Head and Neck Tumors

16

Franklin C.L. Wong, Xiaoyi Duan,
and E. Edmund Kim

Head and neck cancer is the sixth most common cancer worldwide and makes up 2–5% of cancers in the population. In 2009, the estimated number of new diagnosed head and neck cancers was 35,720 in the US, which includes 10,530 tongue cancers, 10,750 mouth cancers, 12,610 pharynx cancers, and 1,830 other oral cavity cancers [1]. Head and neck cancers are more common in men and account for 66–95% of all cases. Most patients with head and neck cancer are between the ages of 50 and 70 years and the number increases with age, especially after 50 years of age [2]. Head and neck cancers are strongly associated with certain environmental and lifestyle risk factors, including tobacco smoking, alcohol consumption, occupational exposure, and certain strains of viruses, such as the sexually transmitted human papillomavirus [3–5].

Most head and neck cancers occur in the tongue base or within the tonsillar fossa (75%). Head and neck squamous cell carcinomas (HNSCC) make up the vast majority of head and neck cancers (90%). It mostly occurs in males over the age of 40 years with a history of heavy alcohol use coupled with smoking.

Staging criteria for head and neck cancer based on the tumor node metastasis (TNM) system, which is outlined in Table 16.1.

There are more than 30,000 new cases of primary thyroid cancers in the US annually, and the incidence is increasing [6]. In 2009, there were 37,200 new cases of thyroid cancers in the US of which 27,200 were in women, accounting for 4% of all cancers occurring in women [1]. According to the histology or cell structure, thyroid cancers are classified into four types: Papillary cancer (70–80%), follicular (10%), medullary (5–10%), anaplastic (2–5%), metastases (3–5%). Papillary and follicular tumors, still named "differentiated thyroid cancer", are the most common types, with a more favorable prognosis than the medullary and undifferentiated types, but, if metastasis occurs, the prognosis is poor [7].

Staging of thyroid cancer depends on the type of cancer and the age of the patient. TNM staging for differentiated thyroid cancer and medullary thyroid cancer are outlined in Table 16.2.

F.C.L. Wong, M.D., Ph.D., J.D. (✉)
Departments of Nuclear Medicine and Neurooncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
e-mail: fwong@mdanderson.org

X. Duan, M.D.
Department of Nuclear Medicine, First Affiliated Hospital, Xìan Jiaotong University, College of Medicine, Shaanxi 710061, China
e-mail: duanxt2009@hotmail.com

E.E. Kim, M.D., M.S.
Departments of Nuclear Medicine and Diagnostic Radiology, The University of Texas MD Anderson Cancer Center and Medical School, Houston, TX 77030, USA

Graduate School of Convergence Science and Technology, Seoul National University, Seoul, South Korea
e-mail: ekim@mdanderson.org

E.E. Kim et al. (eds.), *Clinical PET and PET/CT: Principles and Applications*,
DOI 10.1007/978-1-4419-0802-5_16, © Springer Science+Business Media New York 2013

Table 16.1 TNM staging for head and neck cancer

TX: Cannot be assessed
T0: No primary tumor
Tis: In situ
T1: <2 cm
T2: 2–4 cm
T3: >4 cm
T4: Invades adjacent structures (bone, deep muscle, sinus, skin)
NX: Cannot be assessed
N0: No evidence of regional lymph node metastasis
N1: Metastasis in a single ipsilateral lymph node (≤3 cm)
N2: a. Single ipsilateral lymph node (3–6 cm)
b. Multiple ipsilateral lymph nodes (<6 cm)
c. Bilateral or contralateral lymph nodes (<6 cm)
N3: Metastasis in a lymph node (>6 cm)
MX: Presence of distant metastasis cannot be assessed
M0: No evidence of distant metastasis
M1: Distant metastasis present

Table 16.2 Staging for thyroid cancers

Differentiated thyroid cancer
Less than 45 years of age
Stage I: Tumor of any size with regional node metastasis, no distant metastasis
Stage II: Tumor of any size with regional node metastasis, distant metastasis
45 years of age or older
Stage I: Tumor <2 cm, and remains localized to the thyroid
Stage II: Tumor 2–4 cm, and remains in the thyroid
Stage III: Tumor of any size with regional lymph node metastasis
Stage IV: Tumor of any size with distant metastasis
Medullary thyroid cancer
Stage 0: Cancerous cells have been found through a special screening but there is no tumor
Stage I: Tumor <2 cm, and remains in the thyroid
Stage II: Tumor 2–4 cm, and remains in the thyroid
Stage III: Tumor >4 cm, with regional tissues or lymph node metastasis
Stage IV: Distant metastasis

Imaging of Head and Neck Tumors

Computed Tomography and Magnetic Resonance Imaging

Currently, computed tomography (CT) and magnetic resonance imaging (MRI) with contrast enhancement are the standard imaging techniques for the evaluation of head, neck, and thyroid cancers, which can provide structural information at a high spatial resolution. MRI is superior to CT for laryngeal and hypopharyngeal tumor staging, with high sensitivity and specificity [8]. Soft tissue between the cricoids cartilage and the airway may represent subglottic carcinoma or extension. Thyroid adenomas may appear brighter than normal thyroid tissue on T1-weighted images, possibly related to hemorrhagic degeneration. Thyroid carcinomas show T1 and T2 prolongation. Parathyroid adenomas tend to have longer T2 relaxation times than thyroid adenomas. Tissue characterization of MRI, such as spin-echo sequences, is useful in distinguishing posttreatment fibrosis from recurrent cancer. Discrimination between adenomas and hyperplasia is not possible with MRI [9], because metastatic nodes show contrast enhancement in the rim. MRI has another advantage over CT in the differentiation of lymphadenopathy with various slice orientations and gradient echo techniques revealing vessels [10]. Magnetic resonance angiography allows excellent depiction of the carotid vessels, and is indicated in evaluating vascular displacement or compression by tumor growth and perfusion.

Magnetic Resonance Spectroscopy

Early experience with in vivo magnetic resonance spectroscopy (MRS) has shown its potential for obtaining biochemical information, thus enhancing the diagnostic sensitivity of MRI studies [11]. However, when applied in head and neck tumor, MRS is disappointing because MRS requires a homogeneous magnetic field, while susceptibility artifacts introduced by the paranasal sinuses, airway, and bone, and pulsation artifacts from the carotid artery, severely degrade data. Additionally, a large amount of fat within the neck produces a lipid peak that obscures the relatively small peaks of tumor markers, such as choline. Finally, MRS remains nonspecific. However, with the development of newer techniques, MRS may become practical for evaluating head and neck tumors [12].

Neck Ultrasound

Neck ultrasound (US) has been reported to be superior to palpation in the detection of lymph node metastases [13]. A study reported a sensitivity of 96.8% and a specificity of 93.3% for US in the diagnosis of head and neck cancers, and 91.7% and 91.7%, respectively, in the diagnosis of papillary thyroid cancers [14].

US-guided fine-needle aspiration biopsy (USGFNAB) of thyroid nodules is currently used by many clinicians, with accuracy of 98% in the diagnosis for primary thyroid cancers. The result from FNAB could affect clinical management in 85% of patients with thyroid nodules [15]. The false negative rate of FNAB for benign thyroid lesions is from 1% to 5% [16]. In addition to thyroid nodules, USGFNAB is also applied to neck masses, including cervical nodal metastases from thyroid and other head and neck cancers. Sufficient cells from lymph nodes as small as 3–4 mm can be obtained by USGFNAB [17].

