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Estimating the benefit and cost of radiotherapy for lung cancer

Lisa Barbera
Toronto Sunnybrook Regional Cancer Centre

Hugh Walker
Queen's University Cancer Research Institute

Farshad Foroudi
The Peter MacCallum Cancer Centre

Scott Tyldesley
British Columbia Cancer Agency

William Mackillop
Queen's University Cancer Research Institute

Purpose: To estimate the benefit and cost of using radiotherapy (RT) in the initial management of lung cancer in the general population.
Methods: We identified indications for RT in the initial management of small cell and non–small cell lung cancer through a review of the literature. The proportion of patients with each specific indication for treatment was determined using epidemiological observations from cancer registry data and from the literature. We estimated the benefit gained from RT use for each indication in the model using values published in the literature. We estimated the cost of RT for each indication using published Canadian data. The total benefit and cost was calculated for all indications combined. Results are reported in 2001 Canadian dollars.
Results: The mean benefit was 7 months of survival for each lung cancer patient treated with curative intent and 3 months of symptom control for each patient treated with palliative intent. The average cost was $9,881 per life year gained and $13,938 per year of symptom control gained. Sensitivity analysis revealed values between $7,905 and $19,762 per year of survival gain and between $10,368 and $27,875 per year of symptom control gained.
Conclusions: Using RT in the initial management of lung cancer can provide considerable gains in survival and symptom control. The cost of RT for the initial management of lung cancer is inexpensive compared with a common cut off of $50,000 per life year gained.

Keywords: Radiotherapy, Lung neoplasms, Costs and cost analysis

There is great concern about escalating health care costs (10). Therefore, there is increasing effort directed at measuring the cost-effectiveness of medical treatments (16). Most studies report the incremental benefit of a new intervention for the incremental cost in the setting of a clinical trial. Studies that report cost and benefit at the level of a population are much less common.

Cancer is the third most common cause of death worldwide. Lung cancer is the most common malignancy and has the highest mortality of all cancers (27). Radiotherapy (RT) plays an important role in the management of both small cell

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lung cancer (SCLC) and non-small cell lung cancer (NSCLC) (1;4;17;29;38).

We previously have estimated the need for radiotherapy (RT) in a population of lung cancer patients using an evidence-based, epidemiological approach (42). This approach requires two steps. The first step is to use clinical guidelines to identify all possible indications for delivering RT. The "level of the evidence" supporting each indication is described (34). For example, large randomized trials are given a higher rank than case series because of the superiority of study design. The proportion of patients in a population who are eligible for each of the indications is then estimated using epidemiological observations. The quality of these observations can be described using a standardized ranking system. Higher ranks are given to sources that are more generalizable to the population as a whole. In this case, registry data were given a higher ranking over clinical trial data or single institution case series data. Sources with the highest available rank were chosen for use in the model. These values can be combined to produce an estimate of the total proportion of the population that will require RT.

The purpose of this study is to estimate the benefit and cost of using RT in the initial management of a population of lung cancer patients. To accomplish this, the scope of the model is widened. Information about the indications for RT and the proportion of patients with each indication is taken from the model. This information is combined with estimates of the benefit and cost of RT from the literature.

METHODS

Estimating Benefit

For the purposes of this study, only RT used as part of initial management was considered in the calculations. The indications were taken from the original study (42). The literature was searched for estimates of the benefit of using RT in each of the indications. In general, estimates of benefit were taken from randomized trials or meta-analyses. If these were not available, retrospective institutional series were used. In the absence of any such data a "best guess" estimate of benefit was made.

Benefit was expressed in its natural units: (i) months of survival gained from curative RT, and (ii) months of symptom control gained from palliative RT.

The benefit of using RT in each indication was only counted once; therefore, while there may be symptomatic benefit from using curative RT, if there is a survival benefit, this was the only benefit measured. Because survival is the goal of curative RT, improvements in symptom control tend not to be measured and, therefore, are underestimated. For palliative RT, symptom control is the usual goal, so this was the benefit measured. Survival benefit was quantified as an improvement in median survival. Symptom control benefit was quantified by using the proportion of patients who respond to treatment and the average duration of their response. We chose to express benefit in natural units rather than quality adjusted life years (QALYs). Reasons for this strategy are presented in the discussion section. For NSCLC, RT is also used adjuvantly. Adjuvant RT after surgery is known to improve local control only, not survival (31). For the purposes of the model, local control was considered equivalent to symptom control.

Estimating Cost

The literature was searched for studies reporting the cost of RT. We specifically sought a study that was Canadian, recent, and that reported the planning and delivery costs separately. This latter point allowed the marginal cost of additional fractions to be reflected properly (22).

