Eur Radiol (2007) 17: 3139–3147
DOI 10.1007/s00330-007-0682-2

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Dual-modality FDG-PET/CT in follow-up of patients with recurrent iodine-negative differentiated thyroid cancer

Received: 20 December 2006
Revised: 26 March 2007
Accepted: 27 April 2007
Published online: 22 May 2007

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Abstract The usefulness of combined 2-[^{18}F] fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) in locating suspected recurrence in patients with iodine-negative differentiated thyroid cancer (DTC) was evaluated. Thirty-six patients with DTC and suspected iodine-negative recurrence underwent restaging with FDG-PET/CT. The images of CT, FDG-PET, both modalities viewed side by side (CT+PET), and FDG-PET/CT were evaluated by two physicians separately. Imaging results were correlated with either histology (n=20) and/or clinical follow-up of at least 36 months. Recurrent disease was diagnosed in 22/36 patients. FDG-PET alone, CT alone, CT+PET, and FDG-PET/CT showed a sensitivity of 82%, 73%, 91%, and 96%, respectively. Specificities were 79%, 71%, 79%, and 100%, respectively. FDG-PET/CT significantly improved specificity compared with CT+PET and resulted in a further treatment modification in 5/36 patients (14%). CT alone was especially sensitive for lung metastases, FDG-PET alone for the remainder of the body. Accurate fusion of functional and morphologic data by FDG-PET/CT improves the staging accuracy of patients with suspected recurrence of iodine-negative DTC. This has an impact on patient management in a substantial number of patients.

Keywords Differentiated thyroid cancer · PET/CT · FDG · Dual modality

Introduction

Differentiated thyroid cancer (DTC) generally has a favourable prognosis [1]. However, up to 20% of patients with DTC develop locoregional recurrence and 8% of patients with recurrence will subsequently die from their disease [2–4].

Localisation procedures in routine follow-up of DTC-patients primarily include iodine-131 (^{131}I) whole-body scintigraphy (WBS) and cervical ultrasonography (US). Limitations in detecting locoregional recurrence or distant metastases occur when progressive dedifferentiation of thyroid carcinoma cells leads to a loss of iodine-concentrating capacity, seen in up to 20% of patients with DTC [5]. As patients may have only iodine-negative tumour lesions or both iodine-negative and iodine-positive tumour tissue [6], the presence of iodine-negative tumour tissue decreases the accuracy of iodine scintigraphy. This may provoke a situation in which tumour tissue is not detected by ^{131}I-WBS and will remain untreated [6].

Under these circumstances, conventional imaging techniques to localise tumour deposits, such as US, computed tomography (CT), and magnetic resonance imaging (MRI) may be inconclusive, especially in patients undergoing repeat surgical procedures [5]. In contrast, 2-[^{18}F] fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) has a high accuracy in the detection and staging of

DTC [2, 7] and has been able to improve the diagnostic work-up [6–12]. As surgery is the only curative therapy option for iodine-negative tumour tissue, exact localisation of FDG tumour foci is mandatory.

As FDG-PET provides only limited anatomical information, localisation of a lesion and its potential infiltration into adjacent organs is frequently difficult [13–15]. Thus, for maximal diagnostic benefit, functional data-sets should be read in conjunction with morphological images, e.g. using image fusion. However, accurate retrospective image co-registration of two extracranial image volumes is often compromised by motion-induced misregistration [14, 15]. This limitation can be overcome by collecting functional and morphological data in one examination using PET/CT tomographs [16]. Preliminary studies report promising results when malignant diseases of the head-and-neck area are assessed with combined PET/CT [17–21].

The aim of this study was to determine the diagnostic accuracy of FDG-PET/CT in re-staging of DTC compared with CT alone, PET alone, and PET and CT viewed side by side (CT+FDG-PET).

