The Journal of Laryngology & Otology
November 2005, Vol. **119,** pp. 882–887

Usefulness of technetium-99m methoxyisobutylisonitrile single-photon emission computed tomography and computed tomography in the evaluation of cervical lymph node metastasis

Byung-Joo Lee, MD, Soo-Geun Wang, MD, Eui-Kyung Goh, MD, Jun-Young Kim, MD, In-Ju Kim, MD*, Hak-Jin Kim, MD†

Abstract

The aim of this study was to compare the effectiveness of technetium-99m methoxyisobutylisonitrile (^{99m}Tc-MIBI) single-photon emission computed tomography (SPECT) and computed tomography (CT) in evaluating cervical lymph node metastasis of head and neck cancer. Histopathologic results of 166 cervical lymph node levels in 31 neck-dissected patients were compared with pre-operative CT and ^{99m}Tc-MIBI SPECT findings about cervical lymph node metastasis, retrospectively. Sensitivity, specificity and predictability of CT and ^{99m}Tc-MIBI SPECT were 68.2, 93.1 and 89.8 per cent and 59.1, 87.5 and 83.7 per cent, respectively. When analysing CT and ^{99m}Tc-MIBI SPECT together, sensitivity and specificity were 86.4 and 99.3 per cent, respectively. The combined use of ^{99m}Tc-MIBI SPECT and CT could increase the accuracy of cervical lymph node metastases detection, compared with separate use of either ^{99m}Tc-MIBI SPECT or CT.

Key words: Head and Neck Neoplasms; Tomography, Emission-Computed, Single-Photon; Computed Tomography; Metastasis

Introduction

The accurate evaluation of a tumour's stage is one of the most important steps for successful treatment. Cervical lymph node metastasis is known to be one of the most important prognosis factors in head and neck cancer. However, due to the complex anatomical structures of head and neck lesions, it is very difficult to accurately predict cervical lymph node metastasis. Ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) can effectively show the relations between lymph nodes and surrounding structures as well as the shape and size of lymph nodes.[1] However, these radiological diagnostic methods have limitations; they use only structural transformations as the diagnostic criteria, and it is very difficult to accurately distinguish reactive hyperplasia from lymph node metastasis.

Radionuclide imaging, now widely used, is useful because it may reflect not only morphological characteristics but also metabolic activities. These characteristics can be useful for finding metastatic lesions that could not be detected by other imaging techniques. Radionuclide imaging has had a limited role thus far in evaluating the stage of head and neck cancer. However, positron-emission tomography (PET) imaging using ^{18}F-fluorodeoxyglucose (FDG) has recently been used effectively for the diagnosis of cancer and the evaluation of distant metastasis and recurrence of cancer.[2,3] Unfortunately, PET imaging is very expensive and available to only limited numbers of medical institutions. In the past, thallium-201 single-photon emission CT (SPECT) was used to detect cervical lymph node metastasis but the image was not satisfactory in terms of quality and usefulness.[4] Therefore, technetium-^{99m} methoxyisobutylisonitrile (^{99m}Tc-MIBI) SPECT has been used instead of PET imaging. This new technique was originally developed for the purpose of myocardial imaging, but it is known that ^{99m}Tc-MIBI images are useful for the detection of various malignancies.[5–7]

In the head and neck area, ^{99m}Tc-MIBI SPECT is useful for the detection of cervical lymph node

From the Departments of Otolaryngology, *Nuclear Medicine and †Diagnostic Radiology, College of Medicine, Pusan National University, Pusan, Korea.
Presented at the 76th Korean Otorhinolaryngology Congress, Seoul, Korea, October 25, 2002.
Accepted for publication: 14 April 2005.

