PET in Lung Cancer

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Accurate tumor staging is essential for choosing the appropriate treatment strategy in patients with lung cancer. It has already been shown that FDG-PET is highly accurate in classifying lung nodules as benign or malignant. Integrated PET-CT enables the exact matching of focal abnormalities on PET to anatomic structures on CT. PET-CT is superior in diagnostic accuracy for T staging and differentiation between tumor and peritumoral atelectasis. PET has also proved to be a very effective staging modality for mediastinal nodal staging. It has been demonstrated to assist mediastinoscopy to reveal additional mediastinal disease in 6% of patients. PET detects unexpected extrathoracic metastases in 10-20% of patients and changes therapeutic management in about 20% of patients. A very high accuracy of FDG-PET in distinguishing recurrent disease from benign treatment effects has been shown. Patients should be evaluated after a minimum of 2 months after completion of therapy. FDG-PET can be clinically used for selecting biopsy sites. At our institution PET-CT has become the standard imaging modality for staging patients with lung cancer. Although not all tumors take up FDG, other radiotracers are being studied to expand the utility of PET-CT. PET-CT offers many opportunities for the patients, the clinicians, and the researchers. PET-CT has the potential to become the most efficient oncologic examination in the near future. *(Chang Gung Med J 2005;28:296-305)*

Key words: PET-CT, lung cancer, fluoro-2-deoxy-D-glucose (FDG).

Basic aspects of PET/CT imaging

Introduction

There are several good reasons for combining PET and CT into a single in-line imaging system, where the patient is moved from the CT to the PET gantry by simple table motion. Such a system provides PET and CT images perfectly co-registered by hardware arrangement provided that the patient does not move. This is of major importance because PET scans of the body provide little anatomic information, and software image co-registration has been shown to be cumbersome and inaccurate by many authors.

At least as important is the fact that attenuation correction in a PET/CT scanner can be done as well with the CT data obtained as anatomic reference. This obviates the lengthy standard attenuation procedure used in PET and improves patient throughput by roughly 30%, when a state-of-the-art CT scanner is incorporated into a PET/CT scanner. A CT scan is in fact an attenuation map, albeit measured with 70-140 keV polychromatic X-rays, while the PET attenuation scan is obtained with relatively monochromatic photons at 511 keV. However, measurements have demonstrated that Hounsfield CT maps can be transformed into PET attenuation maps with relatively simple transformations requiring minimal computational efforts. The qualitative and quantitative properties of PET are maintained when CT is used for

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attenuation correction.

The higher patient throughput of a PET/CT scanner compared to a PET only scanner may offset the additional equipment cost, at least in environments where the number of patients to be scanned per PET scanner is high. A net cost advantage results from the fact that FDG decays rapidly with ahalf-life of 110 min, thus faster scanning results in more efficient use of FDG, which may be deliveredas an initial dose for several patients. While a combination of PET and MR is also conceivable, using MR is difficult because the MR images are not attenuation maps like the CT images. In the brain, where MR is superior to CT for anatomic imaging, software image coregistration is much simpler than with body data, and thus a PET/CT scanner is mainly an instrument which is useful in imaging of the human body from the head down to the feet.

It is likely that these synergistic effects obtained when adding CT to PET are responsible for the almost explosive growth of PET/CT imaging worldwide. Three years after the commercial announcement, more than 500 PET/CT systems have been installed. In our group, we always use integrated PET/CT scans in staging lung cancer. We believe PET/CT is the best single imaging modality to scan patients with lung cancer.