Assumptions about dose/fractionation were as follows: the SCLC portion of the model assumed fifteen fractions for curative thoracic RT, ten fractions for prophylactic cranial irradiation, and five fractions for palliative indications; the NSCLC portion of the model assumed that thirty fractions were used for curative indications, twenty-five fractions for adjuvant indications, fifteen fractions for high-dose palliative chest RT, and five fractions for all other palliative indications. The survival in lung cancer is generally quite short; therefore, no attempts were made to discount costs or benefits.

Sensitivity Analysis

A one-way sensitivity analysis was performed around the estimates of benefit and cost.

RESULTS

Estimates of Benefit

All estimates of benefit are summarized in Table 1. In some cases, data from randomized trials or meta-analyses was available (2;5;28;30;39;41). In other cases crude (7) or modeled (35) single institution data were used.

For the survival improvement in locally advanced NSCLC, a "best guess" was made because of a lack of data. There are many trials demonstrating that the addition of chemotherapy to RT improves survival in locally advanced NSCLC (6;12;24;26;32;37). But the use of RT for lung cancer has developed historically, and there are no good descriptions of what the RT adds in this treatment combination. The estimate of survival from the Radiation Therapy Oncology Group (RTOG) trial in the RT alone arm was 11.4 months (this study was the largest trial of those listed). The survival of similar patients without any RT was difficult to quantify. Studies done over 30 years ago had placebo or watchful waiting arms, but they used outdated RT, had different investigations for staging, and reported very few details about the patient characteristics (14;33). For these reasons, an arbitrary assessment was made that the median survival of untreated locally advanced stage III lung cancer patients with good

Table 1. List of Indications and the Expected Type and Amount of Benefit Gained

Indications for RT for SCLC	Number patients	Benefit per patient (source)	Cost per patient ($)	Cost/LYG ($)	Cost/SCYG ($)
Thoracic RT for LS SCLC	255	2.3 mo survival gain (30)	3,943	20,571	
Prophylactic Cranial Irradiation for LS SCLC	255	2.2 mo survival gain (2)	2,516	19,179	
Prophylactic Cranial Irradiation for ES SCLC	53	2.2 mo survival gain (2)	3,516	1,9179	
Palliative Whole Brain RT for ES SCLC	33	39% CR lasting 10 mo (7)	3,090		9,506
alternative value		*34% lasting 5 mo*			
Indications for RT for NSCLC					
Stage I surgery positive margin, adjuvant RT	11	4.8 mo local control gain (39)	4,796		11,991
Stage I curative RT	293	14.1 mo survival gained (35)	5,223	4,445	
alternative value		*minimum 10 mo, maximum 16.3 mo*			
Stage II surgery positive margin, adjuvant RT	2	4.8 mo local control gain (39)	4,796		11,991
Stage II surgery no MLND, adjuvant RT	50	4.8 mo local control gain (39)	4,796		11,991
Stage II curative RT	25	14.1 mo survival gained (35)	5,223	4,445	
alternative value		*minimum 10 mo, maximum 16.3 mo*			
pT1-4 N2-3 negative margin, adjuvant RT	105	4.8 mo local control gain (39)	4,796		11,991
pT1-4 N2-3 positive margin, adjuvant RT	64	4.8 mo local control gain (39)	4,796		11,991
pT3 N0-1 positive margin, adjuvant RT	3	4.8 mo local control gain (39)	4,796		11,991
Stage III curative RT	758	5.4 mo survival gain (24)	5,223	11,606	
Stage III palliative RT	87	2.6 mo survival gain (35)	3,943	18,199	
alternative value		*minimum 1 mo, maximum 3.5 mo*			
Stage IV palliative RT	553	chest 56% improve lasting 91 d (28)	3,090		17,320
alternative value		bone 91% minimal relief lasting 7 mo (41)			
		57% CR lasting 3.8 mo			
		brain 68% RR lasting 10 wks (5)			

Note: The number of patients with each indication is based on a cohort of 5,000 pathologically confirmed lung cancer patients. Values in italics indicate alternatives used in the sensitivity analysis.
CR: complete response; ES, extensive stage; LS, limited stage; LYG, life year gained; MLND mediastinal lymph node dissection; NSCLC, non–small cell lung cancer; RT; radiotherapy, SCLC, small cell lung cancer; SCYG, symptom control year gained.

performance status and no weight loss was approximately 6 months. This finding would mean the benefit gained from RT is 5.4 months.

Estimating Cost

The study that was chosen provides relatively current data in a Canadian (Ontario) setting and did provide separate measures of planning and RT delivery (13). It takes the perspective of a radiation treatment program. It includes direct labor, direct material, general administrative overhead, treatment machine overhead, office and fixed overhead, and maintenance/quality control overhead. All planning and treatment delivery is accounted for. Continuing care is accounted for. Central administrative costs such as finance and human resources are not taken into account.

