

Combined PET-CT in the Head and Neck

Part 2. Diagnostic Uses and Pitfalls of Oncologic Imaging¹

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Positron emission tomography (PET) with 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG) is effective for monitoring head and neck cancer. However, lack of anatomic landmarks, variable physiologic FDG uptake, and asymmetric FDG distribution in the neck can confound image interpretation. This is particularly true in the treated neck, where distortion of normal tissue planes makes detection of early disease recurrence difficult with conventional computed tomography (CT) and magnetic resonance imaging. Combined PET-CT helps prevent the misinterpretation of FDG PET findings in patients with head and neck cancer. Superior localization of FDG uptake with this technique can improve diagnostic accuracy and help avoid interpretative pitfalls. In the future, development of tumor-specific ligands will enhance the usefulness of PET-CT in the detection of initial tumors and tumor recurrence, in the evaluation of tumors with low FDG avidity, and in treatment targeting. Furthermore, improved scanner resolution will help address the limitations of PET-CT with respect to small lesions and may make this modality more valuable in initial tumor staging.

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Abbreviations: FDG = 2-[fluorine-18]fluoro-2-deoxy-D-glucose, SUV = standardized uptake value

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Introduction

Positron emission tomography (PET) provides a unique opportunity to examine a variety of physiologic functions in vivo and thus provides information that is complementary to that obtained with anatomic imaging techniques such as computed tomography (CT) or magnetic resonance (MR) imaging. A highly sensitive tool for noninvasive imaging of the physiologic features of tissue, PET can be used to measure blood flow and to evaluate metabolic processing and receptor-mediated function. The overwhelming majority of clinical PET studies are performed with 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG).

FDG PET is an effective means of detecting head and neck cancer. PET has both greater sensitivity (86%–100%) and greater specificity (69%–87%) than CT (67%–82% and 25%–56%, respectively) for the detection of both primary tumors and lymph node metastases (1,2); however, limited anatomic localization and variable physiologic uptake reduce the effectiveness of PET in the head and neck region (3–6). Nearby anatomic structures, nonspecific FDG uptake by tissues, and limited spatial resolution make it difficult to localize areas of uptake to the tumor site on a PET scan. In addition, inflammation of head and neck tissues due to mucosal ulceration, associated infection, and treatment-related effects may result in nonspecific FDG uptake.

Although the combination of separately acquired CT and PET scans using retrospective or prospective registration methods (7) is more accurate than CT alone (8), this approach is limited by patient movement and by difficulty in exactly correlating points on CT and PET scans. Computer algorithms for coregistering anatomic and functional images, although successful with anatomically fixed organs such as the brain (9), are less so in the more mobile head and neck, whose position can change between scans with changes in patient position; therefore, the two sets of images cannot be precisely aligned with linear transformation. A stereotactic system could be used for scanning the head and neck to ensure use of the same reference system for the PET and CT scans. Alternatively, an immobilization system could be used to ensure stable positioning for separately acquired PET and CT scans; however, this approach would be cumbersome, in addition

to requiring prospective implementation. The most effective solution to the problem of coregistration is to acquire both functional and anatomic images on the same scanner without moving the patient from the scanning table (ie, during a single imaging session). Early experience with scanning suggests that combined PET-CT is superior to PET and CT performed separately in monitoring therapy (10). Minimizing complications of radiation therapy requires that tumor be distinguished from surrounding normal structures, which can be accomplished only with the anatomic detail provided by CT. The coregistration of FDG PET and CT scans on a single device offers the potential for improved detection and localization of head and neck cancer with one imaging tool.

In this article, we review PET-CT technique in our study of over 800 patients with head and neck cancer. We also discuss indications for PET-CT in this patient population, including detection of recurrent thyroid carcinoma or cranial base neoplasm, directing biopsy, detection of the unknown primary tumor site, staging of head and neck cancer, and tumor surveillance. In addition, we discuss various limitations of PET-CT relating to physiologic FDG uptake, inadequate scanner resolution, recent surgery or radiation therapy–chemotherapy, inflammatory tissue, and low FDG avidity, and outline strategies for avoiding misdiagnosis due to these limitations.

PET-CT Technique

Combined PET-CT was performed on three tomographs: (a) a prototype device consisting of an ECAT ART PET scanner (CTI, Knoxville, Tenn) and a Somatom AR.SP CT scanner (Siemens Medical Systems, Iselin, NJ) (11), (b) a commercial device consisting of an ECAT HR+ PET scanner (CPS Innovations, Knoxville, Tenn) and a single-section CT scanner (Siemens Emotion), and (c) a commercial device with a lutetium oxyorthosilicate–based PET scanner (CTI) and a dual-section CT scanner (Siemens Emotion).

PET-CT was performed approximately 1 hour following the intravenous injection of 6–15 mCi (222–555 MBq) of FDG, with acquisition of helical CT data (pitch, 1.1–1.6) immediately preceding acquisition of three-dimensional emission data (5–10 minutes per bed position, two to five bed positions per patient). CT was performed with dynamic injection of 90 mL of intravenous

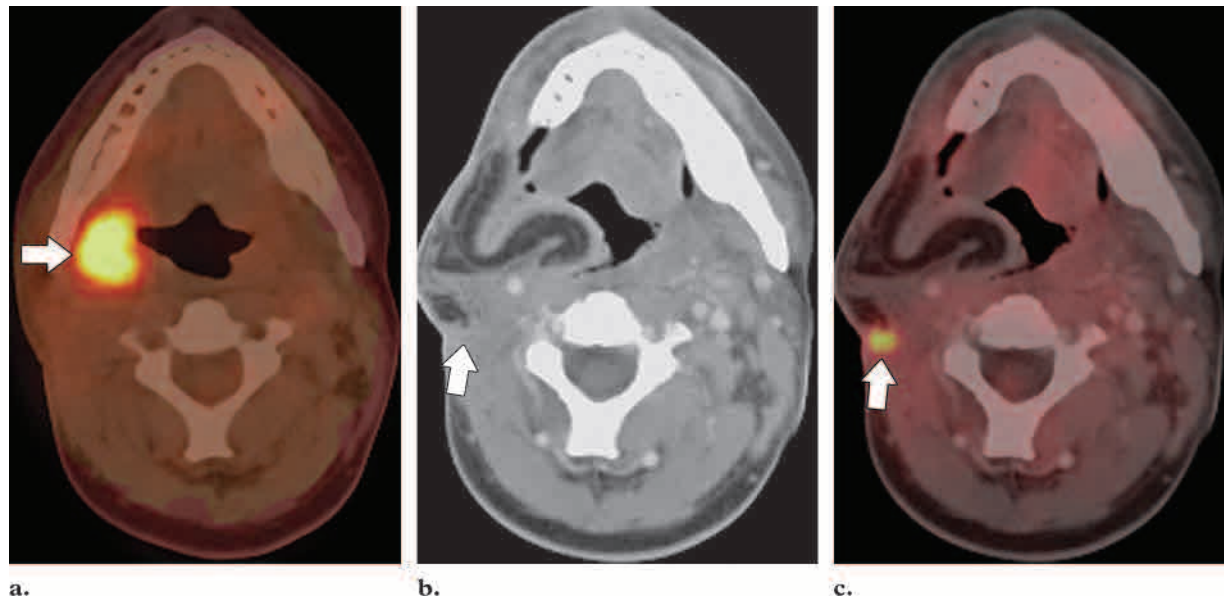


Figure 1. Recurrent tumor. (a) Fused PET-CT scan shows a squamous cell carcinoma of the tonsil (arrow). The patient underwent partial mandibulectomy. (b) CT scan obtained 4 months later fails to demonstrate recurrent disease at the posterior flap margin (arrow), as did physical examination. (c) Follow-up PET-CT scan shows a small (<1-cm) focus of increased FDG uptake (standardized uptake value [SUV] = 2.5) (arrow). Subsequent surgery helped confirm tumor recurrence at the superficial posterior aspect of the muscle flap.

contrast material (ioversol) (Optiray; Mallinckrodt, St Louis, Mo) unless there was a contraindication. The PET scans were corrected for attenuation with coefficients obtained by scaling the CT numbers from the CT scans to the PET energy level (511 kV) (12). The helical CT scans were reconstructed into 512×512 images with a section thickness to match those of the PET scans (2.4–3.4 mm).

Images were evaluated by at least one neuroradiologist and one nuclear medicine physician with experience in PET scan interpretation.

Diagnostic Uses: Indications for PET-CT

In our experience, the most powerful application of PET-CT has been the detection of residual or recurrent head and neck neoplasm after treatment. Posttreatment effects make it difficult to distinguish normal posttherapy tissue changes from tumor recurrence clinically, radiologically, and histologically (13,14). Neck dissection and flap reconstruction distort the normal neck anatomy and make detection of recurrent neoplasm challenging on the basis of structural changes alone. Radiation therapy can further complicate imaging by making tissue planes indistinct and by causing edema that may produce an increase in

tissue volume. Serial imaging with CT and MR imaging is the mainstay for monitoring patients with head and neck tumors. Stability of a lesion over several months suggests scar, whereas interval growth indicates residual or recurrent neoplasm; however, potential treatment time may have been lost, and the stage of cancer may progress. Indeed, the main criterion for tumor recurrence at conventional CT or MR imaging—tumor growth over time—may occur as a normal postirradiation effect (14). Biopsy of residual or recurrent neoplasm may be impeded by inaccessibility and by potential morbidity in irradiated tissue. Aggressive biopsy of radiation-injured soft tissues may lead to frank necrosis and result in increased morbidity but yield a poor return in terms of detection of recurrent neoplasm (15).