TABLE 1

PATIENT DISTRIBUTION, PRIMARY LESION, STAGING AND METHOD OF NECK DISSECTION

	Sex/age (years)	Primary site	Stage	Type of neck dissection	Histological positivity (level)	SPECT positivity (level)	CT positivity (level)
1	F/67	Larynx	$T_3N_2M_0$	Rt MRND Lt LND	3	4	3
2	M/69	Larynx	$T_1N_2M_0$	Lt MRND	2	2	1
3	M/74	Larynx	$T_2N_1M_0$	Rt MRND	1	1	1
4	M/73	Retromolar triangle	$T_1N_0M_0$	Lt MRND	0	0	0
5	F/73	Tongue	$T_2N_2M_0$	Bilat SOND	2	3	2
6	M/66	Larynx	$T_2N_1M_0$	Rt MRND	1	1	1
7	M/65	Larynx	$T_3N_2M_0$	Lt MRND	2	1	3
8	M/66	Larynx	$T_3N_1M_0$	Rt LND Lt MRND	1	2	0
9	M/46	Tongue	$T_2N_0M_0$	Rt MRND Lt SOND	0	0	3
10	M/54	Tongue	$T_1N_0M_0$	Rt SOND	0	0	0
11	M/47	Tongue	$T_1N_0M_0$	Bilat SOND	0	0	1
12	M/63	Tongue	$T_1N_0M_0$	Rt SOND	0	1	0
13	M/55	Tongue	$T_4N_0M_0$	Bilat SOND	0	0	0
14	M/55	Tongue	$T_2N_0M_0$	Bilat SOND	0	0	0
15	M/52	Tongue	$T_2N_0M_0$	Bilat SOND	0	2	0
16	M/62	Tongue	$T_1N_0M_0$	Rt SOND	0	1	0
17	M/64	Tongue	$T_2N_0M_0$	Bilat SOND	0	0	0
18	M/62	Tongue	$T_3N_1M_0$	Bilat SOND	1	1	2
19	M/60	Tonsil	$T_1N_2M_0$	Lt MRND	3	0	2
20	F/38	Larynx	$T_3N_0M_0$	Lt MRND	0	0	0
21	M/64	Larynx	$T_3N_0M_0$	Lt MRND	0	0	0
22	M/64	Larynx	$T_2N_0M_0$	Lt MRND	0	1	0
23	M/66	Larynx	$T_1N_1M_0$	Lt MRND	1	0	1
24	M/55	Soft palate	$T_4N_1M_0$	Lt MRND	1	2	1
25	M/54	MUO	T_xN1M_0	Rt MRND	1	3	1
26	F/41	Tongue	$T_2N_1M_0$	Rt MRND	1	3	1
27	M/59	Larynx	$T_3N_1M_0$	Lt MRND	1	2	1
28	M/63	Tongue	$T_3N_0M_0$	Bilat SOND	0	0	0
29	F/54	Tongue	$T_1N_0M_0$	Bilat SOND	0	0	0
30	M/56	Tongue	$T_2N_1M_0$	Bilat SOND	1	1	0
31	M/63	Larynx	$T_3N_0M_0$	Rt MRND	0	0	0

SPECT = single-photon emission computed tomography; CT = computed tomography; MUO = metastasis of unknown origin; MRND = modified radical neck dissection; LND = lateral neck dissection; SOND = supraomohyoid neck dissection

metastasis[7,8] but the studies on its accuracy are very limited. In this respect, the authors compared the histopathologic results and the results of ^{99m}Tc-MIBI SPECT and CT in order to evaluate usefulness for the detection of cervical lymph node metastasis.

Subjects and methods

Subjects

Subjects included patients who had received neck dissection and undergone pre-operative ^{99m}Tc-MIBI SPECT and contemporaneous CT at the Pusan National University Hospital from February 2001 to January 2003. The Ethical Committee of Pusan National University Hospital approved the study protocol. The subjects were 31 patients (26 men and five women) who were diagnosed as having squamous cell carcinoma of head and neck. The ages of the subjects ranged from 38 to 74 years (average age = 59.7 years). The primary sites were the larynx (12 cases), tongue (15 cases), tonsil (one case), retromolar triangle (one case) and soft palate (one case). In one case, the primary site was not identified. Types of neck dissection used were: modified radical neck dissection type I (six cases), modified radical neck dissection type II (12 cases), supraomohyoid neck dissection (24 cases), and lateral neck dissection (two cases).

