

## A cost-utility analysis of treatments for malignant liver tumours: a pilot project

ANDREW MCKAY, TRISH KUTNIKOFF & MARK TAYLOR

*Department of Surgery, University of Manitoba, Winnipeg, Manitoba, Canada*

### Abstract

**Background.** Hepatic resection is the standard treatment for colorectal liver metastases when feasible. Techniques such as radiofrequency ablation (RFA) have been the subject of ongoing research in hopes of achieving a similar survival to that achieved with hepatic resection, but with less morbidity and better quality of life (QOL). The aim was to generate a hypothesis concerning the cost-utility of various treatments that may be further tested with randomized trials in the future. **Patients and methods.** This was a prospective, non-randomized pilot study comparing the cost-utility of hepatic resection, RFA, systemic chemotherapy, and symptom control alone for colorectal liver metastases. All patients with newly diagnosed liver malignancies were eligible. QOL was measured serially with the Health Utilities Index. Costs, in 2001 Canadian dollars, were captured from the viewpoint of society in general. **Results.** In all, 40 patients were enrolled in the study: 7 underwent hepatic resection, 7 underwent RFA (sometimes in combination with resection), 20 received systemic chemotherapy, and 6 received symptom control alone. Liver resection appeared to be the most effective approach, with an average benefit of 2.58 QALYs (quality-adjusted life years) compared with 1.95 QALYs for RFA, 1.18 QALYs for chemotherapy, and 0.82 QALYs for symptom control alone, resulting in cost-utility ratios of \$7792, \$8056, \$12 571, and \$4788 per QALY, respectively. **Discussion.** The cost-utility of hepatic resection and RFA appeared similar even though patients receiving RFA had more advanced disease. The role of RFA is still being defined; however, if long-term survival proves to be promising, then this study lends support to the conduct of randomized controlled trials in the future.

**Key Words:** *liver neoplasms, cost-utility, liver resection, radiofrequency ablation, quality of life*

### Introduction

Unfortunately, among all patients with metastatic liver disease only a small fraction will be candidates for curative resection [1,2], which currently offers the best chance for long-term survival [3,4]. The complications of surgical resection are significant, however [5]. Newer chemotherapeutic agents may offer median survival rates up to 20 months [6], but long-term survival is rare. Regional techniques such as radiofrequency ablation (RFA) have been the subject of ongoing research in hopes of achieving a similar survival to hepatic resection, but with less morbidity and better quality of life (QOL) [4,7]. Presently, RFA is indicated for patients with tumors that are unresectable on the basis of multifocal disease, poor liver reserve, proximity to major vascular structures, or poor overall medical condition [8]. Longer follow-up is needed before firm conclusions can be made about the effectiveness of RFA.

With limited resources available to healthcare systems, the costs of a particular treatment and the QOL gained survival are also important in decision-making. To date, only a few studies have evaluated the cost-utility of treatments for liver malignancies, none of which have been performed within the context of the Canadian healthcare system. QOL after treatments for liver metastases is not well described in clinical studies and patients must often rely mainly on anecdotal information.

The present study was undertaken to describe the costs and QOL associated with the different treatments available for colorectal liver metastases. Although the initial results of RFA appear promising, this technique is still relatively new. If the long-term survival proves similar to that of hepatic resection, then perhaps randomized controlled trials would be justified in the future. The present study was designed to explore a hypothesis that the cost-utility of RFA

and hepatic resection might be similar enough to justify such a trial. Systemic chemotherapy and symptom control alone (i.e. palliative treatment) were included in the study because the costs and QOL after all treatments for liver metastases are poorly described and the cost-utility of all treatment options should be within an acceptable range [9] if physicians are to continue to recommend them.

## Patients and methods

### *Study design*

This study was a cost-utility analysis comparing surgical resection, RFA, systemic chemotherapy, and symptom control alone (palliative care) for the treatment of malignant liver tumors. The study was purely descriptive and did not influence the treatment received by the patients in any way. The protocol was approved by the University of Manitoba's Health Research Ethics Board.

### *Patient selection*

The primary focus of the study was patients with CRC liver metastases; however, patients with any hepatic malignancy were considered eligible. Patients with liver tumors other than colorectal metastases were considered eligible in order to boost the sample sizes and to allow this pilot study to better explore a hypothesis regarding the cost-utility of liver resection and RFA. These patients were considered eligible because the costs of treatment and the QOL over the time-frame of this study were not expected to be significantly different from those with colorectal metastases. The survival data for these patients were not included in the analysis (see below). All new patients referred to a medical oncology department or to a hepatobiliary surgeon (M.T.) between June 2001 and December 2002 were eligible.

### *Treatment and follow-up*

Patients determined which treatments they wished to pursue based on their physicians' best clinical judgment and the patients' wishes and then informed consent was obtained. Patients were followed up to 2 years after enrolment or until the end of the study period (September 2003).

