Abstract The aims of the present study were (a) to evaluate mediastinal staging in patients with lung cancer with 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG) using a coincidence gamma camera (hybrid PET) in comparison with dedicated positron emission tomography (PET) and computed tomography (CT), and (b) to assess the feasibility to determine standardized uptake values (SUV) with hybrid PET. Forty patients were included in the study. Hybrid PET was performed without and with attenuation correction. Data were rebinned with single-slice (SSRB) or Fourier rebinning (FORE). The SUVs of primary tumors were calculated with hybrid PET and compared with SUVs determined by dedicated PET. Diagnostic accuracy for hybrid with or without attenuation correction was 80 or 74% compared with 82% for dedicated PET, and 63% for CT. Attenuation-corrected hybrid PET revealed a higher specificity than CT (83 vs 52%; \( p < 0.05 \)). The SUVs of primary tumors were similar to those of hybrid PET and dedicated PET with a mean relative difference of 20.8±16.4%. The FORE improved the agreement of SUVs with a mean relative difference of 13.8±9.9 vs 36.0±17.9% for SSRB (\( p < 0.001 \)). Hybrid PET with attenuation correction is more specific than CT for mediastinal staging in patients with lung cancer (\( p < 0.05 \)). It reveals similar results in comparison with dedicated PET. Calculation of SUVs with hybrid PET is feasible.

Keywords Non-small-cell lung carcinoma · Mediastinal staging · Coincidence gamma camera · Positron emission tomography · SUV

Introduction

Lung cancer is the leading cause for cancer-related deaths worldwide as stated by the 1998 WHO report. Histological subtypes include non-small-cell lung cancer (NSCLC) and the less frequent small cell lung cancer (SCLC). Treatment options for NSCLC depend on tumor size, locoregional lymph node involvement, and distant metastases, and include surgery, chemotherapy, radiotherapy, or a combination. Patients without lymph node involvement or ipsilateral hilar lymph nodes (N1) and a primary tumor classification less than T4 (stages I and II) are candidates for complete surgical resection of the tumor. There is a clear advantage to the use of neoadjuvant chemotherapy prior to surgery for locally advanced resectable disease with ipsilateral mediastinal lymph node involvement (stage IIIA; [1, 2]). In locally advanced unresectable disease with contralateral mediastinal or supraclavicular lymph node metastases or tumor classification T4 (stage IIIB), combined-modality therapy with chemotherapy and radiotherapy provides best results [3, 4]. Patients with distant metastases (stage IV) or with malignant pleural effusion are treated with palliative intent with or without cytotoxic drugs; therefore, accurate pre-surgical staging is of paramount clinical interest to avoid unnecessary thoracotomy [5].
The standard procedure for non-invasive staging of lymph node metastases is CT; however, size-related CT criteria fail to detect small lymph node metastases and reveal a considerable number of false-positive results in enlarged lymph nodes [6].

Several reports on the use of 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography (FDG PET) for mediastinal lymph node staging of NSCLC showed that PET is more accurate for lymph node staging than CT [7, 8, 9]. Moreover, it has been recently shown by a randomized multicenter trial that FDG PET can prevent unnecessary surgery in a considerable number of patients with NSCLC [10]; however, the acceptance of FDG PET as a routine imaging procedure is still low because of high costs, limited availability, and reimbursement restrictions. Recently, dual-headed gamma cameras, capable of both single photon emission CT and PET (henceforth referred to as hybrid PET) have been introduced as an alternative to dedicated PET for the diagnosis and staging of lung cancer [11, 12]; however, comparative studies of nodal staging with first-generation non-attenuation-corrected hybrid PET vs dedicated PET revealed a lower sensitivity for hybrid PET [12, 13]. The aim of the present study was to compare the diagnostic performance of hybrid PET, dedicated PET, and CT for mediastinal staging of lung cancer, and to assess the impact of non-uniform attenuation correction.

Patients and methods

Forty patients (age range 43–79 years) with proven or suspected lung cancer were prospectively studied. Thirty-seven patients underwent a dedicated PET scan on the same day prior to hybrid PET. Informed consent was obtained from each patient. The study was approved by the local ethics committee.

Study protocol

All patients were in a fasting state for at least 6 h controlled by blood glucose levels (median 6.1 mmol/l). Two initially hyperglycemic diabetics received regular insulin prior to FDG administration.