TABLE II

SENSITIVITY, SPECIFICITY AND PREDICTABILITY OF ^{99M}Tc-MIBI SPECT AND CT IN THE DIAGNOSIS OF CERVICAL LYMPH NODE METASTASIS

Test	Sensitivity (%)	Specificity (%)	Predictability (%)
SPECT only	59.1	87.5	83.7
CT only	68.2	93.1	89.8
SPECT & CT*	40.9	99.3	91.6
SPECT or CT†	86.4	80.6	81.3

*SPECT & CT = results of both SPECT and CT are positive, consider positive; †SPECT or CT = results of either SPECT or CT is positive, consider positive

https://doi.org/10.1258/002221505774783430 Published online by Cambridge University Press

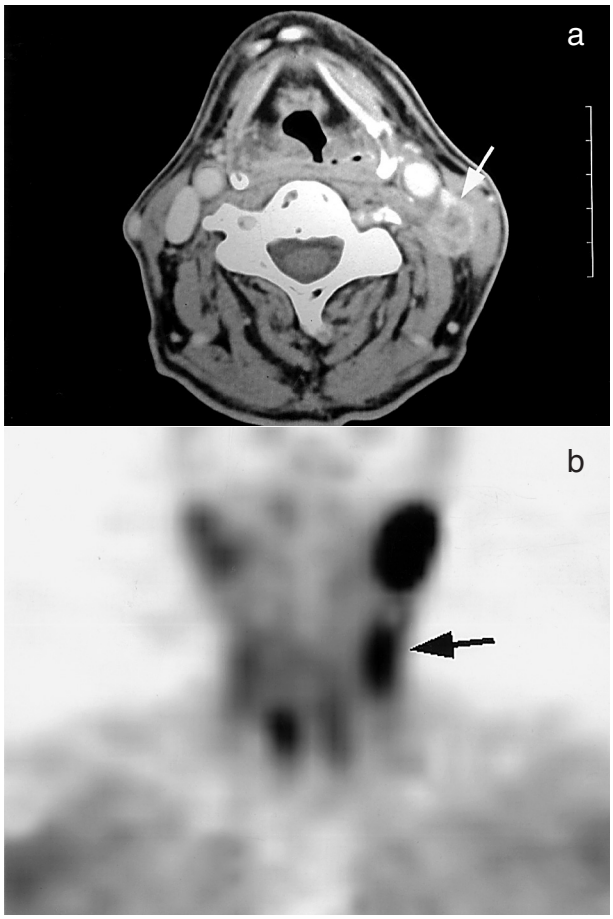

FIG. 1

Both ^{99m}Tc-MIBI SPECT and CT predicted lymph node metastasis correctly (Table I, case 2). (a) CT shows left level III, 2cm, peripheral, enhancing, malignant lymph node (arrow). (b) ^{99m}Tc-MIBI SPECT shows normal uptake of parotid gland, thyroid gland and abnormal uptake of left level III (arrow).