Patients undergoing either surgical resection or RFA were treated by a single surgeon (M.T.). All patients who underwent laparotomy had a preoperative magnetic resonance imaging (MRI) scan in addition to a computed tomography (CT) scan and any other imaging that was done. Patients who were candidates for liver resection were offered the procedure. RFA was offered to patients who were still operative candidates, but had disease that was considered unresectable on the basis of multifocal disease, proximity

to major vascular structures, poor liver reserve, or poor overall medical condition. RFA was performed using the RF 3000<sup>®</sup> Radiofrequency Ablation System (Boston Scientific) at the time of open laparotomy with real-time intraoperative ultrasound (IOUS) guidance. These patients were also considered for adjuvant chemotherapy at the discretion of the medical oncologists. Patients undergoing chemotherapy were assigned to receive one of four chemotherapeutic regimens at the discretion of the treating oncologist: single agent irinotecan, 5-fluorouracil (5-FU) and leucovorin (LV), irinotecan plus 5-FU and LV, or single agent capecitabine.

### *Cost-utility analysis*

This paper has followed the recommendations of the US Panel on Cost-Effectiveness in Health and Medicine [10–12]. QOL was measured by the Health Utilities Index Mark II (HUI2) and Mark III (HUI3), although the HUI3 was used primarily in the cost-utility analysis. The questionnaire was administered to the participants at entry into the study and then at 2 weeks, 3 months, 6 months, 9 months, 12 months, and 18 months after commencing treatment.

Costs (not hospital charges) were measured from the perspective of society as a whole in 2001 Canadian dollars and included the medical resources consumed, the non-medical resources consumed, and the loss of productivity associated with illness or disability. (The term 'productivity costs' has been suggested to refer to these costs [11,13].) Inpatient costs were captured by the hospital's cost-accounting system [14]. Costs from the operating room (OR) were acquired by prospectively tracking the resources consumed in the OR during each case. Overhead costs were calculated to be 16.5% of the total variable hospital costs, based on a previous publication [15]. Costs of delivering chemotherapy were calculated using a case-mix group approach, by calculating the cost of a cycle of each chemotherapeutic regimen and then measuring the costs for each patient based on the number of cycles of the particular chemotherapy regimens received. The cost of blood products was taken from another study [16] and adjusted to 2001 dollars [17]. Costs paid by patients and caregivers including time spent seeking and receiving treatment, travel costs, and drug costs were recorded by patients in diaries that were collected at follow-up visits.

A cost-utility analysis was performed by creating a Markov decision analysis model (see Figure 1) using the computer software Data 3.5<sup>©</sup> (Treeage Software, Inc., 1999). The time-frame of the analysis was 5 years. Survival data were taken from existing literature since the numbers in the current study were small, and then converted to quality-adjusted life years (QALYs) using the utility scores. The annual inflation rate used in the baseline analysis was 1.96% [18] and the discount rate was 3% [11,13].

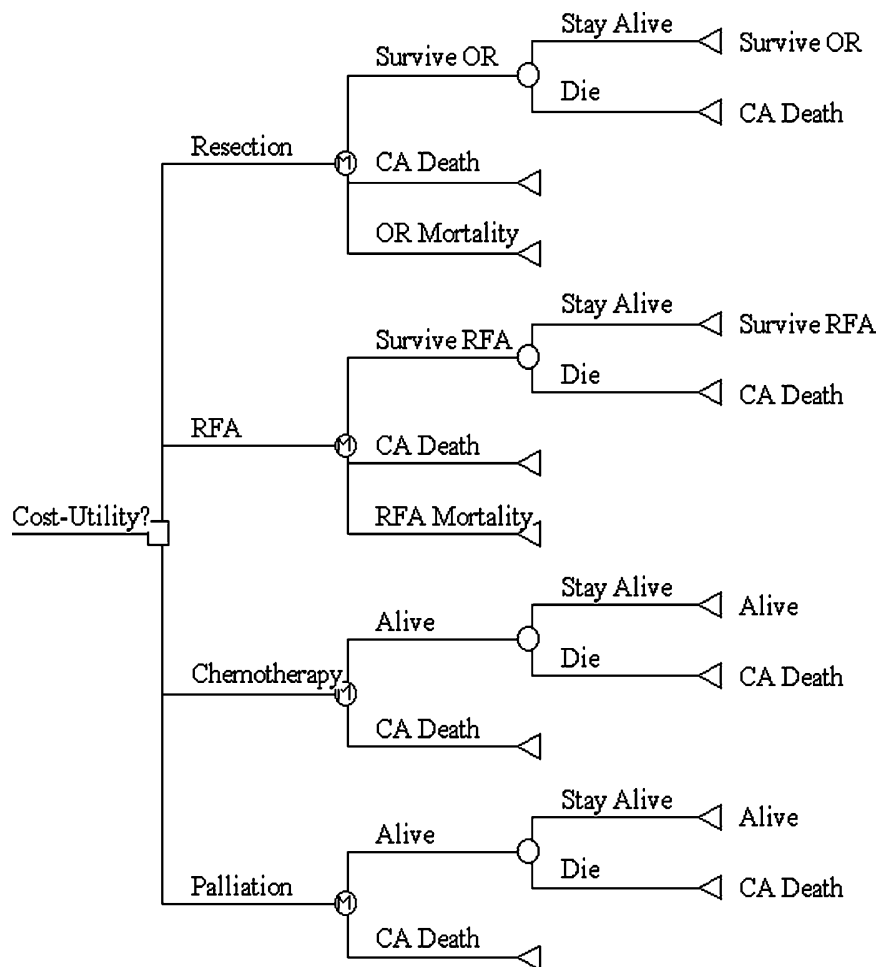


Figure 1. Representation of Markov decision model in the format used by Data 3.5©.

