size benzamides characterized by a lower lipophilicity and lower liver uptake than IDAB to enhance the tumor-to-background ratio. Experiments conducted by John et al. (*6*) using [^{131}I]IPAB (2-piperidinylaminoethyl) 4-iodobenzamide in nude mice bearing human melanoma are promising. At present, however, planar images acquired early after administration of [^{123}I]IDAB must be interpreted with extreme caution.

In comparison to several other studies on scintigraphic detection of ocular melanoma the results presented are superior. Immunoscintigraphy with a commercially available radiolabeled monoclonal antibody, ^{99m}Tc-225.28S, has been evaluated by several groups. Loffler et al. (*7*) performed both planar and SPECT imaging in 28 patients clinically suspected of ocular melanoma. In 16 cases, the tumor was examined histologically. A positive immunoscintigraphy was observed in 56% of the histologically proven cases (and in 42% of the total group). In a study performed by Schaling et al. (*8*) 43 patients with ocular melanoma, six with a lesion suspected of being an ocular melanoma and seven with a benign lesion simulating an ocular melanoma were included. The detection rate of planar scintigraphy was 49%, and this was not increased by the use of SPECT techniques. Detectability by scintigraphy was correlated to the size of the lesions. They conclude that immunoscintigraphy with ^{99m}Tc-225.28S is of limited value especially in small lesions (*8*). Czachonska et al. (*9*) studied 60 patients with suspicion of ocular melanoma. In all patients with positive results the diagnosis of ocular melanoma was confirmed; a sensitivity of 83% was reported. Lietzenmayer et al. (*10*) studied 15 patients with ocular melanoma lesions using ^{18}FDG-PET, 10 (67%) presented positive scan findings.

CONCLUSION

Iodine-123-IDAB scintigraphy might play a role as a noninvasive tool for the imaging of ocular melanoma. In our study, none of the patients with ocular naevi demonstrated increased tracer accumulation. Therefore, [^{123}I]IDAB scintigraphy may be used in the differential diagnosis in cases where ocular melanoma is suspected among other possibilities. Future studies in larger patient cohorts will have to be conducted to determine the role of [^{123}I]IDAB scintigraphy in the diagnostic arsenal more precisely.

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Thallium-201 SPECT in the Diagnosis of Head and Neck Cancer

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The accuracy of SPECT with ^{201}Tl-chloride for the diagnosis of primary tumors, lymph node metastases and recurrences in head and neck cancer was evaluated for clinical applicability. **Methods:** SPECT images, obtained 60 min after administration of 150 MBq ^{201}Tl-chloride, were compared with clinical, CT and/or MRI and histology results. In addition, whole-body images were obtained to detect distant metastases. **Results:** In 79 patients studied for primary tumors (principally larynx, hypopharynx, oropharynx, nasopharynx and oral cavity), ^{201}Tl SPECT correctly identified 69 of 73 (95% versus 88% for CT/MRI) histologically confirmed malignancies including 63 squamous-cell carcinomas. The method localized four occult naso- and oropharynx carcinomas not seen on CT/MRI and was correctly negative in two patients without tumor and in three of four patients with no confirmed primary tumor in the head and neck. With respect to regional spread, only patients who had cervical lymph node dissection were evaluated, and the findings were recorded per side of the neck. Thallium-201 SPECT correctly identified metastases in 31 of 36 neck dissections with proven lymph node involvement (86%), was correctly negative in nine and false-positive in one. Although the sensitivity of CT/MRI was clearly higher (97%), considerably more false-positive cases affected its accuracy (81% versus 87% for SPECT). In 30 patients investigated for recurrences, ^{201}Tl SPECT correctly identified 27 of 29 microscopically confirmed tumor sites (93%) and was correctly negative in seven. Sensitivity of CT/MRI was lower (76%), and a greater number of false-positives (seven versus three for SPECT) further decreased its accuracy (64% versus 87% for SPECT). Distant metastases were detected in five patients. **Conclusion:** Thallium-201 SPECT appears to be an accurate method for the diagnosis of head and neck cancer. The method is particularly useful for detection of occult head and neck tumors and for assessing recurrences. It also may be of complementary value in the staging of primary tumors, in the differentiation of metastatic from reactive lymph nodes in the neck and, on the basis of whole-body scanning, for screening of distant metastases.

Key Words: head and neck cancer; SPECT; thallium-201-chloride

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With more than 500,000 new cases projected annually worldwide, head and neck cancer constitutes approximately 5% of all

TABLE 1
Distribution, Tumor Staging and Imaging Results in Patients Evaluated for Primary Tumors

