Use of a Decision Analysis Model to Assess the Cost-Effectiveness of ^{18}F-FDG PET in the Management of Metachronous Liver Metastases of Colorectal Cancer

Catherine Lejeune, PhD[1,2]; Marie J. Bismuth, MD[3]; Thierry Conroy, MD[4,5]; Catherine Zanni, MD[6]; Pierre Bey, MD[7]; Laurent Bedenne, MD[8]; Jean Faivre, MD[1,2]; Patrick Arveux, MD, PhD[1,2,9]; and Francis Guillemin, MD, PhD[5]

[1]INSERM EMI (Equipe Mixte INSERM) 0106, Dijon, France; [2]Université de Bourgogne, Faculté de Médecine, Dijon, France; [3]CHU de Dijon, Département d'Information Médicale, Dijon, France; [4]Centre de Lutte Contre le Cancer Alexis Vautrin Département d'Oncologie Médicale, Vandoeuvre les Nancy, France; [5]Université Henri Poincaré, Faculté de Médecine, EA (Equipe d'Accueil) 3444, Nancy, France; [6]Caisse Nationale d'Assurance Maladie des Travailleurs Salariés, Direction Régionale du Service Médical (CNAMTS-DRSM) de Bourgogne Franche-Comté, Dijon, France; [7]Institut Curie, Paris, France; [8]Université de Bourgogne, Faculté de Médecine, Fédération Francophone de Cancérologie Digestive (FFCD), Dijon, France; and [9]Centre de Lutte Contre le Cancer Georges-François Leclerc, Département d'Information Médicale, Dijon, France

Few data exist on the medicoeconomic usefulness of PET in the management of metachronous liver metastases from colorectal cancer. This study was designed to assess the cost-effectiveness of PET in the diagnosis and staging of patients with metachronous liver metastases of colorectal cancer using a decision analysis model. **Methods:** Two alternatives were compared: CT and CT associated with PET (CT + PET). Transition probabilities were estimated from published data and consultations with experts. Survival data were provided by the Burgundy Digestive Cancer Registry (France). Costs of imaging techniques and treatments were assessed using reimbursements from the French health care insurance for the year 2004. Evaluation criteria included incremental cost-effectiveness ratios and the proportion of unnecessary operations avoided in patients without metachronous liver metastases. **Results:** CT + PET was the most cost-effective strategy, presenting an expected incremental cost saving of 2,671 € (~$3,213) per patient, for the same level of expected effectiveness as CT alone (1.88-y life expectancy per patient). Sensitivity analyses performed on epidemiologic and economic parameters showed that this model was robust. The model also suggested that CT + PET could avoid exploratory surgery for 6.1% of patients—that is, 88.4% risk reduction compared with CT alone. **Conclusion:** PET for diagnosis and staging does not generate additional survival effectiveness compared with CT alone. However cost savings associated with its use and the improvement of therapeutic management therefore justify its generalization in clinical practice.

Key Words: PET; metachromous metastases; decision modeling; cost-effectiveness; program evaluation

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Colorectal cancer (CRC) is one of the most frequent cancers in France, with >36,000 new cases every year (*1*). About 80% of patients undergo primary tumor resection for cure (*2*). After curative resection, recurrence develops in approximately 30%–40% of patients (*3*). The liver is the most common site of recurrence, metachronous liver metastases, affecting 15%–25% of patients during the first 5 y after curative resection (*4*). Liver resection is potentially curative for patients with metachronous liver metastases. However, this involves about 30% of patients (*4*). The best candidates for resection are patients with <4 metastases, under 5 cm in size, and without extrahepatic dissemination (*5,6*). Therefore, accurate assessment of patients with metachronous liver metastases is essential in defining the appropriate treatment and in avoiding inappropriate surgery. CT is one of the preoperative investigation techniques. However, it may fail in detecting small lesions and extrahepatic dissemination and can be inaccurate in differentiating benign from malignant lesions (*7,8*). ^{18}F-FDG PET, a scintigraphic imaging technique, relies on increased rates of glucose metabolism in malignant cells. Available data suggest that this can be a valuable tool for the detection and staging of recurrent CRC (*9,10*). At present, 60 PET facilities have received authorization for implementation in France. To be generalized on a national scale, any new technique must prove to be more effective and cost-effec-

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For correspondence or reprints contact: Catherine Lejeune, PhD, INSERM EMI 0106, Faculté de Médecine, BP 87900, 21079 Dijon Cedex, France.
E-mail: catherine.lejeune@u-bourgogne.fr.

tive compared with previous strategies. However, the costs and health outcomes associated with PET in addition to CT in clinical practice for CRC have not been assessed in the French clinical and economic context. Two cost-effectiveness analyses based on decision analysis models suggested that CT + PET was cost-effective and a suitable strategy (*11,12*). However, these findings cannot necessarily be extrapolated to the French context because of possible variations in clinical practice and approaches to pricing and reimbursement.

