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ORIGINAL ARTICLE **CME**

Thirteen Years' Experience of Stereotactic Body Radiation Therapy for Ultra-Central Lung Tumours in Hong Kong

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ABSTRACT

Introduction: *Stereotactic body radiation therapy (SBRT) for ultra-central lung tumours is controversial given the proximity of the tumours to critical organs at risk. We undertook a retrospective review of the efficacy and safety outcomes of ultra-central lung SBRT at a major cancer centre in Hong Kong.*

Methods: *We analysed patients with either primary or oligometastatic ultra-central lung tumours treated with SBRT from 2009 to 2022. The primary outcome was local progression-free survival. Secondary outcomes included the incidence of grade ≥2 SBRT-related toxicity and overall survival. Clinical and dosimetric factors were collected and analysed for potential associations with survival outcomes.*

Results: *A total of 66 patients were included. Twenty-four cases were primary lung tumours and 42 were lung metastases, with the majority of metastatic lesions being of lung origin (n = 32). Indications for SBRT for lung metastases included oligoprogression (n = 23), oligoresidual disease (n = 13), and oligorecurrence (n = 6). Most patients (86%) received 50 Gy in five fractions. Median follow-up was 54 months, and median overall survival was 59 months. The 1-year and 3-year local failure-free survival rates were 98% and 88%, respectively. Grade 3 and grade 5 toxicity rates were 4.5% and 6%, respectively. A higher dose to 4 cc of the proximal bronchial tree and tumours located within 1 cm of the mainstem bronchus were associated with grade ≥2 airway toxicity. Oesophageal mean and maximum doses, and dose to 5 cc of the oesophagus were positively associated with grade ≥2 oesophageal toxicity.*

Conclusion: *We demonstrated high rates of local control and acceptable toxicity outcomes with ultra-central lung SBRT. Further results from prospective studies may clarify the optimal dose fractionation and organ-at-risk constraints for this population.*

Key Words: *Lung neoplasms; Organs at risk; Radiosurgery*

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Ethics Approval: This research was approved by the Central Institutional Review Board of Hospital Authority, Hong Kong (Ref No.: CIRB-2024-319-5). The requirement of patient consent was waived by the Board due to the retrospective nature of the research.

中文摘要

香港使用軀體立體定位放射治療超中央型肺腫瘤的十三年經驗

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引言：由於超中央型肺腫瘤接近關鍵的危及器官，因此使用軀體立體定位放射治療（SBRT）這腫瘤具爭議性。我們在香港一所主要癌症中心進行回顧性研究，檢視超中央型肺腫瘤的治療效用及安全性。

方法：我們分析了於2009至2022年期間接受SBRT治療的原位或寡轉移超中央型肺腫瘤患者。主要結果為局部無惡化存活期，次要結果為二級或以上、與SBRT相關的毒性發生率及整體存活期。我們收集並分析了臨床及劑量因素，以找出與存活結果有關的潛在關聯。

結果：本研究共包括66名患者，24名患有原位肺腫瘤，42名出現肺轉移，大部分轉移性病變源自肺部（n = 32）。SBRT治療肺轉移的適應症包括寡進展（n = 23）、寡殘留疾病（n = 13）及寡復發（n = 6）。大部分患者（86%）分五次接受劑量為50 Gy的治療。隨訪中位數為54個月，整體存活期中位數為59個月。一年及三年局部無疾病存活率分別為98%及88%。三級及五級毒性比率分別為4.5%及6%。用於受照射的4 cc近端支氣管樹體積的較高劑量以及位於主支氣管1厘米內的腫瘤與二級或以上毒性相關。食道平均及最高劑量以及用於受照射的5 cc食道體積的劑量與二級或以上食道毒性呈正相關。

結論：研究結果顯示超中央型肺部SBRT的局部控制率高，而且毒性結果可接受。未來可研究釐清適用於相關患者的最佳分次劑量及危及器官的限制。

INTRODUCTION

Stereotactic body radiation therapy (SBRT) is an established treatment for medically inoperable early-stage non–small-cell lung cancer and has been increasingly utilised for treatment of oligometastatic or oligoprogressive lung metastases. In early-stage peripherally located lung tumours, SBRT confers high rates of local control, cancer specificity, and overall survival (OS) with a low incidence of severe toxicity.[1] However, the safety of SBRT to 'ultra-central' lesions, where the gross tumour volume (GTV) and/or planning target volume (PTV) overlaps critical mediastinal structures such as the central airway or oesophagus, remains a matter of debate.[2] This subgroup was underrepresented in the RTOG 0813 trial where ultra-central tumours comprised only 17% of the study population.[2] Alarmingly high rates of fatal airway bleeding (12%) were also reported in the phase II HILUS trial.[3]