The disadvantages of US include the following facts: First, procedures are time consuming and operator-dependent; Second, interpretation of US images is subjective, requiring experience and expertise with head and neck US and anatomy knowledge by individual acquiring the images; Third, regions, such as areas deep to bone or air-filled structures, are not well visualized by US; Fourth, it is limited to regional study, not a whole-body imaging technique.

Single-Photon Emission Computed Tomography

Functional imaging such as ^{99m}Tc-MIBI or ^{201}TI single-photon emission computed tomography (SPECT) has been reported as a useful modality in the staging of primary neck and head tumors, in the differentiation of metastatic from reactive lymph nodes, and is particularly useful for detection of occult head and neck tumors and for assessing recurrences. On the basis of whole-body scanning, SPECT is also helpful for screening of distant metastases [18, 19].

Fused SPECT/CT has emerged during the past decade, which correlates anatomic information from CT with functional information from SPECT. In recent years, SPECT/CT has been used for SN mapping, which is very important clinically if the tumor is located in body parts with ambiguous lymph node drainage. Fused SPECT/CT SN mapping is often performed before SN biopsy and could provide additional data that are of clinical relevance to SN biopsy in patients with trunk or head and neck melanoma and in patients with mucosal head and neck [20].

Some studies have reported on the role of ^{131}I SPECT/CT for investigation of differentiated thyroid cancers. This modality could accurately localize regional and distant metastases and, in the postsurgical patient, may identify residual thyroid tissues. This allows staging and risk stratification of patients prior to ^{131}I therapy [21]. With specific cancer types such as thyroid and parathyroid cancer, SPECT/CT is indeed a useful tool.

Positron Emission Tomography (PET) and PET/CT

The anatomic information from CT or MRI alone cannot completely reveal histopathologic and physiologic characteristics of tumors. Metabolism imaging such as PET might help to characterize the biologic behavior of both primary and metastatic diseases.

Head, neck, and thyroid tumors, either primary or metastatic tumors, have been studied with PET using ^{18}F-fluorodeoxyglucose (FDG) for viability, ^{11}C-methionine for amino acid transport [22], ^{18}F-fluorothymidine for cell proliferation [23], as well as ^{18}F-fluoromisonidazole for hypoxia [24]. The apparent advantages of these agents are their higher specificity and low background. To date, ^{18}F-FDG PET has become an accepted and widely used imaging modality for the evaluation of head and neck cancer [25–28]. However, because of the complex anatomy of the head and neck region, the clinical application of PET is limited by lack of anatomic detail.

Hybrid PET/CT is a promising imaging technique that permits almost synchronous image acquisition of anatomic and metabolic datasets. Compared with PET alone, PET/CT showed a higher accuracy for the detection of head and neck cancer (96% for PET/CT, 90% for PET alone) [29]. Another major advantage of PET/CT is the reduction of scanning time. Single PET examination alone still requires a transmission scan for attenuation correction. Combined CT and PET can obtain anatomic and functional images consecutively in one examination, and attenuation correction by incorporation of fast CT technology (2 min for a whole-body study), which is much faster than using a transmission scan. Therefore, the examination time of PET/CT is notably shortened [30].

Hybrid PET/CT is performed approximately 1 hour after the intravenous injection of ^{18}F-FDG, with acquisition of CT data immediately preceding acquisition of emission data. During the uptake period, patients are advised not to speak, as this may result in vocal cord uptake which could be misinterpreted as pathologic. Patients are also advised not to move or chew during the uptake period. In order for images to be easier illustrated, oral diazepam may be used before the injection of ^{18}F-FDG to help prevent unwanted uptake in neck muscles as a result of tension [31].

Clinically used radiopharmaceuticals include those involved in metabolism of glucose, nucleosides, amino acids, hypoxia, or transporters (Table 16.3).

Clinical Application of 18F-FDG PET/CT in Head and Neck Tumors

As MRI or CT can better evaluate local soft-tissue and bony anatomy, PET/CT is rarely used for initial T staging of primary tumors. Hybrid PET/CT may be helpful in delineation of extent of regional lymph node involvement, detection of distant metastases, identification of an unknown primary tumor, monitoring of the treatment response, long-term surveillance for recurrence and metastases, and planning radiotherapy.

Staging Primary Head and Neck Tumors

Accurate staging has a prognostic value and is important in selecting the appropriate treatment strategy. A recent multicenter prospective study showed that adding whole-body ^{18}F-FDG PET to the pretherapeutic conventional staging modality, such as US, CT, or MRI, can improve the TNM classification of HNSCC and it altered the management of 13.7% of 233 patients [39]. The result supports the implementation of ^{18}F-FDG PET in the routine imaging work-up of HNSCC. Compared with PET alone, PET/CT provides better localization of foci increased FDG uptake, thus reducing the number of equivocal PET [40]. A recent study reported that sensitivity of PET/CT was slightly higher than that of PET alone, while specificity of PET/CT was significantly higher than that of PET alone in patients with initial staging and follow-up of head and neck cancers (initial staging: 90.5% vs. 62.2%; follow-up: 97.2% vs. 74.4%) [41]. Results of PET/CT may alter the treatment plan in some patients with head and neck cancers [42]. For the detection of distant metastases, ^{18}F-FDG PET/CT had a sensitivity of 89%, a specificity of 97%, and an overall accuracy of 96%, while sensitivity and specificity were 61–97% and 21–100% for MRI or CT [43]. The initial staging and detecting metastases of head and neck tumors with ^{18}F-FDG PET/CT are demonstrated in Figs. 16.1 and 16.2.

It is clear that nodal size alone has not been a good discriminator in the assessment of possible malignant involvement. Small nodes can harbor a metastatic tumor and large nodes may simply reflect reactive change. ^{18}F-FDG PET/CT is helpful in the detection of nodal metastases as small as 10 mm. Its sensitivity, specificity, and accuracy were 84%, 91%, and 89% respectively [44]. While false-positives were notable in some patients with lymph nodes smaller than 3 mm [45]. In these cases, selective neck dissection or lymph node biopsy is more definitive.