The purpose of this article was to compare the cost-effectiveness of standard imaging techniques with and without PET in the management of metachronous liver metastases from the French health care system insurance perspective using a decision analysis model.

MATERIALS AND METHODS

Base Case

Using data issued from the Burgundy Digestive Cancer Registry, the base case was considered to be a 68-y-old individual who had previously undergone resection for CRC, with suspected metachronous liver metastases. Metachronous metastases were defined as lesions diagnosed during the follow-up after the resection of the primary tumor by abdominal ultrasonography.

General Description of Model

A decision analysis tree representing the management of metachronous liver metastases was built. In this decision tree, strategies to be compared originated from a decision node. Strategies comprised sequences of clinical events with associated estimated transitional probabilities. These sequences were constructed from data issued from published literature and then validated by a committee of multidisciplinary experts composed of surgeons, oncologists, and gastroenterologists. At the end of each alternative arm of the tree, payoffs were assigned corresponding to the total cost of care (diagnosis + staging + treatment) and life expectancy in years. The expected life expectancy and the expected cost of care associated with each strategy were estimated by weighting life expectancies and costs of each arm of the decision tree by the probability that a patient experiences a clinical event. TreeAge 3.5 data software (TreeAge, Inc.) were used to construct and analyze the decision tree.

Strategies

To decide on the treatment strategy, lesion characteristics must be accurately assessed. In this context, 2 alternative strategies were modeled. The first consisted of CT of the thorax, abdomen, and pelvis (CT) (Fig. 1) and the second consisted of initial CT of the thorax, abdomen, and pelvis followed by PET (CT + PET) (Fig. 2).

