Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 4, pp. 1212–1218, 2006

0360-3016/06/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2006.06.021

CLINICAL INVESTIGATION **Palliation**

COST-EFFECTIVENESS OF SURGERY PLUS RADIOTHERAPY VERSUS RADIOTHERAPY ALONE FOR METASTATIC EPIDURAL SPINAL CORD COMPRESSION

KENNETH C. THOMAS, M.D., M.H.SC., F.R.C.S.C.,* BOHDAN NOSYK, M.A.,† CHARLES G. FISHER, M.D., M.H.SC., F.R.C.S.C.,‡ MARCEL DVORAK, M.D., F.R.C.S.C.,‡ ROY A. PATCHELL, M.D.,§ WILLIAM F. REGINE, M.D.,‖ ANDREW LOBLAW, M.D., M.SC., F.R.C.P.C.,¶ NICK BANSBACK, M.SC.,† DAPHNE GUH, M.SC.,† HUIYING SUN, PH.D.,† AND ASLAM ANIS, PH.D.†#

*Departments of Surgery (Orthopedics) and Neurosciences, University of Calgary, Calgary, AB, Canada; †Center for Health Evaluation and Outcome Sciences, Vancouver, BC, Canada; ‡Department of Orthopedics and #Health Care and Epidemiology, University of British Columbia, Vancouver, BC, Canada; §Departments of Surgery (Neurosurgery) and Neurology, University of Kentucky Medical Center, Lexington, KY; ‖Department of Radiation Oncology, University of Maryland Medical School, Baltimore, MD; and ¶Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

Purpose: A recent randomized clinical trial has demonstrated that direct decompressive surgery plus radiotherapy was superior to radiotherapy alone for the treatment of metastatic epidural spinal cord compression. The current study compared the cost-effectiveness of the two approaches.
Methods and Materials: In the original clinical trial, clinical effectiveness was measured by ambulation and survival time until death. In this study, an incremental cost-effectiveness analysis was performed from a societal perspective. Costs related to treatment and posttreatment care were estimated and extended to the lifetime of the cohort. Weibull regression was applied to extrapolate outcomes in the presence of censored clinical effectiveness data.
Results: From a societal perspective, the baseline incremental cost-effectiveness ratio (ICER) was found to be $60 per additional day of ambulation (all costs in 2003 Canadian dollars). Using probabilistic sensitivity analysis, 50% of all generated ICERs were lower than $57, and 95% were lower than $242 per additional day of ambulation. This analysis had a 95% CI of −$72.74 to 309.44, meaning that this intervention ranged from a financial savings of $72.74 to a cost of $309.44 per additional day of ambulation. Using survival as the measure of effectiveness resulted in an ICER of $30,940 per life-year gained.
Conclusions: We found strong evidence that treatment of metastatic epidural spinal cord compression with surgery in addition to radiotherapy is cost-effective both in terms of cost per additional day of ambulation, and cost per life-year gained. © 2006 Elsevier Inc.

Metastatic spinal cord compression, Cost-effectiveness, Clinical trials, Radiotherapy, Surgery, Secondary neoplasm.

INTRODUCTION

Metastatic epidural spinal cord compression (MESCC), a result of disseminated cancer, has a devastating effect on patient quality of life from severe pain and neurologic dysfunction (1). The natural history of MESCC is unfavorable, with all untreated patients progressing to tetraplegia or paraplegia, paresthesia, and sphincter disturbance (2–4). Further, paraplegia secondary to metastatic disease has been shown to shorten life expectancy while imposing considerable costs on society (5–7).

The mainstays of treatment for MESCC are radiotherapy and surgery. There is controversy as to the optimal treatment strategy. Some authors have concluded that functional outcome after surgery or radiotherapy is equivalent, (4, 8), whereas others have found that both surgery alone and surgery combined with radiotherapy improve ambulatory function and health-related quality of life (6, 9). Whereas, historically, surgery implied a laminectomy of the affected levels, (10) the clinical effectiveness of laminectomy in improving quality of life remains questionable for reasons outlined by McLain *et al.* (11). Renewed interest in the surgical management of MESCC has stemmed from improved imaging techniques, a better understanding of spinal stability, and improved spinal instrumentation and reconstruction (11, 12).

Cost-effectiveness analysis describes the incremental

Reprint requests to: Aslam Anis, Ph.D., Department of Health Care and Epidemiology, Faculty of Medicine, UBC, James Mather Building, 5804 Fairview Avenue, Vancouver, BC, Canada V6T 1Z3. Tel: (604) 822-5550; Fax: (604) 822-4994; E-mail: aslam.anis@ubc.ca

Acknowledgments—Adriane Lewin assisted with the preparation of this manuscript.