Thyroid nodules are relatively common. The prevalence of incidental thyroid FDG uptake (including both focal and diffuse lesions) was

Table 16.3 Clinically used radiotracers for evaluation of head, neck, and thyroid tumors

Radiotracer	Imaging modality	Metabolism	Disease	Sensitivity %	Specificity %	Gold standard	References
^{18}F-FDG	PET/CT	Glucose	Head and neck tumor	89	95	Pathology	[41]
			Differentiated thyroid cancer	95	91	Pathology	[32]
^{18}F-FDOPA	PET/CT	Amino acids	Medullary thyroid cancer	81	–	Pathology	[33]
^{18}F-FLT	PET	Nucleosides	Head and neck tumor	95	–	Pathology	[34]
^{18}F-FMISO	PET	Hypoxia	Head and neck tumor	79	–	Pathology	[35]
^{18}F-FET	PET/CT	Amino acids	Head and neck tumor	64	100	Pathology	[36]
^{124}I NaI	PET/CT	Nucleosides	Differentiated thyroid cancer	90	–	Pathology	[37]
^{99m}Tc-MIBI	SPECT	Perfusion	Head and neck tumor	90	78	Pathology	[18]
^{131}I NaI	SPECT/CT	Nucleosides	Differentiated thyroid cancer	48	–	Pathology	[38]

^{18}F-FDG ^{18}F-fluorodeoxyglucose, *^{18}F-FDOPA* F-18 fluoro didroxyphenylalanine, *^{18}F-FLT* F-18 fluoro-3'-deoxy-L- fluorothymidine, *^{18}F-FMISO* F-18 fluoro-misonidazole, *^{18}F-FET* O-(2-[(18)F]-fluoroethyl)-L-tyrosine, *^{124}I NaI* I-124 sodium iodide, *^{99m}Tc-MIBI* Tc-99m sestamibi, *^{131}I NaI* I-131 sodium iodide

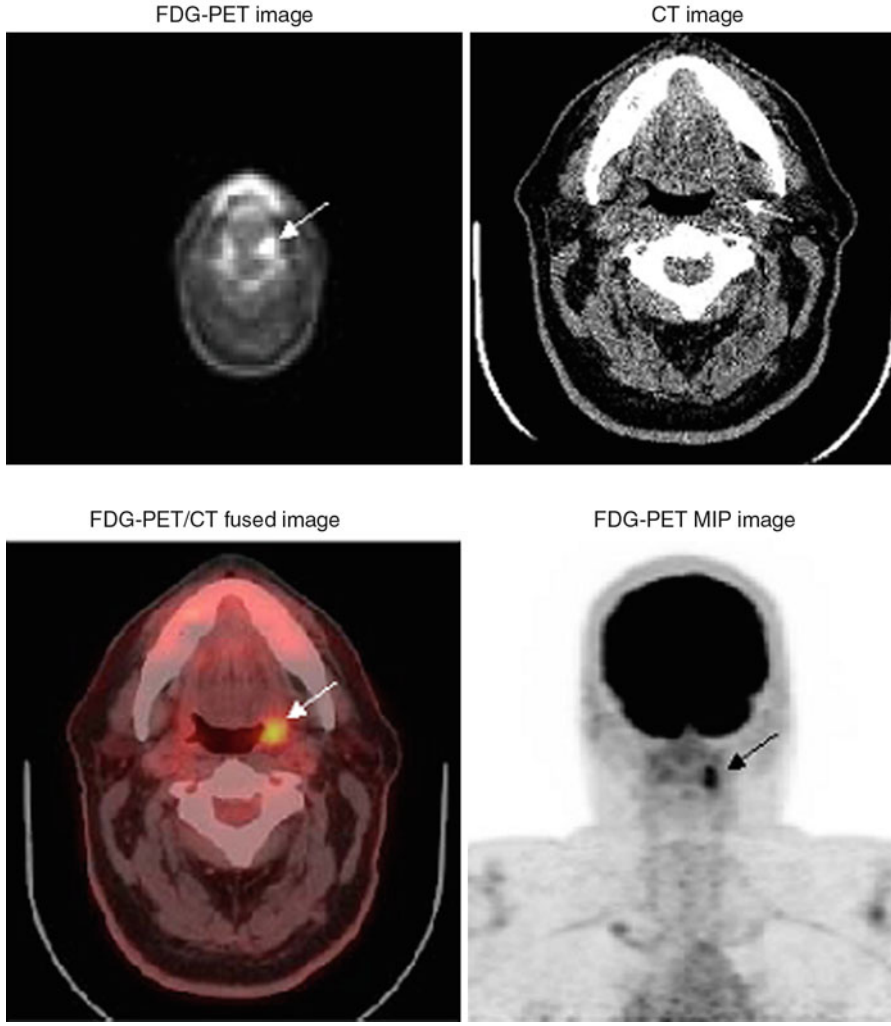

Fig. 16.1 A 62-year-old male with recently diagnosed left tonsillar carcinoma. FDG-PET images show a focal abnormal uptake at the left tonsil represents the patient's known primary tumor with maximum SUV of 5.1 (*arrow*). The corresponding lesion is noted on CT (*arrow*). Fused and MIP images show the lesion clearly (*arrows*). No evidence of active regional nodal or distant metastatic disease

3.8% on FDG PET/CT. Of focal lesions, the cancer risk is 63.6% on pathologic basis [46]. Diffuse thyroid FDG uptake is most probably benign and usually caused by thyroiditis [47].

In thyroid tumors, PET/CT is no better than US and CT for initial evaluation of cervical node [48]. Hybrid PET/CT may be used for detecting recurrent thyroid cancer and localizing neoplasm to facilitate biopsy of incidental findings. The correlation between standard uptake value (SUV) intensity and the risk for a malignant lesion is still controversial [49, 50]. In the case of focal FDG uptake, USGFNAB is likely to obtain a tissue diagnosis, with diagnostic accuracy of 98% [15]. For medullary tumor, PET/CT is superior to anatomic imaging in identifying the source of persistent measurable calcitonin in patients who have undergone total thyroidectomy [51, 52].