Clinical protocols in PET/CT

At our institution we routinely give diluted bowel contrast agent 1 hour prior to scanning followed by supine FDG injection and patient rest of at least 50 minutes. After bladder voiding just prior to scanning, we first perform a low-dose CT scan at 40 mAs. This covers 100 cm of axial field of view with a slice thickness of 4.5 mm, which is matched to the PET slice thickness. The CT scanner is a state-of-the-art 4-slice helical CT with a gantry rotation of 0.5 s minimum. Extensive evaluation of the CT breath hold breathing pattern, best matching the free breathing pattern of PET data acquisition, has led us to conclude that an unforced end-expiratory state is best, during the period where the CT images the regions adjacent to the diaphragm. Thus patients are instructed to expire and hold their breath when the CT scanner scans this body region. CT scanning is accomplished in less than 30 seconds. Subsequently, PET scanning is started from the pelvis up. Starting in the pelvis rather than the head avoids a potential major PET/CT mismatch in the bladder region. This is due to bladder filling between CT data acquisition and the relatively lengthy PET scan, if started at the head. The PET scan is performed using six to seven table positions. As the PET scanner covers an axial field of view of around 15 cm with 32 slices per table position, roughly 90-105 cm of the patient are covered, including the anatomic regions from the brain to the upper thighs in almost all patients. With table position imaging times of 3-4 minutes, typical scan length of a PET/CT partial body scan (head to the mid-upper thighs) is 25-30 minutes.

After this ‘baseline’ PET/CT data acquisition, additional standard CT protocols can be run depending upon the clinical requirements. It is desirable in some settings to also perform a CT scan enhanced with intravenous contrast, which can better delineate the lesions in relation to vascular structures. The overall protocol design for such all-encompassing PET/CT examinations is not defined; where and when additional contrast enhanced CT scanning is useful will have to be evaluated over the next few years.

Non-small-cell lung cancer (NSCLC)

If patients with NSCLC do not show mediastinal lymph node metastasis and if we are able to exclude distant metastasis, then surgery will be performed. But, only in about 50% of all patients can surgery be done. In the situation of ipsilateral mediastinal lymph node metastasis but no contralateral mediastinal lymph nodes and no distant metastasis, neoadjuvant chemotherapy will first be performed followed by surgery. So it is essential to diagnose accurately ipsilateral mediastinal metastasis. In the case of contralateral mediastinal metastasis or distant metastasis, only palliative chemotherapy can be done to increase the quality of life of the patient. What is important is the preoperative staging of these patients. The basic questions we ask are (1) what is the T stage of the primary tumor? (2) where is the tumor localized exactly? and (3) does the tumor invade the surrounding tissue?

Classification and staging

Staging of NSCLC is based on the TNM system and requires accurate characterization of the primary tumor (T stage), regional lymph nodes (N stage), and extrathoracic metastases (M stage).

NSCLCs include adenocarcinomas, squamous cell carcinomas, and large cell carcinomas. Adenocarcinomas develop typically in the periphery of the lung and are most common in women and innonsmokers! Adenocarcinomas have a high incidence of early metastases and tend to grow more rapidly than squamous cell carcinomas. Bronchioloalveolar cell carcinoma (BAC) is a subtype of adenoarcinoma. BACs typically grow along the alveolar spaces without invasion of the stroma. BAC can appear as a solitary pulmonary nodule, a pneumonia-like consolidation or as multiple nodules throughout the lung. Squamous cell carcinomas are strongly associated with smoking. In general, they have the best prognosis because of their slow growth rate and their low incidence of distant metastases. They tend to become large and develop a central necrosis. Metastases to regional lymph nodes are common. Squamous cell carcinoma is the most common cause of Pancoast tumors. These occur typically at the apex of the lung and are associated with Horner's syndrome and bone destruction. Large cell carcinomas are strongly associated with smoking. They tend to grow rapidly, metastasize early and are associated with a poor prognosis.

The TNM staging system is widely used to classify NSCLC. The last revision of the staging system was approved by the AJCC and the IUAC in 1997 (Table 1). The current classification for NSCLC consists of four stages. Stage IV includes only those patients with evidence of distant metastasis or with separate metastatic tumor nodule(s) in the ipsilateral non-primary-tumor lobe(s) of the lung. Stage III is divided into two sub-stages, Stage IIIA and Stage IIIB. Only Stage IIIB is considered unresectable. Tumors with limited invasion of the chest wall and mediastinum are included in the operable stage IIIA (Table 2). Stage T4 is used for extensive invasion of the mediastinum or diaphragm, e.g. invasion of the great vessels, heart, trachea or esophagus. N1 disease refers to peribronchial and ipsilateral hilar metastases including direct extension. All N1 nodes lie distal to the mediastinal pleural reflection and within the visceral pleura. These patients are considered

