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Additional value of PET-CT in the staging of lung cancer: comparison with CT alone, PET alone and visual correlation of PET and CT

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Abstract Integrated positron emission tomography (PET) and computed tomography (CT) is a new imaging modality offering anatomic and metabolic information. The purpose was to evaluate retrospectively the accuracy of integrated PET-CT in the staging of a suggestive lung lesion, comparing this with the accuracy of CT alone, PET alone and visually correlated PET-CT. Fifty patients undergoing integrated PET-CT for staging of a suggestive lung lesion were studied. Their tumor, node, metastasis (TNM) statuses were determined with CT, PET, visually correlated PET-CT and integrated PET-CT. These TNM stages were compared with the surgical TNM status. Integrated PET-CT was the most accurate imaging technique in the assessment of the TNM status. Integrated PET-CT predicted correctly the T status, N status, M status and TNM status in, respectively, 86%, 80%, 98%, 70% versus 68%, 66%,88%, 46% with CT, 46%, 70%, 96%, 30% with PET and 72%, 68%, 96%, 54% with visually correlated PET-CT. T status and N status were overstaged, respectively, in 8% and 16% with integrated PET-CT, in 20% and 28% with CT, in 16% and 20% with PET, in 12% and 20% with visually correlated PET-CT and understaged in 6% and 4% with integrated PET-CT, versus 12% and 6% with CT, 38% and 10% with PET and 12% with visually correlated PET-CT. Integrated PET-CT improves the staging of lung cancer through a better anatomic localization and characterization of lesions and is superior to CT alone and PET alone. If this technique is not available, visual correlation of PET and CT can be a valuable alternative.

Keywords Integrated PET-CT · Visually correlated PET-CT · Lung cancer · Staging

Introduction

Lung cancer is a common disease with approximately 3-million new cases per year worldwide and is the leading cause of cancer-related death in many countries. Eighty percent of the lung cancers are non-small cell lung cancers (NSCLC) and 20% are small cell lung cancers (SCLC) [1]. Tumor, node, metastasis (TNM) staging, as defined by the American Joint Committee on Cancer (AJCC), is a very important tool not only to determine the prognosis but also to choose the most appropriate therapy for patients with NSCLC [2]. Staging a patient with lung cancer implies an accurate determination of the size of the tumor, the potential infiltration of the tumor into the adjacent structures, the involvement of hilar and mediastinal lymph nodes and the detection of distant metastases. Conventional chest radiography, ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy, and positron emission tomography (PET) are all being used for this purpose. However, CT remains the routine imaging procedure for staging patients with NSCLC. The success of CT is related to the fact that very detailed imaging information of the localization and extent of the tumor, the presence of enlarged lymph nodes and the

presence of metastatic disease can be provided [3]. PET has more recently been introduced in tumor staging and it has been used successfully for detection of primary tumors, metastases, and early tumor recurrence [4, 5]. However, the relatively poor spatial resolution, the low contrast between different tissues and the blurring due to motion and partial volume effects in small foci can result in difficulties to localize lesions that show pathologic 2-deoxy-2-[^{18}F] fluoro-D-glucose (FDG) uptake [6]. Furthermore, FDG not only enhances most malignant tumors but can also enhance areas of active inflammation. On the other hand, some tumor tissue shows no or little FDG uptake, like microscopic tumor deposits and biologically weak tumors, such as bronchoalveolar cell carcinoma, carcinoid tumors and some adenomas [7–9]. Combining detailed anatomical information obtained by CT with the metabolic information from FDG-PET seems logical, therefore, because it can solve some of these problems. It has indeed been shown that the accuracy of CT and FDG-PET improves when the PET images are visually correlated with the CT images [10]. PET and CT images can also be fused digitally using software methods. However, these software approaches often provide significant difficulties for the chest and the abdomen due to positional and motion-induced data misregistration, and are generally labor intensive and uncertain of success [11]. In addition, these fusion images seem to add only marginal benefit to correlation [10]. Integrated PET and CT is the most recent approach to post hoc image fusion. It combines these image modalities into one scanner that acquires accurately aligned anatomical and functional images in the same scanning session. The first studies using integrated PET-CT have shown that this technique improves diagnostic accuracy when compared with separately acquired CT and PET [12–14]. While it is obvious that integrated PET-CT will improve TNM staging of lung cancer by combining both techniques, there is some debate in the literature as to whether integrated PET-CT provides better results than visual correlation of PET and CT images arranged side by side. The purpose of our study is to evaluate the accuracy of integrated PET-CT in the staging of lung cancer in comparison with CT alone, PET alone and also with visual correlation of CT and PET side by side.

Materials and methods

Patients

Fifty consecutive patients (44 men, six women) with a median age of 64 years for men (range 26–83) and 60 years for women (range 46–72) were retrospectively included in our study. All these patients underwent an integrated PET-CT in the period from March 2004 till December 2004. The integrated PET-CT was done for staging a lung lesion that was suggestive of a lung tumor without metastases on previous clinical or radiological examinations. Patients with evidence for metastatic disease were excluded from the study. Lesion sampling was performed with bronchoscopy and brushing, transbronchial biopsy, transthoracic or peroperative biopsy. Surgical staging in all these patients was performed during mediastinoscopy (26 patients) or during surgical exploration (24 patients).

If patients showed unexpected metastatic disease on the integrated PET-CT, the most appropriate standard examination technique was performed to evaluate the suspected region: a bone scintigraphy to exclude osteoblastic bone metastases, a dedicated CT of the brain to exclude brain metastases, a coloscopy to exclude pathology of the colon, thoracic surgery to exclude lung metastases. Lesions of the adrenal glands were not explored and the information from PET and CT together with the information of follow-up CT were used to determine the nature of the lesion.