SBRT for ultra-central lung tumours has been performed in our institution, a major cancer centre in Hong Kong, since its introduction in 2009. We sought to undertake a retrospective review of the efficacy and safety outcomes of ultra-central lung SBRT at our centre.

METHODS

Study Design and Patient Population

All consecutive cases of primary or oligometastatic ultra-central lung tumours treated with SBRT from 2009 to 2022 at Pamela Youde Nethersole Eastern Hospital were included for analysis. Patients with incomplete or missing clinical/dosimetric data were excluded. Ultra-central tumours were defined as lesions with the PTV overlapping the trachea, proximal bronchial tree (PBT) or oesophagus.

Procedures

Patients were simulated with arms above their head with arm/shoulder supports and immobilised with the BodyFIX system (Elekta, Stockholm, Sweden). Expiratory breath hold was used for lobe tumours while four-dimensional computed tomography simulation was used for upper/middle lobe tumours or for patients unable to cooperate with the breath-hold procedure. Respiratory motion was monitored using a real-time position management system (Varian; Varian Medical Systems, Palo Alto [CA], US). An additional intravenous contrast-

enhanced simulation scan was performed for tumours adjacent to mediastinal structures; oral contrast was administered at the discretion of the treating physician.

GTV was delineated in the pulmonary window (window width = 1600 Hounsfield unit [HU] and window level = -600 HU), supplemented with images acquired in the soft tissue window (window width = 400 HU, window level = 20 HU). An internal target volume was generated from four-dimensional CT simulation scans and an isotropic margin of 5 mm expanded from the internal target volume to form the PTV. For cases undergoing breath hold, the GTV-to-PTV margin was 8 mm. No clinical target volume was used.

Dose fractionation schemes included 50 Gy in five fractions (57 cases), 60 Gy in eight fractions (seven cases), or 35 Gy in five fractions (two cases). Treatments were administered on alternating days.

Static-field dynamic intensity modulated radiotherapy and/or volumetric modulated arc therapy with 6–mega-voltage photons were used. The prescription isodose level was chosen such that 95% of the PTV received the prescribed dose and 99% of the PTV received ≥90% of the prescribed dose. The prescribed isodose ranged between 80% and 90% for all plans. Dose constraints were adapted from the RTOG 0813 protocol[2] and the American Association of Physicists in Medicine Task Group 101 report.[4] The maximum point doses (D_{max}) to the trachea, the PBT and the oesophagus were limited to 105% of the prescription dose.

Treatment was delivered with linear accelerators (TrueBeam; Varian Medical Systems, Palo Alto [CA], US), with pretreatment cone-beam computed tomography images obtained before each treatment. Online verification and matching were performed. Systemic therapies (excluding hormonal treatments) were withheld at least 24 hours before and after SBRT.

All patients underwent computed tomography scans of the thorax at 6-month intervals for at least 3 years. Clinical follow-up and need for additional imaging were performed at the discretion of treating clinicians.

Outcomes

The primary outcome analysed was local progression-free survival (PFS). Secondary outcomes included the incidence of grade ≥2 SBRT-related toxicity—classified according to the Common Terminology Criteria for Adverse Events version 5.0 grading system[5]—and OS. Clinical and dosimetric factors were collected and analysed for potential associations with survival outcomes.

Statistical Analyses

Local PFS and OS rates were calculated using the Kaplan–Meier method. Local PFS was defined as the time from the date of the first SBRT fraction to either local progression or last follow-up. OS was defined as the time from SBRT to death from any cause or last follow-up.

Clinical and dosimetric variables were analysed using descriptive statistics. Categorical data were represented as numbers with percentages, while continuous data were reported as medians with interquartile ranges. All dosimetric parameters were converted to equivalent doses of 2-Gy fractions (alpha-beta ratio = 3, for dosimetric parameters of organs at risk only) using the linear-quadratic model for comparison across different dose fractionations.

