Lung Cancer 135 (2019) 97–103

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

# Palliative thoracic radiotherapy near the end of life in lung cancer: A population-based analysis

Ian Fraser[a,b], Shilo Lefresne[a,b], Jacqueline Regan[a], Eric Berthelet[a,b], Negar Chooback[c,d,1], Cheryl Ho[c,d], Robert Olson[a,e,*]

[a] Department of Surgery, Faculty of Medicine, University of British Columbia, 2775 Laurel Street, 11th Floor, Vancouver, British Columbia, V5Z 1M9, Canada
[b] Radiation Therapy Program, BC Cancer – Vancouver, 600 West 10th Avenue, Vancouver, British Columbia, V5Z 4E6, Canada
[c] Medical Oncology Program, BC Cancer – Vancouver, 600 West 10th Avenue, Vancouver, British Columbia, V5Z 4E6, Canada
[d] Department of Medicine, Faculty of Medicine, University of British Columbia, 2775 Laurel Street, 10th Floor, Vancouver, British Columbia, V5Z 1M9, Canada
[e] Radiation Therapy Program, BC Cancer – Prince George (Centre for the North), 1215 Lethbridge Street, Prince George, British Columbia, V2M 7E9, Canada

ARTICLE INFO

*Keywords:*
Palliative
Radiotherapy
Thoracic
Lung cancer
End of life

ABSTRACT

*Objectives:* Palliative thoracic radiotherapy (RT) can improve quality of life for patients with advanced lung cancer, but treatment can be associated with acute toxicity and symptomatic relief may take several weeks. The optimal fractionation schedule is not known. Delivery of RT near the end of life (EOL) is an emerging indicator of poor quality care. The aim of this study was to determine utilization of palliative thoracic RT in the last 4 weeks of life, and factors associated with its use, in patients with incurable lung cancer in a population-based healthcare system.

*Materials and methods:* All patients with lung cancer in British Columbia treated with palliative thoracic RT in 2014 and 2015 were identified. Associations between starting a course of palliative thoracic RT within 4 weeks of death and patient/treatment characteristics were assessed using univariate and multivariate logistic regression analysis.

*Results:* 1676 courses of palliative thoracic RT were delivered to 1584 lung cancer patients. Median survival was 20 weeks. 12% of palliative thoracic RT courses were delivered in the last 4 weeks of life, with short fractionation schedules and simple RT planning techniques used more frequently near EOL. Of RT courses delivered in the last 4 weeks of life 89% were courses of 1 – 5 fractions, 75% were completed as prescribed and 94% involved simple 1–2 field RT techniques. Receipt of RT in the last 4 weeks of life was associated with male gender, younger age, poor performance status, metastatic disease, small cell carcinoma histology and no prior chemotherapy.

*Conclusion:* Further study and standardization of quality indicators for palliative RT utilization near EOL is required. Whilst clarification occurs, physicians should consider the prognosis of patients with incurable lung cancer and the realistic expectation of benefit from palliative thoracic RT when considering treatment indications and fractionation schedules.

## 1. Introduction

Lung cancer is the most common cause of cancer death worldwide [1]. Almost 70% of patients with non-small cell lung cancer (NSCLC) in the United States present with stage III or IV disease [2], and most are not suitable for curative-intent treatment due to comorbidities or disease burden. Prognosis is poor, with a median survival of approximately 4 months in both newly diagnosed stage IV NSCLC [3] and extensive stage small cell lung cancer [4].

Almost all patients with advanced lung cancer experience symptoms, with a negative impact on quality of life [5]. Management is therefore largely focused on symptom control, whilst limiting treatment burden and toxicity. Palliative thoracic radiotherapy (RT) is effective for improving symptoms resulting from locally advanced lung cancer, such as hemoptysis, cough, chest pain and dyspnea, with response rates of 50–80% [6,7]. A variety of different regimens are used for palliative

* Corresponding author at: Division Head of Radiation Oncology, University of British Columbia, 1215 Lethbridge Street, Prince George, BC, V2M 7E9, Canada.
*E-mail address:* Rolson2@bccancer.bc.ca (R. Olson).
[1] Present address: Medical Oncology Program, Kingston Health Sciences Centre, Cancer Centre of Southeastern Ontario at Kingston General Hospital, 25 King Street West, Kingston, Ontario, K7L 5P9, Canada.

https://doi.org/10.1016/j.lungcan.2019.02.024
Received 28 September 2018; Received in revised form 5 February 2019; Accepted 21 February 2019

thoracic RT internationally, ranging from a single fraction on 1 day to 30 or more fractions over at least 6 weeks [6,8]. Longer courses of 10 fractions or more with a higher biologically equivalent dose are associated with a modest improvement in survival, whilst shorter courses of 1–5 fractions are more convenient for patients with equivalent palliation of specific symptoms and less toxicity [6,9–12].

One randomized trial comparing two palliative thoracic RT schedules reported an average time to improvement of overall symptom burden of 5–7 weeks [9], but individual symptoms such as hemoptysis may be palliated more quickly [9,12]. Radiation esophagitis is the most common acute toxicity, peaking at 2–6 weeks depending on the RT schedule [9,12–14]. A population-based study of palliative RT at a single center in the United Kingdom identified a 30 day mortality rate of 14% for palliative RT to the chest for lung cancer [15]. Patients with advanced lung cancer are therefore at risk of dying in a timeframe in which they experience toxicity, but no symptomatic benefit, from palliative thoracic RT, having spent much of their remaining lifespan on treatment.

