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^{18}F-FDG PET/CT IN THE POST-OPERATIVE MONITORING OF PATIENTS WITH ADRENOCORTICAL CARCINOMA

A. Ardito[1] MD, C. Massaglia[1] MD, E. Pelosi[2] MD, B. Zaggia[1] MD, V. Basile[1] MD, R. Brambilla[3] MD, F. Vigna-Taglianti[3] MD, E. Duregon[4] MD, V. Arena[2] MD, P. Perotti[1], D. Penna[2] MD, M. Terzolo[1] MD.

[1]Internal Medicine I, Department of Clinical and Biological Sciences, San Luigi Hospital, University of Turin, [2]IRMET, PET-CT Diagnostic Imaging Center, Turin [3]Public Health, Department of Clinical and Biological Sciences, San Luigi Hospital, University of Turin, [4]Pathology, Department of Oncology, San Luigi Hospital, University of Turin, Turin, Italy.

A. Ardito and C. Massaglia contributed equally to the paper.

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Address correspondence to:

M. Terzolo, MD
Internal Medicine I
Department of Clinical and Biological Sciences, University of Turin
San Luigi Gonzaga Hospital
Regione Gonzole, 10
10043 Orbassano, ITALY
Tel: ++ 39 011 9026292
Fax: ++ 39 011 6705456
e-mail:

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ABSTRACT

Context The role of FDG PET/CT in the post-operative monitoring of patients with adrenocortical carcinoma (ACC) is still unclear.

Objective To assess the accuracy of FDG PET/CT to diagnose ACC recurrence in a real world setting.

Design/Methods Retrospective evaluation of data of 57 patients with presumed ACC recurrence at CT scan who underwent FDG PET/CT within a median time of 20 days. We compared the results of either FDG PET/CT or CT with a gold standard confirmation of recurrence (positive histopathology report of removed/biopsied lesions or radiological progression of target lesions at follow-up) to assess their diagnostic performance at different body sites to correctly categorize target lesions. We also assessed whether FDG PET/CT findings may be useful to inform the management strategy.

Results In 48 patients with confirmed ACC recurrence, we found that FDG PET/CT had lower sensitivity than CT in diagnosing liver and lung recurrences of ACC. FDG PET/CT had higher specificity than CT in categorizing liver lesions. FDG PET/CT had a greater positive likelihood ratio than CT to identify liver and abdominal ACC recurrences. The management strategy was changed based on FDG PET-CT findings in 12 patients (21.1%).

Conclusions The greater sensitivity of CT may be partly expected due the specific inclusion criteria of the study; however the greater specificity of FDG PET/CT was particularly useful in ruling out suspected ACC recurrences found by CT. Thus, use of FDG PET/CT as a second-line test in the post-operative surveillance of ACC patients following CT finding of a potential recurrence may have a significant impact on patient management.

INTRODUCTION

Positron emission tomography (PET) with ^{18}F-labeled 2-fluoro-2-deoxy-D-glucose (FDG) has an established role in the diagnostic approach of different types of tumors (1). More recently, PET/CT, a technique combining the anatomic and densitometric applications of CT and the functional and metabolic advantages of PET has been increasingly used in oncology (2, 3).

Several studies have reported the effectiveness of FDG PET or PET/CT to differentiate benign from malignant adrenal tumors (4-11) but only few studies reported on the use of functional imaging techniques in the follow-up of adrenocortical carcinoma (ACC) (9-11). Thus, there is limited evidence that PET/CT may refine staging of ACC patients at initial diagnosis or during follow-up. This is not surprising due to the rarity of ACC that hampers progress in the development of management strategies (12, 13).

It could be expected that PET/CT may provide useful and complementary information to **CT** in the detection of post-operative recurrences. In this clinical scenario, prompt detection of ACC re-growth and precise definition of disease extension is of the utmost importance since surgery is a mainstay for treatment of ACC recurrence whenever it is done with radical intent (12, 14). However, repeating surgery is often technically demanding and not without risk for the patient while debulking does not offer much benefit (14); thus, an accurate pre-operative estimate of tumor burden is mandatory for appropriate selection of patients for surgery. However, no recommendation on the use of FDG-PET or PET/CT in the follow-up of patients following ACC removal, or patients with advanced ACC has been provided in recent reviews (15, 16).

