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REVIEW ARTICLE

^{131}I whole-body scan or ^{18}FDG PET/CT for patients with elevated thyroglobulin and negative ultrasound?

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Abstract The aim of this review is to discuss the current role of iodine-131 (^{131}I) whole-body scanning (WBS) and fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}FDG PET) or PET/computed tomography (PET/CT) in the restaging of differentiated thyroid cancer (DTC), prompted by increasing thyroglobulin serum levels in patients with negative neck ultrasound. Studies in the literature which compared these two imaging methods are discussed in depth. ^{18}FDG PET or PET/CT and ^{131}I WBS may provide complementary information useful for the restaging of DTC patients, and the combined use of these methods should thus be considered to identify recurrent/metastatic DTC patients after total thyroidectomy. The accuracy of ^{18}FDG PET/CT seems to be superior to that of ^{131}I WBS and SPECT/CT in high-risk DTC.

Keywords Iodine-131 · Fluorodeoxyglucose · Positron emission tomography · Thyroid cancer · Restaging

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Introduction

Thyroid tumors account for the vast majority of endocrine neoplasms and their incidence is increasing. Differentiated thyroid cancers (DTCs) are the most frequent thyroid neoplasms and usually have an excellent prognosis; conversely, more aggressive histological subtypes are less frequent and carry a worse prognosis. Recognizing recurrent/metastatic thyroid cancer has a significant impact on clinical decision-making and patient prognosis.

The aim of this review is to discuss the current role of iodine-131 (^{131}I) whole-body scanning (WBS) and fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}FDG PET) or PET/computed tomography (PET/CT) in the restaging of DTC, prompted by increasing thyroglobulin (Tg) serum levels in patients with negative neck ultrasound (US). Furthermore, studies in the literature which compared these two imaging methods are discussed.

^{131}I WBS in patients with detectable Tg levels and negative ultrasound

Diagnostic ^{131}I WBS (DWBS) after thyroid-stimulating hormone (TSH) stimulation has been shown to have low sensitivity at 1-year follow-up of DTC [1, 2]. As a result, its role has been questioned over the past decade. Indeed, several authors have reported that the sensitivity of DWBS is no higher than 50 % of that of post-therapy ^{131}I WBS (PTWBS) [3–7]. The ability of DWBS to reveal sites of disease has been found to be poor, and DWBS findings have not proved to be unequivocally related to serum Tg levels recorded after LT4 withdrawal or after TSH stimulation with recombinant human TSH (Tg-off levels) [1]. In particular, no correlation has been observed between Tg-off

<10 ng/ml and DWBS [8]. Furthermore, in 10–15 % of DTC patients, high levels of Tg may be found despite negative DWBS [6, 9]. DWBS can only confirm successful thyroid remnant ablation, but it is unable to detect new pathological sites of disease that were not detected by PTWBS 1 year earlier [1]. Considering the well-known indolent behavior of DTC, it is likely that metastases detected by DWBS were already present at the time of ablation and already visualized by PTWBS [8]. In other words, when pathological uptake outside the thyroid bed is not detected by PTWBS, DWBS at 1-year follow-up is not necessary in low-risk DTC patients with undetectable Tg under LT4 (Tg-on) and negative neck US [10]. The best markers of complete ablation are considered to be undetectable serum Tg-off levels and normal neck US [11], and patients with undetectable Tg-off levels 1 year after ablation are reported to have an excellent outcome, regardless of residual thyroid bed uptake on DWBS [12]. However, American Thyroid Association (ATA) guidelines reported by Cooper et al. [10] still recommended DWBS in combination with stimulated Tg in high-risk patients with negative basal Tg and US after ablation. This application was recently addressed by Rosario et al. [8] who reported that DWBS can, however, be avoided in high-risk DTC patients with negative initial PTWBS and neck US disease and Tg-on levels <1 ng/ml.

In this diagnostic scenario, the population of DWBS-negative and Tg-positive DTC patients at 1-year follow-up examination is growing. Therefore, localizing the Tg-producing lesions correctly in these patients, to determine the proper treatment, is considered an increasingly important challenge [5–7].