Materials and methods

Patients

Thirty-six consecutive patients (17 men, 19 women; mean age 55 years, range 21–80 years) with treated DTC (21 papillary carcinoma, 15 follicular carcinoma) were included in this retrospective study. All patients included were under regular follow-up in the Department of Nuclear Medicine and presented with clinical or serological signs of recurrent disease. All patients had primarily undergone surgery and ^{131}I-therapies (cumulative activities 4–48 GBq ^{131}I). None of them had residual disease following initial therapy (Tg<0.3 ng/ml). Tumour classification was accomplished according to the American Joint Committee on Cancer system [23]. Patients' characteristics are shown in Table 1. The patients presented pathological or unambiguous findings in cervical (n=11) or abdominal (n=2) US, an increasing Tg (n=19) (range: 0.8–278 ng/ml; median: 10.0 ng/ml), and/or increasing Tg-antibodies (n=4).

All patients were evaluated by medical history, clinical examination, chest radiograph, cervical US, and abdominal ultrasound. Prior to FDG-PET/CT, all patients received a high-dose ^{131}I-WBS using 1,000 MBq ^{131}I (4 weeks after withdrawal of L-thyroxin, the thyroid-stimulating hormone increased to a minimum of 30 mU/l) showing no pathological accumulation of radioiodine and therefore excluding iodine-avid tumour tissue. The study was conducted in full accordance with guidelines issued by the approving local institutional review board.

Table 1 Patient characteristics

Characteristic	Value[a]
Age (years)	55±18
Gender (n)	
Male	17
Female	19
Initial tumour stage (n)	
T1	1
T2	16
T3	10
T4	9
N0	16
N1a	8
N1b	12
M0	30
M1	6
Histology (n)	
Papillary	21
Follicular	15
Suspected recurrence (n)	
Pathological/ambiguous sonography	21
Increasing Tg	19
Increasing Tg-antibodies	4
Tg at study entry (ng/ml)	37±62
Follow-up (months)	45±6

[a]Values are expressed either as mean±standard deviation or number of patients

FDG-PET/CT imaging

FDG-PET/CT was performed on a biograph duo (Siemens Medical Solutions, Hoffman Estates, Ill.). A split acquisition protocol was used to perform a high-quality head and neck CT and a diagnostic whole-body CT with use of intravenous contrast agents [24]. The total examination time was approximately 30 min.

Head and neck FDG-PET/CT After a fasting period of at least 10 h, 350 MBq of FDG were administered intravenously. At 1 h post injection, all patients were positioned on the examination table with arms down and a CT topogram was performed to define the area of the head and neck scan (256 mm CC-range). Afterwards, CT images were acquired in breath-hold (160 mAs, 130 kV, slice width: 3 mm, table feed: 5 mm per rotation). For vascular and parenchymal delineation 60 ml of an iodinated contrast agent (Xenetix 300 mg iodine/ml; Guerbet, Sulzbach, Germany) were administered intravenously with an automated injector (XD 5500; Ulrich Medical Systems, Ulm, Germany) at 3 ml/s. Thereafter,

emission data were acquired (3D mode, 6 min per bed position). CT data were used for PET attenuation correction [24]. Image reconstruction of the corrected emission data was performed after Fourier rebinning (AWOSEM, four iterations, eight subsets, 3-mm Gaussian filter) [24].

Whole-body FDG-PET/CT imaging Afterwards a whole-body FDG-PET/CT was performed with the arms elevated above the head. In a topogram, a whole-body scan from the thorax to the pelvis was defined. Small bowel distension was accomplished using negative contrast-agents [25]. For vascular and parenchymal delineation, 90 ml of a contrast agent were administered. CT images were acquired with 100 mAs, 130 kV, a slice width of 5 mm, and a table feed of 8 mm per rotation. Emission data were acquired in 3D mode for 3 min per bed position over five to eight bed positions. Image reconstruction was performed after Fourier rebinning (AWOSEM, two iterations, eight subsets, 5-mm Gaussian filter).

