# Diagnostic evaluation of separately acquired positron emission tomography and computerized tomography images by nuclear medicine physicians and radiologists in cancer patients

**Henriëtte ME Quarles van Ufford[1,2], Lorentz GBA Quekel[1], Paul FGM van Waes[1], Pien J de Haas[1], John MH de Klerk[1]**

1. *Department of Radiology and Nuclear Medicine, Meander Medical Centre*
2. *University Medical Centre Utrecht, The Netherlands*

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***Correspondence address:***
HME Quarles van Ufford, University Medical Centre Utrecht, Department of Radiology, E01.132, P.O. Box 85500, 3508 GA Utrecht, The Netherlands,
E-mail: *H.M.E.QuarlesvanUfford@umcutrecht.nl*

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## Abstract

*The aim* of our study was to analyze how many oncology patients might benefit from: a) integrated positron emission tomography - multidetector computed tomography (PET/MDCT) and additionally b) clinically relevant information provided by either the CT scan or PET scan. *A total of* 285 consecutive patients 164 male and 121 female, age range 17-84 years, 153 lung cancer, 112 lymphoma, 20 miscellaneous, referred for PET and separate CT scan, were included. The CT scan was performed after the intravenous injection of a soluble contrast media. Patients were retrospectively classified into six Groups: Group I: No pathological uptake on the PET scan, Group II: Suspected lesions were correctly identified by the PET scan alone, Group III: Side-by-side evaluation of PET and CT appeared sufficient to assess the localization of lesions, Group IV: Side-by-side reading was not sufficient and integrated PET/CT was considered beneficial. Additionally all patients with a CT scan with additional clinical relevant information (not visualized by the PET scan) were classified in Group V. Group VI was set for lesions detected by PET alone (not visualized by the CT scan). The CT scan was used as the gold standard to confirm or disprove PET lesion localization. *Our results* showed: A number of 77 patients, (Group I: 77/285, 27%) had no pathologic fluorine-18-fluorodeoxyglucose ($^{18}$F-FDG)-uptake. Lesions were correctly localized by either conventional PET alone (Group II: 76/285, 27%) or side-by-side evaluation of PET and CT scans (Group III: 44/285, 15%). Integrated PET/CT or software fusion, was considered beneficial in 31% (88/285) of the patients with pathological $^{18}$F-FDG-uptake (Group IV). Additionally to the above, in 15% of all patients clinically relevant information, referring to disseminated small pulmonary lesions, abdominal aortic aneurysms >5cm, thrombi or pulmonary emboli, was also provided by the CT scan (Group V). Also, in 7% of all patients, unsuspected pathological lesions, mainly bone metastases, were correctly detected by PET alone (Group VI). *In conclusion,* in 54% of all oncologic patients, PET alone was diagnostic. In 46% of all patients side-by-side reading (15%) or integrated PET/CT images (31%) were considered beneficial for more accurate anatomical localization of the lesions. Additionally, the CT scan added clinically relevant information in 15% of all patients and the PET scan showed unsuspected metastases in 7% of all studied patients. Therefore, integrated reading of PET and MDCT images by nuclear physicians and radiologists may gain quality in the staging of oncology patients.

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## Introduction

Positron-emission tomography (PET) is increasingly used in oncology. PET with fluorine-18-fluorodeoxyglucose ($^{18}$F-FDG) provides functional information, however its main drawback of showing few anatomic landmarks impedes precise localization of sites of pathologic $^{18}$F-FDG uptake. This can be overcome by fusion of PET and computerized tomography (CT) images, especially when acquired with an integrated PET/CT scanner [1, 2]. It produces precisely coregistered molecular and morphologic imaging by allowing them to be obtained on the same scanner without moving the patient [1, 2]. Integrated PET/CT images improve the characterization of equivocal lesions and significantly affect treatment planning by guiding biopsies and surgical interventions, by defining target volumes for radiation therapy fields and by monitoring response to treatment [3-6]. The CT scan performed after intravenous (i.v.) contrast enhancement, differentiates lesions to vascular structures.

Several studies have evaluated integrated PET/CT scans from the nuclear medicine perspective by comparing their diagnostic accuracy with that of PET scans alone. The CT scan is then used for better localization of lesions seen on the PET scan [7-11]. However, only a

few studies have analyzed the situation where a contemporary CT scan is available for side-by-side evaluation and fusion with a PET scan [12, 13]. In the setting of an integrated PET/CT scan, the CT scan is more than a gain in specificity [14]. Besides additional value in staging oncologic disease and treatment monitoring, as mentioned above, CT scan can identify other clinical relevant findings, such as an abdominal aortic aneurysm of more than 5 cm in diameter, thrombi and lung emboli.