Morphological imaging techniques, such as US and CT, are well-established methods of identifying neck and thoracic tumor localizations, respectively [13], especially in the presence of Tg-off values above 5 ng/ml. In particular, US can guide fine-needle aspiration cytology and/or Tg measurement in the aspirate. The added value of US is also related to the possibility of detecting cervical lymph node metastases, even in patients with undetectable Tg-off levels [10]. However, cases with detectable Tg-off levels, negative DWBS, and negative morphological findings are not infrequently reported. In these cases, empirical therapy with ^{131}I should be considered to better detect sites of disease and for the treatment of disease not amenable to surgery [10]. The characteristics of the patient and the tumor must be taken into account before administering further empirical ^{131}I therapy. In particular, age, tumor dimension (*T*), lymph node involvement (*N*), DTC subtype, and serum Tg-off levels are important factors in predicting the efficacy of further ^{131}I therapy. On one hand, old age and aggressive subtypes are more often related to low ^{131}I avidity of the tumor; while on the other hand, it must be remembered that greater *T* and *N* values are associated with a higher possibility of locoregional and distant metastases [14].

The two main (Tg-based) factors taken as the basis for proposing a second empirical ^{131}I treatment are a post-ablation WBS with foci of uptake outside the thyroid bed and Tg-off levels above 10 ng/ml [15]; moreover, it has been suggested that a corresponding Tg rhTSH level would be 5 ng/ml [10]. If, on these grounds, a second ^{131}I treatment is administered, 60 to 80 % of PTWBSs show uptake sites outside the thyroid bed, indicating tumor sites [5–7]. This confirms the intrinsic diagnostic utility of PTWBS in DTC patients with high Tg-off levels and no further evidence of disease. The highest sensitivity of PTWBS is often found in young patients (<45 years old) affected by a nonaggressive DTC subtype, in whom the percentage of false-negative results on DWBS is more often related to the small dimensions of metastatic lesions [7] than to a reduced capability of the ^{131}I uptake mechanism. The principal sites of metastatic disease revealed by PTWBS in cases with negative morphological imaging, e.g., neck US and chest CT, are the cervical lymph nodes and lungs [5–7]. In this setting, the administration of a second dose of ^{131}I ranging from 3,700 to 11,100 MBq [6] can have a considerable diagnostic and therapeutic significance. PTWBS may allow sites of metastasis to be identified before they emerge clinically some years later and may, at the same time, lead to partial or complete remission, especially in the case of small lung metastases [6, 16]. With regard to small cervical lymph nodes, PTWBS may be helpful, above all, in identifying the "culprit" cervical level warranting further lymph node dissection [15]. In this anatomical district, the retropharyngeal lymph nodes, which are not identifiable on US, are the principal sites of mismatching findings between US and PTWBS [10].

However, the key question that has arisen in recent years is that which patients need a further empirical ^{131}I therapy and when this therapy should be performed. As reported by Padovani et al. [17], in the absence of structural disease, Tg-on levels may continue to decline over time after ^{131}I administration, independently of other therapies. Moreover, the time needed to achieve undetectable Tg-on levels depends on the initial risk stratification. As previously demonstrated, Tg-on <1 ng/ml is achieved within 2 years of ablation in 84 % of low-risk patients, but in only 39 % of high-risk patients [18]. Since the natural history of intermediate and high-risk DTC patients is characterized by a slow decline in Tg-on levels over time, a conservative approach may be suggested for high-risk DTC patients with persistent stable Tg-on levels and no evidence of structural disease [17]. In the absence of any evidence of structural disease on conventional imaging (CI) (e.g., CT, US), additional empirical ^{131}I therapy should be reserved for

those DTC patients in whom the Tg-on value rises over time after ablation. This approach may reduce the possibility of administering further, inappropriate therapies to patients who are likely to show a late response to initial treatment.

^{18}FDG PET or PET/CT in patients with detectable Tg levels after thyroidectomy

The literature contains increasing evidence of the usefulness of ^{18}FDG PET or PET/CT in patients with thyroid tumors [19]. ^{18}FDG is the most used PET tracer in oncology; this glucose analog is trapped by cells via the glucose transporters (GLUTs). Overexpression of GLUTs is particularly prevalent in aggressive thyroid tumors; in addition, overexpression of hexokinase-1 promotes ^{18}FDG uptake in thyroid cancer cells [20].

DTC cells expressing the sodium–iodine symporter take up radioiodine; as cells dedifferentiate and the disease becomes more aggressive, their ability to concentrate iodine is lost (leading to reduced radioiodine uptake) and cellular glucose metabolism is activated (with increased ^{18}FDG uptake) [20]. This pattern of differential tracer uptake was defined as the "flip-flop phenomenon" by Feine [21] in 1995. However, contrary to what the original name suggested, differential tracer uptake is not absolute. Patients with thyroid cancer can have a positive ^{131}I-WBS with negative ^{18}FDG PET, the opposite pattern, or a mixed pattern where some lesions show radioiodine uptake, other lesions show ^{18}FDG uptake, and some lesions may show a different degree of uptake of both tracers [22].

