Davetli Derleme / ***Invited Review***

Multimodal Imaging with PET-CT in Oncology

Onkolojide PET-BT ile Multimodal Görüntüleme

Hans-Jürgen BIERSACK, Mahmut YÜKSEL, Holger PALMEDO, Roland RÖDEL, Michael REINHARDT, Ursula JAEGER

The combination of PET (positron emission tomography) with CT (computed tomography) has considerably enhanced the clinical application of PET. PET-CT combines the high resolution of CT with the high sensitivity of PET. As PET and CT results are obtained with one machine during one investigation, an optimal fusion of both procedures is possible. The accuracy of PET can be increased by about 15% by PET-CT, compared to conventional fusion of PET and CT images. The potential of PET-CT can only be fully used if contrast agents -either orally or intravenously- are applied. The X-rays of CT may also be used for attenuation correction. This article focuses mainly on PET-CT in lung cancer, malignant melanoma, head and neck tumors, thyroid tumors, and colorectal cancer, with illustrations of some cases documenting the potentials of PET-CT.

Key Words: Fluorodeoxyglucose F18/diagnostic use; image enhancement; image processing, computer-assisted/methods; neoplasm metastasis; positron-emission tomography/methods; tomography, X-ray computed/methods.

Pozitron-emisyon tomografi (PET) ile bilgisayarlı tomografinin (BT) birlikte kullanımı (PET-BT) PET'in klinik kullanımını önemli ölçüde artırmıştır. PET-BT, BT'nin yüksek çüzünürlüğünü PET'in yüksek duyarlığıyla birleştirmektedir. PET ve BT sonuçlarının tek incelemede ve aynı cihazla elde edilmesi nedeniyle her iki prosedürün en uygun birleşimi mümkündür. PET ve BT görüntülerinin klasik birleştirilmesine oranla, PET-BT ile PET'in doğruluğu yaklaşık %15 oranında artırılabilir. PET-BT'nin gücünden tam olarak yararlanmak sadece oral veya intravenöz kontrast ajanların kullanılmasıyla mümkündür. BT'nin X-ışını aynı zamanda atenüasyon düzeltmesi için kullanılır. Bu makalede ağırlıklı olarak akciğer kanseri, malign melanom, baş-boyun tümörleri, tiroid tümörleri ve kolorektal kanserler üzerinde durulmuş ve PET-BT'nin görsel gücü olgulara ait görüntüler aracılığıyla ortaya konmuştur.

Anahtar Sözcükler: Fluorodeoksiglukoz F18/tanısal kullanım; görüntü artırma; görüntü işleme, bilgisayar destekli/yöntem; tümör metastazı; pozitron-emisyon tomografi/yöntem; bilgisayarlı tomografi/yöntem.

For the past four years, PET-CT has become a routine procedure in nuclear medicine. The primary purpose of combining x-ray computed tomography (CT) and positron emission tomography (PET) scanners is to delineate the precise anatomical localization of regions identified on the PET tracer uptake images.[1-4] While PET-alone attenuation correction is performed using a transmission scan with a 68Ge/68Ga source, in PET-CT, CT is used for attenuation correction by density values. Thus, PET-CT combines attenuation correction

Departments of Nuclear Medicine (Biersack, Palmedo, Prof. Dr.; Rödel, Ph.D.; Reinhardt, Asisst. Prof.) and Radiology (Jaeger, M.D.) University Hospital, Bonn, Germany; Department of Nuclear Medicine, Medicine Faculty of Trakya University (Yüksel, Assoc. Prof.).

Correspondence: Prof. Dr. Hans-Jürgen Biersack. Klinik und Poliklink für Nuklear Medizin Sigmund-Freud-Str. 25, 53127 Bonn, Germany.

Tel: ++49.228.287 5183 Fax: ++49.228.287 6615 e-mail: hans-juergen.biersack@ukb.uni-bonn.de

(and therefore quantification) and anatomical localization.

PET-CT BASICS

Attenuation correction

Current methods of measuring attenuation use positron sources, gamma-ray sources, or x-ray sources. Each type of transmission scans involves different trade-offs of noise *vs* bias, with positron transmission scans having the highest noise but lowest bias, whereas x-ray scans have a negligible noise but the potential of increased quantitative errors.[1] The sensitivity of x-ray-based attenuation correction to artifacts and quantitative errors depends on the method of translating the CT image from the effective x-ray energy of approximately 70 keV to attenuation coefficients at the PET energy of 511 keV. Errors in the PET emission image arise from positional mismatches due to patient motion or respiration differences between the PET and CT scans. Other sources of error comprise CT contrast agents or metallic implants and scatter.[1] Another problem is the different field of view of the PET and the CT scanner. The proper fusion of different fields of view is of crucial importance.

The potentials of PET-CT (Fig. 1) can only be fully used if contrast agents - either orally or intravenously - are applied. X-rays used for attenuation correction of the PET image show different mass attenuation coefficients. As shown by Kinahan et al.,[1] above 100 keV there are only minor differences for bone, muscles, tissue, and air. Therefore, the CT data can be used for the correction of attenuation when positron emitters (511 keV) are used. Contrast artifacts may occur only in cases with high contrast of these agents, for example, when the stomach is filled with contrast media.

