Clin Transl Imaging (2013) 1:163–173
DOI 10.1007/s40336-013-0020-4

REVIEW ARTICLE

# $^{131}$I SPECT/CT: a one-station imaging modality in the management of differentiated thyroid cancer

**Yan-Li Xue · Zhong-Ling Qiu · Germano Perotti · Massimo Salvatori · Quan-Yong Luo**

Received: 6 May 2013 / Accepted: 11 May 2013 / Published online: 12 June 2013


**Abstract** In patients with differentiated thyroid carcinoma (DTC), single-photon emission computed tomography/computed tomography (SPECT/CT) applied to diagnostic or therapeutic radioiodine ($^{131}$I) whole-body scintigraphy (WBS) may accurately localize and help to distinguish benign from malignant sites of $^{131}$I uptake, with the potential to alter the management plan. $^{131}$I SPECT/CT is increasingly being used to evaluate patients with DTC and shows promise for improving imaging specificity and reducing false-positive results. Pre-ablation scans with $^{131}$I SPECT/CT contribute to the staging of thyroid cancer and the identification of regional and distant metastases prior to radioiodine therapy. Post-therapy scans with $^{131}$I SPECT/CT improve detection and localization of $^{131}$I accumulation in lymph node metastases and distant metastases compared with planar WBS and reduce the number of equivocal diagnoses and the need for additional cross-sectional imaging.

**Keywords** Differentiated thyroid carcinoma · $^{131}$I · SPECT/CT · Diagnostic scan · Post-therapy scan · Risk classification

Differentiated thyroid carcinoma (DTC) is the most common endocrine cancer accounting for 1 % of all cancers diagnosed each year [1]. The incidence of thyroid cancer has more than doubled since the early 1970s and, in women, it is the cancer showing the fastest-growing number of new cases. Papillary and follicular carcinomas account for the majority of DTCs and these histological variants are characterized by radioiodine ($^{131}$I) uptake. After initial thyroidectomy, $^{131}$I treatment is performed in most patients to ablate thyroid remnants and to treat locoregional or distant metastases [2].

For many years, planar $^{131}$I whole-body scintigraphy ($^{131}$I WBS), performed using diagnostic ($^{131}$I DxWBS) or therapeutic ($^{131}$I TxWBS) activities of radioiodine, was the standard method used to identify thyroid remnants or metastases [3].

Although $^{131}$I WBS boasts good sensitivity and high specificity, because of the lack of anatomical landmarks, it shows limitations in anatomical localization of the tumor and in differentiation of neoplastic from normal iodine-avid tissue. Low resolution and a paucity of anatomical information, along with a long list of physiological variants, make interpretation of $^{131}$I WBS challenging. Multiple maneuvers and strategies to aid in the differentiation of physiological from pathological foci of activity (e.g. swallowing water, separate-day imaging, oblique and lateral imaging, washing the patient’s skin, correlation with other imaging techniques, etc.) have traditionally been used to improve the diagnostic accuracy [4].

Hybrid SPECT/CT systems integrating a SPECT (single photon emission computed tomography) gamma camera with an X-ray computed tomography (CT) scanner in one gantry have been in use ever since they were first described in 2001 [5]. Thanks to a dual imaging modality, they allow combination of scintigraphic functional imaging (SPECT) data with anatomical (CT) information in a single examination. In the management of DTC patients, SPECT/CT

Y.-L. Xue · Z.-L. Qiu · Q.-Y. Luo (✉)
Department of Nuclear Medicine, Shanghai Sixth People’s Hospital, Shanghai Jiao Tong University, 600 Yishan Rd, Shanghai 200233, China
e-mail: lqyn@sh163.net

G. Perotti · M. Salvatori
Istituto di Medicina Nucleare, Università Cattolica Sacro Cuore, Policlinico Universitario A. Gemelli, 00198 Rome, Italy

with $^{131}$I ($^{131}$I SPECT/CT) provides metabolic and anatomical information about a lesion, allows accurate alignment of anatomical and functional images, and by allowing morphological and metabolic data to be collected in an all-in-one procedure, makes for better cost-effectiveness [6].

Several studies have demonstrated that $^{131}$I SPECT/CT has incremental diagnostic value in the diagnosis, treatment, and management of DTC [6–17].

In this article, we discuss the contribution of $^{131}$I SPECT/CT to better identification and localization of radioiodine uptake sites, its emerging role in staging and patient management, its role in $^{131}$I therapy based on dosimetry data, and finally the limitations and disadvantages of this technology.

## Detection and localization of $^{131}$I uptake sites

The human sodium iodide symporter (NIS) gene, which is located on chromosome 9p12–13.2 and was cloned in 1996, determines expression of NIS and consequent uptake of radioiodine both in normal thyroid tissues and in up to 80 % of thyroid carcinoma cells through an electrochemical sodium gradient generated by sodium–potassium adenosine triphosphatase [18].

NIS is normally expressed in: thyroid cells, ductal cells of salivary glands, parietal and mucus-secreting cells of the gastric mucosa, lacrimal glands, choroid plexus, ciliary bodies of the eye, thymus, placenta, and lactating mammary glands; NIS expression is also detected in most neoplastic cells of locoregional and distant metastases of DTC [18, 19].

As consequence, $^{131}$I WBS can show radioiodine uptake not only in thyroid remnants or metastases from DTC, but also in non-thyroid tissue showing physiological expression of NIS [19]. Several physiological variants and pitfalls may occasionally lead to mimicking of residual disease on $^{131}$I WBS, and these variants are usually recognized on planar imaging.

However, it is difficult to establish the precise anatomical localization of foci of $^{131}$I uptake on planar images because of the lack of anatomical landmarks and the low resolution, and $^{131}$I SPECT/CT has been demonstrated have incremental value over $^{131}$I WBS in characterizing and localizing pathological and physiological sites of radioiodine uptake [9, 10].

There are many studies showing the value of $^{131}$I SPECT/CT in cases that are difficult to resolve due to unusual biodistributions of radioiodine, such as ectopic thyroid tissue, ovarian teratoma, struma ovarii, kidney cysts, or accumulation of physiological secretions in the thorax, abdomen or genitourinary tract [4].

In a recent study, Aide et al. [14] reported that indeterminate findings on $^{131}$I WBS after ablation in 16 out of 55 patients (29 %) were reduced to 7 % after $^{131}$I SPECT/CT and that these results closely correlated with persistence or absence of disease at the end of follow-up. Blum et al. [15] highlighted the role of SPECT/CT in resolving cryptic findings in 40 out of 184 (22 %) whole-body scans performed after diagnostic or therapeutic administration of radioiodine.

By using the one-station $^{131}$I SPECT/CT procedure, the multiple maneuvers and strategies to improve the diagnostic accuracy mentioned earlier (e.g. swallowing water, using laxatives, washing skin, removing and scanning clothing, separate-day imaging, oblique and lateral imaging, correlation with other imaging modalities) may become redundant and can possibly be avoided. Similarly, it is no longer necessary to remain vigilant for pitfalls such as dentures (Fig. 1) and other sources of contamination (Fig. 2).