Site	Number	According to tumor staging	^{201}Tl-SPECT		CT/MRI	
			Pos	Neg	Pos	Neg
Nasopharynx	7	2 T1, 3 T2, 1 T3, 1 T4	7	—	6	1
Oropharynx	21	3 T1, 7 T2, 9 T3, 2 T4	20	1	16	4
Hypopharynx	10	2 T1, 1 T2, 7 T3	8	2	10	—
Oral cavity	8	2 T1, 1 T2, 4 T3, 1 T4	7	1	6	2
Larynx	21	2 T1, 8 T2, 6 T3, 5 T4	21	—	19	1
Other	6		6	—	4	—
Maxilla/mandible	3					
Non-Hodgkin's tonsil	2					
Esophagus	1					
Remained unknown	4		1	3	—	4
No tumor	2		—	2	—	2
Total	79		70	9	61	14

malignancies (*1,2*). Although endoscopic examination under anesthesia is considered to be the definitive diagnostic and staging procedure (*2*), there is an increasing use of diagnostic imaging methods such as CT and MRI to noninvasively assess the extent of local and regional spread of tumor, the depth of invasion and the presence of lymphadenopathy (*3*). The difficulties of these imaging methods in differentiating metastatic from reactive lymph nodes in the neck has led to the use of ultrasound-guided fine-needle aspiration cytology (USG-FNAC) in recent years, which has reached high accuracy levels in the diagnosis of regional spread by combining detection by ultrasound with tissue-characterization by microscopy (*4*).

In spite of these advances, there are still objective shortcomings in the diagnosis of head and neck malignancies, particularly in the localization of occult primary tumors, detection of distant metastases, assessment of tumor response to therapy and differentiation of recurrence from scar tissue as well as the noninvasive characterization of lymphoadenopathies detected by palpation, CT, MRI or ultrasound.

To overcome these limitations, various nuclear medicine procedures aimed to image metabolic aspects of tumors have been tested. PET using [^{18}F]fluorodeoxyglucose (FDG) has been found to be effective for primary and secondary squamous-cell carcinoma (*5–9*). However, the difficulties of the method in differentiating between reactive and metastatic lymph nodes, probably by tracer accumulation in inflammatory tissue (*9*), as well as its costs and availability, limits its applicability. These same cancers also may limit the widespread use of radioimmunoscintigraphy with monoclonal antibodies, which has been evaluated for clinical imaging of head and neck cancer (*10*).

In this study, the clinical experience with ^{201}Tl-chloride and SPECT in more than 100 patients with head and neck malignancies is evaluated. The recognized affinity of ^{201}Tl for malignant tumor cells, its general availability, the ample experience obtained at The Netherlands Cancer Institute using this tracer in the follow-up of patients with thyroid carcinoma (*11*), the promising results reported for ^{201}Tl SPECT in nasopharyngeal carcinoma (*12,13*), as well as our own positive preliminary findings with this method in head and neck cancer (*14*), determined the choice of ^{201}Tl over other radiopharmaceuticals, such as ^{99m}Tc-pentavalent DMSA and ^{99m}Tc-sestamibi, that have been used for the same purpose (*15–17*).

The aims of the study were to:

1. Assess the accuracy of the method in detecting primary lesions and lymph node metastases of head and neck malignancies.
2. Establish the clinical value in tumor recurrences.
3. Establish scintigraphic pattern recognition of ^{201}Tl SPECT imaging in head and neck cancer by comparative evaluation with CT/MRI.

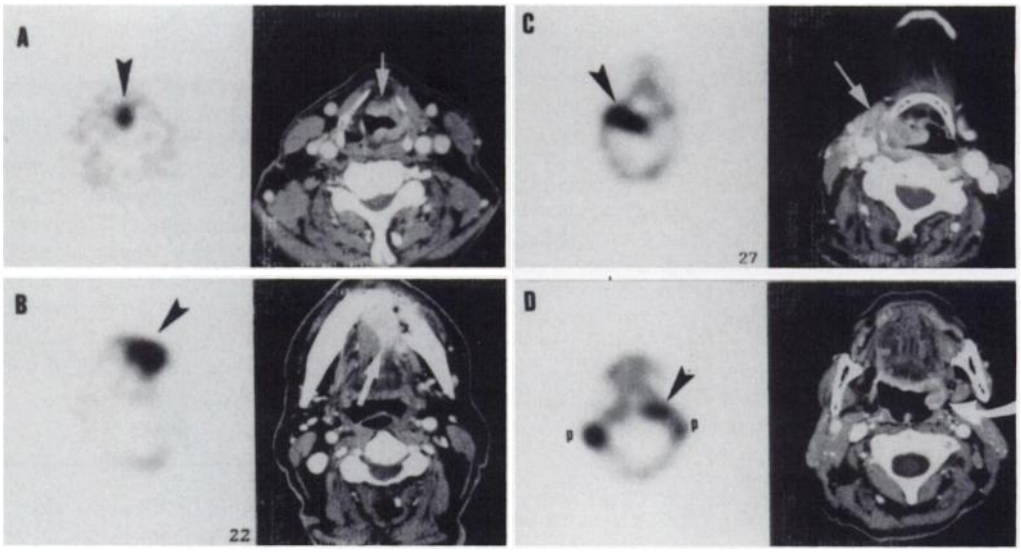

FIGURE 1. (A) Transaxial ^{201}Tl SPECT (left) and CT images after contrast material injection (right) showing (black arrows on SPECT, white arrows on CT) a T2 carcinoma of the larynx, (B) a T3 carcinoma of floor of the mouth, (C) a T3 hypopharyngeal carcinoma and (D) a T2 carcinoma of the oropharynx. In the latter SPECT image, uptake in parotid glands (P) is also observed.

