



## Evidence-based Series 7-16 version 2 - IN REVIEW

A Quality Initiative of the  
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

### The Role of High Dose Rate Brachytherapy in the Palliation of Symptoms in Patients with Non-Small Cell Lung Cancer

*Y Ung, E Yu, C Falkson, A Haynes, WK Evans, and the Lung Cancer Disease Site Group*

An assessment conducted in December 2016 placed Evidence-based Series (EBS) 7-16 version 2 IN REVIEW. This means that it is undergoing review for currency and relevance. The Lung Cancer Disease Site Group has determined that it is still appropriate for this document to continue to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document.

[\(PEBC Assessment & Review Protocol\)](#)

EBS 7-16 Version 2 reviewed EBS report, which is available on the [CCO website](#), consists of the following four sections:

- Section 1: Clinical Practice Guideline (ENDORSED)
- Section 2: Systematic Review
- Section 3: Guideline Development and External Review
- Section 4: Guideline Review Summary and Tool

**Release Date: May 16, 2013**

For information about this document, the PEBC and/or the most current version of all reports, please visit the CCO Web site at <http://www.cancercares.on.ca/> or contact the PEBC office at:

Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: [ccopgi@mcmaster.ca](mailto:ccopgi@mcmaster.ca)

**PEBC Report Citation (Vancouver Style):** Ung Y, Yu E, Falkson C, Haynes A, Evans WK; Lung Cancer Disease Site Group. The role of high dose rate brachytherapy in the palliation of symptoms in patients with non-small cell lung cancer. Toronto (ON): Cancer Care Ontario; [ENDORSED 2013 Sep. In review 2016 Dec]. Program in Evidence-based Care Evidence-based Series No.: 7-16 version 2. IN REVIEW

**Journal Citation (Vancouver Style):** Ung YC, Yu E, Falkson C, Haynes AE, Stys-Norman D, Evans WK, et al. The role of high-dose-rate brachytherapy in the palliation of symptoms in patients with non-small cell lung cancer: a systematic review. *Brachytherapy*. 2006;5(3):189-202.

IN REVIEW

## Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES AND KEY CHANGES
	Search Dates	Data		
Original version October 2005	1966 - 2005	Full Report	Web publication	NA
Version 2 May 2013	2005-2012	New data found in section 4: <a href="#">Document Review Tool</a>	Updated Web publication	2005 recommendations are <a href="#">ENDORSED</a>

## Table of Contents

Section 1: Clinical Practice Guideline .....	1
Section 2: Evidentiary Base .....	5
Section 3: Guideline Development and External Review .....	35
Section 4: Document Review and Summary Tool .....	44

Evidence-based Series #7-16: Section 1

**The Role of High Dose Rate Brachytherapy in the Palliation of  
Symptoms in Patients with Non-Small Cell Lung Cancer:  
A Clinical Practice Guideline**

*Y Ung, E Yu, C Falkson, A Haynes, WK Evans, and the Lung Cancer Disease Site Group*

A Quality Initiative of the  
Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)

These guideline recommendations have been **ENDORSED**, which means that the recommendations are still current and relevant for decision making. Please see [Section 4: Document Review Summary and Tool](#) for a summary of updated evidence published between 2002 and 2012, and for details on how this Clinical Practice Guideline was **ENDORSED**.

Report Date: May 16, 2013

**Guideline Question**

1. Is there a role for high dose rate endobronchial brachytherapy (HDREB) in the palliation of respiratory symptoms in patients with non-small cell lung cancer?
2. If so, what is the optimal dose of HDREB in this setting?

**Target Population**

The recommendations apply to adult patients with symptomatic endobronchial disease in non-small cell lung cancer.

**Recommendations**

- For patients with previously untreated, symptomatic, endobronchial non-small cell lung cancer:
  - External beam radiation therapy (EBRT) alone is more effective for palliation than HDREB alone.
  - The evidence does not provide conclusive results to suggest that HDREB and EBRT would provide improved symptom relief over EBRT alone.
  - For patients with complete collapse of the lung due to endobronchial obstruction, a surgical core out procedure may be needed before EBRT or EBRT with HDREB

- For patients previously treated by EBRT who are symptomatic with endobronchial obstruction due to recurrent disease, HDREB is recommended, providing that endobronchial brachytherapy is technically feasible.
- 

### Qualifying Statements

- This guideline addresses only the use of HDREB for the palliation of symptomatic endobronchial disease and not its use as a radical or adjuvant treatment.
- The occurrence of fatal hemoptysis because of HDREB is a significant risk with that therapy, and occurrence rates as high as 32% of patients have been reported. However, the majority of studies report rates between 4% and 18% of patients.
- Improvement of hemoptysis as a result of HDREB ranges from 19% to 100% of patients, with most studies reporting rates of 69% and higher.
- HDREB should be provided by a team of experts that includes radiation oncologists, thoracic surgeons (or physicians with expertise in bronchoscopy), and medical physicists.
- HDREB is only possible if afterloading catheters can be inserted bronchoscopically. Patients with complete endobronchial obstruction are not suitable for HDREB.
- Treatment alternatives to HDREB include EBRT (if not previously irradiated), Nd-YAG laser therapy, photodynamic therapy (PDT), and surgical core-out procedure.
- The optimal dose and fractionation for HDREB for the palliation of symptoms of airway obstruction has not yet been determined. However, commonly used doses include 1000 cGy at 1cm in a single fraction or 750 cGy at 1cm in one or two fractions.
- HDREB may be effectively combined with other endobronchial treatment modalities such as neodymium-yttrium-aluminum-garnet (Nd-YAG) laser therapy.