PET has proved to be a useful adjunct in detecting tumor and differentiating recurrent tumor from posttherapy tissue necrosis (16). Diminished FDG uptake appears to coincide with a decline in the number of viable tumor cells (17).

In the treated neck, we have been able to detect recurrent tumor earlier and with greater confidence than we would have with CT alone (Figs 1–3).

Figure 2. Recurrent tumor in a 61-year-old patient with a history of squamous cell carcinoma of the right side of the tongue base. The patient had undergone extensive resection of the primary tumor. CT and PET-CT were performed to investigate the cause of recurrent pain. **(a)** CT scan fails to demonstrate recurrent neoplasm (arrow). **(b)** PET-CT scan shows focal intense FDG uptake in the supraglottic larynx (arrow), a finding that proved to be recurrent neoplasm.

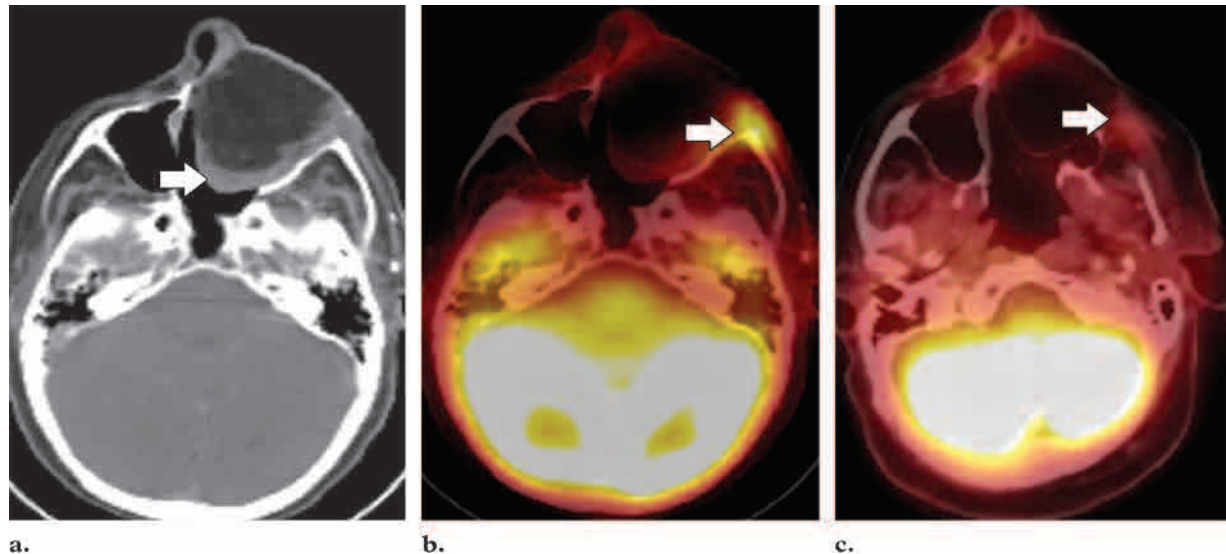
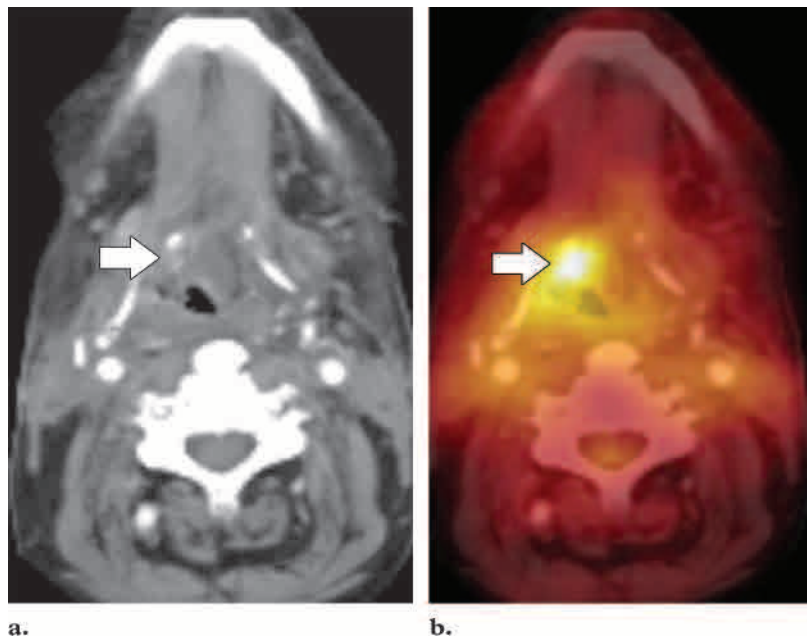


Figure 3. Unsuspected residual tumor in a 72-year-old patient with a history of nasal adenocarcinoma that had invaded the orbit. The patient had undergone left maxillectomy, orbital exenteration, and left ethmoidectomy with flap reconstruction 6 weeks earlier. **(a)** CT scan demonstrates soft tissue along the posterior flap margin (arrow), a finding that was suspicious for neoplasm. **(b)** PET-CT scan demonstrates intense FDG uptake localized to the lateral flap border (arrow), a finding that proved to be residual neoplasm at histologic analysis. **(c)** Follow-up PET-CT scan obtained after resection of the residual neoplasm shows no disease (arrow).

An initial series of 47 patients evaluated for recurrent head and neck neoplasm with PET-CT at our institution were reviewed. Of these 47 patients, 25 underwent biopsy of lesions detected at PET-CT that proved to be recurrent neoplasm. Biopsy demonstrated recurrent squamous cell carcinoma in 18 patients. A variety of other cell types were identified in the remaining seven cases,

including adenocarcinoma, basal cell carcinoma, osteosarcoma, and lymphoma. The sensitivity and specificity of PET-CT for detecting recurrent head and neck neoplasm in this initial series were 95% and 60%, respectively. These findings are similar to those seen in detecting recurrent neoplasm with PET alone. Wong et al (18) reviewed a series of 143 patients with treated squamous cell carcinoma of the head and neck and reported a sensitivity and specificity of 96% and 72%, respectively, for FDG PET in the detection of recurrent neoplasm. In the future, PET-CT evalua-

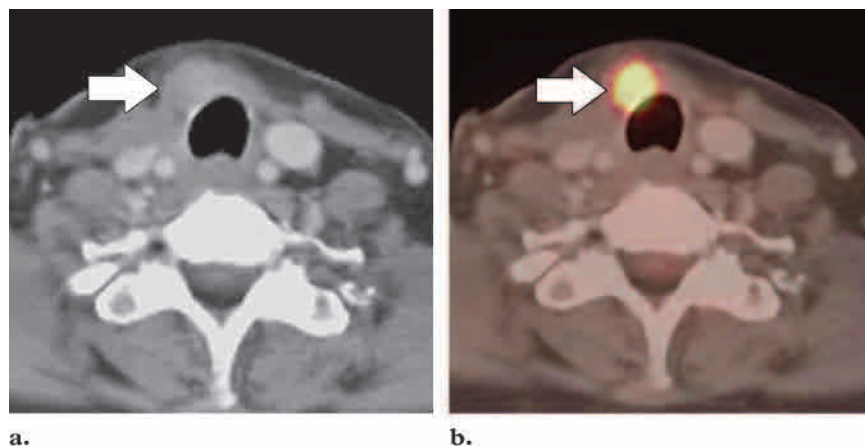


Figure 4. Recurrent papillary carcinoma of the thyroid gland. The patient had a rising thyroglobulin level but a negative ^{131}I scan. **(a)** CT scan shows a paratracheal nodule (arrow) that had not been discovered at two previous surgeries, likely because of distorted anatomy and scar from the original thyroidectomy. **(b)** PET-CT scan demonstrates increased FDG uptake in the thyroidectomy bed (arrow) and provides the additional data needed to justify and guide a third surgical procedure, which helped confirm recurrent neoplasm.

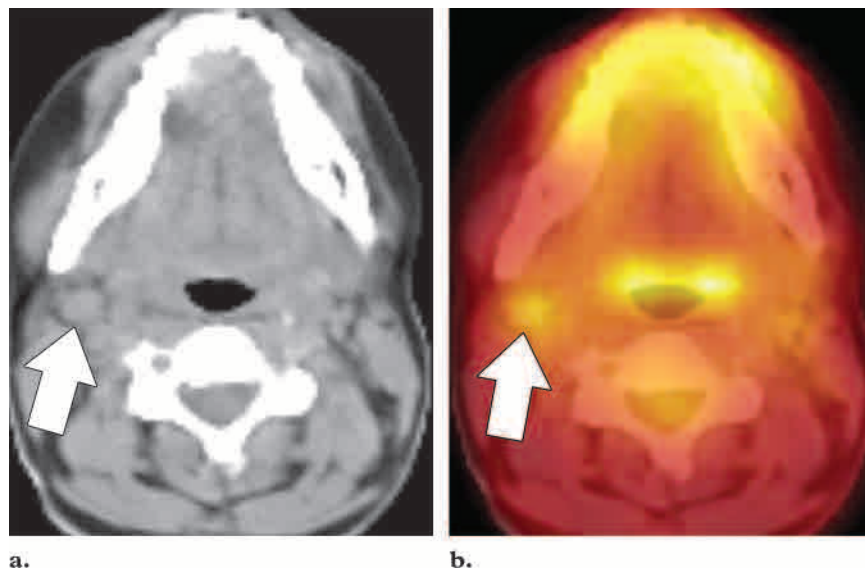


Figure 5. Recurrent thyroid papillary carcinoma in a 28-year-old patient with a rising thyroglobulin level but a negative ^{131}I scan. CT **(a)** and fused PET-CT **(b)** scans show minimal asymmetric FDG uptake in the right side of the neck (arrow), a finding that represents a normal-sized level II lymph node. Recurrent papillary carcinoma was confirmed at histologic analysis.

tion of larger series of patients with recurrent head and neck carcinoma may demonstrate an increase in specificity for the detection of tumor recurrence.