The capacity of $^{131}$I SPECT/CT to better identify physiological and pathological sites of $^{131}$I uptake in the head and neck, thorax, abdomen, pelvis, and bone are examined in the following sections.

### Head and neck

To minimize the risk of surgical complications (e.g., vocal cord paralysis), surgeons commonly leave small amounts of normal thyroid tissue (thyroid remnants) in the thyroid bed, near the expected location of the recurrent laryngeal nerve [4].

Thyroid remnants are depicted on $^{131}$I WBS as focal, intense central neck radioiodine uptake. However, because of the close proximity of adjacent structures in the head and neck and variations in body habitus, it is possible for uptake in the neck to be equivocal or indeterminate on planar imaging [4].

Thyroid remnants and thyroglossal duct remnants (small remains of thyroid tissue that concentrate radioiodine in the setting of elevated TSH levels) have a typical appearance on $^{131}$I SPECT/CT. Thyroid remnants commonly appear as focal (unilateral or bilateral) paratracheal activity associated with surgical clips, while a thyroglossal duct remnant will appear as an intense focal uptake in the midline of the central neck that localizes to the tip of the hyoid bone, along the expected path of descent of the embryological thyroid gland [4, 20].

$^{131}$I SPECT/CT can be helpful for characterizing thyroid remnants and it may influence both the selection of patients and the choice of radioiodine activity for radioiodine treatment (Fig. 3) [9–11]. After radioiodine treatment with empirical activities of $^{131}$I, it has been found that $^{131}$I SPECT/CT has an incremental value over planar imaging, also in terms of its capacity to depict response to radioiodine treatment [9, 14].

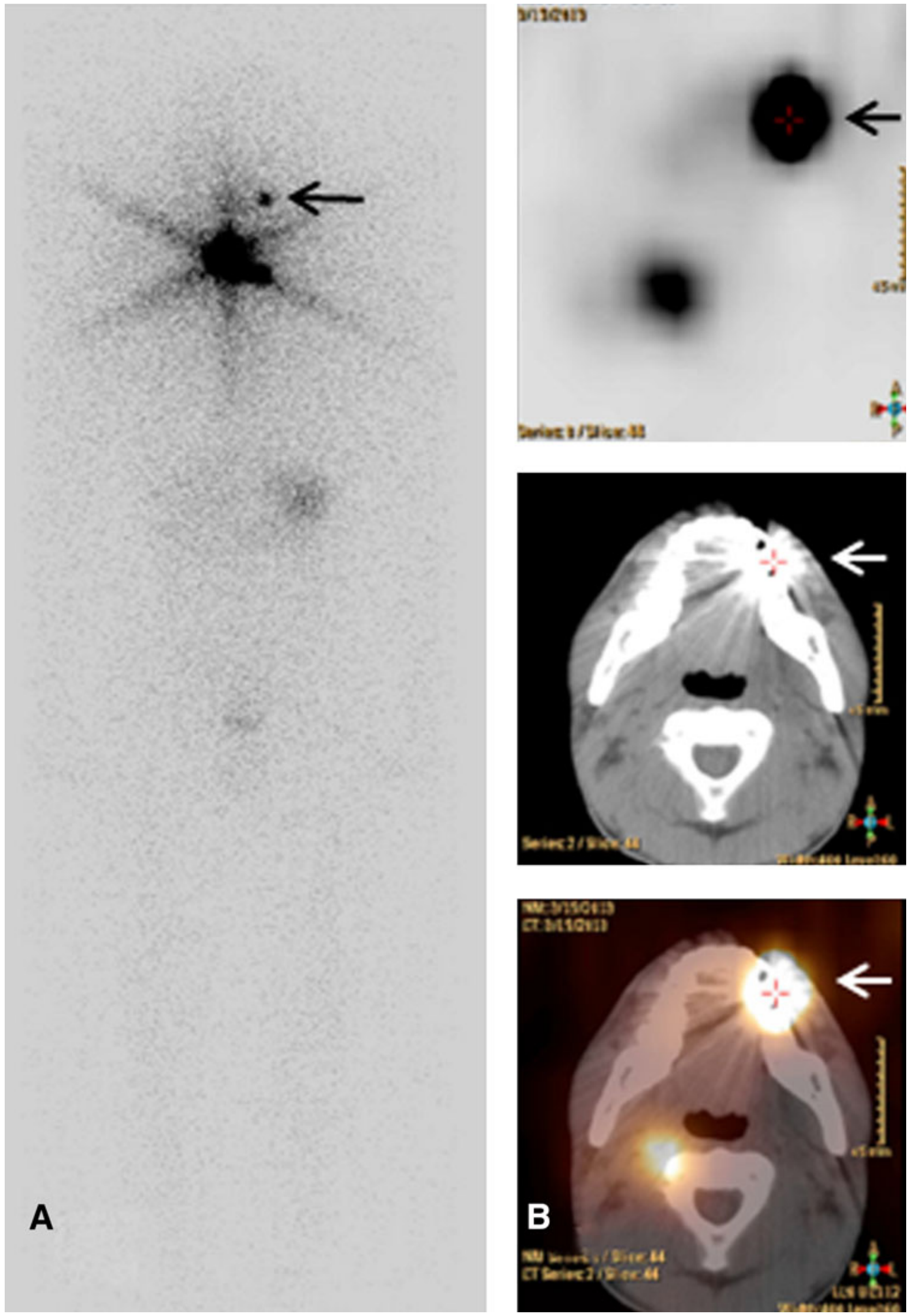


**Fig. 1** Post-therapeutic $^{131}$I WBS showed a small punctiform uptake of $^{131}$I in the left submandibular region (**a**, *arrow*). $^{131}$I SPECT/CT revealed that this lesion was $^{131}$I uptake in dentures (**b**, *arrows*)

To classify a paratracheal central neck activity as benign thyroid remnant or residual tumoral tissue, $^{131}$I SPECT/CT studies must be always evaluated together with the surgical pathology report, which provides information on tumor invasion into local structures and the completeness of the surgical resection [20]. Focal paratracheal central neck activities associated with a total thyroidectomy specimen demonstrating no evidence of extra thyroid tumor extension and negative surgical excision margins on pathology review may be usually characterized as thyroid remnants [21–23].