According to the ATA guidelines, ^{18}FDG PET and PET/CT are currently considered most valuable in the work-up of DTC patients who present post-thyroidectomy, with increasing serum Tg levels and negative ^{131}I-WBS [10]. If no disease sites are identified on CI or ^{131}I-WBS or Tg levels are elevated out of proportion to the minor disease found on CI, ^{18}FDG PET or PET/CT should be performed to detect recurrent or metastatic disease [10, 22].

A meta-analysis of the diagnostic accuracy of ^{18}FDG PET and PET/CT in DTC patients who presented with elevated serum Tg post-thyroidectomy and negative ^{131}I-WBS reported a good diagnostic accuracy of these methods with pooled sensitivity and specificity values of 88.5 and 84.7 %, respectively. The pooled values of sensitivity increased when only ^{18}FDG PET/CT studies were considered in the analysis (93.5 %), demonstrating a superior diagnostic accuracy of PET/CT compared to PET only [23].

Clinical evidence is emerging that the performance of ^{18}FDG PET and PET/CT for the detection of Tg-positive and radioiodine-negative metastases of DTC is also improved after TSH stimulation (either by hormone withdrawal or rhTSH administration) [24]; however, the clinical significance of this superior diagnostic performance remains uncertain.

The current ATA guidelines suggest that ^{18}FDG PET or PET/CT should be performed when Tg levels are >10 ng/mL [10]. However, no clear cutoff value of Tg has, as yet, been established in clinical practice; indeed, although the proportion of true-positive ^{18}FDG-PET findings increases with elevated Tg levels, true-positive findings have also been reported in 10–20 % of DTC patients with Tg levels <10 ng/mL [22, 25]. A recent article suggested that both serum Tg levels and Tg doubling time independently predicted a positive ^{18}FDG PET/CT scan in patients with biochemical recurrence of DTC. The accuracy of ^{18}FDG PET/CT significantly improved when the serum Tg level was above 5.5 ng/mL during LT4 treatment or when the Tg doubling time was <1 year, irrespective of the absolute Tg value [26].

In daily practice, the decision on when to perform ^{18}FDG PET or PET/CT in patients with recurrent DTC should be tailored to the single patient, considering not only Tg levels and ^{131}I WBS findings, but also, on the basis of clinical and histopathological features, their individual risk [22].

Additional clinical uses of ^{18}FDG PET or PET/CT in DTC have been reported, i.e., the use of these techniques as prognostic tools for identifying which patients with known distant metastases are at highest risk for disease-specific mortality [10, 27]. ^{18}FDG PET or PET/CT are also used as selection tools for identifying patients unlikely to respond to additional radioiodine therapy, and they may allow the measurement of post-treatment response following external beam irradiation, surgical resection, embolization, or systemic therapy [10].

Low-risk patients with DTC are very unlikely to require ^{18}FDG PET or PET/CT as part of their initial staging or follow-up. Moreover, at present, ^{18}FDG PET and PET/CT are not recommended for preoperative assessment of DTC [10].

Conversely, in patients with more aggressive thyroid cancers (such as Hürthle cell carcinoma, aggressive variants of DTC, poorly differentiated thyroid carcinomas, and anaplastic carcinomas), which usually show low or absent radioiodine uptake, ^{18}FDG PET and PET/CT are very useful methods for determining the extent of metastatic disease [28, 29] and for prognostic purposes; in the subset of patients with advanced disease, these imaging methods may also be helpful for treatment response assessment [10, 30].

Comparison of ^{131}I WBS and ^{18}FDG PET or PET/CT

Several authors have compared ^{131}I-WBS and ^{18}FDG PET or PET/CT results in patients with DTC with suspected metastases [31–44].

Direct comparisons of diagnostic accuracy

Grunwald et al. [31] evaluated the clinical significance of ^{18}FDG PET and compared the results obtained using this technique with those obtained using ^{131}I WBS. The sensitivity of ^{18}FDG PET was found to be 75 % for the whole patient group ($n = 222$) and 85 % for the group with negative radioiodine scan ($n = 166$). The specificity was 90 % in the whole patient group. The sensitivity and specificity of ^{131}I WBS were 50 and 99 %, respectively. When the results of ^{18}FDG PET and ^{131}I-WBS were combined, tumor tissue was missed in only 7 % of cases [31].