Received April 25, 2006, and in revised form June 9, 2006. Accepted for publication June 9, 2006.

costs and benefits incurred by a particular intervention or test compared with conventional care (13, 14). Economic analysis has a small role in a specific doctor-patient encounter because the physician seeks the best possible treatment and outcome for the specific patient. By providing information on the efficiency or "value for money" of a new technology, however, it may play a key role for policy makers and physician administrators in making optimal decisions on resource allocation using a fixed or limited budget (15). Ideally, all new health interventions would be subject to economic analysis and then funded accordingly.

Recently, the first prospective randomized trial comparing contemporary surgery in addition with radiotherapy (S+RT) vs. radiotherapy alone (RT) has demonstrated improved ambulatory function in the S+RT treatment group (16). Given the limited survival of this patient population, however, coupled with the high resource demands of surgical treatment, one may question whether surgical management represents efficient spending of limited health care dollars. The objective of this study was to determine the incremental cost-effectiveness ratio (ICER), from a societal perspective, of radical surgical decompression plus radiotherapy compared with radiotherapy alone in the treatment of MESCC based on the results of this trial.

METHODS AND MATERIALS

Data

Clinical effectiveness data for this study came from a recent randomized trial comparing S+RT with RT alone (16). The results of that trial have been previously reported and the study methods and sample fully described previously (16). In brief, of 123 patients assessed for eligibility, 101 patients with MESCC were randomized to receive S+RT ($n = 50$) or RT alone ($n = 51$). Of 22 exclusions, 9 patients failed to meet the inclusion criteria, 5 refused to participate, and 8 were excluded because of physician refusal. No patients were lost to follow-up, but 10% of the sample (7 S+RT, 3 RT) was censored when the trial ended prematurely after the interim analysis revealed S+RT to be the more effective method of care. Patients were followed prospectively from trial entry until death, and the primary endpoint was the ability to walk after treatment. Metastatic tumor types excluded were lymphomas, myelomas, leukemias, and germ cell tumors. No previous history of RT to the site and an expected survival of 12 weeks were part of the inclusion/exclusion criteria. Before randomization, patients were stratified according to treating institution, tumor type, ambulatory status, and relative stability of the spine, determined using Cybulski's guidelines (17). Surgery was performed within 24 h of study entry with the intent to remove as much tumor as possible, provide immediate decompression, and stabilize the spine. Both groups received total RT doses of 30 Gy at 3 Gy/fraction/day inclusive of one vertebral body above and below the visible lesion. Radiotherapy began within 2 weeks of surgery in the S+RT group and within 24 h of study entry in the RT group.

Clinical effectiveness data from Patchell *et al.* (16) were used to determine the ICER associated with S+RT compared with RT alone. Discounting was not incorporated into this design because of the short time horizon. A societal perspective was used to capture direct medical and nonmedical costs such as out-of-pocket expenses for home care.

For the purposes of economic evaluation, outcome variables that most accurately permit the measurement of effectiveness are characterized by clinical credibility, responsiveness to change, and a lack of bias in the efficacy estimate (18). Ambulatory status meets these criteria and is an accepted measure of effectiveness for MESCC within the published literature (6–8, 19). Ambulation was therefore chosen as the baseline measure of effectiveness for this evaluation, whereas survival was also considered in the sensitivity analysis.

Costs

Both direct intervention and nonintervention related costs were considered. Costs associated with diagnostic tests, treatment planning, surgery, and hospital ward stay were calculated using the St. Paul's Hospital Cost Model (20), which provides fully allocated costs of all activities performed in hospital. Costs per patient day after surgery, which included the cost of the particular ward, meals and necessary intravenous therapy, were derived from the St. Paul's Hospital Cost Model. Surgeon and anesthetist fees were taken from the *British Columbia Medical Association Guide to Fees* (21), whereas workload unit values of diagnostic tests were derived from the 2002 *Management Information Systems Guidelines* (22). Pharmaceutical costs were derived from the 2003 *British Columbia Pharmacare Low Cost Alternative Drug Booklet* (23) and included a prescription fee. Costs of institutionalization were derived from Hollander *et al.* (24) and national average hourly costs of in-home nursing care, obtained from Statistics Canada (25), were applied for the proportion of patients expected to be treated at home. All costs were reported in 2003 Canadian dollars ($1 CAD = $0.82 US).

Costs for RT treatment were derived from a published study concerning the cost of radiotherapy at an Ontario regional cancer center (26), from a perspective of the government as payer in a universal health care system. Direct treatment and nontreatment related costs were included in the calculation of cost per fraction of radiation.

Resource use data were not available from the randomized clinical trial (16). Therefore, with institutional review board approval, data were collected from a prospective cohort of patients with spinal metastases treated by radical decompression and stabilization at Vancouver Hospital and Health Sciences Center. This allowed for the determination of resource utilization for surgery and associated hospitalization.

