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Title	Clinical Value and Limitations of [¹¹ C]-Methionine PET for Detection and Localization of Suspected Parathyroid Adenomas
Author(s)	Herrmann, Ken; Takei, Toshiki; Kanegae, Kakuko et al.
Citation	Molecular Imaging and Biology, 11(5), 356-363 https://doi.org/10.1007/s11307-009-0205-4
Issue Date	2009-09
Doc URL	https://hdl.handle.net/2115/43808
Rights	The original publication is available at www.springerlink.com
Type	journal article
File Information	MIB11-5_356-363.pdf



Clinical Value and Limitations of [¹¹C]-Methionine PET for Detection and Localization of suspected parathyroid adenomas

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Running title: Imaging HPT with ¹¹C-MET-PET.

Word count: 4142.

Abstract: 259.

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Abstract

Purpose:

The aim of this study was to assess the clinical value of [¹¹C]methionine-PET (MET-PET) for detection and localization of parathyroid adenomas in patients without prior thyroidectomy.

Methods:

A retrospective analysis of patients with suspected hyperparathyroidism undergoing imaging with MET-PET was performed. Prior thyroidectomy was an exclusion criterion. 41 patients with a total of 49 MET-PET scans were included. MET-PET consisted of whole-body images obtained 15 - 20 min after injection of 430 ± 81 MBq of MET using a dedicated PET scanner. Imaging findings were validated by histology or other imaging studies and clinical follow-up on a lesion, side and location basis. Comparison of PET results to other imaging modalities including ultrasound, MIBI scintigraphy and morphological imaging (CT and/or MRI) and subgroup analysis of primary vs. secondary hyperparathyroidism was performed.

Results:

23/49 PET scans revealed pathologic findings, whereas 26/49 scans were negative. Validation of PET findings for detection and localization of hyperthyroidism resulted in an overall sensitivity of MET-PET of 54%, 49% and 35% on a lesion, side and location basis, respectively. Sensitivity of MET-PET was inferior compared to ultrasonography (50% vs. 93%), MIBI scintigraphy (53% vs. 74%) and morphological imaging (52% vs. 74%). Subgroup analysis revealed higher sensitivity for MET-PET in sHPT than pHPT (62% vs. 43%; side basis).

Conclusions:

In patients with initial diagnosis of hyperparathyroidism and no prior thyroidectomy, the sensitivity of MET-PET for detection and localization of hyperparathyroidism is markedly

lower compared to previous reports. While performance was better in sHPT, MET-PET can not be recommended for pHPT localization in this clinically relevant subcollective.

Key words: MET-PET; MIBI scintigraphy; ultrasound; hyperparathyroidism; diagnosis;

Introduction

Hyperparathyroidism (HPT) is a common endocrine disorder affecting approximately one in 500 women and one in 2000 men, commonly diagnosed in the fifth through seventh decade of life [1]. HPT is characterized by an increased secretion of parathyroid hormone (PTH) leading to hypercalcemia by promoting the renal tubular absorption of calcium, decreasing tubular reabsorption of phosphate, stimulating osteoclasts and vitamin D production. Current treatment approaches comprise surgery and percutaneous ethanol injection. Both therapeutic procedures are demanding for pretherapeutical imaging methods to detect and locate abnormal parathyroid gland tissue accurately. Especially the recently developed minimally invasive surgical techniques require reliable preoperative disease localization [2,3]. Commonly used imaging techniques comprise sonography, scintigraphy, CT and MRI. Especially the first two methods have been emerged as dominant for HPT detection and localization of parathyroid adenomas [1]. Positron emission tomography (PET) with the radiopharmaceutical ^{11}C -methionine has been considered to improve diagnosis due to a superior spatial resolution and higher specificity compared to other radiotracers [4,5]. ^{11}C -methionine is considered to be very specific since synthesis of the PTH precursor hormone prepro-PTH comprises seven methionine and stimulates amino acid influx into parathyroid tissue. Recently published studies reported promising results by revealing true-positive localization in up to 85% of patients [5-7]. Further studies recommended to restrict the application of [^{11}C]methionine-PET (MET-PET) to patients in which scintigraphy or ultrasound failed to localize the parathyroid adenoma [4,8]. For parathyroid scintigraphy, initially published sensitivities and specificities were not always reproducible in clinical routine [9]. We therefore aimed to evaluate the clinical value of MET-PET for detection and localization of HPT in patients referred to our institution for further diagnostic work-up. We analyzed retrospectively all patients undergoing MET-PET with suspected HPT without prior

thyroidectomy and correlated the findings to histology, results of other imaging modalities and to clinical follow-up.

Materials and Methods

Patient Population

From September 2002 to September 2006, we retrospectively identified [¹¹C]methionine PET studies performed on patients with suspected HPT referred for further diagnostic work-up. During that time, a total of 41 patients underwent 49 PET scans for pre- or posttherapeutic staging and localization of abnormal parathyroid tissue. All evaluated patients did not undergo previous thyroidectomy. The majority of patients referred to our institution were sent by regional hospitals for further diagnostic workup after initial diagnostic methods failed in HPT detection.

In our study individuals were only eligible if imaging findings could be correlated with histology, other imaging modalities and/or clinical follow-up. Serial follow-up scans were included when the prior study was negative or when the prior study was positive but the patient had undergone surgical resection of disease sites in the interim or when there was an increase in PTH level by at least 20%. Each serial scan thus reflects a snapshot of a patient in time that is different from the previous scan and can stand on its own as a diagnostic test [10,11]. Concurrent available ultrasound, MIBI scintigraphy, CT and MRI reports within 2 months of the time of the [¹¹C]methionine PET study were also retrieved and catalogued. Patient consent was not required for this retrospective study. During retrospective analysis, a total of 66 scans had been retrieved from the database of which 14 scans were omitted because of missing corresponding clinical information and additional 3 scans because of prior thyroidectomy (exclusion criteria).