These findings were confirmed by Shiga et al. [32] who compared these two methods in 32 DTC patients. The number of lesions detected was 47; 87 % of the lesions were detected by both methods, but ^{18}FDG PET uptake was concordant with ^{131}I uptake in only 38 % of the lesions [32].

Hsu et al. [33] evaluating 15 patients with local invasive and/or aggressive DTC found that ^{18}FDG PET was useful for detecting dedifferentiated lesions and was superior to ^{131}I WBS in detecting residual cervical or mediastinal lesions and suspected small metastatic foci in the lung. ^{18}FDG PET was inferior to ^{131}I WBS in detecting diffuse lung metastases and distant bone metastases [33].

Iwata et al. [34] compared ^{18}FDG PET and PTWBS in 19 patients. A total of 32 lesions were diagnosed as metastases; 96.9 % of the lesions were detected by at least one of the two modalities. Small lung metastases were not visualized by either modality in one patient. No false-positive lesions were identified by PTWBS. ^{18}FDG PET and PTWBS revealed a total of 26 (81.3 %) and 22 (68.8 %) lesions, respectively. ^{18}FDG PET was positive in 17 (78.3 %) out of 22 ^{131}I WBS-positive lesions, and also in 9 (90 %) out of 10 PTWBS-negative lesions. When the size of metastases was compared between ^{18}FDG-positive and negative groups, the maximal diameter of ^{18}FDG-positive lesions was found to be significantly greater than that of the ^{18}FDG-negative lesions. The ^{18}FDG-positive and PTWBS-positive lesions were significantly larger than both the ^{18}FDG-negative and PTWBS-positive lesions and the ^{18}FDG-positive and PTWBS-negative lesions. Only 18 lesions (56.3 %) showed concordant results between ^{18}FDG PET and ^{131}I uptake. Thus, there was no significant association between ^{131}I uptake and ^{18}FDG uptake [34].

In a study performed by Caleo et al. [36] in 13 DTC patients after thyroidectomy, ^{18}FDG PET and ^{131}I WBS yielded concordant negative results in the majority (77 %) of patients; the two imaging techniques gave concordant positive results in just one patient. In three patients, the results were discordant [36].

Oh et al. [37] compared the performance of ^{131}I WBS, ^{131}I SPECT/CT, and ^{18}FDG PET/CT in the detection of distant metastases of DTC; 140 patients with 258 foci of suspected distant metastases were evaluated. The imaging modalities showed the following sensitivity, specificity, and accuracy values on patient-based analyses: 65, 55, and 59 % for ^{131}I WBS; 65, 95, and 85 % for ^{131}I SPECT/CT, and 61, 98, and 86 % for ^{18}FDG PET/CT, respectively. Lesion-based analyses demonstrated that both ^{131}I SPECT/CT and ^{18}FDG PET/CT were superior to ^{131}I WBS in all patient groups; ^{131}I SPECT/CT was superior to ^{131}I WBS and ^{18}FDG PET/CT in patients who received a single challenge of radioiodine therapy, whereas ^{18}FDG PET/CT was superior to ^{131}I WBS and ^{131}I SPECT/CT in patients who received multiple challenges [37].

The complementary role of these methods was confirmed by Nagamachi et al. [38] who, in 70 patients, compared the capacity of ^{131}I-WBS and ^{18}FDG PET/CT to detect postoperative DTC metastases. On the patient-basis analysis, the detectability by ^{131}I WBS and ^{18}FDG PET/CT was 67.1 and 84.2 %, respectively. ^{131}I-WBS provided information complementary to that provided by ^{18}FDG PET/CT in 11 of the 70 (15.7 %) cases. On the organ-basis analysis, ^{131}I WBS was found to be the best detector of lymph node metastases (72.4 %), while ^{18}FDG PET/CT was superior to ^{131}I WBS for detecting bone metastases (85.7 versus 71.4 %, respectively) and lung metastases (94.1 versus 62.7 %, respectively) [38].

Overall, the literature suggests that ^{18}FDG PET (or PET/CT) and ^{131}I WBS provide complementary information for detecting metastases in postoperative DTC patients. ^{131}I WBS is useful for determining the differentiation of tumor lesions, identifying thyroid remnants, and looking for distant metastases; while ^{18}FDG PET (or PET/CT) is useful in cases of dedifferentiated thyroid carcinoma in which ^{131}I WBS and Tg measurements are unable to detect tumor lesions. Furthermore, ^{18}FDG PET (or PET/CT) has been shown to be a valuable diagnostic tool for the detection not only of ^{131}I-negative lesions, but also of ^{131}I-positive lesions of metastatic DTC (Figs. 1, 2, 3).

