Technetium-99m-pertechnetate whole-body SPET/CT scan in thyroidectomized differentiated thyroid cancer patients is a useful imaging modality in detecting remnant thyroid tissue, nodal and distant metastases before ^{131}I therapy. A study of 416 patients

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Abstract

Objectives: In this study we aimed to evaluate the role of technetium-99m pertechnetate whole body scan (^{99m}Tc WBS) with single photon emission tomography/computed tomography (SPET/CT) in detecting remnant thyroid tissue, nodal and distant metastases, in differentiated thyroid cancer (DTC) patients before radioiodine (^{131}I) therapy. **Subjects and Methods:** A retrospective analysis was performed in 416 pathologically confirmed DTC patients with total/near-total thyroidectomy. All patients had undergone ^{99m}Tc WBS, followed by ^{131}I therapy and post therapy scans, under thyroid hormone withdrawal protocol. Eighteen patients had an additional ^{99m}Tc SPET/CT of certain lesions. Foci of uptake on the ^{99m}Tc WBS and when indicated additional foci on the SPET/CT scan were assessed and compared with findings from post-therapy ^{131}I scans study which served as gold standard. **Results:** The ^{99m}Tc WBS showed a sensitivity and positive predictive value of 79% and 100%, respectively, for remnant thyroid tissue detection, while 60% and 98%, respectively for metastatic lymph nodes evaluation. High specificity (99%) and negative predictive value (93%) but low sensitivity (37%) was found in detecting distant metastases. By adding ^{99m}Tc WBS to ^{99m}Tc SPET/CT findings, 2/18 patients were confirmed as false-positive. **Conclusion:** Our findings suggested that ^{99m}Tc WBS is a useful imaging modality in detecting remnant thyroid tissue, nodal and distant metastases before ^{131}I therapy. The additional SPET/CT scan when needed in 18 cases supported the ^{99m}Tc WBS diagnosis

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Introduction

Thyroid cancer is the most common malignant tumor in the endocrine system. It ranks the 10th highest incidence of cancer in China with an increase of four times in the past ten years [1]. Differentiated thyroid cancer (DTC) accounts for about 90% of all thyroid cancers [2]. Total thyroidectomy, iodine-131 (^{131}I) therapy, and thyroid stimulating hormone (TSH) suppression are well established treatments for thyroid carcinoma [3-5].

However, the standard process for ^{131}I therapy after thyroidectomy has not been sufficiently studied. A pre-radioiodine therapy evaluation with a whole body scan (WBS) with low dose of ^{131}I may be inconclusive in cases of a stunning thyroid [6, 7]. Iodine-125 (^{125}I) has shown improved quality of imaging compared with 131I, but it is expensive and lacks of supply.

An alternative imaging agent is techetium-99m pertechnetate (^{99m}Tc O_4^-), which is inexpensive, immediately available, widely used in evaluating the remnant tissues in patients with DTC but in a few studies with inconsistent results [8-10]. Single-photon emission tomography/computed tomography (SPET/CT) of certain lesions on ^{99m}Tc scan has been shown to potentially change the management strategy in part of post-surgical patients with DTC [11, 12], but more data are needed for verification.

The purpose of this study is to evaluate the role of ^{99m}Tc WBS supplemented with SPET/CT prior to ^{131}I therapy in the assessment of remnant thyroid tissues and metastases.

Subjects and Methods

Study population

A total of 416 pathologically confirmed DTC patients (152 male, 264 female; mean age±SD, 45.2±12.8y; 409 papillary cancers, 7 follicular cancers) were collected from January 2014 to January 2017 in our hospital. All patients underwent total/near-total thyroidectomy, with/without lymph nodal dissection followed by ^{131}I therapy under hormone withdrawal protocol with TSH＞30mU/L. All patients had ^{99m}Tc WBS before radioiodine therapy. Eighteen patients with equivocal radioactive uptake areas in ^{99m}Tc-WBS underwent an additional SPET/CT. After ^{131}I therapy, all patients underwent post therapy ^{131}I WBS, supplemented with SPET/CT of the neck and chest. The study was approved by our intuitional IRB.