### Key Evidence

- A total of six small randomized trials were identified. One trial compared EBR with HDREB, each as primary palliative treatments. Three studies randomized patients to either EBR alone or EBR with HDREB, one trial randomized patients to Nd-YAG laser therapy with or without HDREB, and one trial compared two different schedules of HDREB. Sample sizes ranged from 29 and 108 patients.
- One randomized trial compared two different doses and schedules of HDREB (four fractions of 3.8 Gy administered weekly versus two fractions of 7.2 Gy administered every 3 weeks) and obtained similar response rates (36% versus 37%), survival (median, 4.2 versus 4.4 months; one-year, 11% versus 20%), and rates of fatal hemoptysis (22% versus 21%), respectively.
- One randomized trial involving 99 previously untreated patients obtained better overall palliation with EBRT alone compared with HDREB alone (physician preference ratings for EBRT,  $p=0.09$ ; patient preference ratings for EBRT,  $p=0.029$ ). The incidence of fatal hemoptysis was comparable in both groups (6% to 8%). Although survival was not a specified endpoint of that study, a significant survival advantage for EBRT alone over HDREB alone ( $p=0.04$ ) was found (median, 9.4 versus 8.2 months, one-year, 38% versus 22%).
- One randomized trial evaluated HDREB in combination with EBRT to EBRT alone using biologically equivalent doses for both arms. Symptom control for cough was better in patients who were treated with EBRT alone compared to HDREB and EBRT, and survival at one year was the same in each group.
- Two trials obtained comparable median survival (6.2 versus 6.5 months and 7.0 versus 8.5 months) and incidence of fatal hemoptysis (14% versus 20% and 13% versus 15%) for

patients treated with EBRT alone or EBRT with HDREB. Combined treatment improved mean dyspnea scores over time ( $p=0.02$ ) and atelectasis improved for a significantly greater proportion of patients with prior atelectasis in the combined group (57% versus 35%,  $p=0.009$ ), although individual symptom scale scores were comparable for both treatments. The other trial reported a tendency toward improved local control with combined therapy ( $p=0.052$ ), but symptom control was not evaluated.

- Median survival (7.4 versus 10.3 months) and incidence of fatal hemoptysis (0 versus 1 patient) were similar for Nd-YAG laser therapy alone or combined with HDREB. The symptom-free period was significantly longer with the combined treatment (8.5 versus 2.8 months,  $p<0.05$ ), although toxicity and symptom palliation were not reported by treatment group.
- Eighteen non-comparative prospective studies evaluated HDREB in doses ranging from 4 Gy at 2 cm from the source axis twice daily over two days to a single fraction of 20 Gy at 1cm from the source axis. Response rates varied between 20% and 98%, median survival between three and 28 months, and one-year survival between 7% and 78%. Hemoptysis improved for most patients, although fatal hemoptysis occurred in between 4% and 32% of patients.
- Five retrospective studies, involving more than 100 patients, reviewed the role of HDREB alone or in combination with EBRT. Treatment intent varied from palliation to radical, using single dose or fractionated treatments. Symptom improvement ranged from 74% to 94%. The risk of fatal hemoptysis ranged from 3.6% to 8%.

### Treatment Alternatives

High dose rate endobronchial brachytherapy can only be given when there is an adequate lumen to allow for insertion of the treatment catheter. If there is complete endobronchial obstruction, then initial therapy could include other treatment modalities such as surgical core out, endobronchial stent for more proximal tumours, Nd-YAG laser therapy, or PDT. Those modalities of therapy could then be followed by HDREB.

### Future Research

Future research on the role of HDREB should focus on two objectives:

1. Defining the optimal dose and fractionation as well as defining the physical aspects of radiation delivery (e.g., dose prescription, optimal length, and the effects of catheter curvature on dose).
2. Evaluating the role of combination therapies (e.g., Nd-YAG laser therapy and PDT).

### Related Evidence Summary

- Evidence Summary Report #7-15: *The Role of Photodynamic Therapy (PDT) in Patients with Non-small Cell Lung Cancer.*

#### *Funding*

The PEBC is supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from its funding agencies.

#### *Copyright*

This guideline is copyrighted by Cancer Care Ontario; the guideline and the illustrations herein may not be reproduced without the express written permission of Cancer Care Ontario. Cancer Care Ontario reserves the right at any time, and at its sole discretion, to change or revoke this authorization.

*Disclaimer*

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

*Contact Information*

For further information about this practice guideline report, please contact  
**Dr. William K. Evans**, Co-Chair, Lung Cancer Disease Site Group, McMaster University and Juravinski  
Cancer Centre, 699 Concession Street, Hamilton ON L8V 5C2;  
TEL (905) 387-9711 ext. 63001; FAX (905) 575-6323

or

**Dr. Yee C. Ung**, Co-Chair, Lung Cancer Disease Site Group, Toronto-Sunnybrook Regional Cancer  
Centre, 2075 Bayview Avenue, Toronto, ON, M4N 3M5;  
TEL (416) 480-4951; FAX (416) 480-6002.

For information about the PEBC and the most current version of all reports,  
please visit the CCO website at <http://www.cancercare.on.ca/>

or contact the PEBC office at:

Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: [ccopgi@mcmaster.ca](mailto:ccopgi@mcmaster.ca)