

The value of scintigraphy, computed tomography, magnetic resonance imaging, and single-photon emission computed tomography/computed tomography for the diagnosis of ectopic thyroid in the head and neck

A STROBE-compliant retrospective study

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Abstract

Because of its rarity, the exact imaging features of ectopic thyroid are poorly known.

To analyze the value of scintigraphy, computed tomography (CT), magnetic resonance imaging (MRI), and single-photon emission computed tomography (SPECT)/CT in the diagnosis of ectopic thyroid in the head and neck.

First, we retrospectively analyzed the scintigraphy, CT, MRI, and SPECT/CT images from 25 masses (22 patients) suspected of head and neck ectopic thyroid from 2006 to 2017 at the Shanghai Ninth People's Hospital. Each mass was imaged by nuclear imaging (scintigraphy with or without SPECT/CT) and radiological exam (CT and/or MRI). Pathological examination was considered as the gold standard. Secondly, thirteen malignant ectopic thyroids in the head and neck reported in the English literature from 2001 to 2017 were retrieved for comparison.

The accuracy of scintigraphy was not significantly higher than that of CT (94.7%, vs 89.5%, $P > .99$) or MRI (92.3%, vs 84.6%, $P > .99$). Five masses which underwent scintigraphy with SPECT/CT were all true positive, while 1 was false negative on MRI, and 2 were false negative on CT. Compared to the benign ectopic thyroids in our study, the 13 malignant ectopic thyroids retrieved from the literature were grossly the same in shape, margins, and invasion on CT or MRI.

The number of patients was limited, but scintigraphy combined with SPECT/CT could be a reliable method for the diagnosis of ectopic thyroid. Benign and malignant ectopic thyroids appear to be similar in shapes, margins, and invasion on CT or MRI.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, PET/CT = positron emission tomography/computed tomography, SPECT/CT = single-photon emission computed tomography/computed tomography.

Keywords: computed tomography, ectopic thyroid, magnetic resonance imaging, scintigraphy, single-photon emission computed tomography/computed tomography

1. Introduction

Ectopic thyroid is uncommon, with a reported prevalence in the range of 1 per 100,000 to 300,000 in the general population, but the prevalence is higher in patients with thyroid diseases, ranging

from 1 in 4000 to 8000 patients.^[1] Lingual thyroid is the most common site and found in 90% of ectopic thyroid cases. Other locations of ectopic thyroid in head and neck are rare, but they may present like lymph nodes with metastatic disease, submandibular tumors, inflammatory lesions, branchial cleft cysts and lymphadenopathy of various etiologies.^[2] Asymptomatic euthyroid patients with ectopic thyroid do not usually require therapy but are kept under observation.^[1] Surgical intervention for an ectopic thyroid is recommended when severe obstructive symptoms, bleeding, ulceration, cystic degeneration, and malignancy occur.

As is reported in the literature, ultrasonography, scintigraphy, computed tomography (CT), and magnetic resonance imaging (MRI) are valuable modalities used to detect an ectopic thyroid.^[3] CT is better to discriminate hard tissues, while MRI is better in soft tissues. Scintigraphy is based on the uptake of isotopes and usually reflect the metabolic rate of a lesion. Nevertheless, misdiagnoses are still common when based on scintigraphy, CT, or MRI because of the low prevalence of the disease. Recently, some studies^[4–7] indicated that single-photon emission computed tomography (SPECT)/CT could be a useful tool to detect ectopic thyroids. Indeed, benign and malignant thyroid can take up

Editor: Gaurav Malhotra.

The authors report no conflicts of interest.

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Medicine (2018) 97:13(e0239)

Received: 12 November 2017 / Received in final form: 27 February 2018 /

Accepted: 1 March 2018

<http://dx.doi.org/10.1097/MD.00000000000010239>

tracers ($^{99m}\text{TcO}_4^-$, ^{131}I , or ^{123}I)^[8–12] and some benign ectopic lingual thyroids can be disguised as thyroid cancer metastases on scintigraphy.^[13] Nevertheless, because of the rarity of ectopic thyroid, the exact imaging features are still poorly known. In addition, it is unclear whether there were some differences between benign and malignant ectopic thyroid among different imaging modalities.