Comparison of clinical and dosimetric parameters between patients with or without grade ≥2 toxicity was done with Chi squared/Fisher's exact test for categorical variables, and the Mann-Whitney *U* test for continuous variables.

Simple Cox proportional hazards regression analyses were conducted to identify potential associations between clinical/dosimetric variables and survival outcomes. Variables with a p value < 0.1 were entered into multivariable analysis. A p value of < 0.05 was considered statistically significant.

Statistical analyses were performed using commercial software SPSS (Windows version 27.0; IBM Corp, Armonk [NY], US). The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist was followed in the preparation of the study.

RESULTS

Patient Population

A total of 66 patients were analysed. The median follow-up was 54 months (range, 4-114). Baseline patient characteristics and dosimetric parameters are detailed in Table 1. The median age was 71.5 years. Most patients (76%) had an Eastern Cooperative Oncology Group performance status score of 0 to 1.

Table 1. Baseline demographic, clinical and dosimetric parameters of the study population (n = 66).*

Sex	
Male	32 (48%)
Female	34 (52%)
Age, y	71.5 (59-78)
ECOG PS score	
0-1	50 (76%)
2-3	16 (24%)
FEV_1	1.91 (1.49-2.23)
History of COPD	
Yes	4 (6%)
No	62 (94%)
Smoking status	
Yes	18 (27%)
No	48 (73%)
Type of tumour†	
Group A	22 (33%)
Group B	44 (67%)
PTV overlap	
Overlapping trachea/PBT	56 (85%)
Overlapping oesophagus	5 (7.5%)
Overlapping trachea/PBT and oesophagus	5 (7.5%)
Endobronchial tumour	
Yes	7 (11%)
No	59 (89%)
Use of anticoagulant/anti-angiogenesis inhibitor within 3 months of SBRT	
Yes	4 (6%)
No	62 (94%)
PBT dose, Gy	
D_{mean}‡	10.28 (5.17-17.9)
D_{max}‡	138.27 (126.77-140.11)
D_{4cc}‡	23.72 (11.6-40.55)
Oesophageal dose, Gy	
D_{mean}‡	3.65 (2.82-5.81)
D_{max}‡	41.13 (22.95-79.5)
D_{5cc}‡	12.45 (8.08-20.65)
Lung V_{20Gy}§	7.55% (5.19%-9.65%)
GTV, cm^3	22.35 (12.68-39.6)
PTV, cm^3	58.90 (41.1-92.33)
Prescription isodose	85.55% (84.6%-86.7%)
PTV covered by the prescription isodose	95.15% (95.08%-95.26%)

Abbreviations: COPD = chronic obstructive bronchopulmonary disease; ECOG = Eastern Cooperative Oncology Group; GTV = gross tumour volume; PBT = proximal bronchial tree; PS = performance status; PTV = planning target volume; SBRT = stereotactic body radiation therapy.

* Data are shown as No. (%) or median (interquartile range).

† Group A tumours are tumours ≤1 cm from the main bronchi and trachea while Group B tumours are all other tumours. See reference 3.

‡ Expressed as mean point dose, maximum point dose, or dose to 4 cc or 5 cc volume of the organ at risk as specified.

§ Percentage of lung receiving a dose ≥20 Gy.

Table 2. Histological subtypes of primary lung and metastatic tumours in the study population (n = 66).*

Primary lung tumours	
Adenocarcinoma	15
Squamous cell carcinoma	3
Non–small-cell carcinoma NOS	2
Adenoid cystic carcinoma	1
Adenosquamous carcinoma	1
Histological confirmation not obtainable	2
Metastatic tumours	
Lung adenocarcinoma	
EGFR exon 19 deletion or exon 21 *L858R* mutation	26
EGFR exon 18 *G719A*	1
ALK fusion	1
RET fusion	1
No known driver mutation	3
Colorectal adenocarcinoma	3
Breast invasive ductal carcinoma	2
Renal cell carcinoma	2
Nasopharyngeal carcinoma	1
Oropharyngeal squamous cell carcinoma (p16-positive)	1
Hepatocellular carcinoma	1

Abbreviations: *ALK* = anaplastic lymphoma kinase; *EGFR* = epidermal growth factor receptor; NOS = not otherwise specified; *RET* = rearranged during transfection.