Table 1. TNM Staging System

Tumor location	Stage	Definition
Primary tumor (T)	T1	Tumor 3 cm or less at the greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus.
	T2	Tumor with any of the following features of size and extent: More than 3 cm at the greatest dimension; involves main bronchus, 2 cm or more distal to the carina; invades the visceral pleura; associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung.
	T3	Tumor of any size that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina, but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung.
	T4	Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, esophagus, vertebral body, carina; or tumor with a malignant pleural or pericardial effusion; or with satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung.
Regional lymph nodes (N)	N0	No regional lymph node metastasis.
	N1	Metastasis to ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intrapulmonary nodes involved by direct extention of the primary tumor.
	N2	Metastasis to ipsilateral mediastinal and/or subcarinal lymph node(s).
	N3	Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).
Distant metastasis (M)	M0	No distant metastasis.
	M1	Distant metastases and/or separate metastatic tumor nodule(s) in the ipsilateral non-primary-tumor lobe(s) of the lung.

Table 2. TNM Classification

Stage grouping	TNM
Stage IA	T1 N0 M0
Stage IB	T2 N0 M0
Stage IIA	T1 N1 M0
Stage IIB	T2 N1 M0
	T3 N0 M0
Stage IIIA	T3 N1 M0
	T1 N2 M0
Stage IIIB	T4 N0 M0
	T1 N3 M0
	T4 N3 M0
Stage IV 1	Any T any N M

resectable. However, the presence of ipsilateral hilar lymph node metastases decreases the overall survival rate. N2 disease refers to ipsilateral paratracheal and/or subcarinal lymph node metastases. These patients have potentially resectable disease. Today, at our institution, most patients with N2 disease receive neoadjuvant chemotherapy for reduction of the tumor mass before surgery. N3 disease refers to contralateral mediastinal nodal metastases, contralateral hilar nodal metastases, and ipsilateral or contralateral scalene or supraclavicular nodal metastases. N3 disease is considered unresectable.

Clinical application of PET/CT

Accurate tumor staging is essential for choosing the appropriate treatment strategy in patients with NSCLC. It has already been shown that FDG-PET is highly accurate in classifying lung nodules as benign or malignant. Whole-body PET improves the rate of detection of mediastinal lymph node metastases as well as extrathoracic metastases when compared to conventional imaging methods, such as CT, MR, ultrasound or bone scan. Since commercial PET scanners provide nominal spatial resolution of 4.5-6 mm in the center of the axial field of view, even lesions less than 1 cm with an increased FDG uptake can be detected. This represents a critical advantage of PET over CT and MR. Integrated PET/CT enables the exact matching of focal abnormalities on PET to anatomic structures on CT. Our results show that PET/CT is superior in diagnostic accuracy in comparison to PET alone, CT alone, and visual correlation of PET and CT.

Solitary lung nodule

The ability of PET to differentiate benign and malignant lesions is high, but not perfect. For benign lesions, a high specificity for FDG-PET has been demonstrated. It has been shown that FDG-PET is highly accurate in differentiating malignant from benign solitary pulmonary nodules (0.6-3 cm) when radiographic findings were indeterminate. In a series of 61 patients, PET had a sensitivity of 93% and a specificity of 88% for detecting malignancy. However, FDG-PET may show negative results for pulmonary carcinoid tumors and bronchiolo-alveolar lung carcinoma. Lesions with increased FDG uptake should be considered malignant, although false-positive results have been reported in cases of inflammatory and infectious processes, such as histoplasmosis, aspergillosis, or active tuberculosis. PET is clinically useful in patients with a solitary pulmonary nodule less than 3 cm in diameter, especially where biopsy may be risky or where the nodule carries a low risk for malignancy based on patients' history or radiographic findings. With integrated PET/CT, additional certainty of the presence or absence of FDG uptake in the pulmonary nodule can be achieved.