Thus, the combination of ^{131}I WBS and ^{18}FDG PET (or PET/CT) should be considered when seeking to detect metastatic thyroid cancer after total thyroidectomy.

Other findings from the comparison between ^{131}I WBS and ^{18}FDG PET or PET/CT

Compared with DWBS and PTWBS, ^{18}FDG PET scans are more likely to reveal uptake outside the thyroid bed and to correlate with the disease stage and long-term outcome, as

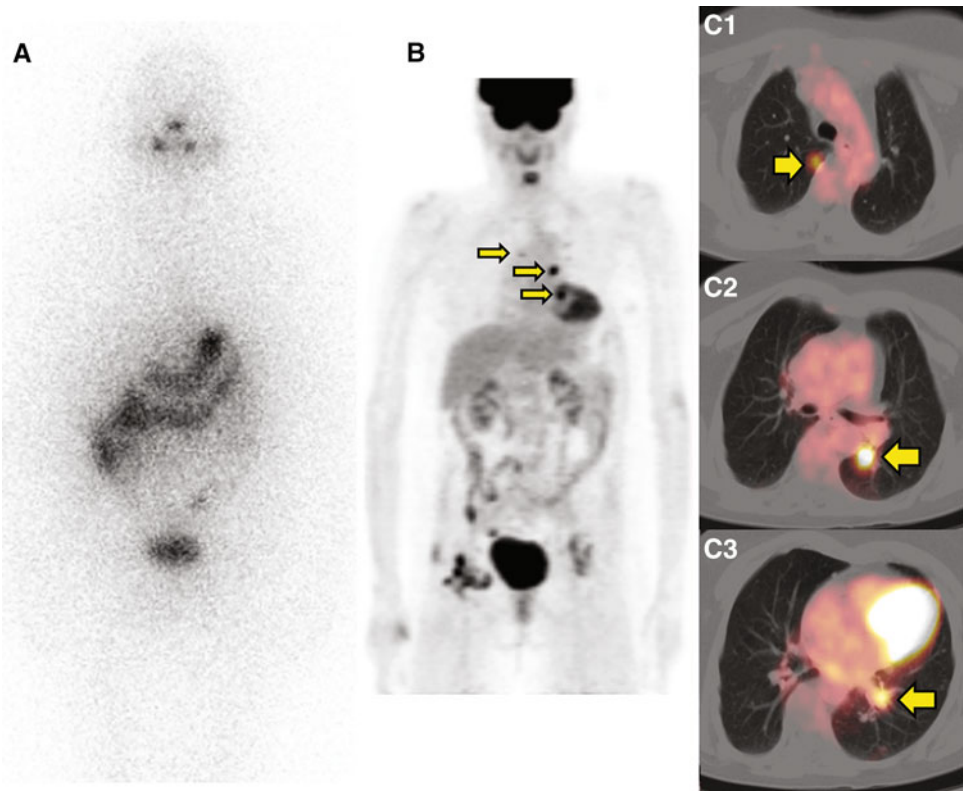

Fig. 1 ^{131}I WBS (**a**), ^{18}FDG PET (**b**) and axial ^{18}FDG PET/CT (**C1–C3**) images in a 48-year-old female patient with increased Tg levels after thyroidectomy for a high-risk DTC. ^{131}I WBS was negative, whereas ^{18}FDG PET and PET/CT showed increased radiopharmaceutical uptake corresponding to lung metastases (*arrows*) (color figure online)

