

PET-FDG scan enhances but does not replace preoperative surgical staging in non-small cell lung carcinoma[☆]

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Abstract

Objective: To assess the effectiveness of positron emission tomography with radiolabeled [¹⁸F]-2-fluoro-deoxy-D-glucose (PET-FDG) imaging in mediastinal lymph node (LN) staging for non-small cell lung carcinoma (NSCLC) and to compare it to conventional clinical and surgical staging. **Methods:** From June 1998 to February 2000, we enrolled 64 potentially resectable NSCLC patients in a prospective study of PET-FDG imaging of the mediastinum to assess LN involvement. Results of this technique were compared to conventional clinical and surgical staging. Diagnostic efficacy was determined by calculating sensitivity, specificity, overall accuracy, and positive and negative predictive values for each method. **Results:** PET-FDG imaging correctly identified nodal stage (N0–N1 vs. N2) in 50 out of 61 patients (82%), overstaging occurred in eight patients (13%), and understaging in three patients (4.9%). The sensitivity, specificity, accuracy, and positive and negative predictive values for PET-FDG scan imaging were 67, 85, 82, 43, and 93.6%, respectively. Conventional staging correctly identified nodal stage (N0–N1 vs. N2) in 51 out of 62 patients (82%), overstaging occurred in five patients (8.1%), and understaging in six patients (9.7%). The sensitivity, specificity, accuracy, and positive and negative predictive values for conventional staging were 33, 90.6, 82, 37, and 89%, respectively. With regard to N2 disease, conventional staging showed a poor sensitivity (33%). Indeed, six out of 64 patients were understaged for mediastinal LN involvement. Even though the improvement was not statistically significant (McNemar $P = 0.08$), the combined use of PET-FDG scan and computerized tomography (CT) scan allowed a two-fold increase in the sensitivity of our clinical preoperative staging. Moreover, relying on the PET-scan high negative predictive value might have contributed to a three-fold decrease in the number of required surgical staging procedures. **Conclusions:** Our study shows that the PET-FDG imaging strength lies in its very high negative predictive value and increased sensitivity. In this study, the overall accuracy of PET-FDG scan (82%) was lower than previously reported. Combined with chest CT-scan preoperatively, it may alleviate the need for surgical staging when PET-FDG studies of the mediastinum are negative. However, with a positive PET-FDG scan result, further diagnostic procedures should be pursued in order to avoid overstaging and allow better surgical patient selection. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: PET-FDG scan; Non-small cell lung carcinoma; Mediastinal lymph node

1. Introduction

Improvements in the staging modalities of non-small cell lung carcinoma (NSCLC) should define more accurately

subgroups of patients and, simultaneously, decrease the number of unwarranted surgical procedures while improving patient survival in selected groups of surgical candidates.

Most recent studies [1,2] have underlined the importance of ipsi-lateral (N2) or contra-lateral (N3) mediastinal lymph node (LN) involvement as a key prognostic factor for long-term survival. Unfortunately, sensitivity and specificity of chest computerized tomography (CT) scan in mediastinal staging for lung cancer has proved to be insufficient. Gambhir et al. [3] reported sensitivity and specificity of 67 and 73%, respectively, whereas more recently, Pieterman et al. [4] reported values of 75 and 66% on a series of 102 patients

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with a diagnostic accuracy of 69%. Thus, a large percentage of false-positive patients either are overstaged and misclassified or undergo additional surgical diagnostic procedures. Those procedures have their own morbidity, mortality, and costs that one has to account for. Moreover, false-negative patients represent a group of patients likely to benefit more from multimodal treatment than from surgical exploration [5,6].

Positron emission tomography with radiolabeled [^{18}F]-2-fluoro-deoxy-D-glucose (PET-FDG) has been shown to have superior sensitivity and specificity than chest CT-scan in the diagnosis of malignant solitary pulmonary nodule [7] while being an extremely safe non-invasive procedure [8]. Several studies have been conducted on the efficacy of PET-FDG scan in the assessment of mediastinal LN involvement. However, only few of these reported extensive mediastinal pathological results. Chin et al. [9] first reported sensitivity, specificity, diagnostic accuracy, and positive and negative predictive values of 78, 81, 80, 64, and 89%, respectively, in a prospective study of 30 patients. PET-FDG scan results combined with chest CT-scan enhanced the diagnostic accuracy up to 90%.