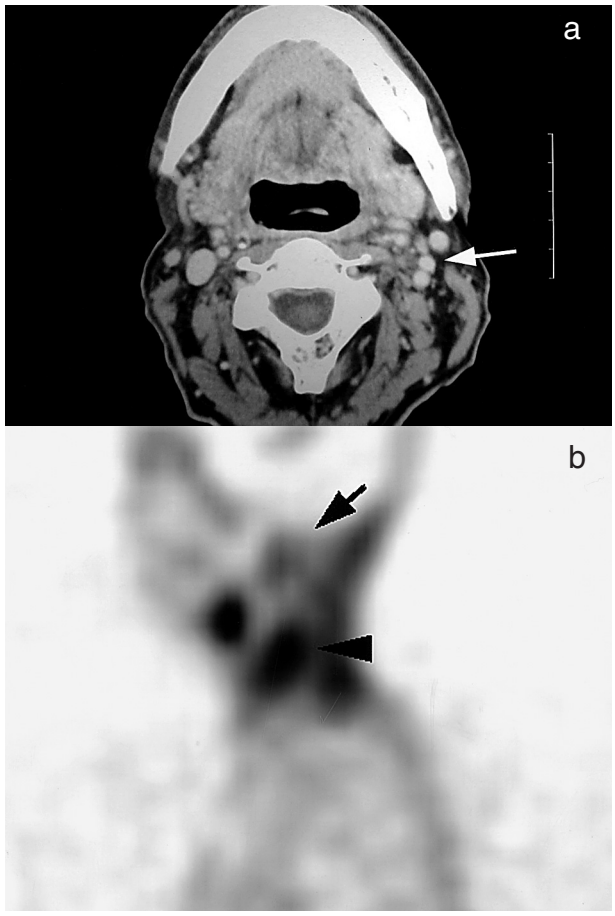

FIG. 2

^{99m}Tc-MIBI SPECT predicted lymph node metastasis correctly but CT missed lymph node metastasis (Table I, case 2). (a) CT shows no significant lymph node enlargement on left level II (arrow). (b) ^{99m}Tc-MIBI SPECT shows abnormal uptake on left level II (arrow) and left level III (arrow head). Histopathologic results were lymph node metastasis on left level II and level III.

Methods

^{99m}Tc-MIBI SPECT.

The SPECT scans of the head and neck were performed 15 minutes after intravenous injection of 740 MBq (20 mCi) ^{99m}Tc-MIBI. The patient was positioned supine on the imaging table with the forehead and chin strapped to prevent motion. The equipment consisted of a rotating, double-head gamma camera (Vertex^{TM}, ADAC, Milpitas, California, USA) fitted with a low-energy, high-resolution collimator. Each image was stored in a 256 × 256 pixel matrix. A magnification coefficient of 1.5 was used when obtaining the lateral images. Each ^{99m}Tc-MIBI SPECT image was interpreted by two experienced physicians and a consensus was reached regarding the finding. Any ^{99m}Tc-MIBI uptake in both necks other than physiological uptake (pituitary glands, nasal and oral cavity, bilateral pharyngeal recesses, maxillary sinus, parotid, palatine, submandibular, and sublingual salivary gland) was considered as positive for cervical lymph node metastasis. Reorientation of images was performed following plans similar to those used for the CT images, with sagittal, coronal and transverse one-pixel slices, to identify cervical lymph node metastasis.

Computed tomography.

A spiral CT scanner (Lightspeed Qx/i, Milwaukee, Wisconsin, USA) was used. The first image was obtained parallel to the hard palate after administering 80–120 ml of contrast medium, and the section interval was 5 mm. Reading of cervical CTs was conducted by radiological doctors unaware of patients' clinical information. The criteria of Mancuso *et al.*[9] were used to evaluate metastasis evident on the CT image.

Analysis.

For topographical evaluation, the findings of SPECT and CT were recorded according to a standardized classification that divides each neck side into six levels.[10] Findings from CT, ^{99m}Tc-MIBI SPECT and histopathology were compared for each level. Sensitivity, specificity and predictability were

https://doi.org/10.1258/002221505774783430 Published online by Cambridge University Press