If patients were N2 or N3 negative, a thoracotomy with lobar or pulmonary resection and a complete thoracic lymph adenectomy were performed. If patients were N2 positive, chemotherapy or radiotherapy was given. If a lesion was not confirmed as malignant follow-up was done.

Forty-five lesions were malignant (23 adenocarcinoma, one carcinoid, one metastasis, two squamous cell carcinoma, 14 spinocellular carcinoma, three spinocellular epithelioma, one undifferentiated tumor) and five benign (one granuloma, two chronic infection, one eosinophilic pneumonia, one arterio-venous malformation).

PET-CT acquisition

All patients were examined on a dual-modality PET-CT tomograph (Biograph LSO Duo; Siemens Medical Solutions). The CT component of the biograph LSO duo correspond to a Somatom Emotion Duo (Siemens Medical Solutions), a two-row spiral CT system with a maximum continuous scan time of 100 s and a maximum rotation speed of 75 rpm. CT images were acquired with 85 mAs, 130 kV, slice thickness of 5 mm, and table feed of 12 mm per rotation. The scanning area for CT and PET was defined on a CT topogram. Single-section whole-body spiral CT was performed starting with the head and subsequently covering the neck, thorax, abdomen, and pelvis. To ensure diagnostic CT image quality, 120 ml of a contrast agent containing 300 mg iodine per milliliter (Xenetix 300; Guerbet, Sulzbach, Germany) was administered intravenously using an automated injector (1.6 ml/s, scan delay 100 s). CT was performed during breath-hold at expiration tidal volume. This limited breath-hold technique was used to avoid respiration artifacts on the CT images and is necessary for a good matching between the CT images and the PET images, since the latter are obtained during normal breathing [15, 16].

The PET component of the combined PET-CT tomograph is based on an ECAT ACCEL (Siemens Medical

Solutions), a full-ring Lutetium ortho silicate (LSO)-based PET system with an in-plane spatial resolution of 4.6 mm and an axial field of view of 15.5 cm for each bed position. PET images were corrected for attenuation on the basis of the CT data, and iterative reconstruction algorithms with two iterations and eight subsets were performed. PET imaging was performed 75 min after the administration of 4.5 MBq/kg of FDG. Patients had been instructed to fast for a minimum of 4 h prior to starting the examination. Blood samples collected before the injection of the radioactive tracer ensured blood glucose levels in the normal range.

Data analysis

CT images

CT staging was performed using the CT images obtained from the integrated PET-CT scanner. A radiologist experienced in chest CT reading interpreted these CT images blinded to the information from the PET part of the integrated PET-CT and, when performed, also to the information from a previous CT scan. Only the information that a PET-CT was performed to stage a lesion suggestive of a lung tumor was given. The radiologist was asked to assign a T, N, and M status of the tumor using the International System for Staging [17]. Tumor assessment was based on lesion size and localization of the lesion, on contrast enhancement and its relation to the surrounding structures. Lymph node assessment was based on size and consistency of the lymph node. Lymph nodes with a short-axis diameter greater than 10 mm were defined as containing tumor [18]. Enlarged lymph nodes with a lipoid centre were considered as benign. Assessment of the M status for lung, liver, adrenal glands, brain and bone was performed using criteria such as size, localization and contrast enhancement.

PET images

PET staging was performed by a nuclear medicine physician, who interpreted the PET part of the integrated PET-CT without knowledge of the information from CT or other previous examinations. Again, only the information that an integrated PET-CT was performed to stage a lesion suggestive of a lung tumor was given. Qualitative analysis of the images was performed by visual identification of areas of increased FDG uptake. A focally increased FDG activity above physiologic levels was considered abnormal and displaying potential malignancy. Number and location of foci were registered, and T, N and M status of each patient was assigned again using the International System for Staging [17].

Combined analysis of CT and PET: side by side correlation and inherent image fusion

PET-CT staging was performed with PET and CT images visually correlated side by side and using the fusion images produced by the integrated PET-CT scanner. The visual correlation was performed by a radiologist at least 1 month after he had finished the CT staging. At the time of the visual correlation not only the images but also the report of the PET examination were available. A second radiologist and nuclear medicine physician interpreted together in consensus the PET-CT fusion images and the T, N and M status were assigned [17]. To decide this TNM status, the same criteria for CT and PET as mentioned above were used. When there was a discordance between CT and PET the decision whether the lesion was suspicious or not depended on the following criteria: (1) a lesion suggestive of a primary tumor on CT but negative on PET was considered as positive when there were other signs on CT (contrast enhancement, feeding vessel sign) which made this lesion suggestive, (2) a lesion not suggestive on CT but positive on PET was made positive for tumor on integrated PET-CT, (3) pulmonary nodules suggestive for lung metastases on CT but PET negative were considered as lung metastases, (4) enlarged and suspected lymph nodes on CT but negative on PET were considered as negative on integrated PET-CT, (5) mediastinal hotspots on PET but without a visible lesion on CT were considered as negative (e.g., brown fat tissue) on integrated PET-CT, (6) an enlarged adrenal gland on CT but PET negative was considered as not tumoral invaded, (7) lesions in the liver and in the brain suspicious of metastases on one of the two examinations were considered as positive for metastases, (8) PET-positive lesions in the abdomen not related to liver or adrenals were correlated with the corresponding structure on CT to decide if they were metastatic or not.