Aggressive anti-cancer treatment near the end of life (EOL) is an emerging indicator of poor quality care [16–19]. Published quality indicators include receipt of chemotherapy in the last 14 and 30 days of life [16,20], but there is no agreed definition regarding palliative RT in this setting. Most studies reporting utilization rates of palliative RT near EOL have included a heterogeneous mix of primary cancer types and anatomic sites treated [21], but lung cancer patients are consistently identified as receiving the highest rates of palliative RT in the last 14 and 30 days of life [15,22–28]. Studies specifically describing palliative thoracic RT near EOL are limited to single institution series with small numbers of NSCLC patients [29–32]. The purpose of this study was therefore to describe the patterns of palliative thoracic RT utilization in patients with advanced lung cancer in a publicly-funded population-based provincial healthcare system. In particular, we sought to describe the proportion of patients receiving RT to the chest in the last 4 weeks of life and identify factors associated with this, which may help physicians avoid overly aggressive treatment near EOL.

## 2. Materials and methods

### 2.1. Data source and extraction

BC Cancer is comprised of 6 regional cancer centers and is the sole provider of RT for the residents of British Columbia (BC). The BC Cancer Agency Information System was used to retrospectively identify all individuals with lung cancer in BC who received palliative RT to the thorax in 2014 and 2015. The BC Cancer RT database contains RT information including site of RT, date of RT, delivered dose and fractionation [33]. These databases were used to abstract patient, provider and treatment characteristics. Epidermal growth factor receptor (EGFR) mutation status was extracted from a separate departmental database of lung cancer patients receiving tyrosine kinase inhibitor therapy. Chart review was performed for all patients who did not complete a course of RT, to identify the intended dose and fractionation schedule, and for all RT courses with delivered doses of 40 Gy or above, to confirm palliative intent. Each course of RT was considered a separate case for data analysis as each course represents an individual clinical decision with a risk of early death. Therefore, patients who received more than one course of thoracic RT during the study period could be counted more than once. This study was approved by the joint University of British Columbia and BC Cancer Research Ethics Board.

### 2.2. Study population

The study included all patients with a diagnosis of non-small cell or small cell lung cancer who received palliative intent RT to thoracic disease at BC Cancer between 1st January 2014 and 31st December 2015. Patients who received re-irradiation for thoracic disease were included. Patients were identified as receiving prior systemic therapy if they received at least one cycle of systemic therapy at any point before the first fraction of RT. RT technique was divided into 3 categories: 1–2 fields, ≥3 field 3-dimensional conformal RT (3DCRT), and intensity modulated RT (IMRT, including volumetric arc therapy). No patients received stereotactic body radiotherapy (SBRT) with palliative intent for thoracic disease during the study period. RT fractionation was classified into 1, 2–5, 6–10 and > 10 fractions. Patients who received more than one course of RT were considered independently for each course.

**Table 1**
Patient, treatment and provider characteristics.

| | | All courses of palliative thoracic RT (n = 1676) | Courses of palliative thoracic RT delivered in the last 4 weeks of life (n = 203) |
|---|---|---|---|
| Male | | 53% (n = 882) | 65% (n = 131) |
| Age (years) | Median | 71.6 | 70.5 |
| | Range | 37.5 – 97.7 | 37.9 – 94.0 |
| ECOG Performance Status | 0 | 6% (n = 99) | 4% (n = 9) |
| | 1 | 21% (n = 358) | 9% (n = 19) |
| | 2 | 19% (n = 316) | 13% (n = 27) |
| | 3 | 21% (n = 351) | 27% (n = 55) |
| | 4 | 4% (n = 58) | 12% (n = 25) |
| | Unknown | 30% (n = 494) | 34% (n = 68) |
| AJCC Stage | I | 2% (n = 25) | 1% (n = 1) |
| | II | 3% (n = 50) | 1% (n = 3) |
| | III | 26% (n = 442) | 19% (n = 38) |
| | IV | 69% (n = 1159) | 79% (n = 161) |
| Histology | Adenocarcinoma | 42% (n = 700) | 32% (n = 65) |
| | Squamous cell carcinoma | 25% (n = 420) | 27% (n = 54) |
| | NSCLC NOS | 13% (n = 209) | 16% (n = 33) |
| | Small cell carcinoma | 11% (n = 189) | 13% (n = 27) |
| | Other | 9% (n = 158) | 12% (n = 24) |
| Sensitizing EGFR mutation | | 3% (n = 47) | 1% (n = 3) |
| Prior systemic therapy | | 28% (n = 467) | 13% (n = 26) |
| BC Cancer center | Abbotsford | 7% (n = 123) | 9% (n = 19) |
| | Kelowna | 20% (n = 337) | 21% (n = 43) |
| | Prince George | 6% (n = 103) | 6% (n = 12) |
| | Surrey | 17% (n = 285) | 15% (n = 31) |
| | Vancouver | 27% (n = 454) | 21% (n = 43) |
| | Victoria | 22% (n = 374) | 27% (n = 55) |
| Number of fractions prescribed | 1 | 16% (n = 273) | 29% (n = 58) |
| | 2-5 | 54% (n = 908) | 60% (n = 121) |
| | 6-10 | 22% (n = 362) | 7% (n = 15) |
| | > 10 | 8% (n = 133) | 4% (n = 9) |
| Completed prescribed course of RT | | 95% (n = 1584) | 75% (n = 152) |
| RT technique | 1-2 fields | 80% (n = 1333) | 94% (n = 190) |
| | ≥3 fields conformal | 12% (n = 202) | 4% (n = 8) |
| | IMRT | 8% (n = 141) | 2% (n = 5) |

Abbreviations: RTradiotherapy; ECOGEastern Cooperative Oncology Group; AJCCAmerican Joint Committee on Cancer; NSCLC NOSnon-small cell lung cancer not otherwise specified; EGFRepidermal growth factor receptor; IMRTintensity modulated radiotherapy.

