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Originals

Head and Neck Cancer : Comparative Evaluation by CT, MRI and FDG-PET

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SUMMARY

Purpose : To investigate the diagnostic accuracy of head and neck cancer, lymph node metastasis, and local tumor recurrence, by FDG-PET compared with CT and MRI, and to validate the results with the histopathological data.

Patients and Methods : Forty one patients with head and neck cancer were enrolled. Our patients presented for primary staging of head and neck cancer ($n=23$) or monitoring after therapy ($n=18$). The three imaging modalities (FDG-PET, MRI and CT) were compared.

Results : Overall 82 head and neck regions were analyzed for detection of malignancy (for primary tumors ; $n=23$, for lymph node metastasis ; $n=41$, for local tumor recurrence after therapy ; $n=18$). The overall sensitivity and specificity were ; CT 88.9% and 89.2% (95% CI ; 80.2－94.9%, $r=0.7791$, $P<0.0001$), MRI 88.9% and 91.9% (95% CI ; 81.9－95.8%, $r=0.8049$, $P<0.0001$), and FDG-PET 97.78% and 86.49% (95% CI ; 84－96.9%, $r=0.8551$, $P<0.0001$). Only FDG-PET by its unique advantage as a whole-body examination could detect distant metastases in 4/41 (9.8%) patients, all outside the head and neck region (liver, lung, paraortic lymph nodes, and bone metastases), and synchronous breast cancer in 1/41 (2.4%) patient.

Conclusion : Compared with CT and MRI, FDG-PET was found to have the highest sensitivity with lower specificity than CT and MRI. Moreover, the whole-body FDG-PET imaging proves useful tool for detection of distant metastasis and synchronous tumors.

Key Words : FDG-PET, lymph node metastasis, head and neck cancer, CT, MRI

INTRODUCTION

Head and neck cancer is the third most frequent cancer, constitute approximately 5% of all malignancies worldwide with 500,000 new cases every year[1,2]. Lymph node involvement is the most important prognostic factor affecting survival in evaluating patients with head and neck cancer. Overall, head and neck cancer 5-year survival is >50%, and 30% in patients without and with cervical lymph node metastases, respectively, though the rate varies widely depending on the type and extent of disease[3,4].

The diagnosis and staging of head and neck cancer is obtained by patient history, physical examination, endoscopy, CT or MRI as anatomical imaging and sometimes ultrasound with fine-needle aspiration biopsy and histopathological tissue evaluation is still mandatory to establish the type of cancer and the most appropriate subsequent treatment plan[4].

CT and MRI are the standard techniques provide

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structural information in a high spatial resolution and are therefore used routinely in the initial staging of tumors in these patients. On the other hand, they rely on certain criteria, such as nodal size and contrast-enhancement patterns, that are not very specific[5]. For instance, specificities of as low as 39% for CT and 48% for MRI have been reported for the detection of nodal metastases in patients with head and neck cancer[6].

After radiation/chemotherapy, changes in tumor metabolism precede morphologic changes. Similarly, after radical surgery or radiation therapy for head and neck malignancies, normal tissue planes are altered substantially. Therefore, CT and MRI have relatively poor specificity in the assessment of residual or recurrent disease following radical therapy[7]. Positron emission tomography (PET), on the other hand, helps in evaluation of tumor metabolism. For these reasons, FDG-PET with the glucose analogue fluorodeoxyglucose (FDG) has been used successfully for the assessment of tumor aggressiveness[8], staging of nodal disease in the neck[3,9], treatment evaluation[8], and detection of recurrent disease[10] in patients with head and neck cancer. Unfortunately, the lack of anatomic details remains a major limitation of FDG-PET if used without CT fusion.

Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) is a marker of tumor viability, based upon the increased glycolysis that is associated with malignancy as compared with most normal tissues. It has also been suggested that tumors with increased FDG uptake appear more aggressive and are associated with less favorable prognosis[3]. Head and neck carcinomas have high glycolytic activity and increased FDG uptake[11]. Therefore, FDG-PET has been advocated more and more acceptance as an additional diagnostic tool in the staging of head and neck carcinoma and for the staging of otherwise N0 necks[12]. However, to interpret FDG-PET images accurately, it is essential to be fully familiar with the normal patterns of physiologic tracer uptake, intensities, and frequencies of FDG distribution in the head and neck area[13].

The aim of our study, therefore, was to evaluate FDG-PET in localizing primary sites of head and neck cancer, lymph node metastasis and local tumor recurrence after therapy and to analyze the additional value of FDG-PET compared with CT and MRI using recent examination techniques.

PATIENTS AND METHODS

1. Patients Population and Study Design

This is a retrospective review of a prospective database. The study group included 41 patients (26 male and 15 female). They were referred to the Radiology Department, National Cancer Center Hospital East, Japan, for diagnostic imaging. Mean age was 57.7±13 years (range 19-80 years). Various head and neck tumors were investigated. Clinical examination was performed by head and neck surgeon. Twenty three patients were investigated with the aim of initial staging of primary head and neck cancer (group A), while 18 patients were evaluated for recurrence after therapy (group B). Patient's evaluation for detection of recurrence or residual tumor after therapy was performed not less than 8 weeks after therapy to avoid post operative or post radiation inflammatory reaction. According to the histopathological examinations and follow up studies, there was 15/41 (36.6%) lymph node metastasis (group A ; $n=9$, group B ; $n=6$), and 7/18 (38.9%) local tumor recurrence after therapy (group B). In all patients 23/23 examined for primary tumors, cancer was confirmed (group A).