Therefore, the aim of the present study was to analyze the value of scintigraphy, CT, MRI, and SPECT/CT in the diagnosis of ectopic thyroid in a relatively large series of cases (16 confirmed masses in 13 patients). Since carcinoma arising from ectopic thyroid is extremely rare, with an incidence of only 1%,^[10] and all of the 16 ectopic thyroids in the present study were benign, we reviewed the reports of malignant ectopic thyroids in the head and neck that were examined using CT and/or MRI in the English literature during the 2001 to 2017 period for comparison.

2. Materials and methods

This retrospective study was approved by the institutional review board of our hospital. Written informed consent was waived for the use of patients' medical and imaging data. All of the patients' information was anonymized prior to the analysis.

2.1. Patients

This was a retrospective analysis of the images of 25 masses (22 patients) which were suspected to be ectopic thyroid by head and neck evaluation at the Department of Oral & Maxillofacial - Head & Neck Oncology during the period 2006 to 2017. The inclusion criteria were: suspicion of ectopic thyroid, available imaging data (at least 1 nuclear imaging and 1 radiological imaging), and available pathological examination. The patients were excluded if the patient had a history of thyroidectomy or thyroid treatment before imaging. All pathological diagnoses were performed by 2 pathologists with 10 to 15 years of experience. All masses were examined within 4.1 ± 1.9 days of surgery or biopsy.

Because no case of malignant ectopic thyroid was found at our center, the English literature was reviewed to analyze the cases of malignant ectopic thyroids in head and neck that underwent CT and/or MRI from 2001 to 2017. PubMed was searched using the keywords "ectopic thyroid" and "malignant". Retrieved literature was examined manually. Reference lists were scanned to identify additional studies. A total of 13 malignant ectopic thyroids were selected for comparison.^[8–12,14–21]

2.2. Scintigraphy and SPECT/CT

An Infinia Hawkeye SPECT/CT (GE Medical system, Haifa, Israel) was used for scintigraphy. Twenty patients were injected with 111–185 MBq (3–5 mCi) of $^{99m}\text{TcO}_4^-$ intravenously 20 min before imaging. Another 2 patients were orally administered 3.7 or 5.5 MBq (100 or 150 μCi) of ^{131}I 48 h before imaging. The scan parameters were: low-energy high resolution collimators for $^{99m}\text{TcO}_4^-$ imaging, and high-energy general purpose for ^{131}I imaging; and total time of 5 min using body contour (256 \times 256 matrix). The imaging was completed with a spot view from the base of skull to the upper mediastinum in anterior projections. SPECT/CT was performed in 5 patients (5 masses) during the same session as scintigraphy with the patient in the same position. A SPECT study with a matrix of 128 \times 128 was acquired; zoom factor of 1.2 to 1.5, according to the individual patient; and a

rotation of 360° (180° per head) 30-s images (1 image every 6°). The CT was acquired in helical mode with a matrix of 512 \times 512 and energy of 2.5 mA and 140 kV.

2.3. CT and MRI

All CT images were obtained with a Lightspeed 16 (GE Healthcare, Waukesha, WI, USA) after scintigraphy. The scan parameters were: 5-mm slice thickness reconstructions; 23-cm field of view (FOV); 120 kV voltage; 200 to 300 mA current; and 256 \times 256 matrix. A total of 80 mL of iopamidol (Iopamiro, Bracco, Milan, Italy) was administered into an antecubital vein at 2.5 mL/s with a power injector. Enhanced CT scans were started 50–60 s after the administration of the contrast agent.

MRI images were obtained with a Signa 1.5T MRI unit (GE Healthcare, Waukesha, WI, USA) with head and neck coil. The MRI protocol contained an unenhanced axial T1-weighted (TR/TE, 600/11 ms) spin-echo sequences, axial or sagittal T2-weighted (TR/TE, 4700/85 ms) fast spin-echo sequences, and enhanced axial or sagittal T1-weighted (TR/TE, 600/11 ms) sequences. An intravenous dose of 0.1 mmol/kg of contrast agent (gadolinium-DTPA; Magnevist; Bayer HealthCare Pharmaceuticals, Montville, NJ, USA) had been administered for enhanced MRI imaging. Images were obtained with FOV of 20 to 24 cm, 3 acquisitions, matrixes of 256 \times 256, and section thicknesses of 5 mm.