### 2.3. Statistical analysis

Descriptive statistics were used to present patient and provider characteristics for all courses of RT, and courses of RT commenced within 4 weeks of death. Patient, tumor and treatment factors included age, gender, Eastern Cooperative Oncology Group (ECOG) performance status, cancer center where RT was delivered, treating physician, stage of disease at start of RT, histology of the primary disease, presence of

**Table 2**
Univariate and multivariable logistic regression analysis of palliative thoracic RT utilization in last 4 weeks of life.

| | | Univariate analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|---|
| Characteristic | | Odds ratio of receiving palliative RT in the last 4 weeks of life (> 1 favors RT in last 4 weeks of life) | 95% Confidence Interval | p value | Odds ratio of receiving palliative RT in the last 4 weeks of life (> 1 favors RT in last 4 weeks of life) | 95% Confidence Interval | p value |
| Patient gender | Female (n = 794) | Reference | | | Reference | | |
| | Male (n = 882) | 1.75 | 1.28-2.37 | < 0.001 | 1.78 | 1.29-2.48 | 0.001 |
| Age of patient (continuous) | | 0.99 | 0.98-1.01 | 0.34 | 0.98 | 0.96-0.99 | 0.009 |
| ECOG Performance status | 0 (n = 99) | Reference | | | Reference | | |
| | 1 (n = 358) | 0.56 | 0.25-1.28 | 0.17 | 0.56 | 0.24-1.32 | 0.18 |
| | 2 (n = 316) | 0.93 | 0.42-2.06 | 0.87 | 0.79 | 0.35-1.79 | 0.57 |
| | 3 (n = 351) | 1.86 | 0.88-3.91 | 0.10 | 1.27 | 0.58-2.78 | 0.55 |
| | 4 (n = 58) | 7.58 | 3.21-17.90 | < 0.001 | 4.25 | 1.70-10.63 | 0.002 |
| | Unknown (n = 494) | 1.60 | 0.77-3.32 | 0.21 | 1.21 | 0.56-2.61 | 0.62 |
| AJCC Stage | I-III (n = 517) | Reference | | | Reference | | |
| | IV (n = 1159) | 1.82 | 1.28-2.61 | 0.001 | 1.84 | 1.23-2.74 | 0.003 |
| Histology | Adenocarcinoma (n = 700) | Reference | | | Reference | | |
| | Squamous cell carcinoma (n = 420) | 1.44 | 0.98-2.11 | 0.06 | 1.50 | 0.98-2.28 | 0.06 |
| | NSCLC NOS (n = 209) | 1.83 | 1.17-2.88 | 0.01 | 1.56 | 0.96-2.53 | 0.07 |
| | Small cell carcinoma (n = 189) | 1.63 | 1.01-2.63 | 0.047 | 2.48 | 1.43-4.32 | 0.001 |
| | Other (n = 158) | 1.75 | 1.06-2.90 | 0.03 | 1.49 | 0.86-2.58 | 0.16 |
| Sensitizing EGFR mutation | Yes (n = 47) | Reference | | | Reference | | |
| | No (n = 1629) | 2.05 | 0.63-6.68 | 0.23 | 0.85 | 0.24-2.99 | 0.81 |
| Prior systemic therapy | Yes (n = 467) | Reference | | | Reference | | |
| | No (n = 1629) | 2.91 | 1.90-4.46 | < 0.001 | 3.04 | 1.84-4.99 | < 0.001 |
| BC Cancer center | Vancouver (n = 454) | Reference | | | Reference | | |
| | Abbotsford (n = 123) | 1.75 | 0.98-3.12 | 0.06 | 1.38 | 0.72-2.64 | 0.33 |
| | Kelowna (n = 337) | 1.40 | 0.89-2.19 | 0.14 | 1.31 | 0.79-2.16 | 0.30 |
| | Prince George (n = 103) | 1.26 | 0.64-2.49 | 0.50 | 1.11 | 0.53-2.32 | 0.79 |
| | Surrey (n = 285) | 1.17 | 0.72-1.90 | 0.54 | 1.02 | 0.60-1.73 | 0.96 |
| | Victoria (n = 374) | 1.65 | 1.08-2.52 | 0.02 | 1.00 | 0.60-1.68 | 0.99 |
| Number of fractions prescribed | 1 (n = 273) | Reference | | | Reference | | |
| | 2-5 (n = 908) | 0.57 | 0.40-0.81 | 0.002 | 0.66 | 0.43-1.00 | 0.05 |
| | 6-10 (n = 362) | 0.16 | 0.09-0.29 | < 0.001 | 0.25 | 0.13-0.49 | < 0.001 |
| | > 10 (n = 133) | 0.27 | 0.13-0.56 | < 0.001 | 1.16 | 0.38-3.55 | 0.80 |
| RT technique | 1-2 fields (n = 1333) | Reference | | | Reference | | |
| | ≥3 fields conformal (n = 202) | 0.25 | 0.12-0.51 | < 0.001 | 0.30 | 0.12-0.76 | 0.01 |
| | IMRT (n = 141) | 0.22 | 0.09-0.55 | 0.001 | 0.29 | 0.09-0.98 | 0.04 |