In our study, we prospectively analyzed the sensitivity, specificity, diagnostic accuracy, and positive and negative predictive values of PET-FDG scanning and compared them to the results of staging by chest CT-scan alone. The integrated results of CT-scan and mediastinal surgical procedures, which represent our conventional staging method, were then compared to PET-FDG scan results.

Endpoints of the study were two-fold: first, to analyze sensitivity, specificity, and accuracy of PET-FDG scan imaging in our institutional series and second, to determine whether this new imaging modality could have a clinical impact on our patient selection and, overall, on our clinical practice.

2. Materials and methods

2.1. Patient selection

From June 1998 until February 2000, we included in the study 64 out of the 92 patients (70%) referred to our department with potentially resectable primary NSCLCs. Patients with N0, N1, and N2 disease determined by chest CT-scan without histological confirmation were eligible for this study. Patients with N3 disease on CT-scan were also included except if the N3 site was also detected by the PET-FDG scan.

Out of the 92 referred patients, eight patients presented on initial evaluation with such N3 disease and 20 patients presented with metastatic (M1) disease as detected by PET-FDG scanning and correlated with other imaging modalities. These 28 patients were excluded from the present study while the remaining 64 patients represent the study cohort. All data were prospectively entered into

our database. Overall, there were 1240 LNs available for pathologic analysis (mean number LN/patient = 19.3, range 3–40). This study was approved by our Institutional Review Board.

2.2. Radiological staging

Most CT examinations (42 out of 64) were performed at our institution on a helical scanner (SR 7000, Philips, Eindhoven, The Netherlands). Images were obtained from the lung apices down to the adrenal glands with 6.5-mm-thick sections, after intravenous injection of 60–100 cm³ of contrast medium (Meglumine ioxitalamaat, Telebrix 35, Guerbet, Aulnay-sous-bois, France). All CT-scans were interpreted by one radiologist (E.C.) blinded to the PET-FDG scan imaging results. LNs were considered positive if they were greater than 1.0 cm in their short-axis diameter.

2.3. PET-FDG acquisition

2-[^{18}F]Fluoro-2-deoxy-D-glucose (FDG) was produced by an automated nucleophilic method based on the Hamacher procedure [10]. Sixty minutes after injection of 370 MBq FDG, patients were positioned on the PET device (ECAT EXACT HR, CTI, Knoxville, TN, USA). Attenuated and non-attenuated images were simultaneously displayed on a high-resolution color monitor and interpreted by one nuclear medicine physician (M.L.) blinded to the results of other imaging modalities. Nodes were described as ipsi- or contra-lateral to the primary tumor and whenever possible, were labeled according to the American Thoracic Society (ATS) classification [11]. In this study, there were neither ‘co-registration’ nor ‘co-lecture’ of CT-scan and PET-FDG scans. Unexpected findings from the PET-FDG scan (extra-thoracic and/or contra-lateral lung uptake) were reported to the responsible physician.

2.4. Surgical staging

Surgical mediastinal staging diagnostic procedures were performed according to the following criteria: (1) patients with ipsi- or contra-lateral mediastinal LN with a diameter >10 mm in its shorter axis on chest CT-scan; (2) patients with a histology of adenocarcinoma on bronchoscopy or transthoracic needle biopsy; or (3) high-risk surgical candidates (associated co-morbidities, elderly patients, etc.). Patients with early stage NSCLC (I–II) and squamous histology were not routinely submitted to mediastinal surgical procedures. All nodal stations were labeled according to the ATS guideline [11]. Biopsy and/or removal of LNs from stations 1–4 and station 7 were routinely performed through a cervical mediastinoscopy. For left-sided tumors and/or stations 5 and 6 sampling, left anterior mediastinotomy was performed as well.

At the time of surgical resection, surgeons were aware of the results of both conventional staging and PET-FDG scan, but regardless of the imaging results, all ipsi-lateral mediast-

Table 1
Demographics and clinico-pathological data

	Study group
<i>n</i>	64
M/F ratio	4:1
Mean age (range)	65.2 (45.2–83.2)
Pathology ^a	
SCC	29
AdC	33
Undifferentiated	1
pTNM stage ^b	
Stage I	34
Stage II	16
Stage III	11
Stage IV	2
Mediastinal procedures	28

^a One patient in the study group presented with neuroendocrine tumor and is not listed in the pathology results.

