the lungs was 3.5 Gy (range, 0.6–12.5 Gy, SD =2.1 Gy).

Discussion

Within the treatment of lung cancer, several studies have shown improved symptomatic palliation with higher radiation doses (1) while others have shown equal palliation of symptoms and survival regardless of dose (2,3). Recent work in the setting of palliative SBRT for other treatment sites has demonstrated a potential role for SBRT for the purposes of palliation. Specifically, several recent studies have shown the possible benefit of improved palliation in the setting of bone metastases. This has included SBRT in the setting of spine metastases in which SBRT was found to be superior to CRT at improving the complete pain response rate at 3- and 6-month post radiation compared to CRT (13). Higher rates of pain response have also been corroborated in non-spine bone metastasis treated with SBRT compared to MFRT (14). In contrast, other studies showed in localized spine metastases that pain control was not improved following SBRT (15,16). This study presents the first evaluation of the efficacy of SBRT for palliation of intra-thoracic tumors. Both symptomatic progression and local control were assessed for this cohort. See *Table 4* for further details of these trials. The differences among these trials have resulted in an ongoing debate without clarity on the role for SBRT in palliation (21).

In our study, 90% of advanced lung cancer patients did not symptomatically progress following SBRT. The small rate of early progression at 1–6 months is partially expected and explained due to the non-ablative doses in the non-curative setting. Palliative SBRT was shown to be most likely to be beneficial in the setting of hemoptysis, cough, and chest pain. Follow-up CT imaging showed 93% of patients with either stability or partial/complete response following SBRT while most patients (64%) showed no local failure at their most recent CT imaging to date or prior to death.

Regarding local control, CT imaging demonstrated 79% (73 of 92) of treated lesions with either partial response (PR =48) or stable disease (SD =25) at follow-up. Regarding local control of our symptomatic cohort, CT imaging demonstrated 93% (41 of 45) of symptomatic patients showing initial PR or SD following SBRT. Of these patients, 71% (29 of 41) then went on to have long-term local control of treated lesions. Within our total cohort, 89% of patients had either improvement or stable symptoms following palliative SBRT. Based on our study, palliative SBRT represents a reasonable treatment modality in the palliation of advanced, incurable NSCLC.

There are limitations of our study to be acknowledged.

Table 4 Table of existing RCTs evaluating the role of SBRT for palliation

Trial	Disease site	SBRT arm			Conventional arm			Pain response	Toxicity
		Dose (Gy/fx)	n	Response	Dose (Gy/fx)	n	Response		
RTOG 0631 (Ryu)	Bone (spine)	16–18/1	230	40.3%	8 in 1	130	57.9%	No difference	No differences
SC.24 (Sahgal)	Bone (spine)	24/2	114	53%	20/5	115	30%	Improved with SBRT at 3 months	No differences
MDACC trial (Nguyen)	Bone (non-spine)	12–16/1	81	38%	30/10	79	21%	Improved with SBRT at 3 months	No differences
VERTICAL trial (Pielkenrood)	Bone (all)	18/1, 30/3, or 35/5	45	40%	8/1, 20/5, or 30/10	44	32%	No difference	No grade 3 or 4 in either arm
Heidelberg (Sprave)	Bone (spine)	24/1	23	25.5%	30/10	23	23.2%	Improved with SBRT at 6 months (trend at 3 months)	No grade 3+ toxicities with SBRT

RCT, randomized controlled trial; SBRT, stereotactic body radiation therapy.

First, because our cohort involved only a single institution review this limits our study's representation of symptom and local control at other institutions with a different patient population and different radiation oncologists. Additionally, our cohort of 76 patients is small; however, we believe this study represents the largest published cohort of patients with SBRT in the palliative lung setting. Additionally, several patients had no follow-up within 1–6 months from SBRT and decreased our cohort size accordingly to involve only those with appropriate follow-up to determine the effect of SBRT on treated patients. We believe that our study is also limited in terms of toxicity reporting based on poor follow-up and likely underreporting of acute symptoms which may have self-resolved by the time of first follow up post treatment. We would encourage future studies to evaluate toxicity data associated with SBRT in advanced lung malignancies such as pulmonary fibrosis, pneumonitis, esophagitis, and strictures which would be far more likely to be helpful when evaluated in the prospective setting. Finally, reviewing notes retrospectively within a chart review of various physicians and their varied documentation of symptoms ushers in the possibility of inconsistency. For example, symptoms were noted on a subjective scale of 0-4 symptom deducing possible symptomatic improvement at follow-up compared to time of initial consult as "stable" with no improvement or worsening analyzed despite the possibility of subtle changes without a prospective protocol to pay particular attention to the subtlety of symptom change.