Detection of Recurrent Thyroid Carcinoma

Several special circumstances regarding recurrent thyroid neoplasm are worthy of mention. Thyroid carcinoma may demonstrate variable FDG uptake, depending on its degree of differentiation; well-differentiated thyroid cancers tend to take up less FDG than do undifferentiated cancers (19). PET has helped detect recurrent thyroid carcinoma that was suspected on the basis of an

elevated thyroglobulin level despite a negative iodine 131 (^{131}I) scan (20,21). PET-CT has helped both detect recurrence and localize neoplasm to facilitate biopsy.

An initial series of eight patients with thyroid carcinoma underwent PET-CT (22). Half of these cases ($n = 4$) demonstrated recurrent neoplasm at PET-CT, with initial histologic findings of papillary carcinoma in three cases and medullary carcinoma in one case. Eight lesions in three cases were sampled, with 75% of lesions demonstrating recurrent neoplasm (Figs 4, 5) (22).

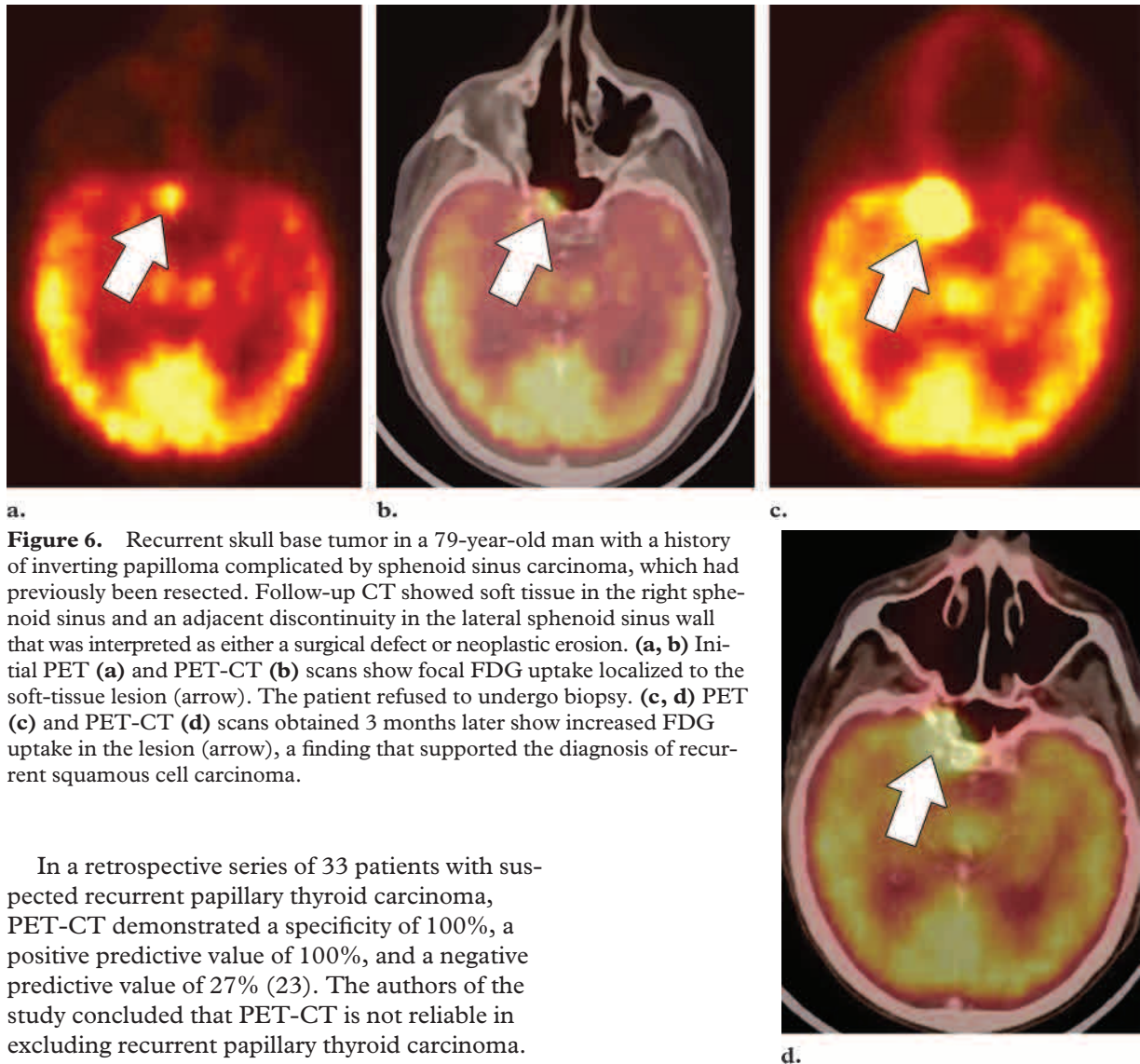


Figure 6. Recurrent skull base tumor in a 79-year-old man with a history of inverting papilloma complicated by sphenoid sinus carcinoma, which had previously been resected. Follow-up CT showed soft tissue in the right sphenoid sinus and an adjacent discontinuity in the lateral sphenoid sinus wall that was interpreted as either a surgical defect or neoplastic erosion. (**a, b**) Initial PET (**a**) and PET-CT (**b**) scans show focal FDG uptake localized to the soft-tissue lesion (arrow). The patient refused to undergo biopsy. (**c, d**) PET (**c**) and PET-CT (**d**) scans obtained 3 months later show increased FDG uptake in the lesion (arrow), a finding that supported the diagnosis of recurrent squamous cell carcinoma.

In a retrospective series of 33 patients with suspected recurrent papillary thyroid carcinoma, PET-CT demonstrated a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 27% (23). The authors of the study concluded that PET-CT is not reliable in excluding recurrent papillary thyroid carcinoma. However, we have found PET-CT to be useful in detecting recurrent thyroid cancer that is no longer ^{131}I avid, in addition to medullary thyroid cancer.

Detection of Recurrent Cranial Base Neoplasm

Recurrent skull base neoplasm is notoriously difficult to detect with anatomic imaging techniques owing to distortion of anatomy caused by flap reconstruction and irradiation. Use of structural

imaging (CT and MR imaging) alone typically requires serial scans to document tumor growth and may potentially result in lost treatment time. PET-CT may help detect these recurrences in a single imaging session (Fig 6) (24). Successful treatment of skull base neoplasm is predicated on precisely localizing tumor and differentiating it from scar. Combined radiation therapy and surgical treatment for skull base cancer results in soft-tissue changes (bone or cartilaginous necrosis, edema, desmoplastic changes) that distort the normal anatomy. These changes most frequently

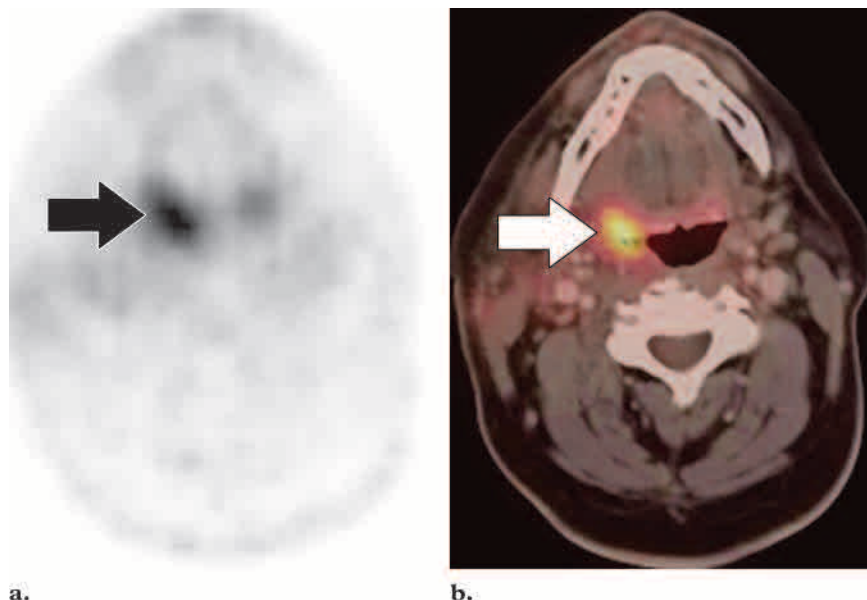


Figure 7. Squamous cell carcinoma in a patient with a known right-sided level II lymph node. Primary site of neoplasm was unknown. Neoplasm was not identified in five tissue samples obtained at direct laryngoscopy and directed biopsies of the tongue base, tonsils, and nasopharynx. PET (a) and PET-CT (b) scans show an area of intense FDG uptake ($SUV = 8$) in the right tonsil (arrow). The next day, the patient again underwent direct laryngoscopy and multiple biopsies of the right side of the tongue base; analysis of six additional samples showed squamous cell carcinoma.

manifest in the 1st year after completion of adjuvant therapy, the same time period during which tumor is most likely to recur (25). Biopsy of recurrent or residual skull base neoplasm is impeded by inaccessibility at surgery and by potential morbidity.