2.4. Image analysis

Scintigraphy images were interpreted by 2 nuclear medicine physicians (A.C.G. and Y.F.P, with 10 and 8 years experience in nuclear medicine, respectively) who were blinded to clinical data and other images. If a consensus could not be reached, a third nuclear medicine physician could be consulted. CT images were interpreted by 2 dedicated head and neck radiologists (M.D.J. and G.X.Y., with 10 and 7 years experiences in radiology, respectively) who were blinded to clinical data and other images. If a consensus could not be reached, a third radiologist could be consulted.

2.5. Statistical analysis

Continuous data were verified for normality with the Kolmogorov-Smirnov test. Normally distributed data were presented as mean \pm standard deviation and analyzed using the Student t test. Categorical data were presented as frequencies and analyzed using the Fisher's exact test. The accuracy of scintigraphy in diagnosing the ectopic thyroid was compared with CT and MRI respectively using McNemar. Statistical analyses were performed using SPSS 17.0 (IBM, Armonk, NY, USA). Two-sided *P*-values $< .05$ were considered statistically significant.

3. Results

3.1. Characteristics of the patients

The characteristics of the 22 patients are shown in Table 1. Compared with the patients with other diseases, the patients with confirmed benign ectopic thyroid had a lower rate of cervical thyroid (7.6% vs 100%, $P < .001$), while there were no differences in sex ($P = .116$) and age ($P = .374$).

Each mass was imaged by nuclear imaging [20 masses (17 patients) with scintigraphy only, 5 masses (5 patients) with

Table 1

The characteristics of the 22 patients with masses suspected of ectopic thyroid in head and neck.

	Suspected masses confirmed to be		P
	Ectopic thyroid	Other disease*	
No. of patients	13	9	
Females: Males	12:1	5:4	.116
Age	36.7 ± 18.9	44.6 ± 25.2	.374
Patients with cervical thyroid	1 (7.6%)	9 (100.0%)	<.001
Thyroid status			—
Euthyroidism	5	4	
Sub-hypothyroidism	2	0	
Hypothyroidism	2	0	
Not done	4	5	
Type of ectopic thyroid			—
Dual ectopic thyroid	3	—	
Lingual or sublingual thyroid	9	—	
Accessory thyroid	1	—	
Benign:malignant	16:0	7:2	—

* Confirmed by histological exam finally including thyrolingual cyst (n=3), submaxillary lymphadenitis (n=1), veno-lymphatic malformation (n=1), neurilemmoma (n=1), vascular malformation (n=1), mucoepidermoid carcinoma (n=1) and non-Hodgkin's lymphoma (n=1).

scintigraphy and SPECT/CT] and radiological exam [12 masses (12 patients) with enhanced CT only, 6 masses (5 patients) with enhanced MRI only, 7 masses (6 patients) with both].

Table 2

Sensitivity, specificity, and accuracy of scintigraphy, CT, and MRI in diagnosing the ectopic thyroid in the head and neck.

Modality	No. of patients	No. of masses	Sensitivity	Specificity	Accuracy
Scintigraphy	14	19	92.3% (12/13)	100% (6/6)	94.7% (18/19)
CT	14	19	84.6% (11/13)	100% (6/6)	89.5% (17/19)
P					>.99
Scintigraphy	11	13	85.7% (6/7)	100% (6/6)	92.3% (12/13)
MRI	11	13	71.4% (5/7)	100% (6/6)	84.6% (11/13)
P					>.99

CT=computed tomography, MRI=magnetic resonance imaging.

3.2. Value of scintigraphy, CT, MRI and SPECT/CT in diagnosing the ectopic thyroid

The value of scintigraphy, CT, and MRI in diagnosing the ectopic thyroid is shown in Table 2. Among the masses examined by scintigraphy and CT, sensitivity, specificity, and accuracy were 92.3%, 100%, and 94.7% for scintigraphy and 84.6%, 100%, and 89.5% for CT. Among the masses examined by scintigraphy and MRI, sensitivity, specificity, and accuracy were 85.7%, 100%, and 92.3% for scintigraphy and 71.4%, 100%, and 84.6% for MRI. The accuracy of scintigraphy was not significantly higher than that of CT (94.7% vs 89.5%, $P > .99$) or MRI (92.3%, vs 84.6%, $P > .99$). An accuracy of 100% was

