Eur J Med Res (2004) 9: 241-246

Technical Innovation

PET / CT: Fundamental Principles

M. D. Seemann, S. Nekolla, S. Ziegler, F. Bengel, M. Schwaiger

Department of Nuclear Medicine, Technical University of Munich, Germany

Abstract: Positron emission tomography (PET) facilitates the evaluation of metabolic and molecular characteristics of a wide variety of cancers, but is limited in its ability to visualize anatomical structures. Computed tomography (CT) facilitates the evaluation of anatomical structures of cancers, but can not visualize their metabolic and molecular aspects. Therefore, the combination of PET and CT provides the ability to accurately register metabolic and molecular aspects of disease with anatomical findings, adding further information to the diagnosis and staging of tumors. The recent generation of high performance PET/CT scanners combines a state of the art full-ring 3D PET scanner and a high-end 16-slice CT scanner. In PET/CT scanners, a CT examination is used for attenuation correction of PET images rather than standard transmission scanning using ^{68}Ge sources. This reduces the examination time, but metallic objects and contrast agents that alter the CT image quality and quantitative measurements of standardized uptake values (SUV) may lead to artifacts in the PET images. Hybrid PET/CT imaging will be very important in oncological applications in the decades to come, and possibly for use in cancer screening and cardiac imaging.

Key words: Positron emission tomography (PET); Computed tomography (CT); PET/CT; PET-CT; Image fusion

Introduction

The most important clinical application of positron emission tomography (PET) is currently oncological imaging. The use of PET enables the assessment of metabolic alterations and molecular aspects that are fundamental to cancer detection, therapeutical response and recurrence. PET imaging can be performed with different radiotracers. The most commonly used radiopharmaceutical is a glucose analogue, 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (^{18}F-FDG). It relies on the detection of an increased rate of aerobic glycolysis. In most cancers, malignant cells are associated with increased metabolic activity. Therefore, increased uptake of ^{18}F-FDG molecules can be used to spot areas of malignancy and tumor growth. In general, this accelerated metabolic activity occurs before anatomical structure changes. Other imaging modalities, such as computed tomography and magnetic resonance imaging rely primarily on anatomical structure changes for disease detection.