T staging

Without image fusion, the use of PET in T staging lung cancer is limited. Recently, it has been shown that integrated PET/CT is superior to CT alone, PET alone, and visual correlation of PET and CT in T staging of patients with NSCLC. Due to the exact anatomic correlation of the extent of FDG uptake, the delineation of the primary tumor can be defined precisely. Therefore the diagnosis of chest wall infiltration and mediastinal invasion by the tumor is improved (Fig. 1, 2). Lesions with chest wall infiltration are classified as Stage T3 and are potentially resectable. Integrated PET/CT provides important information on mediastinal infiltration too. However, PET/CT imaging is unable to distinguish contiguity of tumor with the mediastinum from the direct invasion of the walls of mediastinal structures. It has been shown that FDG-PET is a useful tool for differentiation between tumor and peritumoral atelectasis. This is particularly important for the planning of radiotherapy in patients with lung cancer associated with an atelectasis. The information provided by FDG-PET results in a change in the radiation field in approximately 30-40% of patients.

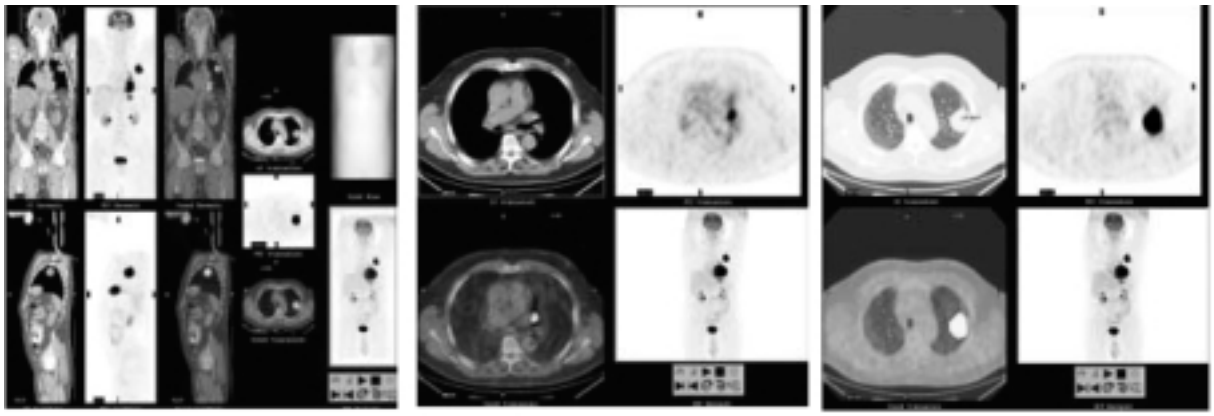

Fig. 1 A 64-year-old man with a non-small-cell lung carcinoma (squamous cell carcinoma) of the left upper lobe with intrapulmonary lymph node metastasis. (A) Full computer screen with CT, PET, PET/CT scans and maximal intensity projection (MIP) showing the extent of disease. Physiological FDG uptake in the brain, myocardium, kidneys and bladder. No evidence of mediastinal or extrathoracic metastases. (B) Transaxial CT (pulmonary window), PET, and PET/CT scans showing the primary tumor which has contact with the pleura but does not invade the thoracic wall. (C) Transaxial CT (soft tissue window), PET, and PET/CT scans showing the ipsilateral peribronchial lymph node metastasis.

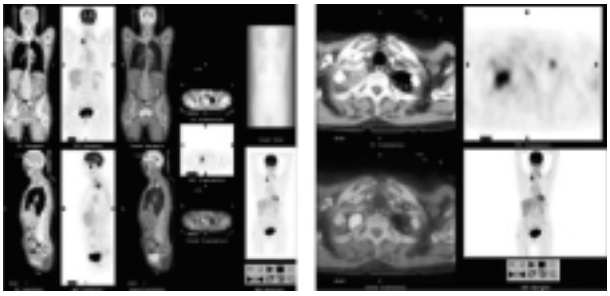

Fig. 2 A 61-year-old woman with a Pancoast tumor of the right lung. (A) Full computer screen with CT, PET, PET/CT scans and maximal intensity projection (MIP) showing the extent of disease. No evidence for further malignant lesions. (B) Transaxial contrast enhanced CT, PET, and PET/CT scans showing that the tumor has contact with the right A. subclavia which represents tumor infiltration of the thoracic wall.