In addition to its use in the evaluation of thyroid remnants, $^{131}$I SPECT/CT can also be used to characterize other sites of benign radioiodine uptake in the head and neck region, e.g. in the nasal mucosa or nasolacrimal duct. Such uptake may be due to secretions or inflammation, pooling of salivary secretions, dental abscesses or recent dental or periodontal procedures, and secretions in a

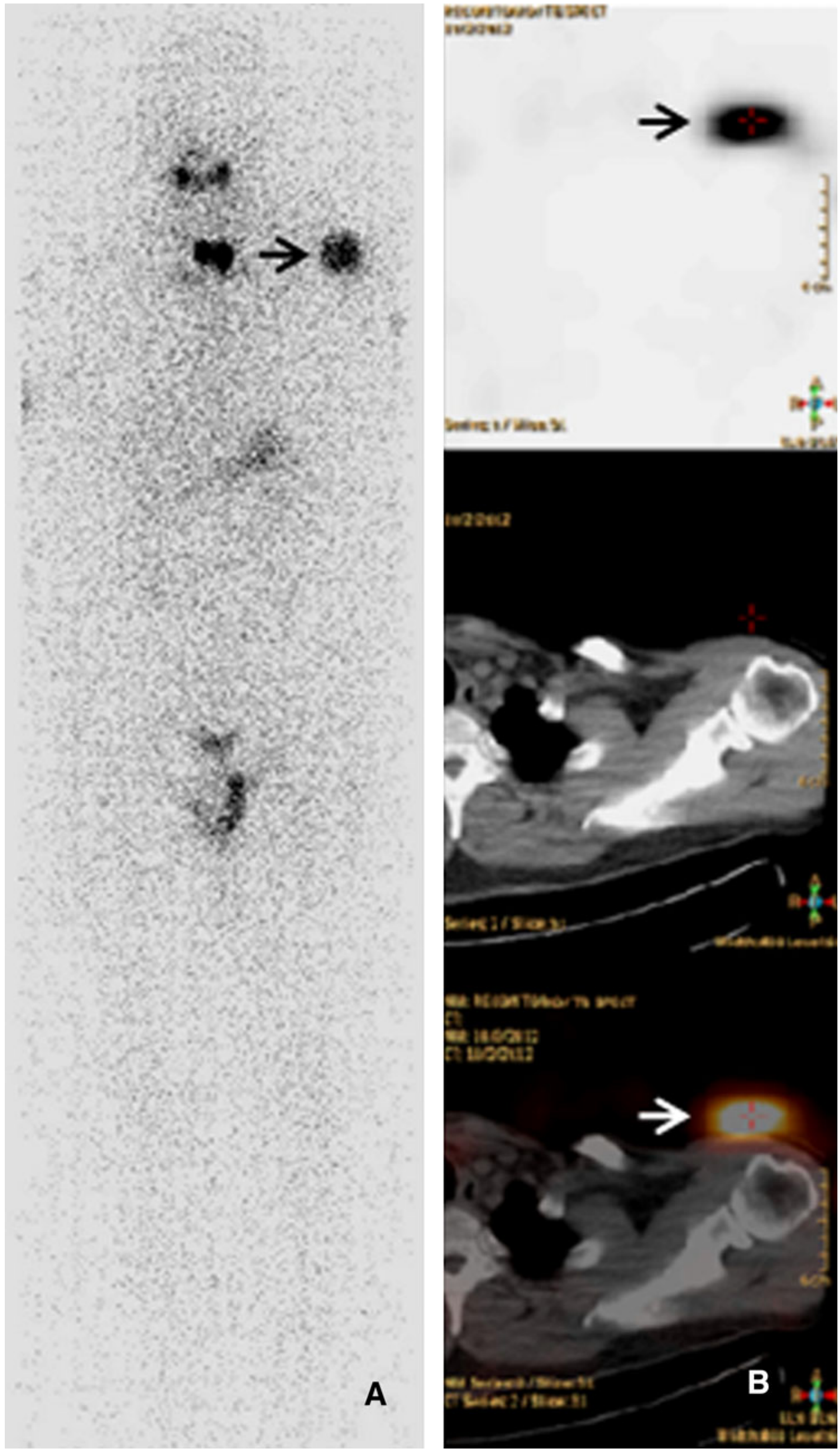


**Fig. 2** Post-therapeutic $^{131}$I WBS demonstrated intense radioactivity in the area of left shoulder (**a**, *arrow*). To accurately locate the $^{131}$I uptake lesion, $^{131}$I SPECT/CT was performed and the $^{131}$I uptake was found to be skin contamination (**b**, *arrows*)

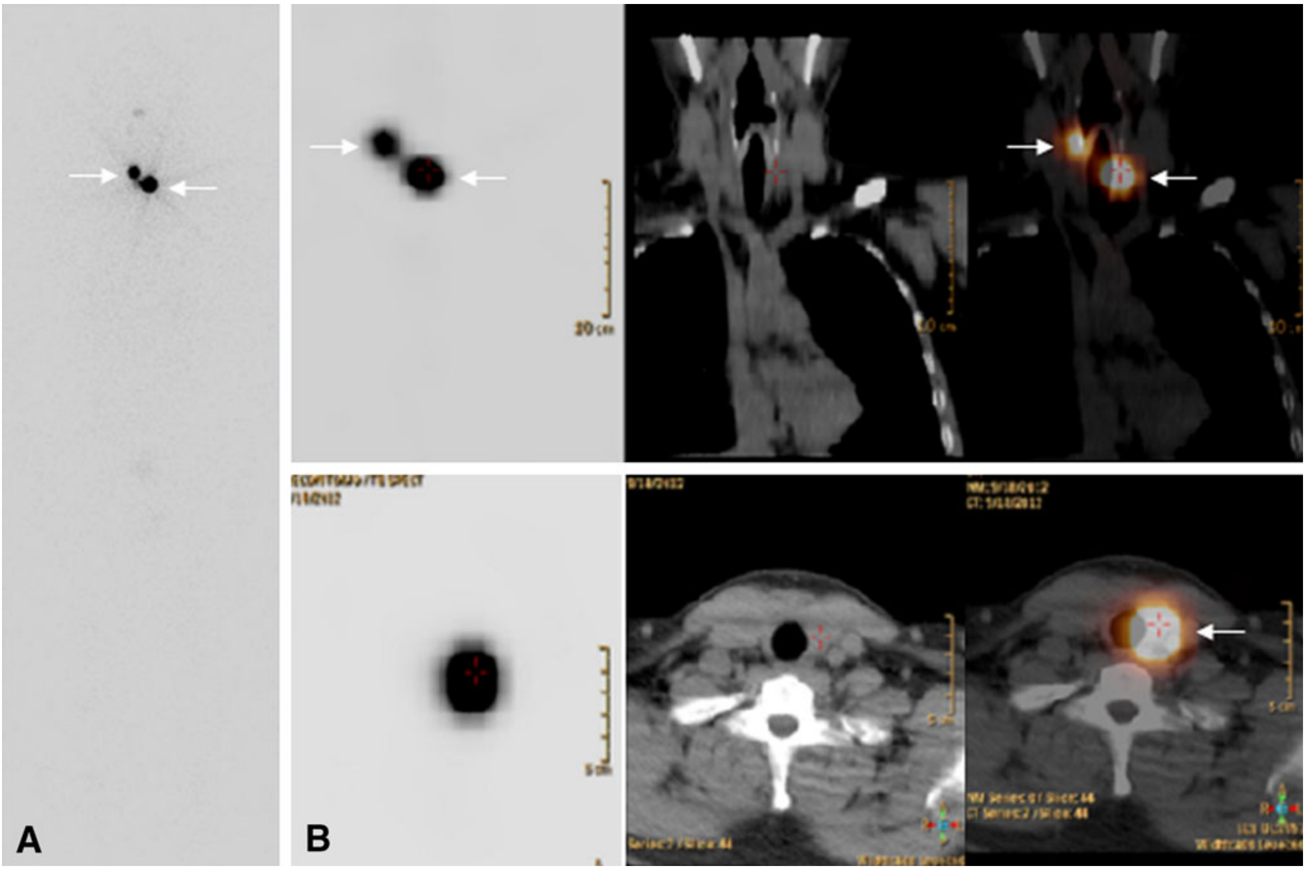


**Fig. 3** Post-therapeutic $^{131}$I WBS revealed two rounded foci of $^{131}$I uptake in the neck. It was difficult to distinguish whether these corresponded to residual thyroid or cervical lymph node tissue (**a**, *arrows*). The subsequent $^{131}$I SPECT/CT fusion images showed the two lesions to be residual thyroid tissue (**b**, *arrows*)