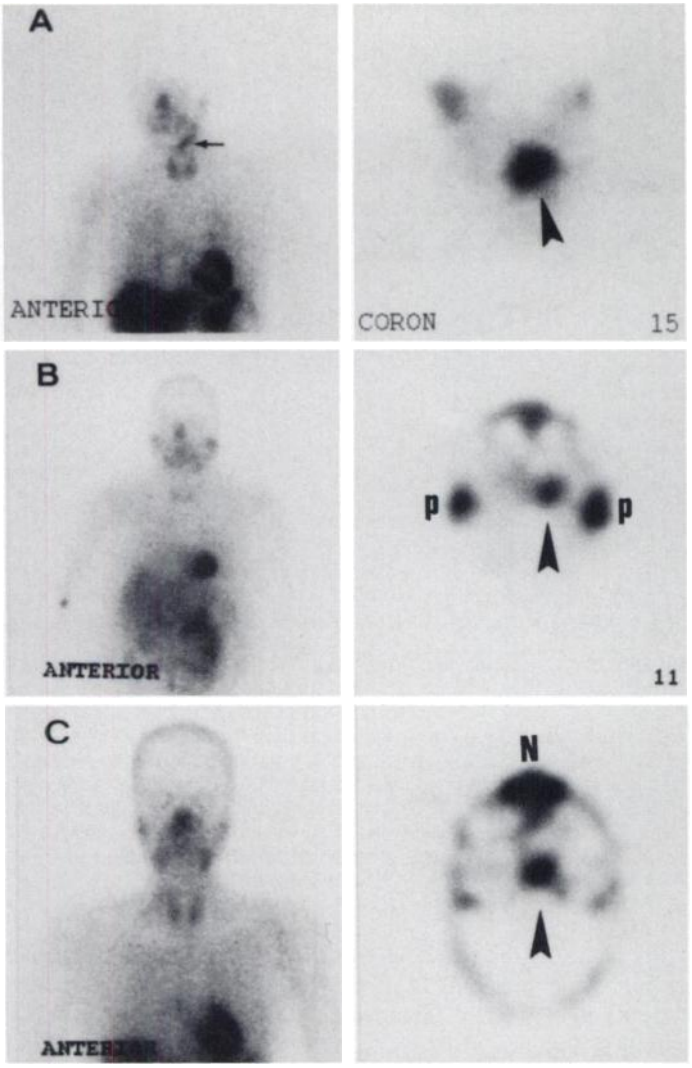

FIGURE 2. Planar (left) and SPECT (right) ^{201}Tl images. (A) For a hypopharyngeal carcinoma, both planar and coronal SPECT show the tumor (arrows). (B) For malignancies localized in the oropharynx and (C) nasopharynx, only SPECT can indicate the tumor site in, respectively, the left tonsil and left nasopharyngeal (arrows) by differentiating tumor uptake from activity in normal structures (p = parotid glands, n = nose).

MATERIALS AND METHODS

Patients

One-hundred and two consecutive patients (75 men, 27 women; mean age 59.5 yr; age range 18–87 yr) clinically suspected for head and neck cancer were evaluated. Clinical assessment was performed by the head and neck surgeon and subsequently patients had CT or MRI scanning and ^{201}Tl SPECT. Seventy patients had CT, 17 MRI and 11 CT and MRI; in four patients neither CT nor MRI could be performed. All patients had ^{201}Tl whole-body studies in addition to SPECT. Results were compared with histologic findings. Classification of the primary tumor and neck lymph nodes was based on the TNM system of the International Union Against Cancer (UICC, 1992). Seventy-nine patients (63 men, 16 women) were examined before initial treatment for malignancies of the nasopharynx, oropharynx, hypopharynx, oral cavity, larynx and other sites (Table 1); 11 patients in this group presented with palpable neck nodes of unknown cause and were evaluated for occult primary lesions in the head and neck. A second group of 30 patients (22 men, eight women) was investigated for diagnosis of recurrence; this group included seven patients who had already been evaluated for initial treatment and were suspected for a recurrence during follow-up.