### Statistical analysis

The sample was one of convenience. Formal power calculations were not performed because this study was not designed to draw firm conclusions, but to develop hypothesis data. Continuous variables were analyzed with the Mann-Whitney U test. For categorical variables, the Fisher's exact test was used. When testing for differences in QOL over time, repeated measures ANOVA was used. Statistical significance was defined using  $p=0.05$ . The statistical analysis was performed using SPSS® Base 14.0 for Windows®.

## Results

### Patient characteristics

Forty patients were recruited: 7 underwent hepatic resection, 7 underwent RFA (4 had RFA in combination with resection), 20 received systemic chemotherapy, and 6 received symptom control alone. Patient characteristics are shown in Table I, and the characteristics of the patients undergoing surgical treatments (resection and RFA) are shown in Tables II and III. Patient characteristics were generally similar

between groups in terms of age, gender, and types of tumors, with no significant differences. Patients who underwent RFA had a greater number of liver lesions than patients who underwent liver resection ( $p < 0.01$ ). Patients who received chemotherapy as the primary treatment had more lesions than patients receiving other treatments ( $p < 0.05$ ).

### Treatment and follow-up

Unfortunately, several patients either withdrew or were lost to follow-up. One patient who underwent resection (1 of 7), one patient who received RFA (1 of 7), three patients who received chemotherapy (3 of 20), and three who elected to receive symptom control alone (3 of 6) were either lost to follow-up or withdrew from the study.

For the majority of patients who underwent surgical procedures, the planned procedure was performed. Three patients who underwent hepatic resection, three patients who underwent RFA, and two patients who initially decided to receive symptom control alone also received systemic chemotherapy. Three patients in the group receiving chemotherapy as the primary treatment had an initial exploratory

Table I. Characteristics of overall study population.

Category		Overall	Resection	RFA	Chemotherapy	Palliative care
<i>n</i>		40	7	7	20	6
Age	Mean	64.4	66.6	57.9	63.4	73.2
	SD	11.1	10.8	12.1	11.3	4.7
Male:female	Male	29	6	5	12	6
	Female	11	1	2	8	0
No. of lesions*	≤3	19	7	3	4	5
	>3	19	0	4	14	1
Tumour type*	Colorectal	32	5	6	17	4
	Other	8	2	1	3	2
Time of metastases*	Synchronous	17	3	4	7	3
	Metachronous	18	4	2	10	2
Extrahepatic disease*	Yes	7	0	1	4	2
	No	30	7	6	14	3
ASA score*	Value	2.61	2.71	2.43	2.70	3.00
	<i>n</i>	28	7	7	10	2

\*For some categories, information was not available for all patients.

laparotomy with the intent to perform hepatic resection or RFA, but exploration and intraoperative ultrasound (IOUS) found inoperable disease that was not detected on preoperative imaging. These costs were included in the analysis.

#### Cost-utility analysis

Survival data were taken from existing literature. For resection of colorectal liver metastases, a recent review of all large case series reported a 5-year survival of 34% and a mortality rate of 3.3% [5]. For RFA, only one study has so far reported 5-year survival (30%) [19]. The simple averages of the 1-, 2-, and 3-year survival figures from other available series are 90.2%, 66.5%, and 48.3%, respectively [19–26]. The mean of reported mortality rates from two large series was 0.8% [27,28]. For systemic chemotherapy, the survival data used in the analysis were taken from two recent randomized controlled trials (RCTs) involving irinotecan, 5-FU, and leucovorin, where the median survival was 14.8 months to 17.4 months [29,30]. The survival beyond 1 year was modeled, using a logarithmic survival curve. For symptom control alone, the survival data for this group of patients came from previously published studies [31–37]. Simple averages of the reported survival rates for ‘all comers’ at 1, 2, 3, and 5 years are 31%, 10%, 3%, and 1%, respectively.

The initial costs for patients who underwent hepatic resection or RFA were similar (Tables IV and V). Surgeons’ fees and anesthesiologists’ fees were included in the OR costs, while the radiologists’ fees were included in the costs of the diagnostic imaging.

The average initial treatment costs for patients receiving systemic chemotherapy and for patients receiving symptom control alone were \$439 and

\$500, respectively. These costs included the costs of the initial consultation, the costs involved in the diagnostic work-up, and the costs associated with exploratory laparotomy. The cost of receiving chemotherapy for all patients was entered into the cost-utility model as a function of time (Table VI).