Directing Biopsy

FDG PET has proved superior to both CT and MR imaging in detecting recurrence and distinguishing tumor from postirradiation effects and scar in extracranial head and neck cancer (2,26–31). Lowe et al (32) determined the sensitivity and specificity of FDG PET for detecting residual disease to be 90% and 83%, respectively; PET studies were followed by biopsies to confirm the radiologic findings. The authors also reported two cases in which initial biopsy was negative for malignant cells despite increased FDG uptake at PET (32). Subsequent biopsy demonstrated tumor, a finding that underscores the limitation caused by sampling errors. Combined PET-CT has facilitated directed biopsies and allowed more accurate sampling of tissue that is highly suspicious for tumor (Figs 1, 3, 7). In addition, follow-up PET-CT that demonstrates diminished FDG uptake (ie, reduced metabolism) may sug-

gest a response to treatment and thus obviate biopsy.

Detection of the Unknown Primary Tumor Site

Detection of the unknown primary site may be limited by physiologic uptake in the lymphoid tissue of the Waldeyer ring. When positive, however, PET-CT may allow more effective directed biopsies (Fig 7), thereby permitting more focused treatment and reducing morbidity.

Cervical metastasis is a common manifestation of occult carcinoma. Previous studies have demonstrated a sensitivity of 30%–47% for FDG PET alone in detecting the undiscovered head and neck primary tumor (33–35). Although FDG uptake in primary neoplasms is usually greater than that observed in even the most metabolically active normal structures (3), overlap between tumor and physiologic uptake proved to limit sensitivity in our experience. Currently, this overlap is likely an important limitation of FDG PET in localizing the occult head and neck primary neoplasm (Fig 8) (36).

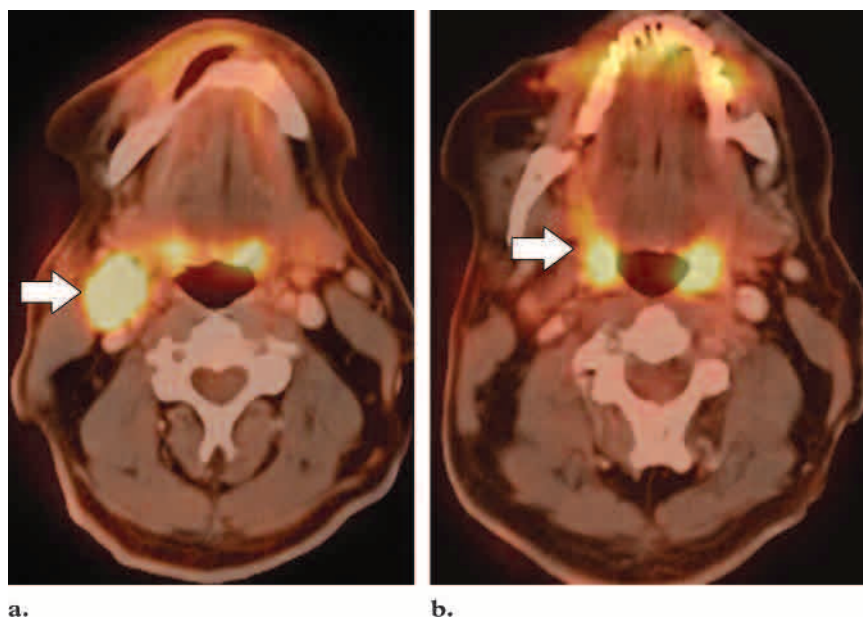


Figure 8. Occult carcinoma. **(a)** PET-CT scan shows intense FDG uptake in a right-sided level II lymph node (arrow) that proved to be squamous cell carcinoma at pathologic analysis. FDG uptake in the tongue base was symmetric. Direct laryngoscopy and directed biopsies failed to reveal the primary site of neoplasm. **(b)** PET-CT scan obtained at the level of the tonsils also shows symmetric FDG uptake (arrow). Because PET-CT also failed to demonstrate the primary site of neoplasm, bilateral tonsillectomies were performed. Histologic examination showed hyperplasia in the left tonsil and squamous cell carcinoma in the right tonsil.

Staging of Head and Neck Cancer

Unfortunately, PET-CT has some of the same limitations as CT and MR imaging in the staging of head and neck cancer. The most salient of these limitations is related to lesion size. Reliable detection of malignancy at PET spatial resolution requires a minimum lesion size of approximately 1 cm. Lesions are evaluated for malignant potential both subjectively (visually) and objectively (using an FDG uptake index with SUVs). The SUV method takes into account the injected dose of FDG as well as the patient's body mass (37) as follows:

$$\text{SUV} = \frac{\text{ROI counts}}{\text{injected dose/body weight}},$$

where ROI = region of interest, ROI counts are in megabecquerels per milliliter, injected dose is in megabecquerels, and body weight is in grams.

Typically, a lesion with an SUV greater than 2.5–3.0 is considered suspicious for malignancy (18,38). However, these values may vary considerably depending on the clinical scenario; inflammatory lesions may also demonstrate high SUVs in the range associated with malignant lesions.

In the evaluation of lesions less than 1 cm in size, PET sensitivity may be reduced; as a result, SUVs in the typically benign range may indicate malignancy. This reduced sensitivity results from partial volume averaging of the metabolic activity of a small lesion with that of the normal surrounding tissue, a phenomenon that is especially relevant in the search for lymph node metastases (Fig 9). However, PET-CT may increase confidence in determining the extent of the primary lesion or in identifying recurrent carcinoma at the primary site. In certain cases, PET-CT may provide information that permits more conservative surgery than would be anticipated on the basis of CT findings alone (Fig 10). Detection of distant metastases at presentation may be challenging at

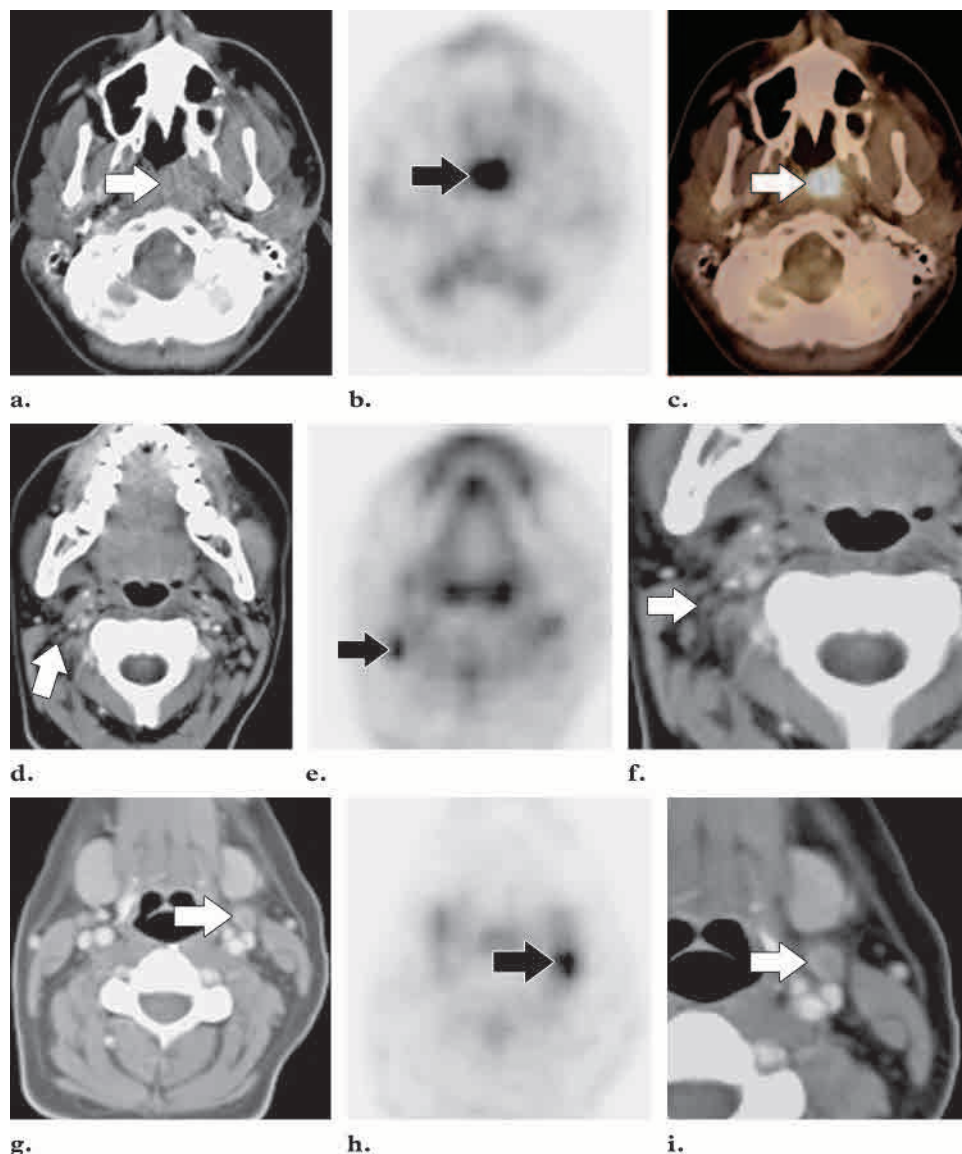


Figure 9. Lymph node metastases in a 23-year-old patient with squamous cell carcinoma of the left ethmoid sinus. The patient had undergone two previous surgeries. (a–c) CT (a), PET (b), and PET-CT (c) scans obtained 10 months after presentation show local recurrence in the nasopharynx (arrow). (d–i) CT scans (d, f, g, i; f and i are magnified views) and PET scans (e, h) show bilateral focal FDG uptake in small (<1-cm) cervical lymph nodes (arrow). These findings prompted resection of the local recurrence as well as bilateral modified neck dissections, the results of which confirmed recurrent neoplasm in both lymph nodes.