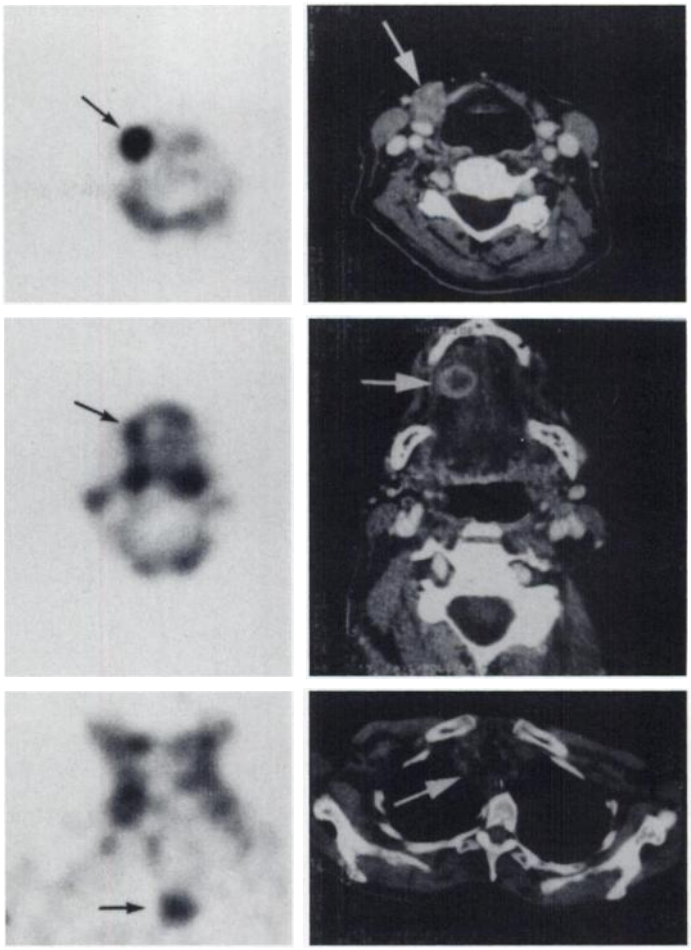

FIGURE 3. Transaxial ^{201}Tl SPECT images (left) and enhanced CT (right) of a patient presenting with metastases in the neck and tongue. SPECT findings (black arrows on top and middle images) match those of CT (white arrows), showing intense uptake in the lymph node metastasis but discreet accumulation in the tongue metastasis that is characterized by necrotic changes. Primary tumor was localized in the esophagus by coronal SPECT images and subsequently by CT (bottom).

Thallium-201 Imaging

SPECT studies of the head and neck were performed with a Vertex dual-head gamma camera (ADAC, Milpitas, CA) equipped with low-energy, high-resolution collimators 60 min after intravenous injection of 150 MBq ^{201}Tl-chloride. Acquisition was based on 360° noncircular rotation with 7° step angles, 60 sec per frame, 64 × 64 × 64 matrix, zoom factor 1.85. Reconstruction was performed with Butterworth filter, order 5, cutoff 0.35; one-pixel images, obtained in the sagittal, coronal and transverse planes, as well as additional three-dimensional volume reconstruction were used to identify tumor sites. In addition, simultaneous anterior and posterior planar 30-min whole-body studies (512 × 1024 matrix) were performed just before the SPECT studies in order to detect distant metastases.

CT and MRI

CT scans were performed with and without contrast material. Three- to 5-ml-thick continuous sections were acquired.

MRI images (T1- and T2-weighted pulse sequences with transaxial and sagittal slices of 3- to 5-mm thickness) were obtained with a Siemens Magnetom 63 SP4000 (Erlangen, Germany) 1.5 Tesla scanner before and after intravenous administration of Gd-diethylenetriaminepenta-acetic acid (DTPA). In addition, coronal short-TI inversion recovery sequences, that suppress fat signal, were obtained to evaluate neck lymph nodes.

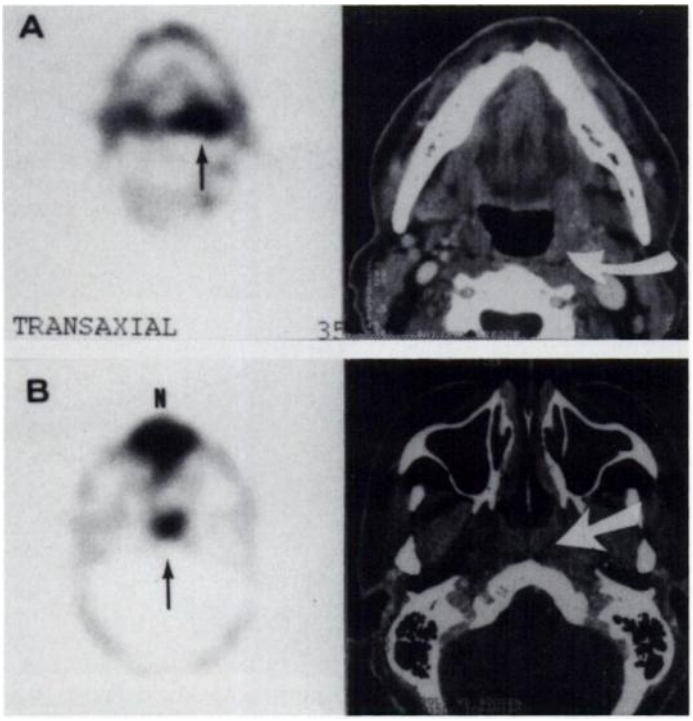

FIGURE 4. Transaxial SPECT images show increased ^{201}Tl uptake (black arrows) in (A, left) a T1 carcinoma of the oropharynx and (B, left) a T2 carcinoma of the nasopharynx in two patients presenting with neck metastases of unknown origin. On the right, enhanced CT shows only a slight asymmetry of left tonsillar region (curved white arrow on A), and unenhanced CT shows no abnormalities in the nasopharynx (straight white arrow on B). (B) Nasal activity (N) is also seen on SPECT images.