Data analysis FDG-PET data sets were evaluated by two nuclear medicine physicians in consensus, CT images were read by two radiologists. The physicians were blinded to the other imaging modality and clinical course of the patients. Interpretation of CT+FDG-PET was performed by the same physicians using the same images, which were manually misregistered by a fifth physician to simulate the clinical situation of FDG-PET and CT acquired in two separately examinations. Finally, FDG-PET/CT data sets were viewed by the same physicians in consensus. FDG-PET images were evaluated for regions of focally increased tracer uptake. Thus, tumours were primarily identified by qualitative interpretation of the PET images. In all identified lesions, the maximum standard uptake values (SUV) were determined for tracer uptake quantification. In otherwise ambiguous findings a maximum SUV of >2.5 was considered to represent malignancy. CT images were evaluated for contrast-enhancing masses or asymmetries typical for malignancies.

Standard of reference

Histology and clinical follow-up served as the standards of reference. The presence or absence of disease and the number and localization of malignant lesions of every patient were defined by a tumour board consisting of two nuclear medicine physicians and two radiologists.

Histopathologic verification was available in all patients with suspective tracer-uptake in FDG-PET (surgery, $n=13$; fine-needle aspiration, $n=7$).

Since some of the patients were considered tumour-free, not all patients were evaluated by histology. In these patients, we defined the sum of all imaging procedures and follow-up data as the standard of reference for the extent and status of the disease. All patients were followed-up clinically for at least 36 months (follow-up time: 36–57 months) and all underwent follow-up Tg measurements, Tg-antibodies measurements, US, and CT. Furthermore, bone-scintigraphy ($n=9$), follow-up FDG-PET ($n=8$), MRI ($n=5$), and other imaging modalities ($n=4$) were acquired. Patients with absence of disease showed neither abnormalities in Tg or Tg-antibodies, nor pathological glucose metabolism on follow-up FDG-PET or enlarging masses on follow-up in anatomical imaging.

Statistical analysis

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the imaging examinations were determined. Confidence intervals were calculated using Jeffrey's equal-tailed confidence interval [26]. The differences in the results were analysed statistically using Fisher exact test. P values<0.05 were considered statistically significant.

Results

Recurrent disease was diagnosed in 22/36 patients; in 21 patients, localisation of recurrence was successful; in one patient, no morphologic or anatomical correlate for tumour recurrence was detected, although Tg continuously rose during the follow-up period of 36 months from 0.4 ng/ml up to 4.6 ng/ml. Six patients showed loco-regional disease, nine patients presented distant metastases and six patients suffered from both. Overall 86 malignant lesions were detected, 26 loco-regional lesions (T/N) and 60 distant metastases (M). Fourteen patients were free of tumour and showed no evidence of recurrence in later follow-up examinations. All patient-based results are summarised in Table 2.

Re-staging

Evaluated on a patient basis, CT correctly re-staged 18/36 patients (50%), FDG-PET correctly assessed 25/36 patients (69%), CT+FDG/PET was correct in 30/36 patients (83%), and FDG-PET/CT in 35/36 patients (97%). The sensitivities of each modality were 73%, 82%, 91%, and 96%, respectively; the specificities were 71%, 79%, 79% and 100%, respectively. All results of the patient-based analysis are presented in Table 3. The differences between CT and combined FDG-PET/CT in the sensitivity, the specificity, the PPV, and the NPV were statistically significant ($P=0.04$, $P=0.03$, $P=0.03$, and $P=0.04$). The comparison of the other imaging modalities showed advantages for combined FDG-PET/CT, which, however, did not reach the level of statistical significance.