N staging

PET has proved to be a very effective staging modality for mediastinal nodal staging. 7-11 CT and MR imaging are limited in depicting small mediastinal lymph node metastases. Several studies have demonstrated that FDG-PET is significantly more accurate than CT in determination of nodal status. In our own study of 47 patients, PET assigned the correct N stage in 96% of cases; CT was correct in 79% of cases. Dwamena et al performed a meta-analytic comparison of PET and CT in mediastinal staging of NSCLC. The mean sensitivity and specificity ($\pm$ 95% CI) were 0.79 $\pm$ 0.03 and 0.91 $\pm$ 0.02, respectively, for PET and 0.60 $\pm$ 0.02 and 0.77 $\pm$ 0.02, respectively, for CT. These results were confirmed in another meta-analysis with a total of more than 1,000 patients.

Even if mediastinoscopy remains the gold standard for mediastinal staging, not all mediastinal lymph nodes are routinely accessed by use of mediastinoscopy, particularly in the para-aortic region and in the aorto-pulmonic window. The limited view through the scope and the single direction in which biopsies can be carried out prevents 100% accuracy. The accuracy of mediastinoscopy is approximately 90% and is surgeon dependent. Recently, it has been demonstrated that PET is useful to assist mediastinoscopy. Due to prior knowledge of PET information, mediastinoscopy revealed additional mediastinal disease in 6% of patients.

Exact allocation of focal abnormalities on PET to specific lymph nodes is difficult or even impossible due to the poor anatomic information provided by PET alone. The presence and site of lymph node metastases should be recorded according to the revised American Thoracic Society lymph node station-mapping system (Table 3). In patients with bulky mediastinal disease or multilevel nodal involvement the assessment of N stage is easy. However, the exact localization of lymph node

metastases in the hilus is difficult. Lymph nodes distal to the mediastinal pleural reflexion and within the visceral pleura are classified as N1 nodes. Lymph nodes within the mediastinal pleural envelope are classified as N2 nodes. Because the pleura are visible neither in CT nor in PET, the exact classification of a hilar node as an N1 node or an N2 node remains difficult. The difficulty of PET is the localization of small single nodes, particularly in patients with a mediastinal shift due to an atelectasis or anatomical variants. In our experience, integrated PET/CT imaging will become the new standard of mediastinal staging. The high reliability of integrated PET/CT in the exact localization of extrathoracic versus intrathoracic and mediastinal versus hilar lymph nodes might have very important therapeutic implications.

Table 3. Lymph Node Map Definitions (Nodal Stations)

N2 nodes*	1 Highest mediastial nodes
	2 Upper paratracheal nodes
	3 Prevascular and retrotracheal nodes
	4 Lower paratracheal nodes
	5 Subaortic nodes (aorto-pulmonary window)
	6 Para-aortic nodes (ascending aorta or phrenic)
	7 Subcarinal nodes
	8 Paraesophageal nodes (below carina)
	9 Pulmonary ligament nodes
N1 nodes†	10 Hilar nodes
	11 Interlobular nodes
	12 Lobar nodes
	13 Segmental nodes
	14 Subsegmental nodes

* All N2 nodes lie within the mediastinal pleural envelope;
† all N1 nodes lie distal to the mediastinal pleural reflection and within the pleura visceralis.

Until now, our group has used non-enhanced CT scans for integrated PET/CT imaging. We could not ethically justify the use of vascular contrast material because all patients had a conventional contrast enhanced CT for staging before. In non-enhanced CT scans delineation of vessels was considerably poorer than with contrast enhancement, or impossible. However, in our patient series non-enhanced PET/CT scans are sufficient for planning surgery in approximately 80% of patients.