^{99m}Tc pertechnetate whole body scan

The ^{99m}Tc WBS was obtained 10-20 min after intravenous injection of 370MBq of ^{99m}Tc (Shanghai GMS Pharmaceutical Co., Ltd, Shanghai, China). Images were captured by Philips Precedence SPET/CT (Philips Medical Systems, Bothell, Wisconsin, USA). The gamma camera was fitted with low-energy and high-resolution collimators. A 512×1024 matrix was used matching a 140keV photo peak with a symmetrical 20% windows.

Post ^{131}I therapy whole body scans

Iodine-131 was provided by Shanghai GMS Pharmaceutical Co., Ltd, Shanghai, China. Iodine-131 dose for therapy ranged from 1480-7400MBq among the patients. Post-therapy ^{131}I WBS was performed in 2-4 days after therapy, captured by Philips Precedence SPET/CT (Philips Medical Systems, Bothell, Wisconsin, USA) with a gamma camera fitted with high-energy and high-resolution collimators. The photo peak was 364keV. A 512×1024 matrix with a symmetrical 20% window was used. Iodine-131 SPET/CT from neck to chest was performed for all patients in 4 days after the therapy, with additional scan of lesions with abnormal radioactive uptake.

Image interpretation

The ^{99m}Tc WBS and post ^{131}I therapy images were evaluated qualitatively (positive or negative) by two experienced nuclear medicine physicians. A clearly visible focus of uptake was defined as positive. A positive focus limited to the thyroid bed was labeled as remnant thyroid tissue (Figure 1), while the positive focus outside the thyroid bed was labeled as nodal or distant metastases (Figure 2). Performance of the pre-therapy ^{99m}Tc WBS in detecting the lesions was compared with the post ^{131}I therapy images which served as the gold standard.

Statistical analysis

Sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and accuracy (ACC) of ^{99m}Tc WBS for detecting remnant tissue, nodal and distant metastases were calculated respectively and then were compared with those on post therapy ^{131}I scans by using the standard R×C table of diagnostic test.

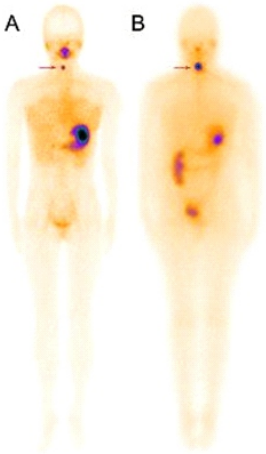

Figure 1. A representative case of remnant thyroid tissues (A: ^{99m}Tc WBS; B: post ^{131}I therapy WBS) which shows a focal uptake corresponding to remnant tissue in the thyroid bed (red arrow).

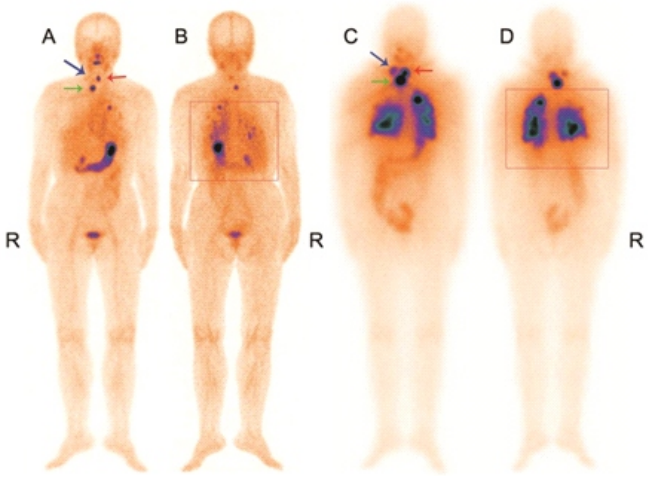

Figure 2. A representative case of remnant thyroid tissue, nodal and distant metastases (A and B: ^{99m}Tc WBS; C and D: post ^{131}I therapy WBS) which shows activity in the lung field (red outline) representing lung metastases, with remnant tissues (red arrow) and nodal metastases (blue and green arrows).