* Data are shown as No.

Twenty-four cases were primary lung tumours and 42 cases were lung metastases. The histological diagnoses for primary lung and metastatic lesions are shown in Table 2. Most metastatic lesions (32/42) were of lung origin. Indications of SBRT for lung metastases included oligoprogression (n = 23), oligoresidual disease (n = 13), and oligorecurrence (n = 6).

Breath hold was used in 11 patients (17%), with the remainder utilising four-dimensional CT simulation. The median prescription isodose was 85.55%. Median GTV and PTV were 22.35 cm^3 and 58.90 cm^3, respectively. Tumour PTV overlapped with the PBT or trachea in 61 lesions and oesophagus in 10 lesions. The median PTV coverage by the prescription isodose was 95.15% (Table 1).

Local Control and Survival Outcomes

The 1-year and 3-year local failure-free survival rates were 98% and 88%, respectively. Mean local failure-free survival was 79 months (95% confidence interval [CI]=65-94) [Figure 1]. OS ranged from 4 to 148 months, with a median OS of 59 months (95% CI = 54-85) [Figure 2]. The 1-year and 3-year OS rates were 89.4% and 69.7%, respectively.

Safety Outcomes

Grade ≥2 toxicity occurred in 18 patients (27%). Three patients (5%) had grade 3 toxicity, including oesophageal stricture, radiation pneumonitis, and lung collapse for each. Four patients (6%) had grade 5 toxicity (one case

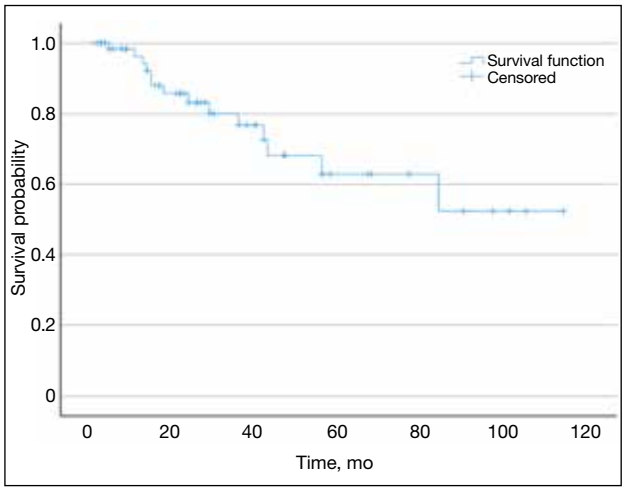

Figure 1. Kaplan–Meier curve for local failure-free survival.

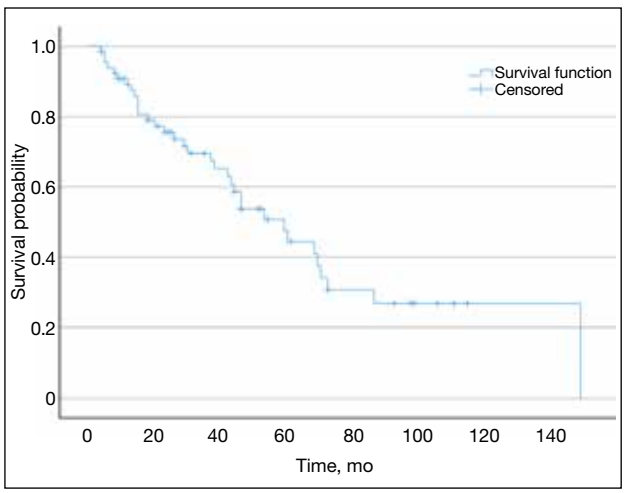

Figure 2. Kaplan–Meier curve for overall survival.

of oesophageal ulcer bleeding, two cases of airway bleeding, and one case of multifactorial respiratory failure). The median time to grade ≥3 toxicity was 4.5 months.

Among the 61 patients with PTV overlapping the PBT or trachea, grade ≥2 pulmonary toxicity occurred in 14 cases (23%). Airway obstruction and/or bleeding occurred in all 14 patients, and eight also had radiation pneumonitis. Among the 10 patients with PTV overlapping the oesophagus, four (40%) developed grade ≥2 oesophageal toxicity, including two with odynophagia, one with oesophageal stricture, and one with oesophageal ulcer bleeding.