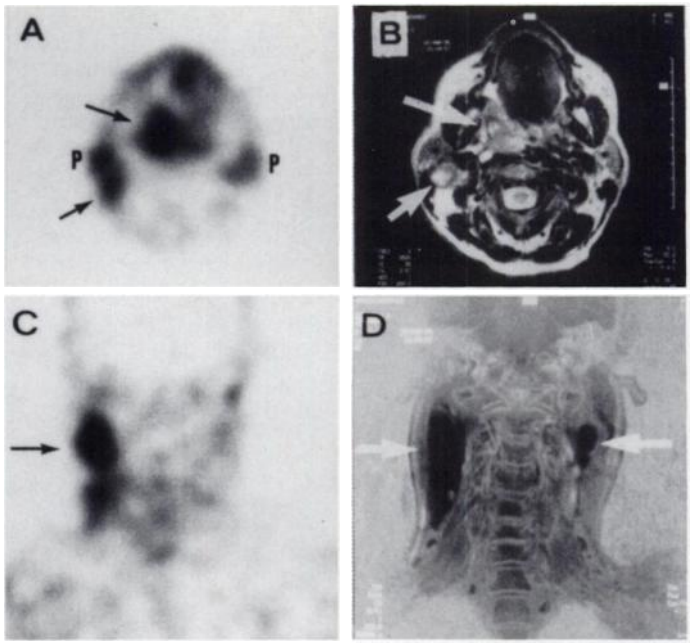

FIGURE 5. (A) Transaxial and (C) coronal ^{201}Tl SPECT images as well as (B) MRI transaxial T1-weighted spin-echo and (D) coronal short-TI inversion recovery sequence that suppresses fat signal of a patient with a T4 oropharyngeal carcinoma (long arrows on A and B) and lymph node metastases (short arrows on A and B). Histological lymph node analysis after bilateral neck dissection demonstrated two metastases on the right side and reactive nodes on the left. Note that coronal MRI displays both reactive and metastatic lymph nodes (white arrows on D) with similar signal intensities, whereas on SPECT only metastases are displayed (black arrows on C). (A) Also, bilateral parotid uptake (P) is observed.

Image Analysis

SPECT images and CT/MR scans were evaluated in joint panel sessions that included a otolaryngologist/head and neck surgeon, a head and neck radiologist and a nuclear medicine specialist. Studies were graded by consensus. For SPECT, tumor uptake was scored as intense (++), moderate (+), weakly positive (±) or absent (-). For CT/MRI, primary lesions with contrast enhancement were considered malignant. Lymph nodes with a diameter greater than 10 mm as well as nodes with central necrosis were classified as positive.

Subsequently, results of the primary lesions were correlated with histologic findings (biopsy or surgery). For regional lymph node spread, only patients who had neck dissection with histologic confirmation of the nodal status were evaluated, and the findings were recorded per side of the neck. For tumor recurrences, the analysis was limited to tumor sites in which histologic or cytological (USG-FNAC) evaluation was possible. For all three categories (primary lesions, neck dissection and recurrence sites), sensitivity, specificity and accuracy were calculated.

RESULTS

Primary Lesions

Histologic findings of 79 patients were as follows: 63 had squamous-cell carcinoma, 10 had poorly undifferentiated large-cell carcinoma, 1 adenocarcinoma, 1 rhabdomyosarcoma, 2 non-Hodgkin's lymphoma and 2 no tumors. In 72 patients, the primary lesions were localized in the head and neck and in the esophagus in one patient. In six other patients with palpable nodal disease in the neck, the primary tumor remained clinically unknown in four, and no malignancy was found in two patients (Table 1).

Thallium-201 SPECT, evaluable in all 79 patients, correctly identified 69 of 73 (sensitivity 95%) primary tumors (Table 1). Thallium-201 SPECT was true-negative in five patients presenting with palpable neck nodes of unknown cause: three without tumor in the head and neck and two with reactive lymphadenopathies. SPECT was false-positive in one patient (specificity 83%) with unknown primary tumor in whom biopsy samples obtained from endoscopy under general anesthesia were negative. In general, the primary tumors were easily distinguished on SPECT images from normal uptake in the salivary glands, mouth, nose and other structures (Fig. 1). Sixty-four of these tumors showed intense or moderately intense uptake. Only in five patients, who had lesions with some necrotic changes, there was discreet tumor uptake. The false-negative ^{201}Tl SPECT studies also concerned primary tumors with necrotic changes. Tumors located in the larynx or hypopharynx area were also frequently seen on planar ^{201}Tl images, whereas for tumors in other head and neck areas, only SPECT was conclusive in distinguishing tumor from overprojection from normal activity in the salivary glands and anterior areas of mouth and nose (Fig. 2). In one patient presenting with metastases in the tongue and cervical lymph nodes, the primary tumor was localized by SPECT in the esophagus (Fig. 3).

CT and/or MRI, evaluable in 75 patients, was correctly positive in 61 of 69 primary lesions (sensitivity 88%). No false-positives were found, and in five cases CT/MRI was correctly negative (specificity 100%).