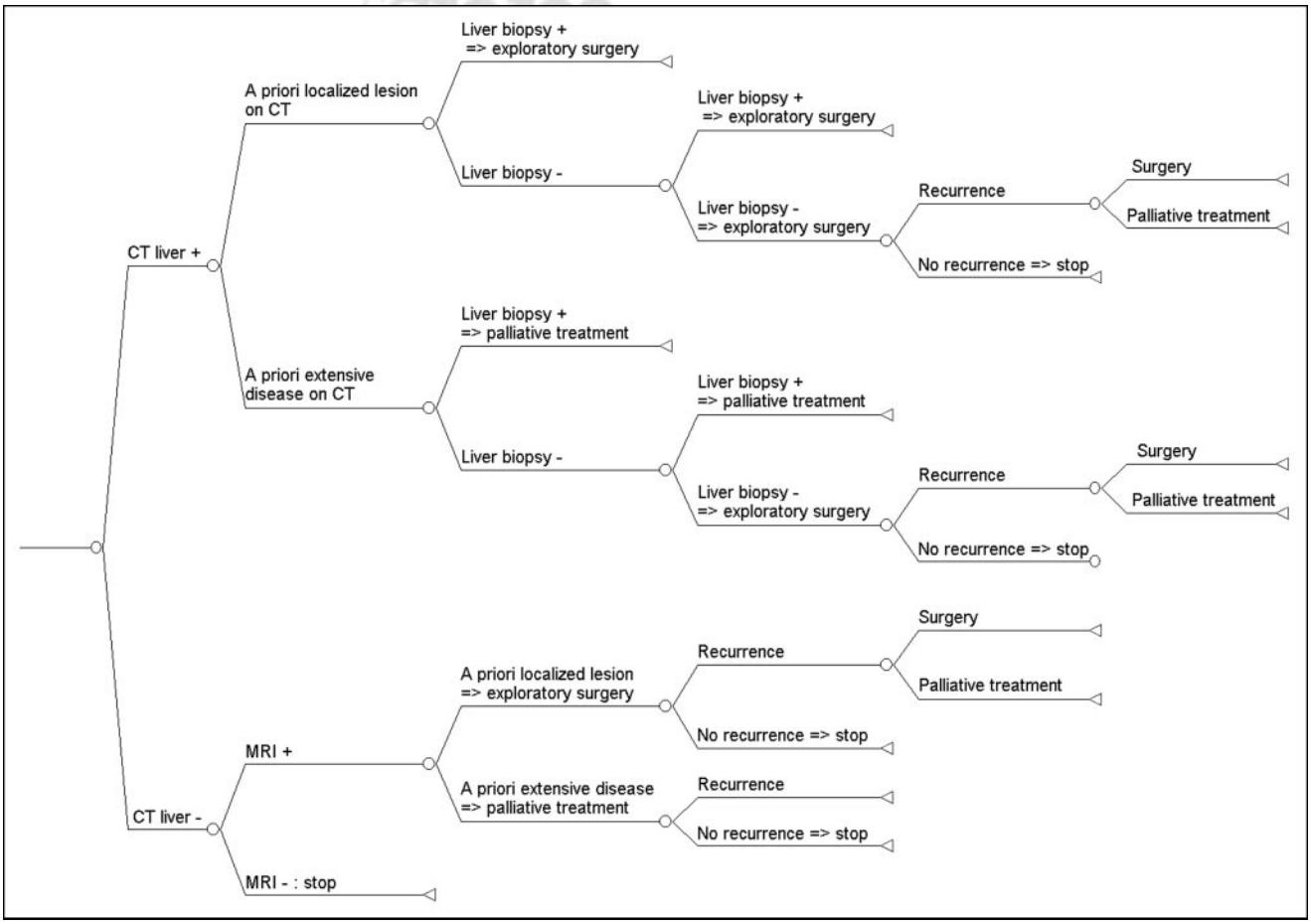

FIGURE 1. Outline of decision tree shows diagnosis and staging of metachronous liver metastases with CT. ○, Chance nodes; ◁, termination nodes.