tracheostomy tube [24–27]. $^{131}$I SPECT/CT can also be useful for evaluating asymmetry of salivary gland uptake (related to radiation-induced salivary duct narrowing or sialadenitis due to prior radioiodine treatment), which can be another potentially misleading pattern [28].

## Chest, lungs, and mediastinum

Radioiodine uptake in the chest can be due to several benign conditions or to residual thyroid tumor, such as skeletal (in the sternum, thoracic spine or ribs), lung and mediastinal lymph node metastases [20].

$^{131}$I SPECT/CT may be used to differentiate benign causes and sites of radioiodine uptake in the chest that may cause diagnostic difficulties. These include esophageal secretions, Zenker's diverticulum, thymus, hiatal hernia, intrathoracic stomach created after esophagectomy or gastric pull-through surgery, lactating or non-lactating breast tissue, pleural and pericardial effusions, pulmonary infections, and skin contamination [4, 29].

In lactating women, focally increased uptake in the chest can be due to accumulation of radioiodine in breast tissue resulting from excretion of radioiodine into breast milk [30, 31]. Although rare, active transport by NIS can also cause symmetric or asymmetric radioiodine uptake in breast tissue in young, non-lactating women [32].

$^{131}$I SPECT/CT can also be of diagnostic assistance in the assessment of mediastinal physiological radioiodine accumulation due to retention in the gastrointestinal system, as in the case of secretion in the esophagus [20] or accumulation in gastric pull-up [33], for example. $^{131}$I SPECT/CT can be used in pediatric patients to evaluate physiological thymic activity mimicking lymph node metastases [34] and in cases in which radioiodine may, by passive diffusion, concentrate in pleural and pericardial effusions, a finding that may be more common in some patients because of the hypothyroidism used before the administration of radioiodine [35].

Lung metastases on $^{131}$I WBS appear as either focal (macronodular disease) or diffuse (micronodular disease) radioiodine uptake. In patients with lung metastases $^{131}$I SPECT/CT may offer several advantages, including the possibility of avoiding a diagnostic thoracic CT, the possibility of using the study as baseline for assessment of therapy response, and the possibility of demonstrating mediastinal adenopathy not easily characterized on planar imaging (Fig. 4) [4].

Abdomen and pelvis

The stomach, bowel, kidneys, and bladder are the most common sites of normal radioiodine uptake in the abdomen and pelvis on $^{131}$I WBS. In addition to these physiological sites, non-neoplastic accumulation of $^{131}$I should also be anticipated and recognized in other unusual locations, such as hiatal hernias, inguinal and abdominal hernias, pelvic or transplanted kidneys, and bladder diverticula, as well as in diverticulitis and in patients previously submitted to bowel surgery [4, 36]. In the liver, hepatic metabolism of radio-iodinated thyroid hormones released by remnant thyroid tissues can be responsible for diffuse uptake on $^{131}$I TxWBS. This pattern should be distinguished from the