Table 2 Summary of restaging, results of different imaging modality, clinical consequences and follow-up in each patient (*T/N* loco-regional lesions, *M* distant metastases, *TP* true positive, *FP* false positive, *FN* false negative, *NT* no therapy, *CTh* chemotherapy, *EBR* external beam radiation)

Patient	Recurrence	Malignant lesions		PET			CT			PET and CT			PET/CT			Clinical consequences	Follow–up (months)	Status on last follow-up
		T/N	M	TP	FP	FN	TP	FP	FN	TP	FP	FN	TP	FP	FN			
1	Yes	3	11	9	0	5	14	0	0	14	0	0	14	0	0	CTh	57.3	Progressive disease
2	No	0	0	0	0	0	0	1	0	0	0	0	0	0	0	Surgery	36.0	Disease free
3	Yes	0	2	2	0	0	1	0	1	2	0	0	2	0	0	EBR	42.9	Stable disease
4	No	0	0	0	1	0	0	0	0	0	1	0	0	0	0	NT. follow-up	45.9	Disease free
5	Yes	1	0	1	0	0	1	0	0	1	0	0	1	0	0	Surgery	38.0	Disease free
6	Yes	2	0	2	0	0	1	0	1	2	0	0	2	0	0	Surgery	42.7	Disease free
7	Yes	0	6	6	0	0	6	1	0	6	0	0	6	0	0	NT. follow-up	41.0	Progressive disease
8	Yes	3	0	3	0	0	0	0	3	3	0	0	3	0	0	Surgery	46.0	Disease free
9	Yes	2	4	5	1	1	3	1	3	5	1	1	6	0	0	Surgery (palliative), EBR	36.0	Progressive disease
10	Yes	2	4	5	0	1	4	6	2	5	0	1	6	0	0	Surgery (palliative)	39.9	Progressive disease
11	Yes	1	0	1	0	0	0	0	1	1	0	0	1	0	0	Surgery	36.5	Disease free
12	Yes	2	0	1	0	1	0	0	2	1	0	1	2	0	0	Surgery	37.0	Disease free
13	Yes	1	0	1	0	0	1	1	0	1	0	0	1	0	0	Surgery	51.0	Disease free
14	No	0	0	0	1	0	0	0	0	0	1	0	0	0	0	NT, follow-up	41.8	Disease free
15	Yes	3	8	11	0	0	9	1	2	10	0	1	11	0	0	Surgery (palliative)	36.5	Progressive disease
16	No	0	0	0	0	0	0	2	0	0	0	0	0	0	0	NT, follow-up	45.9	Disease free
17	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	49.8	Disease free
18	Yes	0	3	0	1	3	3	0	0	3	1	0	3	0	0	NT, follow-up	42.0	Progressive disease
19	Yes	0	2	2	0	0	2	1	0	2	0	0	2	0	0	CTh	41.0	Progressive disease
20	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	48.9	Disease free
21	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	40.0	Disease free
22	No	0	0	0	0	0	0	1	0	0	0	0	0	0	0	NT, follow-up	48.0	Disease free
23	Yes	0	2	2	0	0	0	1	2	2	0	0	2	0	0	Surgery (palliative)	37.0	Stable disease
24	Yes	1	2	3	0	0	2	1	1	3	0	0	3	0	0	Surgery	54.0	Disease free
25	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	47.3	Disease free
26	Yes	1	0	0	0	1	0	0	1	0	0	1	0	0	1	NT, follow-up	36.0	Still no tumour found
27	Yes	0	7	2	0	5	5	0	2	7	0	0	7	0	0	NT, follow-up	37.0	Progressive disease
28	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	51.0	Disease free
29	Yes	0	3	0	0	3	3	0	0	3	0	0	3	0	0	NT, follow-up	48.5	Progressive disease
30	Yes	0	3	3	2	0	0	0	3	3	2	0	3	2	0	NT, follow-up	41.0	Progressive disease
31	Yes	0	1	1	0	0	0	1	1	1	0	0	1	0	0	NT, follow-up	59.0	Progressive disease
32	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	Surgery	50.5	Disease free
33	Yes	4	2	4	1	2	2	0	4	6	1	0	6	0	0	NT, follow-up	45.0	Progressive disease
34	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	54.0	Disease free
35	No	0	0	0	2	0	0	1	0	0	2	0	0	0	0	NT, follow-up	51.0	Disease free
36	No	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NT, follow-up	47.3	Disease free