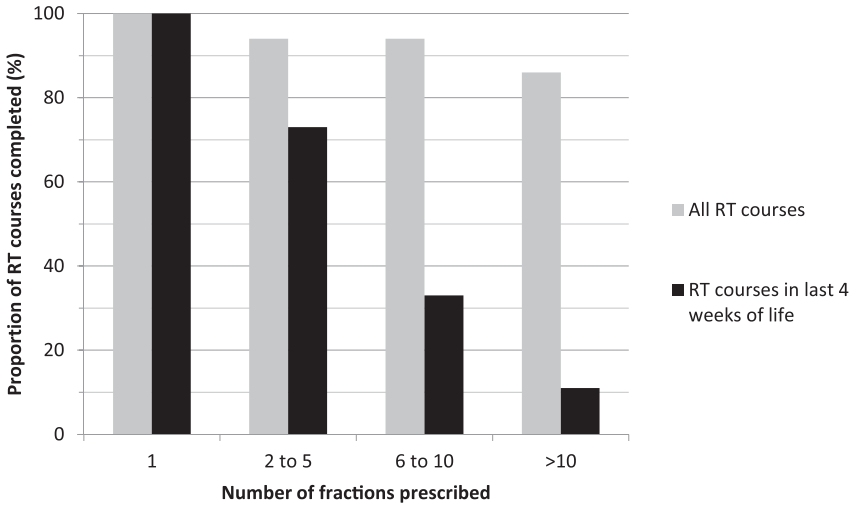
Abbreviations: RT = radiotherapy; ECOG = Eastern Cooperative Oncology Group; AJCC = American Joint Committee on Cancer; NSCLC NOS = non-small cell lung cancer not otherwise specified; EGFR = epidermal growth factor receptor; IMRT = intensity modulated radiotherapy.

sensitizing EGFR mutation, whether systemic therapy was delivered prior to RT, whether the prescribed course of RT was completed, dose and fractionation of RT (both prescribed and delivered) and RT technique. Time to death was calculated from the first day of RT for each course. Associations between starting a course of RT within 4 weeks of death and patient/treatment characteristics were analyzed using univariate and multivariable logistic regression analysis. P values were two-sided, and values less than 0.05 were considered statistically significant. Analyses were conducted using SPSS version 14.0 software (Chicago, IL).

## 3. Results

1676 courses of palliative thoracic RT were delivered to 1584 patients by 38 radiation oncologists in 2014 and 2015. Of the 1676 RT courses delivered, 1584 were the first course of palliative thoracic RT for a patient during the study period, 88 were second courses and four were third courses. The median number of RT courses prescribed by an individual radiation oncologist was 33 (range 5–114). Table 1 summarizes the baseline patient, treatment and provider characteristics. The median number of fractions delivered was 5 (range 1–30) and the median total dose delivered was 20 Gy (range 2–66 Gy). The most commonly prescribed regimes were 20 Gy in 5 fractions (46%), 30 Gy in 10 fractions (17%) and 8 Gy in 1 fraction (13%). Median survival for the entire cohort was 20 weeks from the start of RT, with 1 year survival of 18% and 2 year survival of 3%. Of the 1676 courses of palliative RT, 203 (12%) were delivered to patients in the last 4 weeks of life.

The characteristics associated with receipt of palliative RT in the last 4 weeks of life by univariate and multivariate analysis are presented in Table 2. All of the significant associations found on univariate analysis persist on multivariate analysis. Receipt of RT in the last 4 weeks of life was statistically associated with male gender, younger age (on multivariate analysis only), poor performance status (ECOG 4), metastatic disease, small cell carcinoma histology and no prior systemic therapy. Delivery of RT in the last 4 weeks of life was less common when 2–5 or 6–10 fractions were prescribed, in comparison to 1 fraction, and when the RT technique involved ≥3 fields or IMRT, in comparison to 1–2 fields. Receipt of RT in the last 4 weeks of life was not associated with the cancer center where treatment was delivered. However, for the 38 individual radiation oncologists who prescribed treatment during the study period, the proportion of all of the palliative thoracic RT courses they prescribed which were in the last 4 weeks of life ranged from 0 to 60%.




| | All RT courses | | | | Courses of RT delivered in the last 4 weeks of life | | | |
|---|---|---|---|---|---|---|---|---|
| Number of fractions prescribed | 1 | 2 to 5 | 6 to 10 | >10 | 1 | 2 to 5 | 6 to 10 | >10 |
| Completed courses | 273 | 856 | 340 | 115 | 58 | 88 | 5 | 1 |
| Total courses | 273 | 908 | 362 | 133 | 58 | 121 | 15 | 9 |
| % completed | 100% | 94% | 94% | 86% | 100% | 73% | 33% | 11% |

**Fig. 1.** Proportion of all palliative thoracic radiotherapy (RT) courses and RT courses starting in the last 4 weeks of life which were completed, in relation to number of fractions prescribed.

