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Clinical Utility of Positron Emission Tomography with ^{18}F-Fluorodeoxyglucose in Detecting Residual/Recurrent Squamous Cell Carcinoma of the Head and Neck

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PURPOSE: The use of positron emission tomography with ^{18}F-fluorodeoxyglucose (FDG-PET) to detect residual/recurrent squamous cell carcinoma of the head and neck has been tested only in small groups of patients. Our purpose, therefore, was to evaluate the ability of this technique to detect the presence of tumor at both primary and nodal sites in a large cohort of patients.

METHODS: All patients referred for PET scanning over a 2.5-year period with a question of residual or recurrent squamous cell carcinoma of the head and neck were identified. Thirty-five of 44 patients had sufficient follow-up to be meaningful to our analysis (range, 6–33 months). PET scans were interpreted visually with knowledge of the clinical history and correlative anatomic imaging findings. Detection of disease involving primary and nodal sites was assessed independently. Additionally, because each patient had been referred in an attempt to resolve a specific clinical problem, the usefulness of PET in accurately addressing these questions was assessed.

RESULTS: At the primary site, sensitivity and specificity for residual/recurrent disease were 100% and 64%, respectively; for nodal disease, sensitivity and specificity were 93% and 77%, respectively. In helping to resolve the clinical question being asked, the positive predictive value of the test result was 65% and the negative predictive value was 91%.

CONCLUSION: The high sensitivity and negative predictive value of PET scanning in our cohort of patients suggest an important role for this technique in the care of patients with suspected residual/recurrent head and neck carcinoma. The lower figures obtained for specificity and positive predictive value reflect the fact that increased FDG uptake may be due to either tumor or inflammation.

Squamous cell carcinoma of the upper aerodigestive tract has a high rate of involvement of local and regional lymph nodes (1), and the primary site and involved or at-risk lymph nodes are generally treated with surgical resection, radiation therapy, or both. Complete remission of primary site and/or nodal disease is achieved in 65% to 90% of patients with stage T2 to T4 disease, but control rates fall to 45% to 50% by 3 years (2, 3). Recurrent carcinoma may develop either at the site of the original primary tumor or in the ipsilateral or contralateral cervical nodes. Distant metastasis as the sole manifestation of recurrent disease, without local recurrence at the primary site, occurs in only 3% to 8% of patients (4–6).

Surgery and radiation therapy result in a variety of acute and chronic tissue effects and considerable anatomic distortion (7, 8), which complicate the detection of recurrent disease by clinical examination or conventional anatomic imaging. Biopsy may miss viable tumor if not properly directed and may cause significant complications in previously irradiated tissue (9). Despite these difficulties, prompt recognition of recurrence is critical when salvage therapy is available. The glucose analogue 2-[^{18}F] fluoro-2-deoxy-D-glucose (FDG) is an indicator of glucose metabolism

in both normal and neoplastic tissues (10). Positron emission tomography (PET) with FDG (FDG-PET) has proved to be of use in detecting residual or recurrent tumors in the CNS after radiation therapy (11, 12), and this technique has been extended to the extracranial head and neck (13–19). The use of PET avoids issues of posttherapeutic anatomic distortion by detecting tumor on the basis of abnormal glucose uptake; however, correlative anatomic imaging (CT, MR) is still essential for directing biopsies, precisely locating PET abnormalities, and planning salvage therapy.

The purpose of this study was to analyze the ability of FDG-PET to detect residual and/or recurrent disease after primary therapy in a large cohort of patients with squamous cell carcinoma of the head and neck. We hypothesized that FDG-PET is sensitive but not specific in the detection of recurrent disease, and that a negative FDG-PET scan reliably excludes disease. As the examinations that form the basis of this study were requested by the referring physicians to address specific clinical questions, the ability of this method to assist the referring head and neck surgeon with patient management could be directly assessed.

Methods

Patients

All patients who underwent FDG-PET scanning to assess residual or recurrent disease after primary therapy for squamous cell carcinoma of the head and neck were identified from our PET center database. We then identified a subgroup of 35 patients (with a total of 36 PET scans) who had sufficient post-PET follow-up to be meaningful to our analysis. Scans were performed between August 1994 and January 1997. Patients ranged in age from 30 to 82 years (mean age, 59 years). Follow-up information was obtained from in-depth chart review and discussion with the referring physician.