When comparing patients with or without grade ≥2 airway toxicity (bleeding or obstruction), there was a statistically significant difference for higher D_{max} (p = 0.035) and higher dose to 4 cc (D_{4cc}) of the PBT (p = 0.002) [Table 3].

For grade ≥2 airway bleeding, a statistically significant difference was found with group A tumours (≤1 cm from the main bronchi and trachea)[3] [p = 0.039], while a higher D_{4cc} of the PBT (p = 0.075) and endobronchial tumour location (p = 0.083) did not reach statistical significance. The use of anticoagulant or antiangiogenic therapy was not significantly associated with grade ≥2 bleeding (p = 0.276) [Table 4].

Baseline forced expiratory volume in 1 second, smoking status, history of chronic obstructive pulmonary disease, and the percentage of lung receiving a dose ≥20 Gy were not significantly associated with grade ≥2 radiation pneumonitis. For grade ≥2 oesophageal toxicity, statistically significant differences were found in higher mean dose (D_{mean}) [p < 0.001], higher D_{max} (p = 0.004), and higher dose to 5 cc (D_{5cc}) of the oesophagus (p = 0.005) [Table 3].

No postmortems were performed; thus, all deaths classified as grade 5 events were based on clinical grounds alone.

Simple and Multivariable Analyses

Simple Cox regression found age (hazard ratio [HR] = 0.957, 95% CI = 0.917-0.999; p = 0.047), and group A tumours (HR = 0.316, 95% CI = 0.106-0.945; p = 0.039) were predictors for local failure; however, these variables were not significant in the multivariable analysis (Table 5). Simple cox regression did not find any significant predictors for OS (Table 6).

DISCUSSION

Our study provides some of the longest follow-up data on the real-world outcomes of SBRT to ultra-central lung tumours. With a median follow-up of 54 months, our 3-year local control rate of 88% and grade 3 and grade 5 toxicity rates (5% and 6%, respectively) were comparable to prior studies.[6] In a recent meta-analysis of ultra-central SBRT including 1183 patients over 27 studies,[6] the pooled 2-year local control rate was 89%, while the grade 3 to 4 toxicity rate was 6% and the grade 5 toxicity rate was 4%.

Table 3. Mann-Whitney *U* test for grade ≥2 radiotherapy-related toxicities (n = 66).*

	Grade 0-1 airway toxicity (n = 51)	Grade ≥2 airway toxicity (n = 15)	p Value
PBT D_{mean}, Gy†	9.42 (5.4-12.53)	12.09 (7.29-20.59)	0.061
PBT D_{max}, Gy†	137.65 (122.74-140)	139.5 (137.13-141.27)	0.035
PBT D_{4cc}, Gy†	20.41 (5.13-30.63)	56.36 (24.17-117)	0.002
GTV, cm^3	19.5 (12.6-38.7)	27.4 (12.5-42.2)	0.426
PTV, cm^3	56 (40.4-90.3)	73.3 (41-94.8)	0.392
	Grade 0-1 airway bleeding (n = 61)	Grade ≥2 airway bleeding (n = 5)	p Value
PBT D_{mean}, Gy†	9.63 (5.93-13.29)	13.04 (8.3-24)	0.195
PBT D_{max}, Gy†	138.27 (125.6-140)	138.36 (80.65-141.44)	0.553
PBT D_{4cc}, Gy†	22.07 (9.31-37.67)	61.43 (29.9-105.42)	0.075
GTV, cm^3	21.6 (11.0-38.1)	27.4 (16.85-67.95)	0.27
PTV, cm^3	56 (40.7-91.65)	73.3 (43.55-126.5)	0.357
	Grade 0-1 oesophageal toxicity (n = 59)	Grade ≥2 oesophageal toxicity (n = 7)	p Value
Oesophagus D_{max}, Gy†	39.35 (19.06-57.79)	112.21 (71-139.93)	0.004
Oesophagus D_{5cc}, Gy†	11.51 (7.5-17.53)	30.19 (19.22-101.66)	0.005
Oesophagus D_{mean}, Gy†	3.58 (2.8-4.9)	9.36 (7.43-27.74)	< 0.001
GTV, cm^3	21.7 (12.55-39.3)	18.6 (7.75-39.6)	0.672
PTV, cm^3	56 (40.7-91.65)	73.3 (30.7-102.65)	0.725

Abbreviations: GTV = gross tumour volume; PBT = proximal bronchial tree; PTV = planning target volume.
* Data are shown as median (interquartile range).
† Expressed as mean point dose, maximum point dose, or dose to 4 cc or 5 cc volume of the organ at risk as specified.