[¹¹C]Methionine PET Imaging

Patients were asked to fast three hours prior to MET injection. A whole-body MET-PET image was obtained from 15 min to 20 min after the injection of 430.7 ± 80.9 MBq (mean \pm

SD, range 272–603 MBq) of [^{11}C]MET. Whole-body PET acquisitions were carried out from the skull base to the pelvis with a 2-min emission scan and a 3-min transmission scan per bed position, using a full-ring PET scanner (Siemens ECAT EXACT 47) in 3D mode. Acquisition matrix was 128 x 128. Non-attenuation correction images were reconstructed with the filtered back projection method. Attenuation correction was performed using rotating ^{68}Ge – ^{68}Ga rod sources. The scans were reconstructed with the ordered subsets expectation maximization algorithm.

Ultrasound acquisition

Ultrasound studies were performed by specially trained technicians specialized in ultrasonography of endocrine organs. The ultrasound device employed was a Aloka Pro Sound SSD 5500 (Aloka, Tokyo, Japan) focus with 7.5 or 10MHz transducers. A routine real-time sonography combined with color-Doppler imaging was acquired to evaluate vascularity of the lesion and to aid differentiating lymph node from parathyroid lesions. Transverse and longitudinal views were recorded.

[$^{99\text{m}}\text{Tc}$]Sestamibi scintigraphy

Dual time point scans were performed 20 and 120 minutes after intravenous injection of 600 MBq [$^{99\text{m}}\text{Tc}$]Sestamibi (Cardiolite®; Lantheus Medical Imaging Inc., N. Billerica, MA, USA) on dual-head gamma camera systems (ECAM; Siemens Medicals Systems, Erlangen, Germany; or Millennium VG; GE Medical Systems, Milwaukee, USA). For parathyroid imaging low-energy, high-resolution parallel hole collimators were used. Additionally, first and second image were acquired from neck to mediastinum, and followed by SPECT acquisition. SPECT data was collected with a 128 x 128 matrix from 64 views (32 view

angles x 2 camera heads; 30 seconds each). Images were reconstructed with FBP without attenuation correction.

Image Analysis

All PET scans were evaluated by two experienced nuclear medicine physicians (K.H. and T. T.) blinded to the clinical data and the results of other imaging studies. PET images were interpreted in a binary fashion as either normal/probably normal or abnormal/probably abnormal. In cases of disagreement between the two readers, the images were reviewed together and a consensus was reached. In all cases, attenuation-corrected images were reviewed on a workstation displaying 3 orthogonal planes (transaxial, coronal, and sagittal) and a maximum intensity-projection image. If rated as abnormal/probably abnormal MET uptake was evaluated using the maximum standardized uptake value (SUV_{max}), as reported earlier [12,13]. For all other imaging studies, the official clinical reports from US, MIBI scintigraphy, CT and MRI studies, generated by staff physicians at this institution, were used. Only imaging studies obtained within 2 months before or after MET-PET were considered.

Reference methods for validation of imaging findings

For validation of the PET findings following standard of reference was used: Imaging findings were considered true positive for local disease if they were confirmed by any one of the following: (a) positive histology, (b) concurrent other imaging studies within 2 months of PET and decrease in PTH after ethanol injection therapy, (c) concurrent other imaging studies within 2 months of PET, elevated PTH- and calcium levels, or (d) concurrent other imaging studies or elevated PTH- and calcium levels. Imaging findings were classified as true negative if concurrent other imaging studies were negative and/or PTH- and calcium levels were normal. All imaging studies without clear abnormality in patients with elevated PTH- and

calcium levels were classified as false negative. Sensitivity, specificity and accuracy were determined on this basis.

Statistical analysis

Statistical analyses were performed using SPSS software (version 15.0; SPSS, Inc. Chicago, IL). Quantitative values were expressed as mean \pm standard deviation or median and range if appropriate. Comparisons of related metric measurements were performed using Wilcoxon-signed rank test and Mann-Whitney-U test in case of two independent samples. Fisher's exact tests were used for comparison of frequencies. Exact 95 percent confidence limits (CL) were reported for estimates of sensitivity, specificity and accuracy. All analyses were performed two-sided at a 5 % level of significance. Interobserver agreement was assessed by calculating kappa coefficients. While a kappa coefficient about 0.0 represents agreement at a chance level, kappa values in the range of 0.41–0.60 indicate moderate agreement, 0.61–0.80 indicate substantial agreement, and 0.81–1.00 indicate excellent agreement [14].

RESULTS

Patient information

41 patients (12 men, 29 woman, mean age: 57 ± 13 years, range: 26 – 81 years) referred for suspected hyperparathyroidism underwent a total of 49 scans for pre- or posttherapeutic staging, localization of abnormal parathyroid tissue and monitoring treatment response (Table 1). Staging and restaging procedures included ultrasound performed at our institution (n=46), MIBI scintigraphy (n=21) and morphologic imaging (n=33) comprising magnetic resonance imaging (MRI) and/or computed tomography (CT) of the neck and thorax if appropriate and employed for validation if performed within two months of MET-PET. In 36 cases primary HPT and in the remaining 13 cases secondary HPT was suspected. PET findings were validated by histology in 10 cases, by concurrent other imaging studies within 2 months of PET and decrease in PTH after ethanol injection therapy (CI and post Tx) in 21 cases, by concurrent other imaging studies within 2 months of PET and conclusive PTH- and calcium levels (CI and lab) in 15 cases, and by concurrent other imaging findings or conclusive PTH- and calcium levels (CI or lab) in 3 cases.