In conclusion, we believe that palliative SBRT for thoracic malignancies is a reasonable option to consider for patients who are not candidates for curative intent therapies. Given the potential role for a higher biologic dose in palliation of symptomatic thoracic malignancies, we believe that palliative SBRT represents a safe, convenient option for patients which prevents undue delay to their ability to proceed with additional therapies. Prospective studies would be required to further confirm the role of palliative SBRT for symptomatic thoracic tumors.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1779

Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-21-1779

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1779). AB is a consultant for Courage Health. AS reports research funding and honoraria from Pfizer and Varian Medical Systems, consultant fees from Astrazeneca and Jounce Therapeutics outside the submitted work. AS is the scientific founder and has an

equity interest in Toragen Inc. outside the submitted work. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. IRB approval (#190568) was obtained by the institution's Human Research Protections Program. Individual consent for this retrospective analysis was waived in accordance with HIPAA Privacy rule, 45 CFR 164 section 512(I) and satisfied criteria for waiver of individual authorization. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Teo P, Tai TH, Choy D, et al. A randomized study on palliative radiation therapy for inoperable non small cell carcinoma of the lung. Int J Radiat Oncol Biol Phys 1988;14:867-71.
2. Abratt RP, Shepherd LJ, Salton DG. Palliative radiation for stage 3 non-small cell lung cancer--a prospective study of two moderately high dose regimens. Lung Cancer 1995;13:137-43.
3. Sundstrøm S, Bremnes R, Aasebø U, et al. Hypofractionated palliative radiotherapy (17 Gy per two fractions) in advanced non-small-cell lung carcinoma is comparable to standard fractionation for symptom control and survival: a national phase III trial. J Clin Oncol 2004;22:801-10.
4. Jung J, Yoon SM, Park JH, et al. Stereotactic body radiation therapy for locally advanced pancreatic cancer. PLoS One 2019;14:e0214970.
5. Timmerman RD, Kavanagh BD, Cho LC, et al. Stereotactic body radiation therapy in multiple organ sites. J Clin Oncol 2007;25:947-52.
6. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010;303:1070-6.
7. Theelen WSME, Peulen HMU, Lalezari F, et al. Effect of Pembrolizumab After Stereotactic Body Radiotherapy vs Pembrolizumab Alone on Tumor Response in Patients With Advanced Non-Small Cell Lung Cancer: Results of the PEMBRO-RT Phase 2 Randomized Clinical Trial. JAMA Oncol 2019;5:1276-82.
8. Buwenge M, Macchia G, Arcelli A, et al. Stereotactic radiotherapy of pancreatic cancer: a systematic review on pain relief. J Pain Res 2018;11:2169-78.
9. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet 2019;393:2051-8.
10. Zeng KL, Tseng CL, Soliman H, et al. Stereotactic Body Radiotherapy (SBRT) for Oligometastatic Spine Metastases: An Overview. Front Oncol 2019;9:337.
11. Ryu S, Pugh SL, Gerszten PC, et al. RTOG 0631 Phase II/III Study of Image-Guided Stereotactic Radiosurgery for Localized (1-3) Spine Metastases: Phase II Results. Int J Radiat Oncol Biol Phys 2011;81:S131-2.
12. Nguyen QN, Shiu AS, Rhines LD, et al. Management of spinal metastases from renal cell carcinoma using stereotactic body radiotherapy. Int J Radiat Oncol Biol Phys 2010;76:1185-92.
13. Sahgal A, Myrehaug SD, Siva S, et al. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial. Lancet Oncol 2021;22:1023-33.
14. Nguyen QN, Chun SG, Chow E, et al. Single-Fraction Stereotactic vs Conventional Multifraction Radiotherapy for Pain Relief in Patients With Predominantly Nonspine Bone Metastases: A Randomized Phase 2 Trial. JAMA Oncol 2019;5:872-8.
15. Ryu S, Deshmukh S, Timmerman RD, et al. Radiosurgery Compared To External Beam Radiotherapy for Localized Spine Metastasis: Phase III Results of NRG Oncology/RTOG 0631. Int J Radiat Oncol Biol Phys 2019;105:S2-S3.
16. Pielkenrood BJ, van der Velden JM, van der Linden YM, et al. Pain Response After Stereotactic Body Radiation Therapy Versus Conventional Radiation Therapy in Patients With Bone Metastases-A Phase 2 Randomized Controlled Trial Within a Prospective Cohort. Int J Radiat Oncol Biol Phys 2021;110:358-67.
17. Sprave T, Verma V, Förster R, et al. Quality of Life

Following Stereotactic Body Radiotherapy Versus Three-Dimensional Conformal Radiotherapy for Vertebral Metastases: Secondary Analysis of an Exploratory Phase II Randomized Trial. Anticancer Res 2018;38:4961-8.
18. Johnstone C, Lutz ST. The role of hypofractionated radiation in the management of non-osseous metastatic or uncontrolled local cancer. Ann Palliat Med 2014;3:291-303.
19. Moeller B, Balagamwala EH, Chen A, et al. Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 Update of an American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline. Pract Radiat Oncol 2018;8:245-50.
20. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-47.
21. Hoskin Md Frcr P. Pain Response After Stereotactic Body Radiation Therapy Versus Conventional Radiation Therapy in Patients With Bone Metastases-A Phase 2, Randomized Controlled Trial Within a Prospective Cohort. Int J Radiat Oncol Biol Phys 2021;110:368-70.

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