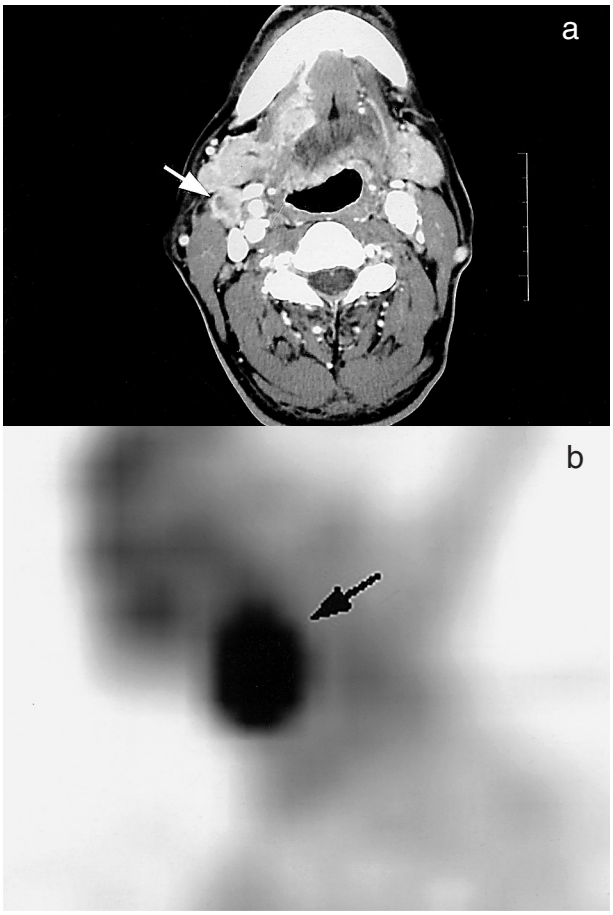

FIG. 3
^{99m}Tc-MIBI SPECT missed lymph node metastasis but CT correctly predicted lymph node metastasis (Table I, case 18). (a) CT shows right internal jugular chain malignant lymph node and right-sided tongue mass (arrow). (b) ^{99m}Tc-MIBI SPECT shows only normal uptake in left submandibular gland (arrow).

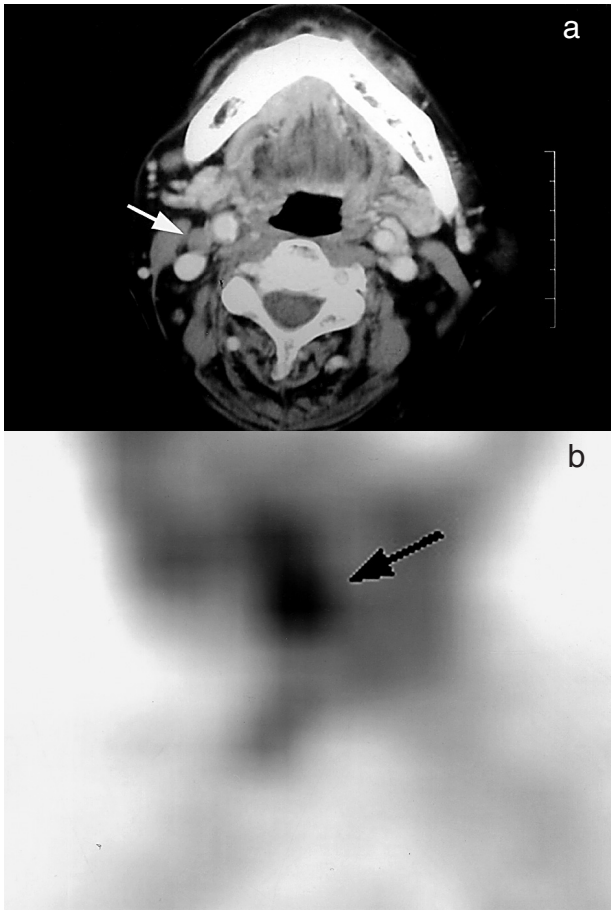

FIG. 4
Both ^{99m}Tc-MIBI SPECT and CT missed lymph node metastasis (Table I, case 1). (a) CT shows 1cm, right carotid space, radiologically insignificant lymph node (arrow). (b) ^{99m}Tc-MIBI SPECT shows only normal submandibular gland uptake (arrow).

calculated for each imaging modality and for the combination of both methods.

Statistical analysis

A McNemar test and a receiver operating characteristic (ROC) curve were used, and the level of significance was set at $p < 0.05$.

Results

Among 31 patients, 15 patients showed cervical lymph node metastasis (Table I). One hundred and sixty-six levels were histopathologically evaluated, and lymph nodes with tumour involvement were found in 22 levels.

With regard to ^{99m}Tc-MIBI SPECT, sensitivity, specificity, and predictability were 59.1 per cent, 87.5 per cent and 83.7 per cent, respectively (Table II). With regard to CT, sensitivity, specificity, and predictability were 68.2 per cent, 93.1 per cent, and 89.8 per cent, respectively (Table II). The ^{99m}Tc-MIBI SPECT technique showed less sensitivity and specificity in predicting cervical lymph node metastasis than did CT; however, this difference was not significant ($p > 0.05$).