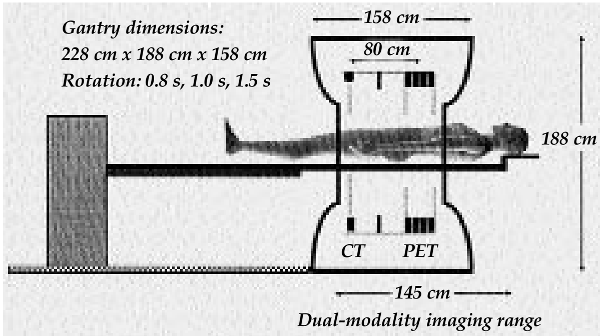

Fig. 1. *PET/CT, with courtesy of reference 1.*

A very important and frequent artifact is caused by breathing. Usually, the CT scan is obtained during breath hold while PET, with its long acquisition time, can only be acquired during shallow breathing.

PET-CT scans are usually a whole body investigation, so that the protocol has to be split. The head and neck regions are visualized with an arms-down protocol, while an abdominal scan requires an arms-up protocol to avoid scatter. Figures 2 to 4 show artifacts associated with breathing, contrast agent use, and enteral implants, respectively.

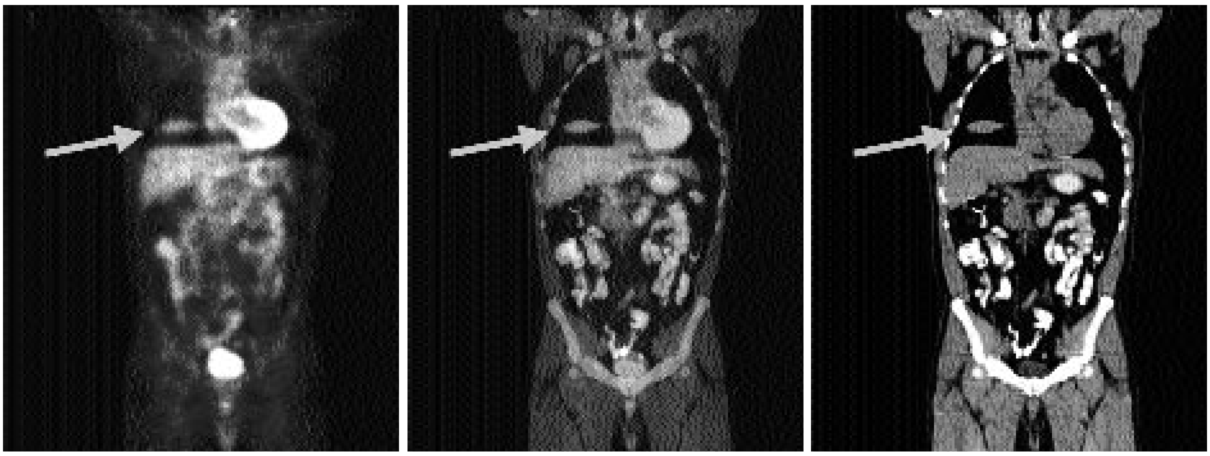

Fig. 2. *Breathing artifact.*

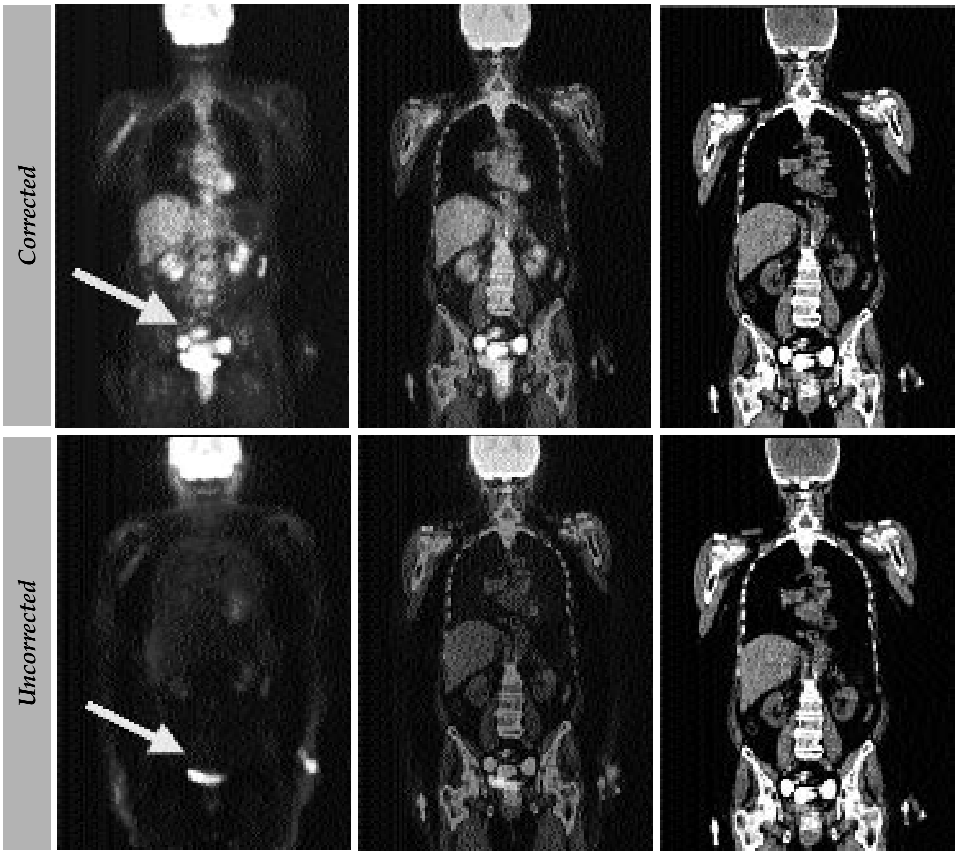

Fig. 3. *Contrast agent artifact (bladder).*

PET-CT is a rapidly growing market, and today PET-CT systems with a 64-detector row CT are available. However, 2-slice CT seems to be sufficient in oncology, while 64-slice machines are only useful if PET-CT of the heart is to be performed.