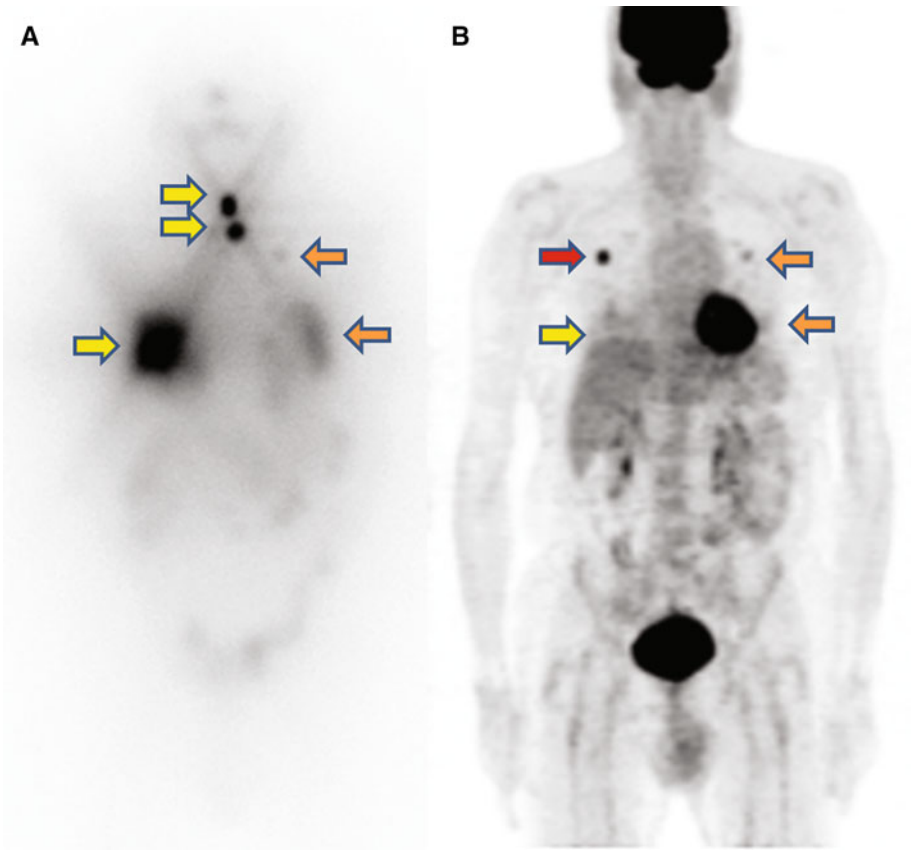

Fig. 2 ^{131}I WBS (**a**) and ^{18}FDG PET (**b**) in a 70-year-old male patient with increased Tg levels after thyroidectomy for a DTC. ^{131}I WBS detected increased tracer uptake corresponding to local recurrence and pulmonary lesions. ^{18}FDG PET detected an additional lung lesion missed by ^{131}I WBS (*red arrow*), whereas other lesions showed similar (*orange arrows*) or lower or absent radiopharmaceutical uptake compared to ^{131}I WBS (*yellow arrows*) (color figure online)