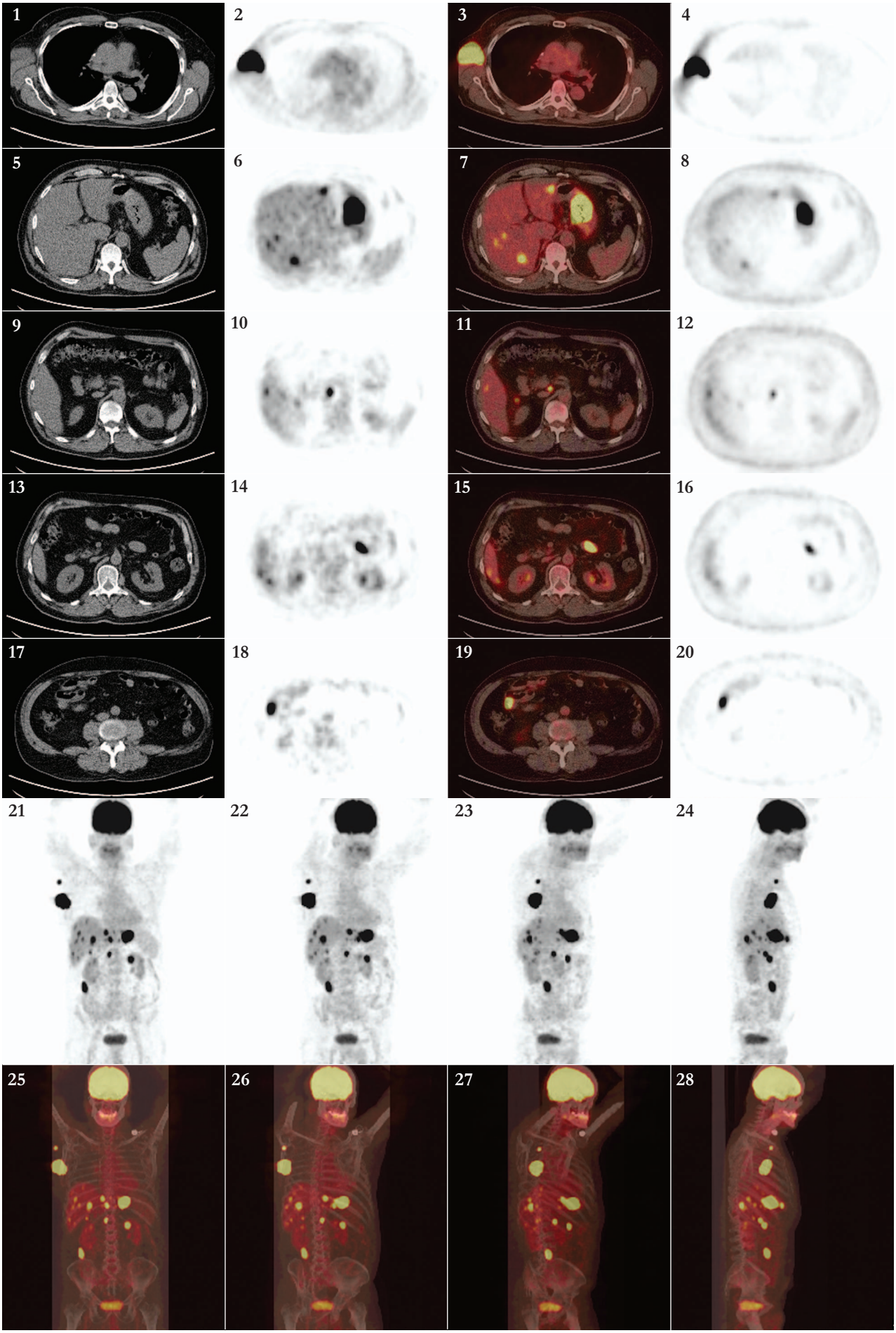
Since the American Food and Drug Administration (FDA) approved ^{18}F-FDG as a safe and effective radiopharmaceutical for oncologic applications (1997), and since the Health Care Financing Administration (HCFA) authorized Medicare to reimburse for ^{18}F-FDG PET imaging for certain indications (1998), ^{18}F-FDG PET imaging has become an accepted and valuable diagnostic imaging tool for patients with cancer. The main difficulty with PET, however, is the lack of an anatomical reference frame.

The fusion of PET and CT images improves the diagnostic value of both imaging modalities in identifying and characterizing of malignancies. The published data about the value of hybrid PET/CT scanners in oncological imaging are very encouraging, but detailed and systematic studies are necessary to clearly define the value and clinical impact of this novel diagnostic imaging technology. In this article, we report on our experience with a biograph Sensation 16 (Siemens AG, Erlangen, Germany).

Fundamental Principles

The combination of PET and CT imaging devices into a single scanner offers several advantages in comparison to PET or CT imaging alone. In combined systems, the CT can be used for the precise anatomical localization of the radiotracer uptake, for the attenuation correction and to reduce the PET examination time. However, the CT-based attenuation correction can lead to artifacts, and thus a review of the uncorrected images may be necessary to differentiate between true radiotracer uptake and tracer activity overestimation caused by artifacts. Only the absence of increased activity in the uncorrected images can truly confirm missing radiotracer activity in the region of the object, preventing "false" interpretations of infection, inflammation, or even malignancy around the object. It is important to take these technical principles into account when interpreting changes qualitatively or quantitatively.

If a diagnostic CT is required, the following protocol is recommended: 1. low dose CT without contrast agent for the attenuation correction, 2. PET emission data, and 3. intravenous contrast enhanced CT with higher currents for diagnostic interpretation [7, 14, 16]. The diagnostic CT can be performed for the whole body, or to limit the radiation dose to the patient, centered on the specific region of interest in the body.