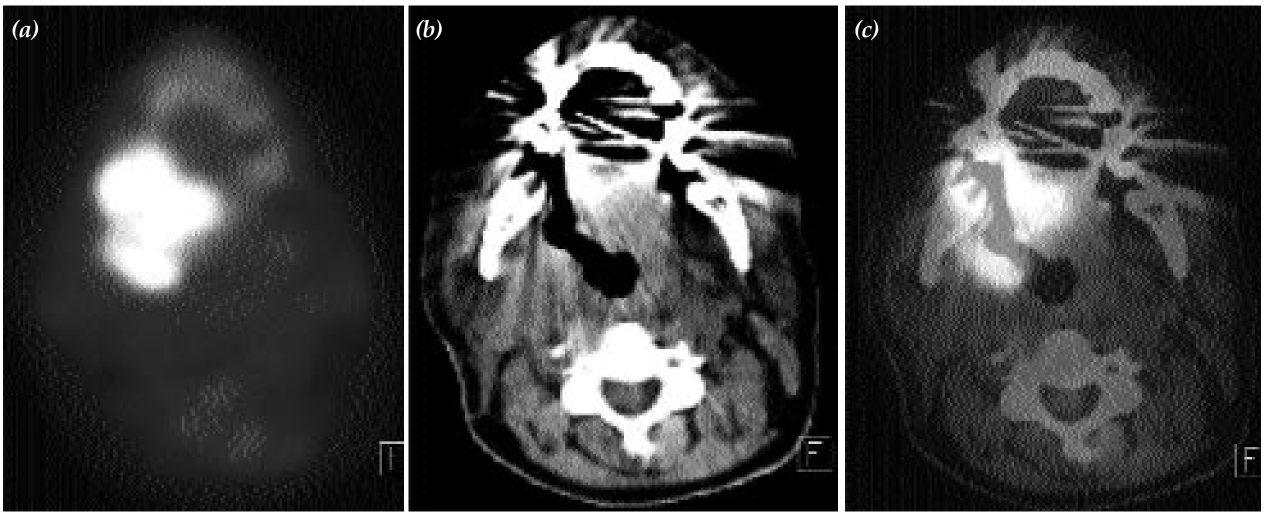

Fig. 4. *Metal implant artifact. State after preliminary resection of oropharyngeal cancer after 19 months.* ***(a)*** *Pathologic uptake (SUV = 9.7) in PET* ***(b)*** *with only asymmetrical change of structure of oropharyngeal tissue in CT.* ***(c)*** *Superposition yields the area of uptake in the floor of the oral cavity behind the right mandible. Histological finding showed a multilayered noncornified squamous cell carcinoma.*

CLINICAL RESULTS

Lung cancer

The use of PET offers much promise as an aid to noninvasive evaluation of lung cancer. 18F-FDG-PET is currently indicated for the characterization of lung lesions, staging of non-small cell lung carcinoma, detection of distant metastases, and diagnosis of recurrent disease. Furthermore, PET is useful for monitoring the treatment of lung cancer.[5] During the past four years, PET-CT has significantly improved the metabolic diagnosis of lung cancer. However, some limitations have to be mentioned: Misalignment of PET-CT - even if the investigation is performed with a dedicated PET-CT scanner - may cause differences between the PET lesion and the CT finding of up to 14 mm

Table 1. Differences between the PET lesion and the CT lesion in lung cancer

PET-CT - Lung cancer
7.55±4.73[6]
10.2 mm lower lungs
6.67 mm upper lungs
1.7 - 5.4 mm apex[7]
0.5 - 14.7 mm periphery[7]
0.7 - 5.9 mm centrally
2.9 - 11.3 mm lung base[7]