Statistical analysis

Analysis for the tumor (T status), lymph nodes (N status), and metastases (M status) with CT alone, PET alone, visually correlated PET-CT and integrated PET-CT was performed and compared with the surgical staging which was used as standard of reference. The relative accuracies of the different imaging techniques in the assessment of the T, N, and M status and of the TNM system stage were compared by McNemar (exact) test (95% confidence interval). Sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV) and accuracies were calculated regarding their ability to detect malignant lymph nodes (N status).

Results

T status

In 43 (86%) patients, integrated PET-CT evaluated correctly the T status, while CT was correct in 34 (68%), PET in 23 (46%) and visually correlated PET-CT in 38 (72%) patients (Figs. 1, 2). The difference between integrated PET-CT and CT and integrated PET-CT and PET was significant (P=0.0269 and P<0.0001, respectively). However, there was no statistically significant difference between integrated PET-CT and visually correlated PET-CT (P=0.2888). There was an overstaging in only four (8%) patients with integrated PET-CT versus ten (20%) with CT, eight (16%) with PET and six (12%) with visually correlated PET-CT and an understaging in only three (6%) patients using integrated PET-CT versus six (12%) using CT, 19 (38%) using PET and six (12%) using visually correlated PET-CT (Fig. 3). Table 1 shows these findings in more detail.

N status

Integrated PET-CT evaluated the N status correctly in 40 (80%) patients, while CT was correct in 33 (66%), PET in 35 (70%) and visually correlated PET-CT in 34 (68%) patients. However, there was no statistical difference. There was an overstaging in eight (16%) patients with integrated PET-CT versus 14 (28%) with CT, ten (20%) with PET and ten (20%) with visually correlated PET-CT and an understaging in two (4%) with integrated PET-CT versus two (6%) with CT, five (10%) with PET and six (12%) with visually correlated PET-CT (Fig. 4). The

Table 1 Details of accuracy of tumor (T) status for integrated PET-CT compared with CT, PET and visually correlated PET-CT

Surgical staging (number)	Imaging T status (number)	CT (number)	PET (number)	Visually correlated PET-CT (number)	Integrated PET-CT (number)
sT0 (5)	0	0	3	2	3
	1	4	1	2	1
	2	1	1	1	1
	3	0	0	0	0
	4	0	0	0	0
	0	0	0	0	0
sT1 (6)	1	5	5	6	6
	2	0	1	0	0
	3	0	0	0	0
	4	1	0	0	0
	0	0	0	0	0
	1	4	15	4	3
sT2 (31)	2	24	11	25	26
	3	0	4	0	0
	4	3	1	2	2
	0	0	0	0	0
	1	1	2	1	1
	2	0	0	0	0
sT3 (6)	3	4	4	4	5
	4	1	0	1	0
	0	0	0	0	0
	1	0	0	0	0
	2	0	0	0	0
	3	1	2	0	0
sT4 (2)	4	1	0	2	2

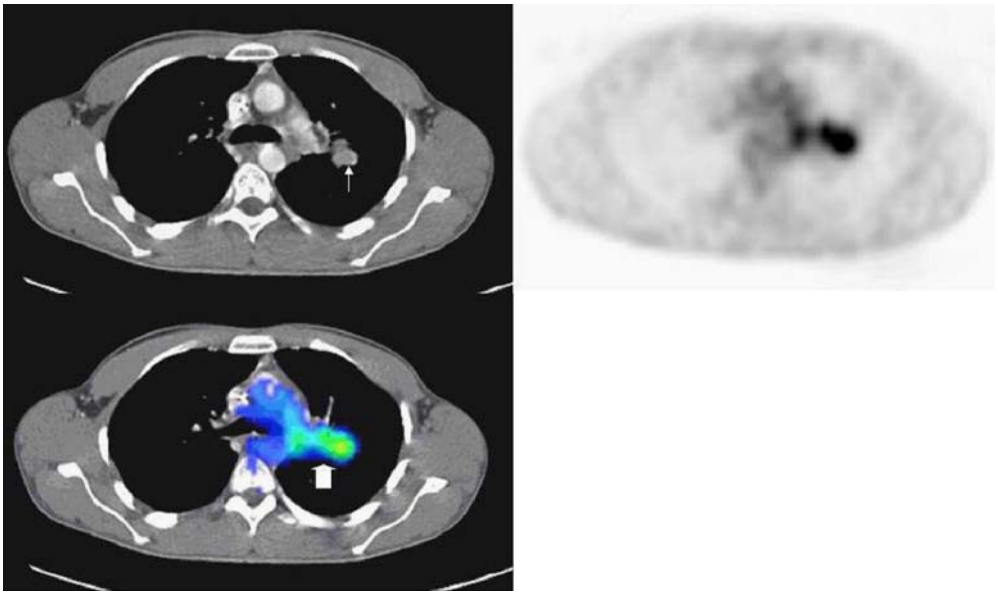

Fig. 1 A 26-year-old man with a tumor in the left lung. On CT, this tumor (*arrow*) was staged as a T1 tumor: a tumor with greatest diameter less than 3 cm. No hilar lymph nodes were seen on CT. The area of FDG uptake on integrated PET-CT was larger than the nodule seen on CT and the tumor was staged as a T2 tumor due to its greatest diameter larger than 3 cm and its extension into the visceral pleura. The surgical staging was also a T2 tumor