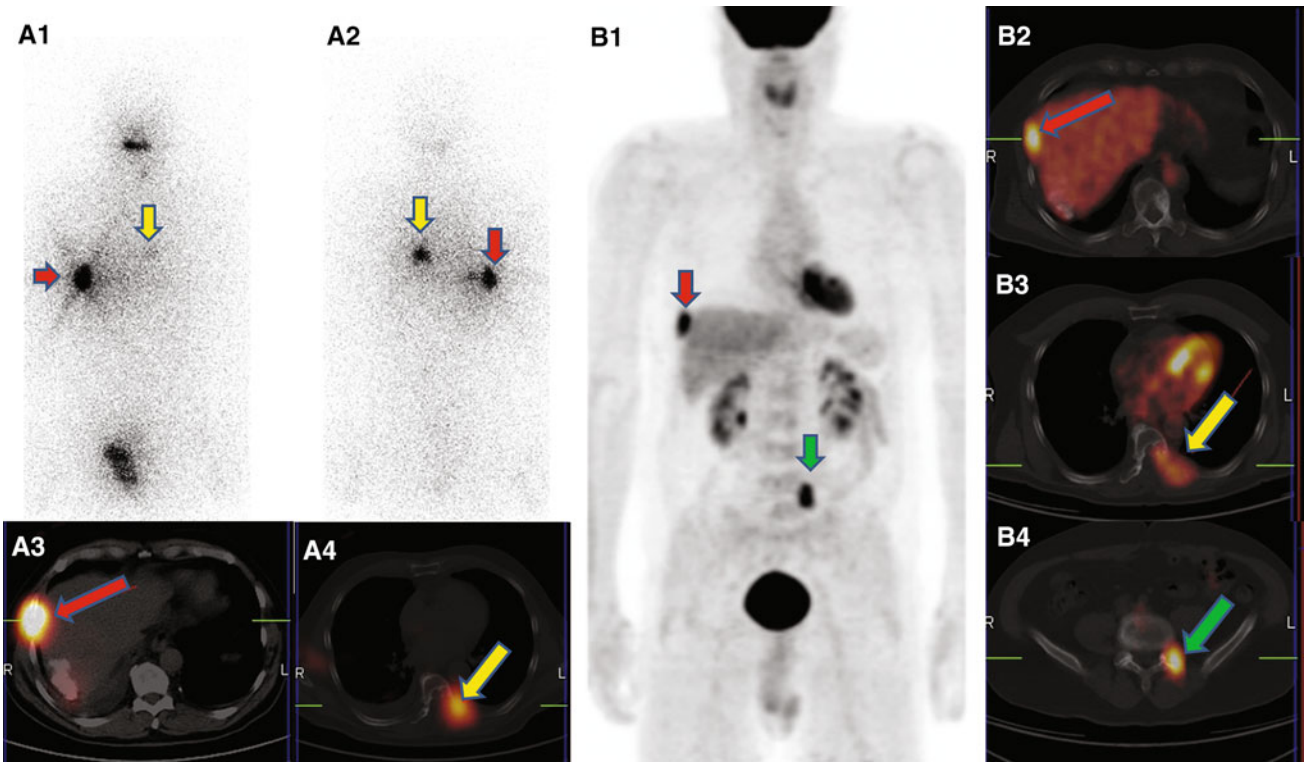

Fig. 3 PTWBS in anterior (**a1**) and posterior (**a2**) view, axial ^{131}I SPECT/CT (**a3, a4**), ^{18}FDG PET (**b1**) and axial ^{18}FDG PET/CT (**b2–b4**) images in a 65-year-old male patient with increased Tg levels after thyroidectomy for a DTC. PTWBS detected increased ^{131}I uptake corresponding to bone metastases on a right rib (*red arrow*) and a dorsal vertebra (*yellow arrow*). ^{18}FDG PET/CT detected an additional bone lesion in a lumbar vertebra (*green arrow*) (color figure online)

demonstrated by Al-Zahrani et al. [35]. These authors compared ^{18}FDG PET with DWBS and PTWBS to assess its prognostic value in 26 newly diagnosed DTC cases. Overall, 18 ^{18}FDG PET scans (69.2 %) were positive, showing a total of 40 foci; while eight ^{18}FDG PET scans (30.8 %) were negative. The corresponding 26 DWBS were all positive and showed a total of 47 foci. DWBS and PTWBS showed similar foci in the 24 patients who had ablation therapy. In contrast to the ^{18}FDG PET scans, which showed 26 foci of uptake (65 %) outside the thyroid bed, on DWBS, 45 foci (95.7 %) were in the thyroid bed; while two foci (4.3 %) were in cervical lymph nodes and no focus was seen outside the neck area. A clear correlation was found between the ^{18}FDG PET results, the stage of the disease, and the long-term outcome; seven of the eight negative ^{18}FDG PET scans were in stage I, while all patients with a disease stage higher than I (six patients) had positive scans. Over a median of 30 months, seven of the eight patients (87.5 %) with negative ^{18}FDG PET scans were in remission compared with only eight (44.4 %) of those with positive ^{18}FDG PET [35].

^{18}FDG PET/CT can be recommended for papillary thyroid cancer (PTC) patients with detectable serum Tg levels to detect residual lymph node metastases, as described by Kaneko et al. [39]. These authors evaluated the incidence of residual lymph node metastases in 37 high-risk PTC patients receiving adjuvant ^{131}I therapy, especially in those without ^{131}I accumulation and assessed the clinical usefulness of ^{18}FDG PET/CT for detecting these lesions. A total of 33 lesions in nine patients were diagnosed as residual lymph node metastases. ^{18}FDG accumulated in all of the lesions, but 19 (57.6 %) of them had no ^{131}I accumulation. These results indicated that residual lymph node metastases were relatively common in high-risk PTC patients receiving adjuvant ^{131}I therapy whose serum Tg levels remained detectable, and these lesions often had no ^{131}I accumulation [39].

Yoshio et al. [40] evaluated the local efficacy of ^{131}I therapy for ^{18}FDG PET/CT-positive lesions in patients with DTC after total thyroidectomy. Their analysis was performed on 44 lesions in 37 patients. In the group with positive accumulation on ^{18}FDG PET/CT and negative accumulation on ^{131}I (F+/I− group), 16 lesions (70 %) were found to be increased while seven (30 %) showed no change or reduction. In the group with positive accumulation for both ^{18}F-FDG and ^{131}I (F+/I+ group), five lesions (63 %) were increased and three (37 %) showed no change or reduction after ^{131}I therapy. The tendency to increase in size was not found to differ significantly between the F+/I− and the F+/I+ groups. Lesions which

showed positive accumulations on ^{18}FDG PET/CT had a greater tendency to increase in size, suggesting that the ^{18}FDG-avid lesions were resistant to radioactive iodine therapy with or without ^{131}I uptake [40].