An estimation of resource use for diagnostic tests, treatment planning, the probabilities of complications arising from radiotherapy along with treatment of both major and minor complications, probabilities of institutionalization as well as resource utilization of in-home care posttreatment, and necessary medication after acute treatment for the initial 12 weeks of follow-up were derived from median responses given by two expert panels (spine surgeons and radiation oncologists; $n = 13$). Median responses were chosen to minimize the effects of outlying parameter estimates. Postintervention costs were extrapolated to the mean survival time of each cohort.

Statistical methods

To account for the censoring of 10% of the sample (7 S+RT, 3 RT), Heitjan *et al.* (27), among others (28, 29), suggest that the appropriate means of extrapolating the outcome data are to fit a Weibull regression onto observed patient-level data. This technique has recently gained favor in the health technology assessment literature for its ability to produce unbiased estimates of extrapolated mean survival and its ease of applicability to probabilistic sensitivity analysis. In our case, both survival and ambulation data were extrapolated to the end of follow-up for the entire cohort, producing estimates of expected mean survival and ambulation.

Fixed costs of surgery, radiotherapy, and diagnostic tests were added to the daily costs of hospital care and postintervention care multiplied by the mean days of survival for each treatment arm, as predicted by the Weibull model. It was assumed that patients in the RT arm would not incur a hospital stay for treatment purposes. The baseline ICER was calculated by dividing the difference between the two groups in costs of therapy by the difference in mean ambulatory days.

Survival was chosen as an alternate measure of effectiveness, which yielded an ICER of cost per life-year saved.

Sensitivity analysis

To establish the robustness of the model, one-way sensitivity analyses were performed on several parameters. This permitted determination of the variation in the ICER that would result from change in a single parameter in the model. The cost of surgery and the number of days spent in the ICU or the general care ward were each varied by the upper and lower bounds of their respective 95% confidence intervals. Hospital costs were varied ±25% to account for variability across institutions. Postintervention and pharmaceutical treatment costs were considered to be equal between cohorts.

A probabilistic sensitivity analysis using Monte Carlo simulation was performed to evaluate the uncertainty associated with the ICER. The probability distributions of the cost of surgery, length of hospital stay in the intensive care unit and in the general care ward, and the total time of ambulation and survival were sampled 5000 times for each cohort. A log-normal distribution was fitted on the cost of surgery, whereas gamma distributions were used for days of hospitalization in the intensive care unit and general care wards. In addition, estimates of survival and ambulation derived from the Weibull regression were fitted with multivariate log-normal distributions. A cost-effectiveness acceptability curve was produced, which indicates the probability that the experimental intervention is cost effective for a range of threshold cost-effectiveness ratios.

Finally, estimates of mean survival and ambulation were varied at the 25th and 75th percentiles derived using results from our Monte Carlo simulation in two-way sensitivity analysis.

Analysis was carried out using STATA version 7.0 and Microsoft Excel.

RESULTS

Demographic characteristics for both the randomized clinical trial and the resource use cohorts are summarized in Table 1. Whereas patients from the resource use cohort were similar in age to the trial participants, a smaller proportion were indicated as having lung cancer, a greater proportion were female, and a greater proportion had breast cancer.

Clinical effectiveness data for ambulatory days and survival is presented in Table 2, along with Weibull parameters and the derived expected values. Patients randomized to S+RT had a greater expected mean survival time (377.06 vs. 221.11 days) and ambulatory time (312.47 vs. 92.34) than patients who received RT alone. A parametric Weibull survival curve is plotted against a Kaplan-Meier curve to

Table 1. Baseline characteristics of study patients: resource use and clinical effectiveness cohorts

	Resource utilization (n = 70)	Clinical effectiveness (16) (n = 101)
Mean age (range)	55.18 (30–76)	59.76 (25–84)
Female (%)	30 (42.9)	31 (30.69)
Tumor type 1: lung (%)	13 (18.6)	26 (25.7)
Tumor type 2: breast (%)	18 (25.7)	13 (12.9)
Tumor type 3: other (%)	39 (55.7)	62 (61.4)

Table 2. Actual and expected clinical outcomes (16)

	RT alone (n = 51)	S+RT (n = 50)
Patients able to ambulate at study entry (%)	35 (69)	34 (68)
Patients able to ambulate postintervention (%)	29 (57)	42 (84)
Days of survival (mean)	216.86	351.96
Ambulatory days (mean)	91.25	289.64
Weibull results and parameters*		
Expected days of survival (mean)	221.11	377.06
Expected days of ambulation (mean)	92.34	312.47
Survival:		
Shape (λ)	0.013	0.012
Scale (γ)	0.826	0.771
Ambulation:		
Shape (λ)	0.048	0.162
Scale (γ)	0.667	0.720

