Cardiovasc Intervent Radiol (2014) 37:1306–1311
DOI 10.1007/s00270-013-0793-x

Comparison of CT-Guided Percutaneous Biopsy with and Without Registration of Prior PET/CT Images to Diagnose Mediastinal Tumors

Koichi Yokoyama · Osamu Ikeda · Koichi Kawanaka · Yutaka Nakasone · Yoshitaka Tamura · Seijiro Inoue · Fumi Sakamoto · Morikatsu Yoshida · Shinya Shiraishi · Yasuyuki Yamashita

Received: 4 May 2013 / Accepted: 1 September 2013 / Published online: 22 November 2013

Abstract
Purpose To compare computed tomography (CT)-guided percutaneous biopsy with and without registration of prior positron emission tomography (PET)/CT images in the diagnosis of mediastinal tumors.
Methods We performed clinically indicated percutaneous biopsy in 106 patients with mediastinal tumors in the anterior ($n = 61$), posterior ($n = 21$), middle ($n = 16$), and superior mediastinum ($n = 8$). The final diagnosis was based on surgical outcomes, or imaging findings and the results of at least 6-month follow-up. The patients underwent CT-guided percutaneous biopsy with (group 1, $n = 56$) or without (group 2, $n = 50$) registration of prior PET/CT images obtained no more than 22 days earlier. The registered images were used to plan the procedure and help target the tumors.
Results CT-guided percutaneous needle biopsy yielded adequate samples in 101 of 106 (95 %) patients (group 1, $n = 53$; group 2, $n = 48$); in 95 patients (94 %), the diagnosis was confirmed by specific histological typing (group 1, $n = 51$; group 2, $n = 44$). The diagnostic accuracy of CT-guided percutaneous biopsy with and without the registration of prior PET/CT images was not statistically different (group 1, 96 %; group 2, 93 %, $p = 0.324$).
Conclusion CT-guided percutaneous biopsy is an easy and safe procedure that can provide a precise diagnosis in the majority of mediastinal tumors. PET/CT-guided biopsy yielded no special diagnostic advantages.

Keywords 18-F FDG PET/CT · CT-guided percutaneous biopsy · Mediastinal tumors

Introduction

Imaging-guided percutaneous transthoracic needle biopsy is adequate for characterizing mediastinal lesions and can be used before invasive surgical diagnostic procedures [1–7]. Core needle biopsy with large needles usually provides samples of good quality that facilitate evaluation of the

K. Yokoyama · O. Ikeda (✉) · K. Kawanaka · Y. Nakasone · Y. Tamura · S. Inoue · F. Sakamoto · M. Yoshida · S. Shiraishi · Y. Yamashita
Department of Diagnostic Radiology, Graduate School of Medical and Pharmaceutical Sciences, Kumamoto University, 1-1-1, Honjo, Kumamoto 860-8505, Japan
e-mail: osamu-3643ik@do9.enjoy.ne.jp

K. Yokoyama
e-mail: ftst19@yahoo.co.jp

K. Kawanaka
e-mail: kawan37@yahoo.co.jp

Y. Nakasone
e-mail: n-yutaka@cd5.so-net.ne.jp

Y. Tamura
e-mail: t-yosh@s2.kcn-tv.ne.jp

S. Inoue
e-mail: seuoni@gmail.com

F. Sakamoto
e-mail: fumi19790526@yahoo.co.jp

M. Yoshida
e-mail: y_morikatsu@hotmail.com

S. Shiraishi
e-mail: shiraish@kumamoto-u.ac.jp

Y. Yamashita
e-mail: yama@gpo.kumamoto-u.ac.jp

tumor architecture, immunohistochemical staining, and in some cases molecular biology studies [8, 9]. Computed tomography (CT)-guided transthoracic needle biopsy has been recommended as the initial diagnostic procedure in patients with mediastinal masses [8–11].

Positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) is now used to evaluate and manage oncology patients and for initial staging, early response evaluation, posttreatment assessment, and follow-up. Nonenhanced CT is often performed to guide percutaneous biopsies [12]. However, because some lesions detected with PET may have few or no correlative CT findings [13, 14], it may not be possible to perform a biopsy based on PET findings alone, and nonenhanced CT-guided biopsy of such lesions may return false-negative results because of sampling error. Therefore, if PET information could be integrated into CT-guided biopsy procedures, more lesions would be available for biopsy, and the accuracy of biopsy results may be improved [12, 15–19].

In the current study, we compared the diagnostic value of CT-guided percutaneous biopsy with and without registration of prior PET/CT images in patients with mediastinal tumors.

Materials and Methods

Patients

Our institutional review board approved this retrospective study; prior written informed consent was obtained from all patients for CT-guided percutaneous biopsy. Between January 2006 and June 2012, we performed clinically indicated percutaneous biopsy of mediastinal tumors in 106 patients (53 men, 53 women; mean age 57 years, range 15–67 years). The final diagnosis was based on surgical outcomes and imaging findings; clinical follow-up lasted at least 6 months. The mean tumor size was 5.3 cm (range 1.4–14 cm).

On enhanced CT or magnetic resonance (MR) images obtained before the procedure that had been obtained no more than 14 days (mean 5.8 days) earlier, the lesions were solid homogenous masses with a regular ($n = 53$, 50 %) or an irregular or invasive tumor border ($n = 35$, 33 %), and were cystic or necrotic tumors ($n = 18$, 17 %). Their diameter ranged from 1.4 cm to 14.0 cm (mean 5.3 cm). The lesions were located in the anterior ($n = 61$, 57.5 %), posterior ($n = 21$, 19.8 %), middle ($n = 16$, 15.1 %), and superior mediastinum ($n = 8$, 7.5 %).

Initial Diagnostic PET/CT Scan

Our patients were referred from 12 hospitals in our local area. All patients from 3 hospitals that had access to a PET/CT scanner received PET/CT examination (group 1), and all patients from another 9 hospitals that did not have access to a PET/CT scanner did not receive PET/CT examination (group 2). There were no differences between these two groups in terms of patients' age, sex, tumor size, stage, and histologic type. When malignant tumor was diagnosed via biopsy in group 2 patients, PET/CT scans were obtained thereafter. They were divided into two groups; group 1 ($n = 56$) underwent CT-guided percutaneous biopsy with, and group 2 ($n = 50$) without, registration of prior PET/CT images that had been obtained no more than 22 days (mean 7.3 days) earlier. The clinical characteristics of the two groups are presented in Table 1.

Table 1 Clinical characteristics of 106 patients

Characteristic	With PET/CT-guided biopsy (group 1)	Without PET/CT-guided biopsy (group 2)	*p* value
No. of patients	56	50	
Age (years)	55.1	58.5	0.36
Sex (M/F)	28/25	25/28	0.77
Mean tumor size (cm)	5.5	5.3	0.67
Tumor location			0.21
Anterior mediastinum	37	24	
Posterior mediastinum	7	14	
Middle mediastinum	7	9	
Superior mediastinum	5	3	
Tumor characteristics			0.01
Tumor border regular	28	31	
Tumor border irregular	24	9	
Cystic tumor	4	10	

PET positron emission tomography, *CT* computed tomography

PET/CT-Guided Biopsy Procedure

All biopsy procedures were performed by two members of the abdominal interventional radiology staff who had 20 years of experience. For all interventional procedures, we used an IVR CT unit comprising an angiographic suite and a CT instrument (Axiom Artis dTA/VB30E; Siemens, Erlangen, Germany). All biopsy specimens were acquired with a coaxial core-needle biopsy technique; the needles were 15- or 17-gauge coaxial introducer needles and 16- or 18-gauge coaxial needles (Tru-Core II; Angiotech, Vancouver, BC, Canada).