The selected study reports that the assessment, planning, and follow-up costs are $2,466 in 1997 Canadian dollars. The cost of delivering each daily fraction is $79. We have used the health consumer price index to inflate the costs to 2002 dollars (CPI 1.08) (9).

There were other sources of Canadian RT cost data. One is over 14 years old (43). Two other studies modeling the cost of treating lung cancer rely on these data (18;19). Another study was conducted in a different province with data collected many years ago (11). Another Canadian (Ontario) study was more recent but did not allow the cost of delivering a fraction of RT to be separated into assessment, planning, and delivery processes (15).

Model Results

Table 1 (final 3 columns) indicates the cost/patient and the cost/benefit for each indication. The average cost per patient

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Table 2. Estimate of Benefit per Patient Using Radiotherpay for SCLC and NSCLC

	SCLC		NSCLC		All lung cancer	
	Average survival gain (months)	Average duration SC gain (months)	Average survival gain (months)	Average duration SC gain (months)	Average survival gain (months)	Average duration SC gain (months)
Measured per incident case	1.7	0.2	2.1	0.5	2.0	0.5
Measured per treated case	4.1	3.9	7.6	2.9	7.1	3.1

NSCLC, non–small cell lung cancer; SC, symptom control; SCLC, small cell lung cancer.

Table 3. Results of sensitivity analysis

	SCLC		NSCLC		All Lung Cancer	
Changes	Cost/LYG ($)	Cost/SCYG ($)	Cost/LYG ($)	Cost/SCYG ($)	Cost/LYG ($)	Cost/SCYG ($)
Model	19,826	9,506	8,126	14,720	9,881	13,938
Different RR bone metastasis NSCLC				17,990		16,718
Different RR brain metastasis SCLC		21,809				15,783
Assume no survival gain for palliative RT in stage III, changed to symptom relief[a]			8,341	13,842	10,064	13,192
Minimum NSCLC survival benefit			9,721		11,237	
Maximum NSCLC survival benefit			7,466		9,320	
NSCLC fewer palliative fractions				14,217		13,511
80% cost	15,860	7,605	6,501	10,856	7,905	10,368
120% cost	23,791	11,408	9,751	16,284	11,857	15,552
Decrease all benefits by 50%	39,651	19,013	16,252	29,439	19,762	27,875

[a] The model assigns a survival gain for palliative chest RT used in stage III NSCLC as reported by Schaafsama et al. (35). In the sensitivity analysis, the survival gain was replaced with the palliative benefit reported by the MRC.
LYG, life year gained; NSCLC, non–small cell lung cancer; RR, response rate; SCLC, small cell lung cancer; SCYG, symptom control year gained.

for Stage I NSCLC is $5,207, Stage II NSCLC is $4,937, and Stage III is $5,041.

Table 2 shows the results of benefit/patient, including details by histology. Overall, the average survival gained per case of lung cancer treated with curative intent is 7 months. The average duration of symptom control gained per case treated with palliative intent is 3 months. The survival and symptom control gained per incident lung cancer case is 2 and .5 months respectively.

Overall, the cost per life year gained is $9,881 and the cost per year of symptom control gained is $13,938. The details of cost/benefit by histology are reported in the first row of Table 3.

Sensitivity Analysis

We tested the following conditions: using an alternative response rate for RT for bone metastases in NSCLC and brain metastases in SCLC; assuming that patients receiving palliative RT for stage III NSCLC have only symptom control benefit; using the minimum and maximum possible survival benefit reported for localized NSCLC (35); assuming a hypofractionated RT scheme for palliating bone and chest disease (one fraction for bone and two for chest versus five fractions for all palliative indications); increasing and decreasing the cost arbitrarily by 20 percent; and reducing all benefits arbitrarily by 50 percent. The values used in the sensitivity analysis are listed in italics in Table 1.

For lung cancer as a whole, the range of values for cost/life year gained and year of symptom control gained are $7,905 to $19,762 and $10,368 to $27,875, respectively. Results of the sensitivity analysis by histology are presented in Table 3. Results were most sensitive to large systematic changes in the estimate of benefit. The model was reasonably robust to all other changes.

DISCUSSION

The study illustrates that the use of RT for lung cancer has the potential to provide significant benefits at a population level. This is at relatively inexpensive cost.