As for false-negative CT/MRI and SPECT results, ^{201}Tl images were unable to detect two tumors located in the hypopharynx; conversely, one larynx and one oral cavity tumor as well as three oropharynx and 1 nasopharynx carcinomas were detected by ^{201}Tl SPECT (Fig. 4). The latter four cases concerned patients presenting with neck nodes of unknown primary tumors; in this subgroup (n = 11), ^{201}Tl SPECT localized five primary tumors (against one for CT/MRI), two resulted no tumor (SPECT and CT/MRI correctly negative) and four tumors remained unlocalized.

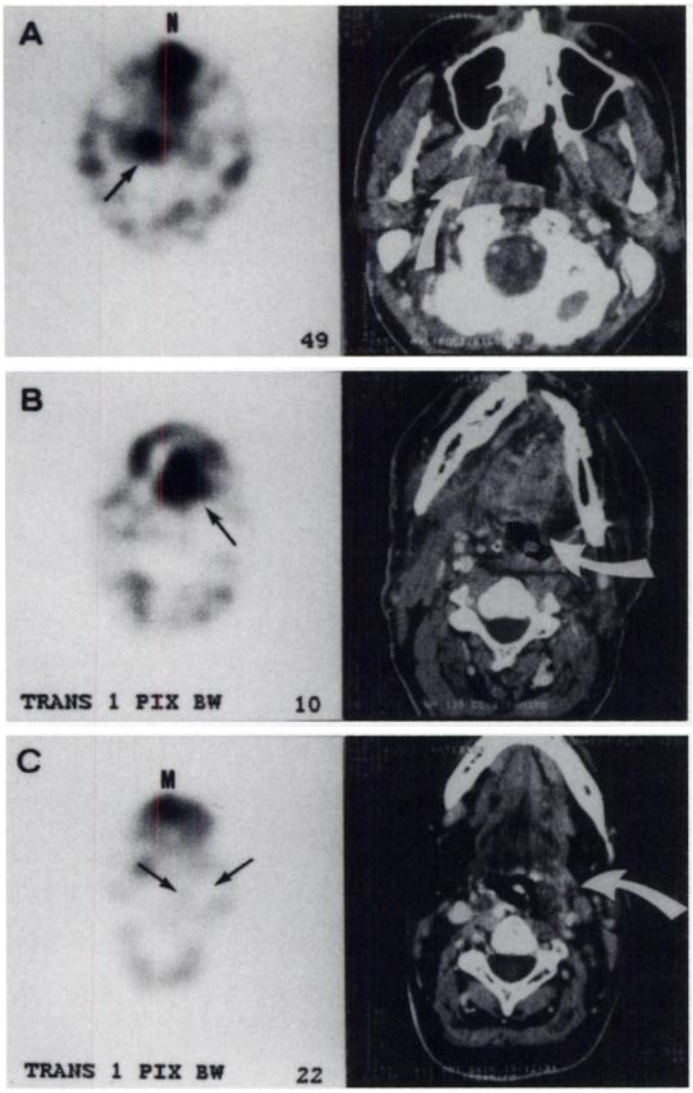

FIGURE 6. Transaxial images of ^{201}Tl SPECT (left) and enhanced CT (right) of three patients suspected for tumor recurrences in (A) nasopharynx, (B) floor of mouth and (C) supraglottis. SPECT, confirming recurrences in nasopharynx and floor of mouth, shows viable tumor (black arrows on A and B) more accurately than CT (white arrows) especially for recurrence of floor of mouth in which CT was not conclusive. By contrast, SPECT is negative in left supraglottis area (black arrows on C), whereas CT is not conclusive in excluding recurrence (white arrow). Activity in mouth (M) and nose (N) are also observed on SPECT.

Neck Metastases

A total of 34 patients with various malignancies had neck dissection (Table 2). In 12 patients, neck dissection was bilateral, which resulted in a total of 46 evaluated neck sides (24 right, 22 left).

Histologically, lymph node metastases were found in 36 neck dissections. Thallium-201 SPECT identified correctly metastases in 31 patients (sensitivity 86%) and had true-negative results in 9 and a false-positive result in 1 (specificity 90%) (Table 2).

CT/MRI, evaluable for 42 neck sides, was true-positive in 31 of 32 neck sides with proven lymph node involvement (sensitivity 97%). However, CT/MRI was true-negative in three and false-positive in seven (specificity 30%), which decreased its accuracy (81% versus 87% for SPECT). False-positive results were mainly found in enlarged reactive lymph nodes with mostly no uptake on ^{201}Tl SPECT scans (Fig. 5).

Recurrences

A total of 30 patients with various primary malignancies (11 larynx, 3 hypopharynx, 4 oral cavity, 6 oropharynx, 3 nasopharynx, 2 auricle, 1 parotid gland) and 39 evaluable sites of tumor recurrences after radiotherapy and/or surgery were analyzed. Thallium-201 SPECT could detect recurrences in 27 of 29 sites with confirmed tumor at microscopy (sensitivity 93%), whereas CT/MRI detected only 22 (76%). Considerably more false-positive (*7*) and false-negative findings (*7*) in comparison with SPECT (three and two, respectively) further decreased the accuracy of CT/MRI (64% versus 87% for ^{201}Tl SPECT).