* Where the expected value of mean survival is given by the equation:

$$E(\theta) = \frac{1^{\frac{1}{\gamma}}}{\lambda}\Gamma\left(1 + \frac{1}{\gamma}\right).$$

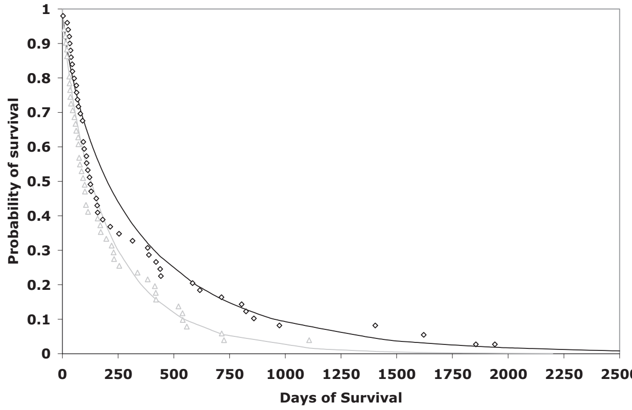

Fig. 1. Kaplan-Meier vs. Weibull survival estimates for contemporary surgery in addition with radiotherapy (S+RT) and radiotherapy alone (RT) groups. *Abbreviations:* S = surgery; RT = radiotherapy. Kaplan-Meier days of survival: S+RT (◇). Weibull expected days of survival: S+RT ---. Kaplan-Meier days of survival: RT (△). Weibull expected days of survival: RT ---. Data from Patchell *et al.* (16).

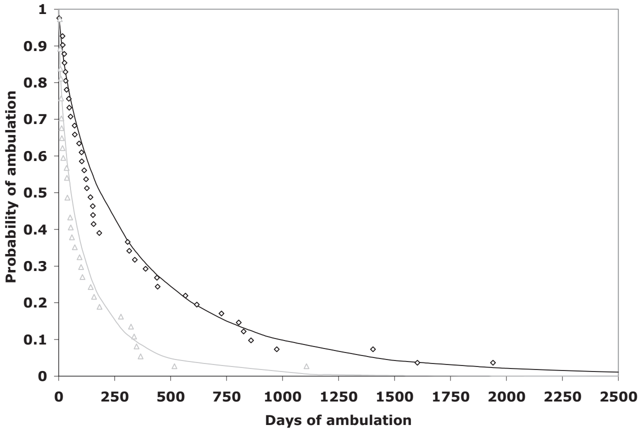

Fig. 2. Kaplan-Meier vs. Weibull ambulation estimates for contemporary surgery in addition with radiotherapy (S+RT) and radiotherapy alone (RT) groups. *Abbreviations:* S = surgery; RT = radiotherapy. Kaplan-Meier days of ambulation: S+RT (◇). Weibull expected days of ambulation: S+RT ---. Kaplan-Meier days of ambulation: RT (△). Weibull expected days of ambulation: RT ---. Data from Patchell *et al.* (16).

compare actual and predicted time until death (Fig. 1) and time until loss of ability to ambulate (Fig. 2).

All unit costs, including the sources of resource use and cost data, are listed in Table 3. Patients in both cohorts incurred costs of diagnostic procedures, radiotherapy, and associated costs of complications, and post-treatment care, which is listed as a daily cost to the final day of expected survival. Patients in the S+RT cohort incurred the additional costs of surgery plus surgical hospitalization (mean length of stay, based on the resource use cohort: intensive care unit = 1.1 day, recovery ward = 16.9 days).

One-way sensitivity analysis showed that equalizing postintervention costs (institutionalization and in-home care costs) brought about the largest change in the ICER. Table 4 summarizes the baseline, one-way, two-way, and probabilistic sensitivity analysis results.

The cost-effectiveness plane shown in Fig. 3 displays graphically the findings from the Monte Carlo simulation for the S+RT and RT cohorts. Eighteen percent of all simulations showed the S+RT strategy to be cost-saving.

The cost-effectiveness acceptability curve is illustrated in Fig. 4. The probabilistic sensitivity analysis found that 50% of the generated ICERs were less than \$57, and 95% were less than \$242 per additional patient day of ambulation.