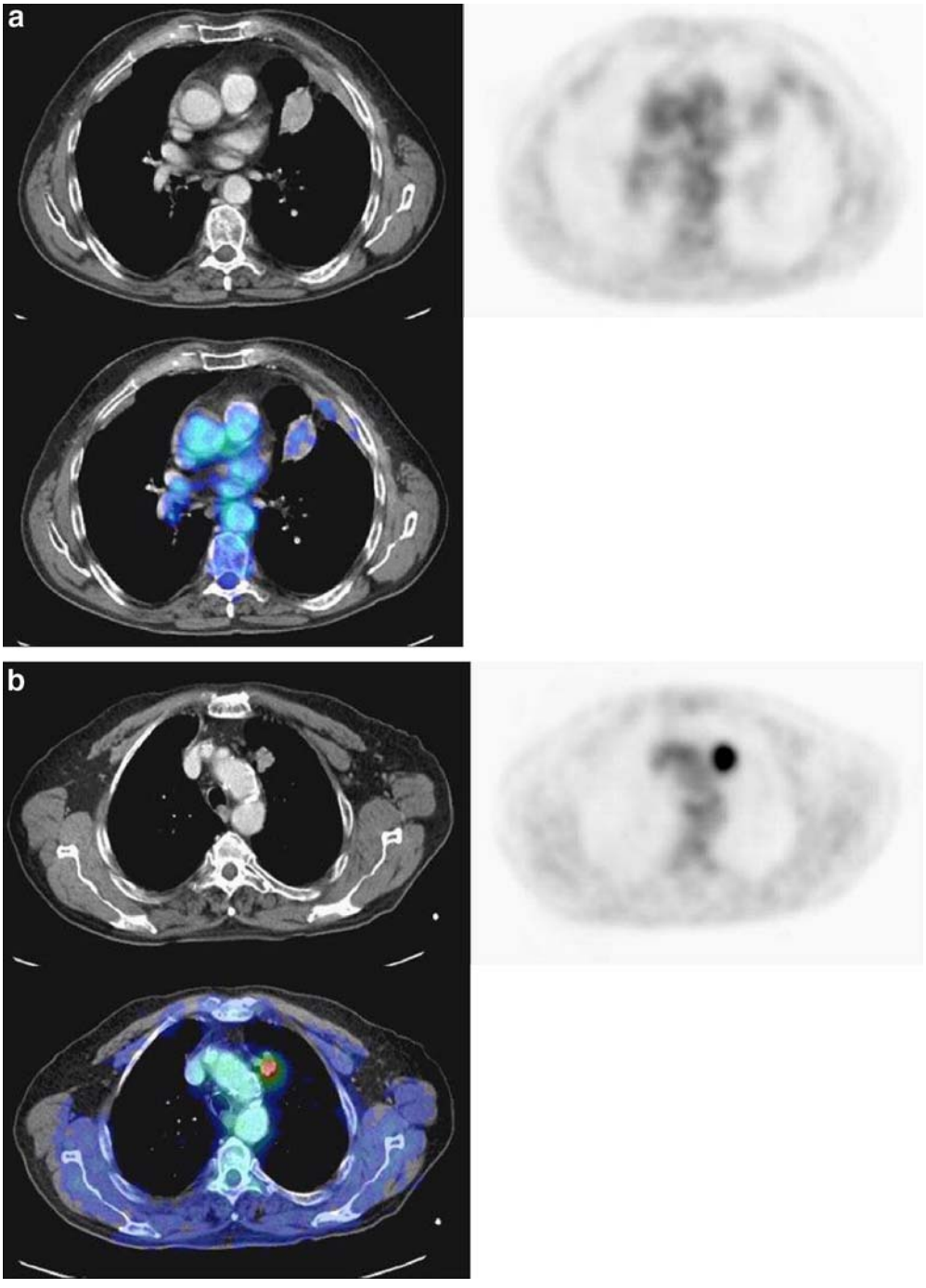

Fig. 2a, b A 76-year-old man with a tumor in the left upper lobe. On CT (**a**) the nodular mass in the lingula was considered as a tumor and the smaller nodular mass more apical in de left upper lobe was considered as a satellite lesion (**b**). There were no enlarged lymph nodes or metastases. The tumor was staged on CT as T4 N0 M0. Integrated PET-CT showed that the tumor was situated in the smaller nodular lesion, but there was no pathologic FDG uptake in the larger lesion in the lingula. The staging with integrated PET-CT was T1 N0 M0. Peroperative the findings of integrated PET-CT were confirmed. The larger mass in the lingula was a fibrotic mass on histopathology without tumor

sensitivity, specificity, PPV, NPV and accuracy of integrated PET-CT, CT, PET and visually correlated PET-CT for the detection of malignant lymph nodes are summarized in Table 2. Table 3 shows these findings in more detail. In our study, integrated PET-CT was the best predictor of the N status in surgical N0 (sN0) and surgical N2 (sN2) status, however the difference was not statistically significant.

Table 2 Sensitivity, specificity, PPV, NPV and accuracy of integrated PET-CT, CT, PET and visual correlated PET-CT for the detection of malignant lymph nodes

	Sensitivity	Specificity	PPV	NPV	Accuracy
Integrated PET-CT	83%	84%	75%	90%	84%
CT	83%	68%	60%	88%	74%
PET	83%	81%	71%	89%	82%
Visual PET-CT fusion	83%	78%	68%	89%	80%