Dedicated PET (ECAT EXACT 922/47, Siemens CTI, Knoxville, Tenn.) was started 64±17 min after intravenous administration of 229±40 MBq FDG. Applying a 1-day protocol, hybrid PET (Solus MCD/AC, ADAC Labs, Milpitas, Calif.) followed 66±22 min after the start of dedicated PET and 129±30 min after administration of FDG.

Hybrid PET was performed using the following parameters for acquisition and reconstruction: emission scanning in coincidence mode covering 180° with 32 steps with an average acquisition time of 39 s. The detector radius was 30.96 cm for all studies. The emission scan was followed by 360° transmission scanning in singles mode with 96 azimuths and an acquisition time of 2 s each. The acquisition matrix was 128×128 pixels. The emission data were corrected for decay by adjusting the frame duration of each step. A dual-window technique was used, accepting coincidences between photopeak events and photopeak and Compton events. The preset windows (photopeak 511 keV±15%, Compton 310 keV±15%) were adjusted for each scan. The Compton window was set relative to the photopeak window according to the manufacturers guidelines. After single-slice rebinning (n=14, SSRB) or Fourier rebinning (n=26, FORE) into 96 projections, an iterative algorithm (ordered subset expectation maximization, eight subsets, 16 steps) was applied for reconstruction. Additionally, a non-attenuation corrected data set was reconstructed. The field of view extended from the supravacular region to the kidneys corresponding to one bed position with an axial extension of 38.5 cm.

For dedicated PET the field of view extended from the base of the skull to the pelvis. The acquisition parameters of seven studies performed with the ECAT 7.0 acquisition software were as follows: five to six bed positions with an acquisition time of 10–12 min per bed position for emission scanning, preceded by a transmission scan of 12–15 min per bed position with 68-Ge rod sources performed prior to FDG administration. Attenuation correction was performed applying measured attenuation coefficients. Data were transferred to ECAT 6.4 file format and reconstructed using a modified algorithm (maximum likelihood expectation maximization; 16 steps) based on the algorithm of Shepp and Vardi [14]. Thirty studies were performed with the whole-body tool implemented in the standard software ECAT 7.1. Acquisition time was 8 min for emission and 4 min for transmission. A segmented attenuation map with empirical attenuation coefficients was used for attenuation correction. For iterative reconstruction an ordered subsets expectation maximization algorithm (30 subsets, 1 step) implemented in the standard software was used.

Computed tomography

All images were obtained in supine position during full inspiratory breath-hold with a Somatom Plus CT scanner (Siemens, Erlangen, Germany) or a CT Twin CT scanner (Elscent, Haifa, Israel). Scans were obtained with 1.0-cm collimation and 1.0-cm interval from the apices to the adrenals. Acquisition parameters were 140 kV and 165 mA. Scanning started 30 s after injection of 100 ml iodinated contrast material by a mechanical power injector (injection rate 3 ml/s). Images were photographed at lung (level –800 HU, width 1600 HU) and mediastinal (level 40 HU, width 400 HU) window settings. Both PET and CT were performed within a maximum of 4 weeks and a median of 1 week.

Image analysis

Hybrid PET with and without attenuation correction (AC/noAC) and dedicated PET were evaluated by one experienced observer (M.Z.) without knowledge of clinical data and results of other imaging or staging procedures using a gray-scale or color-scale screen display. The three PET modalities were analyzed sequentially starting with non-attenuation corrected hybrid PET followed by attenuation corrected hybrid PET and finally dedicated PET. The data sets were analyzed with regard to primary tumor and lymph node metastases. The CT (primary tumor and mediastinum) was interpreted by one experienced radiologist (R.L.). For classification of lymph node metastases the ATS-LCSG map was applied [15].

The findings of dedicated PET, hybrid PET, and CT were compared with the final staging obtained from histology after thoracotomy and/or mediastinoscopy, and from follow-up. At mediastinoscopy lymph nodes of stations two, four, and seven were sampled. At thoracotomy visible ipsilateral lymph nodes were removed. Histopathological analysis of the lymph nodes was performed according to a standard protocol. After formalin fixation and embedding in paraffin, 4-µm sections were cut and stained with hematoxylin and eosin.

Contrast- and signal-to-noise ratio (SNR) of the primary tumor and lymph node metastases were assessed with rectangular regions of interest (ROI) of 4×4 pixels (2.4 cm²) for hybrid PET and 3×3