As a large general secondary hospital, performing separate PET and CT scans with the option of software fusion, we were interested in how many of our oncology patients an integrated PET/CT scan might aid to better staging and patient management. The aim of our study was to analyze how many oncology patients might benefit from: a) an integrated PET/CT and additionally b) clinically relevant information provided by either the CT scan or the PET scan.

## Subjects and Methods

### Subjects

From August 2003 to February 2005, a total of 285 consecutive patients, 164 male and 121 female, age range 17-84 years, were included in the study. The only inclusion criteron was that all patients were referred for a PET scan and a separate CT scan, ordered by their oncologist and performed on the same day or the previous day. This was done in order to include a random realistic group of patients in a general secondary hospital tested for staging or treatment monitoring of neoplastic disease. Our patients suffered from lung cancer (n=153), lymphoma (n=112), colo-rectal cancer (n=8), malignant melanoma (n=2), head and neck cancer (n=2), breast cancer (n=2), pancreatic cancer (n=1), adrenal cancer (n=1), sarcoma (n=1), metastases of unknown primary (n=3). All patients gave their informed consent for the PET/CT examination.

### Positron emission tomography

Patients were scanned with a mobile (Alliance Medical, The Netherlands) PET scanner with lutetium oxyorthosilicate (LSO) crystals, ECAT ACCEL, Siemens Medical Solutions Inc., Germany). After a fasting period of at least 6 h, patients were i.v. injected with 370 MBq of $^{18}$F-FDG. Imaging was performed from the base of the skull to the proximal femora in 7 bed positions. Data acquisition started 45 min post-injection. All patients were advised complete immobility during the uptake period of the radiopharmaceutical and during the scan. Acquisition time was 5 min per bed position, with a transmission time of 60 sec each. PET images were reconstructed with and without attenuation correction using a weighted "iterative ordered subsets expectation maximization" (OSEM) algorithm (2 iterations, 8 subsets). In a final step, a three dimensional isotropic Gaussian filter was applied to a final image resolution of 5 mm with in full width half maximum (FWHM). Transverse, coronal and sagittal slices with and without attenuation correction, were reconstructed.

### Computed tomography

Separate CT scans (Siemens Medical Solutions Inc. Sensation 16 MDCT, Germany) were performed and acquired after the i.v. administration of a water-soluble contrast medium containing iodine (omnipaque 300, Guerbet, Nederland) at i.v. infusion rate: 3 ml/sec with bolus tracking. The following parameters were used: 120 kV peak 90 mA, 0.5 sec tube rotation time and 1.5 mm slice width. All patients were scanned in accordance with the PET acquisition protocol: supine position, arms raised and normal expiration breath hold, from the base of the skull to the proximal femora. Because the abdomen according to the PET protocol was scanned, contrast medium telebrix gastro, (Guerbet, the Netherlands) in a volume of 700 ml was administrated orally, starting one hour before the imaging procedure. Subsequently, transverse, coronal, and sagittal slices were reconstructed. All CT scans were evaluated by two experienced radiologists (LBGA and PFGM) in consensus and compared to the nuclear physicians findings.

### Assessment

Retrospective evaluation of the PET scans was performed according to Reinartz et al (2004) [13]. All PET scans were analysed by two experienced nuclear medicine physicians (P.J. and J.M.H.) who were blinded to the clinical data and the results of other examinations such as laboratory findings and previous radiological examinations. Groups were assigned as follws: a) All scans without pathological lesions were assigned to Group I. For these patients the CT scan was useful for additional clinical relevant findings, but irrelevant for lesion localization. b) If a pathological lesion was found, the nuclear physicians localized by consensus the lesion analyzing the PET scan alone. The CT scan was used as a gold standard to confirm or disprove lesion localization. Patients with lesions which could be correctly localized by PET alone were assigned to Group II. c) If localization was incorrect or inconclusive and/or the CT scan was used for side-by-side reading, patients were assigned to Group III. d) Patients with an inconclusive CT scan (side-by-side reading was not sufficient for lesion localization), were assigned to Group IV. For all lesions assigned to Group IV, integrated PET/CT or software fused imaging was considered beneficial. Additionally to the above, patients with additional clinically relevant findings provided by the CT scan (disseminated small pulmonary lesions, abdominal aortic aneurysms >5cm, thrombi or pulmonary emboli ) were assigned to Group V. Patients with lesions on the PET scan, not visualized on the CT scan were assigned to Group VI.

## Results

Group I consisted of 77 patients-27%, Group II of 76 patients-27%, Group III of 44 patients-15% and Group IV consisted of 88 patients-31%. Groups V and VI referring to the total number of patients, consisted of 42 and 21 patients, 15% and 7%, respectively.