The sensitivity for lesion detection of tumour recurrence was 74% and 66% for FDG-PET and CT (Table 4). While local and loco-regional tumour recurrence could be visualised in 89% with FDG-PET and only 42% with CT, distant metastases were detected with a sensitivity of 67%, and 77%, respectively. FDG-PET showed superiority compared with CT with respect to detection of local recurrence and bone metastases (Fig. 1). CT, on the other

Table 3 Patient-based sensitivities, specificity, positive predictive values, and negative predictive value of CT, FDG-PET, and combined imaging (95% CI=95% confidence interval)

	Sensitivity		Specificity		PPV		NPV	
	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
CT	73	(52–88)	71	(45–89)	80	(59–93)	63	(38–83)
FDG-PET	82	(62–94)	79	(53–94)	86	(67–96)	73	(48–90)
FDG-PET + CT	91	(74–98)	79	(53–94)	87	(69–96)	85	(59–97)
Combined FDG-PET/CT	96	(80–99)	100	(83–100)	100	(89–100)	93	(73–99)

hand, was superior to FDG-PET in diagnosing lung metastases (Table 5). As some of the CT and FDG-PET findings were complementary, evaluation of CT+FDG-PET and co-registrated PET/CT yielded an increasing overall sensitivity for lesion detection of 94% and 99%, respectively. Accordingly, the differences in sensitivity between stand-alone CT and the other imaging modalities were in each case statistically significant ($P<0.001$). Compared with CT+FDG-PET, PET/CT images revealed 5% (4/84) additional tumour manifestations: two bone metastases otherwise interpreted as unspecific abdominal uptake (patient 10) or cervical uptake (patient 9) were found. Furthermore, two cervical lymph node metastases were depicted by combined FDG-PET/CT that were otherwise assessed as unspecific tracer-uptake after repeated surgical procedures (patient 12 and 15, see Fig. 1 as an example). However the differences were not statistically significant ($P=0.096$).

False positive findings were present with all imaging modalities resulting in a PPV of 75%, 88%, 90%, and 98% for CT, FDG-PET, CT+FDG-PET, and FDG-PET/CT, respectively. While CT+FDG-PET did not show significant improvement in PPV compared with FDG-PET, combined FDG-PET/CT allowed to significantly reduce false-positive findings compared with CT, FDG-PET, and CT and FDG-PET side-by-side ($P<0.001$, $P=0.01$, and $P=0.03$ respectively), e.g. by localising contra-lateral vocal-cord-palsy (Fig. 2), physiological intraesophageal tracer-accumulation, or unspecific tracer-uptake.

Clinical consequences and follow-up

Compared with CT, FDG-PET changed therapy management in 9/36 patients (25%); due to unknown metastases undetected on CT ($n=7$) or additional local recurrence ($n=2$; patient 6 and 24). Furthermore, FDG-PET was negative in nine patients with false positive findings in CT, suggesting absence of recurrent disease.

Compared with CT+FDG-PET, FDG-PET/CT resulted in a treatment modification in 5/36 patients (14%). In two patients, additional cervical lymph-node metastases were operated on (patient 12 and 15) and in three patients with false positive or inconclusive findings on CT+FDG-PET no therapy was initiated (patient 4, 14, 35). Follow-up showed no evidence of recurrent disease in these patients.

All patients with only loco-regional recurrence (6/36) were operated on with curative intent with a compartment-oriented systemic lymphadenectomy. Further follow-up in these patients showed no evidence of recurrent DTC.