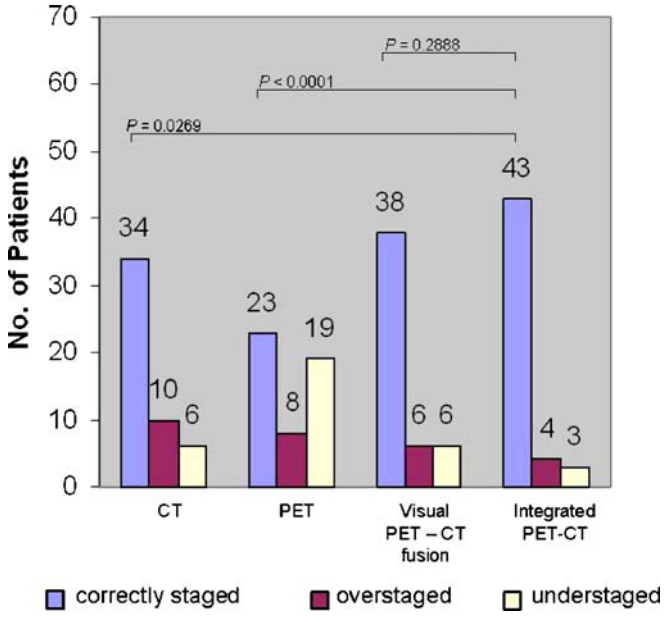

Fig. 3 Accuracy of tumor (T) status for integrated PET-CT compared with CT, PET and visually correlated PET-CT

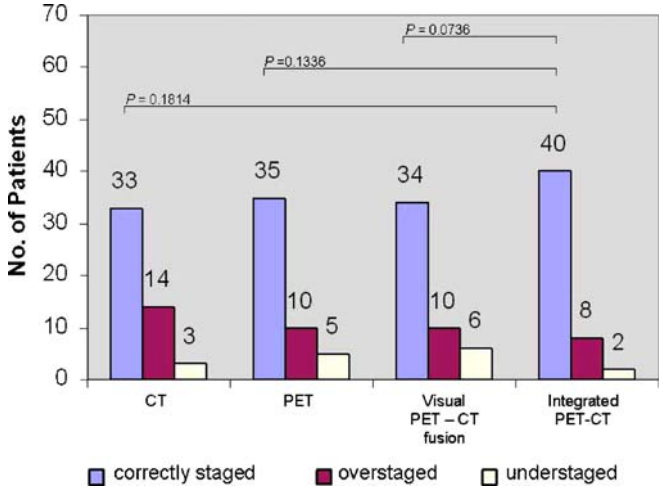

Fig. 4 Accuracy of nodal (N) status for integrated PET-CT compared with CT, PET and visually correlated PET-CT

M status

In our study population, three patients had unsuspected metastatic disease (two lung metastases, one brain metastasis) which was not detected on previous examinations. CT showed nine sites suggestive of metastases: five lung (two true positives, three false positives), one brain (true positive), two adrenals (two false positives), two bone (false positive). PET showed three sites suggestive of metastases: two lung (two true positives) and one colon (false positive). Integrated PET-CT showed four sites suggestive of metastases: three lung (two true positives, one false positive) and one brain (true positive). Integrated

Table 3 Details of accuracy of nodal (N) status for integrated PET-CT compared with CT, PET and visually correlated PET-CT

Surgical staging (number)	Imaging N status	CT (number)	PET (number)	Visually correlated PET-CT (number)	Integrated PET-CT (number)
sN0 (32)	0	22	26	25	27
	1	0	1	1	0
	2	8	3	4	4
	3	2	2	2	1
	0	2	2	2	2
sN1 (7)	1	4	3	3	4
	2	1	1	1	0
	3	0	1	1	1
	0	1	1	1	1
	1	0	2	2	0
sN2 (10)	2	6	5	5	7
	3	3	2	2	2
	0	0	0	0	0
	1	0	0	0	0
	2	0	0	0	0
sN3 (1)	3	1	1	1	1

PET-CT evaluated correctly the M status in 49 (98%) patients, CT in 44 (88%), PET in 48 (96%) and visually correlated PET-CT in 48 (96%) patients (Fig. 5). However, these differences were again not statistically different. There was an overstaging in one patient with integrated PET-CT versus six with CT, one with PET and four with visually correlated PET-CT. Only PET missed 1 metastatic site (Fig. 5).

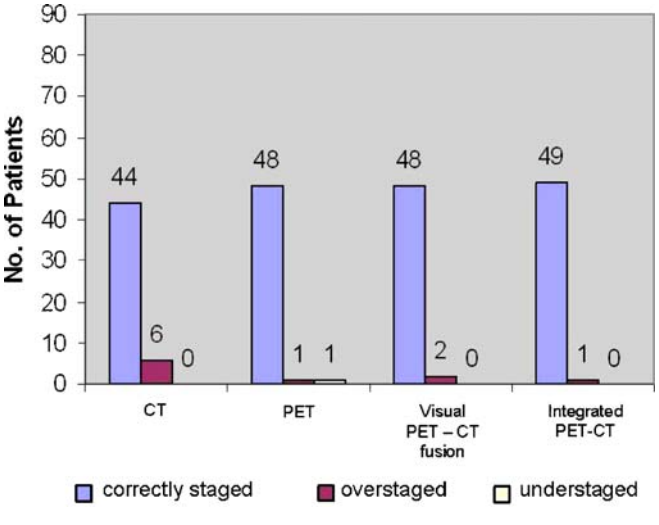

Fig. 5 Accuracy of metastatic (M) status for integrated PET-CT compared with CT, PET and visually correlated PET-CT

Global staging (TNM status)

Integrated PET-CT is more accurate than CT, PET and visually correlated PET-CT in evaluating the TNM status. In 35 (70%) patients global TNM stage was correct with integrated PET-CT versus 23 (46%) with CT, 15 (30%) with PET and 27 (54%) with visually correlated PET-CT. We found a statistical difference between integrated PET-CT and CT alone (P=0.0153) and between integrated PET-CT and PET alone (P=<0.0001), but there was no statistical difference between integrated PET-CT and PET-CT images visually correlated side by side (P=0.0704) (Fig. 6). When there was a mismatch between PET and CT findings at the integrated PET-CT, previously decided criteria were used to determine whether these findings were considered suggestive or not.