Before biopsy, group 1 patients were subjected to FDG PET/CT scanning. A needle path was defined on the monitor that simultaneously displayed CT fluoroscopic and PET/CT images. The patients were placed and immobilized into a proper position with respect to the location of the lesion and the biopsy approach.

The skin entry site was marked and prepared, and sterile drapes were applied. For the moderate sedation of all patients, we used midazolam (1–2 mg, i.v.) and fentanyl (50–200 mg, i.v.), and local anesthesia was inducted with 2 % lidocaine.

A suitable coaxial needle was inserted at the previously identified puncture site. Under CT fluoroscopic imaging guidance, the angle and direction of the 15- and 17-gauge coaxial introducer needles were chosen to accommodate the position of the suspicious lesion.

The tip of the coaxial needle was placed at the border of the suspected lesion exhibiting a solid portion on enhanced CT or MR images acquired before the procedure. Default PET/CT images were obtained to confirm its correct position. The needles were then pulled out and a 16- or 18-gauge coaxial needle was inserted. Satisfactory puncture was confirmed on the CT scan, the biopsy site was recorded, and three or four specimens measuring 1 or 2 cm were obtained. If the lesion was small or difficult to differentiate from important structures such as peripheral vessels, enhanced CT was used to optimize the images. The coaxial needle was withdrawn, and manual pressure was applied for 2–3 min at the puncture site. The specimens were fixed in 10 % formalin and submitted for histopathologic study.

After the biopsy procedure, all patients were monitored for at least 3 h to ensure hemodynamic and respiratory stability. CT scans were acquired immediately and 3 h after the biopsy procedure.

Statistical Analysis

Biopsy samples were considered inadequate if they did not provide sufficient pathological material for diagnostic evaluation as a result of necrotic debris or blood only; these were excluded from further analysis. The biopsy results were later compared with the final diagnosis returned upon surgical histopathological study or clinicoradiologic follow-up. We compared the diagnostic value of CT-guided percutaneous biopsies with and without registration of prior PET/CT images.

Complications related to the interventional radiology techniques (including pneumothorax, hematoma, hemoptysis, and death) were classified as major and minor according to the reporting standards of the Society of Interventional Radiology. We also compared the incidence of complications encountered in CT-guided percutaneous biopsies with and without registration of prior PET/CT images.

For analysis, we applied the Pearson chi squared test; to determine the diagnostic accuracy of the two methods, we used the Fisher exact test for final outcomes.

Table 2 Overall results of the 106 PET/CT-guided percutaneous biopsy samples

Characteristic	With PET/CT-guided biopsy (group 1)	Without PET/CT-guided biopsy (group 2)	*p* value
No. of cases	56	50	
Sampling error	3/56	2/50	0.47
Correct diagnosis	51/53	44/48	0.32
Complications	11/53	9/53	0.81

PET positron emission tomography, *CT* computed tomography

Table 3 Overall correct diagnosis with specific histological typing

Characteristic	With PET/CT-guide biopsy (group 1)	Without PET/CT-guided biopsy (group 2)
No. of cases with correct diagnosis	51	44
Malignant tumor		
Non-Hodgkin lymphoma	8	9
Metastatic tumor	8	5
Thymic carcinoma	6	2
Lung cancer	4	2
Hodgkin lymphoma	1	1
Malignant mesothelioma	1	1
Germ cell tumor	4	
Neuroendocrine carcinoma	1	
Leukemia		1
Benign tumor		
Thymoma	12	9
Sarcoidosis	2	
Granuloma	2	4
Castleman disease	1	
Neurilemmoma	1	4
Teratoma		1
Thymic cyst		1
Aberrant thyroid		1
Amyloidosis		1
Pericardial cyst		1
Extramedullary hemopoiesis lesion		1