1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

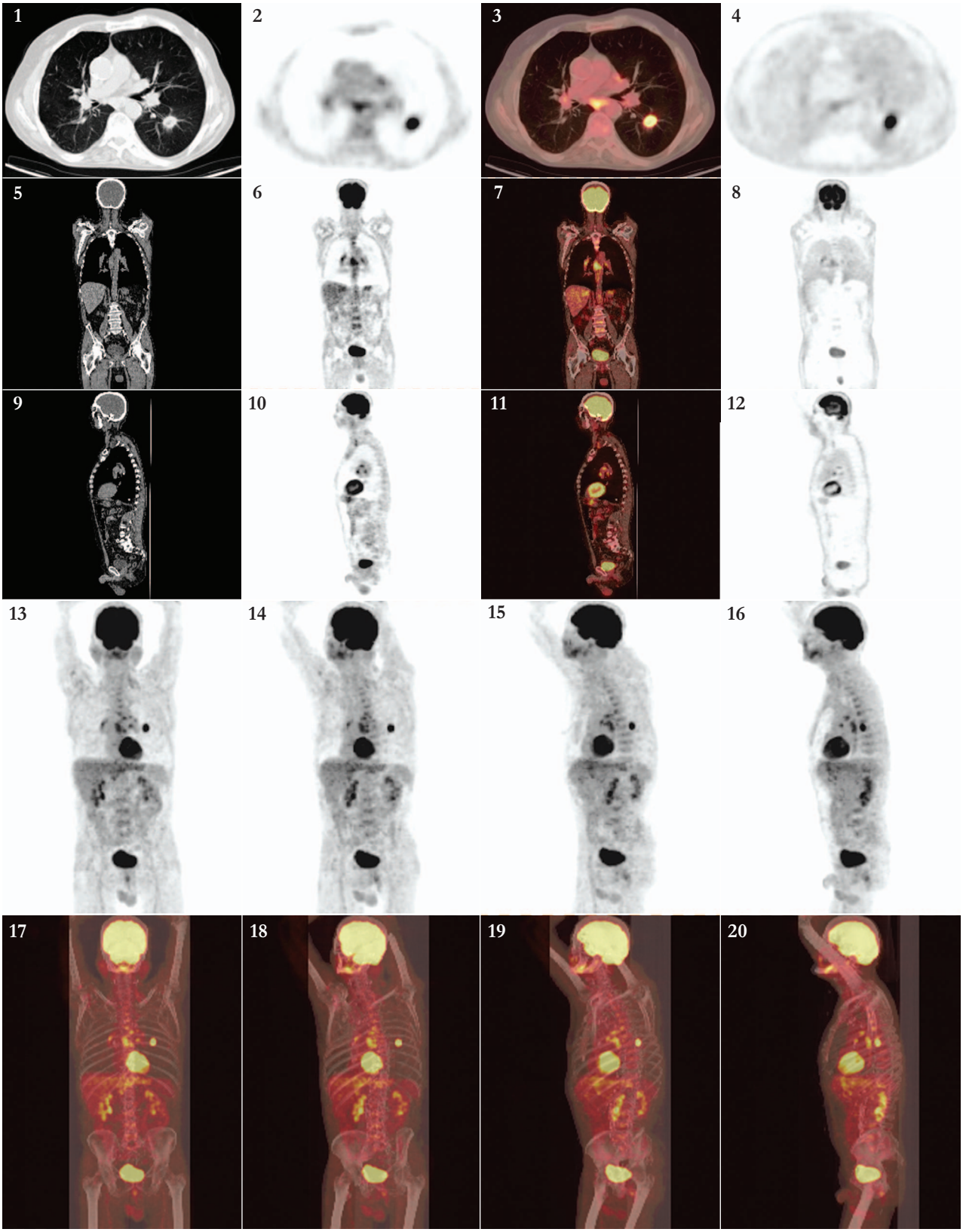


Fig. 1. 64-year-old male patient with an extended metastatic spread of a resected malignant melanoma. CT-based attenuation corrected PET images (2,6,10,14,18), fused PET/CT images (3,7,11,15,19), non-attenuation-corrected PET images (4,8,12,16,20), maximum intensity projection (MIP) reconstructions of the CT-based attenuation corrected PET images (21-24) and MIP reconstructions of the fused PET/CT images (25-28) shows focal increased ^{18}F-FDG uptake of the metastases in the lymph nodes of the axilla (1-4) and the retroperitoneum (9-12), in the liver (5-8), in the stomach (5-8), in the jejunum (13-16) and in the ileum (17-20). The low-dose CT images (1,5,9,13,17) are used for the attenuation correction and the anatomical correlation.

Fig. 2. 70-year-old male patient with an extended mediastinal lymphogen metastatic spread of a peripheral bronchial carcinoma in the left lower lobe. CT-based attenuation corrected PET images (2,6,10), fused PET/CT images (3,7,11), non-attenuation-corrected PET images (4,8,12), maximum intensity projection (MIP) reconstructions of the CT-based attenuation corrected PET images (13-16) and MIP reconstructions of the fused PET/CT images (17-20) shows focal increased ^{18}F-FDG uptake of the peripheral bronchial carcinoma and the metastases in the mediastinum. The low-dose CT images (1,5,9) are used for the attenuation correction and the anatomical correlation.

Precise Anatomical Localization of Radiotracer Uptake of the PET Imaging

Hybrid PET/CT scanners offer the advantage of inherent coregistration and fusion of PET and CT images if patient motion can be neglected.