Discussion

In this study, 50 lung lesions suggestive of lung cancer were scanned with an integrated PET-CT scanner. First, the CT images and the PET images were analyzed separately, then the CT and PET images were correlated visually side by side, and finally the integrated PET-CT images were evaluated. Analysis of the primary tumor (T status), lymph nodes (N status), and metastases (M status) was performed and compared with the surgical staging, which was available for each patient and which was used as standard of reference.

Our study showed that integrated PET-CT correctly evaluated the T status in 86% of patients, which is significantly better than with CT alone and PET alone. In the literature, the percentages of correctly evaluated T-status with integrated PET-CT are 70% (Cerfolio et al. [14]), 86% (Shim et al. [19]),

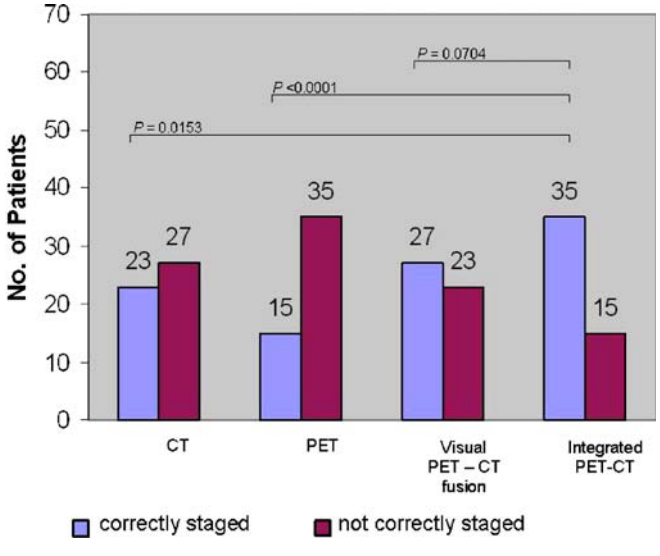

Fig. 6 Accuracy of global TNM staging for integrated PET-CT compared with CT, PET and visually correlated PET-CT

93% (Antoch et al. [12]) and 98% (Lardinois et al. [20]). Differences in patient selection (inclusion of T0 or not) and data acquisition (IV contrast or not) can be responsible for this heterogeneity. Like Lardinois et al. [20], we did not find a significant difference between T status determined by integrated PET-CT and visually correlated CT and PET images side by side. The fact that the anatomic landmarks in the chest (mediastinal structures, chest wall structures) are rather constant and easier to recognize on PET than, for example, the anatomical landmarks in the abdomen, can be one of the reasons why visual correlation of CT and PET images is easier in the chest than in the abdomen, although this advantage is more reliable in the estimation of the N staging [9]. In addition, we did not have any tumor surrounded by athelectatic tissue, a situation where integrated PET-CT could have an advantage over visual correlation since integrated PET-CT allows a better differentiation between tumor and athelectatic lung tissue [20]. The fact that CT was false positive in five sT0 lesions is in part related to the selection of patients, which was on the basis of the presence of a suggestive lesion on chest X-ray, previous CT or bronchoscopy. Both by visually correlating the CT and PET images and by looking at the integrated PET-CT images, the number of false positives could be reduced to three lesions. It has indeed been shown that correlating the anatomical information of CT and the metabolic information of PET can help in excluding malignancy [3, 14, 21] and to differentiate between a mass extending into the hilum or mediastinum and a mass with adjacent enlarged hilar and mediastinal lymph nodes. A striking finding was the downstaging from T1 to T0 status with integrated PET-CT in one patient. This lesion was a nodular lesion with feeding vessel sign on CT suggestive of lung tumor, but after resection histopathology showed that it was an arterio-venous malformation. FDG-PET alone showed no hotspot but only discrete FDG-uptake and was considered negative. During visual correlation of CT and PET the discrete FDG-uptake was located in the nodule, and since this could correspond with a carcinoid it was considered as positive. Integrated PET-CT, which was evaluated by two other physicians, however considered the lesion as negative for a lung tumor. The discrete FDG-uptake of the region and the fact that different physicians evaluated the different images could explain this difference. Integrated PET-CT was better in evaluating the surgical T1, T2, T3 and T4 (sT1, sT2, sT3, sT4) tumor status. It is striking that in the sT2 group PET alone both underestimated and overestimated the T-category of many lesions. This is probably related to the fact that it is difficult to exactly measure the real dimensions of a small hot spot on PET images.

Integrated PET-CT was the best evaluation technique of the sN status. However, the difference with the other imaging modalities and with the results of visually correlated PET and CT was not statistically significant. The most important difference was observed between CT and integrated PET-CT when their potential to predict the presence of normal