PET positron emission tomography, *CT* computed tomography

Results

Our overall results are summarized in Table 2. CT-guided percutaneous needle biopsy yielded adequate samples in 101 of 106 patients (95.3 %; group 1, $n = 53$; group 2, $n = 48$). Sample errors occurred in the other five patients; on prebiopsy CT and MR scans, their lesions appeared to be cystic tumors. The difference in sample errors was not

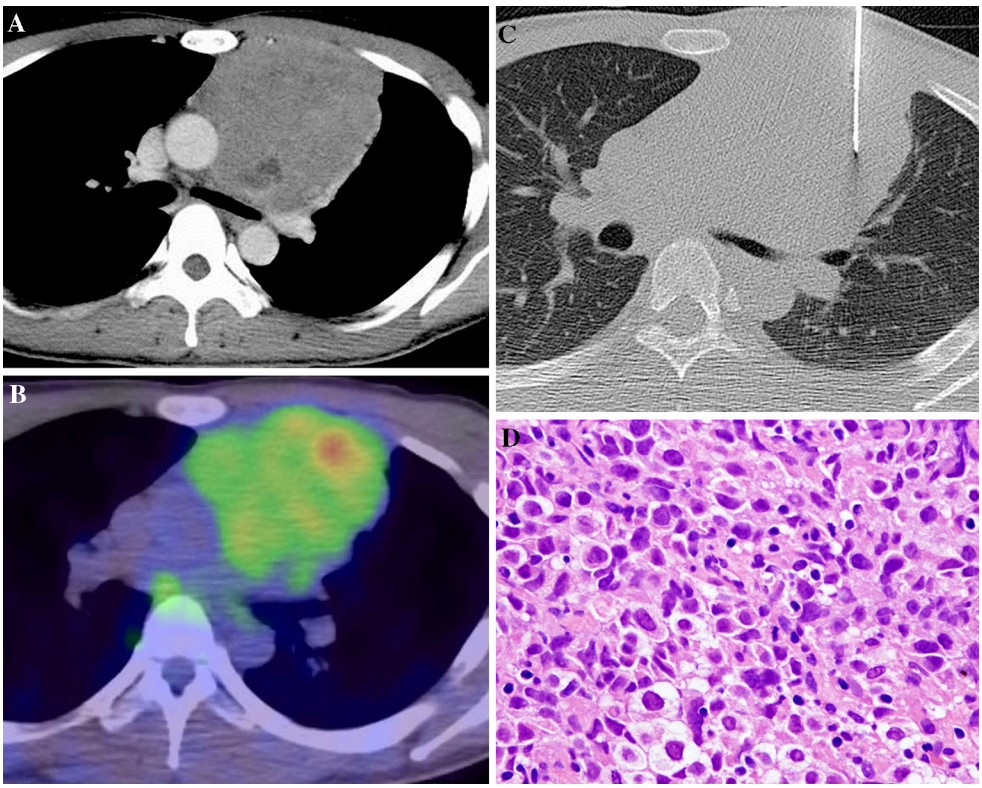

Fig. 1 A 27-year-old man with mediastinal seminoma who underwent PET/CT-guided biopsy. **A** Enhanced CT shows solid homogenous masses with a regular tumor border in the anterior mediastinum. **B** The PET/CT fusion image acquired 1 week before CT-guided biopsy shows the location of the metabolic lesion. **C** The image acquired during CT-guided biopsy shows the placement of the coaxial needle in the metabolic lesion on the PET/CT fusion image. **D** Pathological examination of the lesion confirmed mediastinal seminoma (hematoxylin–eosin staining, original magnification, ×400)

statistically significant (group 1, $n = 5.4$ %; group 2, $n = 4$ %) ($p = 0.47$) (Table 2).