DISCUSSION

On average, patients in the S+RT arm were able to ambulate an additional 220 days and survive an additional 156 days in comparison to those receiving radiotherapy alone at an average additional cost of \$13,220 per patient. Baseline results showed an incremental cost-effectiveness ratio of \$60 per additional patient day of ambulation. When survival was used as the measure of effectiveness, this translates into an ICER of \$30,940 per life-year gained, which compares very favorably with other new interventions such as vaccination programs, implantable cardioverters, screening for colorectal cancer, and abdominal aortic aneurysm surgery (30–35). Given the source of our resource utilization data, we have presented all costs in

Table 3. Unit cost estimates

Cost item	Cost (\$CAD)	Sources: Resource use	Sources: Costs
Diagnostics	1280.08	EP	SPHCM (20)
Surgery (SE)	11,769.58 (3212.89)	VDB	VH OR, SPHCM, BCMA fee schedule (21)
Surgical hospitalization*	12,095.24	VDB	SPHCM
Radiotherapy: no complications (p = 0.706)	3705.60	Earle *et al.* (26)	Earle *et al.*
Radiotherapy: minor complications† (p = 0.273)	85.10	EP	BC Pharmacare (23)
Radiotherapy: major complications‡ (p = 0.021)	1020.72	EP	BC Pharmacare, SPHCM
Posthospitalization treatment: S+RT	67.30	EP	BC Pharmacare
Posthospitalization treatment: RT	289.82	EP	BC Pharmacare
Posthospitalization: S+RT (per day)	108.39	EP	BC Pharmacare, Hollander *et al.* (24), Statistics Canada (25)
Posthospitalization: RT (per day)	223.20	EP	BC Pharmacare, Hollander *et al.*, Statistics Canada

Abbreviations: BCMA = British Columbia Medical Association; EP = expert panel; SE = standard error; SPHCM = St. Paul's Hospital Cost Model; S+RT = surgery in addition to radiotherapy; VDB = Vancouver database; VH OR = Vancouver hospital operating room department.

* Including costs of admission, surgery, stay in postanesthetic recovery room, intensive care unit, and general care ward, intravenous insertion, and meals. Based on an intensive care unit length of stay of 1.01 days and a general care ward length of stay of 16.90 days. Surgical complications included urinary tract infection, psychosis, deep venous thrombosis, acute renal failure, pneumonia, respiratory distress, distress with resultant tracheostomy, sepsis, *C. difficile* diarrhea, wound infection/dehiscence, cerebrospinal fluid leak, postoperative gastrointestinal bleed, and wound hematoma. These complications resulted in longer lengths of hospital stay and therefore higher costs.

† Minor complications indicated by the expert panel included nausea, bone pain, pain, diarrhea, esophagitis.

‡ Major complications indicated by the expert panel included myelopathy, vertebral fracture, and neurologic deficit.

CDN$. Although practices and unit costs of hospital resource utilization will differ between countries, the purchasing power parity-adjusted 2003 US$ costs per additional day of ambulation was found to be US$48, whereas the cost per life-year saved was US$24,752.

Despite the costs associated with surgery and postoperative recovery, 18% of the Monte Carlo simulations showed this treatment resulting in a cost savings in comparison to the standard treatment of radiotherapy alone. When this treatment strategy was not cost saving, the cost of an additional day of ambulation was less than $242 95% of the time.

Although the presence of metastases usually signifies incurable disease, the majority of these patients have a relatively favorable intermediate-term life expectancy. Because these cancer patients live longer from improved medical, surgical, and adjuvant therapies, spinal metastases pose a greater threat to their independence and survival. Several contemporary studies have reported the advantages of surgical treatment of MESCC (6, 9, 11, 12, 36–38) in this very complex patient population. Until recently, there have been no prospective randomized studies on surgery and RT for metastatic spinal disease using modern spinal reconstructive techniques. Although there are many published case series, a comparison or control group is essential because numerous authors have shown that clinical outcome is strongly influenced by pretreatment functional status (1, 8, 19). Patchell *et al.*, using appropriate inclusion/exclusion criteria and thus designing an externally valid study, have clearly shown the effectiveness of modern spine surgery combined with RT, beyond RT alone, on ambulatory function in patients with MESCC (16). It has been noted, however, that the clinical outcome of RT patients in the study by Patchell *et al.* (16) was less favorable than other prior literature; (4) this is due to the exclusion of patients with radiosensitive tumor types noted within the methods section. Furthermore, the centers involved in the study represented a relatively high level of surgical expertise. As such, it is important to interpret the results of this analysis in the context of each clinical setting.