Table 4 Lesion-based sensitivities and positive predictive values of CT, FDG-PET, and combined imaging

		Sensitivity		PPV	
		%	(95% CI)	%	(95% CI)
Overall	CT	66	(56–76)	75	(64–84)
	FDG-PET	74	(64–83)	88	(79–94)
	FDG-PET+CT	94	(88–98)	90	(83–95)
	Combined FDG-PET/CT	99	(95–100)	98	(92–99)
T/N staging	CT	42	(25–61)	55	(34–75)
	FDG-PET	88	(72–97)	85	(69–95)
	FDG-PET+CT	89	(72–97)	85	(68–95)
	Combined FDG-PET/CT	96	(83–99)	100	(91–100)
M staging	CT	77	(65–86)	82	(71–90)
	FDG-PET	67	(54–78)	89	(77–96)
	FDG-PET+CT	97	(90–99)	92	(83–97)
	Combined FDG-PET/CT	100	(96–100)	97	(90–99)

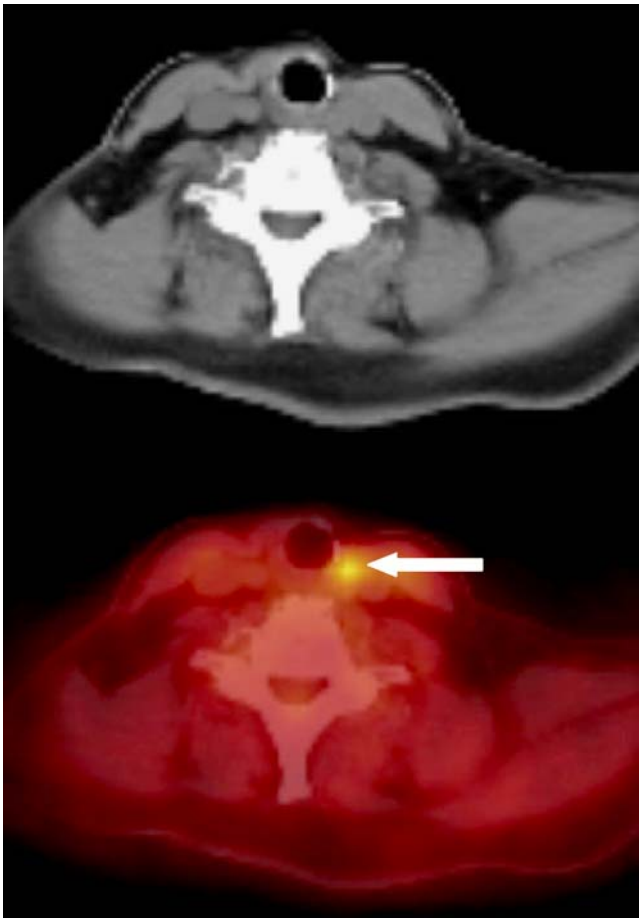

Fig. 1 CT (*upper image*) and FDG-PET/CT (*lower image*) of a patient with loco-regional DTC recurrence (patient 11) showing a pathologic FDG-uptake (*arrow*). FDG-PET/CT allows exact localisation of the tumour not visible in CT alone. The finding was histologically verified

The initial therapeutic strategy based on CT staging was altered in six patients who showed additional mediastinal, skeletal, or lung metastases besides loco-regional recurrence on FDG-PET/CT. One patient with additional mediastinal findings was operated on with curative intent using a transsternal approach; follow-up showed no evidence tumour (patient 24). In three patients, sole selective lymph node dissection or palliative tumour debulking in the neck was performed; followed by external beam radiation in one patient for extended disease. One patient primarily received chemotherapy due to undifferentiated histology and the risk of rapid deterioration. One patient was followed-up without treatment. In the later patients, progressive disease was documented on further follow-up.

Patients with distant metastases underwent palliative tumour debulking of mediastinal lymph node metastases using a transsternal approach ($n=1$), palliative external beam radiation ($n=1$), palliative chemotherapy ($n=1$) or were followed without current treatment ($n=6$). Except one patient with stable disease, all patients suffered from progressive disease.