Of the 101 successful biopsies, 95 (94.1 %; group 1, $n = 51$; group 2, $n = 44$) yielded a correct diagnosis with specific histological typing (Table 3). In the other six patients (5.9 %), the lesions were thymic cysts ($n = 2$), granuloma, reactive lymph node, unknown carcinoma, and thymoma ($n = 1$ each) based on CT-guided percutaneous biopsy. However, surgical histopathologic study and/or clinicoradiologic follow-up identified thymic carcinoma in 2 cases and B cell lymphoma, Castleman disease (plasma cell type), lung cancer, and thyroid carcinoma in 1 case each. Nonetheless, the difference in diagnostic accuracy between group 1 and group 2 (95.8 and 91.8 %) was not statistically significant ($p = 0.32$) (Table 2) (Figs. 1, 2).

Complications encountered in this series were pneumothorax and hemothorax ($n = 4$ each), mediastinal hematoma ($n = 3$), and hemopneumothorax, mediastinal emphysema, and hemoptysis below grade 2 ($n = 1$ each). Chest drainage or degassing was required in five patients with pneumothorax and in one patient with grade 3 hemopneumothorax. The rate of complications between group 1 (20.8 %) and group 2 (17.0 %) was not statistically significant ($p = 0.81$) (Table 2).

Discussion

As PET/CT can demonstrate, malignancy even before morphologic changes is evident at image-guided biopsy. This information may facilitate the early histologic diagnosis and staging of malignancies. Furthermore, the metabolic information provided by PET/CT on viable malignant tissue in masses containing nonmalignant (e.g., necrotic) or fibrotic tissue may improve the diagnostic accuracy of image-guided biopsy [13–19]. To our knowledge, ours is the first investigation to compare the value of CT-guided percutaneous biopsy with and without registration of prior PET/CT images for the diagnosis of mediastinal tumors.

We found that PET/CT-guided biopsy of mediastinal tumors offered no special advantages. The uptake of FDG is not specific to cancer cells. Not all cancers are detected with FDG PET/CT, and the reasons for false-positive and false-negative FDG uptake findings must be considered, especially when there is a discrepancy between the biopsy result and the associated PET/CT interpretation [13–19]. Considerable overlap between the standardized uptake value of malignant and benign lesions renders PET/CT-guided biopsy of mediastinal tumors devoid of intrinsic