Further evaluation is necessary to define conditions in which the application of intravascular contrast material might have an additional diagnostic impact in integrated PET/CT imaging. However, regarding infiltration of hilar and mediastinal vessels, a relatively low sensitivity, specificity and accuracy (68%, 72% and 70%, respectively) of conventional CT scans with contrast enhancement has been observed. Microscopic foci of metastases within very small lymph nodes cannot be detected with any imaging modality. If there is no increased FDG uptake in PET, integrated PET/CT will not provide further information based on FDG accumulation. Recently, it has been reported that FDG-PET after induction therapy is less accurate in mediastinal staging than in staging of untreated NSCLC. PET overstaged nodal status in 33% of patients, understaged nodal status in 15%, and was correct in 52%. Future studies are required to correlate FDG-PET results prior to and after treatment.

M staging

Whole-body FDG-PET is an excellent method to screen for extrathoracic metastases. In a meta-analysis of 581 patients, sensitivity, specificity and accuracy of FDG-PET were 94%, 97% and 96%, respectively. Current imaging methods are inadequate for accurate M staging of patients. PET detects unexpected extrathoracic metastases in 10-20% of patients and changes therapeutic management in about 20% of patients. FDG-PET is more accurate than CT in the evaluation of adrenal metastases (Fig. 3). Marom et al. compared the accuracy of FDG-PET to conventional imaging in 100 patients with newly diagnosed NSCLC. Comparing bone scintigraphy and FDG-PET in detecting bone metastases, the accuracy was 87% and 98%, respectively. All hepatic metastases were correctly identified with PET and CT. With CT, however, benign liver lesions were over-staged as metastases; thus the accuracy of PET was superior to CT in the diagnosis of liver metastases.

The clinical significance of a single focal abnormality on PET remains unclear, especially when no morphological alterations occur on CT images. The advantage of integrated PET/CT imaging is the exact localization of a focal abnormality on PET. This was the case in 20% of all patients with extrathoracic metastases in our study on the value of integrated PET/CT.

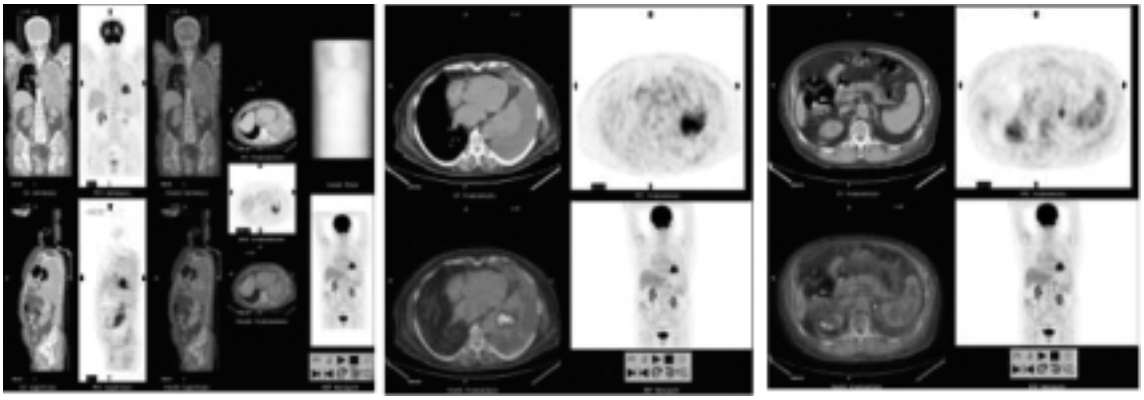

Fig. 3 A 73-year old woman with a non-small-cell lung carcinoma (adenocarcinoma) of the left lower lobe with ipsilateral metastasis of the adrenal gland. No evidence for mediastinal metastases. (A) Full computer screen with CT, PET, PET/CT scans and maximal intensity projection (MIP) showing the extent of disease. (B) Transaxial CT, PET, and PET/CT scans showing the primary tumor and the pulmonary effusion. (C) Transaxial CT, PET, and PET/CT scans showing the metastasis of the left adrenal gland.