Discussion

In DTC patients with iodine-negative metastases, early diagnosis and subsequent surgical resection remains the optimal therapeutic approach [5, 27]. Morphological imaging using US, the first-line tool in follow-up shows a sensitivity of 94% focusing on detection of neck recurrences [28]. However, in our study only patients with negative neck ultrasonography or with ambiguous findings were included, thus the results cannot be compared.

Other morphological imaging techniques, such as CT, have limited value in follow-up of DTC due to their low sensitivity and low specificity in the head-and-neck area, particularly in cases of altered anatomy after surgery [29].

Table 5 Sensitivities and positive predictive values of CT, FDG-PET, and combined imaging in staging of distant metastases

M staging		Sensitivity (%)	PPV (%)
Lung metastases ($n=37$)	CT	100	97
	FDG-PET	51	91
	FDG-PET+CT	100	97
	Combined FDG-PET/CT	100	100
Bone metastases ($n=8$)	CT	13	25
	FDG-PET	88	100
	FDG-PET+CT	88	88
	Combined FDG-PET/CT	100	100
Other distant metastases ($n=15$)[a]	CT	82	57
	FDG-PET	93	82
	FDG-PET+CT	93	82
	Combined FDG-PET/CT	100	88

[a]Mediastinal and hilar lymph nodes ($n=13$) and abdominal tumour manifestation ($n=2$)

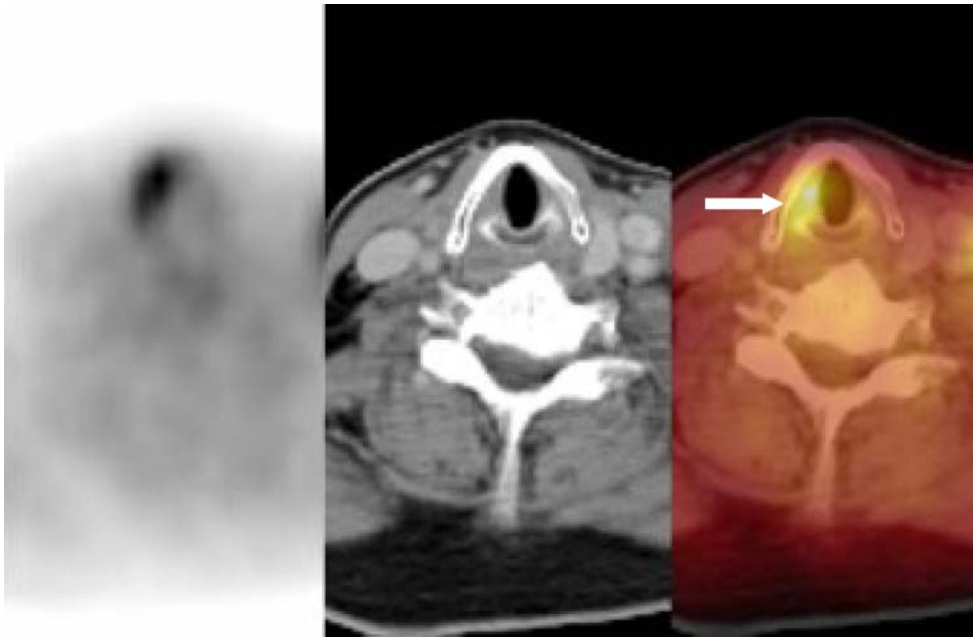

Fig. 2 FDG-PET (*left*), CT (*middle*), and FDG-PET/CT (*right*) of patient 9 showing an increased tracer-uptake in right larynx, inconclusive in FDG-PET alone. FDG-PET/CT allows to localise the FDG-uptake in the right vocal cord representing physiological activation (*arrow*). Due to contrallateral phrenic palsy, the left vocal cord is not activated

Accordingly, contrast-enhanced CT alone had a sensitivity of 43% for loco-regional metastases in our patients. On the other hand, CT demonstrated a sensitivity of 76% in the assessment of distant metastases, with particular strength in diagnosing lung metastases.

