

(ILD) experience a high-risk of treatment-related morbidity and mortality after any pulmonary radiotherapy. The purpose of this study is to systematically review existing literature on SABR-related mortality and ILD-specific toxicity for patients with co-existing ES-NSCLC and ILD.

**Methods and Materials:** The MEDLINE and Embase databases were queried from their respective dates of inception to January 21, 2016. A total of 3101 records were reviewed. Studies involving advanced stage NSCLC, non-SABR radiotherapy technique, guidelines, reviews, meta-analyses, correspondences, or pediatric populations were excluded. SABR-related mortality was defined as any death secondary to radiation pneumonitis or deaths determined to be directly related to radiation therapy by individual study investigators. Treatment-related ILD-specific toxicity was defined as Grade  $\geq 3$  radiation pneumonitis following SABR. Data on treatment-related mortality and ILD-specific toxicity for surgical studies were also extracted for reference. Mortality and morbidity results were summarized with weighted means.

**Results:** A total of 13 SABR studies published between 2003 and 2015 were included in this systematic review. Ten studies were retrospective in design, with the others being a mixed retrospective/prospective observational study, a Phase I clinical trial and a case report. A total of 122 patients were included in the reports, with most studies including medically inoperable patients. Weighted mean for treatment-related mortality was 15.6% after SABR in patients with co-existing ES-NSCLC and ILD. Treatment-related ILD-specific toxicity occurred in 25.9% of SABR patients. An additional 28 surgical studies were reviewed, which included a total of 1681 patients. From 1999 to 2015, medically operable patients with co-existing ES-NSCLC and ILD who underwent surgery experienced treatment-related mortality of 2.0% and ILD-specific toxicity of 11.7%.

**Conclusions:** A high incidence of treatment-related mortality (16%) and ILD-specific toxicity (26%) was observed after SABR for patients with co-existing ES-NSCLC and ILD. Many SABR patients were medically inoperable, preventing direct comparisons with surgical outcomes. Patients should be cautioned about this increased risk of toxicity. Future studies should aim to establish a specific diagnosis of the type and severity of ILD prior to the treatment of any patient with ES-NSCLC and co-existing pulmonary comorbidity.

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SARCOPENIA IS ASSOCIATED WITH WORSE OVERALL SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

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**Purpose:** Sarcopenia, a depletion of a skeletal muscle with or without loss of fat mass, has been studied as a prognostic factor in several cancers. It has been shown to be associated with poorer survival and worse post-operative outcomes independent of patients' body weight. However, it has not been used in routine clinical evaluation nor has its prognostic significance in lung cancer been evaluated. This study examined the value of sarcopenia as a prognostic factor in patients with locally advanced non-small cell lung cancers treated with radical radiation and chemotherapy.

**Methods and Materials:** This study included all patients with Stage III non-small cell lung cancer treated with radical radiation and chemotherapy at a regional cancer centre using the Glans Look database between 2006 and 2012. Body composition analysis of planning or pre-treatment diagnostic CT scans was performed using Eclipse (Varian, Palo Alto, CA) per a previously validated and reported technique. Total skeletal muscle area was calculated on a single axial abdominal CT slice at the level of L3 vertebral body and adjusted for stature. Patients were classified as sarcopenic or nonsarcopenic using validated sex-specific cut-offs of L3 skeletal muscle index ( $52.4 \text{ cm}^2/\text{m}^2$  for

males and  $38.5 \text{ cm}^2/\text{m}^2$  for females). Kaplan-Meier survival estimates and Cox proportional-hazard models were used to determine the impact of sarcopenia on overall survival.

**Results:** A total of 106 patients (53% males, 47% females), with mean age 65 years (SD = 8.7) were analyzed. Mean BMI was  $26.3 \text{ kg}/\text{m}^2$  (SD =  $6.7 \text{ kg}/\text{m}^2$ ). Only one patient was underweight (BMI < 18.5), 40% patients had normal weight and 60% of patients were either overweight or obese. Overall, 38.7% patients were sarcopenic. The prevalence of sarcopenia was 56% among patients with normal weight and 27% among overweight or obese patients. Sarcopenia was identified as an independent predictor of overall survival on multivariate analysis (hazard ratio 1.71; 95% CI 1.09 - 2.72,  $p = 0.019$ ). Other significant predictors for worse overall survival included age over 65 years and absence of concurrent chemotherapy. Median survival in sarcopenic patients was 21 months (95% CI 13 - 28 months) compared with 31 months (95% CI 20 - 39 months) in nonsarcopenic patients.