mediastinal lymph nodes (sN0) was studied. Integrated PET-CT evaluated the sN0 status correctly in 27 out of 32 patients, while CT was correct in 22 patients. Also the number of false positives was reduced with integrated PET-CT: five with integrated PET-CT and ten with CT. However, PET and visually correlated PET-CT images also reduced the number of false positives. This is not surprising due to the high negative predictive value of PET. The number of correctly evaluated N1 and N2 nodes is comparable between the four techniques. Although integrated PET-CT was slightly better than CT alone, PET alone and visually correlated PET-CT. Underestimation of sN1 with the four techniques was probably related to the fact that some nodes in the hilum close to the central located tumor were considered as part of this tumor. The underestimation of the sN2 nodes was most important with PET and with visually correlated PET-CT. Probably this is related to the fact that the small nodules among them were not identified with PET and considered as normal with CT, while due to the low anatomical detail of PET the large nodules were considered as hilar instead of mediastinal lymph nodes. The overestimation of the N2 nodes as N3 nodes with the four techniques is probably related to an inflammatory enlargement of these nodes. The sensitivity, specificity, PPV, NPV and accuracy of integrated PET-CT was in our study, respectively, 83%, 84%, 75%, 90% and 84%. PET has already a very good negative predicted value, but by combining this metabolic information with the exact anatomic information from CT integrated PET-CT does better. The initial reports in the literature also suggest that integrated PET-CT is superior in accuracy of N-staging in comparison with PET alone, with CT alone, and with visually correlation of PET and CT images arranged side by side [3, 10, 12, 20, 22, 23]. The results for integrated PET-CT in the N staging in the literature show sensitivities of between 71% and 89%, specificities of between 89% and 96%, PPV of between 70% and 89%, NPV of between 90% and 94%, and accuracies of 93% [12, 14, 19, 20]. Our results were in the same range.

Integrated PET-CT evaluated the M status correctly in 98% of the patients, while CT was correct in 88%, PET in 96%.When PET-CT images were visually correlated, M staging was correct in 96% of patients. As can be expected and due to the small number of metastatic lesions these differences were not statistically significant. Also, Cerfolio et al. [14] showed that integrated PET-CT is only a little better to assess metastatic disease compared with PET alone: 92% versus 87%. In their study, the M status was overstaged with integrated PET-CT in eight patients versus 13 with PET and understaged in two patients versus four with PET.

Defining a correct TNM status of course implies that the T status, the N status and the M status are all correctly evaluated. In our study, integrated PET-CT evaluated the TNM status correctly in 70% of the patients, while CT, PET and visually correlated PET-CT were correct in, respectively, 46%, 30% and 54% of the patients. The difference between integrated PET-CT and CT (P=0.0153) and PET (P<0.0001) was significant, and almost significant between integrated PET-CT and visually correlated PET-CT (P=0.0704). Our results were different from the results of Sung et al. [19], who showed a correct overall staging with PET-CT in 87% of patients and with CT in 66% of patients. Their overall staging was only based on tumor and lymph node staging and not on the prediction of metastases. Also, other investigators confirmed the additional value of integrated PET-CT in the staging of lung cancer [12, 14, 24].

Our study has some limitations related to the technique and the selection of the patients. The CT images evaluated in this study have a lower image quality than what can be expected when a stand-alone spiral CT or multislice CT would have been used. The CT part of the integrated PET-CT is performed with a lower dose (80 mAs versus 120 mAs for a dedicated chest CT in our centre) [25]. Although Hany et al. [3] compared different CT doses and found no significant differences in accuracy when 80 mAs was used in comparison with that of a dedicated chest CT. The CT was performed at normal inspiratory breath-hold versus at deep inspiration for a dedicated chest CT. This could induce problems in the detection of small lung lesions [15, 26]. All CT examinations were performed with intravenous (i.v.) contrast administration. The systematic use of i.v. contrast was considered necessary for a good interpretation of the mediastinum, liver and adrenal glands on CT, but could have caused problems during attenuation correction for PET imaging. Although, artifacts due to the use of i.v. CT contrast media are minimalized [27–29]. On the other hand, the fact that no precontrast CT scans were performed probably also has negatively influenced the results of the CT scan, especially in the evaluation of the adrenals.

Because CT is used for attenuation correction PET images obtained from the integrated PET-CT are qualitatively better than “regular” PET images [11]. This improved quality can also have influenced the evaluation of PET and can be to some degree responsible for differences between our results and those found in the literature.

Also our patient selection could have influenced the results of the T staging of the tumor. Indeed all patients had a suggestive lesion on a previous examination and this was known by the radiologists and nuclear medicine physicians.

Conclusion

The major added value of integrated PET-CT is its ability to directly link PET information on metabolic changes of

structures to highly detailed anatomic CT information on these structures [30]. We have confirmed previous reports which concluded that global TNM staging is most accurately performed with integrated PET-CT. Integrated PET-CT has an additional value in comparison with CT and PET alone in a better differentiation of for tumor suggestive lesions as benign or not. If this technique is not available, visually correlation of PET and CT images can be a valuable alternative.