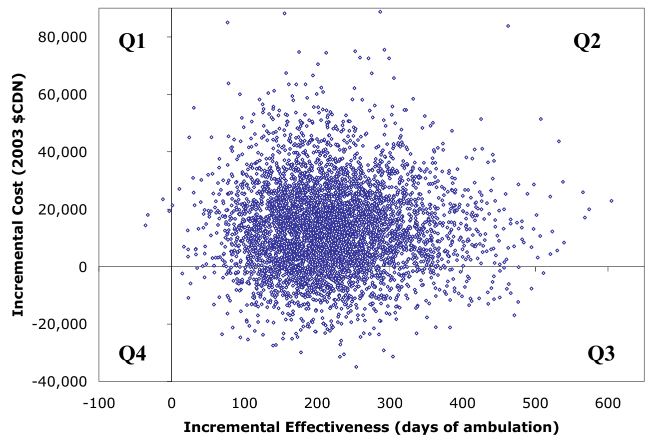

Fig. 3. Scatterplot of differences in cost and days of ambulation based on Monte Carlo simulations for the contemporary surgery in addition with radiotherapy (S+RT) and radiotherapy alone (RT) cohorts. *Abbreviations:* S = surgery; RT = radiotherapy. Q1: S+RT strategy more costly, less effective. Q2: S+RT strategy more costly, more effective. Q3: S+RT strategy less costly, more effective. Q4: S+RT strategy less costly, less effective.

Table 4. Baseline and sensitivity analysis cost results

Baseline measure of effectiveness	ICER* (2003$CAD)
Ambulation	60.06
Survival	84.76 30,940.16/life-years saved
One-way sensitivity analysis	ICER resulting from variation in a single cost parameter
Cost of hospitalization (±25%)	46.37–73.75
Intensive care unit LOS (95% CI)	53.27–66.87
General care ward LOS (95% CI)	53.28–66.87
Surgery (95% CI)	56.64–63.48
Common posthospitalization costs	198.02
Common treatment costs	61.07
Two-way sensitivity analysis	ICER resulting from variation in both ambulation and survival
RT: survival/ambulation (P25, P75)	91.93–(−138.50)
S+RT: survival/ambulation (P25, P75)	54.60–73.62
Probabilistic sensitivity analysis†	ICER generated on simulated data
Median (95% CI)‡	56.89 ((−72.47)–309.44)

Abbreviations: ICER = incremental cost-effectiveness ratio; LOS = length of stay; RT = radiotherapy alone; S+RT = surgery plus radiotherapy.

* Interpreted as the cost per additional day of ambulation, except where noted.

† The probability distributions of cost of surgery, length of hospital stay in the intensive care unit (ICU) and in the general care ward, and the total time of ambulation and survival were sampled 5000 times for each cohort.

‡ 95% Credibility interval stated; (2.5–97.5%).

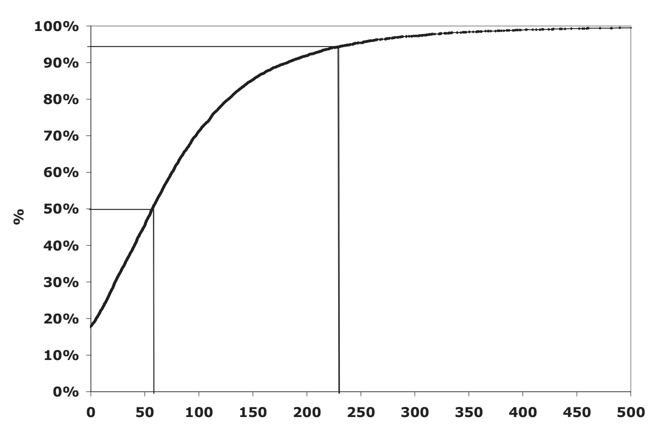

Fig. 4. Incremental cost-effectiveness acceptability curve for contemporary surgery in addition with radiotherapy and radiotherapy alone.

Metastatic epidural spinal cord compression treated with surgery lends itself to economic analysis as it is an expensive treatment for an incurable disease. Cost-effectiveness analysis, as opposed to cost-utility or cost-benefit analysis, was chosen in this study for several reasons. To the best of our knowledge, there are no studies evaluating the effectiveness of radiotherapy in patients with MESCC that have used health utilities as the outcome measure; the lack of published utilities prevented the use of a more conventional cost-utility economic assessment. Cost-effectiveness analysis has several advantages. It is easy to understand, making it the most commonly used approach to economic evaluation in health care (39). It allows for a comparison of costs as well as outcomes for two similar interventions for a specific disease (15). On the other hand, the use of a clinical measure of effectiveness such as ambulation excludes other relevant patient-focused measures such as health-related quality of life (15). A more common metric in the denominator of an ICER has been the number of life-years saved, included in our alternate model where we used survival as the primary outcome measure. In any case, given the uncertainty in the threshold cost-effectiveness ratio, the cost-effectiveness acceptability curve (displayed in Fig. 4) is the most informative tool for policy makers to base their decisions on. This graph may be interpreted as indicating the probability that the new intervention will be cost effective for a range of threshold values, which will differ according to the size of the health care budget within a community.