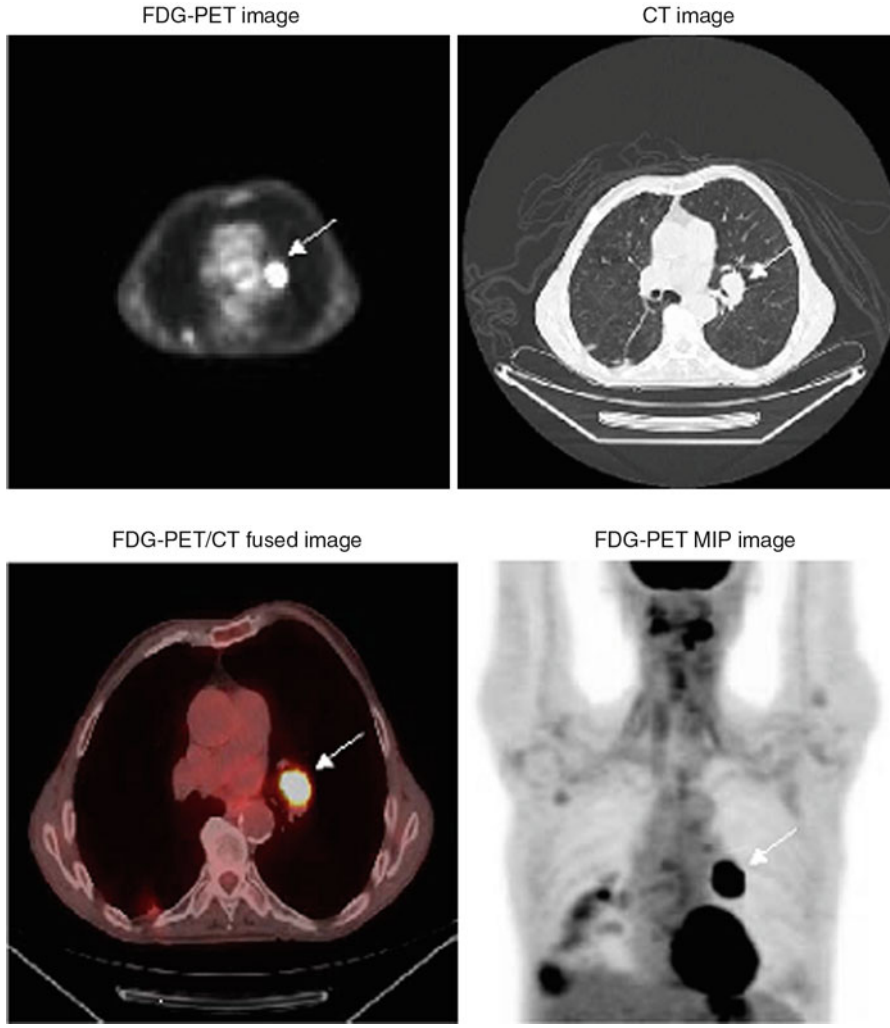

Fig. 16.2 A patient with squamous cell cancer in the tongue who has undergone chemoradiation. FDG-PET/CT images show an active area at left hilar with maximum SUV of 14.5, which may represents a head/neck metastatic lesion (*arrows*). Deep FNA confirms metastatic squamous carcinoma

Detecting Recurrent Tumors

After therapy, early detection of recurrence is critical to achieve an optimal outcome. After surgery or radiation therapy for head and neck tumors, the regional anatomy is distorted. Therefore, anatomic imaging such as CT and MRI has relatively poor specificity in the assessment of residual or recurrent disease [53, 54]. There is a relatively high sensitivity for ^{18}F-FDG PET/CT to detect recurrent disease at the primary tumor site (Fig. 16.3). It also finds regional lymph node metastases at earlier stage than conventional imaging [28, 55, 56]. Approximately 70% of patients with head and neck cancer with positive PET/CT findings were confirmed to have recurrent tumor by histopathology [57]. Abnormal physiologic uptake, metabolically active tissues such as brown adipose tissue and muscle contractions are the main reasons of false-positive results for PET/CT [58]. FNAB should be performed if PET/CT findings could not settle the issue.

Fig. 16.3 A 54-year-old male with history of T1 squamous cell cancer in the left glottis and underwent laser resection in 09/2006. FDG-PET/CT images note a hypermetabolic lesion measuring 2.5×2 cm in the left oropharynx with SUV of 11, which is consistent with recurrence of tumor (*down arrows*). There is also hypermetabolic adenopathy in the left neck measuring 1.9×1.7 cm and SUV of 15.8 (*arrows*), which is confirmed to be metastatic squamous cell carcinoma by lymph node biopsy

Although well-differentiated papillary and follicular thyroid cancers are treatable, 20% of patients have a recurrence associated with an 8% death rate. Earlier detection and effective management of local recurrence can improve the prognosis for these patients. Whole-body ^{131}I scintigraphy (WBS) and serial thyroglobulin measurement are standard methods for detecting differentiated thyroid cancer recurrence. However, WBS is negative in 10–15% of patients with detectable serum Tg levels [59]. A meta-analysis reported the sensitivity and specificity of ^{18}F-FDG PET/CT in detection of recurrent or metastatic differentiated thyroid cancer were 93.5% and 83.9% respectively in patients with elevated serum thyroglobulin and negative ^{131}I scan [60], as demonstrated in Fig. 16.4. When used as a predictor for survival of thyroid cancer, ^{18}F-FDG

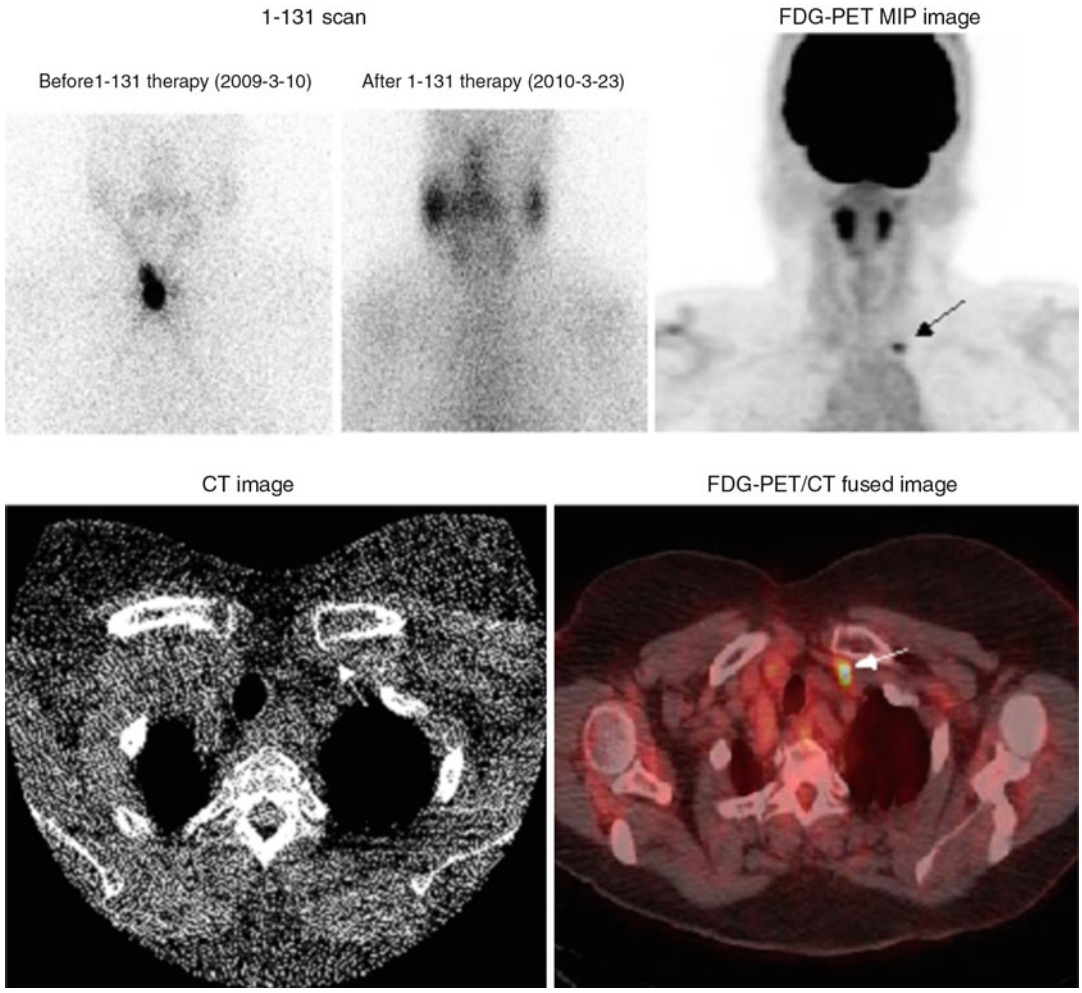

Fig. 16.4 A 64-year-old female with poorly differentiated thyroid cancer. Thyroidectomy was performed in 10/2008, followed by radioiodine ablation therapy. Of note, she has rising thyroglobulin level, with negative I-131 whole body scan. FDG-PET/CT images show focal hypermetabolism in the left supraclavicular region with SUV 6.3, which is consistent with recurrent thyroid cancer (*arrows*)

uptake of thyroid tumor correlated with elevated Tg and negative ^{131}I scan. High ^{18}F-FDG uptake may mean shorter survival [61].