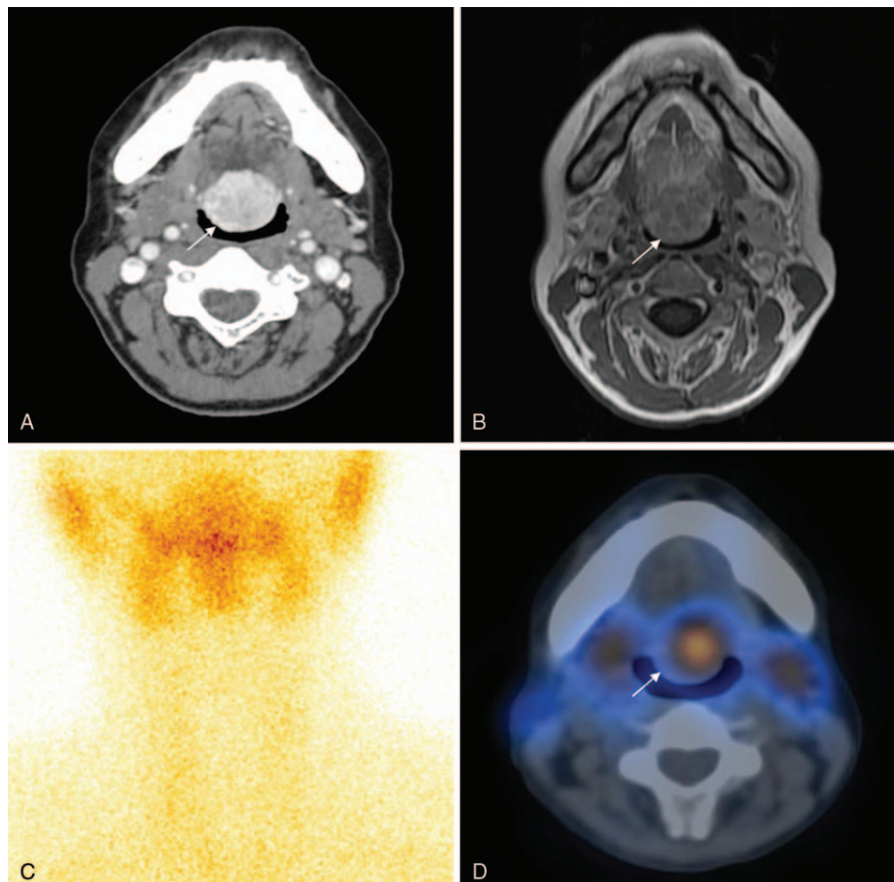


Figure 1. A sublingual mass in a 54-year-old female was diagnosed of ectopic thyroid by enhanced CT (A) (arrow), but it was misdiagnosed as benign tumor by enhanced MRI (B) (arrow). On scintigraphy with $^{99m}TcO_4^-$ (C), the mass was obscured by the tracer in the mouth, and the patient was misdiagnosed of subacute thyroiditis. SPECT/CT (D) made it clear that the mass (arrow) was an ectopic thyroid. CT=computed tomography, MRI=magnetic resonance imaging, SPECT/CT=single-photon emission computed tomography/computed tomography.