Table 4. Chi squared/Fisher's exact test for grade ≥2 radiotherapy toxicities.

	X^2	p Value*
Grade ≥2 airway toxicity		
Endobronchial tumour		0.634
Group A vs. Group B tumour†	1.553	0.229‡
Anticoagulant/Anti-angiogenesis inhibitor use	N/A	0.653
COPD	N/A	0.653
Smoking status	N/A	0.616
Grade ≥2 airway bleeding		
Endobronchial tumour		0.083
Group A vs. Group B tumour†		0.039
Anticoagulant/Anti-angiogenesis inhibitor use		0.276
COPD		0.724
Smoking status		0.192

Abbreviations: COPD = chronic obstructive pulmonary disease; N/A = not applicable.
* Generated with Fisher's exact test, unless otherwise specified.
† Group A tumours are tumours ≤1 cm from the main bronchi and trachea while Group B tumours are all other tumours. See reference 3.
‡ Generated with Chi squared test.

A primary concern in ultra-central lung SBRT is radiation-induced airway bleeding. In our study, grade ≥2 airway bleeding occurred in only five patients (8%), including three fatal haemorrhages, representing 5% of the study population. A possible reason may be our institutional practice of limiting hotspots to 120%, in contrast to the HILUS trial[3] where hotspots of up to 150% were allowed.

Our univariate analysis revealed that grade ≥2 airway toxicity was associated with a higher D_{4cc} of the PBT, and airway bleeding occurred more frequently in group A tumours. This is consistent with findings of prior dosimetric studies[7,8] where the majority of fatal lung haemorrhages were observed in group A tumours, with rates of 70% to 89%.

Our grade 5 toxicity rate of 6% is comparable to previous studies on ultra-central lung SBRT.[6] Among these, two patients had bronchoscopy-proven endobronchial tumour involvement. Although endobronchial tumour location was more common in patients with grade ≥2 airway bleeding the association did not reach statistical significance (p = 0.083) [Table 4]. This parallels findings from Tekatli et al[9] where endobronchial tumours comprised 46% of all SBRT-related grade ≥3 lung haemorrhages.

In our cohort, 10 patients had the PTV overlapping the oesophagus, and grade 3 to 5 events occurred in three of them. Literature focusing specifically on oesophageal toxicity in SBRT is limited, with small sample size. In Wang et al's retrospective study[10] of 88 patients, 23 tumours had the PTV overlapping the oesophagus. Grade ≥3 oesophageal toxicity rate was 13%, including

Table 5. Simple and multivariable Cox regression analyses of predictors for local failure.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Sex	0.585 (0.195-1.760)	0.340		
Age	0.957 (0.917-0.999)	0.047	0.967 (0.917-1.021)	0.228
ECOG PS score (0-1 vs. 2-3)	28.537 (0.82-9909.834)	0.262		
FEV_1	2.612 (1.144-5.962)	0.023	1.909 (0.776-4.694)	0.159
COPD	22.728 (0.003-192866)	0.499		
Smoker	1.561 (0.432-5.643)	0.497		
Endobronchial tumour	0.746 (0.179-3.626)	0.778		
Group A vs. Group B tumour*	0.316 (0.106-0.945)	0.039	0.591 (0.170-2.061)	0.409
% PTV covered by prescription isodose	0.966 (0.916-1.018)	0.198		
GTV	1.001 (0.973-1.030)	0.933		
PTV	0.996 (0.980-1.013)	0.653		

Abbreviations: 95% CI = 95% confidence interval; COPD = chronic obstructive bronchopulmonary disease; ECOG = Eastern Cooperative Oncology Group; FEV_1 = forced expiratory volume in 1 second; GTV = gross tumour volume; HR = hazard ratio; PS = performance status; PTV = planning target volume.