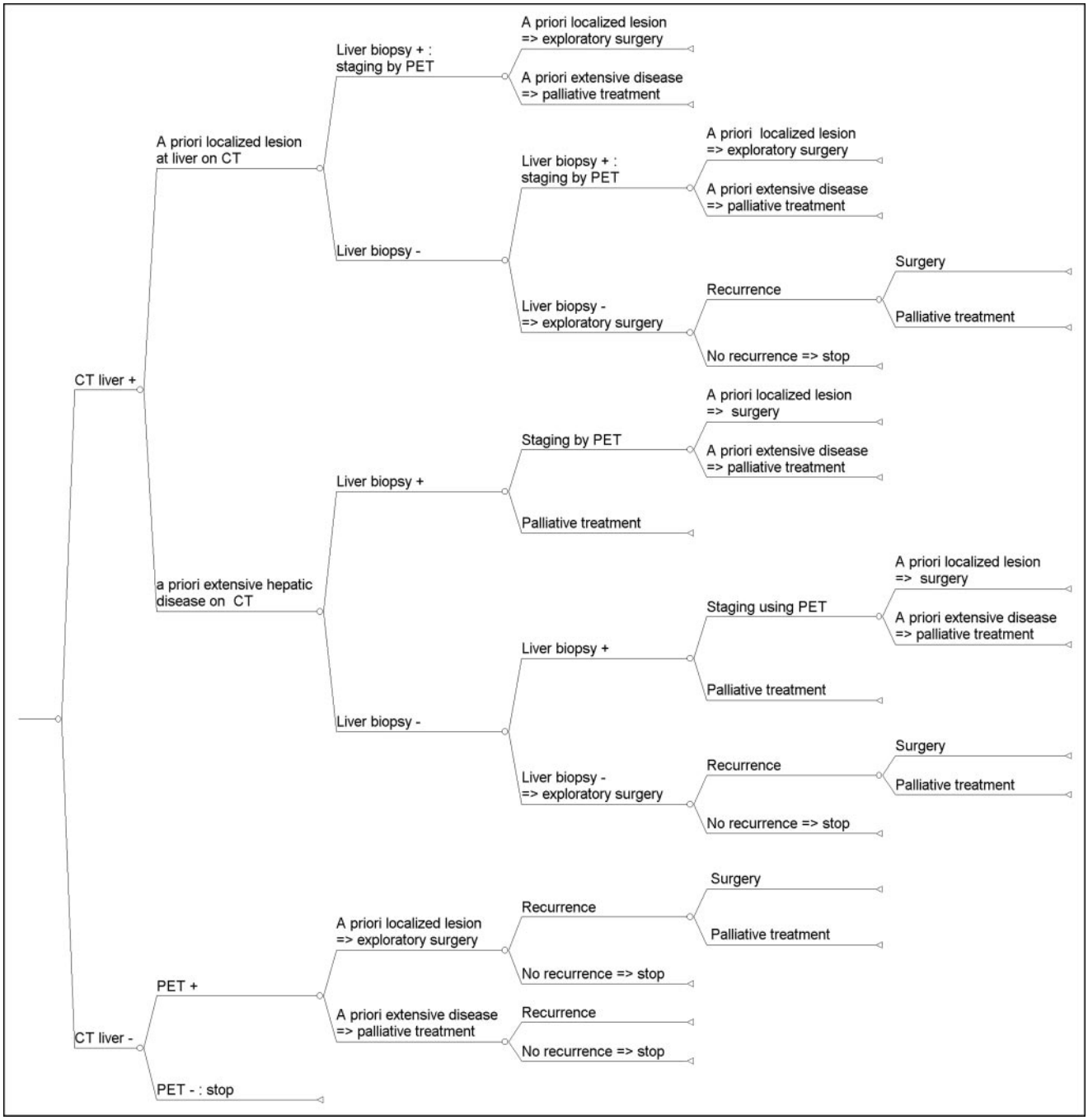

FIGURE 2. Outline of decision tree shows diagnosis and staging of metachronous liver metastases with CT + PET. ○, Chance nodes; ◁, termination nodes. PET = ^{18}F-FDG PET.

CT Strategy. In the CT strategy, a transparietal liver biopsy was performed in the case of positive CT findings (indicating a high presumption of metachronous liver metastases). If the biopsy confirmed the diagnosis (positive biopsy), the patient was oriented either to exploratory surgery if the disease appeared resectable or to palliative treatment if the patient presented an a priori extensive disease. The "exploratory surgery" event was then weighted by the proportion of patients presenting in fact a nonresectable lesion. In this case, palliative treatment was proposed. Similarly, the "palliative treatment" event was weighted by the proportion of patients presenting a localized lesion. In this case, patients were assumed to be reoriented toward surgery for cure after 2 cycles of chemotherapy (*13*). Liver biopsy could also be negative. Because the imperfect sensitivity of the biopsy is well established (*14*), the probability of false-negative results was considered and a second biopsy was performed. In the case of positive findings at the second biopsy, the same management as described above was applied. In the case of a new negative biopsy, exploratory surgery was performed. If evidence of metachronous liver metastases was found, the patient underwent either surgery for cure or palliative treatment

according to the staging of the lesion. If no evidence of the disease was found, the work-up was stopped.

When CT findings were negative (indicating a high presumption of absence of metachronous liver metastases), MRI was performed. In the case of negative MRI, the work-up was stopped. Diagnostic errors associated with MRI due to its imperfect sensitivity were considered (*7,15*). Indeed, a small proportion of patients was assumed to present a malignant lesion despite negative MRI and was oriented toward surgery or palliative treatment according to the extent of the disease. If MRI findings were positive, the patient was directed toward exploratory surgery if the disease appeared localized on MRI or toward palliative treatment in the case of suspected extensive disease. Similarly, imperfect MRI specificity allowed us to model the case of patients oriented toward treatment, even though presenting a benign lesion.

CT + PET Strategy. In the case of positive CT findings, a biopsy was performed, followed by a second biopsy in the case of negative results. In the case of positive findings at the first or second biopsy and if the lesion was considered to be resectable by CT, it was assumed that the patient would be systematically reevaluated with PET and then oriented toward the most suitable treatment. If the patient was considered to have nonresectable hepatic disease by CT, experts considered that reassessment using PET would be performed in 10% of cases because of clinical uncertainty. Otherwise (in the remaining 90% of cases), the patient was oriented directly to a palliative treatment. In the case of negative biopsy, the same management as described in the CT-alone strategy was applied.

If CT findings were negative, PET was immediately performed to confirm the CT results. If PET was negative, the work-up was stopped. Possible diagnostic errors due to its imperfect sensitivity (*16,17*) were modeled. If PET was positive, the same scenario as described with MRI was modeled.

Epidemiologic Parameters

Transition Probabilities. Epidemiologic data are reported in Table 1. The probability of having metachronous liver metastases after abnormal abdominal ultrasound was estimated to be 0.85