## 4. Discussion

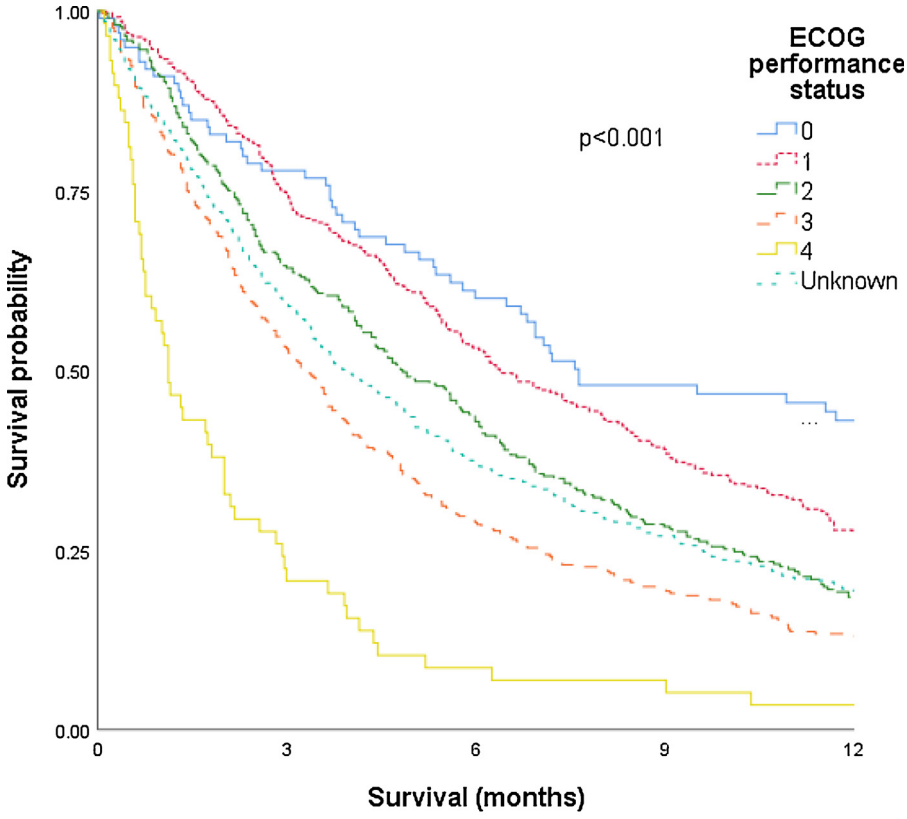
This large, population-based study found that 12% of palliative thoracic RT courses were delivered in the last 4 weeks of life. Receipt of RT in the last 4 weeks of life was associated with male gender, younger age, poor performance status (ECOG 4), metastatic disease, small cell carcinoma histology and no prior systemic therapy. Short fractionation regimes and simple RT planning techniques were appropriately used more commonly near EOL.

Previous studies have reported death within 30 days or 4 weeks of palliative thoracic RT of 8–42% [15,29–32], with variation in study cohorts and whether survival was measured from the start or end of RT course. Our finding of 12% of palliative thoracic RT courses being delivered in the last 4 weeks of life is consistent with the two studies with similar methodology to our own, which reported 30 day mortality from the start of RT of 14% [15] and 16% [29]. The median survival of our cohort is similar to that reported in retrospective unselected series of patients receiving palliative thoracic RT [29,34–37].

American Society for Radiation Oncology (ASTRO) clinical practice guidelines recommend palliative thoracic RT schedules using 1–5 fractions for patients with poor performance status or those requesting a shorter treatment course, and 30 Gy in 10 fraction equivalent or greater in patients with good performance status [38]. Despite these recommendations, recent population-based studies of patients with metastatic NSCLC receiving palliative thoracic RT in the United States report only 10% of patients receiving 1–5 fractions [8] and 70% receiving more than 10 fractions [39]. By comparison, 1–5 fractions were prescribed for 70% of RT courses in our study, and more than 10 fractions in only 8%. Short fractionation regimes were prescribed more commonly near EOL, with 89% of RT courses in the last 4 weeks of life involving 5 fractions or less. The frequent use of short fractionation regimes is likely to contribute to the high proportion of RT courses which were completed as prescribed. Ninety five per cent of all RT courses were completed, compared to completion rates of 71–95% published in the literature [29,30,36,40]. Of the 203 courses of RT delivered in the last 4 weeks of life, 75% were completed as prescribed, with 100% of 1 fraction, but only 11% of > 10 fraction courses in this group being completed (Fig. 1). There is strong evidence for the use of short palliative thoracic RT regimes, such as 10 Gy in 1 fraction and 16–17 Gy in 2 fractions, with the benefit of more protracted schedules generally limited to patients with better performance status or without metastatic disease [6,9–13]. Increased use of these short regimes in patients with limited life expectancy could further improve the proportion of patients completing treatment and reduce the burden of treatment near EOL.

More complex RT planning techniques, involving 3DCRT with 3 or more fields or IMRT, were used relatively infrequently in our study, and in only 6% of RT courses delivered in the last 4 weeks of life. Planning studies have demonstrated dosimetric benefits with IMRT in the radical and palliative setting [41,42], with use of IMRT for locally advanced lung cancer rapidly increasing despite a lack of prospective evidence [43]. A randomized phase 3 study of Palliative Radiation of Advanced Central lung Tumors with Intentional avoidance of the Esophagus (PROACTIVE) is currently accruing patients with the aim of assessing the clinical benefit of IMRT in this setting [44]. Should esophageal-sparing IMRT be shown to decrease acute toxicity, increasing the complexity of palliative thoracic RT planning could be an area for improvement in BC for appropriately selected patients. However, given the resources required for IMRT planning, a cost-benefit analysis would be wise, particularly for single fraction treatments.