The objective of this work was to assess the accuracy of FDG PET/CT to diagnose ACC recurrence in a real world setting. Due to limited availability of the technique and cost issues, we have employed FDG PET/CT as a second-line test in patients with a potential ACC recurrence found by CT during post-surgical follow-up. We have retrospectively correlated FDG PET/CT and CT findings with histopathologic results for patients who underwent surgery or biopsy, or radiological progression of target lesions (RECIST criteria) for patients who were not operated on.

SUBJECTS AND METHODS

Patients

Patient data were retrieved from the ACC database of the San Luigi Hospital, a tertiary referral center for patients with adrenal tumors. The database was established in 2001 with the development of a structured data form to collect comprehensive information of all patients with ACC treated at our center. Data of patients before 2011 were collected retrospectively, while in the following years data were input prospectively. Data were retrieved by trained medical personnel using specifically tailored data forms. For the purpose of this study, patients diagnosed between January 1998 and July 2012 were considered and follow-up for this study was closed on December 2013. The institutional ethics committee of our hospital approved the study, and all patients provided written informed consent. Selected patients underwent surgery either at the San Luigi Hospital or at other institutions.

Inclusion criteria for the study were: age ≥18, pathologically confirmed diagnosis of ACC (in 50 of 57 cases, diagnosis was made or confirmed by the pathologists of San Luigi Hospital), availability of pre-operative and post-operative computed tomography (CT) scans; ACC stage I-III at diagnosis, radical resection of primary tumor; confirmed diagnosis of ACC recurrence during follow-up of a previously tumor-free patient; availability of concomitant FDG PET/CT; complete follow-up information until death or end of the study period. Exclusion criteria were: incomplete tumor staging; ENSAT stage IV ACC; history of other previous/concomitant malignancies; incomplete resection; follow-up of less than 12 months or incomplete follow-up information, time elapsed between the index CT showing potential ACC recurrence and FDG PET/CT >60 days.

We collected data on patients' demographic and clinical characteristics, their tumor stage at diagnosis, hormonal workup, surgical approach, pathology report, adjuvant mitotane treatment, date and modality of recurrence, either the date and cause of death or the date of the last follow-up. Staging at diagnosis was based on imaging studies and corroborated by pathological findings at surgery. Staging was reported according to the ENSAT staging system (17). Radical resection was defined as no evidence of microscopic residual disease at pathological analysis. Follow-up visits, which included physical examination, routine laboratory and hormone evaluation, and cross-sectional imaging of the chest and abdomen, were performed every 3 to 6 months until either disease progression or end of study occurred. For this study, suspected disease recurrence was defined as CT evidence of a possible new tumor site during follow-up (target lesion). The study included only patients with a presumed recurrence (target lesion) found on CT during follow-up.

Imaging techniques

FDG-PET images were acquired using the PET tomography Discovery ST (General Electric Medical Systems, Waukesha, Wisconsin, USA). Patients were asked to fast for at least six hours before the exam and a serum glucose level below 160 mg/dL was ensured. Image acquisition was performed after 60 minutes from intravenous administration of 222-370 MBq of FDG. Firstly an imaging field (CT scout view, with thickness of slices of 3.75 mm) was determined performing a CT scan (140 kV, tube current 80 mA/S) for both anatomical localization and calculation of attenuation correction. Then, PET data were acquired in a 3-dimensional mode from the pelvic floor to the skull basis in 6 to 7 bed positions. The acquisition time for PET was 2.5 minutes per bed position. Coronal, sagittal, and transverse data sets were reconstructed. Co-registered scans were displayed by using dedicated software (Advantage 4.2; GE Healthcare) and integrated FDG-PET/CT data sets were prospectively evaluated in consensus by 3 nuclear medicine physicians. **To qualify a PET imaging as positive, we used qualitative visual criteria following the guidelines of the European Association of Nuclear Medicine (18). The rationale is that there is no single lower limit of the intensity of FDG uptake for the detection of abnormal uptake within lesions as it depends on the degree of contrast between the tumor and its immediate surroundings.** Thoraco-abdomino-pelvic CT scans were performed after intravenous iodinated contrast with multi-slices CT whose thickness of slices varied from 0.5 to 1 mm. Images were captured every 3 to 6 months and were compared to the previous ones with a storage system (PACS). Lesions observed with CT and FDG PET/CT were analyzed by location and number, categorizing the findings according to the district (local, abdominal and peritoneal, liver, lung, bone, peritoneal lymph nodes, thoracic lymph nodes, other districts). **Results of CT scans were also evaluated in consensus and compared to results of FDG PET/CT scans. All evaluations were blinded to the subsequent patient management.**

Confirmation of recurrence

The gold standard test for categorizing any target lesion found in a given patient by imaging as ACC recurrence was one of the following: 1) positive histopathology report of removed, or biopsied, lesions; 2) radiological progression according to RECIST criteria of target lesions at follow-up when they were not removed or biopsied.