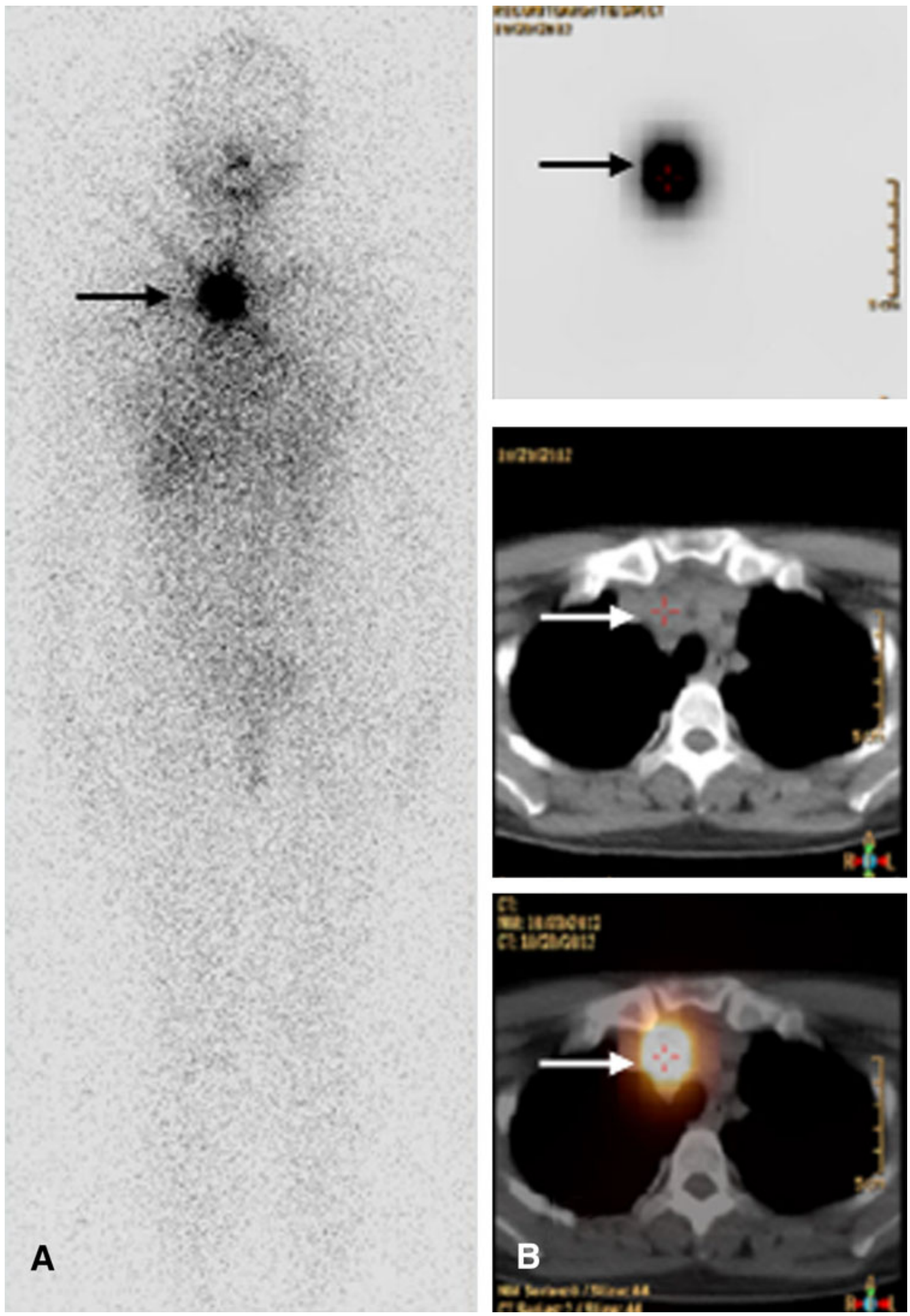


**Fig. 4** Post-therapeutic $^{131}$I WBS showed a single uptake of $^{131}$I in the right upper chest (**a**, *arrow*). It was not clear whether this was bone or lymph node uptake. $^{131}$I SPECT/CT identified and localized the $^{131}$I uptake lesion in the upper mediastinal lymph node (**b**, *arrows*)

focal uptake caused by benign tumors or liver metastases [37].

Radioiodine uptake in the above-mentioned sites of may simulate skeletal metastases in the lumbar spine or pelvic bones, and $^{131}$I SPECT/CT improves reader confidence in interpretation by setting the focal activity seen on planar images in a clear anatomical context and accurately characterizing the uptake [4].

$^{131}$I SPECT/CT may also distinguish Meckel's diverticulum (which may manifest as focal radioiodine uptake in the abdomen because of active transport by ectopic gastric mucosa) [38], inguinal hernia that contains a loop of small bowel and serous cavities, and simple epithelial cysts of renal and ovarian origin accumulating radioiodine as a result of passive diffusion [4].

### Bone metastases

After the lungs, the skeleton is the second most common site of distant metastases in patients with DTC and $^{131}$I SPECT/CT can play an important role in the accurate diagnosis and characterization of bone metastases. Focal radioiodine activity in bone can occur at any site and needs to be distinguished from skin contamination or adjacent skin and soft-tissue involvement. Although techniques such as additional views, delayed imaging, and washing the skin may be helpful, $^{131}$I SPECT/CT can rapidly localize activity to bone to confirm the diagnosis. Recently, Qiu et al. [39] demonstrated that $^{131}$I SPECT/CT and $^{18}$F-FDG PET/CT were superior to $^{99m}$Tc-MDP bone scintigraphy for the detection of DTC bone metastases in patient-based and lesion-based analyses. $^{131}$I SPECT/CT seemed to show similar diagnostic accuracy to $^{18}$F-FDG PET/CT in the patient-based analysis but a superior performance in lesion-based analysis [39].

### Rare sites of metastases

In patients with DTC, metastases to the brain, breast, liver, kidney, muscle, and skin are rare or relatively rare. Nevertheless, distinguishing rare metastases from DTC has a significant impact on clinical decision-making and on the prognosis of patients. Thanks to the use of $^{131}$I-SPECT/CT imaging fusion techniques, metastasis in rare sites in DTC is increasingly becoming an incidental finding [40]. For example, the recent literature contains reports of parapharyngeal metastasis [41], erector spinae metastasis [42], ovarian metastasis [43], adrenal metastasis [44], and orbital metastasis [45]. With the popularity of $^{131}$I treatment and the emergence of $^{131}$I SPECT/CT fusion imaging techniques, rare metastases in DTC seem to be increasingly common and may not, therefore, be as rare as once thought (Fig. 5).

## Impact on staging and patient management

Risk stratification and staging, based on clinical findings, histopathological criteria, and morphological and functional imaging, are used to predict the probability of DTC recurrence, treatment failure, and tumor-specific mortality [11–13, 46, 47].

The risk of recurrence increases when uptake of radioiodine outside the thyroid bed is present on the first radioiodine treatment after surgery and $^{131}$I SPECT/CT has been shown to be more accurate than $^{131}$I WBS for the completion of DTC staging and, moreover, for evaluating lymph node involvement during radioiodine ablation [48, 49].

$^{131}$I Tx SPECT/CT was found to allow a gain in information on nodal staging in 35–36.4 % of patients and resulted in new risk stratification in 6.4–25 % [48].

Avram et al. [47] reported that $^{131}$I SPECT/CT changed the staging in 4 % of younger and 25 % of older patients before radioiodine treatment. The authors restaged 320 patients post-total thyroidectomy with $^{131}$I SPECT/CT and changed the staging (from N0 to N+) in 38 % of patients aged under 45 years and in 24 % of patients aged over 45 years. They also demonstrated that pre-ablation radioiodine imaging with SPECT/CT detected regional metastases and distant metastases in 35 % and 8 % of patients, respectively [47].

Avram [46], in a recent review, concluded that risk stratification and staging of patients should not be based solely on clinical and histopathological criteria, but should also include $^{131}$I SPECT/CT imaging to evaluate the presence of regional and distant metastases.

Grewal et al. [21] reported that SPECT/CT changed the risk classification in 7 out of 109 patients (6.5 %), modifying the intensity of their management during the subsequent follow-up. This is not a low percentage, if one considers that radioiodine scan is only one of factors determining the risk classification and that the newest guidelines do not recommend radioiodine treatment in low-risk patients.

Beyond the impact on staging, the utility of $^{131}$I SPECT/CT is defined by its impact on clinical management, which may be changed in 23.5–25 % of patients, as reported by Xue et al. [48] in their recent systematic review on the incremental value of $^{131}$I SPECT/CT.

Depending on the location of the iodine uptake sites, the results of the $^{131}$I SPECT/CT may change a patient's planned treatment, the frequency of surveillance, and the need for additional imaging, laboratory tests or biopsy. $^{131}$I SPECT/CT can also avoid unnecessary $^{131}$I therapy in patients in whom residual and/or metastatic disease has been excluded [46].

Identification of regional and distant metastases prior to $^{131}$I therapy has significant potential to alter patient