Poor performance status, male gender and lung cancer have consistently been associated with palliative RT near EOL [15,23,24,26,27,45–47], with poor performance status and the number of organs involved with metastases associated with palliative thoracic RT near EOL [30,48]. In addition to poor performance status, male gender and presence of metastatic disease, our study reports associations with younger age, small cell histology and no prior chemotherapy. Higher rates of chemotherapy and RT near EOL amongst younger cancer patients have previously been described [22], which may be due to an inclination for physicians to be optimistic about prognosis and




| | Number at risk | | |
|---|---|---|---|
| ECOG | 0 months | 6 months | 12 months |
| 0 | 99 | 55 | 35 |
| 1 | 358 | 183 | 83 |
| 2 | 316 | 130 | 52 |
| 3 | 351 | 99 | 41 |
| 4 | 58 | 5 | 2 |
| Unknown | 494 | 174 | 84 |

**Fig. 2.** Survival from the start of palliative thoracic radiotherapy in relation to Eastern Cooperative Oncology Group (ECOG) performance status. Median survival was 7.6 months, 6.4 months, 4.8 months, 3.4 months, 1.1 months and 3.9 months for ECOG 0, 1, 2, 3, 4 and unknown respectively ($p < 0.001$).

recommend more aggressive treatment or younger patients' wishes. The other associations are likely to be a reflection of the poor prognosis of these groups. Poor performance status was most strongly associated with receipt of RT near EOL, with 43% of ECOG performance status 4 patients dying within 4 weeks of starting RT and a median survival of only 5 weeks in this group (Fig. 2). This is similar to the findings of a Polish study of 235 patients with advanced NSCLC, moderate/severe chest symptoms and Karnofsky performance status less than 50 which reported a median survival of 8 weeks and 42% of patients dying within 30 days of RT [32]. Although this was a non-randomized trial, there was no difference in survival or symptom control between patients who opted to receive palliative thoracic RT or supportive care alone, but RT was poorly tolerated with high rates of nausea, vomiting and esophagitis. Therefore, in patients with very poor performance status and advanced lung cancer, best supportive care may be more appropriate than palliative thoracic RT.

There was variation in the proportion of RT courses delivered in the last 4 weeks of life by treating radiation oncologist (range 0–60%). Caution should be exercised when interpreting this analysis given the small sample size, but 32 of the 38 radiation oncologists delivered between 0% and 20% of their palliative thoracic RT courses in the last 4 weeks of life. This may represent an acceptable range in clinical practice given the challenges with prognostication in this patient group. Although this was not testable within the current study design the variation may be due to differences in decision-making and aggressiveness of treatment near EOL amongst individual physicians, as well as differences in referral patterns. A potential area for further research will be to assess whether providing physicians with feedback on the proportion of RT courses they prescribe near EOL in comparison to their peers may change practice. Open discussion of cases where death has occurred within 4 weeks of palliative RT in the forum of a morbidity and mortality meeting may be helpful in this regard. Similarly, in the era of increasing peer review for quality assurance, the inclusion of all palliative RT plans in this process (currently not done in BC) may also lead to a change in practice if choice of fractionation and decision to treat are discussed.

The current study should be interpreted in the context of its strengths and limitations. Our study only included patients who received at least one fraction of palliative RT, so we do not have information on patients who refused treatment, died before starting RT, or were not offered RT because of a predicted short life expectancy. Given the retrospective nature of the study, we were not able to explore physicians' or patients' beliefs in relation to treatment decisions near EOL, efficacy of symptom control or toxicity. In addition, we were not able to assess associations between receipt of RT near EOL and all variables which are included in existing prognostic models for patients

receiving palliative thoracic RT, such as nodal stage, presence of liver or adrenal metastases, elevated C-reactive protein or lactase dehydrogenase and presence of progressive extrathoracic disease [34,37]. However, the large sample size provided sufficient power to detect differences amongst factors associated with RT near EOL, and as a population-based study it is relatively free from referral and selection bias. An interesting topic for further study would be exploring the indication for treatment in this cohort. For example, determining if certain symptoms (e.g. dyspnea, hemoptysis) or clinical presentations (e.g. superior vena cava obstruction) are associated with death within four weeks of RT would be clinically valuable. Additionally, this information could be meaningful in discussing the appropriateness and utility of RT near EOL according to various clinical scenarios.

## 5. Conclusions

This population-based study found that 12% of palliative thoracic RT courses for lung cancer were delivered in the last 4 weeks of life, with use of short fractionation schedules and simple RT planning techniques more common near EOL. RT in the last 4 weeks of life was most frequent amongst patients with poor performance status (ECOG 4), male gender, younger age, metastatic disease, small cell carcinoma histology and no prior chemotherapy. Consideration of these factors, coupled with communication of realistic expectations of prognosis and benefits of palliative thoracic RT, may help to decrease the use of inappropriate or prolonged treatment schedules near EOL. Further study and standardization of quality indicators for palliative RT near EOL is required. Whilst further clarification in this area occurs, physicians should be aware of the poor prognosis of many lung cancer patients referred for palliative thoracic RT when making treatment decisions.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Conflict of interest

There are no conflicts of interest to declare.