QOL is shown in Figure 2. For patients who underwent surgical treatments (hepatic resection or RFA) QOL scores decreased for the first few months postoperatively. The health attribute of pain was largely responsible for this postoperative decrease in QOL. Overall and marginal cost-utility ratios are presented in Figures 3 and 4.

Sensitivity analysis showed that the results were sensitive to the magnitude of the utility scores, the survival associated with each treatment, and the costs of hepatic resection, RFA, and chemotherapy. However, over a wide range of values, uncertainty in these costs and effects changed the magnitudes of the cost-utility ratios, but not the relative ranking of the treatments.

#### Discussion

There are many limitations to the present study, since it was not designed to draw firm conclusions, but to explore a hypothesis that the cost-utilities of hepatic resection and RFA might be similar enough to one day justify a randomized trial. The accrual rate was lower than anticipated and the sample size is small. The study compared patients with different stages of disease, since patients with resectable disease were offered surgery. Patients receiving chemotherapy seemed to have the most advanced disease. Those receiving RFA were considered to have unresectable disease and had significantly more lesions than the patients undergoing hepatic resection. RFA was sometimes used in combination with resection to

Table II. Characteristics of patients undergoing hepatic resection.

Gender	Age (years)	Tumor type	No. of liver lesions	Timing of lesion	Location	Extrahepatic disease	Type of resection	Chemotherapy	Comorbid disease	ASA score
M	61	Rectal	1	Metachronous	Right lobe (segment 6)	No	Wedge	No	COPD	3
M	72	GIST	1	Metachronous	Right lobe (segment 8)	No	Wedge	Yes	DM II	2
M	61	Colon	1	Synchronous	Left lobe (segment 2)	No	Wedge	Yes	COPD, obesity	3
M	48	Testicular	1	Synchronous	Right lobe	No	Right lobe	Yes	HTN	3
M	74	Colon	1	Synchronous	Right lobe	No	Wedge	No	HTN	3
M	69	Rectal	1	Metachronous	Right lobe	No	Wedge	No	HTN, DM II	2
F	81	Colon	1	Metachronous	Left lobe	No	Wedge	No	Nil	3

COPD, chronic obstructive pulmonary disease; DM II, type II diabetes mellitus; HTN, hypertension.

Table III. Characteristics of patients undergoing radiofrequency ablation (RFA).

Gender	Age (years)	Tumour type	No. of liver lesions	Timing of lesion	Location	Extrahepatic disease	Treatment	Chemotherapy	Comorbid disease	ASA score
F	42	Rectal	4	Synchronous	Right lobe	Yes	RFA	No	Nil	2
F	77	Rectal	2	Metachronous	Left + right lobes	No	Resection & RFA	No	DM II, HTN, breast CA	3
M	63	Colon	2	Synchronous	Left + right lobes	No	Resection & RFA	Yes	HTN	2
M	64	Rectal	4	Synchronous	Left + right lobes	No	Resection & RFA	Yes	DM II	2
M	50	HCC	1	NA	Right lobe	No	RFA	No	HCV, HTN, DMII	3
M	60	Rectal	4	Metachronous	Left + right lobes	No	Resection & RFA	No	Nil	3
M	49	Colon	4	Synchronous	Right lobe	No	RFA	Yes	Nil	2

DM II, type II diabetes mellitus; HTN, hypertension; HCV, hepatitis C virus.

Table IV. Initial hospital costs of treatment for patients undergoing liver resection and RFA.

Category	Resection		RFA		<i>p</i> value
	Average	SD	Average	SD	
LOS*	7.3	2.0	6.4	1.7	0.60
Nursing	\$1860.86	\$676.50	\$1608.77	\$456.52	0.66
Lab fees	\$171.83	\$36.61	\$128.30	\$72.26	0.23
Imaging	\$324.37	\$49.46	\$485.81	\$134.99	0.09
Medications	\$115.71	\$69.57	\$86.48	\$67.65	0.34
Other	\$267.28	\$118.07	\$156.76	\$81.43	<0.05
OR costs	\$2907.72	\$517.52	\$3131.98	\$907.65	0.66
Overhead	\$424.74	\$134.12	\$370.56	\$110.91	0.66
Total	\$6064.61	\$1220.75	\$5971.23	\$1142.73	0.66

\*Length of stay in hospital (measured in days).

extend the capabilities of surgical resection. Patients who underwent a combination of RFA and liver resection were grouped with patients who underwent RFA alone, since it was hypothesized that RFA would be less effective than hepatic resection and that the effectiveness of RFA would be the major determinant of survival. Patients with non-colorectal cancers were included since the costs of their treatments and their QOL afterwards were expected to be reasonably similar to those with colorectal cancers and would help explore the hypothesis of the study.

In cost-effectiveness analysis, not every variable must be measured with absolute certainty [13]. Error in certain measurements may not influence the overall results. It may be more important to obtain a reasonable range of values and then test the influence of this uncertainty and the robustness of the conclusions with a sensitivity analysis. The most robust conclusions are those that hold true over a wide range of values. The sensitivity analyses in this study showed that uncertainty in these costs and effects would change the magnitudes of the cost-utility ratios, but not the overall rankings of the treatments and the general conclusions.