2. Histopathological work-up.

Histopathological results confirmed ; SCC ($n=30$), Adenoid cystic carcinoma ($n=3$), Olfactory neuroblastoma ($n=2$), Non Hodgkin's Lymphoma (n=1), Papillary carcinoma ($n=1$), Follicular carcinoma ($n=1$), Carcinosarcoma ($n=1$), Malignant melanoma ($n=1$), Lymphoepithelioma ($n=1$) tumor sites (Table 1). Regional analysis revealed ; 14 tumors localized on the lateral wall of the pharynx (hypopharynx ; $n=7$, oropharynx ; $n=4$, nasopharynx ; $n=3$), 10 in the oral cavity (tongue ; $n=7$, gingiva ; $n=2$, retromolar ; n=1), 6 in the Larynx, 3 on the wall of the esophagus, 3 in the parotid gland, 2 in the thyroid gland, 2 in the nasal cavity, and one in the maxillary sinus (Table 2).

3. Image Acquistion

CT, MRI and FDG-PET images were compared in regard to detect the primary tumor and lymph node metastasis or local tumor recurrence after therapy. All

Table 1 Histopathological Findings

Histology	No. of patients
Squamous cell carcinoma	30
Adenoid cystic carcinoma	3
Olfactory neuroblastoma	2
Non Hodgkin's Lymphoma	1
Papillary carcinoma	1
Follicular carcinoma	1
Carcinosarcoma	1
Malignant melanoma	1
Lymphoepithelioma	1
Total	41

Table 2 Tumor Localization

Localisation	No. of patients	
Pharynx		14
Hypopharynx	7	
Oropharynx	4	
Nasopharynx	3	
Oral Cavity		10
Tongue	7	
Gingiva	2	
Retromolar	1	
Larynx		6
Esophagus		3
Salivary glands		3
Parotid gland	3	
Thyroid gland		2
Nose		2
Paranasal sinuses		1
Maxillary sinus	1	
Total		41

the three imaging modalities were performed within a mean time frame 21.8 ± 11.7 days.

3.1. CT

Scans of the cervical region were obtained with a multi-detector CT scanner (Toshiba Acquilion 16 row). Slice thickness was 2.5 – 3 mm. Contrast material enhancement was achieved by intravenous administration of 100 ml of non-ionic contrast material Iopamidol 300 (Iopamiron 300 ; Schering, Osaka, Japan), or Omnipaque 300 (iohexol ; Daiichi Pharmaceutical, Tokyo, Japan) with a power injector rate of 2 ml/sec.

3.2. MRI

Patients underwent MRI with a 1.5-T unit (Intera ; Philips). We first obtained non-enhanced transversal slices with fast spin-echo T2 technique often with fat saturation and/or STIR images with a slice thickness of 3 – 4 mm (gap 1.4 mm). In addition, coronal and sagittal slices were performed with a slice thickness of 5 mm (gap 2 mm). All patients had transversal T1 slices before and after intravenous administration of contrast medium [0.1 mmol of gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA)/kg body weight ; slice thickness 3 mm and interslice gap 1.4 mm].

3.3. FDG-PET

Patients were scanned on GE Advance NXi full-ring PET camera (GE Medical Systems, Waukesha, Wis., USA). PET camera has an axial field-of-view 15.2 cm, transaxial 55 cm and spatial resolution of 5 mm full-width at half-maximum at the centre of the field of view (slice thickness 5 mm). Prior to the FDG-PET, patients had been fasting for 6 hours. Patients with known diabetes mellitus were excluded from the study, so normal glucose plasma levels (<100 mg%) were confirmed in all patients. The patients were instructed not to chew or talk during the FDG uptake time in order to minimize muscular uptake. Patients were asked to evacuate the urinary bladder before the scan, which was acquired from the pelvic floor to the head. Forty five up to sixty minutes after intravenous administration of 230 – 300 MBq ^{18}F-FDG, PET studies were performed using a whole-body technique (six to seven bed positions ; acquisition time per position : 4 min ; 3 min for emission, 1 min for transmission). In addition, static regional scans of the head and neck region with attenuation correction were acquired by means of a transmission scan acquired by the built-in germanium-68 sources. Attenuation data were segmented (conventional transmission scan) and all images were reconstructed using an iterative algorithm (OSEM, 28 subsets, two iterative steps). FDG was produced in-house using a 18-MeV Cyclotron and an automated FDG synthesis module (HM-18 Cyclotron, Sumitomo Heavy Industries, Japan). The original transverse images were three-dimensionally reconstructed by filtered back-projection.

4. Image Interpretation and Analysis

All study findings were interpreted jointly and in consensus by experienced physicians trained in diagnostic head and neck radiology and nuclear medicine. They were aware of the patients' clinical history, which was provided by the referring physician, but were blinded to the results of other imaging studies if these were performed. Results of imaging for primary tumors were classified preoperatively according to the TNM classification. For lymph node staging, we used the standard VII levels AJCC classification (American Joint Committee on Cancer). Findings were correlated with histology and follow-up. Diagnosis was confirmed either by obtaining histology (32/41) or by follow-up examinations.