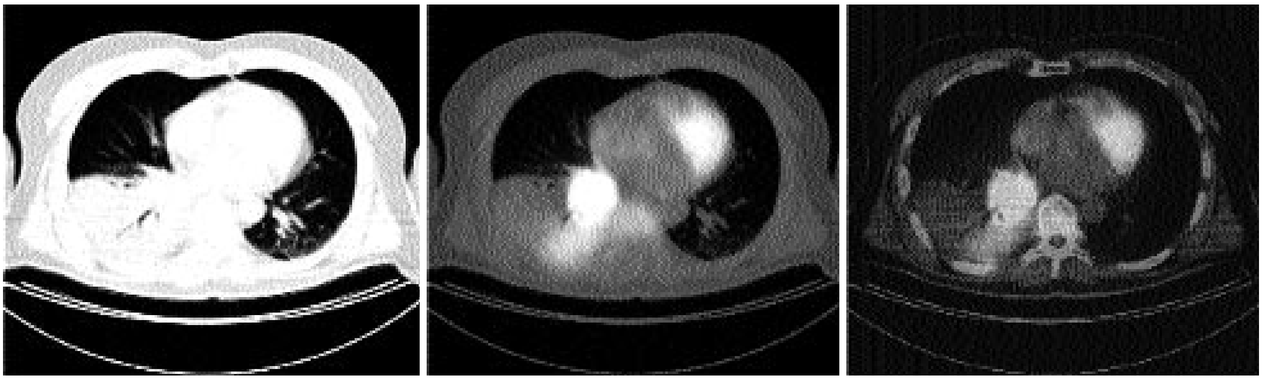

Fig. 5. *Lung cancer and atelectasis.*

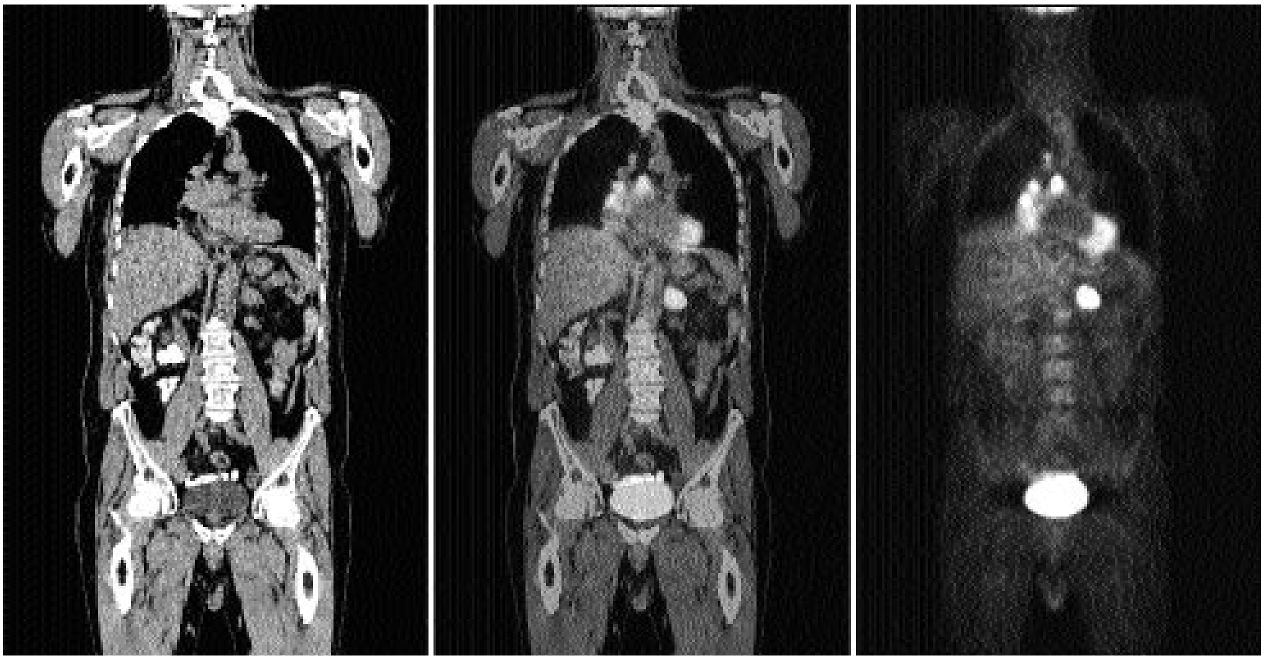

Fig. 6. *Lung cancer with mediastinal metastasis and left adrenal metastasis.*

due to different breathing (Table 1).[6,7] Lardinois et al.[8] compared PET and PET-CT in lung cancer and found additional information in about 41% of patients. Figures 5 and 6 show some results of PET-CT in lung cancer: In Fig. 5, it is evident that PET-CT allows differentiation of atelectasis and lung cancer. Fig. 6 shows mediastinal lymph nodes and left adrenal metastasis.

As mentioned before, the advantage of PET-CT imaging is attenuation correction performed by CT. Reinhardt et al.[9] investigated 92 patients with 438 metastases of the lungs. Of these, 174 were detected with FDG-PET, six of them were detected on non-attenuation-corrected images alone. The sensitivity of FDG-PET increased significantly from 0.405 for metastases of 5-7 mm in diameter to 0.784 for lesions of 8-10 mm and to 0.935 for lesions measuring 11-29 mm in diameter. No metastases smaller than 5 mm in diameter were seen on PET images. This finding necessitates an optimal CT imaging protocol in lung lesions.

