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A prospective analysis of high-dose-rate endobronchial brachytherapy in the palliation of obstructive symptoms in lung cancer patients: A single-institution experience

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ABSTRACT

PURPOSE: Obstructive symptoms that affect quality of life (QOL) are commonly caused by endobronchial disease in many patients with locally advanced, inoperable lung cancer. High-dose-rate endobronchial brachytherapy (HDREBBT) has been used to palliate these symptoms, yet its role is not well defined in the literature.

METHODS AND MATERIALS: Ninety-eight patients with locally advanced, inoperable lung cancer received HDREBBT. They were prospectively followed for survival, QOL, and toxicity endpoints. QOL measures were captured using the Quality of Life Questionnaire−Lung Cancer 30 and −Lung Cancer 13.

RESULTS: At 1-year follow-up, no significant toxicities were seen. Overall survival was 13.4% at 12 months (mean 192 days). Performance status, additional treatment after HDREBBT and treatment intent affected overall survival on univariate analysis ($p < 0.05$). Mean hemoptysis-free survival for all patients was 232.3 days, cough-free survival was 140.3 days, and dyspnea-free survival was 173.5 days. There was no impact of any treatment- or patient-related factors of these outcomes on multivariate analysis, including additional treatment modalities and HDREBBT dose.

CONCLUSIONS: HDREBBT is a safe and effective way to palliate endobronchial symptoms. Additional external-beam radiation therapy, chemotherapy, or chemoradiation after HDREBBT improves survival, but does not affect QOL measures.

Key words: Lung cancer; Brachytherapy; High dose rate; External radiation; Palliation; Symptom-free survival

Introduction

Lung cancer is one of the most common cancers in Canada. It remains the most common cause of cancer death for both sexes (1). Minimal gains in survival rates have been made over the past few decades, with 5-year survival remaining less than 20% (1). Thirty to 40% of patients are inoperable or have metastatic disease at diagnosis (2). In patients who undergo curative resection, 50% develop recurrent disease within 5 years (2). Patients who undergo radical management with concurrent chemoradiotherapy (CRT) relapse within the irradiated field more than 55% of the time (3). Half of patients with lung cancer will ultimately develop symptomatic endobronchial involvement due to their disease (4). These patients present with typical obstructive symptoms of cough, dyspnea, hemoptysis, and postobstructive pneumonitis that affect quality of life (QOL). Previous irradiation could preclude the opportunity for palliative external-beam radiation therapy (EBRT) due to dose constraints of nearby organs at risk.

Alternative interventions for obstructive symptoms include laser photocoagulation, cryotherapy, photodynamic therapy, stenting, low-dose-rate brachytherapy, and high-dose-rate endobronchial brachytherapy (HDREBBT). A randomized study to compare these modalities closed early due to failure to accrue patients (5).

HDREBBT is an ideal approach given the ability to deliver potentially tumoricidal doses in few fractions with short treatment times and low dose to organs at risk. Although HDREBBT has been in practice since the

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1920s (6), advances in technology such as the flexible fiberoptic bronchoscope and remote HDR afterloading have made it safer, faster, and more effective. However, mainstream use of this technique is limited to specially trained radiation oncologists, access to a shielded brachytherapy suite, and appropriate multidisciplinary resources. Moreover, the optimal role for HDREBBT in radical or palliative settings is not well defined in the literature.

At the Juravinski Cancer Centre in Hamilton, Ontario, the HDREBBT program was initiated in 2005. Since that time, more than 600 patients have been treated in the definitive or palliative setting. Between 2005 and 2006, eligible patients undergoing HDREBBT were prospectively followed for QOL measures and survival endpoints. This report represents a prospective analysis of 98 patients with at least 1-year follow-up.

Materials and methods

Inoperable patients with endobronchial disease on bronchoscopy or imaging and obstructive symptoms were eligible for HDREBBT. Patients were followed every 3 months, or earlier if indicated. QOL data were assessed at baseline and at follow-up visits using the Quality of Life Questionnaire−Lung Cancer 30 and −Lung Cancer 13 (7, 8). Treatment toxicity was assessed by the radiation oncologist during follow-up. Bronchoscopies were not performed to assess response unless specifically indicated by patient symptoms. All patients were followed for at least 1 year with institutional review board approval.

Patients were premedicated with topical Xylocaine and sedated with intravenous fentanyl and midazolam. Flexible fiberoptic bronchoscopy was undertaken orally or at times nasally by a respirologist to visualize the tumor. Flexible plastic catheters were inserted into the bronchi adjacent to and beyond the tumor under bronchoscopic and fluoroscopic vision. The number of catheters used varied depending on tumor size and location with the intent of encompassing the entire intraluminal visualized tumor and optimizing dose distribution. The bronchoscope was subsequently withdrawn, leaving only the catheter in situ. A marker wire with a centimeter scale was inserted into the catheter for precise treatment delineation under fluoroscopic vision. Fluoroscopy was used and orthogonal films were taken to image and confirm catheter placement, as well as to delineate the target volume. The plans were created in real-time using the BrachyVision Treatment Planning system (Varian, Palo Alto, CA, USA). A usual dose of 7 Gy (range 5−10 Gy) was prescribed to 1 cm from the source axis for tumors in the mainstem bronchus or 0.5 cm from the source axis for tumors in segmental bronchi. The VariSource (Varian, USA) HDR afterloader was used to place an Iridium-192 source at 0.5-cm dwell positions. The patient's cardiorespiratory status was closely monitored throughout. After the treatment, the catheter (or catheters) was removed and the patient was monitored in a recovery room for approximately 1 hour before discharge. Brachytherapy dose and fractionation was determined based on American Brachytherapy Society Recommendations. Treatment parameters used, including dose and fractionation, are described in Table 1. Multiple fractions were scheduled at 1-week, and less often 2-week, intervals. Brachytherapy was not given concurrently with EBRT or chemotherapy. Patients undergoing subsequent chemotherapy treatments were given a 2-week break between modalities.

Survival, QOL, and toxicity data were collected in a prospective fashion over the follow-up period. Survival was defined as time from first consultation to death. Specific symptom-free survival was defined as time from first brachytherapy insertion to symptom return or progression. Statistical analysis of the data was done using the SAS Statistics software (SAS Institute, Cary, NC). Kaplan-Meier curves were compared using the log-rank test. Multivariate and univariate analyses were done using the Cox proportional hazards model. Ethics approval for the study was obtained from the Hamilton Integrated Research Ethics Board.

Results

The mean age was 69 years (range 47−89 years). Most patients had poor performance statuses with comorbidities, such as smoking, coronary artery disease, congestive heart failure, and chronic obstructive pulmonary disease. Baseline patient characteristics are described in Table 2. Presenting symptoms are presented in Table 3.

Most patients (78%) were treated for newly diagnosed disease, whereas 22% of patients had disease recurrence.

Table 1
High-dose-rate endobronchial brachytherapy treatment parameters

	Treatment parameter	N
Catheters used per patient	1	33
	2	49
	3	14
	4	2
Total dose given, Gy	5	1
	7	12
	10	1
	14	44
	15	1
	18	2
	21	36
	28	1
Dose per fraction, Gy	5	1
	6	2
	7	93
	7.5	1
	10	1
Number of fractions used	1	14
	2	45
	3	38
	4	1