Malignancy of primary tumors and lymph nodes were diagnosed by CT and MRI using established morphologic criteria including a lymph node size larger than 10 mm, a conglomeration of a minimum of three lymph nodes, central necrosis, and indistinct nodal margins or if pathological contrast material enhancement was encountered. Abnormal FDG uptake was defined as radiotracer accumulation that was thought to be outside of the normal anatomic structures, such as normal laryngeal muscle activity, and of higher uptake than background activity in the neck or in the location of the normal anatomic structures but asymmetric and/or of higher intensity than is normally seen. Lesions diagnosis was based on the presumed anatomic location (e.g., a likely benign FDG uptake in lymphoid tissues in nasopharynx or tonsils), as well as the symmetry and intensity of the radiotracer uptake.

5. Statistical Analysis

A receiver operating characteristic (ROC) analysis for all tumor lesions, lymph node metastasis and local recurrence was performed for all techniques. All the imaging modalities were compared in terms of accuracy depending on the histopathological findings and follow up data by using the t test and McNemar test adjusted for clustering and p value was calculated. A p value of less than 0.05 was considered to indicate a statistically significant test.

RESULTS

1. Primary Tumor, Lymph Node Metastasis and Local Recurrence Diagnosis

In 23/41 (56.1 %) patients evaluated for initial staging of primary head and neck cancer (group A) ; the sensitivity of CT, MRI and FDG-PET for primary tumor detection was 100 % (95 % CI ; 82.2 - 100 %), while the sensitivity and specificity for lymph node metastasis were 66.7 (95 % CI ; 30.9 - 91 %) and 85.7 % (95 % CI ; 56.2 - 97.5 %), 66.7 % (95 % CI ; 30.9 - 91 %) and 92.9 % (95 % CI ; 64.1 - 99.6 %), 88.9 % (95 % CI ; 50.7 - 99.4 %) and 78.6 % (95 % CI ; 48.9 - 94.3 %), respectively. For 18/41 (43.9 %) patients assessed for recurrence after therapy (group B) ; the sensitivity and specificity for tumor recurrence detection were ; CT and MRI 85.7 % (95 % CI ; 42 - 99.2 %) and 90.9 % (95 % CI ; 57.1 - 99.5 %), FDG-PET 100 % (95 % CI ; 56.1 - 100 %) and 90.9 % (95 % CI ; 57.1 - 99.5 %), while the sensitivity and specificity for lymph node metastasis were ; CT and MRI 83.3 (95 % CI ; 36.5 - 99.1 %) and 91.7 % (95 % CI ; 59.8 - 99.6 %), FDG-PET 100 % (95 % CI ; 51.7 - 100 %) and 91.7 % (95 % CI ; 59.8 - 99.6 %), respectively (Table 3).

1.1. Primary Tumor

All the three imaging modalities correctly diagnosed 23/23 (100 %) primary tumors.

1.2. Lymph Node Metastasis

Correctly diagnosed metastatic lymph nodes by CT was 34/41 (TP ; n = 11, TN ; n = 23) with sensitivity and specificity ; 73.3 % and 88.5 % (95 % CI ; 65.6 - 91.4 %, r = 0.6277, P < 0.0001), by MRI was 35/41 (TP ; n = 11, TN ; n = 24) with sensitivity and specificity ; 73.3 % and 92.3 % (95 % CI ; 67.8 - 92.7 %, r = 0.6794, P < 0.0001) and by FDG-PET was 36/41 (TP ; n = 14, TN ; n = 22) with sensitivity and specificity ; 93.3 % and 84.6 % (95 % CI ; 75.2 - 96.5 %, r = 0.7566, P < 0.0001) (Fig. 1 & 2).

1.3. Local Tumor Recurrence after Therapy

Correctly diagnosed local tumor recurrence after therapy by CT and MRI were 16/18 (TP ; n = 6, TN ; n = 10) with sensitivity and specificity ; 83.3 % and 91.7 % (95 % CI ; 64.5 - 98.1 %, r = 0.7662, P = 0.0001),

Table 3 Accuracy of CT, MRI and FDG-PET for All Lesions Diagnosis

	Head and Neck Cancer						Cervical Lymph Node Metastasis					
	Primary Tumor (n = 23)											
	Sensitivity	Specificity	PPV	NPV	Correlation coefficient (r)	P Value	Sensitivity	Specificity	PPV	NPV	Correlation coefficient (r)	P Value
CT	100 % (82.2 – 100 %)	N/A	100 % (82.2 – 100 %)	N/A	N/A	N/A	66.7 % (30.9 – 91 %)	85.7 % (56.2 – 97.5)	75.0 % (35.6 – 95.6 %)	80.0 % (51.4 – 94.7 %)	0.5367	0.0041
MRI	100 % (82.2 – 100 %)	N/A	100 % (82.2 – 100 %)	N/A	N/A	N/A	66.7 % (30.9 – 91 %)	92.9 % (64.1 – 99.6 %)	85.7 % (42 – 99.2 %)	81.3 % (53.7 – 95 %)	0.6313	0.0006
FDG-PET	100 % (82.2 – 100 %)	N/A	100 % (82.2 – 100 %)	N/A	N/A	N/A	88.9 % (50.7 – 99.4 %)	78.6 % (48.9 – 94.3 %)	72.7 % (39.3 – 92.7 %)	91.7 % (59.8 – 99.6 %)	0.6591	0.0003
	Recurrent Tumors (n = 18)											
	Sensitivity	Specificity	PPV	NPV	Correlation coefficient (r)	P Value	Sensitivity	Specificity	PPV	NPV	Correlation coefficient (r)	P Value
CT	85.7 % (42 – 99.2 %)	90.9 % (57.1 – 99.5 %)	85.7 % (42 – 99.2 %)	90.9 % (57.1 – 99.5 %)	0.7662	0.0001	83.3 % (36.5 – 99.1 %)	91.7 % (59.8 – 99.6 %)	83.3 % (36.5 – 99.1 %)	91.7 % (59.8 – 99.6 %)	0.7500	0.0002
MRI	85.7 % (42 – 99.2 %)	90.9 % (57.1 – 99.5 %)	85.7 % (42 – 99.2 %)	90.9 % (57.1 – 99.5 %)	0.7662	0.0001	83.3 % (36.5 – 99.1 %)	91.7 % (59.8 – 99.6 %)	83.3 % (36.5 – 99.1 %)	91.7 % (59.8 – 99.6 %)	0.7500	0.0002
FDG-PET	100 % (56.1 – 100 %)	90.9 % (57.1 – 99.5 %)	87.5 % (46.7 – 99.3 %)	100 % (65.5 – 100 %)	0.8919	$<$0.0001	100 % (51.7 – 100 %)	91.7 % (59.8 – 99.6 %)	85.7 % (42 – 99.2)	100 % (67.9 – 100 %)	0.8864	$<$0.0001