The acquisition of PET emission data requires a relative long time (a few minutes) and represents an average of patient movement, and respiratory and cardiac motion. The acquisition of CT data is relatively short (a few seconds) and normally can be performed using a breathhold technique. Therefore, the position of organs could differ markedly between the average position obtained with PET emission and the breathhold technique obtained with CT. At the chest-abdomen interface, the discrepancy in the position of the diaphragm between the PET and CT examination results in the appearance of an infrequently severe curvilinear "cold artifact" paralleling the dome of the diaphragm in 84 % of the patients [21]. This artifact can lead to serious mislocalization of lesions that will appear on the CT-corrected images to be located in the wrong organ [20]. Nevertheless, mislocalization of liver metastases are usually easily recognized because the focal uptake in the lung in the PET image will present without a corresponding lung nodule on CT. On average, misregistration of central lung nodules on PET and CT was determined to be 7.6 mm for ^{18}F-FDG-avid lung lesions, with a tendency to be more marked in the lung base than in the middle lung zone and apex [4, 11]. Therefore, adjusted breathing techniques to improve registration in the lung have been evaluated extensively [10, 11]. Although breath holding is the standard technique for CT, it is impractical for the longer PET emission acquisition. Goerres et al. [10, 11] reported that a normal expiration technique during the CT acquisition, where the patient stops respiration at the level of a normal expiration, provides the best match of PET and CT images.