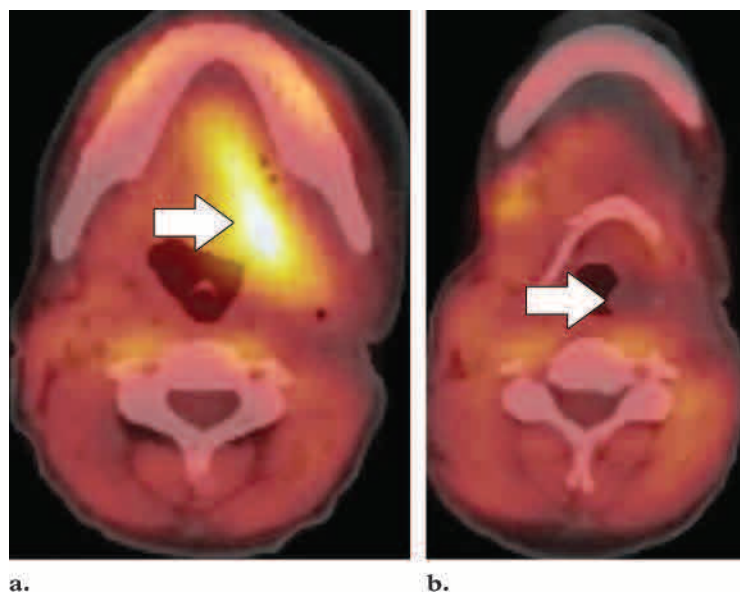


Figure 10. Tumor recurrence in a 50-year-old patient with a history of squamous cell carcinoma of the tongue base. The patient had undergone chemotherapy and radiation therapy in Germany 2 years earlier. MR imaging performed there demonstrated extensive tumor involvement of the tongue base and larynx. PET-CT scans show tumor recurrence in the tongue base (arrow in a) but sparing of the supraglottic larynx (arrow in b), involvement of which had been suspected at CT. The PET-CT findings allowed the patient to undergo more conservative surgery than would have been indicated by the CT data alone.

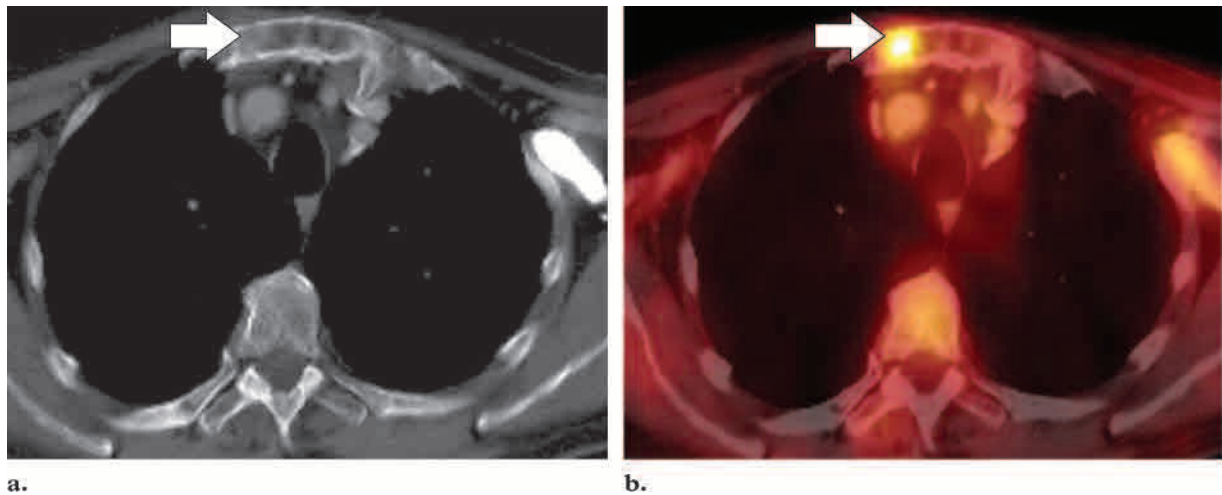


Figure 11. Distant metastasis in a 61-year-old patient with recently diagnosed squamous cell carcinoma of the right side of the oropharynx. The patient had undergone CT, which showed no evidence of distant metastasis. **(a)** CT scan shows no lesion in the sternum (arrow). **(b)** PET-CT scan shows a small focus of FDG uptake localized to the sternum (arrow), a finding that is consistent with metastasis. PET-CT also showed intense FDG uptake at the primary site.

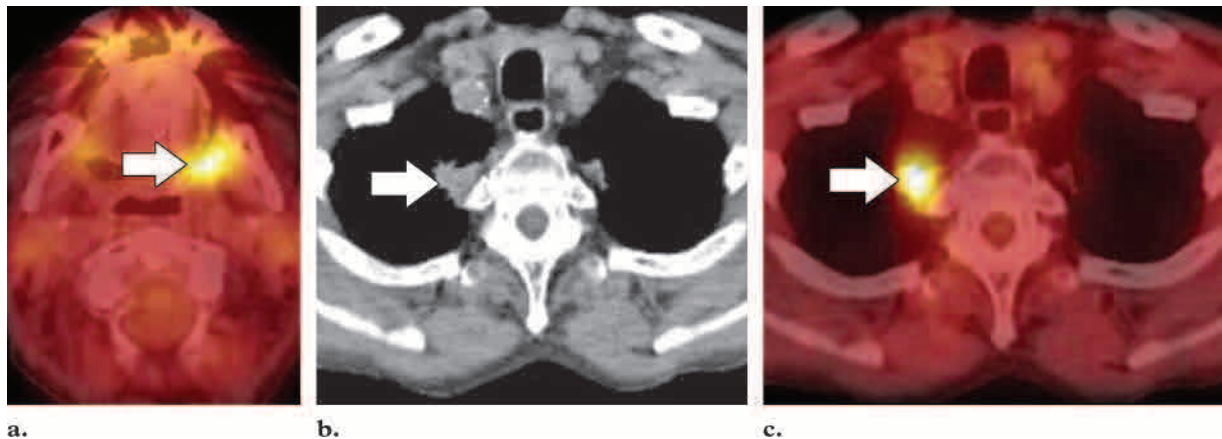


Figure 12. Second primary lung tumor in a patient who presented with throat pain. The patient had undergone chemotherapy and radiation therapy for squamous cell carcinoma of the oropharynx 6 years earlier. **(a)** PET-CT scan demonstrates recurrent neoplasm in the left retromolar trigone (arrow). **(b)** CT scan shows stranding in the lung apices (arrow), a finding that was interpreted as radiation-induced change. **(c)** PET-CT scan demonstrates intense FDG uptake in the right lung apex (arrow), a finding that proved to be a second primary adenocarcinoma.

conventional CT and MR imaging (Fig 11). PET-CT also aids in the detection of a second primary lung tumor, which is why we advocate chest scanning as a routine procedure (Fig 12).

Tumor Surveillance

Combined anatomic (CT) and functional (PET) imaging may provide a more powerful approach for monitoring or targeting therapy than PET and CT performed separately. As mentioned earlier, reduction in FDG uptake appears to coincide with a decline in the number of viable tumor cells

(17). Metabolic response to therapy may precede changes in tumor volume (17,39,40). In a study by Minn et al (40), patients who ultimately had a good response to radiation therapy also had a marked reduction in FDG uptake from basal level during the course of radiation therapy. Lowe et al (32) evaluated FDG PET in assessing the response of stage III-IV head and neck cancer to chemotherapy. They hypothesized that a reduction in tumor metabolism, as evidenced by a decreased SUV, would correlate with tumor response to chemotherapy. The authors further determined the sensitivity and specificity of PET for the detection of residual disease to be 90% and