The QOL measured in this study appears accurate, as it is consistent with measurements by others [38]. Patients who underwent hepatic resection and RFA

had quite good long-term QOL. In the period shortly after surgery these scores dropped, mainly due to postoperative pain, but after 3–6 months the scores returned to baseline or higher for most patients. QOL in patients treated with systemic chemotherapy remained reasonably high for the first 12 months of treatment. Disease invariably progresses with systemic chemotherapy, and this is the likely explanation for the eventual decline. The patients who elected to receive symptom control alone had quite high utility scores, suggesting that the absence of treatment-related side effects may be important, although a third of these patients did choose to receive chemotherapy during the course of their disease.

To put these scores into a clinical perspective, the mean HUI3 utility scores for people considered to be in good health and without chronic medical conditions taken from a population-based sample of over 17 000 Canadians was 0.93 [39], and utility for patients with various chronic conditions ranged from 0.54 to 0.83 [39,40].

The initial costs of hepatic resection and RFA were similar and there were no significant differences in mean operating time or hospital stay. The OR costs found in this study were similar to other Canadian results [41], again supporting the accuracy of our results. The costs of hepatic resection and of RFA in

Table V. Cost of surgery for patients undergoing hepatic resection and RFA.

Category	Resection		RFA		<i>p</i> value
	Average	SD	Average	SD	
OR time (min)	291	77	279	61	0.70
OR staffing	\$477.68	\$126.26	\$457.54	\$99.90	0.70
Supply costs	\$549.98	\$181.89	\$1107.10	\$833.15	0.14
PARR costs*	\$58.96	\$21.91	\$53.30	\$15.49	0.75
Overhead	\$179.29	\$40.62	\$304.25	\$235.96	0.28
MD fees†	\$1641.81	\$324.23	\$1553.80	\$211.71	0.48
Total	\$2907.72	\$517.52	\$3131.98	\$907.75	0.85

\*Post anesthesia recovery room costs.

†MD fees include the fees paid to the surgeons and to the anesthetists.

Table VI. Costs for chemotherapy in patients undergoing other primary treatment modalities.

Treatment	No. receiving chemotherapy	Months until chemotherapy started	Months until chemotherapy stopped	Average total cost	No. of months treated	Cost per month*
Resection	3 of 7	9.7	5.0	\$6008.19	5.0	\$1003.72
RFA	3 of 7	3.7	9.3	\$17 842.87	9.3	\$830.89
Chemotherapy	20 of 20	0.5	11.2	\$21 581.45	11.2	\$1979.27
Palliative care	2 of 6	4.0	5.3	\$1020.97	5.3	\$478.22

\*Cost per month refers to the cost per month for those months when chemotherapy was given. These costs were inputted into the cost-utility model only for the average period of time when patients received their chemotherapy.

the Canadian setting are much lower than reported from American studies (\$23 317 US dollars in 1998 for liver resection) [42,43], likely reflecting fundamental differences in the healthcare systems. Thus, caution must be used when applying the economic data of this study to other healthcare systems (and vice versa).

In this study, RFA was done through a laparotomy. The costs of percutaneous RFA would probably be lower, but there are several reasons as to why this was not done in the current study. Four patients underwent RFA in conjunction with hepatic resection in order to expand the capabilities of resection alone. These patients would have needed a laparotomy regardless. Another reason is that the sensitivity of IOUS is higher than that of other preoperative imaging modalities to detect hepatic lesions. IOUS has been shown to alter decision-making in the operating room in 18–44% of cases [44–46]. Elias et al. found unsuspected metastases in 41% of patients who underwent hepatectomy for CRC liver metastases that would not have been treated with percutaneous techniques [47]. Another advantage of an open surgical approach is the ability to occlude hepatic inflow when tumors are adjacent to major vascular structures to increase the likelihood of

complete tumor necrosis [7]. Tumors abutting the diaphragm are not always amenable to a percutaneous approach [7]. If patients were to undergo RFA in the outpatient setting, we would anticipate a significant difference between the cost of resection and RFA, although it is possible that the effectiveness would suffer.

The costs of chemotherapy were considerable, even in patients undergoing surgical procedures. Because treatment of cancer involves a multidisciplinary approach with specialists from different backgrounds, it was felt that the costs of providing chemotherapy to patients undergoing surgery or symptom control should be included in the analysis, as this approximates what is done in clinical practice. If the benefits of adjuvant treatment are included, the costs should be as well.

Another shortcoming of this study is that subsequent hospitalizations for disease recurrence or treatment complications may have occurred in other hospitals or after the study period ended. The costs of these hospitalizations would not have been captured.