Statistical analysis

All statistical analyses were performed with Statistica (StatSoft) statistical software. Rates and proportions were calculated for categorical data and medians and ranges for continuous data. CT and FDG-PET results were compared with the gold standard test by means of 2 x 2 tables. For FDG PET/CT, we calculated sensitivity (SST = true positive/true positive + false negative), specificity (SPC = true negative/true negative + false positive), positive predictive value (PPV = TP/true positive + false positive), negative predictive value (NPV = true negative/true negative + false negative), positive likelihood ratio (LR+ = SST/1 - SPC) and negative likelihood ratio (LR- = 1 - SST/SPC). The diagnostic accuracy of CT and FDG-PET was analyzed by means of the chi-square test and Fisher's exact test. Since the inclusion criteria of the study required positivity of the CT scan (detection of new lesion(s) during follow-up), we did not make a formal comparison of FDG PET/CT vs. CT to categorize patients as with or without ACC recurrence. However, we compared the results of either FDG PET/CT or CT with the gold standard confirmation of recurrence to assess their diagnostic performance at different body sites to correctly categorize target lesions as ACC recurrences. We also assessed whether FDG PET/CT findings may be useful to inform the management strategy. P values of less than 0.05 were considered to indicate statistical significance.

RESULTS

From the overall series of 214 ACC patients who underwent radical resection between 1998 and 2012, 4 patients were excluded for concomitant malignancies, 3 were minors at the time of diagnosis, 62 patients did not recur during follow-up and 33 patients were lost to follow-up. In 57 of 112 patients with presumed ACC recurrence, FDG PET/CT scan was done within a median time of 20 days (range, 3-60 days) from the index CT suggesting disease recurrence and these patients formed the study cohort. Baseline characteristics of the patients are provided in table 1.

In 40 out of 57 patients (70.2%) with one or more new target lesions at CT as marker of potential ACC recurrence, FDG PET/CT showed at least one significant focal uptake. Assessment of the uptake was performed in a qualitative or quantitative way via the Standardized Uptake Value (SUV). SUV of the target lesions ranged between 1.2 and 15.5, median 6.8. In 48 patients a definitive diagnosis of ACC recurrence was demonstrated by histological analysis of surgically removed lesions (23 cases), fine-needle biopsy (5 cases), or detection of radiological progression (RECIST criteria) at imaging follow-up of target lesions (20 cases). In the remaining 9 patients, ACC recurrence was not confirmed.

When assessing concordance of CT and FDG PET/CT target lesions with confirmed ACC recurrences, we found that FDG PET/CT had lower sensitivity than CT in diagnosing liver and lung lesions as ACC recurrences (Table 2, Table 3); however, FDG PET/CT had higher specificity than CT in categorizing liver lesions. FDG PET/CT had a greater LR+ than CT to identify liver and abdominal ACC recurrences. FDG uptake of a liver lesion increases by 38 times the probability of being a true ACC recurrence. FDG uptake of an abdominal lesion increases by 52 times the probability of being a true ACC recurrence (Table 3). **A list of false positive findings of PET/CT is given in table 4.**

In 26 patients (45.6%), CT and FDG PET/CT findings were superimposable (in 2 of them, both techniques had false positive results because local recurrence was finally excluded). When analyzing the 31 patients (54.4%) with discordant findings between the two imaging tests, CT showed a greater number of target lesions than FDG-PET/CT in 23 patients. Conversely, FDG PET/CT showed **additional** target lesions not found by CT in 4 patients. Finally, in 4 patients FDG PET/CT and CT showed two different target lesions (Figure 1). In 7 of the 23 patients with target lesions at CT without corresponding FDG uptakes, ACC recurrence was excluded (2 hepatic nodular hyperplasia, 2 unspecific pulmonary nodules, 2 post-surgical scars, 1 bone aspecific lesion). In the 8 patients with FDG PET/CT target lesions without corresponding CT findings, the additional lesions found by FDG PET/CT were demonstrated to be ACC recurrences.