Recurrent lung cancer

A very high accuracy of FDG-PET in distinguishing recurrent disease from benign treatment effects has been shown. If PET images demonstrate areas of tumor viability, they can direct biopsy for pathologic confirmation. Patients should be evaluated a minimum of 2 months after completion of therapy. Otherwise post-therapeutic healing processes or radiation pneumonitis may result in false-positive PET findings. These abnormal findings return to normal at variable times without further intervention. In the experience of Inoue et al, a curvilinear contour of increased FDG accumulation was seen, mostly in inflammatory lesions, while focal nodular uptake was seen mostly in recurrent tumors. Their data suggest that FDG-PET can be clinically used for selecting biopsy sites because of its high sensitivity in detecting recurrent lung cancer.

Pitfalls

False-negative FDG-PET results have been reported in pulmonary carcinoid tumors and in bronchioloalveolar carcinomas. Some active infectious or inflammatory lesions may have an increased FDG uptake. Tuberculosis, eosinophilic lung disease, histoplasmosis, aspergillosis and other infections may have a significant uptake of FDG. Furthermore, sarcoid shows a typical bilateral relatively symmetric hilar uptake pattern. Therefore, lesions with an increased FDG accumulation should be histologically confirmed. However, most chronic inflammatory processes do not significantly take up FDG.

It is well known that active muscles accumulate FDG. In some patients with lung cancer an intense focal FDG accumulation is seen in the lower anterior neck just lateral to the midline. Co-registered PET/CT images revealed that the focal FDG uptake was localized in the internal laryngeal muscles. This finding is a result of compensatory laryngeal muscle activation caused by contralateral recurrent laryngeal nerve palsy due to direct nerve invasion by lung cancer of the left mediastinum or lung apices. The knowledge of this finding is important to avoid false-positive PET results.

Effectiveness

Gambhir et al. demonstrated that a combined CT- and PET-based strategy is cost-effective in the staging of patients with NSCLC. The study evaluated the expected costs and projected life expectancy. The combined CT and PET strategy showed savings of more than US$1,000 per patient without loss of life expectancy compared with the alternate strategy of CT alone. The major advantage of FDG-PET is the cost savings that result from a patient with unresectable disease not undergoing unnecessary surgery. The cost savings are the result of improved staging of lung carcinoma before the decision of whether to perform surgery is made. In a subsequent study five decision strategies for selection of potential surgical

candidates were compared: thoracic CT alone or four different strategies that use chest CT plus PET. For all possible outcomes of each strategy, the expected cost and projected life expectancy were compared. A strategy that uses PET after a negative CT study was shown to be a cost-effective alternative to the CT-alone strategy (US$25,286 per life-year saved).

Dietlein et al demonstrated that the implementation of a whole-body FDG-PET using a dedicated PET scanner in the preoperative staging of patients with NSCLC and normal-sized lymph nodes is clearly cost-effective. However, patients with nodal-positive PET results should not be excluded from biopsy. Recently, a randomized controlled trial in patients with suspected NSCLC, who were scheduled for surgery after conventional workup, was performed to test whether FDG-PET reduces the numbers of thoracotomies. Patients were followed up for 1 year. Thoracotomy was regarded as futile if the patient had benign disease, explorative thoracotomy, pathological stage IIIA-N2/IIIB, or postoperative relapse or death within 12 months of randomization. The investigators found that addition of PET to standard workup in routine clinical practice improved selection of surgically curable patients and prevented unnecessary surgery in 20% of patients with suspected NSCLC.

A PET/CT scanner costs around 20-35% more than a PET scanner alone. It has to be taken into account that the use of these various components has some synergistic effects. PET/CT is faster than PET, when attenuation correction is done with CT data, resulting in time savings of up to 30% of examination time of a conventional PET. The time saving increases the patient throughput and decreases imaging cost per patient.