TABLE 1
Epidemiologic Parameters (Baseline Value and Range) Used in Model

Variable	Value	Range	Reference
Probability of metachronous liver metastases if abnormal abdominal ultrasound	0.85	[0.80–0.95]	(*4,18*)
Diagnostic imaging test performances for detection			
CT sensitivity	0.98	[0.90–0.99]	(*7,16,19*)
CT specificity	0.85	[0.80–0.95]	(*7,16,19*)
PET sensitivity	0.90	[0.85–0.99]	(*16,17*)
PET specificity	0.98	[0.80–0.99]	(*16,17*)
MRI sensitivity	0.98	[0.90–0.99]	(*7,15*)
MRI specificity	0.95	[0.80–0.98]	(*7,15*)
1st liver biopsy sensitivity	0.85	[0.70–0.95]	(*14*)
2nd liver biopsy sensitivity	0.99	—	Experts
1st and 2nd liver biopsy specificity	1.00	—	(*14*)
Diagnostic test performances for assessing resectability			
CT sensitivity	0.80	[0.80–0.99]	(*21,22*)
CT specificity	0.90	[0.60–0.95]	(*21,22*)
PET sensitivity	0.95	[0.80–0.99]	(*20*)
PET specificity	0.95	[0.85–0.99]	(*20*)
MRI sensitivity	0.85	[0.80–0.99]	(*21*)
MRI specificity	0.95	[0.80–0.95]	(*21*)
Proportion of resectable metastases	0.20	[0.10–0.40]	(*4*)
Clinical practices			
Frequency of use of PET after a patient is considered as nonresectable after CT	0.10	[0.00–0.80]	Experts
Proportion of patients directed toward chemotherapy in case of extensive disease	0.90	—	Experts
Proportion of patients directed toward symptomatic treatment in case of extensive disease	0.10	—	Experts
Risks associated with surgery for cure			
Morbidity rate	0.10	—	(*23,24*)
Mortality rate	0.03	—	(*23,24*)
Life expectancy (y)			
Absence of recurrence (68-y-old individual)	5.62	—	*
Surgery for cure	1.86	—	*
Chemotherapy	1.11	—	*
Symptomatic treatment	0.60		*

*Burgundy Digestive Cancer Registry.
PET = ^{18}F-FDG PET.

(*4,18*). The probability that the diagnosis of liver metastases would be confirmed by imaging techniques was estimated using the sensitivity and specificity of CT (*7,16,19*), MRI (*7,15*), and PET (*16,17*). The probability that liver metastases would be found resectable by imaging techniques was estimated along with the proportion of resectable metachronous liver metastases (*4*) and the sensitivity and specificity of CT, MRI, and PET in predicting resectability (*20–22*). Sensitivity in predicting resectability was defined as the number of individuals with no evidence of extensive disease (liver invasion or extrahepatic metastases) depicted on imaging tests divided by the number of individuals with no evidence of extensive disease at surgical examination. False-positive patients were those thought to be resectable by imaging test criteria but were not found to be resectable at exploratory surgery. Specificity in predicting resectability was defined as the number of individuals with evidence of extensive disease depicted on imaging tests over the number of individuals with extensive disease at surgical examination. False-negative patients were subjects thought not to be resectable by imaging test criteria but were finally directed toward surgery for cure because of the presence of a localized lesion. Data about morbidity and mortality related to surgical resection were also taken into consideration (*23,24*). Mortality associated with biopsy was not introduced into the model given the small number of such events (*14*). Experts were consulted on the following points: sensitivity of the second liver biopsy, frequency of PET use after the patient has been considered nonresectable by CT, and proportion of patients directed toward chemotherapy or symptomatic treatment in the case of a priori nonresectable disease.

Life Expectancies. Life expectancies were calculated using the DEALE (Declining Exponential Approximation of Life Expectancy) method (*25,26*) (Table 1). Survival rates according to surgery for cure, chemotherapy, and symptomatic treatment were extracted from the Burgundy Digestive Cancer Registry database over the period 1976–1995 (nonpublished data). After 1 y, mean observed survival rates were 62%, 43%, and 20%, respectively, allowing life expectancies to be estimated at 1.86, 1.11, and 0.60 y. Patients reoriented toward surgery for cure after 2 cycles of chemotherapy were assumed to have the life expectancy of a patient initially directed to justified resection. Patients with benign lesions, but falsely considered as presenting malignant disease, were assumed to have the life expectancy of patients resected for cure of a primary basis of data of the Burgundy Digestive Cancer Registry, the mean 1-y observed survival rate was 89% for these patients, leading to an estimated life expectancy of 5.62 y.

Economic Parameters

The economic analysis was performed from the national health insurance perspective. Costs were expressed in euros (€) [U.S. dollars ($)] for the year 2004.

Cost of Diagnostic Tests. CT, MRI, and PET did not require hospitalization. Their costs were obtained from the "Nomenclature Générale des Actes Professionnels" (NGAP), a fixed-costs scale of medical procedures based on practitioners' fees, fixed costs for the medical procedures themselves, and fixed costs for operating the equipment (Table 2). Liver biopsy required a 12-h stay in hospital. Therefore its cost included the cost of an ambulatory hospitalization stay (<24 h) in the medical department of our Dijon university hospital, reimbursed by the French health care insurance (Table 3).