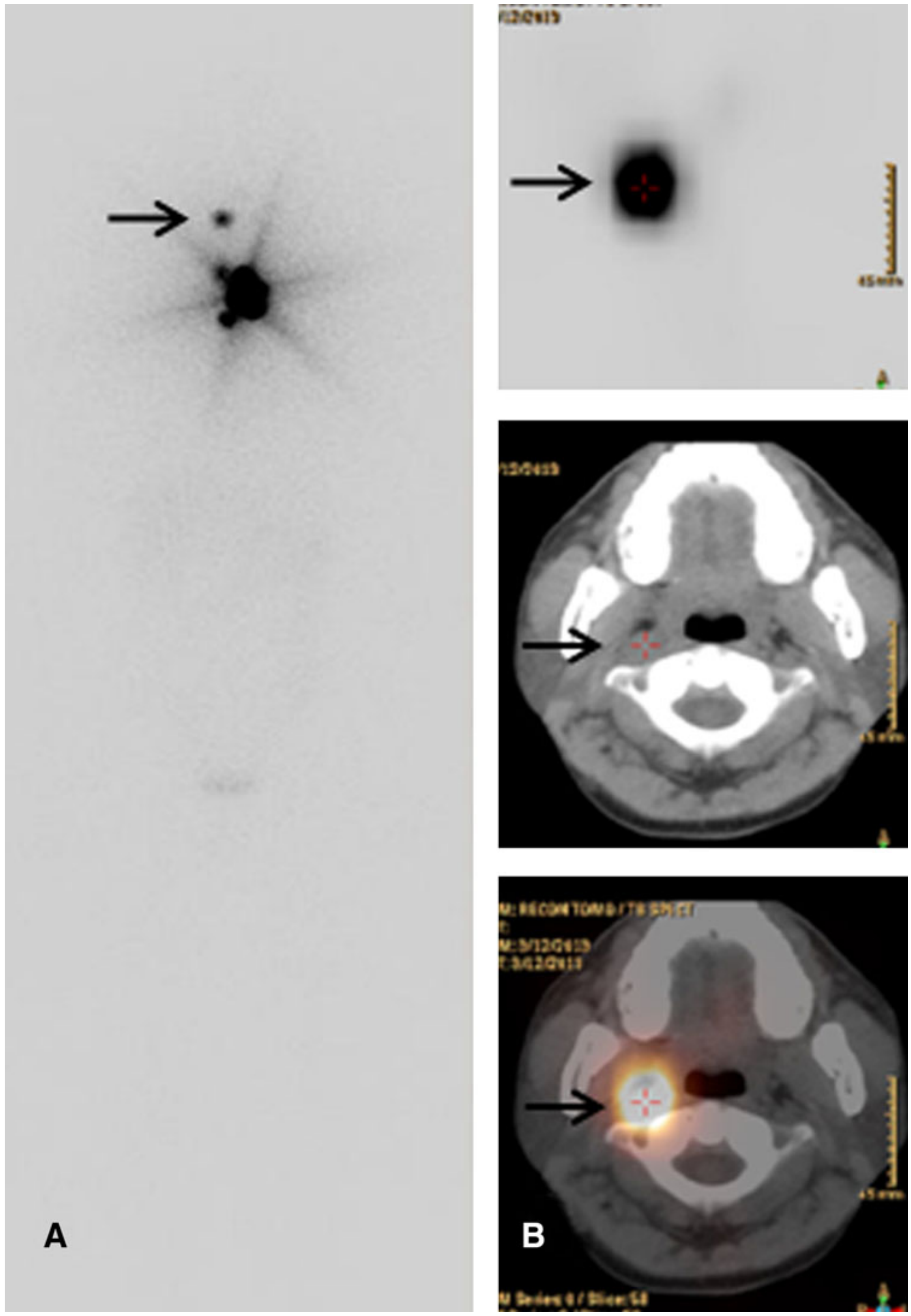


**Fig. 5** Post-therapeutic $^{131}$I WBS detected a focus of $^{131}$I uptake in the right facial region (**a**, *arrow*) in addition to the cervical uptake. $^{131}$I SPECT/CT showed that this focus of $^{131}$I uptake was localized in the right parapharyngeal space (**b**, *arrows*)

management, either by adjusting empirical $^{131}$I activities or by administering activities after dosimetric calculations [46, 48]. In addition, in patients with localized disease the size of the metastasis can be measured by SPECT/CT and this information can be useful in deciding on $^{131}$I therapy (small metastases) vs surgical resection (bulky disease).

Grewall et al. [21] reported that patient management was changed in 20 % of subjects in whom SPECT/CT results reduced the need for additional imaging studies, while Chen et al. [9] conducted 37 SPECT/CT studies in 23 patients with inconclusive foci on WBS and reported a change in management in 34.7 % (8/23) of these cases.

Wong et al. [10] showed that the use of diagnostic $^{131}$I SPECT/CT may lead to both increases and decreases in prescribed doses for initial postoperative $^{131}$I therapy. Prescribing medium or high $^{131}$I activities in high-risk patients can improve patient outcome; conversely, in a younger patient, in whom the risks of radiation may be greater and may extend over a longer time, it can be particularly important to administer a low $^{131}$I activity [2].

## $^{131}$I SPECT/CT for dosimetry

Treatment with $^{131}$I should be aimed at destroying as much of the thyroid carcinoma as possible, with the absorbed dose of radiation in the carcinoma being the best predictor of success of the treatment. However, dosimetric calculations based on planar imaging are hampered by an inability to measure accurately the volumes of the tumor targets, while measurements of absorbed radiation show inherent inaccuracies [50].

The most complete information that can be used to perform accurate quantification in macroscopic tumoral lesions is that derived from SPECT/CT imaging, which allows optimal attenuation correction based on the CT data, scatter correction, and distance-dependent detector response function correction [51]. Fully 3D SPECT/CT imaging yields activity estimates at the voxel level and it is the recommended approach when dosimetry at this level is required.

Flux et al. [52], studying 23 patients receiving 3 GBq $^{131}$I following thyroidectomy, determined the absorbed dose in the voxel with the highest uptake on Tx $^{131}$I SPECT/CT, reporting values ranging from 7 to 570 Gy. The authors found a significant difference in absorbed doses delivered to thyroid remnants between patients who had a successful ablation versus those with a failed ablation.

In patients with distant functioning metastases, dosimetry with SPECT/CT can predict absorbed doses of radiation to the tumor and to the adjacent organs and thus provide a basis for data-based decisions on $^{131}$I therapies. Sisson et al. [53] reported a case of an enlarging metastasis of DTC to the skull that was impinging on the brain and in which dosimetry, enabled by $^{131}$I SPECT/CT, was performed before $^{131}$I treatments. The authors reported that dosimetry indicated delivery, in two treatments, of 1,970 and 2,870 cGy to the tumor and 35 and 42 cGy to the brain, which induced recession of tumor volume, and that the patient was still alive more than 11 years after the diagnosis.

## Limitations of $^{131}$I SPECT/CT

Despite the benefits of $^{131}$I SPECT/CT, this technology has several limitations and disadvantages [10, 21, 46, 47].

First, the low activity administered for $^{131}$I Dx SPECT/CT (111–185 MBq) may lead to poor statistical counting, especially when an iterative reconstruction technique is used. This problem can be corrected with a longer acquisition time, at the expense of greater discomfort for the patient, and with the use of filtered back-projection reconstruction [10].

Second, patient motion during acquisition can cause misregistration of fusion images, also in integrated SPECT/CT cameras; immobilizers could be called for if acquisition time cannot be reduced [10].

Third, the presence of streak artifacts, common with high activity of radioiodine, and attenuation of the neck by the patient' shoulders could give rise to doubts and problems in image interpretation. In these cases the use of a pin-hole collimator and comparison with planar images could be very useful.

Fourth, additional radiation exposure from the CT component of the study (1–4 mSv with each acquisition) should be assessed on a patient-by-patient basis, particularly in the pediatric population [46]. In addition, the spatial resolution of SPECT is limited by the partial-volume effect in small lesions and the method lacks sensitivity for the detection of micrometastatic lesions [46].