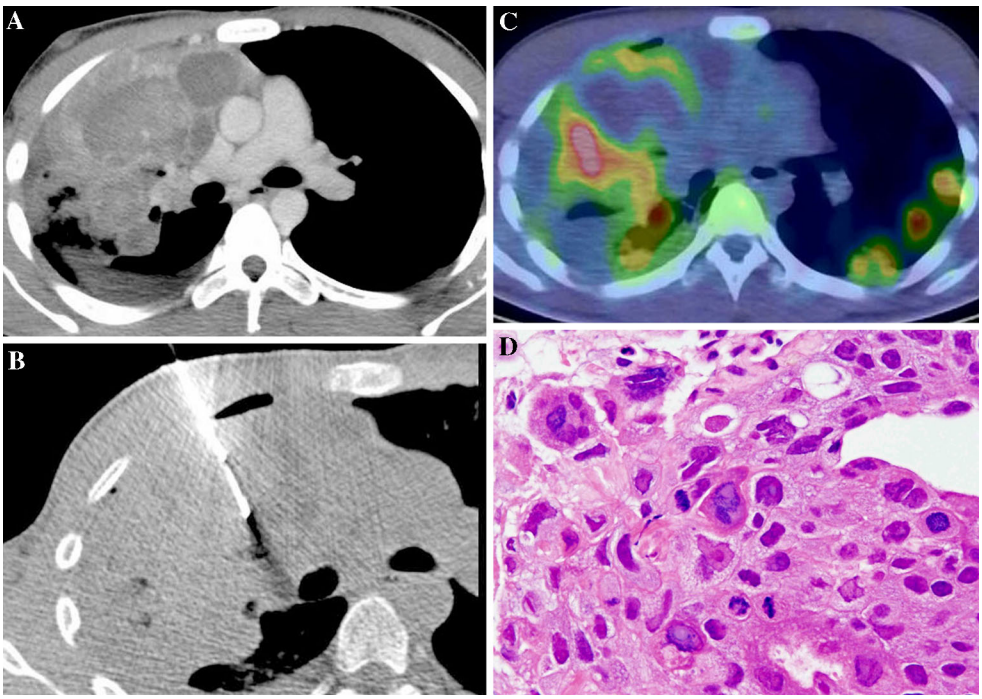

Fig. 2 A 20-year-old man with mediastinal choriocarcinoma who did not undergo PET/CT-guided biopsy. **A** Enhanced CT shows heterogeneous masses with a regular tumor border in the anterior mediastinum. **B** The image acquired during CT-guided biopsy shows the placement of the coaxial needle in the anterior mediastinum. **C** The PET/CT fusion image acquired 2 days after CT-guided biopsy shows the location of the metabolic lesion. At CT-guided biopsy, the metabolic lesion was missed. **D** Pathological examination of the lesion confirmed mediastinal choriocarcinoma (hematoxylin–eosin staining; original magnification, ×400)

diagnostic importance without integration into the proper clinical context and without a correlation with anatomic imaging findings [13–19].

If a mass is not well visualized on nonenhanced CT images, contrast material can be administered intravenously during CT-guided biopsy. However, the usefulness of this method is limited because contrast enhancement of some masses (e.g., hepatocellular carcinoma) may be transient and insufficient and thus not available for guidance throughout the duration of the procedure [20]. Although ultrasound or MR imaging guidance can be used at the biopsy of masses that are not visible on nonenhanced CT images, not all masses are detected by ultrasound and MR imaging requires special wide-bore or open-configuration imaging units. Furthermore, these modalities may still be limited in their depiction of the neoplastic part of masses that also contain nonneoplastic portions. PET/CT guidance may be particularly helpful for biopsies in abdominal masses that are FDG avid but not well visualized on nonenhanced CT images [16]. However, because most mediastinal tumors are clearly visualized and differentiated from normal organs on non-contrast-enhanced CT images, PET/CT-guided needle biopsy is more useful in patients with lesions in other intra-abdominal organs.

Our study has some limitations. First, our study population was small, and the patients presented with similar kinds of tumor and tumor locations. This precluded meaningful statistical analysis of the tumors and their location. Second, because of the study's retrospective nature, our patient population was not randomized between patients who received PET/CT and those who did not. However, there was no intentional bias in receiving PET/CT. All patients from 3 hospitals that had accessible to PET/CT scanner underwent PET/CT examination (group 1), and all patients from the other 9 hospitals that did not have access to a PET/CT scanner did not undergo PET/CT examination (group 2). There were no differences between these two groups in terms of patients' age, sex, tumor size, stage, and histologic type. Further randomized study will be required to eliminate this potential bias. Third, in both types of PET/CT-guided percutaneous biopsy, we used a PET/CT scanner, while in earlier reports, the PET/CT images registered with intraprocedural CT images were acquired with computer software [15, 17, 18, 21]. When a PET/CT scanner is used, biopsy guidance is performed by using the CT elements of the integrated PET/CT system. Needle placement in the targeted area of FDG uptake is confirmed on fused PET/CT images acquired at the same table position used for both unenhanced CT and PET scans [15, 17, 18, 21]. In another technique that uses previously acquired PET/CT images, diagnostic PET/CT images obtained before the procedure and CT images acquired

during the procedure are transferred in the digital imaging and communications in medicine format to a computer via a local area network connection, and the images are fused with the aid of medical image processing [15]. Although we used previously acquired PET/CT images at CT-guided percutaneous biopsy, the images were displayed side by side on the same monitor rather than fused.