Finding Unknown Primary Tumors

Approximately 2–9% of all HNSCCs present in the way how cervical malignant nodes have been detected but primary tumor site has failed to demonstrate [62]. Hybrid PET/CT is useful in these cases. A recent meta-analysis addressed 150 patients who had initial negative MRI findings, in which the primary tumors in 40 patients were detected by ^{18}F-FDG PET [63]. Another study reported patients with biopsy-proved metastatic disease from unknown head and neck primary tumor undergoing further evaluation with ^{18}F-FDG PET/CT. It showed that 57% of unknown primary tumors were detected by PET/CT [64]. The common sites for false-negative ^{18}F-FDG PET/CT scans are often the lingual and palatine tonsils because of their physiologic uptake. In such cases, asymmetric uptake may be an indicator of tumors. One precaution for salivary gland tumor is that the vast majority of FDG

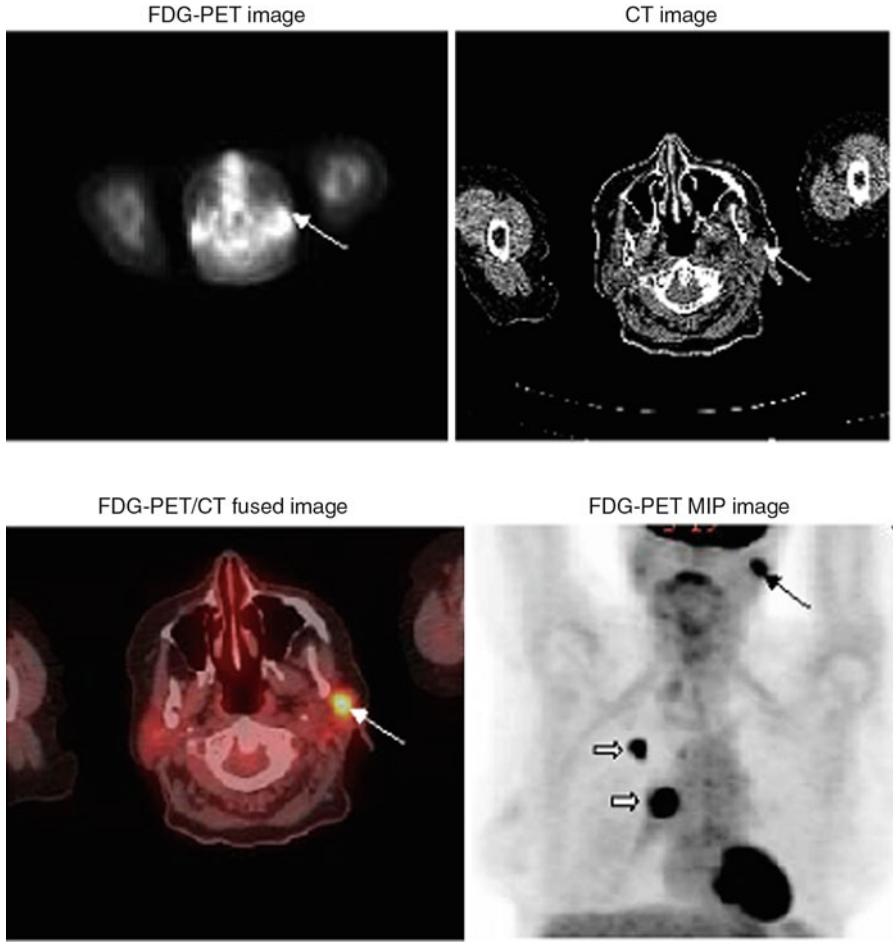

Fig. 16.5 A 73-year old female with diagnosed right non-small cell lung cancer and right hilar nodal metastases (*right arrows*). An incidental finding of pleomorphic adenoma with hypermetabolism is noted in the left parotid gland, likely representing benign lesion such as pleomorphic adenoma or Warthin's tumor (*arrows*)

hypermetabolic lesions in the salivary glands (especially the parotids) are benign tumors including pleomorphic adnoma (80%) or Warthin's tumor (<15%) (Fig. 16.5) [65].

Monitoring the Response to Therapy

Patients could benefit from periodic surveillance after treatment. For example, the early identification of nonresponders to a particular therapy would allow physicians to discontinue ineffective treatments and initiate alternative approaches. Theoretically, metabolic changes of tumor cells are earlier and better predictors of therapeutic effects than anatomic changes shown by CT or MRI [66]. Additionally, because often in cases there is residual fibrosis, edema, or tissue necrosis after surgery, chemotherapy, or radiation therapy, it is difficult for anatomic imaging to differentiate these conditions from tumor recurrence. Therefore, anatomic imaging is not sufficient for assessing response to therapy. Hybrid PET/CT could make up for this limitation and provide valuable information about the efficacy of radiation therapy or chemotherapy regimens (Fig. 16.6).

An early study has suggested that reduced FDG uptake after treatment appeared to coincide with a decline in the number of viable tumor cells