**Conclusions:** Sarcopenia is independently associated with inferior survival in patients with locally advanced non-small cell lung cancers treated with chemoradiotherapy. It can be routinely assessed in clinical practice using radiation planning software. Sarcopenia as independent predictor for survival and toxicity outcomes should be included in larger prospective clinical studies.

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THE MANAGEMENT OF SMALL CELL LUNG CANCER WITH RADIOTHERAPY - A PAN-CANADIAN SURVEY OF RADIATION ONCOLOGISTS

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**Purpose:** The management of small cell lung cancer (SCLC) with radiotherapy (RT) is variable, with many treatment regimens described in the literature. We created a survey to assess patterns of practice and clinical decision making in the management of SCLC by Canadian radiation oncologists (ROs).

**Methods and Materials:** A 35-item survey was e-mailed to Canadian ROs. Questions investigated the role of RT, dose/timing of RT, target delineation, and use of prophylactic cranial irradiation (PCI) in limited stage (LS) and extensive stage (ES) SCLC.

**Results:** Fifty-two eligible ROs responded. For LS-SCLC, staging (98%) and simulation/dosimetric (96%) CT imaging were key determinants of RT suitability. The two most common dose/fractionation schedules were 40-45 Gy/15 once daily (QD) (40%) and 45 Gy/30 twice daily (33%). Elective nodal irradiation was performed by 31% of ROs. Preferred management of clinical T1/2aN0 SCLC favored primary chemoradiotherapy (64%). For ES-SCLC, consolidative thoracic RT was frequently offered (88%), with a preferred dose/fractionation of 30 Gy/10 QD (70%). Twenty-three ROs (44%) would not offer extrathoracic consolidative RT. After response to initial treatment, PCI was generally offered in both LS- (100%) and ES- (98%) SCLC. Performance status, baseline cognition, and pre-PCI brain imaging were important clinical factors assessed prior to offering PCI.

**Conclusions:** There are both variations and alignment in practice in the management of SCLC by Canadian ROs. Future clinical trials and national treatment guidelines may reduce variability in treating early-stage disease, optimizing dose/targeting in LS-SCLC, and defining suitability for both PCI and consolidative RT.

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PROPHYLACTIC CRANIAL IRRADIATION: DOES AGE MATTER?

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**Purpose:** Prophylactic cranial irradiation (PCI) has been shown to provide a survival benefit and decrease occurrence of brain metastases in patients with small cell lung cancer (SCLC).

Detriment to cognitive function is suggested by some studies, but whether this risk changes based on age is unknown. The purpose of this project was to determine patterns of practice of PCI for both limited stage SCLC (LS-SCLC) and extensive stage SCLC (ES-SCLC) across Canada with a focus on how age affects recommendations in clinical practice.

**Methods and Materials:** A survey was created in English and French. It was approved and distributed through Canadian Association of Radiation Oncology (CARO) to all its radiation oncologist members. Answers were collected anonymously using Google Forms over a five week period. Descriptive statistics were used to analyze responses.

**Results:** Fifty-seven responses were collected with representation from all CARO regions. Ninety-eight percent of respondents routinely would recommend PCI for LS-SCLC and 78% for ES-SCLC. For LS-SCLC, age was an independent factor for recommending PCI for 52% of respondents, and 65% used an age cut off of 80 - 84 years. For ES-SCLC, only 46% of respondents would consider age when recommending PCI, and 48% of those also used 80 - 84 years as the cut off. 85% justified this cut point based on poor patient outcome in their own or a colleague's experience. Forty-two percent of respondents who didn't use an age cut off indicated that a patient's performance status was a more relevant criterion.

**Conclusions:** Based on the consensus opinion from this survey, we would suggest PCI for SCLC should be offered to patients with acceptable performance status under 80 years of age. For patients 80 years and older, caution is recommended.

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PHASE I STUDY OF CISPLATIN/DOCETAXEL CHEMOTHERAPY WITH CONCURRENT THORACIC RADIOTHERAPY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

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**Purpose:** The current standard of care for unresectable locally advanced Stage III non-small cell lung cancer (NSCLC) is chemoradiotherapy. However, there is no established consensus for the optimal chemotherapy regimen. We designed a Phase I study of docetaxel and cisplatin (DC) chemotherapy with concurrent thoracic radiotherapy (RT) followed by consolidative DC for locally advanced NSCLC. The primary objective of this study is to determine optimal concurrent and consolidative DC doses, with secondary objectives to describe associated toxicities.