Primary sites of squamous cell carcinoma in our patients were the nasopharynx (n = 6), oral cavity (n = 5), base of tongue (n = 8), tonsil (n = 4), other oropharyngeal sites (n = 2), supraglottic area (n = 1), larynx (n = 4), parotid gland (n = 1), nasal cavity (n = 1), and maxillary sinus (n = 2); one patient had an unknown primary site with squamous cell carcinoma metastatic to the neck nodes. At initial presentation, stages of primary lesions were T1 in five patients, T2 in nine patients, T3 in eight patients, T4 in seven patients, and not known in the patient with the unknown primary site; nodal stages were N0 in 16 patients, N1 in three patients, N2 in nine patients, and N3 in two patients. Staging information was not available in five cases. All patients had been previously treated with surgery and/or radiation therapy.

The average time from the completion of primary treatment to the time of PET scanning was 16 months (range, 2–120 months; median, 8 months). All but six patients were scanned 4 months or longer after primary therapy. One patient was scanned 2 months after completion of therapy, and five patients were scanned 3 months after completion of therapy.

Correlative anatomic imaging with either CT or MR imaging was performed in all patients, usually within 2 weeks and always within 4 weeks of the PET study. The scans themselves or a report were available at the time of interpretation of the PET scan. Residual or recurrent carcinoma was confirmed histologically from specimens obtained from biopsy or surgical resection at primary and/or nodal sites in 15 cases. In three cases, recurrence was inferred from obvious clinical progression. Patients whose PET scans did not suggest recurrent disease were followed up clinically, with biopsy performed if there was concern that the PET scan was underestimating disease. Of this group, five patients underwent biopsy because of clinical findings, and the remaining patients were followed up over 6 to 33 months (average, 18 months).

PET Imaging

PET scans were performed using a Siemens ECAT-EXACT HR system. All patients had fasted for at least 4 hours before scanning. After informed consent as defined by our institutional review board was obtained, approximately 10 mCi of FDG was injected intravenously. Transmission scanning with three germanium-68/gallium-68 rotating rod sources was performed for attenuation correction immediately after FDG administration. This was followed by emission scanning at each bed position, generating two series of 47 axial attenuation-corrected emission images with coverage from the skull base to the level of the thoracic inlet. The first emission sequence was begun approximately 25 minutes after FDG administration. Each transmission scanning series required 20 minutes, while each emission series required 40 minutes. Through-plane resolution was 3 mm, with in-plane spatial resolution of 3.5 mm full-width half-maximum in the center of the field of view. The matrix size was 128 × 128 with a 30-cm FOV, and the nominal section thickness was 3 mm. Images were viewed on a workstation that allows simultaneous viewing of sagittal, axial, and coronal planes, with easy cross-referencing among planes.

PET scans were interpreted by experienced physicians who had access to current clinical data at the time of the interpretation. Recent anatomic imaging studies (MR or CT) were almost always available to the interpreting physician; if studies could not be immediately located, imaging reports were available. The PET interpretation was based on visual analysis of the data, with areas of asymmetric and/or focal uptake reported as positive. If the interpreting physician favored an area of uptake as representing tumor rather than inflammatory or reactive changes, this preference was reported. In most cases, areas of focal and/or asymmetric uptake had to be considered as indeterminate for tumor or inflammation, unless they could be clearly seen to represent a normal structure (ie, pterygoid muscle in a person who talked during the examination). Absence of these findings was reported as negative.

When the PET reports were reviewed retrospectively for purposes of this study, the visual assessment of disease activity was assigned a grade of 0, 1, or 2. A grade of 0 indicated that no abnormal focal or asymmetric activity was noted, a grade of 2 indicated a focal abnormal accumulation of radiopharmaceutical where the possibility of tumor was high, and a grade of 1 suggested that the tracer accumulation could represent tumor but was somewhat less intense and/or more diffuse than would be seen with grade-2 uptake. For the purpose of this study we considered both grades 1 and 2 to represent positive results, as the clinician was required to make a decision about patient management when any abnormal activity was detected.

Outcome Determination

Detailed chart reviews were conducted to evaluate patient outcome. Emphasis was placed on clinical head and neck examinations, follow-up imaging studies, and follow-up cytologic or histopathologic findings. On the basis of this information, PET results were classified as true-positive, true-negative, false-positive, or false-negative.