[¹¹C]methionine-PET findings

Consensus reading resulted in 26/49 negative and in 23/49 positive PET scans detecting a total of 29 lesions. In 4 cases two lesions were described, and in 1 case even three lesions. Mean SUVmax of the lesions with the maximum uptake in the 23 cases was 2.56 ± 0.75 (range: 1.51-4.61). Analysis of PET accuracy was performed on case basis (positive PET), on side basis (prediction of lesion to the correct side) and on location basis (prediction of lesion to the right localization).

Lesion Basis

All 23 positive scans were deemed true positive of which 5 were validated by histology (Figure 1). 12 positive studies were validated by CI and post Tx, 6 positive cases by CI and lab (Table 2). 6 of the 26 negative PET studies were rated as true negative, validated by CI and lab (n=3) and by CI or lab (n=3; concurrent other imaging finding only in 1 case and conclusive PTH- and calcium levels in 2 cases). The remaining 20 negative studies were rated as false negative (Figure 2). Present HPT was confirmed by histology in 5 cases, by CI and post Tx in 9 cases, and by CI and lab in 6 cases. This resulted in a sensitivity of 54% (23/43; 95% confidence limits (CL): 38% to 69%), specificity of 100% (6/6; 95%CL: 54% to 100%) and an accuracy of 59% (29/49; 95% CL: 44% to 73%). Corresponding positive and negative predictive value were 100% (23/23; 95%CL: 85 to 100%) and 23% (6/26, 95%CL: 9% to 44%), respectively.

Side Basis

If only prediction of the disease to the correct side was considered as true positive, then 21/23 positive scans were deemed true positive. Of those 21 cases, 4 were validated by histology, 12 by CI and post Tx and 5 by CI and lab (Table 2). In two cases, PET detected lesions only on one side whereas histology (n=1) and CI and lab (n=1) revealed lesions affecting both sides of the neck (scans no. 22 and 32). Therefore these scans were rated as false negative. The 26 negative PET studies have been validated as true negative (n=6) and false negative (n=20) as listed more detailed in the precedent section. Corresponding sensitivity was 49% (21/43; 95%CL: 33% to 65%), specificity 100% (6/6; 95%CL: 54% to 100%) and accuracy of 55% (27/49; 95%CL: 40% to 70%). Positive and negative predictive values for PET on a side basis were 100% (21/21; 95%CL: 54% to 100%) and 21% (6/28; 95%CL: 8% to 41%), respectively.

Location Basis

On location basis, a PET scan fulfilled the criteria of true positive only if the exact localization had been predicted. Applying these criteria, 15 scans of the 23 PET positive scans were rated as true positive. Of the remaining 8 positive PET scans, PET detected fewer lesions than confirmed by validation in 5 cases (rated as false negative) and in 1 case one lesion more was found (scan no. 41) than actually verified (rated as false positive). In 2 cases, disease was located at the opposite pole than indicated by PET (rated as false negative) (Table 2). The remaining PET studies were validated as listed previously. Corresponding sensitivity, specificity and accuracy were 35% (15/43; 95%CL: 21% to 51%), 100% (6/6; 95%CL: 54% to 100%) and accuracy of 43% (21/49; 95%CL: 29% to 58%), respectively.

Findings of other imaging modalities

Ultrasound

In a subgroup of 46 cases ultrasound reports were available. According to the validation criteria hyperparathyroidism was confirmed in 42 cases, whereas 4 cases were rated as disease free. On a lesion basis, ultrasound reports were positive in 40 cases with hyperparathyroidism present and negative in all four cases without disease. Corresponding sensitivity and specificity were 95% and 100%, respectively. MET-PET in this subgroup revealed a sensitivity of 55% (23/42) and a specificity of 100% (4/4). Ultrasound also revealed higher sensitivities on a side basis (93% vs. 50%) and a location basis (88% vs. 36%) than MET-PET. For both methods, all patients without hyperparathyroidism present revealed no suspicious findings.

MIBI

In 21 of the included cases, a MIBI scan had been performed. On a lesion basis, MIBI scan was rated positive in 15/19 cases with clinical evidence of hyperparathyroidism (sensitivity 79%). Two cases without hyperparathyroidism had no findings in the MIBI scans, resulting in a specificity of 100%. Corresponding values for MET-PET in this subgroup were a sensitivity of 58% (11/18) and a specificity of 100% (2/2), respectively. Sensitivity of MIBI was also superior to MET-PET if validation was performed on side basis (74% vs. 53%) or location basis (68% vs. 42%).

Morphologic imaging

Morphologic imaging (MI; comprising CT and/or MRI) studies were performed in a subgroup of 33 cases. In 24/31 cases with hyperparathyroidism MI scans were rated true positive on a lesion basis, resulting in a sensitivity of 77%. Both cases without disease present revealed no suspicious findings on the MI scan (specificity: 100%). Corresponding values for MET-PET in this subgroup were 58% and 100% for sensitivity and specificity, respectively. If true positive scans were limited to disease detection for the correct side and correct localization, slightly lower sensitivities were found for MI. Again, sensitivity for MET-PET was inferior to the MI results.