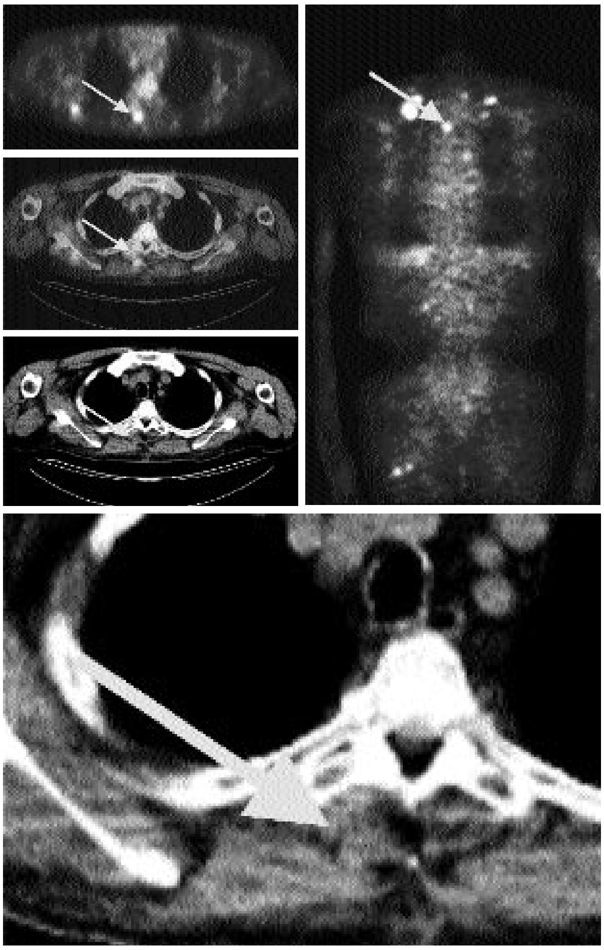

Fig. 7. *Soft tissue metastasis of malignant melanoma surrounded by muscle tissue and normal CT of this region.*

Malignant melanoma

Reinhardt et al.[10] investigated the diagnostic performance of whole body dual modality 18F-FDG-PET-CT imaging for N- and M-staging of

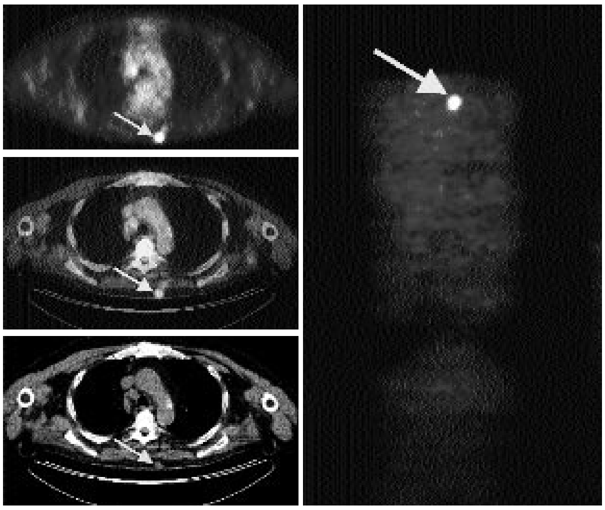

Fig. 8. *Malignant melanoma with metastasis surrounded by fatty tissue.*

Fig. 9. *Malignant melanoma with lymph node metastasis. Bone metastasis is only visualized by PET. Patient 58-y, m, SSM, 4.3 mm, right shoulder, re-staging (3-y).*
(a) *CT: LN right supraclav. (1.2, 1.5 cm Ø) + right axilla (1.0 cm Ø).*
(b) *PET: 2 foci right supraclav. + right humerus head, axilla neg.*
(c) *PET/CT: image fusion enabled detection of possible corticalis disruption; made further diagnostic procedures dispensable.*

Table 2. Detection of visceral and nonvisceral metastasis by CT, FDG-PECT and PDG-PET/CT

	CT		FDG-PET		PET/CT		
	No	%	No	%	No	%	Total no
Nonvisceral	279	74.0	353	93.6	368	97.6	377
Visceral	188	64.2	242	82.6	293	100	293
Total	467	69.7	595	88.8	661	98.7	670

malignant melanoma in 250 consecutive patients. PET-CT detected significantly more visceral and nonvisceral metastases than PET alone and CT alone (98.7%, 88.8% and 69.7%, respectively). PET-CT imaging thus provided significantly more accurate interpretations regarding overall N- and M-staging than those obtained by PET alone and CT alone (Table 2). Overall, N- and M-stages were correctly determined by PET-CT in 243 of 250 patients (97.2%) compared with 232 patients (92.8%) by PET and 197 patients (78.8%) by CT. Change of treatment based on PET-CT findings occurred in 121 patients (48.4%).