CT-based Attenuation Correction

A PET examination usually involves both the acquisition of an emission scan, which consists of detecting coincident 511 keV photons obtained from the decay of a positron emitting isotope that labels the administered tracer, and the acquisition of a transmission scan for attenuation correction, obtained from a 511 keV source or other high energy rotating around the body (usually a ^{68}Ge rod source or a ^{137}Cs point source). PET images can be reviewed without attenuation correction, but are usually reconstructed using an iterative algorithm, which takes an attenuation map obtained from the high-energy transmission scan into account to produce an attenuation correction image. The high-energy transmission map is usually noisy, has limited anatomic details and poor spatial resolution. With the segmentation of the transmission map, the noise level is reduced, allowing the acquisition of a "shorter" 3-min acquisition per bed position with a ^{68}Ge source. CT images are acquired at an X-ray beam effective energy of ~70-80 keV as a result of using photons with a broad energy spectrum from 40-140 keV. They are obtained from the attenuation of high-intensity x-ray sources by the body, and also have high spatial resolution and low noise. To use them to generate a transmission map for PET, they have to be converted from Hounsfield units (HU) into attenuation coefficients at 511 keV. Due to the different energy, the attenuation coefficients are different for the 511 keV and CT x-ray photons. This difference varies depending on the material or tissue that is imaged; therefore, an algorithm is necessary to scale the attenuation coefficient of the much lower x-ray energy levels to 511 keV energy level in order to provide an accurate attenuation correction. The single most accurate method of performing this scaling is the acquisition of CT images at two different energies. However, alternative methods based on a single CT scan applying scaling, segmentation or a combination of the two have been implemented in order to provide a simpler but potentially less accurate solution. Studies carried out with such algorithms have concentrated on correcting errors in the derivation of PET attenuation coefficients, without correlating such errors with resulting biases in recovering activity concentrations from CT-based attenuation-corrected emission images. The CT-based attenuation map has high statistical quality and thus a low-noise level, which introduces less noise and potential noise-related artifacts into the attenuation correction process. Since PET resolution is worser than the CT resolution, for attenuation correction, the CT scan can be performed with the lowest current to apply a minimum of radiation dose to the patient. The CT images were resampled from a 512 x 512 matrix size to the 128 x 128 or 256 x 256 matrix sizes of the PET emission images. The CT pixel values in HU were transformed into linear attenuation coefficients in cm^{-1} at 511 keV by a bilinear function defined by the three coordinates (-1,000 HU, 0 cm^{-1}; 0 HU, 0.0933 cm^{-1}; and +1,326 HU, 0.172 cm^{-1}). These attenuation images are then forward projected according to the PET scanner geometry, and the calculated line integrals exponentiated to obtain the attenuation correction factors. The resulting attenuation correction data is smoothed with a 8-mm gaussian filter to adjust to the spatial PET resolution. These attenuation correction factors are then applied to the emission data, and the attenuation-corrected emission images are finally reconstructed with an ordered-subset expectation maximization (OSEM) iterative reconstruction algorithm [3, 15, 19, 22].

Decrease of Examination Time

Using a 16-slice low-dose CT (voltage of 120 kV and current of 26 mAs) as transmission scan for the attenuation correction, the maximum scan length of 1981 mm lasts less than 1 minute and leads to a radiation exposure of only 1.85 mGy. This shortens the duration in comparison to a standard PET examination by 15 to 21 min [16].

Furthermore, the use of Lutetium Oxyorthosilicate (LSO) detector technology instead of conventionally used Bismuth Germanate (BGO), together with three-dimensional emission data acquisition, will further decrease the examination time. Thus the entire examination time for patients can be reduced to 15 min, excluding the time needed for patient positioning.

Tracer Activity Overestimation Caused by Artifacts

The use of CT-derived transmission maps is adequate for attenuation correction in most situations, but there is a potential risk of over-estimating the true tracer activity with CT-based attenuation correction. In comparison to ^{68}Ge based attenuation correction, the measured activity with CT-based attenuation correction will be overestimated in osseous lesions by 11.1% ($P<0.01$) and in soft tissue by 2.1% ($P<0.01$) [19]. Therefore, the information from the uncorrected PET images may be necessary in regions with increased activity for differentiation of pathological "true" tracer uptake from overcorrection artifacts.

The use of oral and rectal contrast agents in the CT examination is useful for interpreting the abdominal images, especially for the gastrointestinal bowel, but the CT-based attenuation correction leads to artifacts of markedly increased apparent radiotracer uptake, which leads to an overestimation of the measured activity. Low-density contrast can result in minimal overestimation of true tracer uptake in the bowel and appears suitable for clinical use, but high-density contrast results in the presence of artifacts and markedly increased apparent tracer uptake [5, 8].