In conclusion, CT-guided percutaneous biopsy is an easy and safe procedure that can yield a precise diagnosis in the majority of mediastinal tumors. Although we did not find that PET/CT-guided biopsy of mediastinal tumors offered specific advantages, further evaluation of its clinical impact and cost-effectiveness requires larger trials.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Priola AM, Priola SM, Cardinale L et al (2006) The anterior mediastinum: diseases. Radiol Med 11:312–342
2. Priola SM, Priola AM, Cardinale L et al (2006) The anterior mediastinum: anatomy and imaging procedures. Radiol Med 11:295–311
3. Adler OB, Rosenberg A, Peleg H (1983) Fine-needle aspiration biopsy of mediastinal masses: evaluation of 136 experiences. Am J Roentgenol 140:893–896
4. Weisbrod GL, Lyons DJ, Tao LC et al (1984) Percutaneous fine-needle aspiration biopsy of mediastinal lesions. Am J Roentgenol 143:525–529
5. Herman SJ, Holub RV, Weisbrod GL et al (1991) Anterior mediastinal masses: utility of transthoracic needle biopsy. Radiology 180:167–170
6. Protopapas Z, Westcott JL (2000) Transthoracic hilar and mediastinal biopsy. Radiol Clin North Am 38:281–291
7. Gupta S, Seaberg K, Wallace MJ et al (2005) Imaging-guided percutaneous biopsy of mediastinal lesions: different approaches and anatomic considerations. Radiographics 25:786–788
8. Staudt LM (2003) Molecular diagnosis of the hematologic cancers. N Engl J Med 348:1777–1785
9. Loubeyre P, Copercini M, Dietrich PY (2005) Percutaneous CT-guided multisampling core needle biopsy of thoracic lesions. Am J Roentgenol 185:1294–1298
10. Priola AM, Priola SM, Cataldi A et al (2008) CT-guided percutaneous transthoracic biopsy in the diagnosis of mediastinal masses: evaluation of 73 procedures. Radiol Med 113:3–15
11. Greif J, Staroselsky AN, Gernjac M (1999) Percutaneous core needle biopsy in the diagnosis of mediastinal tumors. Lung Cancer 25:169–173
12. Yap JT, Carney JP, Hall NC, Townsend DW (2004) Image-guided cancer therapy using PET/CT. Cancer J 10:221–233
13. von Schulthess GK, Steinert HC, Hany TF (2006) Integrated PET/CT: current applications and future directions. Radiology 238:405–422
14. Wiering B, Ruers TJ, Krabbe PF et al (2007) Comparison of multiphase CT, FDG-PET and intra-operative ultrasound in patients with colorectal liver metastases selected for surgery. Ann Surg Oncol 14:818–826
15. Tatli S, Gerbaudo VH, Mamede M et al (2010) Abdominal masses sampled at PET/CT-guided percutaneous biopsy: initial experience with registration of prior PET/CT images. Radiology 256:305–311
16. Kobayashi K, Bhargava P, Raja S et al (2012) Image-guided biopsy: what the interventional radiologist needs to know about PET/CT. Radiographics 32:1483–1501
17. Klaeser B, Mueller MD, Schmid RA et al (2009) PET-CT-guided interventions in the management of FDG-positive lesions in patients suffering from solid malignancies: initial experiences. Eur Radiol 19:1780–1785
18. Tatli S, Gerbaudo VH, Feeley CM et al (2011) PET/CT-guided percutaneous biopsy of abdominal masses: initial experience. J Vasc Interv Radiol 22:507–514
19. Cerci JJ, Neto CCP, Krauzer C et al (2013) The impact of coaxial core biopsy guided by FDG PET/CT in oncological patients. Eur J Nucl Med Mol Imaging 40:98–103
20. Yoon SH, Lee JM, So YH et al (2009) Multiphasic MDCT enhancement pattern of hepatocellular carcinoma smaller than 3 cm in diameter: tumor size and cellular differentiation. Am J Roentgenol 193:W482–W489
21. Govindarajan MJ, Nagaraj KR, Kallur KG, Sridhar PS (2009) PET/CT guidance for percutaneous fine needle aspiration cytology/biopsy. Indian J Radiol Imaging 19:208–209