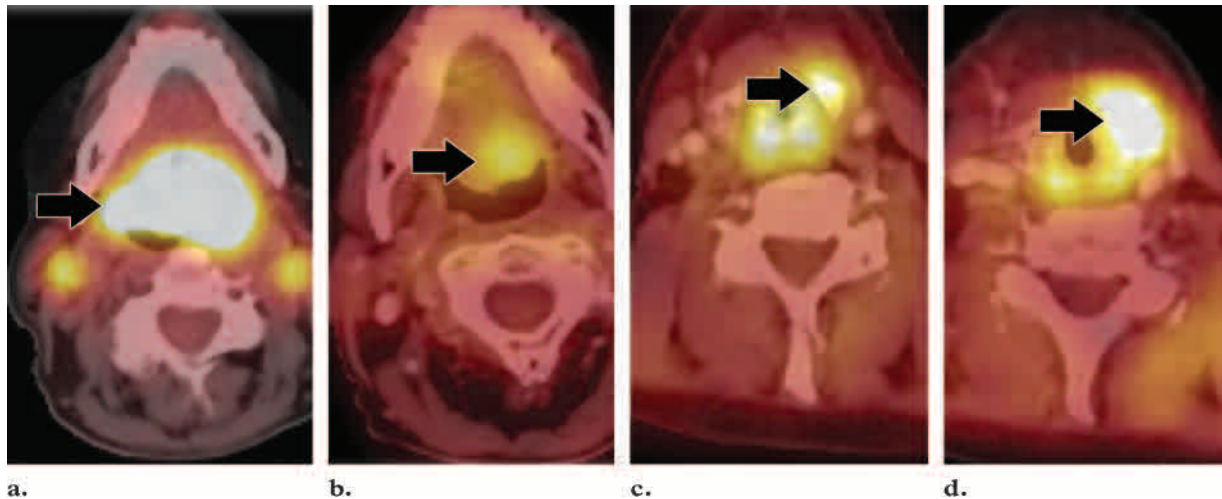


Figure 13. Recurrent neoplasm in a 67-year-old patient with progressive dyspnea in whom squamous cell carcinoma of the tongue base had been diagnosed. **(a)** Initial PET-CT scan shows a large focus of intense FDG uptake in the tongue base (arrow) and uptake in bilateral level II lymph nodes. The patient subsequently underwent chemotherapy and radiation therapy. **(b)** PET-CT scan shows a decrease in FDG uptake in the tongue base (arrow) and resolution of the nodal uptake. **(c)** PET-CT scan reveals new FDG uptake in the vocal cords and sclerosis of the left side of the thyroid cartilage (arrow). These findings were interpreted as representing inflammation. Direct laryngoscopy was performed and showed radiation-induced change in the true vocal cords. **(d)** Follow-up PET-CT scan shows increased FDG uptake in the thyroid cartilage (arrow), a finding that represents recurrent neoplasm in proximity to the vocal cords.

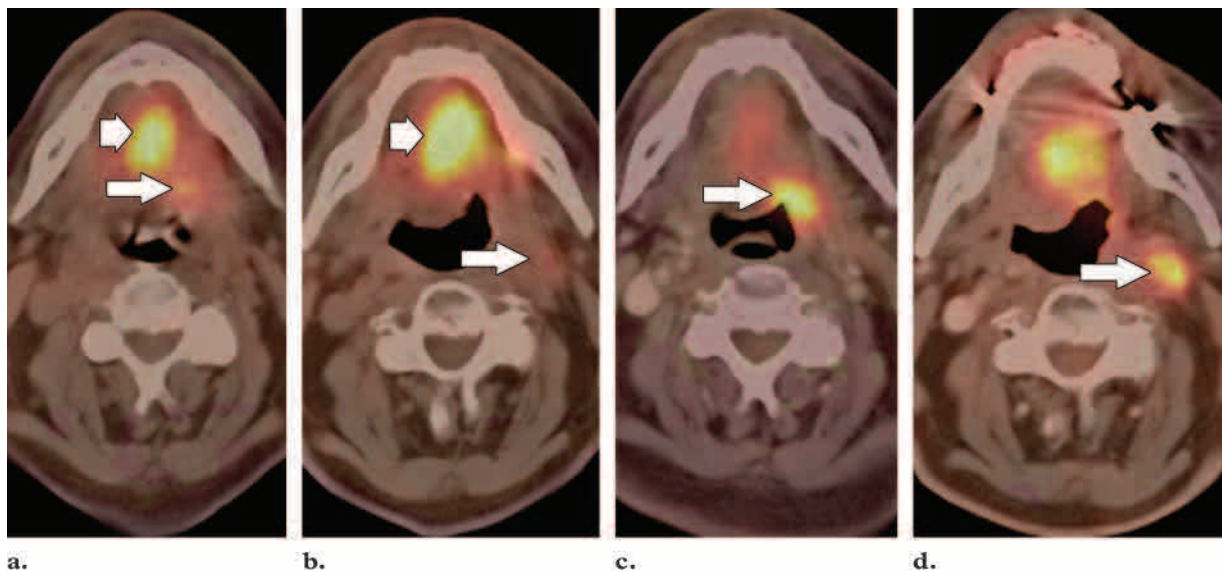


Figure 14. Squamous cell carcinoma of the tongue in a 60-year-old patient who had undergone chemotherapy and radiation therapy 2 years earlier. **(a, b)** PET-CT scans show faint FDG uptake in the left side of the tongue base (primary site) and in a left-sided level II lymph node (long arrow), as well as intense physiologic uptake in the genioglossus muscle (short arrow). The patient subsequently underwent gene therapy. **(c, d)** PET-CT scans obtained 3 months later show disease progression, with increased FDG uptake in the left side of the tongue base and in the lymph node (arrow).

83%, respectively (32). These findings support the notion that FDG PET is valuable in assessing tumor response to chemotherapy.

Further study will be required to determine the usefulness of PET-CT for tumor surveillance. The theory that a decrease in metabolic activity immediately after treatment may herald a response has been controversial. Such a finding is largely dependent on the interval between treat-

ment and imaging: Imaging performed 1 month after treatment may be unreliable in terms of evaluating tumor response, whereas imaging performed 4 months after treatment may provide prognostic information (Fig 13) (41). In addition, a lack of reduction in metabolic activity may signal the need to change treatment or to opt for a more aggressive therapy (Fig 14).

Figure 15. Nasopharyngeal carcinoma in a 62-year-old patient. **(a)** Coronal PET scan shows intense FDG uptake (arrow) in proximity to the brain. **(b)** Axial fused PET-CT scan helps localize the FDG uptake to extensive neoplastic erosion of the sphenoid bone (arrow) rather than the brain.

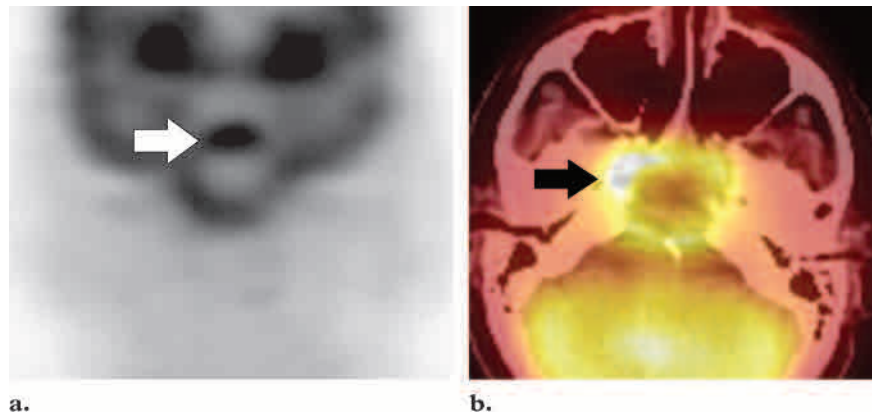
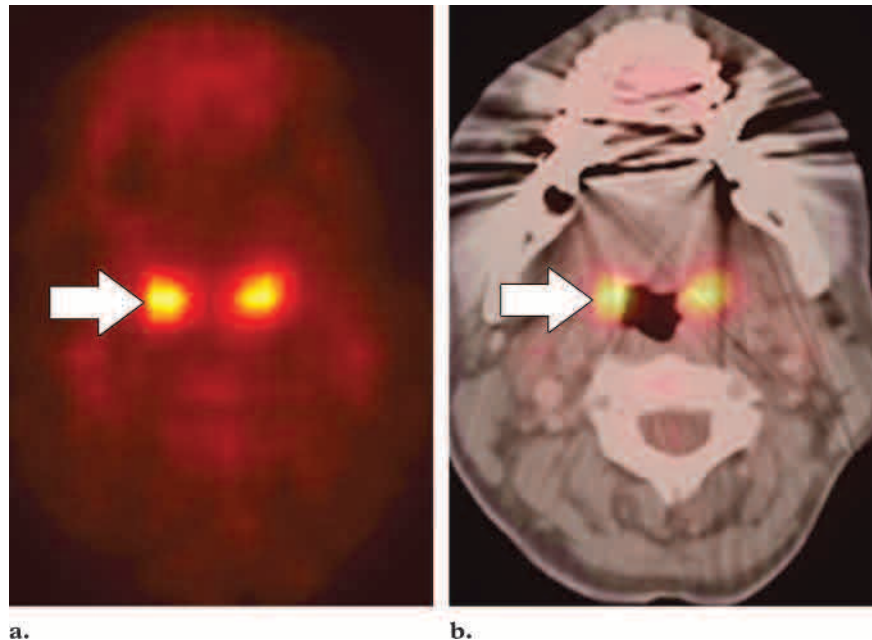


Figure 16. Tonsillar uptake. PET **(a)** and PET-CT **(b)** scans demonstrate intense physiologic FDG uptake in the tonsils (arrow). Such uptake creates high background activity that makes it difficult to detect an unknown primary neoplasm.



Pitfalls: Limitations of PET-CT

Physiologic FDG Uptake

Variable FDG uptake in normal structures such as the nasal turbinates, pterygoid muscles, extraocular muscles, parotid and submandibular glands, and lymphoid tissue of the adenoids and upper Waldeyer ring may confound interpretation and result in false-positive findings (3). Similarly, normal FDG uptake in muscles that are contracting or tensed during the uptake phase (eg, in anxious or talkative patients) may lead to false-positive findings. Although overlap between tumor and physiologic uptake may confound interpretation, PET-CT allows direct correlation of FDG uptake with anatomic structures to reduce false-positive results (4–6).