Parentheses means 95 % Confidence Interval (95 % CI). PPV = Positive Predictive Value, NPV = Negative Predictive Value

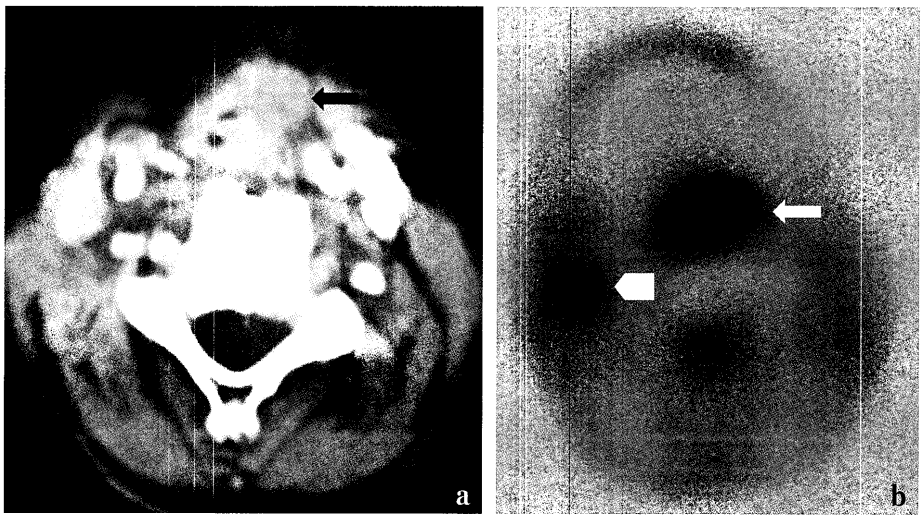


Fig. 1 77-years-old man with subglottic carcinoma, status post laryngectomy. Transaxial scans. a. Contrast enhanced CT. b. FDG-PET. Local tumor recurrence was detected by CT and FDG-PET (arrows). Lymph node metastasis only picked up by FDG-PET (arrow head).

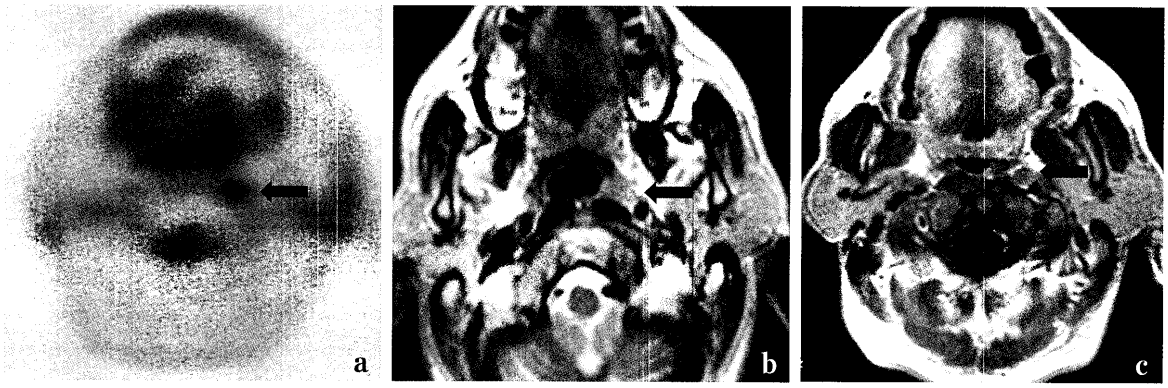


Fig. 2 67-year-old man with history of oropharyngeal carcinoma which was treated surgically. FDG-PET was ordered for evaluation of potentially recurrent or metastatic disease. a. FDG-PET axial scan 8 months post operative... Abnormal left parapharyngeal hot spot (early detection of left Revenuer's lymph node metastasis), b. Concurrent MRI T2W axial image... Post operative granulation tissue could not be differentiated form lymph node metastasis and the result was equivocal, c. MRI T1W axial image 18 months post operative... Left Revenuer's lymph node metastasis becomes clear.

and by FDG-PET was 17/18 (TP ; $n=7$, TN ; $n=10$) with sensitivity and specificity ; 100% and 91.7% (95% CI ; 74.1-98.9%, $r=0.8919$, $P<0.0001$) (Table 4).