## References

[1] M.C.S. Wong, X.Q. Lao, K. Ho, W.B. Goggins, S.L.A. Tse, Incidence and mortality of lung cancer: global trends and association with socioeconomic status, Sci. Rep. 7 (2017) 1.
[2] D. Morgensztern, S.H. Ng, F. Gao, R. Govindan, Trends in stage distribution for patients with non-small cell lung cancer: a national cancer database survey, J. Thorac. Oncol. 5 (2010) 29–33.
[3] J.J. Ko, R. Tudor, H. Li, et al., Reasons for lack of referral to medical oncology for systemic therapy in stage IV non-small-cell lung cancer: comparison of 2003-2006 with 2010-2011, Curr. Oncol. (Toronto, Ont.) 24 (2017) e486.
[4] A. Khakwani, A.L. Rich, L.J. Tata, et al., Small-cell lung Cancer in England: trends in survival and chemotherapy using the national lung cancer audit, PLoS One 9 (2014) e89426.
[5] S. Iyer, A. Roughley, A. Rider, G. Taylor-Stokes, The symptom burden of non-small cell lung cancer in the USA: a real-world cross-sectional study, Support. Care Cancer 22 (2014) 181–187.
[6] A. Fairchild, K. Harris, E. Barnes, et al., Palliative thoracic radiotherapy for lung Cancer: a systematic review, J. Clin. Oncol. 26 (2008) 4001–4011.
[7] S. Lefresne, R. Olson, R. Cashman, et al., Prospective analysis of patient reported symptoms and quality of life in patients with incurable lung cancer treated in a rapid access clinic, Lung Cancer 112 (2017) 35–40.
[8] A.B. Chen, A. Cronin, J.C. Weeks, et al., Palliative radiation therapy practice in patients with metastatic non–small-cell lung cancer: a cancer care outcomes research and surveillance consortium (CanCORS) study, J. Clin. Oncol. 31 (2013) 558–564.
[9] G.W.P.M. Kramer, S.L. Wanders, E.M. Noordijk, et al., Results of the Dutch National study of the palliative effect of irradiation using two different treatment schemes for non-small-cell lung cancer, J. Clin. Oncol. 23 (2005) 2962–2970.
[10] S.C. Erridge, M.N. Gaze, A. Price, et al., Symptom control and quality of life in people with lung cancer: a randomised trial of two palliative radiotherapy fractionation schedules, Clin. Oncol. 17 (2005) 61–67.
[11] A. Bezjak, P. Dixon, M. Brundage, et al., Randomized phase III trial of single versus fractionated thoracic radiation in the palliation of patients with lung cancer (NCIC CTG SC.15), Int. J. Radiat. Oncol. Biol. Phys. 54 (2002) 719–728.
[12] F.R. Macbeth, J.J. Bolger, P. Hopwood, et al., Randomized trial of palliative two-fraction versus more intensive 13-fraction radiotherapy for patients with inoperable non-small cell lung cancer and good performance status. Medical Research Council Lung Cancer Working Party, Clin. Oncol. (R. Coll. Radiol.) 8 (1996) 167–175.
[13] S. Sundstrøm, R. Bremnes, U. Aasebø, 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. 22 (2004) 801–810.
[14] U. Nestle, C. Nieder, K. Walter, et al., A palliative accelerated irradiation regimen for advanced non–small-cell lung cancer vs. conventionally fractionated 60 GY: results of a randomized equivalence study, Int. J. Radiat. Oncol. Biol. Phys. 48 (2000) 95–103.
[15] K. Spencer, E. Morris, E. Dugdale, A. Newsham, D. Sebag-Montefiore, R. Turner, G. Hall, A. Crellin, 30 day mortality in adult palliative radiotherapy – a retrospective population based study of 14,972 treatment episodes, Radiother. Oncol. 115 (2015) 264–271.
[16] C.C. Earle, M.B. Landrum, J.M. Souza, B.A. Neville, J.C. Weeks, J.Z. Ayanian, Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? J. Clin. Oncol. 26 (2008) 3860–3866.
[17] A.D. Falchook, S.B. Dusetzina, F. Tian, R. Basak, N. Selvam, R.C. Chen, Aggressive end-of-life care for metastatic cancer patients younger than age 65 years, J. Natl. Cancer Inst. 109 (2017).
[18] M. Toole, S. Lutz, P.A.S. Johnstone, Radiation oncology quality: aggressiveness of Cancer care near the end of life, J. Am. Coll. Radiol. 9 (2012) 199–202.
[19] J.A. Jones, S.T. Lutz, E. Chow, P.A. Johnstone, Palliative radiotherapy at the end of life: a critical review, CA Cancer J. Clin. 64 (2014) 295–310.
[20] M. Wallington, E.B. Saxon, M. Bomb, et al., 30-day mortality after systemic anticancer treatment for breast and lung cancer in England:a population-based, observational study, Lancet Oncol. 17 (2016) 1203–1216.
[21] K.R. Park, C.G. Lee, Y.D. Tseng, et al., Palliative radiation therapy in the last 30 days of life: a systematic review, Radiother. Oncol. 125 (2017) 193–199.
[22] P. Grendarova, A. Sinnarajah, T. Trotter, C. Card, J. Wu, Variations in intensity of end-of-life cancer therapy by cancer type at a Canadian tertiary cancer centre between 2003 and 2010, Support. Care Cancer 23 (2015) 3059–3067.
[23] B.A. Guadagnolo, K.P. Liao, L. Elting, S. Giordano, T.A. Buchholz, Y.T. Shih, Use of radiation therapy in the last 30 days of life among a large population-based cohort of elderly patients in the United States, J. Clin. Oncol. 31 (2013) 80–87.
[24] K. Angelo, J. Norum, A. Dalhaug, et al., Development and validation of a model predicting short survival (death within 30 days) after palliative radiotherapy, Anticancer Res. 34 (2014) 877.
[25] L.K. Rautakorpi, J.M. Mäkelä, F. Seyednasrollah, et al., Assessing the utilization of radiotherapy near end of life at a Finnish University Hospital: a retrospective cohort study, Acta Oncol. (Stockholm, Sweden) 56 (2017) 1265–1271.
[26] M. Anshushaug, M.A. Gynnild, S. Kaasa, A. Kvikstad, B.H. Grønberg, Characterization of patients receiving palliative chemo- and radiotherapy during end of life at a regional cancer center in Norway, Acta Oncol. 54 (2015) 395–402.
[27] J.D. Murphy, L.M. Nelson, D.T. Chang, L.K. Mell, Q. Le, Patterns of care in palliative radiotherapy: a population-based study, J. Oncol. Pract. 9 (2013) e227.
[28] J. Huang, E.S. Wai, F. Lau, P.A. Blood, Palliative radiotherapy utilization for cancer patients at end of life in British Columbia: retrospective cohort study, BMC Palliat. Care 13 (2014) 49.
[29] M. Støchkel Frank, D. Schou Nørøxe, L. Nygård, G. Fredberg Persson, Fractionated palliative thoracic radiotherapy in non-small cell lung cancer - futile or worthwhile? BMC Palliat. Care 17 (2018) 15.
[30] B. van Oorschot, B. Assenbrunner, M. Schuler, G. Beckmann, M. Flentje, Survival and prognostic factors after moderately hypofractionated palliative thoracic radiotherapy for non-small cell lung cancer, Strahlenther. Onkol. 190 (2014) 270–275.
[31] C. Nieder, R. Yobuta, B. Mannsåker, A. Dalhaug, How should palliative thoracic radiotherapy be fractionated for octogenarians with lung cancer? In vivo (Athens, Greece) 32 (2018) 331.
[32] Tomasz Walasek, Beata Sas-Korczyńska, Tomasz Dąbrowski, Marian Reinfuss, Jerzy Jakubowicz, Paweł Blecharz, Elżbieta Łuczyńska, Zbigniew Darasz, Piotr Skotnicki, Palliative thoracic radiotherapy for patients with advanced non-small cell lung cancer and poor performance status, Lung Cancer 87 (2014) 130–135.
[33] S.M. Jackson, S. Tyldesley, B. Baerg, I.A. Olivotto, Are the creation and maintenance of databases in healthcare worthwhile? An example of a unique, population-based, radiation therapy database, Healthc. Q. 15 (2012) 71–77.
[34] D. Rades, L. Käsman, S.E. Schild, S. Janssen, A survival score for patients receiving palliative irradiation for locally advanced lung cancer, Clin. Lung Cancer 17 (2016) 558–562.
[35] C. Schröder, M. Ivo, A. Buchali, Does high-dose radiotherapy benefit palliative lung cancer patients? Strahlenther. Onkol. 189 (2013) 771–776.
[36] C. Nieder, T. Tollali, R. Yobuta, A. Reigstad, L.R. Flatoy, A. Pawinski, Palliative thoracic radiotherapy for lung cancer: what is the impact of total radiation dose on survival? J. Clin. Med. Res. 9 (2017) 482–487.
[37] C. Nieder, T. Tollåli, E. Haukland, A. Reigstad, L. Randi Flatøy, A. Dalhaug, A four-tiered prognostic score for patients receiving palliative thoracic radiotherapy for lung cancer, Cancer Invest. 36 (2018) 59–65.
[38] G. Rodrigues, G.M.M. Videtic, R. Sur, et al., Palliative thoracic radiotherapy in lung cancer: an American Society for Radiation Oncology evidence-based clinical practice guideline, Pract. Radiat. Oncol. 1 (2011) 60–71.
[39] M. Koshy, R. Malik, U. Mahmood, Z. Husain, R.R. Weichselbaum, D.J. Sher,