**Methods and Materials:** Patients with histologically or cytologically proven and unresectable Stage IIIA or IIIB (dry) NSCLC were eligible for this single-institution research-ethics board approved study. In the concurrent cycles with thoracic RT, C was given every three weeks (fixed at 75mg/m<sup>2</sup>) and D given weekly. The starting dose of D was 20 mg/m<sup>2</sup> weekly escalated in cohorts of three to define the maximum tolerated dose. RT was prescribed to a dose of 60 Gy in 30 fractions. This was followed by two cycles of consolidative DC, which were dose escalated if concurrent chemoradiotherapy was tolerated. Evaluation for dose limiting toxicities was performed on a weekly basis during RT. Tumour response was characterized through the RECIST criteria. Actuarial outcomes of overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan-Meier analysis.

**Results:** Between September 2004 to June 2014, 26 patients were enrolled. One patient did not receive protocol-specified treatment due to metastatic disease on baseline imaging. Of the eligible patients, 18 had Stage IIIA and seven had Stage IIIB disease. The median OS all patients was 33.6 months (95% CI 15.8-71.6). Median PFS was 17.0 months (95% CI 9.2-26.3) with median follow up of 26.6 months (range 0.43 -110.8). The majority of patients (19/26) completed both phases of treatment

and most received concurrent D at 20mg/m<sup>2</sup> weekly. Eight patients tolerated dose escalation of posterior consolidative C or D. Twelve patients experienced Grade 3 toxicities (five esophagitis, one pneumonitis, three nausea, one leukopenia, and two neutropenia). Three patients had Grade 4 neutropenia. No patients died due to early or late treatment toxicities. Complete response, partial response, and stable disease were observed in one, 16 and four patients, respectively. Five patients underwent surgical resection, and three of five did not have evidence of residual disease.

**Conclusions:** Cisplatin and docetaxel (DC) chemotherapy with concurrent radiation treatment followed by consolidative DC achieved promising results in the treatment of Stage III NSCLC in light of reported outcomes from RTOG 0617 (standard arm median PFS 11.8, OS 28.7 months). However, treatment toxicities should be considered. The dose finding results of this study will inform the design of Phase II/III trials.

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TREATMENT OF LOCALLY ADVANCED/RECURRENT CUTANEOUS SQUAMOUS CELL CARCINOMA WITH CETUXIMAB AND CONCURRENT RADIOTHERAPY

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**Purpose:** Cutaneous squamous cell carcinoma (cuSCC) accounts for approximately 30% of all skin cancers and is one of the most common cancers in North America. The standard treatment for locally advanced cuSCC is surgery followed by adjuvant radiotherapy (RT). Patients presenting with locally advanced or recurrent disease are often elderly or immunosuppressed, and may be medically inoperable or technically unresectable. These patients are traditionally treated with radiotherapy alone since adding concurrent chemotherapy may not be well tolerated by this group. The risk of locoregional recurrence is about 40% for RT alone, compared to 15% in those treated by surgery and RT. Cetuximab is an antagonistic monoclonal chimeric IgG1 antibody that binds to the epidermal growth factor receptor (EGFR). EGFR overexpression in cuSCC varies between 43-100% of patients. Small, single institutional studies have retrospectively reported synergistic activity when combining Cetuximab and RT (CRT) for the treatment of metastatic or unresectable cuSCC. In preparation for a larger Phase II study, this project prospectively identified patients with unresectable cuSCC who were candidates for CRT.

**Methods and Materials:** Three patients have been treated with CRT in the last 18 months. Data regarding patient outcome and tolerability was collected prospectively. Cetuximab was delivered weekly, with the first dose timed as a loading dose (400 mg/m<sup>2</sup>) seven days prior to the initiation of radiotherapy. Concurrent with radiation, weekly doses of cetuximab were administered at a dose of 250 mg/m<sup>2</sup>. Radiation doses varied between patients (5500 cGy/22#, n = 1, and 6600 cGy/30#, n = 2).

**Results:** The median age in our cohort was 85 years. All were male patients, with Karnofsky performance scores  $\geq$  60. Two patients were treated for primary SCC (T3N0M0 and T3N1M0) while the third patient was treated for recurrent disease. Notably, one patient presented with Waldenstrom's macroglobulinemia. Treatment was well tolerated, and felt to be comparable to treatment with RT alone. One patient developed a Grade 2 acneiform skin reaction likely related to cetuximab. One patient developed an acute coronary syndrome (Grade 3), most likely unrelated to therapy. Two patients had a complete response to treatment. The first patient is in remission for 18 months and the second patient is in remission for 12 months. The third patient completed CRT two months ago and is waiting for reassessment.

**Conclusions:** Despite the frailty of our cohort, CRT was well tolerated and produced exceptional clinical outcomes. Limitations to this study include its small sample size and non-randomization. This study will serve as the basis for a larger, prospective, randomized Phase II study which is now in