References

1. Ettinger DS (2004) Overview and state of the art in the management of lung cancer. Oncology(Williston Park) 18 (Suppl 4):3–9
2. AJCC Cancer Staging Manual, 6th edn (2002) Greene FL, Page DL, Fleming ID, Fritz A, Balch CM, Haller DG, Morrow M (eds). Springer, Heidelberg New York, pp 165–177
3. Hany TF, Steinert HC, Goerres GW, Buck A, von Schulthess GK (2002) PET diagnostic accuracy: improvement with in-line PET-CT system: initial results. Radiology 225:575–581
4. Scott WJ, Gobar LS, Terry JD, Dewan NA, Sunderland JJ (1996) Mediastinal lymph node staging of non-small-cell lung cancer: a prospective comparison of computed tomography and positron emission tomography. J Thorac Cardiovasc Surg 111:642–648
5. Weder W, Schmid RA, Bruchhaus H, Hillinger S, von Schulthess GK, Steinert HC (1998) Detection of extrathoracic metastases by positron emission tomography in lung cancer. Ann Thorac Surg 66:886–893
6. Wahl RL, Quint LE, Greenough RL, Meyer CR, White RI, Orringer MB (1994) Staging of mediastinal non-small cell lung cancer with FDG PET, CT, and fusion images: preliminary prospective evaluation. Radiology 191:371–377
7. Abouzied MM, Crawford ES, Nabi HA (2005) 18F-FDG imaging: pitfalls and artifacts. J Nucl Med Technol 33:145–155; quiz 162–163
8. Steinert HC (2005) PET in lung cancer. Chang Gung Med J 28:296–305, May
9. Verschakelen JA, De Wever W, Bogaert J, Stroobants S (2004) Imaging: staging of lung cancer. Eur Respir Mon 30:214–240
10. Vansteenkiste JF, Stroobants SG, Dupont PJ, De Leyn PR, De Wever WF, Verbeken EK, Nuyts JL, Maes FP, Bogaert JG (1998) FDG-PET scan in potentially operable non-small cell lung cancer: do anatometabolic PET-CT fusion images improve the localisation of regional lymph node metastases? The Leuven Lung Cancer Group. Eur J Nucl Med 25:1495–1501
11. Townsend DW, Beyer T, Blodgett TM (2003) PET/CT scanners: a hardware approach to image fusion. Semin Nucl Med 33:193–204
12. Antoch G, Stattaus J, Nemat AT, Marnitz S, Beyer T, Kuehl H, Bockisch A, Debatin JF, Freudenberg LS (2003) Non-small cell lung cancer: dual-modality PET/CT in preoperative staging. Radiology 229:526–533
13. Aquino SL, Asmuth JC, Alpert NM, Halpern EF, Fischman AJ (2003) Improved radiologic staging of lung cancer with 2-[18F]-fluoro-2-deoxy-D-glucose-positron emission tomography and computed tomography registration. J Comput Assist Tomogr 27:479–484
14. Cerfolio RJ, Ojha B, Bryant AS, Raghuveer V, Mountz JM, Bartolucci AA (2004) The accuracy of integrated PET-CT compared with dedicated PET alone for the staging of patients with nonsmall cell lung cancer. Ann Thorac Surg 78:1017–1023
15. Goerres GW, Burger C, Kamel E, Seifert B, Kaim AH, Buck A, Buehler TC, von Schulthess GK (2003) Respiration-induced attenuation artifact at PET/CT: technical considerations. Radiology 226:906–910
16. Goerres GW, Kamel E, Heidelberg TN, Schwitter MR, Burger C, von Schulthess GK. (2002) PET-CT image co-registration in the thorax: influence of respiration. Eur J Nucl Med Mol Imaging 29:351–360
17. Mountain CF (1997) Revisions in the international system for staging lung cancer. Chest 111:1710–1717
18. Verschakelen JA, De Wever W, Bogaert J (2004) Role of computed tomography in lung cancer staging. Curr Opin Pulm Med 10:248–255
19. Shim SS, Lee KS, Kim BT, Chung MJ, Lee EJ, Han J, Choi JY, Kwon OJ, Shim YM, Kim S (2005) Non-small cell lung cancer: prospective comparison of integrated FDG PET-CT and CT alone for preoperative staging. Radiology 236:1011–1019
20. Lardinois D, Weder W, Hany TF, Kamel EM, Korom S, Seifert B, von Schultness GK, Steinert HC (2003) Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. N Engl J Med 348:2500–2507
21. Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, Altman H, Keidar Z, Israel O (2003) Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. J Nucl Med 44: 1200–1209
22. Scott WJ, Gobar LS, Terry JD, Dewan NA, Sunderland JJ (1996) Mediastinal lymph node staging of non-small-cell lung cancer: a prospective comparison of computed tomography and positron emission tomography. J Thorac Cardiovasc Surg 111:642–648
23. Magnani P, Carretta A, Rizzo G, Fazio F, Vanzulli A, Lucignani G, Zannini P, Messa C, Landoni C, Gilardi MC, Del Maschio A (1999) FDG/PET and spiral CT image fusion for medistinal lymph node assessment of non-small cell lung cancer patients. J Cardiovasc Surg (Torino) 40:741–748
24. Keidar Z, Haim N, Guralnik L, Wollner M, Bar-Shalom R, Ben-Nun A, Israel O (2004) PET/CT using F-FDG in suspected lung cancer recurrence: diagnostic value and impact on patient management. J Nucl Med 45: 1640–1646
25. Kamel E, Hany TF, Burger C et al (2002) CT vs 68Ge attenuation correction in a combined PET/CT system: evaluation of the effect of lowering the CT tube current. Eur J Nucl Med Mol Imaging 29:346–350

26. Juergens KU, Weckesse M, Stegger L, Franzius C, Beetz M, Schober O, Heindel W, Wormanns D (2006) Tumor staging using whole-body high resolution 16-channel PET-CT: does additional low-dos chest CT in inspiration improve the detection of solitary pulmonary nodules? Eur Radiol 16: 1131–1137
27. Antoch G, Freudenberg LS, Beyer T, Bockisch A, Debatin JF (2004) To enhance or not to enhance? 18F-FDG and CT contrast agents in dual-modality 18F-FDG PET/CT. J Nucl Med 45 (Suppl 1):56S–65S
28. Yau YY, Chan WS, Tam YM, Vernon P, Wong S, Coel M, Chu SK (2005) Application of intravenous contrast in PET/CT: does it really introduce significant attenuation correction error? J Nucl Med 46:283–291
29. Dizendorf E, Hany TF, Buck A, Von Schulthess GK, Burger C (2003) Cause and magnitude of the error induced by oral CT contrast agent in CT-based attenuation correction of PET emission studies. J Nucl Med 44:732–738
30. Schrevens L, Lorent N, Dooms C, Vansteenkiste J (2004) The role of PET scan in diagnosis, staging, and management of non-small cell lung cancer. Oncologist 9:633–643