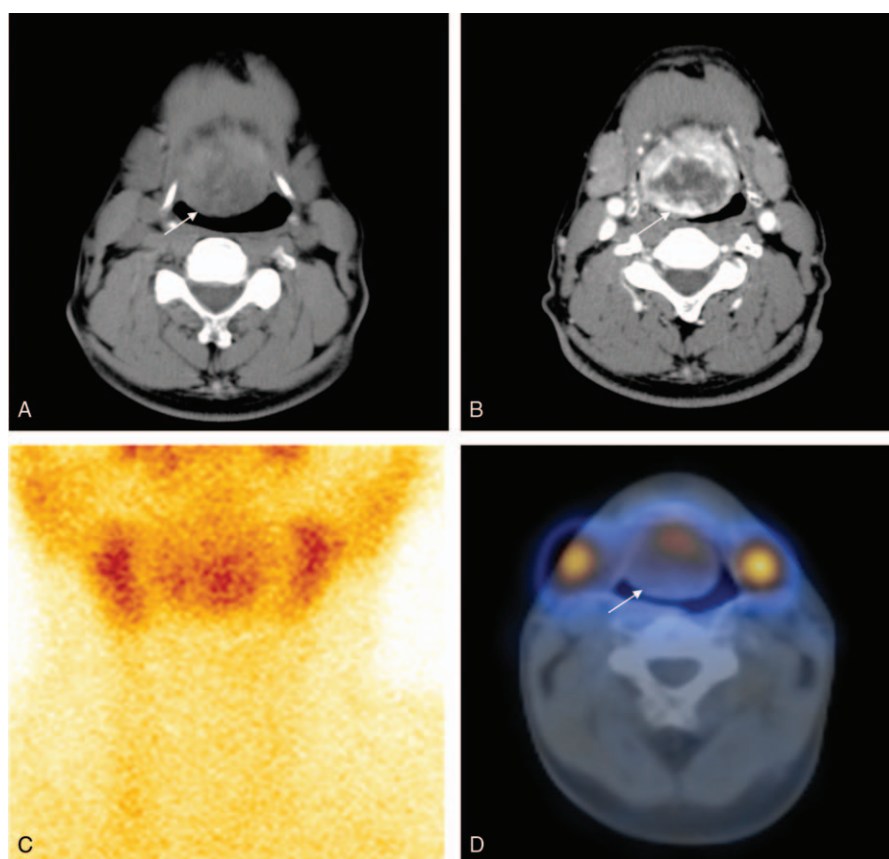


Figure 2. A sublingual mass in a 60-year-old man was misdiagnosed as neurilemmoma by pre- (A) and post-contrast (B) CT (arrows). It was diagnosed as ectopic thyroid by scintigraphy (C) and SPECT/CT with $^{99m}\text{TcO}_4^-$ (D) (arrow). Histological examination revealed that the mass was nodular goiter that originated from ectopic thyroid. CT=computed tomography, SPECT/CT=single-photon emission computed tomography/ computed tomography.

achieved when scintigraphy was combined with SPECT/CT in 5 masses. Among the 5 masses, 1 was false negative on scintigraphy (Fig. 1C) and MRI (Fig. 1B), 2 were false negative on CT (Fig. 2A and B). There was no case of false-positive diagnosis of ectopic thyroid by these 4 imaging modalities.

On scintigraphy, 15 masses of ectopic thyroid were positive, whereas 1 mass was equivocal and the patient was misdiagnosed as subacute thyroiditis, however, SPECT/CT correctly diagnosed it as ectopic thyroid (Fig. 1). On CT, 13 masses of ectopic thyroid displayed obvious (12 masses) and slight (1 mass, Fig. 2A) higher density compared with that of the surrounding soft tissue with homogeneous (3 masses) or heterogeneous (10 masses, Fig. 2B) enhancement. Two of them were misdiagnosed as neurilemmoma (Fig. 2A and B) and angioma, respectively. On MRI, 6 masses of ectopic thyroid were isointense on T1WI and hyperintense on T2WI compared with nearby skeletal muscle with heterogeneous (3 masses), ring (1 mass, Fig. 1B), or no (2 masses, Fig. 3A) enhancement. Another mass was hyperintense on T1WI and isointense on T2WI with heterogeneous enhancement. Two masses were misdiagnosed as benign tumor (Fig. 1B), another mass was misdiagnosed as thyrolingual cyst (Fig. 3C). The 16 benign ectopic thyroids had ovoid shapes, well-defined margins, and no invasion to the surrounding structures on CT and/or MRI.

3.3. Literature review

The characteristics of the 13 malignant ectopic thyroids are summarized in Table 3.^[8–12,14–21] Compared to the benign

ectopic thyroids in our study, the 13 malignant ectopic thyroids were the same in shapes, margins, and invasion.

4. Discussion

Because of its rarity, the exact imaging features of ectopic thyroid are poorly known. Therefore, the present study aimed to analyze the value of scintigraphy, CT, MRI, and SPECT/CT in the diagnosis of ectopic thyroid in the head and neck. Our results showed that scintigraphy, MRI and CT demonstrated similar diagnostic accuracy. While the number of masses examined by scintigraphy combined with SPECT/CT was limited, this technique correctly diagnosed all the false negatives returned by other modalities, with an accuracy of 100% achieved.