^b In the study group, one patient had induction chemotherapy based on clinical Stage IIIa and had complete pathological response (CR). This patient was not included in pTNM of Table 1.

inal LNs stations were systematically sampled. Histologically documented nodal involvement by tumor was the standard criterion to which CT-scan and PET-FDG scan results were compared.

2.5. Statistical analysis

All data were dichotomized with respect to the accurate diagnosis of mediastinal LN involvement (N0–N1 vs. N2 disease). Diagnostic efficacy of CT-scan, PET-FDG imaging and surgical diagnostic procedures was determined by calculating sensitivity, specificity, overall predictive accuracy, and positive and negative predictive values as follows:

$$\text{Sensitivity} = \frac{[\text{True positive}]}{[\text{True positive} + \text{false negative}]} \times 100$$

$$\text{Specificity} = \frac{[\text{True negative}]}{[\text{True negative} + \text{false positive}]} \times 100$$

$$\text{Overall accuracy} = \frac{[\text{True positive} + \text{true negative}]}{[\text{Number of patients studied}]} \times 100$$

Positive predictive value

$$= \frac{[\text{True positive}]}{[\text{True positive} + \text{false positive}]} \times 100$$

Negative predictive value

$$= \frac{[\text{True negative}]}{[\text{True negative} + \text{false negative}]} \times 100$$

The McNemar test was used to compare the effectiveness of chest CT-scan vs. PET-FDG scan in the detection of

pathologic N2 disease. A probability value of less than 0.05 was considered significant.

3. Results

Table 1 summarizes clinical and pathological variables of the study group. One patient had induction chemotherapy initiated on a clinical Stage IIIa and had pathologic complete remission (CR) on the resected specimen (TxNxM0). Another patient was found to be metastatic at thoracotomy (synchronous tumors in different lobes) though the PET-FDG imaging only showed one tumoral uptake and did not undergo mediastinal LN dissection. These two patients were excluded from further statistical analysis. Mediastinoscopy and/or anterior mediastinotomy was performed in 28 out of 64 (43.7%) patients.

As shown in Table 2, CT-scan correctly identified the nodal stage in 35 out of 62 patients (56%). Understaging occurred in nine patients (14%), and overstaging in 18 patients (29%). PET-scan correctly identified the nodal stage in 45 out of 61 patients (74%). Understaging occurred in seven patients (11%), and overstaging in nine patients (15%). Mediastinoscopy/mediastinotomy correctly identified the nodal stage in 23 out of 28 patients (82%). Understaging occurred in five patients (18%); no patient was

Table 2

Results of CT-scan (CT), mediastinoscopy, PET-FDG scan, and CT + mediastinoscopy in the determination of nodal involvement in the study group (*n* = 64)^a

	pN0 (<i>n</i> = 39)	pN1 (<i>n</i> = 14)	pN2 (<i>n</i> = 9)	pN3 (<i>n</i> = 0)
CT				
N0	25	5	2	–
N1	–	6	2	–
N2	12	1	4	–
N3	2	2	1	–
PET-scan ^b				
N0	33	4	3	–
N1	1	6	–	–
N2	3	4	6	–
N3	1	–	–	–
Mediastinoscopy/mediastinotomy (<i>n</i> = 28)				
N0–N1	13	7	5	–
N2–N3	–	–	3	–
CT + mediastinoscopy				
N0	38	4	3	–
N1	1	8	3	–
N2	–	2	3	–
N3	–	–	–	–

^a Two out of the 64 patients were excluded from analysis. One had complete pathological response (CR) after induction chemotherapy initiated on clinical stage IIIa and the other patient was found to be metastatic during thoracotomy (not detected by PET-FDG) and did not undergo mediastinal lymph node dissection.