2. Distant Metastasis and Synchronous Malignancy Diagnosis

Only FDG-PET by its unique advantage as a whole-body examination could detect distant metastases in 4/41 (9.8%) patients, all outside the head and neck region (liver, lung, paraortic lymph nodes, and bone metastases), and synchronous breast cancer in 1/41 (2.4%) patient (Fig. 3).

N.B. TP = True positive, TN = True negative, r = Correlation coefficient.

DISCUSSION

The present management of head and neck cancer mainly consists of resection of the primary tumor, which may be coupled with neck surgery or subsequent radiotherapy and chemotherapy. When distant

Table 4 Findings of CT, MRI, and FDG-PET in Primary tumor, Lymph Node metastasis and Local Recurrence : Frequency of False Ratings Compared with The Results of Other Techniques

CT False Rating ($n=9$)				MRI False Rating ($n=8$)				FDG-PET False Rating ($n=6$)			
OT	T ($n=0$)	N ($n=7$)	R ($n=2$)	OT	T ($n=0$)	N ($n=6$)	R ($n=2$)	OT	T ($n=0$)	N ($n=5$)	R ($n=1$)
MRI	—	5	1	CT	—	5	1	CT	—	3	—
FDG-PET	—	3	1	FDG-PET	—	3	1	MRI	—	3	—

Note.—Dash indicates 0., T = Primary tumor, N = Lymph node, R = Local recurrence, OT = Other techniques

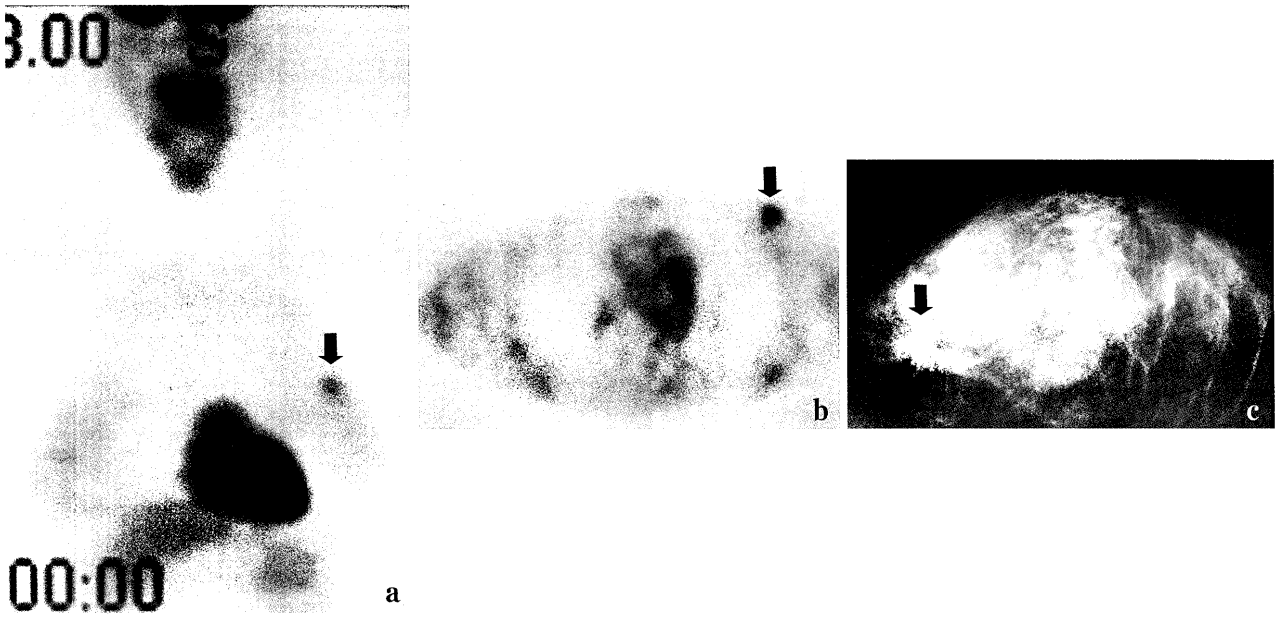


Fig. 3 65-year-old women with thyroid papillary carcinoma. FDG-PET scanning (a. coronal image, b. axial image) easily depicts synchronous second tumor at the left breast which was missed by initial CT and MRI imaging c. Mammography (craniocaudal projection) later shows microcalcifications of malignant pattern at the tumor site. Invasive ductal carcinoma was confirmed after mastectomy.

metastasis is detected preoperatively, appropriate palliation instead of surgical excision or neck dissection is indicated. Therefore, a decision regarding curative or palliative treatment is crucial for untreated head and neck cancer patients.

1. Evaluation of FDG-PET versus CT and MRI

Superior diagnostic accuracy of FDG-PET for detection of recurrent head and neck cancer or metastatic lymph node disease has been shown by many authors[10,14~16,18]. However, only few studies have reported the sensitivity of FDG-PET for preoperative staging of primary head and neck cancer and/or compared it with the conventional diagnostic modalities, for example, functional images such as ^{67}Ga and bone scintigraphy, as well as anatomic images such as CT and MRI[19~23].