The cost-utility of hepatic resection and radio-frequency ablation appear similar. Resection appeared to offer a greater quality-adjusted survival than RFA,

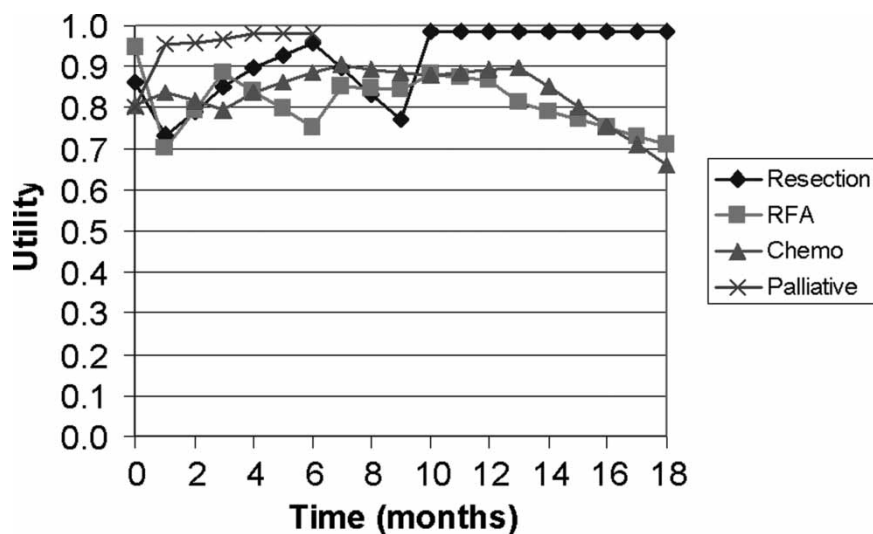


Figure 2. Health Utilities Mark III scores for all treatments.

		<u>Total Cost</u>	<u>Effect</u>	<u>C/E Ratio</u>
Cost-Utility?	Resection	\$20,122	2.58 QALY's	7,792 \$/QALY
	RFA	\$15,730	1.95 QALY's	8,056 \$/QALY
	Chemotherapy	\$15,069	1.18 QALY's	12,751 \$/QALY
	Palliation	\$3,899	0.82 QALY's	4,778 \$/QALY

Figure 3. Overall cost-utility ratios of available treatments for malignant liver tumors using HUI3 data.

but at a higher cost. In addition to overall cost-utility, the marginal cost-utility is important when deciding between alternative treatments. Marginal cost-utility refers to the incremental difference in cost and in effectiveness between two alternative treatments, rather than a simple comparison of the overall cost-utilities. Compared to symptom control alone, systemic chemotherapy had a marginal cost-utility ratio of \$30 537 per QALY. RFA offered a greater number of QALYs than chemotherapy at only a slightly increased cost, yielding a very favorable marginal cost-utility of \$858 per QALY. Hepatic resection had a marginal cost-utility ratio of \$6974 per QALY compared to RFA, which is again quite favorable [9]. Hepatic resection demonstrated a marginal cost-utility ratio of \$3609 per QALY compared to systemic chemotherapy.

The US Panel recommends that health consequences be measured with generic health-state classification systems that express QOL in terms of utilities that are based on community preferences, and that the utility measurements can then be converted to QALYs [11]. The Health Utilities Index was chosen for this study since it fulfils these criteria [48–50]. Another advantage of describing QOL with utility scores is that it allows comparisons across diseases and between studies [11].

Another major assumption necessitated by the limited follow-up period was that the QOL scores for patients surviving longer than 2 years were assumed to be stable after the last measurement at 18 months. The HUI scores were composed of patients who were recurrence-free, patients experien-

cing recurrence, and patients experiencing side effects of the treatments. Thus, these scores would likely reflect the effects of disease recurrence in the future beyond the time-frame of the study.

The purpose of this study was not to draw firm conclusions comparing these treatment options for liver metastases from colorectal cancer, but to explore a hypothesis regarding the feasibility of future comparisons of RFA to hepatic resection. Even with supporting evidence that the cost-utilities may be similar, the long-term survival associated with RFA is still largely unknown and would need to be evaluated before a randomized trial could ethically be carried out. Because RFA cannot be considered an equivalent treatment to liver resection at present, the existing trials have consisted of patients with unresectable disease. In spite of this, some early studies have reported survival similar to that of resection [21–23]. Others have been less enthusiastic [25], so longer-term follow-up is essential.

## Conclusions

The QOL associated with both hepatic resection and RFA appears quite good, and the cost-utility of hepatic resection and RFA for colorectal liver metastases appears similar. The cost-utility ratio of systemic chemotherapy is higher, but still well within the range of what is considered to be medically and economically acceptable [9]. Should the long-term survival benefit of RFA prove to be close to that of hepatic resection, this study would offer support for a randomized trial comparing the two treatments in the future.

		<u>Marginal Cost</u>	<u>Marginal Effect</u>	<u>Marginal C/E</u>
Cost-Utility?	Resection	\$4,391	0.63 QALY's	6,974 \$/QALY
	RFA	\$661	0.77 QALY's	858 \$/QALY
	Chemotherapy	\$11,170	0.37 QALY's	30,537 \$/QALY
	Palliation			

Figure 4. Marginal cost-utility ratios of available treatments for malignant liver tumours using HUI3 data. The marginal cost-utility ratios are given for the next most effective treatment in each case. The marginal cost-utility ratio of chemotherapy is compared to symptom control alone; the marginal cost-utility ratio of RFA is compared to chemotherapy; and the marginal cost-utility ratio of hepatic resection is compared to RFA.