There are limitations to this study. First, the use of data from several different sources increased the potential for measurement error. In addition, sample sizes for each of the cohorts were quite small, and there was a great deal of variation in both cost and effectiveness data. Probabilistic sensitivity analysis was employed for the specific purpose of illustrating how the uncertainty in these parameters affected the overall result; we are confident that the values derived from probabilistic sensitivity analysis are within the range of acceptable interventions.

Second, the use of Weibull regression analysis requires the assumption that the censorship of data is independent of follow-up time. The trial by Patchell *et al.* (16) was stopped early for ethical reasons; using Weibull regression, we implicitly assumed that this discontinuation was independent of the follow-up time of the surviving patients. On the other hand, only 10 patients, or 10% of the cohort, were censored. In addition, although there was left- and right-censoring in terms of ability to ambulate, we assumed that all patients who were able to ambulate postintervention were able to do so from the first day of follow-up.

Third, tumor type, among other covariates, may also influence the ICER. Cox proportional hazard regression, with survival as the dependent variable, was performed using covariates from the Patchell dataset. We found that gender and ability to ambulate postintervention were the only consistent predictors of survival (results not presented). Although similar analyses could not be carried out on resource utilization data, we can infer that females and patients who were able to walk immediately after the intervention were relatively more cost-effective compared with males and those unable to ambulate immediately after the intervention, respectively. Because the resource use cohort had a higher proportion of women, this could have led to cost estimates that were lower than those actually incurred by the clinical effectiveness cohort.

The treatment of patients with spinal metastases presents a mammoth challenge across many disciplines and domains. These patients have multiple medical comorbidities, psychosocial issues, and an unknown life expectancy. Our findings must be interpreted within the context of clinical practice. The addition of surgery before radiotherapy for patients with MESCC improves ambulatory function (16). Metastatic epidural spinal cord compression, left untreated, has devastating physical and psychologic consequences.

Because health care resources are limited, we must seek to use available resources efficiently by maximizing health benefits. Scarce resources in the healthcare system have led to the current atmosphere of cost containment. Efficient use of these resources can only be accomplished through sound economic evaluation of health interventions. Whether the addition of surgery to the standard treatment of radiotherapy is cost effective is dependent on the value placed on ambulatory function by the patient and society and on the alternative uses for scarce resources (18).

REFERENCES

1. Katagiri H, Takahashi M, Inagaki J, *et al.* Clinical results of nonsurgical treatment for spinal metastases. *Int J Radiat Oncol Biol Phys* 1998;42:1127–1132.
2. Bilsky MH, Lis E, Raizer J, *et al.* The diagnosis and treatment of metastatic spinal tumor. *Oncologist* 1999;4:459–469.
3. Helweg-Larsen S. Clinical outcome in metastatic spinal cord compression. A prospective study of 153 patients. *Acta Neurol Scand* 1996;94:269–275.
4. Loblaw DA, Laperriere NJ. Emergency treatment of malignant extradural spinal cord compression: An evidence-based guideline. *J Clin Oncol* 1998;16:1613–1624.
5. Gokaslan ZL, York JE, Walsh GL, *et al.* Transthoracic vertebrectomy for metastatic spinal tumors. *J Neurosurg* 1998;89: 599–609.
6. Hirabayashi H, Ebara S, Kinoshita T, *et al.* Clinical outcome and survival after palliative surgery for spinal metastases: Palliative surgery in spinal metastases. *Cancer* 2003;97:476–484.
7. Helweg-Larsen S, Sorensen PS, Kreiner S. Prognostic factors in metastatic spinal cord compression: A prospective study using multivariate analysis of variables influencing survival and gait function in 153 patients. *Int J Radiat Oncol Biol Phys* 2000;46:1163–1169.
8. Maranzano E, Latini P. Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: Final results from a prospective trial. *Int J Radiat Oncol Biol Phys* 1995;32:959–967.
9. Wai EK, Finkelstein JA, Tangente RP, *et al.* Quality of life in

surgical treatment of metastatic spine disease. *Spine* 2003;28:508–512.