Subgroup analysis pHPT vs. sHPT

In 36/49 cases primary hyperparathyroidism (pHPT) was present or suspected, whereas secondary hyperparathyroidism (sHPT) was reason for referral in 13/49 cases. Subgroup analysis revealed the following results:

pHPT

In 30 cases with clinical evidence of pHPT, 13 MET-PET scans were deemed true positive and in 17 cases PET was rated as false negative if evaluation was done on a lesion basis. Six negative scans were validated as true negative. Thus, on lesion basis, these results lead to a sensitivity of 43%, and a specificity of 100%. If validation of PET findings is performed on a side basis, sensitivity remains to be 43%, whereas it decreases to 33% for location basis.

sHPT

MET-PET was performed in 13 cases with sHPT. All 10 positive PET scans were rated true positive on a lesion basis, resulting in a sensitivity of 77% (Figure 3). Prediction of the lesion to the correct side was obtained in 8/13 cases, whereas prediction of the accurate localization was achieved in only 5/13 cases. Corresponding sensitivities were 62% for side and 39% for location basis.

Histological subgroup analysis

In 10 cases a total of 14 adenomas (1 patient with 5 adenomas) were histologically verified. Mean adenoma weight was 747 mg (median: 432 mg, range: 80 – 2760 mg). In five cases, MET-PET revealed suspicious focal uptake rated as true positive. Corresponding mean adenoma weight was 1265 mg (range: 213 – 2760 mg). However, in one case only one lesion was described but histology revealed a total of five lesions (range: 80 – 1540 mg). Therefore, this case was rated false negative on a side and location basis. In the MET-PET negative subgroup, mean adenoma weight was 363 mg (range: 214 – 554 mg). Comparison of adenoma weight for MET-PET positive vs. negative lesions resulted in a tendency towards MET-PET missing especially smaller adenomas ($p=0.058$).

Agreement of PET readers

PET scans were read by two independent readers in a binary fashion. For evaluation of interobserver reliability the kappa coefficient was assessed. Validation of imaging studies resulted in concordant findings in 80% of the scans. The calculated kappa coefficient was 0.592, indicating a moderate correlation of individual findings of both readers.

DISCUSSION

In patients with no prior thyroidectomy, the overall sensitivity of MET-PET was 54% for detection of primary or secondary hyperparathyroidism. Sensitivity decreased to 49% for prediction of disease to the correct side and to 35% for prediction of the lesion to the correct location. MET-PET revealed clearly lower sensitivity values compared to other imaging methods compared to ultrasound, MIBI scintigraphy, CT and/or MRI. However, higher sensitivities were found in patients with secondary compared to primary hyperparathyroidism. Prediction of disease to the correct side by MET-PET was 62%, and increased to 77% for evaluation on a lesion basis. Additionally, MET-PET was true negative in six cases without clinical evidence of parathyroid adenoma leading to a specificity of 100%. In comparison to the literature, we found clearly inferior values regarding sensitivity and specificity for detection of hyperparathyroidism. Earlier published studies reported sensitivities up to 87% for localizing parathyroid adenoma [5,7]. A more recent study by Beggs et al. including 51 patients with suspected pHPT confirmed these values by claiming a sensitivity of 83% and a specificity of 100% for the localization of primary hyperparathyroidism [6]. Notably, all patients included into this study had negative or equivocal MIBI studies. Interestingly, Beggs et al. reported nine patients with secondary HPT revealing all false negative MET-PET scans. Otto et al. attributed MET-PET an important role in highly pre-selected patients describing a sensitivity of 94% for hyperparathyroidism related to adenomas and carcinomas, and a sensitivity of 69% for detection of secondary and tertiary hyperparathyroidism. All mentioned studies included a considerable fraction of patients (11/30 patients in the study by Otto et al. had prior surgery, in the study by Beggs et al. 29/51 patients were referred for recurrent/persistent hyperparathyroidism) with disease recurrence and prior thyroidectomy [4,6].

Regarding our study population it is important to mention, that Hokkaido University Hospital is a tertiary medical center providing health care for the whole Hokkaido prefecture accounting for 5.5 million people. Patients referred to our institution have mostly gone through an extensive diagnostic work-up in peripheral institutions and therefore our patient population involves a rather complicated patient spectrum. Retrospective analysis of our database of patients referred for suspected parathyroid adenoma revealed that a broad majority of the patients had no prior thyroidectomy (only three patients with prior surgery). For reassuring a homogenous cohort we decided to focus on patients without prior thyroidectomy in contrast to previously published studies. For some part this inclusion criteria might explain the lower sensitivity we found, since it is well known that remaining thyroid tissue reduces the lesion-to-background ratios due to physiological uptake and complicates the reading of parathyroidal MET-PET scans. Another contributing factor to the lower sensitivity for MET-PET may be the PET analysis by the readers blinded to the clinical data and the results of other imaging studies. Since PET results were compared to the official clinical reports of the other imaging studies (US, MIBI scintigraphy, CT and/or MRI) generated in notice of clinical history, this might have resulted in somewhat overestimated sensitivities of the non-PET methods. Furthermore, not every patient underwent all imaging studies and this allows the comparison of performance of the different modalities only the appropriate subgroups as listed in the result section. In the subgroup of patients with histological clarification of parathyroid adenomas (all patients with positive histology) we observed that MET-PET was more likely to miss adenomas with lower weight and therefore smaller size, possibly enabling scanners with a higher spatial resolution to overcome this shortcoming.