^b In one patient with a large hilar mass, PET-FDG could not differentiate nodal status.

overstaged. CT-scan and mediastinoscopy/mediastinotomy together correctly identified the nodal stage in 49 out of 62 patients (79%). Understaging occurred in ten patients (16%), and overstaging in three patients (4.8%). Analysis of these results with respect to discriminating early stage, operable disease (pN0–pN1) from locally advanced disease ($\geq$ pN2) is summarized in Table 3. Sensitivity, specificity, overall accuracy, positive predictive value (+PV), and negative predictive value (–PV) for CT-scan were 55, 68, 66, 23, and 90%; and for PET-FDG scan they were 67, 85, 82, 43, and 93.6%, respectively. With respect to the 28 patients who underwent mediastinal surgical staging, the results obtained were 27, 100, 82, 100, and 80%. For CT-scan and mediastinoscopy/mediastinotomy together, sensitivity, specificity, accuracy, +PV, and –PV results were 33, 90.6, 82, 37, and 89%. Statistical analysis of the diagnostic accuracy of nodal involvement by CT-scan alone or PET-FDG scan alone showed that, even with PET-FDG scan greater sensitivity, the *P* value was only of borderline significance (McNemar's test, *P* = 0.08). Conventional staging (CT-scan and mediastinoscopy) statistically improved diagnostic accuracy when compared to CT-scan staging alone (*P* = 0.02). Finally, comparison between conventional staging and PET-FDG staging showed that PET-FDG scan did not improve diagnostic accuracy significantly (*P* = 0.79, NS). Based on our current algorithm, six out of 64 patients (9.3%) were primarily operated on for N2 disease though our current practice would have been to offer the patient a multimodal treatment with induction chemotherapy. Relying on PET-FDG scan results, only three patients with N2 disease out of the 64 patients (4.7%) would not have been detected prior to surgery.

We reviewed the charts of the three patients with PET-FDG scan false-negative results in detail: the first patient was a 58-year-old female with a preoperative diagnosis of adenocarcinoma. CT-scan staging was T2N1. PET-FDG scan results were T(+)N0M0. A mediastinoscopy with sampling of stations 4R, 7, and 4L was performed. Results were negative. She underwent a right upper lobectomy with standard mediastinal node sampling. At stations 1 and 3,

two out of 10 and one out of three nodes, respectively, were found to be massively invaded by tumor cells. The diameter of metastasis in one of these nodes was superior to 2.5 cm. The second patient was a 75-year-old male who had an initial evaluation in another hospital where he had been treated with induction chemotherapy (CVM) for a cStage IIIa (T2N2M0) squamous cell carcinoma (SCC). After the first cycle of chemotherapy, he solicited a second opinion in our institution where a complete staging reassessment was undertaken. CT-scan staging was T1N2M0 but PET-FDG scan results were T(+)N0M0. Because of partial clinical tumor response to the first cycle, he was offered a second cycle before undergoing a right lower and middle bi-lobectomy. At station 8, two out of nine nodes were found to be invaded by metastatic cells. The diameter of tumor cell islets within one of those nodes was 0.9 cm. The 14 nodes from stations 1, 3, 4, and 7 were negative. The third patient was a 77-year-old heart transplanted male (1991) in whom a lung nodule was discovered during routine follow-up. Percutaneous transthoracic needle biopsy revealed SCC pathology. CT-scan classified a T3N2 lesion but PET-FDG scan results were T(+)N0M0. At mediastinoscopy, all the nodes sampled from stations 4 and 2 remained negative. He underwent a right lower lobectomy with complete mediastinal node dissection. Out of the 16 LNs from stations 4R and 3, six nodes were metastatic. The diameter of tumor burden within one of those nodes was 1.5 cm.

Table 4 shows the details of the eight false-positive patients that were encountered in the study group. Out of these eight patients, three had centrally located tumors and two others had an active inflammatory process (one had active granulomatous disease and another had severe anthroco-silicotic disease on pathological examination of mediastinal LNs).

4. Comments

Our results for the diagnostic sensitivity, specificity, accuracy, and positive and negative predictive values of

Table 3

Results of CT-scan (CT), mediastinoscopy, PET-FDG scan, and CT + mediastinoscopy for the staging of nodal mediastinal involvement in the study group (*n* = 64)

Diagnostic tool	pN0–N1 (<i>n</i> = 53)		pN2–N3 (<i>n</i> = 9) ^a	
	Correctly staged, <i>n</i> (%)	Overstaged (false +)	Correctly staged, <i>n</i> (%)	Understaged (false –)
CT	36/53 (68)	17/53	5/9 (56)	4/9
Mediastinoscopy/ mediastinotomy ^b	20/20 (100)	0/20	3/8 (38)	5/8
PET-scan	44/52 ^c (85)	8/52	6/9 (67)	3/9
CT + mediastinoscopy	48/53 (91)	5/53	3/9 (33)	6/9

^a Out of 11 patients with clinical Stage IIIa or more, one had CR after induction chemotherapy initiated on a clinical staging. One patient was found M1 at thoracotomy and did not undergo lymph node dissection. These two patients were excluded from the analysis.