In the present study, scintigraphy, CT, and MRI were all useful modalities for detecting ectopic thyroids in the head and neck, with no statistical difference in accuracy. Nevertheless, misdiagnoses were still made when these modalities were analyzed individually. On plain CT, ectopic thyroid tissue usually displays higher density than the surrounding soft tissue,^[3] but 1 case in the present study was not obvious. Although enhanced CT demonstrated ectopic thyroid tissue more clearly than plain CT,^[22] some cases in the present study and in the literature^[16] suggest that enhanced CT is still not reliable. On MRI, Takashima et al^[23] reported that ectopic thyroid appears isointense or hyperintense relative to muscle tissue on T1WI and hyperintense on T2WI, which was also observed in the present study. Nevertheless, the same signal appears in some

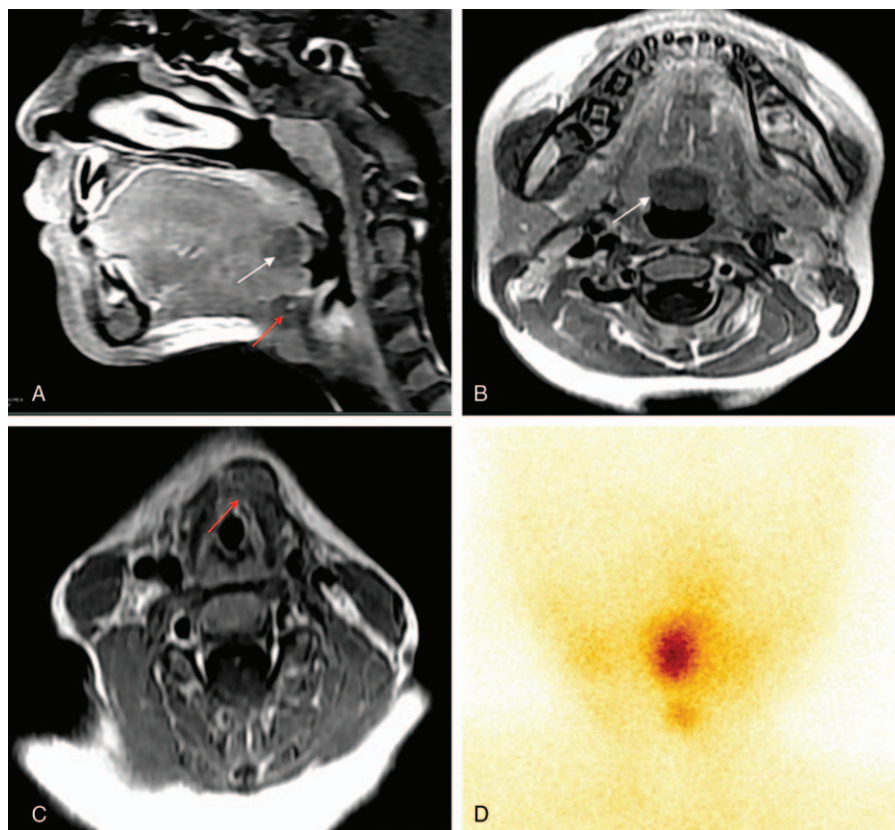


Figure 3. Two masses were found by enhanced MRI (A–C) in a 7-year-old girl. They were diagnosed of ectopic thyroid (white arrows) and thyrolingual cyst (red arrows), respectively, but scintigraphy with $^{99m}\text{TcO}_4^-$ (D) correctly diagnosed them as ectopic thyroids. MRI=magnetic resonance imaging.

cases of non-Hodgkin’s lymphoma and adenoid cystic carcinoma.^[2,3] Furthermore, in the present study, the enhancements of the 7 ectopic thyroids on MRI were of various types. Therefore, there are still some difficulties to diagnose ectopic thyroids by their density on CT, signal on MRI, or their enhancement. Nevertheless, the present study suggest that females without normal cervical thyroid might be useful clues for the diagnosis of ectopic thyroid on CT or MRI, as suggested by previous studies.^[2,10,13,15,16,23,24]

Scintigraphy with $^{99m}\text{TcO}_4^-$, ^{131}I , or ^{123}I is no doubt the most important diagnostic method to detect the existence of thyroid tissue, no matter its location. Nuclear medicine physicians just pay attention to the abnormal foci on scintigraphy images. Nevertheless, the possibility of false positive and false negative diagnostic scintigraphy must be taken into account.^[13] Tracers in the nasal mucosa, salivary glands, and mouth may sometimes obscure the ectopic thyroid, and even if some ectopic thyroids take up some tracer, it will be hard to see. SPECT/CT has been

Table 3
Cases of malignant ectopic thyroid in head and neck from the English literature.