The management strategy was changed based on PET-CT findings in 12 patients (21.1%) **(Table 5).** We did not treat 8 patients with CT lesions not confirmed by PET. The following work-up confirmed no ACC recurrence in 7 of them while a patient has to be considered as a false negative of PET/CT. We changed the treatment plan in 4 out of 8 patients who showed FDG PET/CT target lesions without corresponding CT findings. We gave a systemic treatment instead of surgery in 1 patient and planned a more extensive surgery in 3 patients, in whom surgical and pathologic reports demonstrated the existence of multiple recurrence sites. In the remaining 4 patients with discordant findings between techniques, we chose to base management on CT findings, but following investigations demonstrated the presence of ACC recurrence in the sites of FDG uptake.

DISCUSSION

The role of FDG PET/CT in the post-operative monitoring of ACC patients is yet to be established. A single study evaluated the role of FDG PET/CT to diagnose ACC recurrence and showed that PET was more sensitive than CT in detecting local recurrence, while CT was more sensitive in detecting small lung or peritoneal metastases (9). As a consequence, no formal recommendation on incorporating this technique in the surveillance protocol of ACC patients following complete tumor removal has been provided. However, some expert centers add FDG PET/CT at six-month intervals in the follow-up strategy (16).

In the present study, we have assessed retrospectively our experience at the San Luigi Hospital where FDG PET/CT has been used as a second-line test in patients with a potential ACC recurrence found by CT during post-surgical follow-up. Therefore, we did not make a formal comparison of FDG PET/CT vs. CT to categorize patients as with or without ACC recurrence, but we assessed whether addition of FDG PET/CT in selected cases may refine diagnosis of ACC recurrence and inform the management strategy. To this aim, we have compared the results of either FDG PET/CT or CT with a gold standard confirmation of recurrence (positive histopathology report of removed/biopsied lesions or radiological progression of target lesions at follow-up) to assess the diagnostic performance of both techniques at different body sites to correctly categorize presumed ACC recurrences.

Sensitivity of CT was overall greater than that of FDG PET/CT, and this may be partly expected due the specific inclusion criteria of the study requiring positivity of the CT scan (detection of new lesion(s) during follow-up). Sensitivity of CT was significantly greater than that of FDG PET/CT in the lungs and liver. **The low sensitivity of FDG-PET for lung metastases is already known due to the limited FDG-PET/CT resolution of lung nodules less than 5 mm (9). In our series, many lung metastases were small and frequently located in the inferior lobes, close to the lung bases, where nodules are less detectable due to respiratory movements, compared to nodules in the upper parts of the lung (19).**

Specificity of FDG PET/CT was overall greater than that of CT, and the difference was at the limits of statistical significance in the liver. Moreover, FDG PET/CT had a greater LR+ than CT to identify liver and abdominal ACC recurrences. Thus, FDG PET/CT was of particular value in ruling out suspected ACC recurrences found by CT. FDG PET/CT findings informed patient management in 12 cases (21.1%) and the chosen strategy proved to be correct in all but one. In additional 4 patients with discordant findings between the two techniques, all sites of pathological uptake by FDG PET/CT without a correspondent anatomical lesion at CT were finally demonstrated to be true

ACC recurrences. Results of FDG PET/CT were not considered to guide management in such patients, but the choice proved to be a mistake.

Strengths of the study are the rather large series considering the rarity of ACC, the central review of radiological material with FDG PET/CT scans done in a single center and the completeness of follow-up with unequivocal demonstration of recurrence, while we have to disclose the limit of a retrospective analysis **and lack of standardization of the time interval elapsed between index CT and FDG PET/CT scan. There are no formal recommendations on the optimal time interval between the two imaging procedures, and in previous work a time interval within 3 months was considered as acceptable (20). However, we should strive to achieve PET within one month from CT due to the possibility of fast disease progression. This seems a plausible compromise between the need of the shortest delay possible and the need to face practical problems (i.e. PET availability, travel arrangement for patients living far from the referral center).**

Although retrospective assessment of a decision making process may be partly flawed, the study findings are of clinical relevance showing that the use of FDG PET/CT to confirm anatomical lesions suspected to be ACC recurrences may allow a better selection of patients to surgery. Due to the limited efficacy of available medical treatments, surgical treatment of ACC recurrences still represents the best option to prolong patient survival whenever surgery can be done with radical intent, and proven that recurrence-free survival from primary surgery be of at least one year (21). FDG PET/CT was useful in differentiating liver nodular hyperplasia and post-surgery abdominal inflammatory reactions from ACC recurrence. As a matter of fact, FDG PET/CT pathological uptake of a liver or abdominal lesion increases by 38 or 52 times, respectively, the probability of a target lesion of being a true ACC recurrence.