In 10 cervical lymph node levels, both ^{99m}Tc-MIBI SPECT and CT accurately detected cervical lymph node metastasis (Figure 1). In three cervical lymph node levels, CT failed to detect cervical lymph node metastasis but ^{99m}Tc-MIBI SPECT did detect such metastasis. For example, where the CT failed to show any abnormal findings (e.g. significant hypertrophy) in cervical lymph nodes, the ^{99m}Tc-MIBI SPECT indicated an abnormal local uptake (Figure 2). In five cervical lymph node levels, ^{99m}Tc-MIBI SPECT failed to detect cervical lymph nodes metastasis but CT accurately detected such metastasis (Figure 3). In four cervical lymph node levels, both tests failed to predict cervical lymph node metastasis (Figure 4).

When the cases detected as positive by both ^{99m}Tc-MIBI SPECT and CT were regarded as positive, the specificity was 99.3 per cent. When those cases evaluated as positive by one of the two tests were regarded as positive, the sensitivity was 86.4 per cent. The combined use of ^{99m}Tc-MIBI SPECT and CT gave better results, in terms of specificity and sensitivity, than could be obtained from the single use of one of the two methods (analysis by ROC curve).

https://doi.org/10.1258/002221505774783430 Published online by Cambridge University Press

Discussion

The status of the cervical lymph nodes is an important tumour-related prognostic factor for head and neck cancer patients. The combined use of palpation and image-diagnosis methods like ultrasonography, CT and MRI have been used to determine neck metastasis. However, these methods only reflect the structural transformations of the cervical region, and are therefore limited in their ability to detect tumour micrometastasis or to distinguish reactive lymph node hypertrophy from cervical lymph node metastasis.

- **Accurate evaluation of cervical metastasis is vital in planning treatment of head and neck cancer**
- **This study looks at the combined use of technetium-99m methoxyisobutylisonitrile single-photon emission computed tomography (SPECT) and computed tomography in evaluating cervical lymph node metastasis in 31 patients undergoing neck dissection**
- **The use of these combined imaging techniques has the potential to improve the diagnostic accuracy in prediction of cervical metastasis**

Radionuclide images are valuable tools in evaluating the morphological and functional state of tissues.[11] Therefore, radionuclide images are useful in evaluating primary tumours as well as metastatic or recurrent lesions. The radionuclide image methods that can determine cervical lymph node metastasis are PET and SPECT. The PET technique is known to enable a very high rate of diagnosis, but only a limited number of medical institutions have access to it as it is very expensive. In the case of SPECT, ^{67}Ga citrate, ^{201}Tl and ^{99m}Tc-(V)-dimercaplosuccinic acid (DMSA) can be used to evaluate various cancers. Recently, ^{99m}Tc-MIBI has been shown to produce good image quality and to be more suitable for SPECT imaging than the alternatives.[7,12] The ^{99m}Tc-MIBI technique can be useful for the evaluation of cancer because it is selectively uptaken into tumour cells. The ^{99m}Tc-MIBI SPECT technique shows the internal distribution of radioactive isotopes in the form of tomographic images. Therefore, the radioactivity of the lesions and the surrounding tissues can be separated, making it possible to identify three-dimensional tumour location. Accordingly, ^{99m}Tc-MIBI SPECT is useful for the diagnosis of tumours within complicated anatomical structures, such as head and neck cancer.[7]

In a study that compared the accuracy of the detection of cervical lymph node metastasis in nasopharyngeal cancer using ^{99m}Tc-MIBI SPECT and CT, Sun *et al.*[7] reported that ^{99m}Tc-MIBI SPECT showed less sensitivity but greater specificity than did CT. In our study, however, ^{99m}Tc-MIBI SPECT showed less sensitivity and specificity in predicting cervical lymph node metastasis than did CT, in head and neck cancer (without nasopharyngeal cancer). The sensitivities and specificities obtained by CT for the cervical lymph node metastasis in our study were similar to those found by Feinmesser *et al.*[13] When both methods were employed together in order to obtain more accurate results, the specificity (99.3 per cent) and sensitivity (86.4 per cent) were higher than the specificity and sensitivity obtained from the single use of one of the two methods. False positive results could be reduced significantly with the combined use of both methods. These results are also consistent with those reported by Sun *et al.*[7]

In conclusion, CT was more accurate than ^{99m}Tc-MIBI SPECT in detecting cervical lymph node metastasis, but the most accurate detection was possible when the two methods were employed together. The combined use of ^{99m}Tc-MIBI SPECT and CT may be helpful for the prediction of cervical lymph node metastasis.