In Table 1 the frequency distribution of the different tumour types for the different Groups studied, is displayed. Table 2 dis-

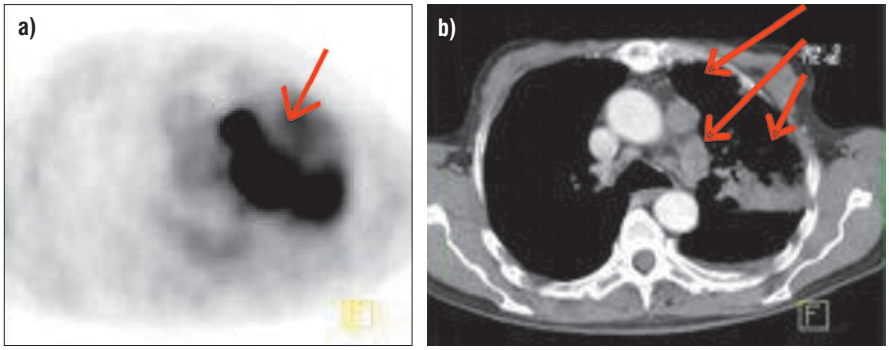


**Figure 1.** Patient presenting with a consolidation in the left upper lobe. The oncologist referred the patient for a PET and CT scan. The PET scan (a) illustrates 3 pathologic lesions. However, exact localization is not possible without the knowledge of the CT scan (b). Patient-based analysis: Group III. The consolidation proved to be a post-obstruction infiltrate of a lung carcinoma (stage IIIa). Both PET and CT were usefull in order to plan the biopsy and acquire histology of the carcinoma instead of the infiltrate.

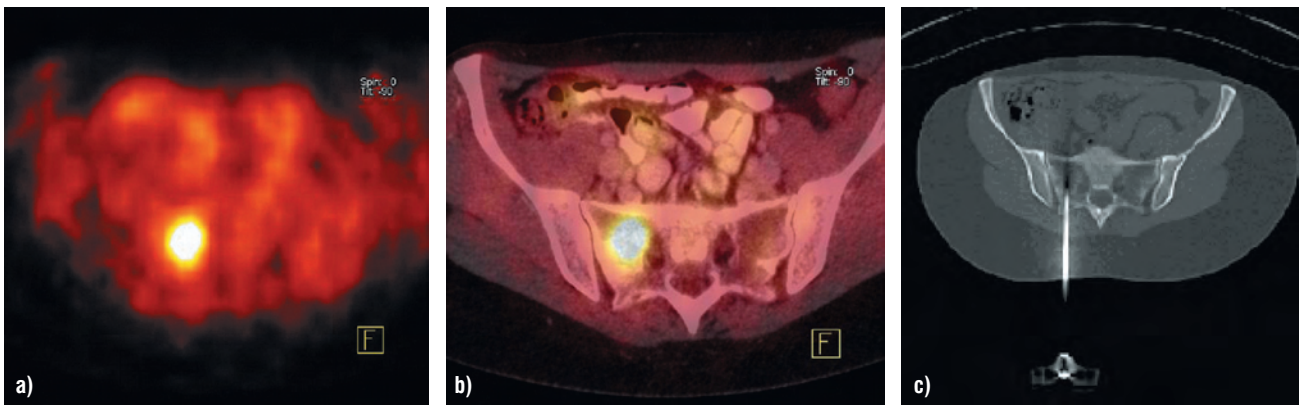


**Figure 2.** Patient referred for malignant lymphoma staging: PET visualized unsuspected bone localization. Exact localization in the sacrum was provided by the software fused PET/CT image. CT could not confirm this localization and a CT-guided bone biopsy was performed. (a) PET scan. (b) CT scan. (c) CT-guided bone biopsy. Classic Hodgkin's lymphoma was confirmed histologically.

plays the pathologic lesions of Group VI patients. Figure 1 presents a patient with pathological $^{18}$F-FDG uptake that needed the CT scan for exact anatomical localization of the lymph nodes. In this case side-by-side reading by both the nuclear medicine physician and the radiologist was sufficient (Group III). Figure 2 shows the PET and CT scans of a patient with lymphoma from Group IV. In this particular case, CT could not confirm the localization of pathological $^{18}$F-FDG uptake in the sacrum (Group VI). A CT-guided bone biopsy was performed. Histologic examination revealed a typical Hodgkin's lymphoma, thus confirming the findings of the PET scan.