10. Young RF, Post EM, King GA. Treatment of spinal epidural metastases. Randomized prospective comparison of laminectomy and radiotherapy. *J Neurosurg* 1980;53:741–748.
11. McLain RF, Bell GR. Newer management options in patients with spinal metastasis. *Cleveland Clin J Med* 1998;65:359–356.
12. Sundaresan N, Rothman A, Manhart K, *et al.* Surgery for solitary metastases of the spine: rationale and results of treatment. *Spine* 2002;27:1802–1806.
13. Korthals-de Bos I, van Tulder M, van Dieten H, *et al.* Economic evaluations and randomized trials in spinal disorders: principles and methods. *Spine* 2004;29:442–448.
14. Drummond MF, O'Brien BJ, Stoddart G. Methods for the economic evaluation of health care programmes. 2nd ed. New York: Oxford University Press; 1997.
15. Earle CC, Coyle D, Evans WK. Cost-effectiveness analysis in oncology. *Ann Oncol* 1998;9:475–482.
16. Patchell RA, Tibbs PA, Regine WF, *et al.* Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: A randomised trial. *Lancet* 2005;366(9486):643–648.
17. Cybulski GR. Methods of surgical stabilization for metastatic disease of the spine. *Neurosurgery* 1989;25:240–252.
18. Anis AH, Tugwell PX, Wells GA, *et al.* A cost effectiveness analysis of cyclosporine in rheumatoid arthritis. *J Rheumatol* 1996;23:609–616.
19. Falkmer U, Jarhult J, Wersall P, *et al.* A systematic overview of radiation therapy effects in skeletal metastases. *Acta Oncol* 2003;42:620–633.
20. Palepu A, Tyndall MW, Leon H, *et al.* Hospital utilization and costs in a cohort of injection drug users. *CMAJ* 2001;165:415–420.
21. British Columbia Medical Association. BCMA guide to fees 2003. Available online at: http://www.bcma.org/public/news_publications/publications/fee_guide.htm. Accessed April 20, 2005.
22. The Management Information Systems Group. Management Information Systems Project Steering Committee: Guidelines for management information systems in canadian healthcare facilities. Ottawa, Canada: MIS Group; 2002.
23. Government of British Columbia. Pharmacare low cost alternative reference drug program booklet, Version 1.1. 2003. Available online at: http://www.health.gov.bc.ca/pharme/lca/lcabooklets.html. Accessed April 20, 2005.
24. Hollander MJ. Unfinished business: The case for chronic home care services: a policy paper. Victoria, BC, Canada: Hollander Analytic Services Ltd.; 2003.
25. Statistics Canada. Table number 2810035 series V1602547. Available online at: http://cansim2.statcan.ca. Accessed April 12, 2005.
26. Earle C, Coyle D, Smith A, *et al.* The cost of radiotherapy at an Ontario regional cancer centre: A re-evaluation. *Crit Rev Oncol Hematol* 1999;32:87–93.
27. Heitjan DF, Kim CY, Li H. Bayesian estimation of cost-effectiveness from censored data. *Stat Med* 2004;23:1297–1309.
28. Al MJ, Van Hout BA. A Bayesian approach to economic analyses of clinical trials: The case of stenting versus balloon angioplasty. *Health Econ* 2000;9:599–609.
29. O'Hagan A, Stevens JW. A framework for cost-effectiveness analysis from clinical trial data. *Health Econ* 2001;10:303–315.
30. Rothberg MB, Rose DN. Vaccination versus treatment of influenza in working adults: A cost-effectiveness analysis. *Am J Med* 2005;118:68–77.
31. Katz DA, Cronenwett JL. The cost-effectiveness of early surgery versus watchful waiting in the management of small abdominal aortic aneurysms. *J Vasc Surg* 1994;19:980–990.
32. Provenzale D. Cost-effectiveness of screening the average-risk population for colorectal cancer. *Gastrointest Endosc Clin N Am* 2002;12:93–109.
33. Larsen G, Hallstrom A, McAnulty J, *et al.* Cost-effectiveness of the implantable cardioverter-defibrillator versus antiarrhythmic drugs in survivors of serious ventricular tachyarrhythmias: Results of the Antiarrhythmics Versus Implantable Defibrillators (AVID) economic analysis substudy. *Circulation* 2002;105:2049–2057.
34. Saab S, Ly D, Han SB, *et al.* Is it cost-effective to treat recurrent hepatitis C infection in orthotopic liver transplantation patients? *Liver Transpl* 2002;8:449–457.
35. Wilson LS, Reyes CM, Lu C, *et al.* Modelling the cost-effectiveness of sentinel lymph node mapping and adjuvant interferon treatment for stage II melanoma. *Melanoma Res* 2002;12:607–617.
36. Ryken TC, Eichholz KM, Gerszten PC, *et al.* Evidence-based review of the surgical management of vertebral column metastatic disease. *Neurosurg Focus* 2003;15:E11.
37. Onimus M, Papin P, Gangloff S. Results of surgical treatment of spinal thoracic and lumbar metastases. *Eur Spine J* 1996;5:407–411.
38. Sundaresan N, Sachdev VP, Holland JF, *et al.* Surgical treatment of spinal cord compression from epidural metastasis. *J Clin Oncol* 1995;13:2330–2335.
39. Williams C, Coyle D, Gray A, *et al.* European School of Oncology Advisory report to the Commission of the European Communities for the "Europe Against Cancer Programme" cost-effectiveness in cancer care. *Eur J Cancer* 1995;31A:1410–1424.