FDG-PET has been shown to be the most accurate method in recurrent iodine-negative DTC, with sensitivities and specificities ranging between 85% and 94% [5–12, 30]. Our results are in concordance with these findings, showing an overall sensitivity for lesion detection of 74% and a patient-based sensitivity of 82% for FDG-PET alone. The somewhat lower detection rate is probably due lower tumour burden in our patients, including patients with low Tg serum concentrations.

Since the introduction of PET/CT, some studies have been published on its value in detection of recurrent DTC as summarised in Table 6. In our cohort, FDG-PET/CT demonstrated a sensitivity of 96% in per-patient analysis, being within the range of previously published data. However, all previous studies must be interpreted with caution due to short follow-up periods, as DTC is known to grow slowly. Thus, intervals for follow-up are larger than for most other tumour entities, leading to a lack of reference standard for many patients with DTC. Nevertheless, FDG-PET/CT seems to enable a more accurate staging of DTC than either FDG-PET or CT, reflecting the inherent limitations of the two imaging modalities when either of these two is used alone. However, as Buell et al. [31] argue correctly, the somewhat unrealistic comparisons of FDG-PET with FDG-PET/CT must necessarily show an advantage for FDG-PET/CT. To allow for a more balanced study design reflecting clinical reality, FDG-PET/CT must be compared with a side-by-side evaluation of conventional FDG-PET and CT scans. Until now, only Palmedo et al. [18] have compared co-registrated PET/CT with both modalities interpreted side by side, showing no differences of sensitivity but an increase of specificity, PPV, and NPV. In our study an increase of sensitivity in re-staging from 91% to 96% and in the lesion-based sensitivity from 93% to 98% could be achieved by means of FDG-PET/CT, not reaching the level of statistical significance.

The essential advantage of FDG-PET/CT in our patients has to be seen in a significant decrease of false positive or inconclusive findings, reflected by a significant improvement of PPV. Thus, FDG-PET/CT allows overcoming one major limitation of FDG-PET, especially in the region of

Table 6 Summarised literature on FDG-PET/CT in recurrent DTC

Study	Patients (*n*)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Zimmer et al. [19]	8	50	–	–	–
Nahas et al. [20]	33	60	100	100	27
Saab et al. [21]	15	60	–	–	–
Ong et al. [22]	17	88	–	–	–
Palmedo et al. [18]	40	95	91	86	95

the neck: the possibility of false-positive FDG accumulations leading to the diagnosis of lymph node metastases [32–34] and, consequently, to the potential scheduling of a futile operation [35]. Consequently, PET/CT can help to increase diagnostic accuracy in re-staging of DTC [32, 36].

FDG-PET/CT resulted in a further treatment modification in 14% of our patients. In contrast Palmedo et al. [18] described a change of therapy in 48% of their patients. These differences can mainly be explained by different acquisition protocols for FDG-PET/CT. While we routinely acquired contrast enhanced CT, Palmedo and co-workers performed CT without contrast agents. Thus, CT is not diagnostic with respect to radiological standards [37], and side-by-side reading of PET and CT is compromised.

Conclusions

In patients with suspected recurrence of DTC with negative ^{131}I-WBS, FDG-PET/CT is a useful technique to improve re-staging accuracy. Furthermore, FDG-PET/CT most likely will be valuable to evaluate the response to treatment, as shown for other tumour entities [15]. Clinical benefit can be expected with respect to planning of further surgery, palliative interventions, and external beam radiation in individual cases. Considering the impact of correct patient treatment, we assume an influence on patient prognosis. Due to the relatively slow progression of DTC, this could, however, not be proven in our study, even with a minimum follow-up of 3 years.

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