* Group A tumours are tumours ≤1 cm from the main bronchi and trachea while Group B tumours are all other tumours. See reference 3.

Table 6. Simple Cox regression analysis of predictors for overall survival.

	HR (95% CI)	p Value
Sex	1.735 (0.838-3.594)	0.138
Age	0.983 (0.954-1.014)	0.283
ECOG PS score (0-1 vs. 2-3)	1.127 (0.458-2.769)	0.795
FEV_1	1.205 (0.689-2.108)	0.513
COPD	1.482 (0.443-4.958)	0.523
Smoker	1.180 (0.564-2.470)	0.661
Endobronchial tumour	2.485 (0.577-10.701)	0.222
Group A vs. Group B tumour*	1.408 (0.650-3.051)	0.386
PBT D_{mean} †	0.982 (0.954-1.010)	0.203
PBT D_{max} †	1.004 (0.992-1.017)	0.486
PBT D_{4cc} †	0.996 (0.985-1.006)	0.437
Oesophagus D_{mean} †	1.082 (0.987-1.186)	0.092
Oesophagus D_{max} †	0.998 (0.989-1.007)	0.635
Oesophagus D_{5cc} †	0.988 (0.951-1.026)	0.531
% PTV covered by prescription isodose	1.005 (0.940-1.075)	0.875
Anticoagulant/Anti-angiogenesis inhibitor use	1.483 (0.200-10.998)	0.700
GTV	0.996 (0.976-1.016)	0.658
PTV	1.002 (0.991-1.012)	0.770
Lung V_{20Gy} ‡	1.026 (0.925-1.138)	0.626
Non-NSCLC histology	1.357 (0.541-3.407)	0.515

Abbreviations: 95% CI = 95% confidence interval; COPD = chronic obstructive pulmonary disease; ECOG = Eastern Cooperative Oncology Group; FEV_1 = forced expiratory volume in 1 second; GTV = gross tumour volume; HR = hazard ratio; NSCLC = non–small-cell lung cancer; PBT = proximal bronchial tree; PS = performance status; PTV = planning target volume.

* Group A tumours are tumours ≤1 cm from the main bronchi and trachea while Group B tumours are all other tumours. See reference 3.

† Expressed as mean point dose, maximum point dose, or dose to 4 cc or 5 cc volume of the organ at risk as specified.

‡ Percentage of lung receiving a dose ≥20 Gy.

two cases of tracheoesophageal fistulisation.[10] Univariate analysis suggested that shorter distance between the tumour and the oesophagus predicted toxicity and suggested the use of more protracted fractionation.[10]

Our dosimetric analysis revealed that oesophageal D_{max}, D_{5cc}, and D_{mean} were associated with higher rates of grade ≥2 oesophageal toxicity. However, the optimal threshold for oesophageal toxicity remains undefined in the literature. Among the 10 patients whose PTV overlapped the oesophagus, D_{5cc} exceeded the RTOG 0813 constraint of 27.5 Gy in three patients, two of whom had grade ≥3 events. This suggests that strict adherence to a D_{5cc} of <27.5 Gy may help to reduce severe toxicity.

Taken together, our results and the literature suggest that lesions close to/abutting the oesophagus carry a substantial risk of SBRT-related toxicity. Protracted fractionations and avoiding tumours with direct invasion or abutment of the oesophagus would be advisable to reduce severe toxicity. Further data are awaited to define optimal dose constraints and fractionation for these tumours.

Limitations

Our study had several limitations, including its retrospective nature and non-randomised design. Our sample size was also small, and the number of events was too limited for detailed statistical analyses and

elucidation of safe dose constraints for the investigated toxicity endpoints. Our database relied on clinical records documented by treating clinicians rather than a prospective database for research purposes; thus, some toxicities may have been underreported. The lack of autopsy information on the exact cause of death also made it difficult to definitively conclude whether they were truly SBRT-related mortalities.

CONCLUSION

In our study of 66 patients undergoing ultra-central SBRT, long-term follow-up showed sustained high rates of local control and acceptable toxicity outcomes. Caution should be taken when delivering SBRT to group A lesions, and attention should be paid to dosimetric constraints such as the D_{4cc} of the PBT and the D_{5cc} of the oesophagus. Further studies are needed to clarify the optimal dose fractionation and organ at risk constraints to minimise toxicity.

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