Fig. 10. *COP: Lymph node metastases at level II.*

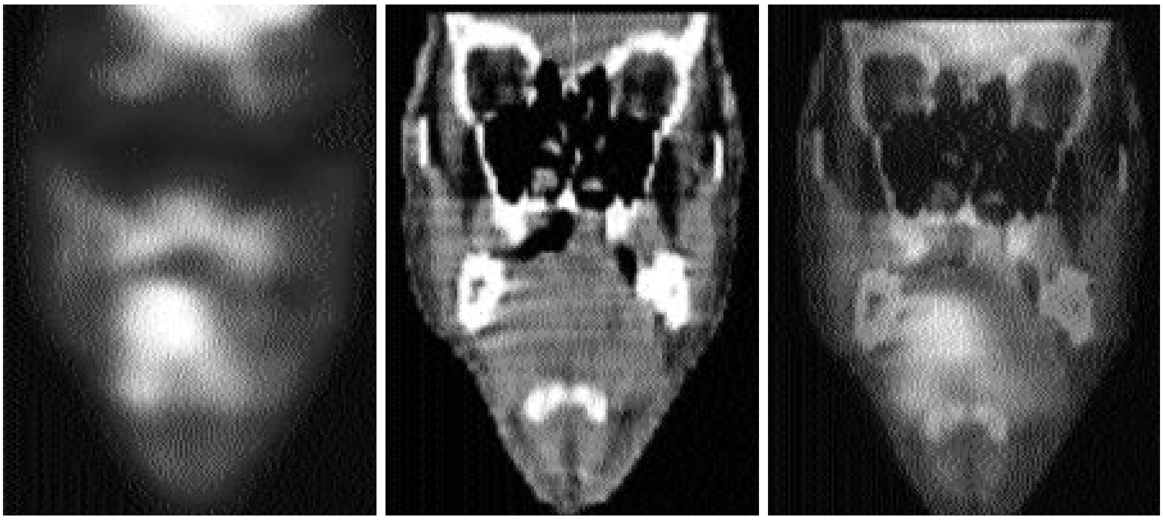

Fig. 11. Recurrence of squamous cell cancer at the floor of the mouth. Uptake on PET asymmetric to CT. Differentiation is only possible by PET/CT.

Figures 7 and 8 clearly demonstrate the power of PET-CT. While soft issue metastases surrounded by muscle cannot be detected by CT, metastases surrounded by fatty tissue are clearly visualized by CT (Fig. 8). Figure 9 shows a case in which bone metastasis could only be visualized by PET.

Head and neck tumors

Rodel et al.[11] investigated 59 patients with head and neck tumors using PET-CT without intravenous contrast media. Figures 10 and 11 show their results. Figure 12 presents a case where small lung metastasis was only seen on CT but not on PET. Figure 13 is a summary of the results comparing PET, CT and PET-CT. It is evident that especially specificity can be increased by PET-CT, while sensitivity remains almost unchanged.

Differentiated thyroid cancer

Palmedo et al.[12] published their data on PET-CT in differentiated thyroid cancer with iodine-negative metastases. Forty patients with differentiated thyroid cancer were included in the study. A total of 127 lesions were evaluated. Diagnostic accuracy was 93% for PET-CT and 78% for PET (per patient analysis). In 17 (74%) of 23 patients with suspicious 18F-FDG foci, integrated PET-CT added relevant information to side-by-side interpretation of PET and CT images and enabled precise localization of the lesions. In tumor-positive PET patients, PET-CT fusion by co-registration led to a change of ther-

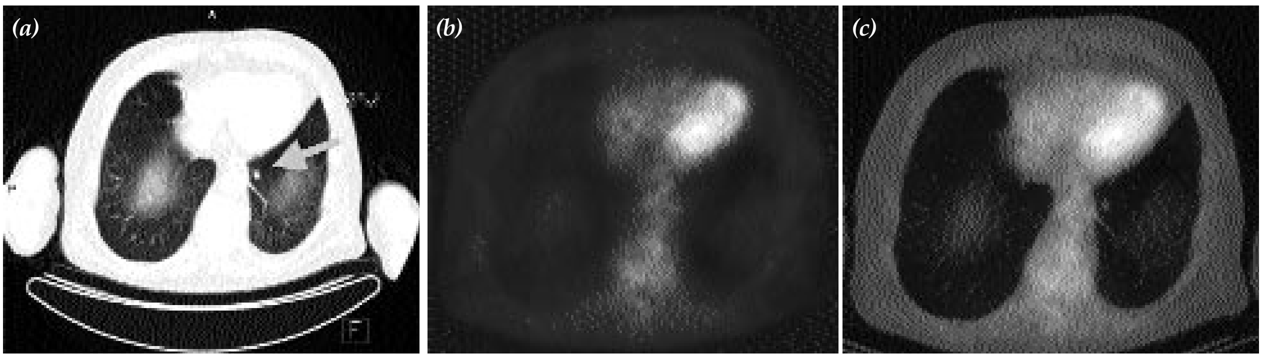

*Fig. 12. Head and neck cancer with small lung metastasis is only visualized on CT. **(a)** Circular focus (green arrow) of suspicious malignant growth in the medial left low lobe of the lung in CT **(b)** without activity accumulation in PET and **(c)** superposition. Further history revealed a metastasis of laryngeal cancer.*

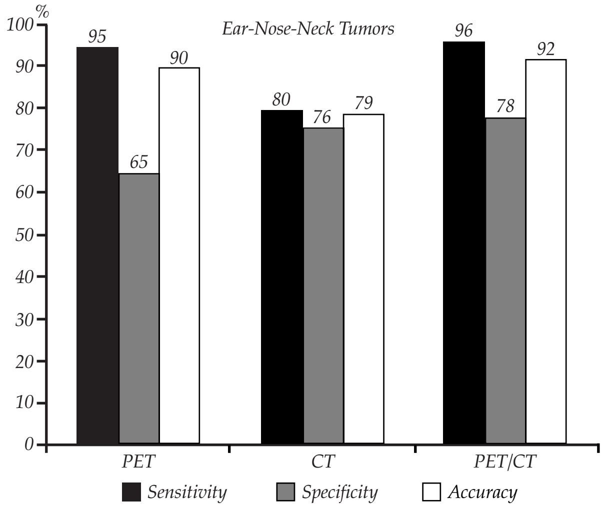

Fig. 13. *Sensitivity, specificity, and accuracy of PET-CT in head and neck tumors.*

apy in 10 patients (48%). Futile surgery was prevented in additional three patients.