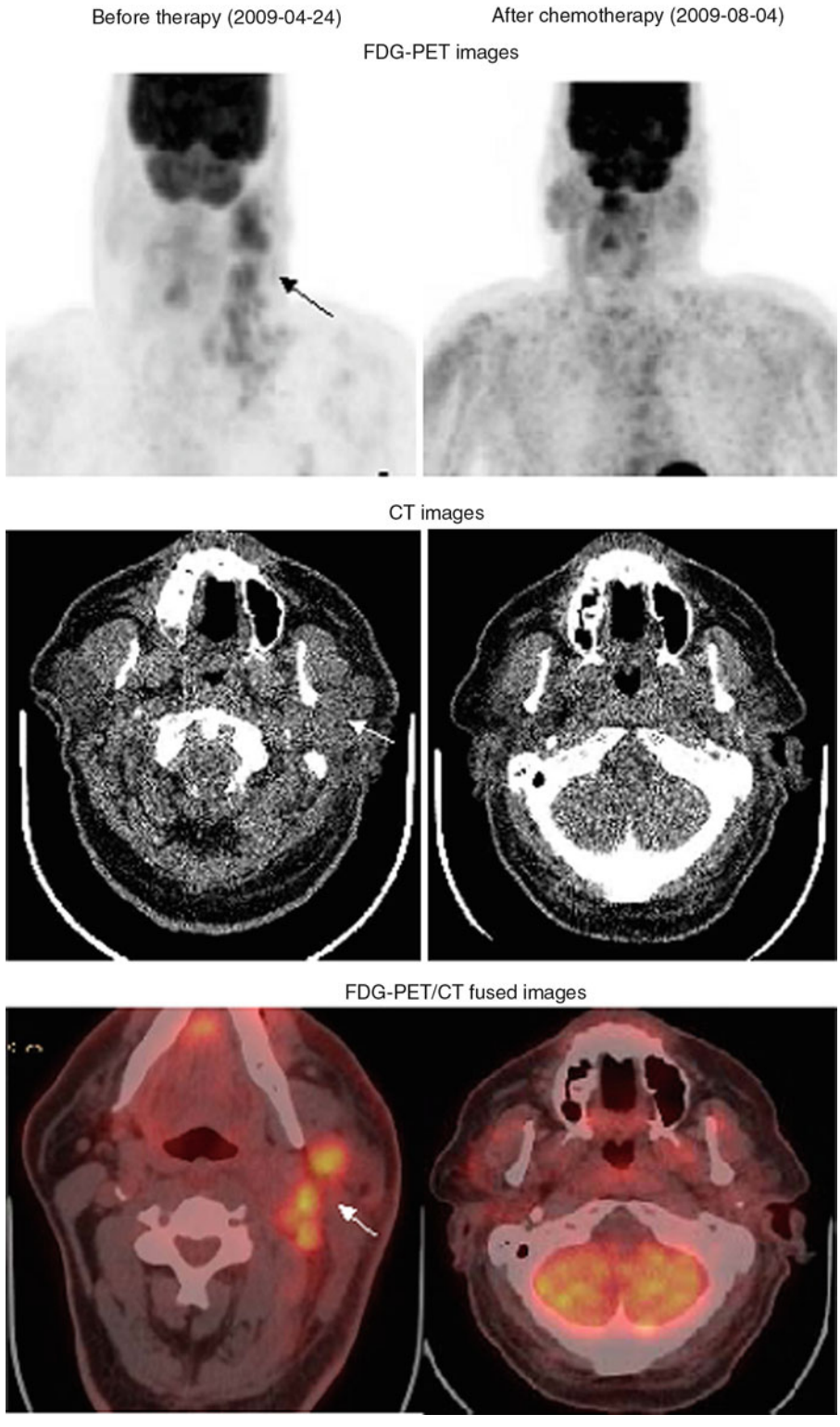

Fig. 16.6 A 69-year-old male with carcinoma of the left parotid. Before chemotherapy, FDG-PET/CT images show extensive nodular hypermetabolism involving left head and neck, extending from left temporalis muscle region to left axillary nodes (*arrows*). After chemotherapy, the primary left parotid tumor has decreased dramatically in intensity, and nodal hypermetabolism in the left neck and left axilla has resolved completely, which are consistent with an excellent response to treatment

[67]. A decline in ^{18}F-FDG uptake during chemotherapy was significantly associated with a clinical response and survival [28, 68]. SUV may be helpful in the evaluation of the response to therapy. A significant reduction in SUV after therapy would be a good response. Tissue inflammation in response to radiotherapy may lead to false-positive results. Normal variants of ^{18}F-FDG uptake in head and neck locations may also pose difficulty in interpreting images. So, there is no fixed quantitative scheme to use SUV to differentiate cancerous tissue from noncancerous tissue. Therefore, it is particularly important to have a baseline PET/CT scan to help differentiate incidental physiologic ^{18}F-FDG-avid foci from malignant foci on subsequent posttreatment scans.

The timing of PET/CT after therapy is very crucial for accurate assessment of treatment response. The metabolic activity of residual viable tumor might be decreased immediately after the completion of radiation therapy, and it may take several weeks to recover their metabolic activity. Additionally, inflammation caused by radiation may result in diffuse increased FDG uptake, which can impair the identification of residual tumor. A report noted an improvement in both sensitivity and specificity of ^{18}F-FDG PET when the scan was obtained at 8 weeks, as compared with 4–8 weeks, after the end of chemoradiotherapy. A false-positive or false-negative result on ^{18}F-FDG PET/CT did not occur later than 8 weeks after radiation therapy [69]. A recent study has the consensus opinion that PET/CT should be performed about 10–12 weeks after the end of therapy [70].

Planning Radiotherapy

Precise and accurate localization of radiotherapy targeted to the gross tumor volume (GTV) is critical for optimizing the radiation therapeutic ratio. With the development of molecular imaging, specific physiologic and molecular information about tumors can now be incorporated into radiation treatment planning. Hybrid PET/CT is a bridge between anatomic imaging and functional imaging, which can provide important information complementary to CT. Therefore, PET/CT appears to be ideally suited to radiotherapy planning in the era of conformal radiotherapy [71]. A recent study reported 42 patients with head and neck cancer of various stages and treated with ^{18}F-FDG PET/CT based intensity-modulated radiation therapy (IMRT). The 2-year overall survival and disease-free survival rates are 83% and 71%, respectively [72], which were notably higher than those in patients receiving standard fractionation (46.1% vs. 37.1%) or receiving accelerated fractionation with concomitant boost (50.9% vs. 39.3%) [73]. ^{18}F-fluoromisonidazole (^{18}F-FMISO) is a nitroimidazole PET tracer that is bound to cell constituents under hypoxic conditions. The feasibility of ^{18}F-FMISO PET/CT in detecting hypoxic subvolume for IMRT has been reported in select patients to achieve favorable outcome [74].

To date, the value of PET/CT for radiotherapy planning is still under investigation. Integrated PET/MRI may further improve the accuracy of GTV delineation, especially for oropharyngeal and oral cavity tumors, because of its higher spatial and temporal resolution.

There has been increasing concern about radiation exposure from PET/CT, especially from the CT portion. The total effective doses from CT and PET scanning ranged from 1.0 to 3.0 cGy [75]. The CT component contributed 54–81% of the total combined dose. However, in light of head and neck cancer, for a patient who is expected to receive 3,000–6,000 cGy to the treatment regions, the exposure from PET/CT should be less of a concern.

Conclusion

Hybrid PET/CT is an effective noninvasive clinical tool for the assessment of head, neck, and thyroid cancer. The primary benefits of this modality are detecting distant metastases, discovering unknown primary tumors, and monitoring response to therapy. This technique can also be used for long-term surveillance. However, the clinical application of PET/CT is currently