^b Out of the 64 patients, 28 underwent mediastinal diagnostic surgical procedures based on selection criteria explained in Section 2.

^c In one patient in the study group, PET-scan could not conclude whether nodal involvement was hilar or mediastinal.

Table 4

Details of patients with false-positive PET-FDG scans results ($n = 8$)

	PET-FDG nodal status	pStage	CT nodal status	(CT + mediastinoscopy) nodal status ^a	Pathological details
Patient 1	N2	T1N1M1	1	1 ^a	Adenocarcinoma, central tumor, hilar N1, no retro-obstructive pneumonia, perioperative findings of pleural metastasis
Patient 2	N2	T1N0M0	1	1 ^a	Adenocarcinoma, peripheral, 3 cm Ø, node (+) for active tuberculosis
Patient 3	N2	T2N1M0	1	–	Adenocarcinoma, peripheral, 5 cm Ø
Patient 4	N2	T3N1M0	3	0 ^a (T3)	SCC, central tumor, hilar N1, no retro-obstructive pneumonia
Patient 5	N2	T3N0M0	2	0 ^a	SCC, central tumor, hilar N1, no retro-obstructive pneumonia
Patient 6	N2	T4N0M0	0	0 ^a	SCC, peripheral, 7 cm Ø, no retro-obstructive pneumonia, severe anthraco-silicosis
Patient 7	N2	T1N0M0	0	0 ^a	SCC, peripheral, 2 cm Ø
Patient 8	N3	T2N0M0	2	0 ^a	SCC, peripheral, 3 cm Ø

^a When available.

CT-scan in our group of patients studied are in agreement with several previously published series. Gdeedo et al. [12] results, in a series of 74 patients, were 48, 53, 51, 40, and 61%, respectively, and Dillemans et al. [13], in a series of 477 patients, reported values of 69, 71, 71, 51, and 84%.

Our results concerning the PET-FDG scan, 67, 85, 82, 43, and 93.6%, respectively, are slightly inferior to those found in the most recent published series. Scott et al. [14] reported values of 100, 98, 99, 91, and 100% in a series of 27 patients. However, only 2.8 LNs were sampled per patient on average and one could argue that some nodal stations remained unexplored, leading to optimistic results. Gupta et al. [15] reported a series of 71 patients with 126 LNs sampled (less than two per patient) with respective values of 93, 94, 96, 92, and 96%. In their series, there were four false-positive and four false-negative results. Finally, Kernstine et al. [16] recently reported their experience in a series of 64 patients and 122 LNs. Sensitivity, specificity, and diagnostic accuracy of PET-FDG scan were 70, 86, and 84% (vs. 65, 79, and 76% for CT-scan) with an 8% (two out of 25) false-negative rate.

In the current study, all 64 patients had complete mediastinal surgical staging with 1240 LNs available for pathological examination (19.4 nodes/patient). Therefore, we believe that the reported results are rather realistic and that there should be minimal bias with respect to the completeness of mediastinal pathological staging. We do not have a clear explanation for the false-negative results of PET-FDG scan. In a previous report, Vansteenkiste et al.

[17] suggested that their five false-negative node results (two out of 68 patients) were due to microscopic tumor burden in the mediastinal LNs and the current limits of the PET-FDG technique. However, in our series, the three false-negative patients had metastatic mediastinal LNs with tumor burden ranging from 0.9 to more than 2 cm in diameter. Thus, it is likely that the biological behavior of the tumor cells has also to be accounted for when considering potential limitations of this non-invasive technique.

Importantly, in our series, eight false-positive patients (eight out of 64), or 12.5% of all patients, would have been denied surgical exploration with a curative intent if no further diagnostic procedures had been performed. In our experience, seven out of the eight false-positive PET-FDG scan patients were correctly staged after mediastinoscopy (Table 4).