Localization of a lesion either within or in proximity to an anatomic structure with inherently high FDG uptake such as the brain or tonsils may make it difficult to distinguish pathologic from physiologic metabolic activity (Figs 6, 8, 15–17).

Inadequate Scanner Resolution

Small malignancies (<1 cm) may not be reliably detected unless intense FDG uptake is present because these lesions are typically below the resolution of current scanners (Fig 18). In small lesions, the FDG uptake may be underestimated owing to partial volume averaging with adjacent normal tissue. Thus, partial volume averaging effects may cause a significant decrease in the perceived SUV relative to actual FDG uptake in lesions that are smaller than twice the scanner resolution at full width half maximum (42). As a re-

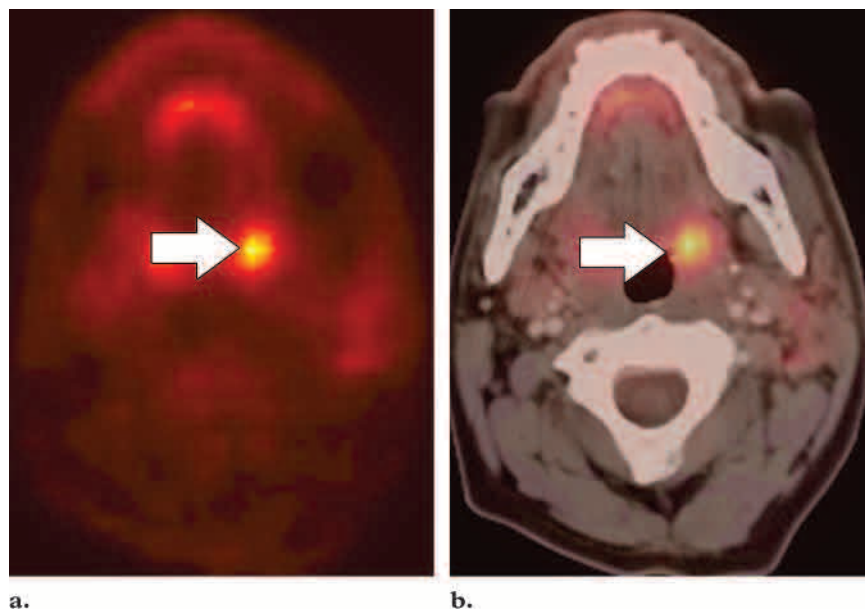


Figure 17. Squamous cell carcinoma in a left-sided level II lymph node. PET and PET-CT were performed to search for the primary site. PET (a) and PET-CT (b) scans demonstrate slightly asymmetric FDG uptake in the left tonsil (arrow), a finding that was initially interpreted as physiologic uptake. Direct laryngoscopy and multiple biopsies of the tongue base and tonsils proved that the left tonsil was in fact the primary site.

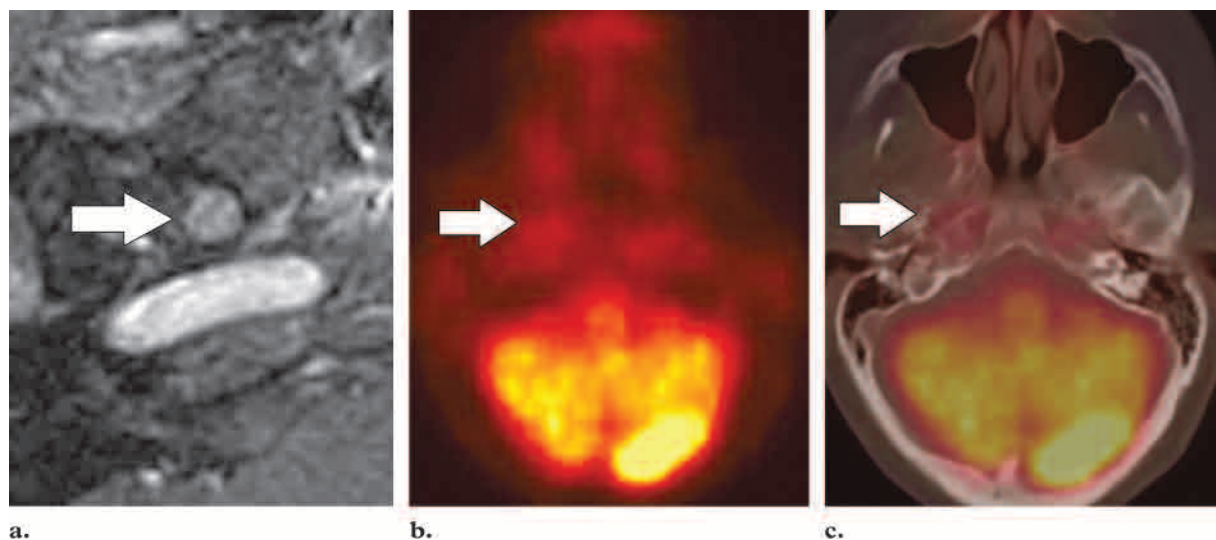


Figure 18. Neoplastic spread in a patient who presented with severe dysesthesia in the distribution of the right fifth cranial nerve (maxillary and mandibular divisions). The patient had undergone resection of a right buccal squamous cell carcinoma 9 months earlier. (a) MR image (magnified view) shows an enhancing 5-mm lesion in the right fifth cranial nerve (mandibular division) in the foramen ovale (arrow). (b, c) PET (b) and PET-CT (c) scans show no FDG uptake in the fifth cranial nerve (mandibular division) (arrow), likely owing to the small lesion size. Perineural spread of neoplasm was confirmed at surgery.

sult, FDG uptake that typically falls in the benign range (<2.5 – 3.0) (18,38) may indicate neoplasm. In the future, improved scanner resolution may help address this limitation.

Recent Surgery

Surgery may incite variable inflammatory response in the surrounding tissue. This inflammation may result in increased glycolysis and there-

fore be associated with increased FDG uptake. Increased uptake at sites of inflammation, including those caused by infection and foreign bodies, is well documented (43,44). In fact, some authors advocate the use of FDG PET for the detection of inflammatory disorders (45).

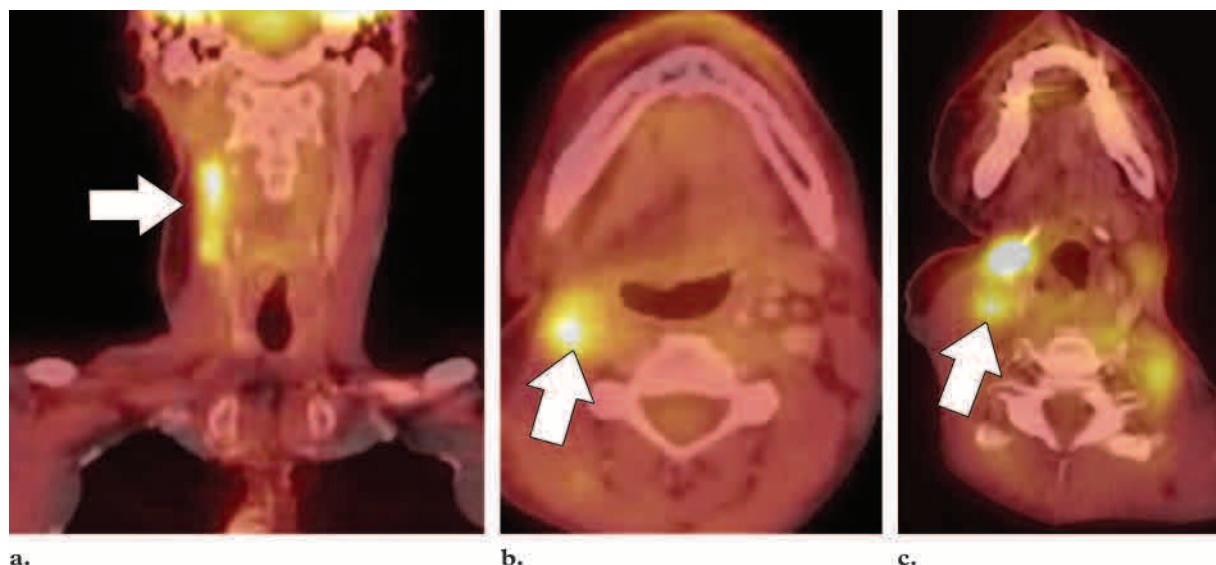


Figure 19. Residual neoplasm in a 42-year-old patient who had undergone radical neck dissection, chemotherapy, and radiation therapy for squamous cell carcinoma of the right side of the tongue base and neck. **(a)** PET-CT scan obtained 3½ weeks after radiation therapy shows linear, intensely increased FDG uptake in the right side of the neck (arrow), a finding that was interpreted as likely representing treatment-related changes. No definite abnormality had been seen at CT. **(b, c)** PET-CT scans obtained 4 months later show globular increased FDG uptake in the same location (arrow), as well as increased FDG uptake anteriorly **(c)**. Thus, the initial FDG uptake represented residual neoplasm rather than treatment-related changes.