The other potential limitation is that although information obtained with diagnostic $^{131}$I SPECT/CT led to changes in staging and management, this may not directly translate into a more favorable outcome [21, 47]. In a slowly growing malignancy such as DTC, assessing the outcome of therapeutic interventions requires prolonged follow-up [21].

Finally, non-iodine-avid disease, which occurs in approximately 30 % of DTC, may remain undetected on SPECT/CT and lead to false negative interpretations [46].

## Conclusion

SPECT/CT is a powerful diagnostic tool that allows accurate anatomical localization and characterization of radioiodine foci and has substantially improved the interpretation of $^{131}$I whole-body scintigraphy.

SPECT/CT may provide an important contribution to the identification of benign or malignant functional thyroid tissue, improving post-operative staging and patient risk stratification, as well as clinical management, in a significant number of patients with DTC.

This improvement in diagnostic performance has been achieved largely thanks to superior anatomical localization of radioactivity and CT-based attenuation correction of functional tomographic images. Moreover, $^{131}$I SPECT/CT can be used to measure volumes of residual tumor and metastases and thus opens the way for highly accurate dosimetry-based $^{131}$I treatments.

**Conflict of interest** Yan-Li Xue, Zhong-Ling Qiu, Germano Perotti, Massimo Salvatori, Quan-Yong Luo declare that they have no conflict of interest related to the publication of this article.

## References

1. Davies L, Welch HG (2006) Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA 295:2164–2167

2. Cooper DS, Doherty GM, Haugen BR et al (2006) Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 16:109–142
3. Haugen BR, Lin EC (2001) Isotope imaging for metastatic thyroid cancer. Endocrinol Metab Clin North Am 30(2):469–492
4. Glazer DI, Brown RK, Wong KK, Savas H, Gross MD, Avram AM (2013) SPECT/CT evaluation of unusual physiologic radioiodine biodistributions: pearls and pitfalls in imaging interpretation. Radiographics 33:397–418
5. Even-Sapir E, Keidar Z, Sachs J, Engel A, Bettman L, Gaitini D et al (2001) The new technology of combined transmission and emission tomography in evaluation of endocrine neoplasms. J Nucl Med 42:998–1004
6. Yamamoto Y, Nishiyama Y, Monden T, Matsumura Y, Satoh K, Ohkawa M (2003) Clinical usefulness of fusion of $^{131}$I SPECT and CT images in patients with differentiated thyroid carcinoma. J Nucl Med 44:1905–1910
7. Tharp K, Israel O, Hausmann J, Bettman L, Martin WH, Daitzchman M, Sandler MP, Delbeke D (2004) Impact of $^{131}$I-SPECT/CT images obtained with an integrated system in the follow-up of patients with thyroid carcinoma. Eur J Nucl Med Mol Imaging 31:1435–1442
8. Ruf J, Lehmkuhl L, Bertram H, Sandrock D, Amthauer H, Humplik B, Munz DL, Felix R (2004) Impact of SPECT and integrated low-dose CT after radioiodine therapy on the management of patients with thyroid carcinoma. Nucl Med Commun 25:1177–1182
9. Chen LB, Luo QY, Shen Y, Yu YL, Yuan ZB, Lu HK, Zhu RS (2008) Incremental value of $^{131}$I SPECT/CT in the management of patients with differentiated thyroid carcinoma. J Nucl Med 49:1952–1957
10. Wong KK, Zarzhevsky N, Cahill JM, Frey KA, Avram AM (2008) Incremental value of diagnostic $^{131}$I SPECT/CT fusion imaging in the evaluation of differentiated thyroid carcinoma. AJR Am J Roentgenol 191:1785–1794
11. Kohlfuerst S, Igerc I, Lobnig M, Gallowitsch HJ, Gomez-Segovia I, Matschnig S, Mayr Z, Mikosch P, Beheshti M, Lind P (2009) Posttherapeutic $^{131}$I SPECT-CT offers high diagnostic accuracy when the findings on conventional planar imaging are inconclusive and allows a tailored patient treatment regimen. Eur J Nucl Med Mol Imaging 36:886–893
12. Spanu A, Solinas ME, Chessa F, Sanna D, Nuvoli S, Madeddu G (2009) $^{131}$I SPECT/CT in the follow-up of differentiated thyroid carcinoma: incremental value versus planar imaging. J Nucl Med 50:184–190
13. Schmidt D, Szikszai A, Linke R, Bautz W, Kuwert T (2009) Impact of $^{131}$I SPECT/spiral CT on nodal staging of differentiated thyroid carcinoma at the first radioablation. J Nucl Med 50:18–23
14. Aide N, Heutte N, Rame JP, Rousseau E, Loiseau C, Amar MH, Bardet S (2009) Clinical relevance of single-photon emission computed tomography/computed tomography of the neck and thorax in postablation $^{131}$I scintigraphy for thyroid cancer. J Clin Endocrinol Metab 94:2075–2084
15. Blum M, Tiu S, Chu M, Goel S, Friedman K (2011) I-131 SPECT/CT elucidates cryptic findings on planar whole-body scans and can reduce needless therapy with I-131 in post-thyroidectomy thyroid cancer patients. Thyroid 21:1235–1247
16. Ciappuccini R, Heutte N, Trzepla G, Rame JP, Vaur D, Aide N, Bardet S (2011) Postablation $^{131}$I scintigraphy with neck and thorax SPECT-CT and stimulated serum thyroglobulin level predict the outcome of patients with differentiated thyroid cancer. Eur J Endocrinol 164:961–969
17. Wakabayashi H, Nakajima K, Fukuoka M, Inaki A, Nakamura A, Kayano D, Kinuya S (2011) Double-phase $^{131}$I whole body scan and $^{131}$I SPECT-CT images in patients with differentiated thyroid cancer: their effectiveness for accurate identification. Ann Nucl Med 25:609–615
18. Filetti S, Bidart JM, Arturi F, Caillou B, Russo D, Schlumberger M (1999) Sodium/iodide symporter: a key transport system in thyroid cancer cell metabolism. Eur J Endocrinol 141(5):443–457
19. Chung JK (2002) Sodium iodide symporter: its role in nuclear medicine. J Nucl Med 43(9):1188–1200
20. Wong KK, Zarzhevsky N, Cahill JM, Frey KA, Avram AM (2009) Hybrid SPECT-CT and PET-CT imaging of differentiated thyroid carcinoma. Br J Radiol 82:860–876
21. Grewal RK, Tuttle RM, Fox J et al (2010) The effect of post-therapy 131-I SPECT/CT on risk classification and management of patients with differentiated thyroid cancer. J Nucl Med 51(9):1361–1367
22. Mustafa M, Kuwert T, Weber K et al (2010) Regional lymph node involvement in T1 papillary thyroid carcinoma: a bicentric prospective SPECT/CT study. Eur J Nucl Med Mol Imaging 37(8):1462–1466
23. Schmidt D, Linke R, Uder M, Kuwert T (2010) Five months' follow-up of patients with and without iodine-positive lymph node metastases of thyroid carcinoma as disclosed by (131)I-SPECT/CT at the first radioablation. Eur J Nucl Med Mol Imaging 37(4):699–705
24. Boxen I, Zhang ZM (1990) Nasal secretion of iodine-131. Clin Nucl Med 15(9):610–611
25. Norby EH, Neutze J, Van Nostrand D, Burman KD, Warren RW (1990) Nasal radioiodine activity: a prospective study of frequency, intensity, and pattern. J Nucl Med 31(1):52–54
26. Herzog G, Kisling G, Bekerman C (1992) Diagnostic significance of dental history in the clinical evaluation of patients with thyroid carcinoma: periodontal surgery mimicking a metastasis on I-131 whole body survey. Clin Nucl Med 17(7):589–590
27. Ain KB, Shih WJ (1994) False-positive I-131 uptake at a tracheostomy site: discernment with Tl-201 imaging. Clin Nucl Med 19(7):619–621
28. Kipper MS, Krohn LD (1996) Increased submandibular gland uptake on thyroid scintigraphy due to Wharton's duct stone. Clin Nucl Med 21(11):881–882
29. Haveman JW, Phan HT, Links TP, Jager PL, Plukker JT (2005) Implications of mediastinal uptake of 131-I with regard to surgery in patients with differentiated thyroid carcinoma. Cancer 103(1):59–67
30. Ahlgren L, Ivarsson S, Johansson L, Mattsson S, Nosslin B (1985) Excretion of radionuclides in human breast milk after the administration of radiopharmaceuticals. J Nucl Med 26(9):1085–1090
31. Mountford PJ, Coakley AJ (1989) A review of the secretion of radioactivity in human breast milk: data, quantitative analysis and recommendations. Nucl Med Commun 10(1):15–27
32. Hammami MM, Bakheet S (1996) Radioiodine breast up-take in nonbreastfeeding women: clinical and scintigraphic characteristics. J Nucl Med 37(1):26–31
33. White JE, Flickinger FW, Morgan ME (1990) I-131 accumulation in gastric pull-up simulating pulmonary metastases on total-body scan for thyroid cancer. Clin Nucl Med 15(11):809–810
34. Davidson J, McDougall IR (2000) How frequently is the thymus seen on whole-body iodine-131 diagnostic and post-treatment scans? Eur J Nucl Med 27(4):425–430
35. Geatti O, Shapiro B, Orsolon PG, Mirolo R, Di Donna A (1994) An unusual false-positive scan in a patient with pericardial effusion. Clin Nucl Med 19(8):678–682
36. Bakheet SM, Hammami MM, Powe J (1996) False-positive radioiodine uptake in the abdomen and the pelvis: radioiodine retention in the kidneys and review of the literature. Clin Nucl Med 21(12):932–937