As recently shown by Piccardo et al. [41], ^{18}FDG PET/CT could detect new radioiodine-negative metastases in advanced DTC patients with unchanged positive ^{131}I WBS and increasing Tg levels. These authors studied stage-IV DTC patients with elevated Tg levels associated with positive ^{131}I WBS. On suspicion of non-iodine concentrating additional metastases, 20 stage-IV DTC patients with increasing Tg levels and stable positive PTWBS were enrolled. Conventional imaging procedures, including neck US, bone scintigraphy, and CT, were performed before ^{18}FDG PET/CT. The ^{18}FDG PET/CT was positive in 16 out of 20 patients (80 %). In nine patients (45 %), it detected a larger number of tumor recurrences/metastatic sites than were detected on ^{131}I WBS + CI [41].

The sensitivity of empirical ^{131}I administration and subsequent ^{131}I WBS versus ^{18}FDG PET/CT in patients who had a normal post-ablation ^{131}I WBS was assessed in a recent article by Leboulleux et al. [42]. Thirty-four DTC patients with a normal post-ablation ^{131}I WBS underwent empirical ^{131}I administration and ^{18}FDG PET/CT. A total of 75 lesions were found in 23 patients, distributed in 36 organs. The sensitivities for the detection of individual lesions and for the diagnosis of metastatic organs were 88 and 97 % for ^{18}FDG PET/CT and 16 and 22 % for post-empirical ^{131}I WBS, respectively. ^{18}FDG PET/CT was abnormal in 22 patients, five of whom also had an abnormal post-empirical ^{131}I WBS. Only one patient was found to have an abnormal post-empirical ^{131}I WBS and a normal ^{18}FDG PET/CT. These authors concluded that in patients with suspicion of recurrence based on the Tg level after a normal post-ablation ^{131}I WBS, ^{18}FDG PET/CT, rather than post-empirical ^{131}I WBS, should be used to localize the disease. Empirical ^{131}I should be used only in patients with no significant ^{18}FDG uptake [42].

^{18}FDG PET performed concurrently with ^{131}I ablation can detect lymph node metastases in which radioiodine does not accumulate and may influence the management and treatment options for DTC patients, as Iwano et al. [43] have shown. These authors evaluated the ability of ^{18}FDG PET, performed concurrently with initial ^{131}I ablation, to detect lymph node metastases, and also examined its role in the management of DTC patients. Fifty-four patients underwent both ^{18}FDG PET and subsequent ^{131}I ablation. ^{18}FDG PET was positive in 25 sites in 18 patients (33 %). Only five out of 16 lymph node metastases (31 %) that were ^{18}FDG PET-positive were also positive on ^{131}I WBS. The success rate of Tg-negative after ablation was significantly lower in patients with ^{18}FDG PET-positive scans than in those with ^{18}FDG PET-negative scans [43].

^{18}FDG PET/CT as an initial staging method has a high impact on the management of patients with high-risk DTC, as recently demonstrated by Rosenbaum-Krumme et al. [44] in a study of 90 consecutive patients with either extensive or metastasized high-risk DTC who received ^{18}FDG PET after the first ^{131}I treatment. ^{18}FDG PET/CT was positive in 26 patients (29 %) and negative in 64 patients (71 %). These findings were compared with the results of ^{131}I WBS. In the 26 patients with ^{18}FDG PET/CT-positive lesions, the lesions were found to be both iodine- and ^{18}FDG-positive in 7 patients, ^{18}FDG-positive only in 15; while in 4 patients some lesions were ^{18}FDG-positive and some were iodine-positive [44].

Comparison of the radiation dose of ^{131}I WBS and ^{18}FDG PET

Diagnostic accuracy apart, it is important to underline the difference in the radiation dose between DWBS, PTWS, and ^{18}FDG PET.

For example 185 MBq of ^{131}I, administered for a DWBS, and 5550 MBq of ^{131}I, administered for a PTWBS, correspond to radiation doses of 11 and 330 mSv, respectively. The administration of 300 MBq of ^{18}FDG corresponds to a radiation dose of about 6 mSv.

Conclusions

This analysis of the literature leads us to conclude that ^{18}FDG PET or PET/CT and ^{131}I WBS may provide complementary information useful in the restaging of DTC patients. Accordingly, the combined use of these methods should thus be considered to identify recurrent/metastatic DTC patients after total thyroidectomy. The accuracy of ^{18}FDG PET/CT seems to be superior to that of ^{131}I WBS in high-risk DTC.

Conflict of interest G. Treglia, F. Bertagna, A. Piccardo, L. Giovanella declare that they have no conflict of interest related to the publication of this article.

Human and Animal Studies This article does not contain any studies with human or animal subjects performed by any of the authors.

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