The potential impact of PET-FDG scan on the overall preoperative work-up is illustrated in Table 5 which represents a comparison between our current strategy and a hypothetical setting with the study group population. Based on our criteria described in Section 2, 17 patients (Group I) should not have had mediastinal staging as part of preoperative work-up whereas 47 patients (Groups II and III) should have undergone mediastinoscopy or anterior mediastinotomy, in 13 cases for clinical T3 or T4 tumors and/or enlarged mediastinal LNs on CT-scan (Group II), and in 34 patients for a non-small and non-SCC histology (Group III). Adding the PET-FDG scan to the preoperative

Table 5

Requirements for mediastinal surgical staging based on standard criteria in the study group ($n = 64$)^a

Mediastinal surgical staging based on	SCC T1/T2, no enlarged LN, Group I ($n = 17$)	SCC T3/T4 and/or enlarged LN, Group II ($n = 13$)	Adenocarcinoma, Group III ($n = 34$)	Surgical staging procedures
CT-scan	0/17	13/13	34/34	47/64
PET-FDG scan	3/17	5/13	7/34	15/64

^a SCC, squamous cell carcinoma; LN, lymph node.

work-up, and taking into consideration its very accurate negative predictive value and its relatively low specificity would have modified our strategy in the initial work-up in such a way that out of the 17 patients of Group I, only three would have undergone mediastinal surgical staging. Out of the 13 patients of Group II, five would have had mediastinoscopy/mediastinotomy and finally, out of the 34 patients from Group III, only seven were PET-FDG scan positive and would have undergone mediastinal surgical staging. Of the 64 patients, 49 patients had negative PET-FDG scan. Three out of these were false-negative (one patient in each group) whereas in one patient, the PET-FDG scan could not differentiate the hilar location of the primary tumor from an ipsi-lateral mediastinal LN. Thus, taking into account the results of the PET-FDG scan and its high negative predictive value, only 15 mediastinal surgical staging procedures would have been performed. This represents a three-fold decrease in the amount of invasive procedures NSCLC patients would have to undergo.

During the study period (1998–2000), based on the Belgian medicare system for medical costs coverage, the estimated cost for a PET-FDG scan study is 818 euro. This diagnostic test is performed on an outpatient basis. During the same period, reviewing our database, we calculated the average costs for a standard mediastinal surgical staging procedure. Routinely, this requires an overnight hospital stay. Including operating room costs, medications, anesthesiologist and surgeon fees, the average cost sums up to 2479 euro.

Following the inclusion criteria for surgical staging strictly, our study group should have had 47 mediastinal surgical procedures out of the 64 patients (total cost = 116 509 euro).

However, 28 surgical staging procedures only were performed in addition to the PET-FDG scan studies, revealing the selection bias in this non-controlled non-randomized trial where throughout the study period, our growing confidence in a negative PET-FDG scan study increased our threshold for invasive surgical staging.

Following strictly PET-FDG scan results and pursuing investigations only with positive results, our study group should have had 15 mediastinal surgical staging procedures out of the 64 patients (37 184 euro), in addition to the PET-FDG scan studies (37 184 euro) (total cost = 89 539 euro).

As shown in Tables 5 and 6, this could have reduced

overall staging costs by about 23%, in addition to a three-fold reduction in the number of surgical procedures required, sparing patients surgical stress, associated morbidities, and the theoretical risk of mortality.

Only three out of 64 (4.7%) patients would not have been accurately stratified preoperatively as to whether a primary surgery (N0–N1 disease) or multimodal therapy (N2–N3 disease) was to be preferred. In contrast, our current strategy left twice as many patients understaged (six out of 64 or 9.4%) for their disease despite an increased number of preoperative invasive surgical staging procedures. The lack of sensitivity of mediastinoscopy and mediastinotomy is well established in the literature [18] and is dependent on the expertise of the surgeon, the completeness of the procedure, and the accessibility of the mediastinal nodes. Indeed, nodes from stations 8 and 9 as well as the lowest nodes from station 7 are out of reach through conventional approaches [19,20]. Even with a thorough dissection of the entire tracheal environment, there is still a potential for sampling error since the nodal biopsy could miss a small metastatic islet of cells within a node unless total LN excision is carried out. Improved accuracy has been reported with the more radical ‘extensive cervical mediastinoscopy’ [19,21]. However, this procedure carries with it an increased risk for injury to major mediastinal structures [22]. Recent data suggest that additional thoracoscopic procedures, which allow inferior and posterior mediastinal LN sampling, could improve the overall sensitivity of invasive surgical staging techniques [23,24]. However, the reported series only included a small number of patients and thus their results have still to be confirmed in larger series.