37. Omür O, Akgün A, Ozcan Z, Sen C, OzkiIiç H (2009) Clinical implications of diffuse hepatic uptake ob-served in postablative and post-therapeutic I-131 scans. Clin Nucl Med 34(1):11–14
38. Caplan RH, Gundersen GA, Abellera RM, Kisken WA (1987) Uptake of iodine-131 by a Meckel's diverticulum mimicking metastatic thyroid cancer. Clin Nucl Med 12(9):760–762
39. Qiu ZL, Xue YL, Song HJ, Luo QY (2012) Comparison of the diagnostic and prognostic values of 99mTc-MDP-planar bone scintigraphy, 131I-SPECT/CT and 18F-FDG-PET/CT for the detection of bone metastases from differentiated thyroid cancer. Nucl Med Commun 33:1232–1242
40. Song HJ, Xue YL, Xu YH, Qiu ZL, Luo QY (2011) Rare metastases of differentiated thyroid carcinoma: pictorial review. Endocr Relat Cancer 18(5):R165–R174
41. Qiu ZL, Xu YH, Song HJ, Luo QY (2011) Localization and identification of parapharyngeal metastases from differentiated thyroid carcinoma by $^{131}$I-SPECT/CT. Head Neck 33(2):171–177
42. Qiu ZL, Luo QY (2009) Erector spinae metastases from differentiated thyroid cancer identified by I-131 SPECT/CT. Clin Nucl Med 34(3):137–140
43. Xu YH, Huang XM, Song HJ, Qiu ZL, Luo QY (2011) $^{131}$I-SPECT/CT found an ovarian metastasis covered by iliac metastasis on $^{131}$I whole-body scan in a patient with papillary thyroid carcinoma. Clin Nucl Med 36(5):363–364
44. Xue YL, Song HJ, Qiu ZL, Luo QY (2012) An unusual $^{131}$I-avid adrenal metastasis from follicular thyroid carcinoma identified by $^{131}$I-SPECT/CT. Clin Nucl Med 37(9):e229–e230
45. Rocha Filho FD, Lima GG, Ferreira FV, Lima MG, Hissa MN (2009) Orbital metastasis as primary clinical manifestation of thyroid carcinoma—case report and literature review. Arg Bras Endocrinol Metabol 52:1497–1500
46. Avram AM (2012) Radioiodine scintigraphy with SPECT/CT: an important diagnostic tool for thyroid cancer staging and risk stratification. J Nucl Med 53:754–764
47. Avram AM, Fig LM, Frey KA, Gross MD, Wong KK (2013) Preablation $^{131}$I scans with SPECT/CT in postoperative thyroid cancer patients: what is the impact on staging? J Clin Endocrinol Metab 98:1163–1171
48. Xue YL, Qiu ZL, Song HJ, Luo QY (2013) Value of 131I SPECT/CT for the evaluation of differentiated thyroid cancer: a systematic review of the literature. Eur J Nucl Med Mol Imaging 40:768–778
49. Maruoka Y, Abe K, Baba S, Isoda T et al (2012) Incremental diagnostic value of SPECT/CT with 131I scintigraphy after radioiodine therapy in patients with well-differentiated thyroid carcinoma. Radiology 265:902–909
50. Van Nostrand D, Atkins F, Yeganeh F, Acio E, Bursaw R, Wartofsky L (2002) Dosimetrically determined doses of radioiodine for the treatment of metastatic thyroid carcinoma. Thyroid 12(2):121–134
51. Bardiès M, Buvat I (2011) Dosimetry in nuclear medicine therapy: what are the specifics in image quantification for dosimetry? Q J Nucl Med Mol Imaging 55(1):5–20
52. Flux GD, Haq M, Chittenden SJ, Buckley S, Hindorf C, Newbold K, Harmer CL (2010) A dose-effect correlation for radioiodine ablation in differentiated thyroid cancer. Eur J Nucl Med Mol Imaging 37(2):270–275
53. Sisson JC, Dewaraja YK, Wizauer EJ, Giordano TJ, Avram AM (2009) Thyroid carcinoma metastasis to skull with infringement of the brain: treatment with radioiodine. Thyroid 19:297–303