Figures 14 and 15 illustrate a case with known lymph node metastases and local

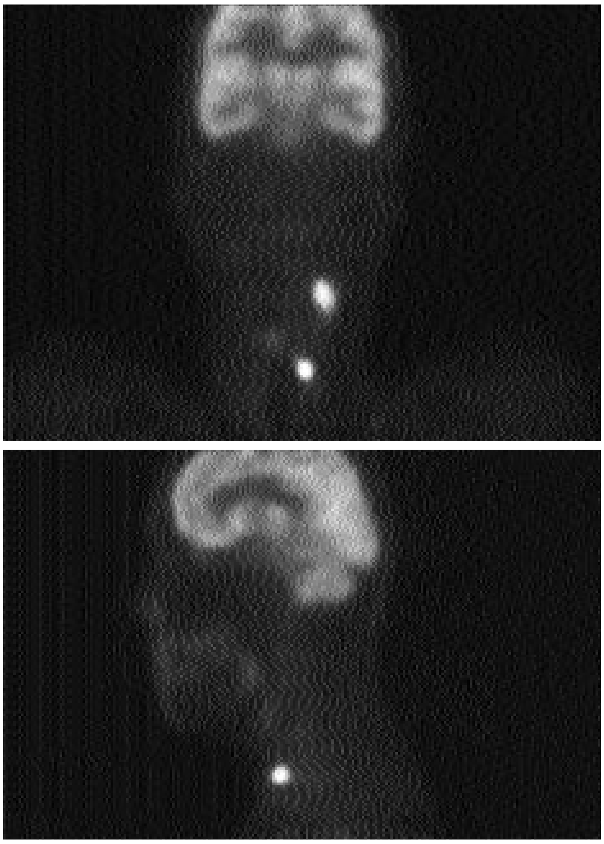

Fig. 14. *Differentiated thyroid cancer with left lymph node metastasis and local recurrence.*

tumor recurrence. Only image fusion demonstrates the site of the local recurrence so that surgery was possible.

Colorectal cancer

Strunk et al.[13] used PET-CT imaging for restaging colorectal cancer patients. The results are summarized in Table 3. Additional information was obtained in nine out of 29 patients (32%) by co-registered PET-CT imaging.

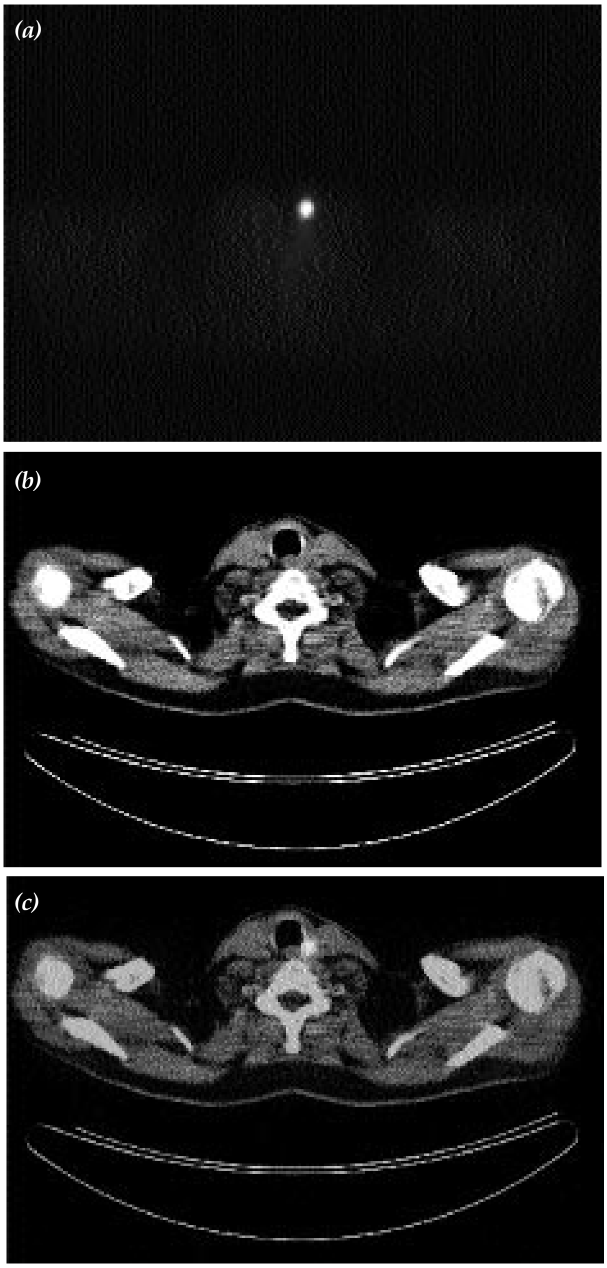

Fig. 15. ***(a)*** *PET,* ***(b)*** *CT, and* ***(c)*** *DTC fused images.*

Table 3. Parameters

	PET analyses		Virtual fusion		True co-registered reading	
	No. of lesions	No. of patients	No. of lesions	No. of patients	No. of lesions	No. of patients
Sensitivity	100 (7/7)	100 (6/6)	100 (7/7)	100 (6/6)	100 (7/7)	100 (6/6)
Specificity	72 (8/11)	72 (8/11)	81 (9/11)	81 (9/11)	100 (11/11)	100 (11/11)
Positive predictive value	70	66	77	75	100	100
Negative predictive value	100	100	100	100	100	100

Figure 16 illustrates a case with elevated CEA. Figures 16a and 16b show lymph node recurrence. Figures 16c and 16d demonstrate that only PET-CT allows the localization of a soft tissue lesion.