Prevalence and predictors of inappropriate delivery of palliative thoracic radiotherapy for metastatic lung Cancer, J. Natl. Cancer Inst. 107 (2015) djv278.
[40] S. Janssen, L. Kaesmann, S.E. Schild, D. Rades, Impact of the radiation dose and completion of palliative radiotherapy on survival in patients treated for locally advanced lung cancer, Anticancer Res. 36 (2016) 1825.
[41] S. Baker, M. Dahele, F.J. Lagerwaard, S. Senan, A critical review of recent developments in radiotherapy for non-small cell lung cancer, Radiat. Oncol. (London, England) 11 (2016) 115.
[42] P.V. Granton, D.A. Palma, A.V. Louie, Intentional avoidance of the esophagus using intensity modulated radiation therapy to reduce dysphagia after palliative thoracic radiation, Radiat. Oncol. (London, England) 12 (2017) 27.
[43] S.M. Shirvani, J. Jiang, D.R. Gomez, J.Y. Chang, T.A. Buchholz, B.D. Smith, Intensity modulated radiotherapy for stage III non-small cell lung cancer in the United States: predictors of use and association with toxicities, Lung Cancer 82 (2013) 252–259.
[44] A Randomized Phase III Study of Palliative Radiation of Advanced Central Tumors With Intentional Avoidance of the Esophagus (PROACTIVE), (2018) Accessed at www.clinicaltrials.gov on August 20.
[45] S. Gripp, S. Mjartan, E. Boelke, R. Willers, Palliative radiotherapy tailored to life expectancy in end-stage cancer patients: reality or myth? Cancer 116 (2010) 3251–3256.
[46] S.G. Ellsworth, S.R. Alcorn, R.K. Hales, T.R. McNutt, T.L. DeWeese, T.J. Smith, Patterns of care among patients receiving radiation therapy for bone metastases at a large academic institution, Int. J. Radiat. Oncol. Biol. Phys. (2014).
[47] C. Nieder, K. Angelo, A. Dalhaug, A. Pawinski, E. Haukland, J. Norum, Palliative radiotherapy during the last month of life: predictability for referring physicians and radiation oncologists, Oncol. Lett. 10 (2015) 3043–3049.
[48] C. Nieder, E. Haukland, B. Mannsåker, A. Pawinski, A. Dalhaug, Early palliative radiation therapy in patients with newly diagnosed cancer: reasons, clinical practice, and survival, Pract. Radiat. Oncol. 5 (2015) e542.