In conclusion, the current study suggests that PET-FDG scan is a valuable adjunct in the preoperative diagnostic staging of NSCLC even though the overall accuracy (82%) was lower than data previously reported by others. PET-FDG scan strength lies mostly in its very high negative predictive value. This should alleviate the need for surgical staging procedures in patients whose PET-FDG scan studies are negative. We believe that with a positive PET-FDG scan result, every effort should be pursued to confirm or infirm mediastinal LN involvement so as not to exclude false-positive patients who otherwise would be denied surgical exploration with a curative intent.

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Table 6
Costs analysis

Diagnostic tool	Conventional staging costs in euro (n patients)	PET-FDG scan-based staging costs in euro (n patients)
Mediastinoscopy/mediastinotomy	116 509 (47)	37 184 (15)
PET-scan	– (0)	52 355 (64)
Total costs	116 509 (64)	89 539 (64)

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Appendix A. Conference discussion

Dr D. van Raemdonck (Leuven, Belgium): Your results accord with the results that we have published previously.

Can I ask you what your current policy is in a patient with a central tumor and a negative PET-scan on the mediastinum?

Dr Poncelet: In this study, in fact, we did not do co-registration of CT-scan and PET-FDG, so that we believe that our false-positive rate is higher than what was published previously. So our aim now would be first to do co-registration. However, we probably would go to mediastinoscopy.

Dr van Raemdonck: It's also our practice for central tumors to still do a mediastinoscopy because the PET-scan is having difficulties in distinguishing lymph nodes from the primary tumor.

Dr Poncelet: That is correct.

Dr T. Dosios (Athens, Greece): Do you think that every patient who is going to be operated on should have a PET-scan preoperatively from now on, and, if so, what about the cost?

Dr Poncelet: What was not studied in this presentation is the number of positive findings outside of the thoracic wall and parenchyma. Several studies have shown that there is probably more than 10% of patients who would be initially operated on without a PET-FDG and who would prove to be metastatic by PET-FDG and histology. So I believe that PET-FDG should be done in every patient, even for the N0 patient. Currently the cost in Belgium is about \$700.

Dr A. Imdahl (Freiburg, Germany): I understand that you miss N1 disease with a PET-scan because N1 is localized near the tumor and you get one hot spot, but I have difficulty understanding why N2 was false-negative. It might be worth it to look at markers, for instance, the proliferation index or whatever. Have you done that?

Dr Poncelet: As we have seen on the slide, we have looked into the diameter of the metastatic cell islets within the lymph nodes, and in contrary to what was published by the Leuven group, in our cases there was a large amount of metastatic cells within the nodes. We haven't studied the biological behavior of these tumors.

Dr K. Jeyasingham (Winterbourne Down, UK): You mentioned that you would do PET-scan for all cases. If you were going to do PET-scan and CT-scan, at what point would you do the PET-scan and at what point would you do the CT-scan in order to reduce cost and time?

Dr Poncelet: I would probably say that with a peripheral small tumor that you see on the chest X-ray and which is centrally located in comparison to the chest wall, you might think that just doing the PET-scan as a preoperative work-up would be enough just because you know that the resection would probably be easy. Now, the CT is an indication for the local information when you need to know whether the chest wall or the mediastinum is invaded.

Dr van Raemdonck: If I can add to this comment, I also agree that PET-scan and CT-scan should be added together because you still need anatomical information next to the biochemical information. So I think you still need both investigations if you have the money to do it.

Dr K. Al Kattan (Riyadh, Saudi Arabia): Obviously we have a bit differ-

ent type of population because we have a higher incidence of TB, which makes the diagnostic differentiation a bit more difficult. But when we started the biologic study using PET-scan, we noted that, yes, we can save some money by detecting extra-thoracic lesions which you wouldn't detect before, but also we started doing too many investigations for suspicious lesions that would have not been significant on CT alone; contralateral lymph node, for example, or on the other side or a small old TB on

another lobe, that you need also to do further investigation, and I think we used to have this when we used to do routine brain CT and bone scan and details for lung cancer, and then we stopped because it's not cost-effective and we started to do it only on symptomatic patients. So I think routine use of PET can have advantages but can also have a lot of disadvantages costwise, even if you bring the cost up to \$700, as you said.