limited because of its inadequate scanner resolution and nonspecificity of FDG. Ultimately, with the progression of hardware and software, and with the application of tumor-specific tracers, PET/CT may be more valuable in evaluation of head, head and thyroid tumors.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. CA: a cancer journal for clinicians. American Cancer Society. Published online May 2009.
2. Ridge JA, Glisson BS, Lango MN, et al. Head and neck tumors. Cancer management: a multidisciplinary approach. 11 ed. 2008.
3. Maier H, Dietz A, Gewelke U, et al. Tobacco and alcohol and the risk of head and neck cancer. Clin Investig. 1992;70:320–7.
4. Cauvin JM, Guénel P, Luce D, et al. Occupational exposure and head and neck carcinoma. Clin Otolaryngol Allied Sci. 1990;15:439–45.
5. Gillespie MB, Smith J, Gibbs K, et al. Human papillomavirus and head and neck cancer: a growing concern. JSC Med Assoc. 2008;104:247–51.
6. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA. 2006;295:2164–7.
7. Hu MI, Vassilopoulou-Sellin R, Lustig R, et al. Head and neck tumors. Cancer management: a multidisciplinary approach. 11 ed. 2008.
8. Castelifns JA, Kaiser MC, Vakl J, et al. Magnetic resonance imaging of the laryngeal cancer. J Comput Assist Tomogr. 1987;11:134–40.
9. Glazer HS, Nimyer JH, Balfe DM. Neck neoplasms: MR imaging. Part II. Posttreatment evaluation. Radiology. 1986;160:349–54.
10. Vogl TJ, Steger W, Balzer J, et al. MRI of the neck, larynx and hypopharynx. In: Hasso AN, Stark DD, editors. Spine and body MRI. Boston: ARKS; 1991. p. 99–110.
11. Mafee MF, Barany M, Gotsis ED, et al. Potential use of in vivo proton spectroscopy for head and neck lesions. Radiol Clin North Am. 1989;27:243–54.
12. King AD, Yeung DKW, Ahuja AT, et al. In vivo proton MR spectroscopy of primary and nodal nasopharyngeal carcinoma. AJNR Am J Neuroradiol. 2004;25:484–90.
13. Prayer L, Winkelbauer H, Gritzmann N, Winkelbauer F, Helmer M, Pehamberger H. Sonography versus palpation in the detection of regional lymph-node metastases in patients with malignant melanoma. Eur J Cancer. 1990;26:827–30.
14. Hwang HS, Perez DA, Orloff LA. Comparison of positron emission tomography/computed tomography imaging and ultrasound in staging and surveillance of head and neck and thyroid cancer. Laryngoscope. 2009;119:1958–65.
15. Ogilvie JB, Piatigorsky EJ, Clark OH. Current status for fine needle aspiration for thyroid nodules. Adv Surg. 2006;40:223–38.
16. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med. 1993;118:282–9.
17. van den Brekel MW, Castelijns JA, Stel HV, et al. Occult metastatic neck disease: detection with US and US-guided fine-needle aspiration cytology. Radiology. 1991;180:457–61.
18. Leitha T, Glaser C, Pruckmayer M, et al. Technetium-99 m-MIBI in primary and recurrent head and neck tumors: contribution of bone SPECT image fusion. J Nucl Med. 1998;39:1166–71.
19. Valdés Olmos RA, Balm AJ, Hilgers FJ, et al. Thallium-201 SPECT in the diagnosis of head and neck cancer. J Nucl Med. 1997;38:873–9.
20. Even-Sapir E, Lerman H, Lievshitz G, et al. Lymphoscintigraphy for sentinel node mapping using a hybrid SPECT/CT system. J Nucl Med. 2003;44:1413–20.
21. Wong K, Zarzhevsky N, Cahill JM, Frey KA, Avram AM. The value of diagnostic 131-I SPECT-CT fusion imaging in the evaluation of differentiated thyroid carcinoma. AJR Am J Roentgenol. 2008;191:1785–94.
22. Leskinen-Kallio S, Lindholm P, Lapela M, Joensuu H, Nordman E. Imaging of head and neck tumors with positron emission tomography and [^{11}C]methionine. Int J Radiat Oncol Biol Phys. 1994;30:1195–9.
23. Shields AF, Grierson JR, Dohmen BM, et al. Imaging proliferation in vivo with [F-18]FLT and positron emission tomography. Nat Med. 1998;4:1334–6.
24. Koh WJ, Rasey JS, Evans ML, et al. Imaging of hypoxia in human tumors with [F-18]fluoromisonidazole. Int J Radiat Oncol Biol Phys. 1992;22:199–212.
25. Adams S, Baum R, Stuckensen T, et al. Prospective comparison of ^{18}F-FDG PET with conventional imaging modalities (CT, MRI, US) in lymph node staging of head and neck cancer. Eur J Nucl Med. 1998;25:1255–60.
26. Stokkel MP, ten Broek FW, Hordijk GJ, et al. Preoperative evaluation of patients with primary head and neck cancer using dual head 18 fluorodeoxyglucose positron emission tomography. Ann Surg. 2000;231 :229–34.
27. Wong RJ, Lin DT, Schoder H, et al. Diagnostic and prognostic value of [(18)F]fluorodeoxyglucose positron emission tomography for recurrent head and neck squamous cell carcinoma. J Clin Oncol. 2002;20: 4199–208.
28. Lowe VJ, Boyd JH, Dunphy FR, et al. Surveillance for recurrent head and neck cancer using positron emission tomography. J Clin Oncol. 2000;18:651–8.
29. Schöder H, Yeung HW, Gonen M, et al. Head and neck cancer: clinical usefulness and accuracy of PET/CT image fusion. Radiology. 2004;231:65–72.
30. Clarke JC. PET/CT "Cometh the hour, cometh the machine?". Clin Radiol. 2004;59:775–6.
31. Barrington SF, Maisey MN. Skeletal muscle uptake of fluorine-18-FDG: effect of oral diazepam. J Nucl Med. 1996;37:1127–9.