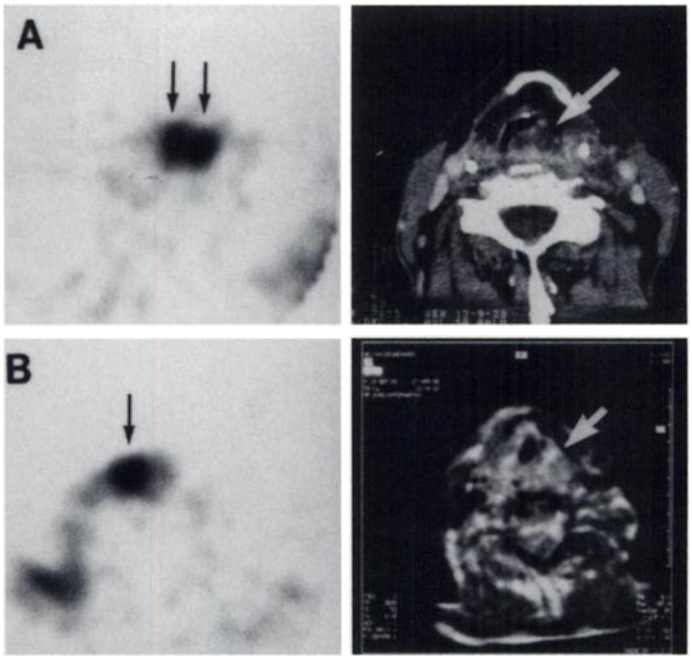

FIGURE 7. (A) Transaxial images of ^{201}Tl SPECT (left) and enhanced CT (right) of a patient with a larynx carcinoma showing an intense uptake (black arrows) at the tumor site in left area of larynx with extension to the right side (white arrow). (B) After radiotherapy, persistent uptake is seen in right part of tumor (black arrow), whereas on MRI (only T1-weighted spin-echo image after intravenous contrast medium is shown) tumor cannot be differentiated from reactive tissue changes (white arrow).

In the comparative analysis of images, ^{201}Tl SPECT could accurately reveal viable tumor, particularly in sites of local recurrence in which CT/MRI was not conclusive (Figs. 6 and 7).

An overview of ^{201}Tl SPECT and CT/MRI results in relation to primary lesions, regional spread and tumor recurrences is given in Table 3. Data of additional whole-body studies are not included in this table. In five patients (two investigated for primary assessment and three for recurrence), ^{201}Tl imaging could detect distant metastases (bone, esophagus, lungs).

DISCUSSION

Thallium-201 SPECT appears to be an accurate method for diagnosing of head and neck cancer. In primary lesions, the method compared well to CT/MRI, with concordant results in approximately 85% of the patients (Table 1). However, a particular advantage of SPECT is the detection of three occult submucosal oropharyngeal tumors of the tonsillar area as well as one nasopharyngeal lesion, which originally presented with neck metastases. SPECT was the only imaging modality that could disclose the site of the primary tumor, enabling histologic confirmation by subsequent endoscopy and biopsy under general anesthesia. In spite of the high accuracy found in this study, the lack of anatomical information of ^{201}Tl SPECT may limit wide applicability of SPECT by itself for staging of primary head and neck tumors: superior anatomical delineation, as is provided by CT and MRI, is required to evaluate local spread and depth of invasion of the tumor (*3*). However, ^{201}Tl SPECT may play a complementary role to USG-FNAC in tumor staging

TABLE 2
Distribution, Clinical Staging and Results of Patients Evaluated for Neck Node Involvement

Primary tumor site	No.	Clinical staging	Neck dissection (Side)	SPECT	CT/MRI	Histology
Oropharynx	9	T1N2	L	+	+	+
		T2N3	L	+	+	+
		T1N2	R	+	+	+
		T3N2b	R	+	+	+
		T3N2b	R	+	+	+
		T2N2	R	+	+	+
		T2N3	R	+	+	+
		T3N0	R	+	−	−
		T2N2	L	+	+	+
Hypopharynx	4	T3N1	L	+	+	+
		T3N1	R	+	+	+
		T3N2	R/L	R+/L−	R+/L−	R+/L−
		T3N1	R	+	+	+
Oral cavity	5	T1N1	R/L	R−/L−	R+/L−	R−/L−
		T3N2c	R/L	R+/L−	R+/L+	R+/L+
		T2N0	R	−	−	+
		T1N2c	R/L	R+/L+	not perf.	R+/L+
		T3N0	R/L	R−/L−	R+/L+	R−/L−
Larynx	9	T2N2a	R/L	R−/L+	R+/L+	R−/L+
		T4N1	L	+	+	+
		T2N3	L	+	+	+
		T4N2	R/L	R+/L+	R+/L+	R+/L+
		T3N0	R	+	+	+
		T2N2c	R/L	R+/L+	R+/L+	R+/L+
		T3N2	R/L	R+/L+	R+/L+	R+/L+
		T3N0	R/L	R−/L−	R+/L+	R−/L−
		T4N2	L	−	+	+
Other (maxilla/ mandible area)	3	−	L	−	+	−
		−	R	−	+	+
		−	R/L	R+/L+	R+/L+	R+/L+
Unknown	4	TXN2b	L	+	+	+
		TXN1	R	+	+	+
		TXN2c	R/L	R+/L−	not perf.	R+/L+
		TXN1	L	+	+	+

by adding metabolic information about the tumor, which may help to select sites of viable tumor for fine-needle aspiration. The satisfactory tumor visualization with ^{201}Tl found in this study, as well as the experimental evidence that the differences in tumor uptake of the tracer before and after radiotherapy correspond with proliferative changes in the tumor (*18*), may also enable the use of the method, preferably assisted by quantification, to assess therapy outcome in tumors that will be irradiated (Fig. 7).