TABLE 2
Baseline Values of Cost of Diagnostic Tests Used in Decision Tree and Performed on Ambulatory Patients (€ [$] in year 2004)

Diagnostic test	Resources utilization	Cost (€ [$])	Total cost (€ [$])
CT	Equipment	213 (256)	313 (377)
	Medical procedure	62 (75)	
	Contrast product	28 (34)	
	Contrast product injection	10 (12)	
MRI	Equipment	282 (339)	365 (439)
	Medical procedure	69 (83)	
	Contrast product	5 (6)	
	Contrast product injection	10 (12)	
PET	Equipment	950 (1,143)	1,034 (1,244)
	Medical procedure	84 (101)	

PET = ^{18}F-FDG PET.

Cost of Treatment Procedures. Treatment costs were calculated in a similar way to liver biopsy cost. These costs varied according to the type of hospitalization—complete (>24 h) or ambulatory (<24 h)—and the type of department (surgical, medical, or drug-specialized). Surgeons from our Dijon university hospital estimated that surgery for cure without complications required 10 d of hospitalization, 12 d if complications occurred, and 7 d for exploratory laparotomy. Palliative treatment consisted of chemotherapy and symptomatic treatment. The association of folinic acid and fluorouracil (5FU) was used as standard protocol for chemotherapy. It required 2 d of ambulatory hospitalization every 2 wk for an optimal period of 6 mo (12 cycles). Its cost was estimated by multiplying the total number of hospitalization days (i.e., 24 d) by the cost of ambulatory hospitalization in a drug-specialized department. If chemotherapy was stopped after 2 cycles, only 4 d were considered (*13*). The hospitalization duration for symptomatic treatment was issued from the national hospital database on diagnosis-related groups (DRGs) in the public health care sector for 2003. This database allowed us to determine which of the 580 existing DRGs covered each of the specific medical procedures modeled in the study. The DRG including the "symptomatic treatment" procedure presented an average hospitalization length of 5 d in a medical department. This duration was also multiplied by the cost for complete hospitalization.

Outcomes

Effectiveness, Costs, and Cost-Effectiveness. A cost-effectiveness analysis was performed using CT alone as the reference strategy. Incremental effectiveness was measured in terms of the difference in expected average life expectancy between the CT + PET strategy and the reference strategy. Incremental costs were evaluated in a similar fashion. The cost-effectiveness analysis was based on an incremental cost-effectiveness ratio (ICER), calculated by dividing the incremental costs by the incremental effects of 2 alternatives according to the following formula: $\text{ICER} = (\text{Cost}_{\text{CT+PET}} - \text{Cost}_{\text{CT}})/(\text{Life expectancy}_{\text{CT+PET}} - \text{Life expectancy}_{\text{CT}})$. The most cost-effective strategy was defined as that with the lowest ICER. Incremental costs were not discounted given the time period elapsed between the diagnosis of recurrence and the first treatment (<1 y). In the case of incremental gains in effec-

TABLE 3
Baseline Values of Cost of Transparietal Liver Biopsy and Treatments Used in Decision Tree and Requiring Hospitalization (€ [$] in year 2004)

Diagnostic test and treatment	Hospitalization length (d)	Hospital cost* (€ [$])	Total cost (€ [$])
Transparietal liver biopsy	1	567.26 (682)	567 (682)
Surgery for cure without complications	10	669.24 (805)	6,692 (8,050)
Surgery for cure with complications	12	669.24 (805)	8,031 (9,660)
Exploratory laparotomy	7	669.24 (805)	4,685 (5,635)
Complete chemotherapy	24†	961.37 (1,156)	23,073 (27,744)
Incomplete chemotherapy	4†	961.37 (1,156)	3,845 (4,624)
Symptomatic treatment	5	550.26 (662)	2,751 (3,310)

*567.26 € is cost for ambulatory hospitalization in a medical department, 669.24 € is cost for complete hospitalization in a surgical department, 961.37 € is cost for ambulatory hospitalization in a drug-specialized department, and 550.26 € is cost for complete hospitalization in a medical department at the Dijon university hospital.

†Chemotherapy protocol consists of 2 d of ambulatory hospitalization every 2 wk over a 6-mo period (12 cycles). In the case of incomplete protocol, patient was assumed to receive 2 cures over the period of 1 mo (2 cycles).

tiveness (Life expectancy$_{CT+PET}$ − Life expectancy$_{CT}$), these were discounted back at the annual discount rate of 5% (*27*).

Clinical Results. The number of true diagnoses of recurrence, the number of unseen recurrences, as well as the number of well-suited treatments (curative resection, palliative treatment) and the number of not well-suited treatments (unnecessary exploratory surgery, palliative treatment), among patients with suspected liver metastases were estimated. Therefore, for each of the 2 model strategies, transition probabilities associated with the arms of the decision tree were applied to a fictitious population of 1,000 individuals. It was also possible to estimate the number of patients reaching the ends of the arms of the decision tree, to add together all those having the same diagnostic status (false or true) or the same type of treatment (well-suited or not well-suited) and then to calculate the proportion of patients according to their diagnostic or therapeutic management.