Small cell lung cancer (SCLC)

The staging procedures for SCLC do not differ from those for NSCLC. The primary role for imaging is to separate accurately limited disease (LD) from extended disease (ED). As you know, patients with extended disease receive only chemotherapy but patients with limited disease receive combined radiation treatment and chemotherapy. In very early disease if you have very limited SCLC, we perform multimodality therapy with adjuvant surgery. The key question is to distinguish limited from extended disease.

Based upon the widespread dissemination of SCLC, a battery of imaging tests is performed such as CT of the chest and abdomen, CT or MRI of the brain and a bone scan. Recently, it has been shown that whole-body FDG-PET is a useful tool for staging SCLC. FDG-PET is superior to conventional staging in the detection of all involved sites, and particularly in the assessment of mediastinal lymph node metastases. Our first experience demonstrated that integrated PET/CT imaging in SCLC is a highly valuable tool for planning radiation treatment. It is useful for accurate target definition by reducing the probability of overlooking involved areas.

Malignant pleural mesothelioma (MPM)

We expect the peak of MPM in the next 10-20 years. In limited disease if we have no diffuse tumor invasion and no metastasis (no mediastinal metastasis and no distant metastasis), a tri-modality therapy will be performed. At first, we use neoadjuvant chemotherapy, followed by surgery, followed by radiation therapy. If a diffuse tumor invasion can be diagnosed, or if we see mediastinal or distant metastasis, the patient has really only a poor outcome of some weeks to months and only palliative therapy can be done. The key question is to assess operability. Similarly to lung cancer, excellent FDG uptake in MPM has been previously described. Schneider et al demonstrated that PET is particularly valuable for distinguishing between benign and malignant pleural processes. FDG is not taken up in pleural fibrosis, thus differential diagnosis of the pleural lesions is possible. PET imaging is useful in localizing the areas involved with MPM. However, PET and CT are unable to differentiate MPM from pleural adenocarcinoma, so that histology is needed for confirmation. The role of PET is to document the extent of pleural disease, to establish mediastinal lymph node involvement, to evaluate tumor invasion, and to diagnose recurrence. Our experience demonstrates that integrated PET/CT imaging is an excellent method for staging patients with MPM (Fig. 4). With the co-registration of anatomic and metabolic information, the extent of the tumor can be precisely defined. Small mediastinal lymph node metastases can be detected and precisely localized. Integrated PET/CT imaging is helpful to identify the optimal biopsy site thereby increasing diagnostic accuracy of the histological examination.

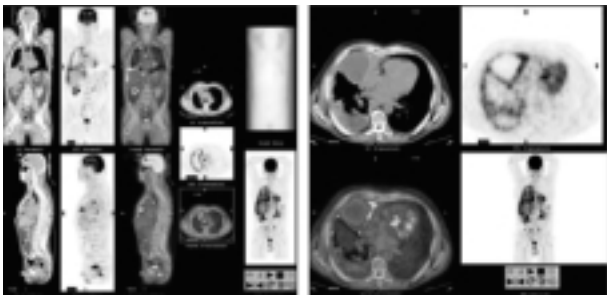

Fig. 4 A 62-year-old man with a malignant pleural mesothelioma of the right lung. (A) Full computer screen with CT, PET, PET/CT scans and maximal intensity projection (MIP) showing the extent of disease. No evidence for extrathoracic metastases. (B) Transaxial CT, PET, and PET/CT scans showing diffuse pleural thickening. Some lesions do not accumulate FDG, demonstrating inactive pleural fibrosis.

Conclusion

PET/CT is a 'one-stop-shot' examination. It requires only one examination time rather than two different appointments. This is increasingly important for patient comfort. In addition, PET/CT has highly improved the quality of interpretation of PET scans. At our institution PET/CT has become the standard imaging modality for staging patients with lung cancer. PET/CT has the potential to become the most efficient oncologic examination in the near future. Although not all tumors take up FDG, other radiotracers are currently being studied to expand the utility of PET and thereby PET/CT. The synergies achieved by integrating PET/CT are manifold. PET/CT offers many opportunities for the patients, the clinicians, and the researchers. Thus, the future of PET/CT is bright.

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