References

1 Haberal I, Celik H, Gocmen H, Akmansu H, Yoruk M, Ozeri C. Which is important in the evaluation of metastatic lymph nodes in head and neck cancer: palpation, ultrasonography, or computed tomography? *Otolaryngol Head Neck Surg* 2004;**130**:197–201

2 Laubenbacher C, Saumweber D, Wagner-Manslau C, Kau RJ, Herz M, Avril N *et al.* Comparison of fluorine-18-fluorodeoxyglucose PET, MRI and endoscopy for staging head and neck squamous-cell carcinomas. *J Nucl Med* 1995;**36**:1747–57

3 Lapela M, Grenman R, Kurki T, Joensuu H, Leskinen S, Lindholm P *et al.* Head and neck cancer: detection of recurrence with PET and 2-[F-18]fluoro-2-deoxy-D-glucose. *Radiology* 1995;**197**:205–11

4 Valdes Olmos RA, Balm AJM, Hilgers FJM, Koops W, Loftus BM, Tan IB *et al.* Thallium-201 SPECT in the diagnosis of head and neck. *J Nucl Med* 1997;**38**:873–9

5 Prats E, Aisa F, Abos MD, Villavieja L, Garcia-Lopez F, Asenjo MJ *et al.* Mammography and ^{99m}Tc-MIBI scintimammography in suspected breast cancer. *J Nucl Med* 1999;**40**:296–301

6 Castellani M, Reschini E, Longari V, Paracchi A, Corbetta S, Marotta G *et al.* Role of Tc-^{99m} sestamibi scintigraphy in the diagnosis and surgical decision-making process in primary hyperparathyroid disease. *Clin Nucl Med* 2001;**26**:139–44

7 Sun SS, Tsai SC, Kao CH. Detection of cervical lymph node metastases in nasopharyngeal carcinoma: comparison between technetium-^{99m} methoxyisobutylisonitrile single photon emission computed tomography and computed tomography. *Anticanc Res* 2001;**21**:1307–10

8 Pui MH, Du JQ, Yueh TC, Zeng SQ. Imaging of nasopharyngeal carcinoma with Tc-^{99m} MIBI. *Clin Nucl Med* 1998;**23**:29–32

9 Mancuso AA, Maceri D, Rice D, Hanafee W. CT of cervical lymph node cancer. *Am J Roentgenol* 1981;**136**:381–5

10 Robbins KT, Medina JE, Wolfe GT, Levine PA, Sessions RB, Pruct CW. Standardizing neck dissection terminology. *Arch Otolaryngol Head Neck Surg* 1991;**117**:601–5

11 Arbab AS, Koizumi K, Toyama K, Araki T. Uptake of technetium-^{99m}-tetrofosmin, technetium-^{99m}-MIBI and thallium-201 in tumor cell lines. *J Nucl Med* 1996;**37**:1551–6

12 Maublant J, de Latour M, Mestas D, Clemenson A, Charrier S, Feillel V *et al.* Technetium-^{99m}-sestamibi uptake in breast tumor and associated lymph nodes. *J Nucl Med* 1996;**37**:922–5

13 Feinmesser R, Freeman JL, Noyek AM, Birt BD. Metastatic neck disease. *Arch Otolaryngol Head Neck Surg* 1987;**113**:1307–10

https://doi.org/10.1258/002221505774783430 Published online by Cambridge University Press

Address for correspondence:
Soo-Geun Wang, MD,
Department of Otolaryngology,
College of Medicine,
Pusan National University,
1-10, Ami-dong, Seo-gu,
Busan, Korea, 602-739.
Fax: 82-51-246-8668
E-mail: wangsg@pusan.ac.kr

Professor Soo-Geun Wang takes responsibility for the integrity of the content of the paper.
Competing interests: None declared

https://doi.org/10.1258/002221505774783430 Published online by Cambridge University Press