The surprisingly high sensitivities for ultrasound could be explained by two factors. Firstly, due to clinical workflow ultrasound stands first in the diagnostic work-up. Patients

without any suspicious findings at ultrasound examination did mostly not proceed to MET-PET. Secondly, ultrasound is performed by very well trained and long time experienced staff members employing also color-Doppler sonography. For this technique, sensitivities of up to 86% for localization of the adenomas to the correct side of the neck have been published [15,16]. Even if due to the mentioned factors ultrasound's sensitivity might be overestimated, ultrasound examination proved to localize hyperparathyroidism with high accuracy - an observation, which agrees with a recently published study by Hessman et al. achieved in a howsoever different clinical setting investigating localization diagnosis prior to parathyroid reoperation [8]. Another contributing factor is a well-known trend that larger studies evaluating imaging methods in a clinical routine setting cannot reproduce initially reported sensitivity values of pilot studies. A similar observation has been recently published by Gotthardt et al. describing clear discrepancies in the sensitivity of parathyroid MIBI scintigraphy results [9].

For the future, introduction of combined PET/CT devices allow the merging of complementary morphological information from CT with the functional information of PET. Thus, leading to an exact anatomic localization of the PET finding and probably contributing to a higher sensitivity and specificity for detection of hyperparathyroidism [17]. A further favorable influence can be expected by the use of high resolution scanners, facilitating especially detection of small lesions due to higher spatial resolution [18].

Several limitations have to be taken into account before generalizing our results. Firstly, we investigated a highly pre-selected patient population without prior thyroidectomy, mainly being referred due to initially negative or equivocal findings. Secondly, MET-PET was mainly performed if ultrasound revealed abnormal or equivocal findings. Thirdly, only a small subgroup of patients underwent surgery enabling us to validate imaging findings by histology. Fourthly, this analysis was retrospectively performed with patients undergoing

MET-PET scans on a dedicated PET only device. Use of more up-to-date equipment such as high-definition PET/CT allows an accurate anatomic localization and higher spatial resolution and therefore may return better sensitivity and specificity values, however, this has not been investigated so far. Fifthly, a short acquisition of 2 minutes per bed position was used as previously reported by Kanegae et al.[19], but a longer acquisition time might contribute to a better accuracy. Nevertheless, we believe that our results as well as the comparably low interobserver agreement reflect reliably the performance of MET-PET in daily clinical routine in a subgroup of patients with suspicion on pHPT or sHPT. Especially in the subgroup of patients with sHPT, MET-PET detected side of disease with an acceptable accuracy and may add valuable information for detection and localization. Moreover, we think that these results may serve as a note of caution even though that they may be less relevant in the era of PET/CT. The true value of MET-PET and MET-PET/CT can only be determined in a prospective study with histologic verification in all subjects.

CONCLUSION

In conclusion, sensitivity of MET-PET for detection and localization of parathyroid adenomas is inferior compared to previously published studies. However, we believe that this study reflects reliably the clinical value of MET-PET in patients with initial diagnosis of hyperparathyroidism without prior thyroidectomy. While performance was better in sHPT, MET-PET can not be recommended for pHPT localization in this clinically relevant subcollective.

Acknowledgments

We appreciate the excellent contributions made by the technical staff members of the Department of Nuclear Medicine, Hokkaido University, Sapporo, Japan.

Table and Figure legends

Table 1: Patient and lesion characteristics (Sex, Age, Activity, primary hyperparathyroidism “1” vs. secondary hyperparathyroidism “2”), PET findings (positive PET “1” vs. negative PET “0”), number of lesions, MET uptake as SUV max if focal lesion was detectable, validation of PET findings on a lesion, side and location basis (true positive or true negative as “1”, false positive or false negative as “0”, and if not performed “2”), presence of disease (hyperparathyroidism present “1”, no disease “2”), and validation of PET findings (histology “1”, concurrent other imaging studies within 2 months of PET and decrease in PTH after ethanol injection therapy “2” (CI and post Tx), concurrent other imaging studies within 2 months of PET and conclusive PTH- and calcium levels “3” (CI and lab) and concurrent other imaging findings or conclusive PTH- and calcium levels “4” (CI or lab)).

Table 2: Validation of PET findings on a lesion basis, side basis and on a location basis). TP: true positive, TN: true negative, FP: false positive, FN: false negative. “CI and post Tx”, “CI and lab” and “CI or lab” used as declared in Table 1.

Figure 1: A: Transaxial views of CT, B: MET-PET and C: MIBI scintigraphy of a patient with a parathyroid adenoma at the right lower pole due to primary hyperparathyroidism. Arrows indicate the positive findings for each modality.

Figure 2: A: Transaxial views of CT, B: MET-PET and C: MIBI scintigraphy of a patient with a parathyroid adenoma at the left lower pole due to primary hyperparathyroidism. Arrows indicate the suspicious findings in CT scan

(A) and MIBI scintigraphy (C), validated as true positive findings. In contrast, no suspicious uptake in the MET-PET scan (B), validated as false negative.

Figure 3: A: Sagittal, B: transaxial and C: coronal views of MET-PET of a patient with a parathyroid adenoma at the left lower, left upper and right upper pole due to secondary hyperparathyroidism. Arrows indicate the suspicious finding in MET-PET, which were validated as true positive findings.