One of the strengths of this study is that, unlike many other cost-effectiveness analyses, it summarizes the benefit and cost over an entire population for a range of RT indications. Our results are consistent with previous analyses that

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Table 4. Examples of Cost per QALY for Cancer and Non–cancer-related Interventions

Intervention and Alternative	Cost Utility (1998 CAD)
Immediate biopsy versus 6 month observation for a 50-year-old woman with abnormal findings on mammography	$3,700
Adjuvant chemotherapy after surgery, assuming a 5% gain in life expectancy, versus surgery alone in Duke's B or C colorectal cancer patients	$41,440
Antiemetic therapy with ondansetron versus metoclopramide for a 70 kg patient receiving cisplatin chemotherapy ($\geq$75 mg/m^2) who had not previously been exposed to antineoplastic agents	$680,800
Driver side air bag versus no air bag in driving population	$39,960
Total hip arthroplasty versus no hip arthroplasty in white 60-year-old women with osteoarthritis in American College of Rheumatology function class III	$8,140

Note: All values were converted from 1998 USD to 1998 CAD ($1 USD $\cong$ $1.48 CAD (41). Examples were taken from Earle et al. (16) and Chapman et al. (8).

suggest that RT is an inexpensive modality of therapy for cancer (3;21;40). The sensitivity analysis shows that, even if we overestimated the benefits of RT by a factor of two, RT would still be inexpensive.

The cutoff commonly used for describing expensive or inexpensive therapy is $50,000 per QALY. Therapies costing less than $20,000 are considered very inexpensive. Therapies costing more than $100,000 are considered expensive (25). The cost (USD) per QALY for other selected cancer- and noncancer-related interventions are provided in Table 4 for comparison (8;16). While our analysis is in natural units, the values in the table provide a frame of reference.

Although our estimates of benefit are admittedly crude, the use of natural units is a transparent way of describing the benefit. Reporting benefit in natural units has been used before in RT (3;20;40). Cost per life year gained is a much more meaningful value than total cost or cost/year of total survival. The use of more than one type of outcome, though, does not allow benefits to be aggregated. QALYs are an alternative way to express the benefits of an intervention. QALYs allow comparisons of different types of health benefits from different types of illnesses treated with different types of therapy. Whereas there are some data available about QALYs in lung cancer (23;36), there is not enough information about all of the possible health status states in lung cancer to be able to use this type of information in the model. Furthermore, there are limitations of utilities (25): techniques for measuring utilities are not standardized, utilities may be unresponsive to clinically important changes that are detectable by other means and QALYs may not always reflect patient preferences.

Another strength of this approach is its flexibility. The model was originally constructed to be generalizable to a typical North American population. However, it can be made relevant to any population by modifying the appropriate epidemiological observations. Similarly, the indications can be modified to fit local interpretations of evidence. Estimates of benefit have been taken from North American and European sources. In practice, this type of information is commonly used in settings different from the one in which the information originated. While costs in this study were estimated using Canadian data, any country's information could be applied.

Finally, this study also demonstrates the breadth of output possible with models using an evidence-based epidemiological approach. The strength of this framework is that all estimates start with accepted indications for RT and then applies them to a population. The alternative is to start with patients who happen to have been referred for RT. This method may allow for useful cost information to be collected but is unlikely to reflect the need for RT or the potential for benefit in the population.

The main limitation of the study is that repeat radiotherapy or radiotherapy delivered later in the course is not accounted for. These factors would result in additional benefits and costs that have not been quantified. Despite this result, we believe that our study provides reasonable information about the value of using RT in the initial management of lung cancer.

Evans and colleagues have published similar work (20) using a microsimulation model to estimate the cost of treating lung cancer in Canada; however, the methodology behind the two models is very different. The Evan's model considers all aspects of diagnosis and management, including continuing care, while our model considers initial RT only. As a result, our model includes a larger number of details about the RT. The microsimulation model made no attempt to quantify nonsurvival benefits, which our model does. Indications for RT in the Evans model were defined by expert opinion and not explicitly guided by principles of evidence-based medicine. Also, the criteria for choosing epidemiological observations were not explicitly described. Some were taken from registry data, but stage distribution was based on retrospective staging of approximately 60 percent of incident cases in Alberta and Ontario. They report a total cost of approximately $11,000 (1988 CAD) per life year gained for NSCLC and approximately $39,000 (1988 CAD) per life year gained for SCLC. Inflated to year 2002 dollars, these values would be approximately $15,000 and $53,000, respectively.

Policy Implications

There are two main policy implications for this model. The first is that it provides information useful for resource planning. Knowledge about the number of fractions required to treat the population and an approximation of the cost to deliver them is useful when planning an RT program. Similar information about RT for other cancer sites would add to the power of this estimate.

Second, the output of the model provides information with which to make judgments about priorities. If a limited budget is available, the model allows one to quantify the expected benefit at a population level, with a certain level of spending. Similar information about other cancers or other illnesses would facilitate explicit decision making about priorities for spending.

We have estimated benefit and cost of RT for lung cancer at a population level based on an evidence-based epidemiological approach to estimating RT need. Future work will be directed at developing similar models for other major cancer sites.

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