## Acknowledgements

We would like to thank Vivian Painter at CancerCare Manitoba and Janelle Zajakowski at the St Boniface General Hospital for their invaluable assistance with the cost analysis, as well as Carla Pindera for her help with the initial design and implementation.

## References

- [1] Tandan VR, Harmantas A, Gallinger S. Long-term survival after hepatic cryosurgery versus surgical resection for metastatic colorectal carcinoma: a critical review of the literature. *Can J Surg* 1997;40:175–81.
- [2] Silen W. Hepatic resection for metastases from colorectal carcinoma is of dubious value. *Arch Surg* 1989;124:1021–2.
- [3] Millikan KW, Staren ED, Doolas A. Invasive therapy of metastatic colorectal cancer to the liver. *Surg Clin North Am* 1997;77:27–48.
- [4] Yoon SS, Tanabe KK. Surgical treatment and other regional treatments for colorectal cancer liver metastases. *Oncologist* 1999;4:197–208.
- [5] Yasui K, Shimizu Y. Surgical treatment for metastatic malignancies. Anatomical resection of liver metastasis: indications and outcomes. *Int J Clin Oncol* 2005;10:86–96.
- [6] Hurwitz H, Fehrenbacher L, Novotny W, Cartwright T, Hainsworth J, Heim W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med* 2004;350:2335–42.
- [7] Curley SA. Radiofrequency ablation of malignant liver tumors. *Oncologist* 2001;6:14–23.
- [8] Ng KK, Poon RT. Radiofrequency ablation for malignant liver tumor. *Surg Oncol* 2005;14:41–52.
- [9] Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *CMAJ* 1992;146:473–81.
- [10] Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. *JAMA* 1996;276:1172–7.
- [11] Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. *JAMA* 1996;276:1253–8.
- [12] Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. Panel on Cost-Effectiveness in Health and Medicine. *JAMA* 1996;276:1339–41.
- [13] Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes, 2nd edn. New York: Oxford University Press; 1997.
- [14] Patient based accounting & budgeting: hospital management & clinical support software. Somerset, NJ: Network Inc.
- [15] Finlayson G, Roos N, Jacobs P, Watson D. Using the Manitoba Hospital Management Information System: comparing average cost per weighted case and financial ratios of Manitoba Hospitals. The next step. Department of Community Health Sciences, Faculty of Medicine, University of Manitoba: Manitoba Centre for Health Policy and Evaluation, 2001.
- [16] Tretiak R, Laupacis A, Riviere M, McKerracher K, Souetre E. Cost of allogeneic and autologous blood transfusion in Canada. Canadian Cost of Transfusion Study Group. *CMAJ* 1996;154:1501–8.
- [17] Statistics Canada. CANSIM. Table 326-0002 and Catalogue nos 62-001-X, 62-010-X and 62-557-X. 29-7-2005.
- [18] Statistics Canada. Consumer Price Index for Canada, Monthly/Health and Personal Care. CANSIM, 2005.
- [19] Gillams AR, Lees WR. Radiofrequency ablation of colorectal liver metastases. *Abdom Imaging* 2005;30:419–26.
- [20] Solbiati L, Goldberg SN, Ierace T, Livraghi T, Meloni F, Dellanoce M, et al. Hepatic metastases: percutaneous radiofrequency ablation with cooled-tip electrodes. *Radiology* 1997;205:367–73.
- [21] Solbiati L, Livraghi T, Goldberg SN, Ierace T, Meloni F, Dellanoce M, et al. Percutaneous radio-frequency ablation of hepatic metastases from colorectal cancer: long-term results in 117 patients. *Radiology* 2001;221:159–66.
- [22] Iannitti DA, Dupuy DE, Mayo-Smith WW, Murphy B. Hepatic radiofrequency ablation. *Arch Surg* 2002;137:422–6.
- [23] Oshowo A, Gillams A, Harrison E, Lees WR, Taylor I. Comparison of resection and radiofrequency ablation for treatment of solitary colorectal liver metastases. *Br J Surg* 2003;90:1240–3.
- [24] White TJ, Roy-Choudhury SH, Breen DJ, Cast J, Maraveyas A, Smyth EF, et al. Percutaneous radiofrequency ablation of colorectal hepatic metastases – initial experience. An adjunct technique to systemic chemotherapy for those with inoperable colorectal hepatic metastases. *Dig Surg* 2004;21:314–20.
- [25] Abdalla EK, Vauthey JN, Ellis LM, Ellis V, Pollock R, Broglio KR, et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Ann Surg* 2004;239:818–25.
- [26] Joosten J, Jager G, Oyen W, Wobbes T, Ruers T. Cryosurgery and radiofrequency ablation for unresectable colorectal liver metastases. *Eur J Surg Oncol* 2005;31:1152–9.
- [27] de Baere T, Risse O, Kuoch V, Dromain C, Sengel C, Smayra T, et al. Adverse events during radiofrequency treatment of 582 hepatic tumors. *AJR Am J Roentgenol* 2003;181:695–700.
- [28] Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. *Radiology* 2003;226:441–51.
- [29] Saltz LB, Cox JV, Blanke C, Rosen LS, Fehrenbacher L, Moore MJ, et al. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. Irinotecan Study Group. *N Engl J Med* 2000;343:905–14.
- [30] Douillard JY, Cunningham D, Roth AD, Navarro M, James RD, Karasek P, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. *Lancet* 2000;355:1041–7.
- [31] Bengtsson G, Carlsson G, Hafstrom L, Jonsson PE. Natural history of patients with untreated liver metastases from colorectal cancer. *Am J Surg* 1981;141:586–9.
- [32] Wagner JS, Adson MA, Van Heerden JA, Adson MH, Ilstrup DM. The natural history of hepatic metastases from colorectal cancer. A comparison with resective treatment. *Ann Surg* 1984;199:502–8.
- [33] Arnaud JP, Dumont P, Adloff M, Leguillou A, Py JM. Natural history of colorectal carcinoma with untreated liver metastases. *Surg Gastroenterol* 1984;3:37–42.
- [34] Stangl R, Altendorf-Hofmann A, Charnley RM, Scheele J. Factors influencing the natural history of colorectal liver metastases. *Lancet* 1994;343:1405–10.
- [35] Scheele J, Stangl R, Altendorf-Hofmann A. Hepatic metastases from colorectal carcinoma: impact of surgical resection on the natural history. *Br J Surg* 1990;77:1241–6.
- [36] Luna-Perez P, Rodriguez-Coria DF, Arroyo B, Gonzalez-Macouzet J. The natural history of liver metastases from colorectal cancer. *Arch Med Res* 1998;29:319–24.
- [37] Gorog D, Toth A, Weltner J. Prognosis of untreated liver metastasis from rectal cancer. *Acta Chir Hung* 1997;36:106–7.