32. Palmedo H, Bucerius J, Joe A, et al. Integrated PET/CT in differentiated thyroid cancer: diagnostic accuracy and impact on patient management. J Nucl Med. 2006;47:616–24.
33. Beheshti M, Pöcher S, Vali R, et al. The value of ^{18}F-DOPA PET-CT in patients with medullary thyroid carcinoma: comparison with ^{18}F-FDG PET-CT. Eur Radiol. 2009;19:1425–34.
34. Linecker A, Kermer C, Sulzbacher I, et al. Uptake of (18)F-FLT and (18)F-FDG in primary head and neck cancer correlates with survival. Nuklearmedizin. 2008;47:80–5.
35. Rajendran JG, Schwartz DL, O'Sullivan J, et al. Tumor hypoxia imaging with [F-18] fluoromisonidazole positron emission tomography in head and neck cancer. Clin Cancer Res. 2006;12:5435–41.
36. Balogova S, Périé S, Kerrou K, et al. Prospective comparison of FDG and FET PET/CT in patients with head and neck squamous cell carcinoma. Mol Imaging Biol. 2008;10:364–73.
37. Capoccetti F, Criscuoli B, Rossi G, et al. The effectiveness of 124I PET/CT in patients with differentiated thyroid cancer. Q J Nucl Med Mol Imag. 2009;53:536–45.
38. Wong KK, Zarzhevsky N, Cahill JM, et al. Incremental value of diagnostic 131I SPECT/CT fusion imaging in the evaluation of differentiated thyroid carcinoma. AJR Am J Roentgenol. 2008;191:1785–94.
39. Lonneux M, Hamoir M, Reychler H, et al. Positron emission tomography with [^{18}F]fluorodeoxyglucose improves staging and patient management in patients with head and neck squamous cell carcinoma: a multicenter prospective study. J Clin Oncol 2010;28(7): 1190–95.
40. Schoder H, Yeung HW, Gonen M, et al. Head and neck cancer: clinical usefulness and accuracy of PET/CT image fusion. Radiology. 2004;231:65–72.
41. Ishikita T, Oriuchi N, Higuchi T, et al. Additional value of integrated PET/CT over PET alone in the initial staging and follow up of head and neck malignancy. Ann Nucl Med. 2010;24:77–82.
42. Gordin A, Golz A, Keidar Z, et al. The role of FDG-PET/CT imaging in head and neck malignant conditions: impact on diagnostic accuracy and patient care. Otolaryngol Head Neck Surg. 2007;137:130–7.
43. Ryan WR, Fee JR WE, Le QT, et al. Positron-emission tomography for surveillance of head and neck cancer. Laryngoscope. 2005;115:645–50.
44. Piao Y, Bold B, Tayier A, et al. Evaluation of ^{18}F-FDG PET/CT for diagnosing cervical nodal metastases in patients with oral cavity or oropharynx carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108:933–8.
45. Schoder H, Carlson DL, Kraus DH, et al. ^{18}F-FDG PET/CT for detecting nodal metastases in patients with oral cancer staged N0 by clinical examination and CT/MRI. J Nucl Med. 2006;47:755–62.
46. Chen W, Parsons M, Torigian DA, et al. Evaluation of thyroid FDG uptake incidentally identified on FDG-PET/CT imaging. Nucl Med Commun. 2009;30:240–4.
47. Karantanis D, Bogsrud TV, Wiseman GA, et al. Clinical significance of diffusely increased ^{18}F-FDG uptake in the thyroid gland. J Nucl Med. 2007;48:896–901.
48. Jeong HS, Baek CH, Son YI, et al. Integrated ^{18}F-FDG PET/CT for the initial evaluation of cervical node level of patients with papillary thyroid carcinoma: comparison with ultrasound and contrast-enhanced CT. Clin Endocrinol (Oxford). 2006;65:402–7.
49. Kim TY, Kim WB, Ryu JS, et al. ^{18}F-fluorodeoxyglucose uptake in thyroid from positron emission tomogram (PET) for evaluation in cancer patients: high prevalence of malignancy in thyroid PET incidentaloma. Laryngoscope. 2005;115:1074–8.
50. Eloy JA, Brett EM, Fatterpekar GM, et al. The significance and management of incidental [^{18}F]fluorodeoxyglucose-positron-emission tomography uptake in the thyroid gland in patients with cancer. AJNR Am J Neuroradiol. 2009;30:1431–4.
51. Diehl M, Risse JH, Brandt-Mainz K, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in medullary thyroid cancer: results of a multicentre study. Eur J Nucl Med. 2001;28:1671–6.
52. Szakall Jr S, Esik O, Bajzik G, et al. ^{18}F-FDG PET detection of lymph node metastases in medullary thyroid carcinoma. J Nucl Med. 2002;43:66–71.
53. Kao CH, ChangLai SP, Chieng PU, Yen RF, Yen TC. Detection of recurrent or persistent nasopharyngeal carcinomas after radiotherapy with 18-fluoro-2-deoxyglucose positron emission tomography and comparison with computed tomography. J Clin Oncol. 1998;16:3550–5.
54. Anzai Y, Carroll WR, Quint DJ, et al. Recurrence of head and neck cancer after surgery or irradiation: prospective comparison of 2-deoxy-2-[F-18]fluoro-D-glucose PET and MR imaging diagnoses. Radiology. 1996;200:135–41.
55. Li P, Zhuang H, Mozley PD, et al. Evaluation of recurrent squamous cell carcinoma of the head and neck with FDG positron emission tomography. Clin Nucl Med. 2001;26:131–5.
56. Fukui MB, Blodgett TM, Meltzer CC, et al. PET/CT imaging in recurrent head and neck cancer. Semin Ultrasound CT MR. 2003;24:157–63.
57. Zimmer LA, Snyderman C, Fukui MB, et al. The use of combined PET/CT for localizing recurrent head and neck cancer: the Pittsburgh experience. Ear Nose Throat J. 2005;84:108–10.
58. Castellucci P, Zinzani P, Pourdehnad M, et al. ^{18}F-FDG PET in malignant lymphoma: significance of positive findings. Eur J Nucl Med Mol Imag. 2005;32:749–56.
59. Pacini F, Agate L, Elisei R, et al. Outcome of differentiated thyroid cancer with detectable serum Tg and negative diagnostic 131I whole body scan: comparison of patients treated with high 131I activities versus untreated patients. J Clin Endocrinol Metab. 2001;86:4092–7.
60. Dong MJ, Liu ZF, Zhao K, et al. Value of ^{18}F-FDG-PET/PET-CT in differentiated thyroid carcinoma with

radioiodine-negative whole-body scan: a meta-analysis. Nucl Med Commun. 2009;30:639–50.
61. Wang W, Larson SM, Fazzari M, et al. Prognostic value of [^{18}F]fluorodeoxyglucose positron emission tomographic scanning in patients with thyroid cancer. J Clin Endocrinol Metab. 2000;85:1107–13.
62. Jereczek-Fossa BA, Jassem J, Orecchia R. Cervical lymph node metastases of squamous cell carcinoma from an unknown primary. Cancer Treat Rev. 2004;30:153–64.
63. Menda Y, Graham MM. Update on ^{18}F-fluorodeoxyglucose/positron emission tomography and positron emission tomography/computed tomography imaging of squamous head and neck cancers. Semin Nucl Med. 2005;35:214–9.
64. Nanni C, Rubello D, Castellucci P, et al. Role of ^{18}F-FDG PET-CT imaging for the detection of an unknown primary tumour: preliminary results in 21 patients. Eur J Nucl Med Mol Imag. 2005;32:589–92.
65. Uchida Y, Minoshima S, Kawata T, et al. Diagnostic value of FDG PET and salivary gland scintigraphy for parotid tumors. Clin Nucl Med. 2005;30:170–6.
66. Findlay M, Young H, Cunningham D, et al. Noninvasive monitoring of tumor metabolism using fluorodeoxyglucose and positron emission tomography in colorectal cancer liver metastases: correlation with tumor response to fluorouracil. J Clin Oncol. 1996;14:700–8.
67. Abe Y, Matsuzawa T, Fujiwara T, et al. Assessment of radiotherapeutic effects on experimental tumors using ^{18}F-2-fluoro-2-deoxy-d-glucose. Eur J Nucl Med. 1986;12:325–8.
68. Brun E, Kjellén E, Tennvall J, et al. FDG PET studies during treatment: prediction of therapy outcome in head and neck squamous cell carcinoma. Head Neck. 2002;24:127–35.
69. Andrade RS, Heron DE, Degirmenci B, et al. Posttreatment assessment of response using FDG-PET/CT for patients treated with definitive radiation therapy for head and neck cancers. Int J Radiat Oncol Biol Phys. 2006;65:1315–22.
70. Ong SC, Schöder H, Lee NY, et al. Clinical utility of ^{18}F-FDG PET/CT in assessing the neck after concurrent chemoradiotherapy for locoregional advanced head and neck cancer. J Nucl Med. 2008;49:532–40.
71. Ciernik IF, Dizendorf E, Baumert BG, et al. Radiation treatment planning with an integrated positron emission and computer tomography (PET/CT): a feasibility study. Int J Radiat Oncol Biol Phys. 2003;57:853–63.
72. Vernon MR, Maheshwari M, Schultz CJ, et al. Clinical outcomes of patients receiving integrated PET/CT-guided radiotherapy for head and neck carcinoma. Int J Radiat Oncol Biol Phys. 2008;70:678–84.
73. Fu KK, Pajak TF, Trotti A, et al. A Radiation Therapy Oncology Group (RTOG) Phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas: First report of RTOG 9003. Int J Radiat Oncol Biol Phys. 2000;48:7–16.
74. Lee NY, Mechalakos JG, Nehmeh S, et al. Fluorine-18-labeled fluoromisonidazole positron emission and computed tomography-guided intensity-modulated radiotherapy for head and neck cancer: a feasibility study. Int J Radiat Oncol Biol Phys. 2008;70:2–13.
75. Huang B, Law MW, Khong PL. Whole-body PET/CT scanning: estimation of radiation dose and cancer risk. Radiology. 2009;251:166–74.