To conclude, we have showed that use of FDG PET/CT as a second-line test in the post-operative surveillance of ACC patients following CT finding of a potential recurrence may have a significant impact on patient management, in particular for an appropriate selection of patients to surgery. **Therefore, we suggest that FDG PET/CT becomes part of the post-operative work-up protocol of ACC patients following a CT scan that has identified morphological lesions compatible with ACC recurrences. Despite** limited availability of the technique and cost issues, this strategy seems particularly appealing also with the aim of reducing the psychological burden of repeated testing in such patients. It remains to be demonstrated whether the routine use of FDG PET/CT in addition to cross-sectional imaging in the post-operative follow-up of ACC patients may improve detection and, more importantly, treatment of recurrent disease.

DECLARATION OF INTEREST

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AUTHOR CONTRIBUTION

A. Ardito, E. Pelosi, M. Terzolo; study concept and design.

A. Ardito, B. Zaggia, M. Terzolo; patient management.

E. Pelosi, V. Arena, D. Penna; FDG-PET scan and analysis, analysis of CT scans.

E. Duregon, pathological analysis.

A. Ardito, C. Massaglia, V. Basile; data collection and capture.

P. Perotti; database management, submission to EC.

R. Brambilla, F. Vigna-Taglianti; statistical analysis.

C. Massaglia; manuscript drafting

All, critical input in the manuscript

M. Terzolo; final manuscript review.

REFERENCES

1. Rohren EM, Turkington TG, Coleman RE. Clinical applications of PET in oncology. *Journal of Radiology..* 2004 **231** 305–332. (doi: 10.1148/radiol.2312021185)

2. Elaini AB, Shetty SK, Chapman VM, Sahani DV, Boland GW, Sweeney AT, Maher MM, Slattery JT, Mueller PR, Blake MA. Improved detection and characterization of adrenal disease with PET-CT. *RadioGraphics.* 2007 **27** 755–67. (doi: 10.1148/rg.273055031)

3. Chong S Chong S, Lee KS, Kim AH. Integrated PET-CT for the characterization of adrenal gland lesions in cancer patients: diagnostic efficacy and interpretation pitfalls. *RadioGraphics*. 2006 **26** 1811–26. (doi: 10.1148/rg.266065057)

4. Blake MA, Slattery JM, Kalra MK, Halpern EF, Fischman AJ, Mueller PR, Boland GW. Adrenal lesions: characterization with fused PET/CT im- age in patients with proved or suspected malignancy—initial experience. *Radiology.* 2006 **238** 970–7. (doi: 10.1148/radiol.2383042164)

5. Boland GW, Blake MA, Holalkere NS, Hahn PF. PET/CT for characterization of adrenal masses in patients with cancer: qualitative versus quantitative accuracy in 150 consecutive patients. *American Journal of Roentgenology*. 2009 **192** 956-62. (doi: 10.2214/AJR.08.1431)

6. Dong A, Cui Y, Wang Y, Zuo C, Bai Y. (18)F-FDG PET/CT of adrenal lesions. *American Journal of Roentgenology.* 2014 **203** 245-252. (doi: 10.2214/AJR.13.11793).

7. Song JH, Mayo-Smith WW. Current status of imaging for adrenal gland tumors. *Surgical Oncology Clinics of North America.* 2014 **23** 847-861. (doi: 10.1016/j.soc.2014.06.002).

8. Nakajo M, Nakajo M, Fukukura Y, Jinguji M, Shindo T, Nakabeppu Y, Kamimura K, Yoneyama T, Takumi K, Yoshiura T. Diagnostic performances of FDG-PET/CT and diffusion-weighted imaging indices for differentiating benign pheochromocytoma from other benign adrenal tumors. *Abdominal Imaging.* 2014 Nov 11 (doi: 10.1007/s00261-014-0291-x).

9. Deandreis D, Leboulleux S, Caramella C, Schlumberger M, Baudin E. FDG PET in the management of patients with adrenal masses and adrenocortical carcinoma. *Hormones & Cancer*. 2011 **2** 354-62. (doi: 10.1007/s12672-011-0091-5) .

10. Mackie GC, Shulkin BL, Ribeiro RC, Worden FP, Gauger PG, Mody RJ, Connolly LP, Kunter G, Rodriguez-Galindo C, Wallis JW, Hurwitz CA, Schteingart DE. Use of [18F]fluorodeoxyglucose positron emission tomography in evaluating locally recurrent and metastatic adrenocortical carcinoma. *The Journal of Clinical Endocrinology & Metabolism*. 2006 **91** 2665-2671. (doi: 10.1210/jc.2005-2612).