Overall 82 head and neck regions were analyzed for detection of malignancy in our study (for primary tumors ; $n=23$, for lymph node metastasis ; $n=41$, for local tumor recurrence after therapy ; $n=18$). The overall sensitivity and specificity for diagnosis of head and neck primary cancer, lymph node spread and local recurrence were ; CT 88.9 % and 89.2 % (95 % CI ; 80.2 − 94.9 %, $r=0.7791$, $P<0.0001$), MRI 88.9 % and 91.9 % (95 % CI ; 81.9 − 95.8 %, $r=0.8049$, $P<0.0001$),

and FDG-PET 97.78% and 86.49% (95% CI ; 84-96.9%, $r=0.8551$, $P<0.0001$). The overall sensitivity and specificity in group (A) versus group (B) were ; CT 90.6/84.6 and 85.7/91.3, MRI 90.62/84.62 and 92.86/91.30, and FDG-PET 96.87/100.0 and 78.57/91.3

1.1. Primary Tumor

Most of the head and neck tumors can be detected easily by clinical examination. Additional information about tumor extension into the deep spaces, the relationship to adjacent structures, and bone infiltration is needed for treatment planning. Both CT and MRI met these requirements in all tumors of our series. CT and MRI, by virtue of their higher anatomic resolution, remain the methods of choice for evaluation of the primary tumor with reliable T-staging in 80% - 90% of cases[24]. FDG-PET had no additional value in this situation because of the lack of morphologic information. The sensitivity of FDG-PET reported by other groups, range from 88% to 100%[9,19,20,22]. Our results are in agreed with the previous reports.

It is evident from the literatures[9,21,25,26] that FDG-PET is very sensitive for detecting primary tumors in head and neck region, and our data further support these findings. Our data demonstrate sensitivity, 100% for the three imaging modalities in the detection of primary tumors. In our series, the sensitivity of FDG-PET was significantly higher than those of CT and MRI but the specificity is slightly lower than them. Previous reports[9,19~22,27,28] showed that FDG-PET has a higher sensitivity (range, 78% - 100%) than did CT and MRI (57% - 82%). Also, Yoshimasa et al.[23], in his study compared the FDG-PET sensitivity with CT and MRI for detection of head and neck carcinoma, concluded that the sensitivity of FDG-PET for primary tumor detection was 100% (similar to our results) and it was lower for MRI and CT, 78.3% and 68.2% respectively (lower than our results). The higher CT and MRI sensitivity recorded in our series, could be explained in view of technical improvement (CT examinations was performed by using 16 mutislice CT scanner with high spatial resolution, moreover, the MR examinations were performed by using 1.5-T machine, which ensure higher image quality (higher signal-to-noise ratio, better spatial resolution through lowering the section thickness and increasing image matrices). Cumulative experience is another impact factor due to pooling of many cancer patients to our hospital (National Cancer Center, Japan).

1.2. Lymph Node Staging

The prognosis for patients with head and neck cancer is strongly influenced by the presence of lymph node metastases[19]. Less than the findings of the previous reports[3], metastatic lymph node disease was confirmed in 15/41 (36.6%) patients in our series. Complete removal of all metastatic lymph nodes is a prerequisite to achieve curative treatment. Morphologic imaging methods, including CT and MRI, are reported to provide a high rate of false-negative diagnoses, which can be explained by micrometastases within otherwise normal lymph nodes[6,11]. It should be noted that more than 40% of all lymph node metastases are localized in nodes

smaller than 1.0 cm in diameter[29]. FDG-PET, as a functional imaging method, might solve this problem. In previous studies, FDG-PET was able to detect metastatic disease in lymph nodes only 4-6 mm[3,11,30,31]. On the other hand, false-negative FDG-PET results were reported in large lymph nodes up to 20 mm in diameter[30] or in necrotic lymph nodes[11]. The reported sensitivities of FDG-PET for nodal disease range from 67% to 91%[3,11,21,22,27,30~32], similar values were found for CT (67-90%)[3,6,11,30,33] and MRI (71-91%)[3,6,11,19,27]. The results of our series are within this range. Reported sensitivity and specificity for diagnosis of lymph node metastasis in our study were ; CT 73.3% and 88.5% (95% CI ; 65.6-91.4%, $r=0.6277$, $P<0.0001$) MRI 73.3% and 92.3% (95% CI ; 67.8-92.7%, $r=0.6794$, $P<0.0001$), FDG-PET 93.3% and 84.6% (95% CI ; 75.2-96.5%, $r=0.7566$, $P<0.0001$), respectively.

High specificity and high negative predictive value for the diagnosis of lymph node disease are required to restrict the extent of a neck dissection so that subsequent morbidity can be minimized[22]. The reported specificity of FDG-PET ranges from 88% to 100%[3,21,27,30,31] compared with a wide range of reported specificity values for CT (38-97%) and MRI (48-94%)[3,6,30,34]. In contrast, all three imaging techniques yielded high specificity (84.5-92.3%) and high negative predictive value (85.2-95.7%) in our study. This

Table 5 Sensitivity and Specificity of CT, MRI, and FDG-PET for Diagnosis of Head and Neck Lymph Node Metastasis, Current Literatures Report

Study	Patients Total (n)	CT		MRI		FDG-PET	
		sensitivity	specificity	sensitivity	specificity	sensitivity	specificity
Laubenbacher et al. 1995 [26]	22	—	—	78 %	71 %	90 %	96 %
Braams et al. 1995 [30]	12	—	—	36 %	94 %	91 %	88 %
Wong et al. 1997 [21]	54	67 %	25 %	67 %	25 %	67 %	100 %
Adams et al. 1998 [2]	60	82 %	85 %	80 %	79 %	90 %	94 %
Yoshimasa et al., 2003 [23]	23	—	76.2 %	—	85 %	—	73.9 %
Shu-Hang et al., 2005 [25]	124	52.6 %	93 %	52.6 %	93 %	74.7 %	94.5 %
Current study	41	73.3 %	88.5 %	73.3 %	92.3 %	93.3 %	84.6 %

discrepancy might be explained by the inhomogeneity of the examination protocols [6] or the limited number of patients [27] included in these studies.