The use of intravenous contrast agents in the CT examination is necessary to improve the diagnostic quality. Nevertheless, the use of intravenous contrast CT images as transmission images can produce artifacts of increased radiotracer uptake in regions of high-density, as shown in phantom, animal, and human studies [1, 18]. This affects the qualitative interpretation of PET studies and the quantitative measurements by inducing an overestimation of the true uptake. In a canine model, presence of a contrast agent also increased emission activity, but the percentage bias was less than 15% in the liver and smaller in all other organs except the kidney (26%) [18]. This effect was independent of ^{18}F-FDG concentration [18].

In addition, when using CT-based attenuation correction, the presence of metallic objects (dental metalwork, dental implants, bullets, pacemakers, injection ports, and metallic orthopedic hardware) results in an overestimation of attenuation correction measured at x-ray energies and incorrectly scaled to the 511 keV energy, and leads to focal apparent increased radiotracer uptake in regions nearby [9,15]. These artifacts were more evident when the object was moved between the CT and PET scan [12].

Arms are positioned above the head for most procedures, whereas they are positioned along the torso when the region of interest is the head and neck. Minimal patient motion is important in PET/CT imaging, otherwise the PET and CT acquisition are misaligned, creating inconsistent fusion data. The risk of motion is significantly increased by a long time interval between the data acquisitions of the two modalities. This will be particularly deleterious in the head and neck area. Instructions to the patient and careful positioning are warranted. Depending on the level of patient cooperation, immobilization devices can be used.

Conclusions

A hybrid PET/CT offers the ability for accurate registration of metabolic and molecular aspects of the diseases with exact correlation to anatomical findings. This yields a clear improvement of diagnostic accuracy by combining two already excellent modalities. The precise correlation of radiotracer uptake with CT allows the differentiation of the normal physiological variants of radiotracer uptake (urinary, bowel, fat, muscle) that can mimic metastatic lesions from pathological uptake, and can help avoid potential false-positive interpretations [6, 13, 17]. Furthermore, PET/CT adds further information to diagnoses, allowing adequate characterization and proving improved tumor staging. In addition, malignancies with low or normal metabolic activity (e.g. mucinous carcinomas, primary renal cell carcinoma and prostate cancer) may show clearly positive or suspicious findings in the CT image component of the PET/CT [2]. On the other hand, PET will identify lesions with the highest FDG uptake, while the CT component will provide anatomical details to precisely guide the biopsy. Hybrid PET/CT imaging will be very important in oncological applications in the decades to come, and possibly for use in cancer screening and cardiac imaging.

References

1. Antoch G, Freudenberg LS, Egelhof T, Stattaus J, Jentzen W, Debatin JF, Bockisch A (2002) Focal tracer uptake: a potential artifact in contrast-enhanced dual-modality PET/CT scans. J Nucl Med 43: 1339-1342
2. Berger KL, Nicholson SA, Dehdashti F, Siegel BA (2000) FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. Am J Roentgenol 174: 1005-1008
3. Burger C, Goerres G, Schoenes S, Buck A, Lonn AH, von Schulthess GK (2002) PET attenuation coefficients from CT images: experimental evaluation of the transformation of CT into PET 511-keV attenuation coefficients. Eur J Nucl Med Mol Imaging 29: 922-927
4. Cohade C, Osman M, Marshall LN, Wahl RN (2003) PET-CT: accuracy of PET and CT spatial registration of lung lesions. Eur J Nucl Med Mol Imaging 30: 721-726
5. Cohade C, Osman M, Nakamoto Y, Marshall LT, Links JM, Fishman EK, Wahl RL (2003) Initial experience with oral contrast in PET/CT: phantom and clinical studies. J Nucl Med 44: 412-416
6. Cohade C, Osman M, Pannu HK, Wahl RL (2003) Uptake in the supraclavicular area fat ("USA-Fat"): description on ^{18}F-FDG PET/CT. J Nucl Med 44: 170-176
7. Cohade C, Wahl RL (2003) Applications of positron emission tomography/computed tomography image fusion in clinical positron emission tomography – clinical use, interpretation methods, diagnostic improvemnts. Semin Nucl Med 33: 228-237
8. Dizendorf EV, Treyer V, von Schulthess GK, Hany TF (2002) Application of oral contrast media in coregistered positron emission tomography-CT. Am J Roentgenol 179: 477-481
9. Goerres GW, Hany TF, Kamel E, von Schulthess GK, Buck A (2002) Head and neck imaging with PET and PET/CT: artifacts from dental metallic implants. Eur J Nucl Med Mol Imaging 29: 367-370