Recent Radiation Therapy and Chemotherapy

The performance of FDG PET-CT after radiation therapy and chemotherapy is a controversial topic. PET performed in the 1st month following radiation therapy may yield false-negative findings (2). A small prospective study of 12 patients with advanced (stage II or stage IV) head and neck cancer that evaluated the usefulness of FDG PET before and after definitive radiation therapy showed that a positive PET study performed 1 month after radiation therapy accurately indicated the presence of disease, but that a negative PET study was unreliable in demonstrating the absence of disease (negative predictive value, 14%) (46). CT and MR imaging were more reliable than PET in demonstrating the absence of disease in that series (negative predictive value, 50%) (46). PET-CT performed within 3 months of radiation therapy may still yield false-positive or false-negative findings (Figs 13, 19). Early data from Greven et al (47) suggest that PET performed 4 months after the completion of radiation therapy more accurately reflects disease status than does PET performed immediately after therapy.

Lowe et al (48) prospectively evaluated 44 patients with stage II or stage IV head and neck can-

cer with FDG PET to detect recurrence at 2 and 10 months following treatment (chemotherapy, radiation therapy, surgical salvage) and found that initial PET had yielded no false-positive results. More recent data suggest that PET surveillance as early as 6 weeks after completion of a regimen of combined chemotherapy and radiation therapy may yield highly sensitive and specific information regarding the presence of residual neoplasm, distant metastases, or a second primary tumor (sensitivity, 90.9%; specificity, 93.3%) (49).

Inflammatory Tissue

Benign conditions that exhibit increased glycolysis may also demonstrate FDG uptake; these conditions include inflammation, infection, and granulomatous processes (45). Macrophages in inflammatory lesions, as well as neoplasms, may demonstrate a concentration of FDG (50). The affinity of FDG for inflammatory tissue has been exploited in cases of fever of unknown origin (45,51) but may produce false-positive findings in cancer patients (Fig 20) (18,52,53). Wong et al (18) evaluated the use of FDG PET in detecting recurrent disease in a cohort of 143 patients with treated head and neck squamous cell carcinoma. They reported that one-fifth of false-positive foci of FDG uptake occurred at sites of known infection or inflammation (18).

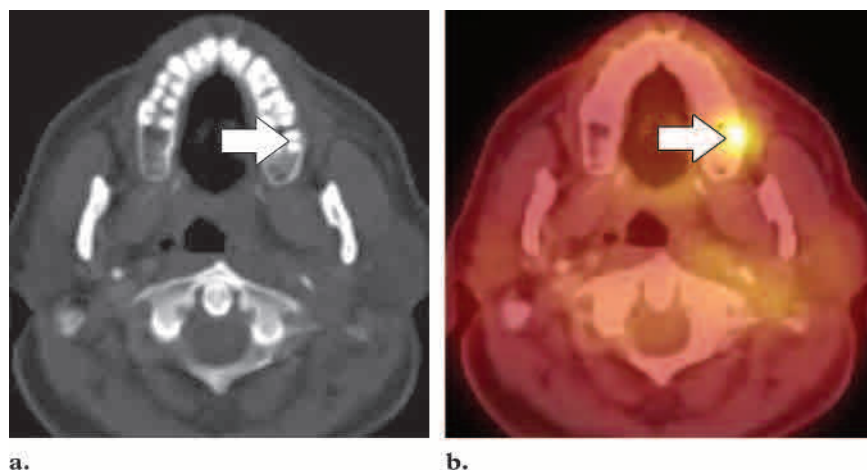


Figure 20. Dental abscess in a 56-year-old man with a history of squamous cell carcinoma of the left side of the tongue base. The patient had undergone resection and radiation therapy and presented with new left-sided facial pain. **(a)** CT scan shows no abnormality in the left maxilla (arrow). **(b)** PET-CT scan shows a focal area of intense FDG uptake in the left maxilla (arrow). Although neoplasm was suspected, the FDG uptake proved to represent a dental abscess.

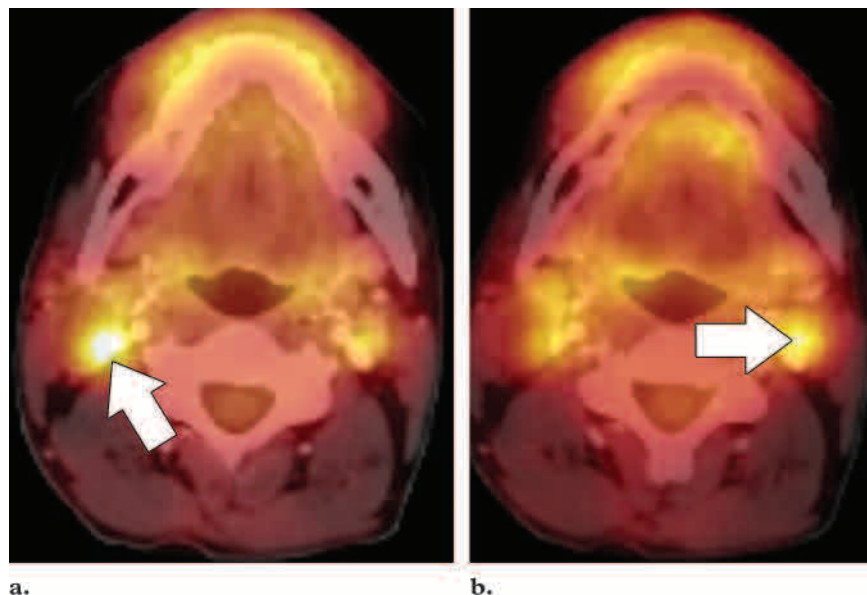


Figure 21. Lack of FDG uptake in a necrotic lymph node metastasis in a patient with squamous cell carcinoma of the right side of the tongue base. The patient underwent PET-CT for staging. **(a)** PET-CT scan shows a necrotic right-sided level II lymph node with focal uptake in the solid portion (arrow). However, no FDG uptake is noted in the more anterolateral necrotic component of the lymph node, a finding that represents a potential pitfall. **(b)** PET-CT scan shows unsuspected tumor involvement of a contralateral level II lymph node (arrow). This finding had not been detected at CT earlier, likely because the lymph node was inseparable from the left sternocleidomastoid muscle.

Low FDG Avidity

Tumors with inherently low FDG uptake such as salivary gland neoplasms and necrotic neoplasms may yield false-negative results (54). Necrotic lymph nodes may simply not contain sufficient metabolically active tissue to take up FDG, despite FDG uptake in solid neoplasms with the

same histologic features (Fig 21). Salivary gland neoplasms and spindle cell neoplasms may not be FDG avid (Fig 22) (55,56). FDG PET-CT cannot currently be recommended in this setting unless a baseline study demonstrates FDG uptake in the tumor.

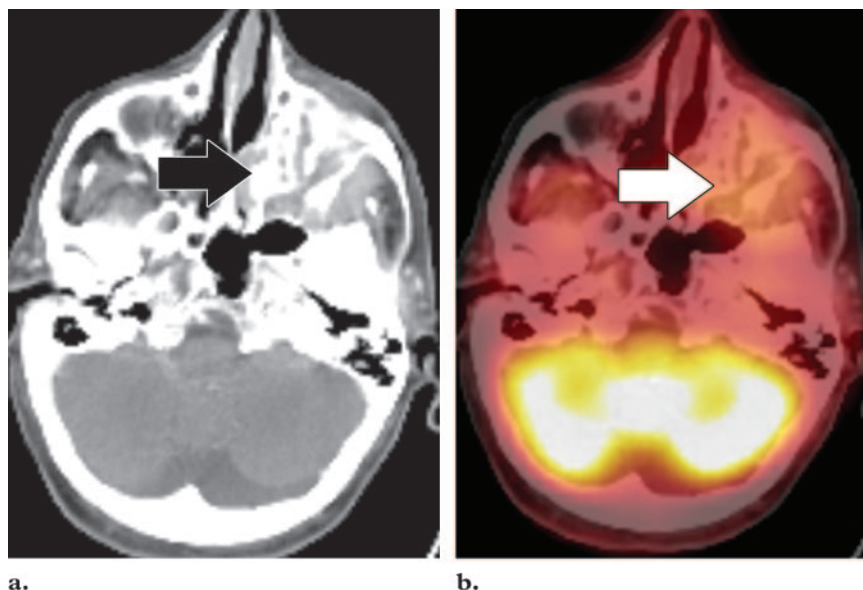


Figure 22. Spindle cell neoplasm in a 76-year-old patient. CT (a) and PET-CT (b) scans show sclerosis of the left maxillary sinus walls, in addition to a mass in the masticator space (arrow). The latter finding proved to be neuroendocrine carcinoma with bone invasion at histologic analysis. Spindle cell neoplasms, like some other neoplasms, may have low FDG avidity, thereby representing a potential pitfall.

Artifacts, including attenuation correction artifacts, are discussed in part 1 of this two-part series (6).

Conclusions

Our experience at the University of Pittsburgh indicates that combined PET-CT optimizes the interpretation of FDG PET findings in head and neck cancer. Superior localization of radiotracer uptake with this technique can improve diagnostic accuracy and help avoid interpretative pitfalls. Ultimately, improved scanner resolution will help address the limitation related to lesion size and may make PET-CT more valuable in initial tumor staging. Development of tumor-specific ligands will enhance the usefulness of PET-CT in the detection of initial tumor and tumor recurrence and in the evaluation of tumors with low FDG avidity. Successful treatment of neoplasm with irradiation or radiosurgery is predicated on accurately differentiating tumor from scar and on precise localization of the tumor. In the future, treatment targeting may be more effective if based on metabolic or tumor-specific markers rather than morphologic data alone.

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