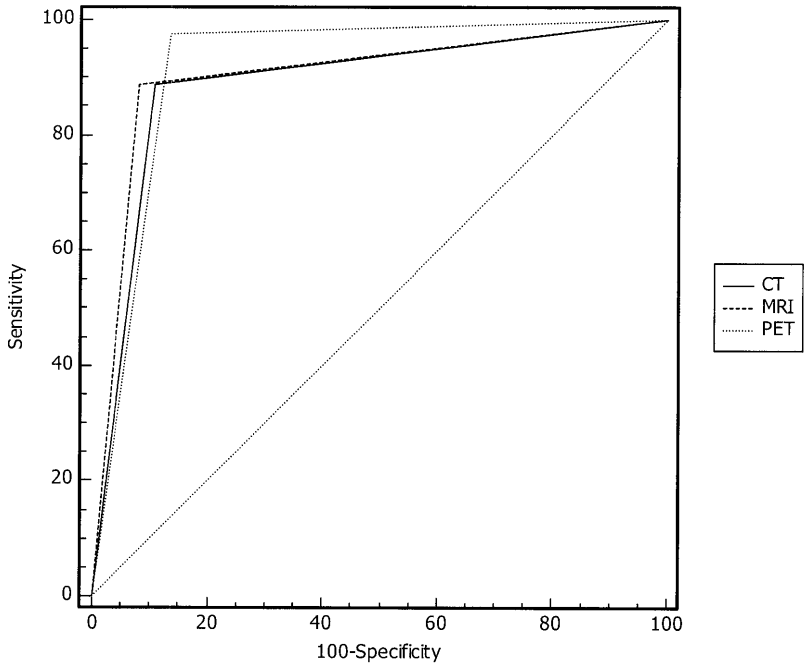
Previous studies [35,36] showed that the extent of the intranodal tumor deposit is a more limiting determinate to surgical dissection than the nodal size. FDG-PET has been reported to have higher specificity than CT/MRI in detecting cervical nodal disease in most of the published literature [3,9,11,21,22,25,27,30,35,37,38]. Three articles [26,31,39] reported that, FDG-PET had a lower specificity. Our study showed the specificity of FDG-PET was lower than CT and MRI (84.5 % vs. 88.5 and 92.3 %). In our study ; false-positive FDG-PET findings (n =4) were mainly due to its inherent inability to discriminate inflammatory processes from tumor infiltration since high-level metabolic changes occur in both instances. Spatial inaccuracy contributed to a portion of the false-positive results. We summarized the outcome of the current literatures versus our study in (Table 5).

ROC analysis did not reveal significant differences among the performances of FDG-PET, CT, and MRI (Fig. 4). However, with respect to surgical planning, FDG-PET provided additional information in 9/41 (22 %) patients, whereas CT (n =5), MRI (n =4), or both (n =2), have unsatisfactory outcome. Furthermore, the potential of FDG-PET (5/8) to improve or correct CT results was superior to that of MRI (3/8), and to correct MRI results was superior to that of CT (4/7 for FDG-PET vs 2/7 for CT) due to superior accuracy (Table 6).

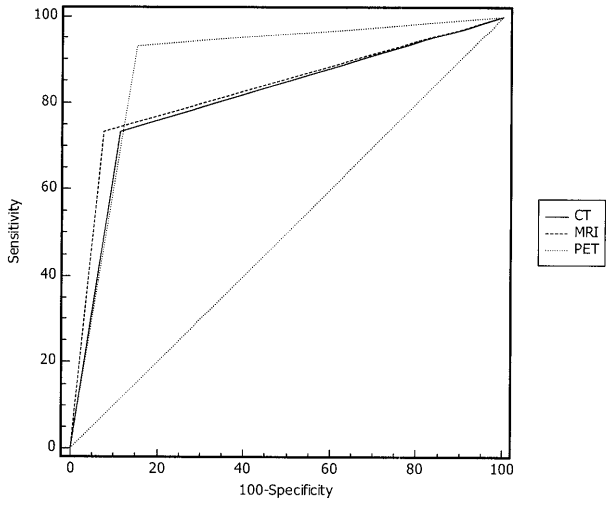
1.3. Local Tumor Recurrence after Therapy

For early detection of local tumor recurrence after therapy FDG-PET recorded higher sensitivity 100 % versus 85.7 % for CT and MRI. Precise evaluation of the presence or absence of residual viable tumor is particularly important to the preservation of vital organs and functions by avoiding unnecessary surgery or performing a reduced form of surgery after neoadjuvant chemoradiation therapy. Eighteen out of forty one patients were investigated for detection of residual tumors or local recurrence after therapy (monitoring). CT and MRI had almost equal sensitivity 85.7 %, FDG-PET recorded the highest sensitivity (100 %). All the three modalities share a similar specificity rate (90.9 %). In patients with no viable tumor cells, the specificity of the three modalities was similar, since by they can not differentiate post operative reaction from residual tumor in one patient.