10. Goerres GW, Kamel E, Heidelberg TN, Schwitter MR, Burger C, von Schulthess GK (2002) PET-CT image coregistration in the thorax: influence of respiration. Eur J Nucl Med Mol Imaging 29: 351-360
11. Goerres GW, Kamel E, Seifert B, Burger C, Buck A, Hany TF, von Schulthess GK (2002) Accuracy of image coregistration of pulmonary lesions in patients with non-small cell lung cancer using an integrated PET/CT system. J Nucl Med 43: 1469-1475
12. Goerres GW, Ziegler SI, Burger C, Berthold T, von Schulthess GK, Buck A (2003) Artifacts at PET and PET/CT caused by metallic hip prosthetic material. Radiology 226: 577-584
13. Hany TF, Gharehpapagh E, Kamel EM, Buck A, Himms-Hagen J, von Schulthess GK (2002) Brown adipose tissue: a factor to consider in symmetrical tracer uptake in the neck and upper chest region. Eur J Nucl Med Mol Imaging 29: 1393-1398
14. 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
15. Kamel EM, Burger C, Buck A, von Schulthess GM, Goerres GM (2003) Impact of metallic dental implants on CT-based attenuation correction in a combined PET/CT scanner. Eur Radiol 13: 724-728
16. Kamel EM, Hany TF, Burger C, Treyer V, Lonn AH, von Schulthess GK, Buck A (2002) CT vs ^{68}Ge 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
17. Kluetz PG, Meltzer CC, Villemagne VL, Kinahan PE, Chander S, Martinelli MA, Townsend DW (2000) Combined PET/CT Imaging in Oncology. Impact on Patient Management. Clin Positron Imaging 3, 223-230
18. Nakamoto Y, Chin BB, Kraitchman DL, Lawler LP, Marshall LT, Wahl RL (2003) Effects of nonionic intravenous contrast agents at PET/CT imaging: phantom and canine studies. Radiology 227: 817-824
19. Nakamoto Y, Osman M, Cohade C, Marshall LT, Links JM, Kohlmyer S, Wahl RL (2002) PET/CT: comparison of quantitative tracer uptake between germanium and CT transmission attenuation-corrected images. J Nucl Med 43: 1137-1143
20. Osman MM, Cohade C, Nakamoto Y, Marshall LT, Leal FP, Wahl RL (2003) Clinically significant inaccurate localization of lesions with PET-CT: frequency in 300 patients. J Nucl Med 44: 240-243
21. Osman MM, Cohade C, Nakamoto Y, Wahl RL (2003) Respiratory motion artifacts on PET emission images obtained using CT attenuation correction on PET-CT. Eur J Nucl Med Mol Imaging 30: 603-606
22. Visvikis D, Costa DC, Croasdale I, Lonn AHR, Bomanji J, Gacinovic S, Ell PJ (2003) CT-based attenuation correction in the calculation of semi-quantitative indices of [18F]FDG uptake in PET. Eur J Nucl Med 30: 344-353

Received: February 24, 2004 / Accepted: March 17, 2004

Address for correspondence:
Marcus D. Seemann, M.D.
Associate Professor of Radiology
Department of Nuclear Medicine
Technical University of Munich
Ismaninger Strasse 22
D-81675 Munich, Germany
Tel.: +49 89-4140 2971
Fax: +49 89-4140 4841
e-mail: m.seemann@lrz.tum.de