Other studies support the significance of PET-CT in gastrointestinal malignancies.[14-16]

CONCLUSION

This report is mainly based on the personal experiences of our institution. Due to a limited budget, we are not able to perform more than 700-800 patient studies a year. As the budget of our National Health Service System for inpatients covers not more than 300 investigations, we had to focus on some tumor entities in which our referring colleagues had already evaluated the clinical significance of PET-CT. However, our experiences may easily be transferred to other tumors like lymphoma or breast and lung cancer. Since January 2006, the N- and M-staging of lung cancer has been the only indication which is covered by the National Health Service System. This represents the first break-

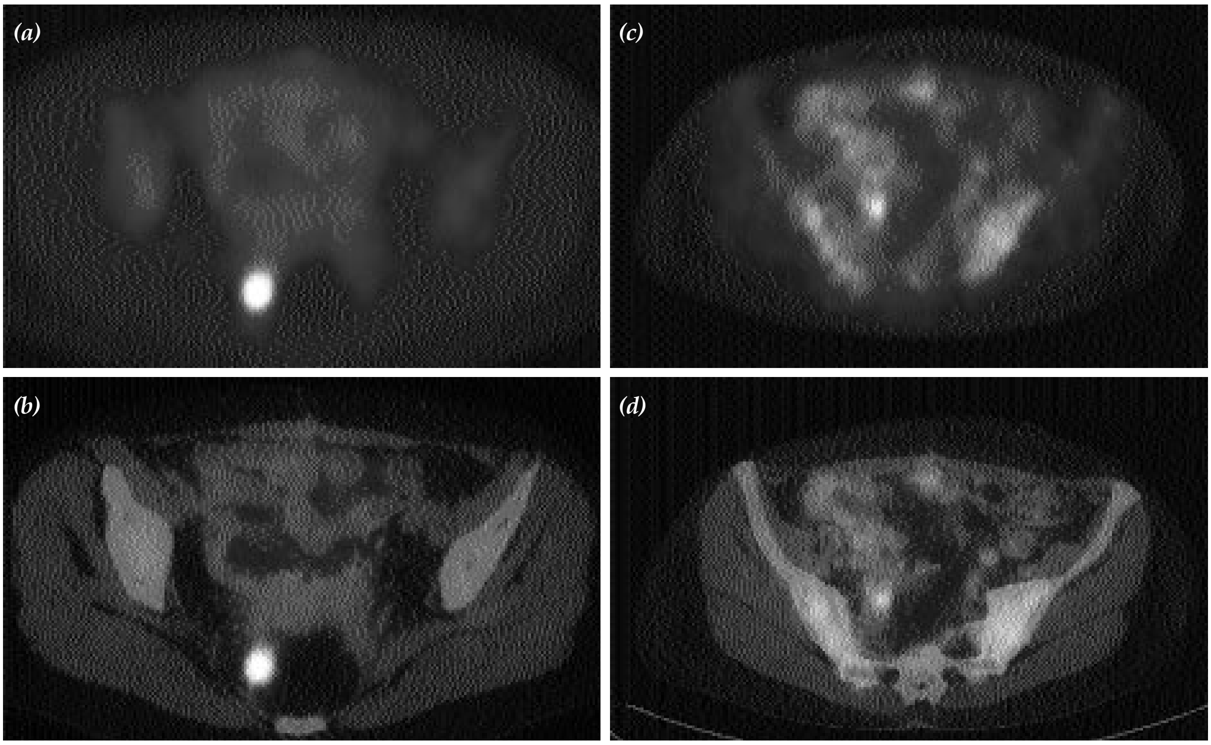

Fig. 16. ***(a)*** *Colorectal cancer, elevated CEA. A "hot" lesion in the pelvic area.* ***(b)*** *PET-CT, correct localization of the lesion by CT.* ***(c)*** *Another soft tissue lesion, PET with increased FDG uptake on the right side.* ***(d)*** *Correct localization of the PET lesion by the fused image.*

through after 2.5 years of "Evidence Based Medicine". Knowing the situation in Turkey, it has to be stated that Turkey offers better reimbursement to PET (CT) than in Germany.

One of the major problems which has to be solved is the cooperation of radiologists and nuclear medicine specialists. Even in Germany, in many places a certain "fight" is observed between these two diagnostic specialities. However, PET-CT can only become the tumor imaging modality of choice in oncology if intravenous and oral contrast agents are used. The interpretation and reporting of PET-CT scans should be done jointly by the radiologist and the nuclear medicine physician. Worldwide accepted investigation protocols allow proper quantitation and evaluation of PET-CT scans. The combination of morphological data with absent or positive glucose uptake allows a superb tumor diagnosis with accuracy rates above 90%. PET-CT may be considered the tool of choice for the evaluation of patients with malignancies.

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