Sensitivity Analysis

One-way sensitivity analyses were performed on epidemiologic and economic parameters. Threshold values were determined and used as cutoff points beyond which the hierarchy between strategies could be modified, therefore changing the conclusions of the study.

RESULTS

Cost-Effectiveness Modeling Baseline Value

Table 4 shows the cost-effectiveness results of CT and CT + PET in the management of an average 68-y-old individual who was previously resected for CRC and with suspected metachronous liver metastases after an abnormal abdominal ultrasound. CT was a dominated strategy, presenting an extra cost of 2,671 € (~$3,213) and a similar expected effectiveness-per-patient compared with CT + PET (1.88-y life expectancy per patient).

Sensitivity Analyses

Sensitivity Analysis Performed on Natural History of the Disease. The probability of having liver metastases after an abdominal ultrasound with suggestive findings was tested first over the [0.80–0.95] interval. No thresholds were found and CT remained dominated by CT + PET. The increase in the proportion of nonresectable metastases (baseline value of 0.80, varying between 0.60 and 0.90) led to the same conclusion.

Sensitivity Analysis Performed on Parameters Characterizing PET Strategy. The following parameters characterizing PET were changed: sensitivity and specificity for detecting liver lesion, sensitivity and specificity for assessing respectability, and frequency of PET use among patients considered as nonresectable by CT. The model was not sensitive to any of these parameters.

Sensitivity Analysis Performed on Epidemiologic Parameters Characterizing CT Strategy. Similarly, no thresholds were found for diagnostic performance associated with biopsy, CT, or MRI as well as for CT and MRI performance in assessing resectability.

Sensitivity Analysis Performed on Economic Parameters. Costs of CT, MRI, biopsy, and treatment procedures were separately increased and decreased by 20%. The conclusion of the cost-effectiveness analysis remained unchanged. The only threshold found was related to the cost of PET. The baseline cost used was 1,034 € (~$1,244). Sensitivity analysis showed that above 8,992 € (~$10,817), CT + PET

TABLE 4
Cost-Effectiveness Results of CT and CT + PET in Management of Metachronous Liver Metastases

Strategy	Cost (€ [$])	Life expectancy* (y)	Incremental cost-effectiveness ratio
CT + PET	17,064 (20,526)	1.88	—
CT	19,735 (23,739)	1.88	Dominated

*All life expectancies were rounded up to 2 decimal places.
PET = ^{18}F-FDG PET.

TABLE 5
Modification of Diagnosis and Therapeutic Orientation of Patients with Metachronous Liver Metastases Induced by CT and CT + PET

Management	CT (%)	CT + PET (%)
Absence of recurrence	14.4	14.7
Unseen recurrence	0.0	0.3
Curative resection	13.6	13.2
Palliative treatment*	61.3	67.1
Unnecessary exploratory surgery†	6.9	0.8
Unnecessary palliative treatment‡	3.9	3.9

*Palliative treatment includes chemotherapy and symptomatic treatment.

†Exploratory surgery performed although tumor was nonresectable.

‡Palliative treatment adopted although malignant tumor could be resected for cure in first intention.

PET = ^{18}F-FDG PET.

became dominant by CT alone. However, this cost was not a reasonable range cost for PET.

Outcomes Relating to Diagnostic and Therapeutic Management of Patients

The introduction of PET did not greatly modify the diagnostic management of patients with suspected metachronous liver metastases (Table 5). The main difference between the 2 strategies related to the therapeutic management of patients. Compared with CT + PET, CT alone was associated with a relative risk reduction of 9.5% in correctly assessing patients with nonresectable disease. The relative risk that patients undergo inappropriate surgery was estimated to be reduced by 88.4% when PET was associated with CT compared with CT alone.