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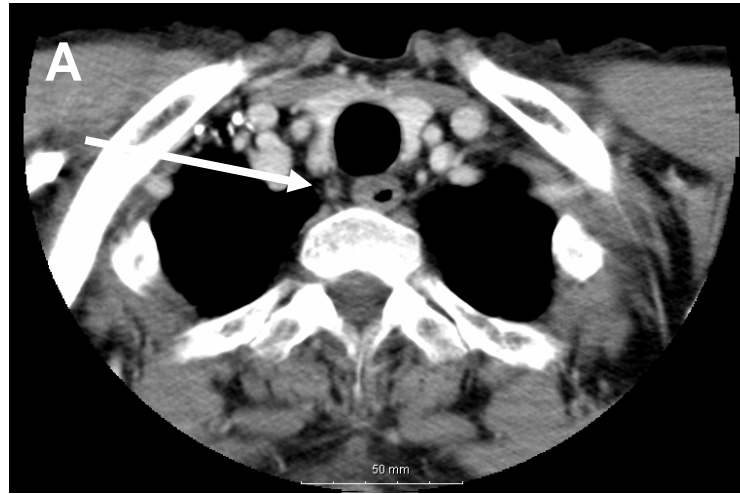
Table 1:

Pat. No.	Scan No.	Sex	Age	HPT(p/s)	PET positive?	no lesions	SUVmax	Lesion	Side	Location	Disease	Validation
1	1	2	62	s	1	1	2.99	1	1	0	1	2
1	2	2	63	s	1	1	1.81	1	1	1	1	2
1	3	2	64	s	1	1	1.51	1	1	1	1	2
2	4	2	78	p	1	1	1.86	1	1	0	1	3
3	5	2	69	p	0	0	n. a.	0	0	0	1	3
4	6	2	56	p	0	0	n. a.	0	0	0	1	3
5	7	2	57	s	1	1	2.97	1	1	1	1	2
5	8	2	58	s	1	1	2.40	1	1	1	1	2
6	9	2	56	p	1	1	1.91	1	1	1	1	2
6	10	2	56	p	0	0	n. a.	1	1	1	0	4
7	11	2	54	s	0	0	n. a.	0	0	0	1	2
8	12	1	61	p	1	1	1.81	1	1	1	1	2
9	13	2	67	p	0	0	n. a.	0	0	0	1	2
10	14	2	58	p	0	0	n. a.	0	0	0	1	1
11	15	1	42	s	1	3	1.9	1	1	1	1	2
11	16	1	42	s	0	0	n. a.	0	0	0	1	2
12	17	1	52	s	1	2	3.14	1	1	0	1	2
12	18	1	52	s	0	0	n. a.	0	0	0	1	2
13	19	2	73	p	0	0	n. a.	1	1	1	0	3
14	20	1	54	p	0	0	n. a.	0	0	0	1	2
15	21	2	46	p	0	0	n. a.	0	0	0	1	2
16	22	1	58	s	1	2	3.89	1	0	0	1	3
17	23	1	31	p	1	1	3.29	1	1	0	1	1
18	24	2	56	p	0	0	n. a.	0	0	0	1	1
19	25	1	42	p	1	1	2.67	1	1	1	1	1
20	26	2	57	p	0	0	n. a.	0	0	0	1	3
21	27	2	81	p	1	1	2.61	1	1	1	1	2
21	28	2	81	p	0	0	n. a.	1	1	1	0	4
22	29	2	53	p	0	0	n. a.	0	0	0	1	2
22	30	2	54	p	0	0	n. a.	1	1	1	0	4
23	31	2	56	p	0	0	n. a.	0	0	0	1	2
24	32	1	51	s	1	1	1.81	1	0	0	1	1
25	33	2	65	p	0	0	n. a.	0	0	0	1	3
26	34	2	28	p	0	0	n. a.	0	0	0	1	2
27	35	2	53	p	1	1	2.56	1	1	1	1	2
28	36	2	64	p	0	0	n. a.	1	1	1	0	3
29	37	1	44	p	1	1	4.61	1	1	1	1	3
30	38	2	62	p	1	1	3.06	1	1	1	1	2
31	39	2	47	s	1	2	2.37	1	1	0	1	3
32	40	1	54	p	0	0	n. a.	0	0	0	1	3
33	41	2	61	p	1	2	2.01	1	1	0	1	3
34	42	2	81	p	0	0	n. a.	0	0	0	1	1
35	43	1	26	p	0	0	n. a.	1	1	1	0	3
36	44	2	62	p	1	1	2.53	1	1	1	1	3
37	45	2	76	p	0	0	n. a.	0	0	0	1	1
38	46	1	52	p	1	1	3.11	1	1	1	1	1
39	47	2	55	p	0	0	n. a.	0	0	0	1	1
40	48	2	79	p	1	1	2.23	1	1	1	1	1
41	49	2	62	p	0	0	n. a.	0	0	0	1	3

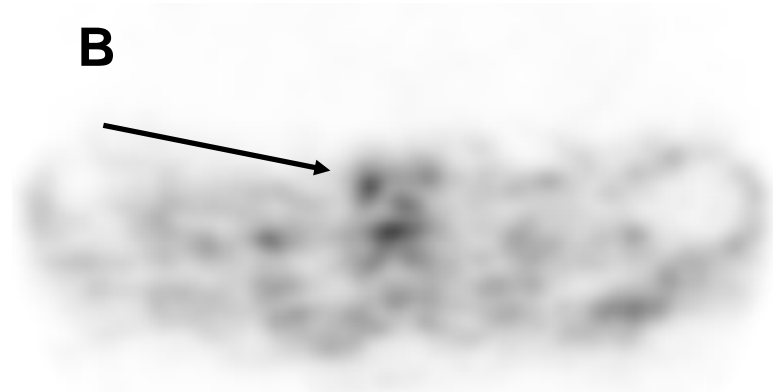
Table 2:

Lesion Basis					
Validation	No.	Histology	CI and post Tx	CI and Lab	CI or Lab
TN	6	0	0	3	3
FN	20	5	9	6	0
TP	23	5	12	6	0
Side Basis					
Validation	No.	Histology	CI and post Tx	CI and Lab	CI or Lab
TN	6	0	0	3	3
FN	22	6	9	7	0
TP	21	4	12	5	0
Location Basis					
Validation	No.	Histology	CI and post Tx	CI and Lab	CI or Lab
TN	6	0	0	3	3
FN	27	7	11	9	0
TP	15	3	10	2	0
FP	1	0	0	1	0

CT



MET-PET



MIBI

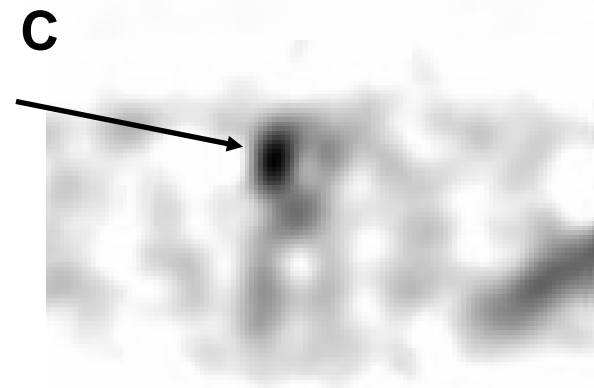


Figure 1

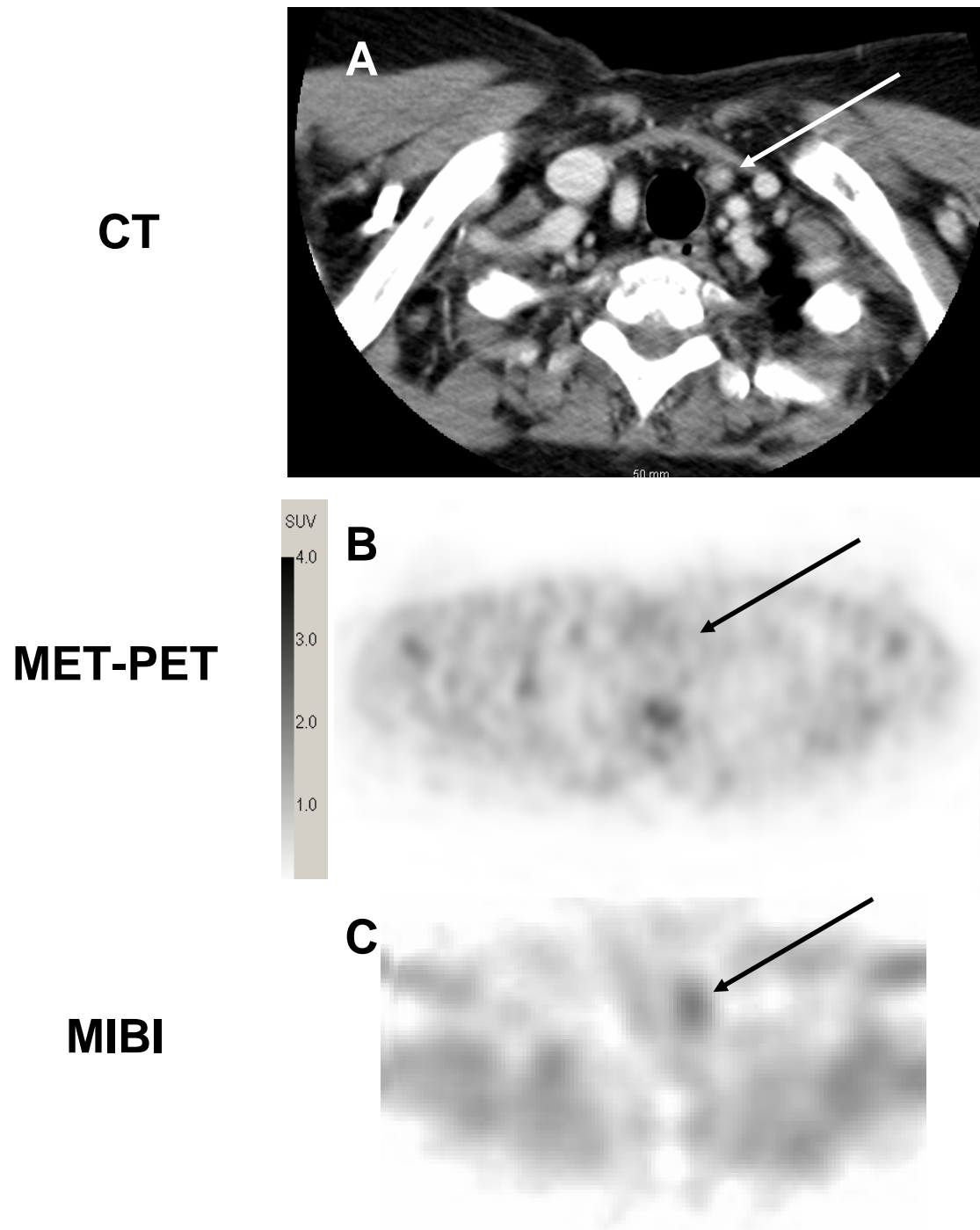


Figure 2

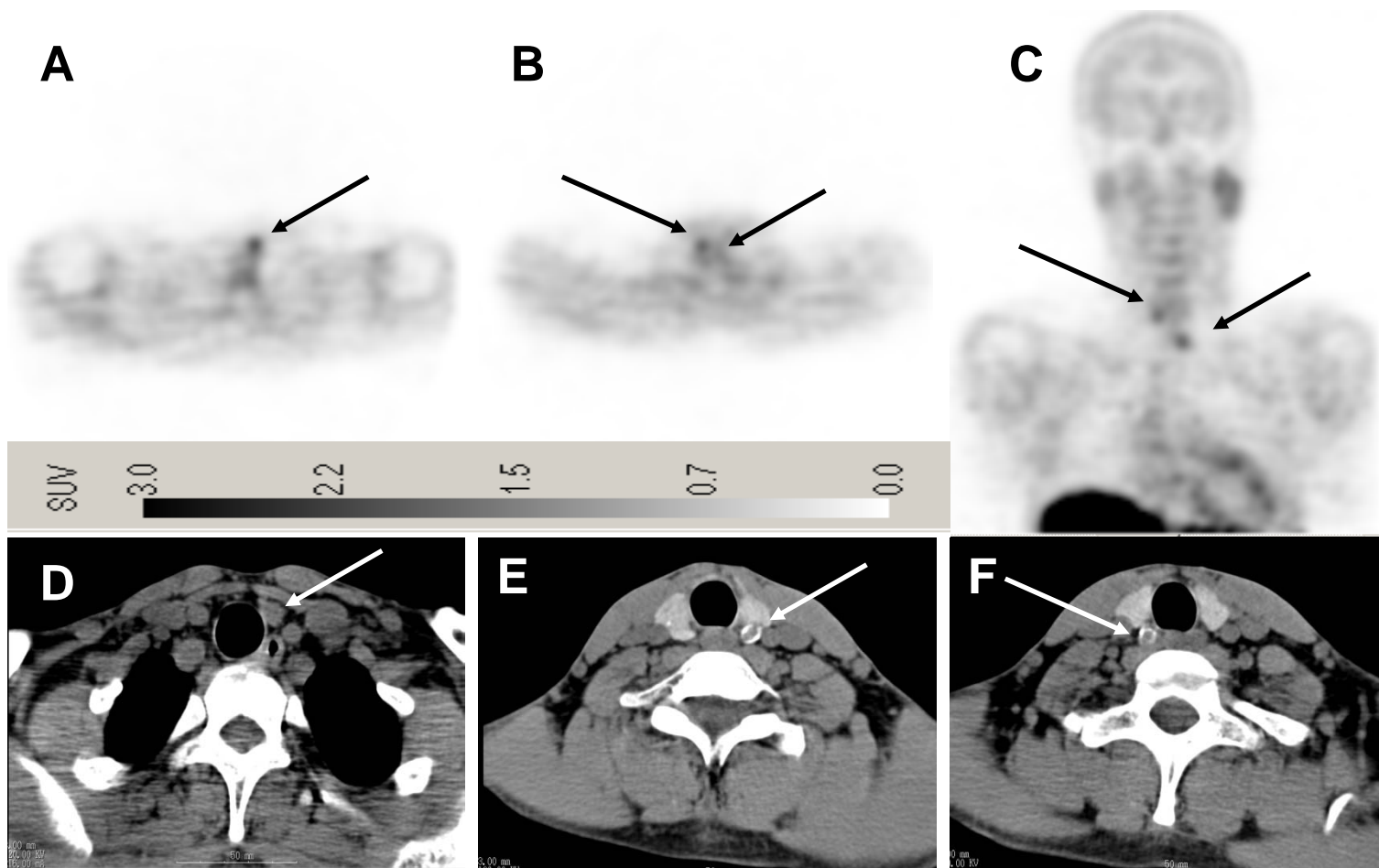


Figure 3

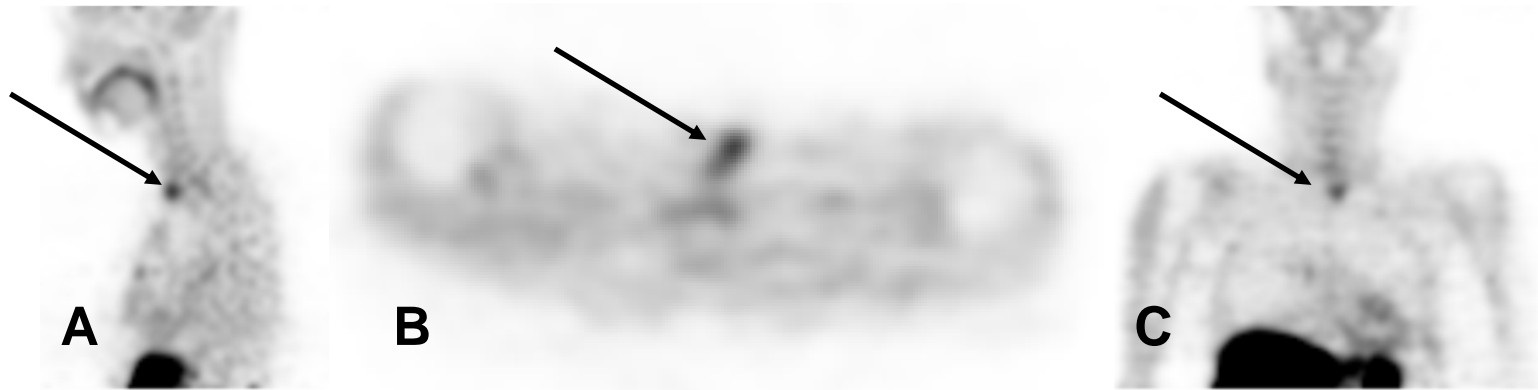


Figure 4