Results

A total of 416 consecutive DTC patients who had undergone pre therapy ^{99m}Tc WBS, ^{131}I therapy, and post ^{131}I therapy WBS were included in this research. Results were analyzed on per-patient basis in different regions (remnant thyroid, lymph nodal and distant metastases).

In terms of remnant thyroid tissue detection (Table 1), all patients had positive scans on the post ^{131}I therapy WBS. Of them, 328 (79%) had the same positive results on the pre therapy ^{99m}Tc WBS, while 88 (21%) were negative. The Se, PPV and ACC of the pre therapy ^{99m}Tc WBS were 79%, 100%, 79% respectively.

In terms of lymph nodal metastases, Se, Sp, PPV, NPV and ACC of the pre therapy ^{99m}Tc WBS were 60%, 99%, 98%, 82% and 86%, respectively. Similarly, for distant metastases evaluation, the ^{99m}Tc WBS showed a Se of 37%, but a high Sp of 99%

NPV of 93%, and ACC of 93% for detection of distant metastases of DTC (Table 1).

Table 1. *Performance of ^{99m}Tc WBS for detecting remnant thyroid tissue, nodal and distant metastases in comparison with post ^{131}I therapy scan.*

^{99m}Tc WBS		^{131}I scans (+)	^{131}I scans (-)	Total 416
Remnant thyroid tissues	(+)	328	0	328
	(-)	88	0	88
Nodal metastases	(+)	90	2	92
	(-)	59	265	324
Distant metastases	(+)	16	3	19
	(-)	27	370	397

(+) positive, (-) negative.

Eighteen out of one hundred eleven (16%) patients had undergone the additional ^{99m}Tc SPET/CT WBS for equivocal radioactive uptake areas, mainly in the neck, mediastinum and apex pulmonis (Table 2). The results showed that two patients were positive for lesions in mediastinum by ^{99m}Tc WBS, while both had physiological uptake on the esophagus (Figure 3). The other patients were confirmed with postoperative residual metastases.

Table 2. *Performance of ^{99m}Tc SPET/CT for patients with equivocal lesions area by ^{99m}Tc WBS.*

Lesions	No. of patients
Remnant thyroid tissue	2
Cervical nodal metastases	6
Mediastinum nodal metastases	4
Physiological uptake of esophagus	2
Lung metastases	2
Bone metastases	2

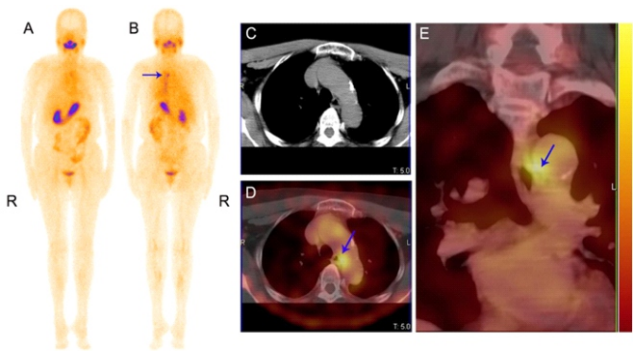

Figure 3. A representative case of abnormal radioactive uptake lesions in the mediastinum (A, B: ^{99m}Tc WBS; C, D and E: ^{99m}Tc SPET/CT) which show activity in esophagus (blue arrows) representing physiological uptake.

Discussion

Remnant thyroid tissues are commonly existed in post-thyroidectomy patients with DTC. Iodine-131 therapy is considered for patients of intermediate or high risk, after total thyroidectomy by American Thyroid Association. An effective pre ^{131}I therapy imaging evaluation is needed to guide the ind-ividualized treatment of these patients. In this study, we evaluated ^{99m}Tc WBS SPET/CT in detecting remnant thyroid tissues and metastases before radioiodine therapy.