DISCUSSION

To our knowledge, this study is the first to attempt to estimate and clarify the clinical and medicoeconomic implications of PET in France among patients with metachronous metastases. Metachronous metastases were defined as lesions discovered during the follow-up after the resection of the primary tumor (in contrast with synchronous metastases, which are diagnosed in the preoperative work-up or during surgery). Results indicated that CT + PET was a more cost-effective strategy than CT alone. Only 2 other studies have been published with regard to the use of PET for detecting and staging patients with suspected metachronous liver metastases (*11,12*). Gambhir et al. compared carcinoembryonic antigen (CEA) + CT, with CEA + CT + PET, with the absence of monitoring. CT + PET was associated with a 2-d increase in life expectancy and savings of $220 per patient compared with CT (*11*). In the study of Park et al., the population introduced into the decision tree was also selected after a positive CEA finding. CT + PET generated a gain in life expectancy of 9.5 d and an ICER of $16,437 per life-year gained compared with CT (*12*). In the present study, CEA testing was not modeled. Patients were selected after an abdominal ultrasound with suggestive findings, as recommended by French clinical guidelines (*28*). Moreover, MRI was introduced into the model when the absence of metachronous liver metastases using CT was suspected. This point also reflects French guidelines that recommend using MRI when CT fails in characterizing detected lesions (*29*). The introduction of liver biopsy into the decision tree could be argued. Its use depends mainly on the degree of uncertainty associated with radiologic findings and the treatment to be considered (*29*). Generally, if palliative chemotherapy is planned, the use of biopsy is justified. On the other hand, if the lesion appears resectable, the use of liver biopsy is more controversial because of a possible risk of dissemination of the disease (*30*). In this work, liver biopsy was modeled in both cases because of the imperfect diagnostic performance of CT for recurrence detection. One can reasonably assume that introducing biopsy only if resection was planned will not change considerably the conclusion of the analysis given the similar survival rates between strategies.

Another choice in the model related to percutaneous radiofrequency, which was not taken into consideration. This is a promising complementary treatment to surgery for nonresectable lesions. However, this new treatment protocol still needs to be assessed (*31,32*).

The place of PET in the decision tree can also be discussed. Recent French guidelines issued by the National Agency for Accreditation and Evaluation in Health Care (ANAES) recommended that PET could be considered when CT was not sufficient in determining the most appropriate treatment for the patient and when a resection is considered (*33*). Therefore, PET was systematically modeled before any therapeutic decision when the liver lesion was a priori considered as localized using CT and after negative CT findings. However, to take into account possible different clinical practices, PET was also assumed to be performed in 10% of the cases when CT suggested the presence of nonresectable hepatic disease. Sensitivity analysis on this parameter did not modify the conclusion of the analysis.

Our study suggests a positive influence of PET on the management of metachronous liver metastases of CRC. A total of 6.1% of patients could avoid inappropriate exploratory surgery because of its introduction, whereas Park et al. found a smaller figure (2.8%) in his cost-effectiveness analysis (*12*). Conversely, PET was estimated to reduce the number of futile laparotomies by 25% in a study reporting the first 5-y overall survival in patients considered to have resectable liver disease after conventional imaging (*34*). The difference between the results from the 2 model studies and this population-based study can be explained by the fact that models are affected by the choice of sequences of clinical events and epidemiologic parameters. In this work,

the main uncertainty related to the probability that imaging techniques falsely downstage the lesion. Studies suggested that extrahepatic lesions were missed by CT in the range of 30%–40%, with the introduction of PET decreasing this proportion to a 17%–32% range (*20,35–37*). Even less data exist relating to MRI. It has been suggested that MRI sensitivity in detecting extrahepatic lesions was 90% (*21*). Uncertainty also related to the probability that imaging techniques falsely upstage the lesion. According to studies, the proportion of these patients was estimated to range between 6% and 10% (*20,21*). On the basis of these data, 33.3% of patients with liver recurrence were assumed to be directed toward inappropriate surgery after CT, 19% after MRI, and 17.4% after PET in our model. Similarly, 5.3%, 3.8%, and 1.3% of patients were falsely upstaged after CT, MRI, and PET, respectively. The uncertainty associated with these parameters led us to perform several sensitivity analyses. Our results showed the robustness of the model. Some other parameters (survival, probability of having metachronous metastases) were not tested because they were provided by a population-based cancer registry—thus, without the selection bias of specialized units.

Quality of life was not considered in this work. Patients directed toward surgery for cure after 2 cycles of chemotherapy were assumed to have the life expectancy of a patient initially directed to justify resection. Therefore, one of the perspectives of this work could be to determine whether results change using cost per QALY (Quality-Adjusted Life Year) instead of cost per life-year gained.

Another choice was made not to model the PET/CT combination because of a lack of relevant data in published studies and the fact that it is too early in France to evaluate this technology, which is just at the beginning.

At present, PET units are planned throughout France, even though the medico-economic consequences of PET use have been poorly analyzed. This work demonstrated the value of the association of CT + PET from an economic point of view but also the nonrelevance of this association if only survival effectiveness was taken into consideration. The main advantage of the introduction of PET consists in decreasing the number of inappropriate exploratory surgical acts. Clinical trials are necessary to back up these results and to determine over a long period of time the effectiveness and costs incurred by introducing PET into the management of patients with suspected metachronous liver metastases.

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