## Discussion

Many studies have compared PET and integrated PET/CT and demonstrated the increase in accuracy of lesion localization by PET/CT and the improvement of management of cancer patients at different stages of their disease [1-11]. In a clinical setting, the CT scan should be read as a diagnostic scan, not just as a localizer of lesions illustrated by a PET scan. According to the opinion of the authors this is probably one of the last studies analyzing the value of stand-alone PET with a separately acquired MDCT scan, as currently integrated PET/CT scanners tend to replace the stand-alone PET cameras.

In the present study a relatively large proportion of patients (77/285, 27%) did not have any pathological $^{18}$F-FDG uptake (Group I). Most of the negative PET scans were performed for treatment monitoring of lymphoma patients (52/77, 68%). In many of these patients a residual mass was seen on the CT scan. A negative follow-up PET scan in patients with lymphoma, usually performed after 3 cycles of chemotherapy, is an important prognostic factor as it indicates a longer period of progression-free survival [15, 16]. Masses often do not regress completely after curative treatment because of fibrosis and necrotic debris. This is why the

**Table 1.** *Frequency distribution of tumour types classified according to the patient-based analysis (Groups I-IV, n=285)*

| Tumour type | Group I No $^{18}$F- FDG | Group II PET alone | Group III PET and CT | Group IV PET/CT | Total |
|---|---|---|---|---|---|
| Lung cancer | 19 | 48 | 21 | 65 | 153 |
| Lymphoma | 52 | 23 | 18 | 19 | 112 |
| Miscellaneous | 6 | 5 | 5 | 4 | 20 |
| Total | 77 | 76 | 44 | 88 | 285 |
| | 27% | 27% | 15% | 31% | 100% |

**Table 2.** *Classification of the lesions detected by PET alone (Group VI)*

| | Bone | Lymph nodi |
|---|---|---|
| Lung cancer | 12 | 3 |
| Lymphoma | 3 | 2 |
| Sarcoma | 1 | |

anatomic response criteria indentified by CT often underestimate the chemotherapeutic effect.

A total of 208 patients showed pathological $^{18}$F-FDG uptake on the PET scan. For 76 patients the localization of the lesions was correctly assessed by conventional PET alone (Group II). This means that for 27% (76/285) of all included patients, the CT scan had no additional value for lesion localization and an integrated PET/CT scan was not needed. Accurate staging of disease (majority lung cancer and lymphoma) was possible by the PET scan, without knowledge of the CT scan.

In 31% of our patients (Group IV, 88/285 patients) integrated PET/CT was considered beneficial because even side-by-side reading of PET and CT scans was insufficient. In lymphoma patients, for example, it can be difficult to distinguish between a bone localisation and a lymph node close to the spine. Another example is a patient with non-small cell lung cancer and a positive lymph node localized in either the hilus of in the mediastinum. In these patients the accurate assessment of mediastinal lymph node involvement is of great relevance for treatment and prognosis. According to the international TNM classification patients with ipsilateral mediastinal lymph nodes (N2) metastasis have stage IIIa disease, which is usually not surgically resectable [17, 18].

The result of 31% in this series is relatively large, as others have concluded that if both the PET scan and the CT scan were evaluated side-by-side, in only 7% of the patients, the integrated PET/CT would be considered beneficial [13]. A possible explanation for this difference is the studied patient cohort. Patients with lymphoma as in our study 39% of all patients, will benefit from integrated PET/CT regarding lesion localization, because in these patients pathologic uptake can be seen in many structures such as lymph nodes, bone marrow, spleen and other. In the other study only 7% of the patients had lymphoma.

As stated in literature, the radiation dose must be considered in nuclear medicine and radiology examinations [19]. Especially for tumor staging, CT scan alone is usually performed in a full-dose manner having a sufficient spatial resolution with an acceptable signal-to-noise ratio. The radiation dose from a CT scan may amount to approximately 15-20 mSv for a scan from the head to the upper thighs [20]. The major portion of radiation exposure in a PET/CT scan (25 mSv) can therefore be attributed to the CT component [20]. In the setting that the CT scan is only used for localization of PET lesions and not for diagnostic purposes, a low-dose CT component (3-4 mSv) may be used for attenuation correction [14, 21]. This type of scanning can be used for monitoring of therapy, which is mainly based on functional data rather than morphology. The indication of the PET/CT scan must be known instead of using rigid scanning protocols [21].

*In conclusion,* a) in 54% of all oncologic patients PET alone was diagnostic. In 46% of all patients side-by-side reading (15%) or integrated PET/CT images (31%) were considered beneficial for more accurate anatomical localization of the lesions. Additionally, the CT scan added clinically relevant information in 15% of all patients and the PET scan showed unsuspected metastases in 7% of all studied patients. Therefore, integrated reading of PET and MDCT images by nuclear physicians and radiologists may gain quality in the staging of oncology patients.

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