Compared with the findings of remnant thyroid tissues on post ^{131}I therapy scans (serving as gold standard), the results of ^{99m}Tc WBS showed that the sensitivity and accuracy were lower than those of another reported study [13]. This could be related to the rapid washout of ^{99m}Tc, or to the small size of the remnant. Future work will evaluate whether early imaging (less than 10 minutes after injection) could increase the sensitivity and accuracy and decrease the false negative rate.

Lymph nodal metastases are a risk factor for increased recurrence and decreased survival rate of patients with DTC [14, 15]. As shown in Table 1, pre-therapy ^{99m}Tc WBS had a high specificity and PPV in detecting lymph nodal metastases but with a sensitivity of 60%, which means that it may miss 40% of patients with nodal metastases. Different from post ^{131}I therapy scan, in our study, the SPET/CT portion of ^{99m}Tc was only applied to patients with equivocal radioactive uptake areas in the post treatment ^{131}I WBS. This may explain the relatively low sensitivity for cervical nodal metastases detection of the ^{99m}Tc WBS in comparison with the ^{131}I WBS. We consider adding ^{99m}Tc SPET/CT of the neck in our practice, in order to test this hypothesis that may improve the sensitivity for cervical node detection.

Similarly, ^{99m}Tc WBS showed high specificity and negative predictive value with a low sensitivity for detecting distant metastases. The low sensitivity of our study differs from several previously published studies in which a relatively small number of patients with distant metastases were studied by ^{99m}Tc WBS SPET/CT [16, 17]. This difference could be related to different patient populations and metastases on different organs. Further studies are needed to confirm the role of ^{99m}Tc WBS on the basis of different metastases sites. Nevertheless, our results showed that ^{99m}Tc WBS may miss some of the distant metastatic lesions, which is critical for nuclear medicine physicians in interpreting the imaging findings.

In eighteen cases with additional ^{99m}Tc SPET/CT scan, two of them were prevented from over-treatment by ^{131}I therapy.

In conclusion, our results showed that in DTC patients after thyroidectomy, a pre ^{131}I therapy with ^{99m}Tc WBS SPET/CT had an acceptable sensitivity for detecting remnant thyroid tissue and regional nodal metastases and also a high specificity. For detecting distant metastases this scan showed a relatively low sensitivity. Given its low price and availability compared with ^{123}I and having no stunning effect compared with ^{131}I, ^{99m}Tc was an alternative tracer for pre ^{131}I therapy evaluation, also considering that the majority of thyroid cancers are detected at early stages without distant metastases. The time of performing the ^{99m}Tc WBS SPET/CT scan may further

improve its diagnostic accuracy.

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The authors declare that they have no conflicts of interest.

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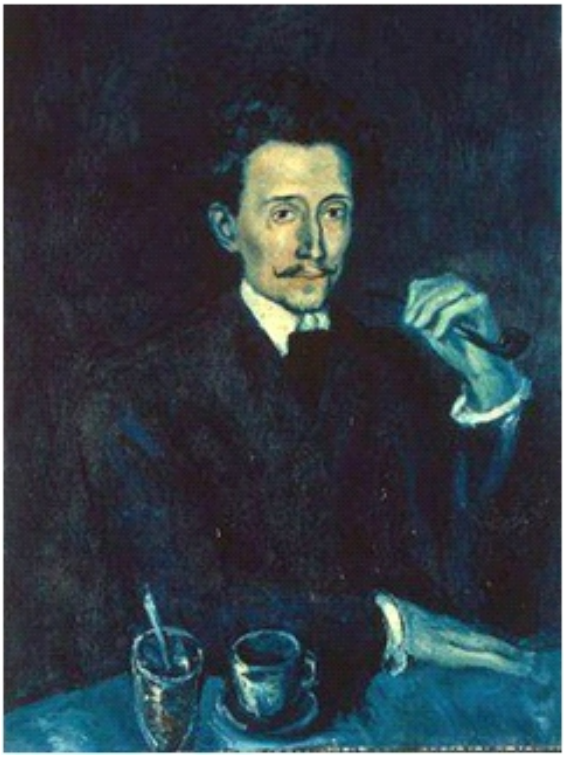

Pablo Picasso. Portrait of Benet Soler (1903). Oil in canvas. 100x71cm.