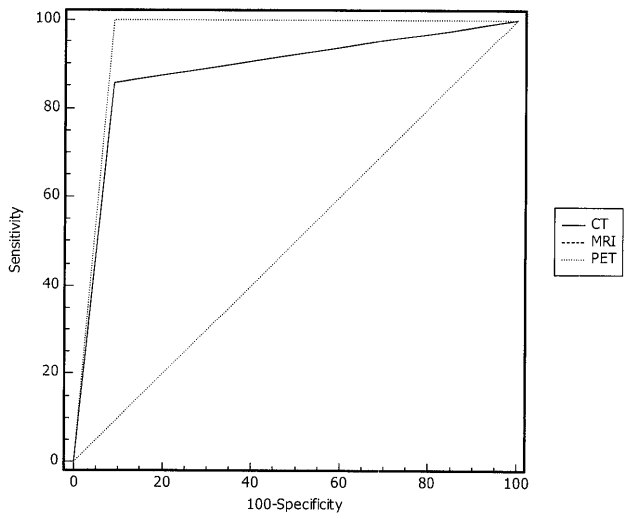
Yoshimasa et al. [23], settled the superiority of FDG-PET in the investigation of the floor of the mouth, the parapharyngeal space, the base of the tongue, and the cheek where these areas were sometimes difficult to assess using anatomic imaging because posttreatment fibrosis, diffuse edematous swelling, and granulation tissue demonstrated such contrast enhancement could not differentiate the persistent residual tumor. Also the artifact created by teeth is a problem during CT and MRI examination that could mask an important data. FDG-PET correctly identified residual tumors independent of their site and can exclude residual tumors with high specificity. We agree with Yoshimasa et al. in his conclusion that increased FDG uptake on FDG-PET images obtained >4 weeks after treatment strongly indicated the presence of residual tumor, whereas the absence of FDG uptake suggested that no viable tumor remained.



(Fig. 4.1.)



(Fig. 4.2.)



(Fig. 4.3.)

Fig. 4 Receiver operating characteristic analysis of findings of CT, MRI, and FDG-PET in overall diagnosis (Fig. 4.1.), lymph node spread (Fig. 4.2.) and local tumor recurrence (Fig. 4.3.). Overall diagnosis ; Area under curve (Az) ± SE for CT = 0.890 ± 0.036, Az for MRI = 0.904 ± 0.034, and Az for FDG-PET = 0.921 ± 0.031. Lymph node spread ; Area under curve (Az) ± SE for CT = 0.809 ± 0.076, Az for MRI = 0.828 ± 0.072, and Az for FDG-PET = 0.890 ± 0.060. Local tumor recurrence ; Area under curve (Az) ± SE for CT and MRI = 0.883 ± 0.092, and Az for FDG-PET = 0.955 ± 0.059. Differences are not significant.

Table 6 Characterization of Neck Lesions Misdiagnosed by CT, MRI and FDG-PET and Frequency of Correction

Characterization of Neck Lesions Misdiagnosed by CT Correctly Diagnosed with MRI and FDG-PET Corrected with CT Findings			
	False-negative ($n=5$)	False-positive ($n=4$)	Total ($n=9$)
MRI	2	1	3
FDG-PET	4	1	5
Characterization of Neck Lesions Misdiagnosed by MRI Correctly Diagnosed with CT and FDG-PET Corrected with MRI Findings			
	False-negative ($n=5$)	False-positive ($n=3$)	Total ($n=7$)
CT	2	-	2
FDG-PET	4	-	4
Characterization of Neck Lesions Misdiagnosed by FDG-PET Correctly Diagnosed with CT and MRI Corrected with FDG-PET Findings			
	False-negative ($n=1$)	False-positive ($n=5$)	Total ($n=6$)
CT	0	2	2
MRI	0	2	2

2. Distant Metastatic Workup and Secondary tumors

Synchronous secondary tumors are found in about 8 % of all head and neck malignant carcinomas[40,41]. In his series, Florian[42], a simultaneous malignancy was histologically confirmed in five (8.5 %) of the 59 patients, including three lesions outside the head and neck region. Regarding our study, there is only one patient (2.4 %) with synchronous tumor (breast cancer) and 4 patients (9.8 %) with distant metastases (liver, lung, paraortic lymph nodes, and bone metastases). All were outside the head and neck region. Similar to Florian, in his series, all of the synchronic tumors and the distant metastasis were clearly diagnosed by a FDG-PET whole-body scan and missed by the initial CT and MRI examinations of the head and neck region. As for whole-body evaluation, FDG-PET has a clinical impact on the management of patients with head and neck cancer through reliable detection of second primary malignancies as well as distant metastases[43]. FDG-PET with whole-body imaging would replace the conventional functional imaging modalities of ^{67}Ga and bone scintigraphy. However, the sensitivity for osteoblastic bone metastases is limited with FDG-PET and bone scintigraphy still has the upper hand in that field[44].

The results of the current study indicate that patients with head and neck cancer could be diagnosed before and followed up after therapy by FDG-PET with high accuracy, although the results must be evaluated with consideration of some important limitations. Firstly ; the results were achieved with a retrospective study and not with randomized, controlled trials. Secondly ; No quantification of SUVs. Thirdly ; FDG-PET studies were performed by PET scanner and fused CT and PET images were not available.

CONCLUSION

This histopathologically controlled study proves FDG-PET as the procedure with the highest sensitivity for overall diagnosis of primary cancer, local tumor recurrence and lymph node metastases of head and neck cancer and has become a routine method in many institutims. Although FDG-PET provides information not available by means of MRI or CT, it cannot replace these anatomic modalities. We conclude that FDG-PET, MRI and CT are essential imaging tools for the management of head and neck cancer.

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