- [38] Ramsey SD, Andersen MR, Etzioni R, Moinpour C, Peacock S, Potosky A, et al. Quality of life in survivors of colorectal carcinoma. *Cancer* 2000;88:1294–303.
- [39] Mittmann N, Trakas K, Risebrough N, Liu BA. Utility scores for chronic conditions in a community-dwelling population. *Pharmacoeconomics* 1999;15:369–76.
- [40] Grootendorst P, Feeny D, Furlong W. Health Utilities Index Mark 3: evidence of construct validity for stroke and arthritis in a population health survey. *Med Care* 2000;38:290–9.
- [41] Jacobs P, Shanahan M, Roos N, Farnsworth M. Cost list for Manitoba Health Services. Department of Community Health Sciences, Faculty of Medicine, University of Manitoba: Manitoba Centre for Health Policy and Evaluation, 1999.
- [42] Gazelle GS, Hunink MG, Kuntz KM, McMahon PM, Halpern EF, Beinfeld M, et al. Cost-effectiveness of hepatic metastasectomy in patients with metastatic colorectal carcinoma: a state-transition Monte Carlo decision analysis. *Ann Surg* 2003;237:544–55.
- [43] Gazelle GS, McMahon PM, Beinfeld MT, Halpern EF, Weinstein MC. Metastatic colorectal carcinoma: cost-effectiveness of percutaneous radiofrequency ablation versus that of hepatic resection. *Radiology* 2004;233:729–39.
- [44] Zacherl J, Scheuba C, Imhof M, Zacherl M, Langle F, Pokosier P, et al. Current value of intraoperative sonography during surgery for hepatic neoplasms. *World J Surg* 2002;26:550–4.
- [45] Cervone A, Sardi A, Conaway GL. Intraoperative ultrasound (IOUS) is essential in the management of metastatic colorectal liver lesions. *Am Surg* 2000;66:611–5.
- [46] Conlon R, Jacobs M, Dasgupta D, Lodge JP. The value of intraoperative ultrasound during hepatic resection compared with improved preoperative magnetic resonance imaging. *Eur J Ultrasound* 2003;16:211–6.
- [47] Elias D, Sideris L, Pocard M, de Baere T, Dromain C, Lassau N, et al. Incidence of unsuspected and treatable metastatic disease associated with operable colorectal liver metastases discovered only at laparotomy (and not treated when performing percutaneous radiofrequency ablation). *Ann Surg Oncol* 2005;12:298–302.
- [48] Feeny D, Furlong W, Boyle M, Torrance GW. Multi-attribute health status classification systems. *Health Utilities Index. Pharmacoeconomics* 1995;7:490–502.
- [49] Furlong WJ, Feeny DH, Torrance GW, Barr RD. The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. *Ann Med* 2001;33:375–84.
- [50] Torrance GW, Furlong W, Feeny D, Boyle M. Multi-attribute preference functions. *Health Utilities Index. Pharmacoeconomics* 1995;7:503–20.