For neck metastases, ^{201}Tl SPECT was clearly less sensitive than CT/MRI and could not identify other abnormal lymph nodes not already localized by these imaging modalities. However, the method was highly effective in excluding cervical lymph node involvement by scoring significantly more true-negative results than CT/MRI. This may lead to a complementary role of ^{201}Tl SPECT in the characterization of enlarged lymph nodes already detected by CT or MRI (Fig. 4). At present, the most accurate technique to stage the neck is USG-FNAC that is able to differentiate metastases from reactive changes in lymph nodes by combining ultrasound detection with fine-needle cytological tissue characterization (*4*). However, its accuracy depends on the skill of the ultrasonographer

TABLE 3
Thallium-201-SPECT and CT/MRI Results in Primary Lesions, Neck Metastases and Tumor Recurrences in Head and Neck

Condition	True-Positive	False-Negative	False-Positive	True-Negative	Sensitivity	Specificity	Accuracy
Primary tumors							
^{201}T1-SPECT	69	4	1	5	95%	83%	94%
CT/MRI	61	8	0	6	88%	100%	89%
Neck metastases*							
^{201}T1-SPECT	31	5	1	9	86%	90%	87%
CT/MRI	31	1	7	3	97%	30%	81%
Tumor recurrences†							
^{201}T1-SPECT	27	2	3	7	93%	78%	87%
CT/MRI	22	7	7	3	76%	30%	64%

*Neck side with lymph node involvement: 46 neck sides evaluated in 34 patients.
†Thirty-nine evaluated tumor sites in 30 patients.

and the cytopathologist, and the technique may require multiple aspirations. This has led to the use of various PET tracers for the assessment and staging of neck metastases. Fluorine-18-FDG, thanks to its high sensitivity and negative predictive value, is useful in clinically negative neck metastases, but its relatively high false-positive rate (*9*) probably makes other compounds such as L-[^{11}CH3-] methionine (*19*) and L-1-[^{11}C]-tyrosine (*20,21*) more suitable in the evaluation of patients with palpable neck lymph nodes by its potential to differentiate between cancerous and inflammatory cells. In this study, the accuracy of ^{201}Tl SPECT was determined on the basis of data recording per dissected neck side, which made it possible to correlate the histologic and imaging data. This is of practical relevance to characterize the neck as positive or negative and to determine the clinical management. A complementary study, including analysis per lymph node level, is necessary in the future in order to test the precision and reproducibility of the method for the localization of lymph node metastases during surgery (*22*). An important disadvantage of ^{201}Tl imaging is the uptake of the tracer in thyroid and salivary glands. Principally, uptake in submandibular glands may camouflage the presence of nodal disease in the high-jugular and submandibular regions. Probably the combined interpretation with CT or MR images may help to overcome these difficulties. However, only co-registration of SPECT, CT and MRI along with matched images that will permit incorporation of superior anatomical information may enable a better diagnostic approach of the neck.

One of the most relevant findings of this study is the high accuracy reached by ^{201}Tl SPECT in the diagnosis of recurrences of head and neck cancer. Although in 22 tumor sites ^{201}Tl SPECT and CT/MRI were concordant in detecting recurrences, the additive value of SPECT was observed in the correct identification of viable tumor in five sites of local recurrence in which CT/MRI was not conclusive. The method was also effective in characterizing tumor-free lesions as negative and may constitute an alternative to PET with ^{18}F-FDG, which also appears to be effective in the diagnosis of recurrences of head and neck cancer (*23*). Finally, an additional benefit of ^{201}Tl imaging, as established in this study, is the possibility to obtain whole-body studies in combination with SPECT to detect distant metastases.

CONCLUSION

Thallium-201 SPECT appears to be an accurate method for diagnosing head and neck cancer: particularly in assessing primary lesions and tumor recurrences. This study data suggest that this method is particularly useful for detecting occult head and neck tumors in patients presenting with enlarged cervical lymph nodes of unknown cause. Although CT and MRI are the preferred imaging modalities because of their superior anatomical definition, ^{201}Tl SPECT, however, may be of complementary value in tumor staging especially in guiding biopsy or aspiration. For regional spread, the method may be helpful to characterize the neck as negative or positive by differentiating metastatic from reactive lymph nodes in suspected cases. For tumor recurrences, the high accuracy of ^{201}Tl SPECT justifies its prompt incorporation in the clinical routine use. Imaging pitfalls may be caused by uptake of the tracer in the salivary glands, thyroid and anterior areas of mouth and nose. However, adequate interpretation in conjunction with CT and MRI may overcome these difficulties. Additional ^{201}Tl whole-body studies may help to detect distant metastases.

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