Case*	Author, date	Age (years), sex	Location	CT or MRI findings		
				Shape	Margin	Invasion
1	Massine, 2001 ^[8]	57, M	Lingual	Ovoid	Well-defined	No
2	Perez, 2003 ^[9]	28, M	Lingual	Ovoid	Well-defined	No
3	Falvo, 2005 ^[10]	30, F	Submandibular	Ovoid	Well-defined	No
4	Kennedy, 2007 ^[11]	25, F	Lingual	Ovoid	Well-defined	No
5	Wang, 2010 ^[14]	42, M	Submental	Ovoid	Well-defined	No
6	Sevinc, 2010 ^[15]	31, F	Subhyoid	Ovoid	Well-defined	No
7	Bhojwani, 2012 ^[16]	28, F	Lingual	Ovoid	Well-defined	No
8	Chen, 2013 ^[12]	42, M	Lingual	Ovoid	Well-defined	No
9	Karras, 2013 ^[17]	35, F	Neck	Round	NA	NA
10	Tian, 2014 ^[18]	16, F	Nasopharynx	Ovoid	Well-defined	No
11	Ma, 2016 ^[19]	67, F	Trachea	NA	Well-defined	No
12	Cao, 2016 ^[20]	65, F	Temporal skull	Ovoid	Well-defined	Yes
13	Agosto-Vargas, 2017 ^[21]	33, M	Neck	Round	Well-defined	No

* Cases 1 to 11 and 13 were with papillary thyroid carcinoma. Cases 8 and 12 were with follicular thyroid carcinoma.

used clinically for decades and it can be performed immediately after scintigraphy with better emission resolution. Until recently, there were few reports^[4–7] about its use in the diagnosis of ectopic thyroid. In the present study, SPECT/CT correctly diagnosed the ectopic thyroids with false negative result on scintigraphy due to its better emission resolution. The number of cases was limited, but the present study could suggest that scintigraphy combined with SPECT/CT is a reliable method for the diagnosis of ectopic thyroids.

When a mass is diagnosed as ectopic thyroid, it is important to distinguish its benign/malignant nature. It had been shown that the value of scintigraphy alone is limited because both benign and malignant ectopic thyroid can show uptake of tracer.^[8–12] Compared to scintigraphy, CT and MRI provide more details on the ectopic thyroid. Takashima et al^[23] reported that benign ectopic thyroids had well-defined margins, whereas malignant tumors tended to have ill-defined margins and to invade the surrounding structures on MRI, but malignant ectopic thyroids were not included for comparison in their study. In the present study, a comparison was made between the 16 benign ectopic thyroids and 13 malignant ectopic thyroids from the literature.^[8–12,14–21] To the best of our knowledge, this is the first study to make such a comparison. Surprisingly, all 13 malignant ectopic thyroids from the literature had an ovoid or round shape, well-defined margins, and no invasion to the surrounding structures, just like the benign ones in the present study. These features suggest that CT and MRI cannot distinguish the nature of ectopic thyroids. Therefore, histology might remain the only way to correctly diagnose ectopic thyroids. In recent years, positron emission tomography (PET)/CT become widely used for the detection of thyroid cancer and metastases.^[25] In 2016, Park et al^[26] reported the use of F-18 FDG PET/CT in distinguishing benign ectopic thyroid from malignant in a single patient. The potential usefulness of F-18 FDG PET/CT needs to be explored in a cohort of such patients in future studies.

The present study is not without limitations. The number of cases was small and the malignant cases had to be taken from the literature.^[8–12,14–21] In addition, the retrospective nature of the study limited the available data. Additional studies are necessary to determine the imaging characteristics of ectopic thyroids.

In conclusion, the number of patients was limited, but scintigraphy combined with SPECT/CT could be a reliable method for the diagnosis of ectopic thyroid. Benign and malignant ectopic thyroids appear to be similar in shapes, margins, and invasion on CT or MRI.

Author contributions

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Resources: Z. Shao.

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Writing – review & editing: Y. Ma.

Acknowledgments

The authors acknowledge the support of the oral pathology department

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