11. Leboulleux S, Dromain C, Bonniaud G, Aupérin A, Caillou B, Lumbroso J, Sigal R, Baudin E, Schlumberger M. Diagnostic and prognostic value of 18-fluorodeoxyglucose positron emission tomography in adrenocortical carcinoma: a prospective comparison with computed tomography. J *The Journal of Clinical Endocrinology & Metabolism*. 2006 **91** 920-925. (doi: 10.1210/jc.2005-1540).

12. Fassnacht M, Libé R, Kroiss M & Allolio B. Adrenocortical carcinoma: a clinician's update. *Nature Reviews. Endocrinology* 2011 **7** 323-335. (doi: 10.1038/nrendo.2010.235).

13. Terzolo M, Zaggia B, Allasino B & De Francia S. Practical treatment using mitotane for adrenocortical carcinoma. *Current Opinion in Endocrinology, Diabetes, And Obesity* 2014 **21** 159-65. (doi: 10.1097/MED.0000000000000056).

14. Schteingart DE, Doherty GM, Gauger PG, Giordano TJ, Hammer GD, Korobkin M & Worden FP. Management of patients with adrenal cancer: recommendations of an International Consensus Conference. *Endocrine-Related Cancer* 2005 **12** 667–680. (doi:10.1677/erc.1.01029).

15. Berruti A, Baudin E, Gelderblom H, Haak HR, Porpiglia F, Fassnacht M, Pentheroudakis G & ESMO Guidelines Working Group. Adrenal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 2012 **23** (Supplement 7): vii131–vii138. (doi:10.1093/annonc/mds231).

16. Zini L, Porpiglia F, Fassnacht M. Contemporary management of adrenocortical carcinoma. *European Urology*. 2011 **60** 1055. (doi: 10.1016/j.eururo.2011.07.062).

17. Fassnacht M, Johanssen S, Quinkler M, Bucsky P, Willenberg HS, Beuschlein F, Terzolo M, Mueller H-H, Hahner S, Allolio B, for the German Adrenocortical Carcinoma Registry Group and the European Network for the Study of Adrenal Tumors. Limited prognostic value of the 2004 International Union Against Cancer staging classification for adrenocortical carcinoma: proposal for a revised TNM classification. *Cancer.* 2009 **115** 243–250. (doi:10.1002/cncr.24030).

18. Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, Verzijlbergen FJ, Barrington SF, Pike LC, Weber WA, Stroobants S, Delbeke D, Donohoe KJ, Holbrook S, Graham MM, Testanera G, Hoekstra OS, Zijlstra J, Visser E, Hoekstra CJ, Pruim J, Willemsen A, Arends B, Kotzerke J, Bockisch A, Beyer T, Chiti A, Krause BJ. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imaging*. 2015 **42** 328–354. (DOI 10.1007/s00259-014-2961).

19. Kim SK, Allen-Auerbach M, Goldin J, Fueger BJ, Dahlbom M, Brown M, Czernin J, Schiepers C. Accuracy of PET/CT in characterization of solitary pulmonary lesions. *J Nucl Med.* 2007 **48** 214–220.

20. Pelosi E, Messa C, Sironi S, Picchio M, Landoni C, Bettinardi V. Value of integrated PET/CT for lesion localization in cancer patients: a comparative study. *Eur J Nucl Med Mol Imaging*. 2004 **7** 932-9.

21. Erdogan I, Deutschbein T, Jurowich C, Kroiss M, Ronchi C, Quinkler M, Waldmann J, Willenberg HS, Beuschlein F, Fottner C, Klose S, Heidemeier A, Brix D, Fenske W, Hahner S, Reibetanz J, Allolio B, Fassnacht M, on behalf of the German Adrenocortical Carcinoma Study Group. The role of surgery in the management of recurrent adrenocortical carcinoma. *Journal of Clinical Endocrinology and Metabolism*. 2013 **98** 181-191. (doi: 10.1210/jc.2012-2559).

LEGENDS

Figure 1. Discordant results between CT and FDG-PET/CT scans: patients with a greater number of target lesions in CT than in FDG-PET/CT scans are identified as CT > PET/CT; patients with a greater number of target lesions in FDG-PET/CT than CT scans are identified as PET/CT > CT; patients with CT and FDG-PET/CT scans showing target lesions in different districts are identified as CT ≠ PET/CT. Analysis is done per site of lesion.