Data Analysis

To assess the performance of PET scanning, we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of this technique at both primary and nodal sites. These were separately assessed to determine

TABLE 1: Summary of PET results at primary sites

	Biopsy	Clinical Follow-up	Total
True-positive	11	3	14
True-negative	1	13	14
False-positive	3	5	8
False-negative	0	0	0

TABLE 2: Summary of PET results at nodal sites

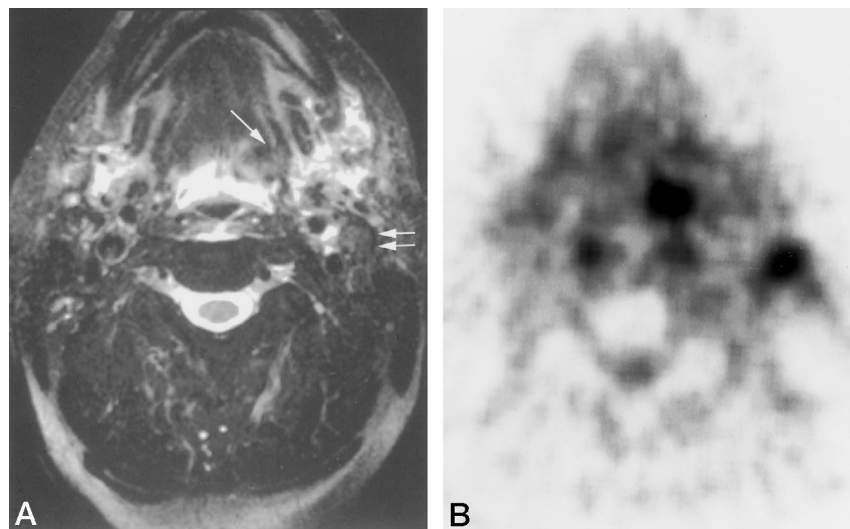|	Biopsy	Clinical Follow-up	Total
True-positive	10	3	13
True-negative	1	16	17
False-positive	3	2	5
False-negative	1	0	1

Fig 1. 52-year-old man with a T2N2M0 squamous cell carcinoma of the tongue base, which had been treated with radiation therapy.

A, Follow-up T2-weighted fast spin-echo MR image with fat saturation (4000/102$_{eff}$/2 [TR/TE/excitations]) shows extensive postradiation change. No definite tumor can be seen at the left base of the tongue (*single arrow*). A left-sided jugulodigastric lymph node (*double arrows*), measuring 11 mm in diameter, is homogeneously low in signal intensity on the T2-weighted image, and is significantly decreased in size relative to that on a pretherapy examination (*not shown*). This study was interpreted as indeterminate for residual disease.

B, PET scan obtained 1 week after the MR study shows abnormal accumulation of FDG at both the left tongue base and the jugulodigastric lymph node. Mild symmetric activity is also noted in the prevertebral muscles. The patient went on to partial glossectomy, supraglottic laryngectomy, and modified radical neck dissection. The presence of tumor was histologically confirmed at both the primary and the nodal sites.

whether PET did equally well in depicting residual/recurrent disease at both these locations. We had 36 data points to evaluate at each location. In general, we were unable to correlate PET and histopathologic results for individual nodes owing to the retrospective nature of this study. One patient whose neck showed no evidence of disease at PET scanning was eliminated from consideration because he died of such rapidly progressive disease at the primary site that the true status of disease in the neck was uncertain.

These parameters also were evaluated in light of the specific clinical question being asked. This was done to prevent our results from being falsely improved by, for example, the detection of clinically obvious nodal disease in a patient in whom the clinician desired only to know the status of disease at the primary site.

Results

Primary Site

There were 22 positive scans and 14 negative scans at the primary site of disease. These results are summarized in Table 1. Eight positive scans were judged to be false-positive on the basis that there was no evidence of tumor on multiple biopsy specimens (n = 3) or there was no evidence of disease on clinical follow-up over a period averaging 22 months (range, 9–33 months) (n = 5). All 14 negative results were considered true-negative based on stable clinical follow-up findings over a period averaging 16 months (range, 6–32 months) (n = 13) and on a biopsy specimen of a clinically suspicious area that revealed only fibrotic and inflammatory changes (n = 1). FDG-PET had a sensitivity of 100%, a specificity of 64%, a positive predictive value of 64%, a negative predictive value of 100%, and overall accuracy of 78% for residual/recurrent disease at the primary site.

Of the 14 true-positive cases, only five had evidence of a mass at the primary site on CT or MR studies or at clinical examination. The remainder had scans that showed only posttherapeutic changes at the primary site of disease (Fig 1).

Nodal Disease

There were 18 positive and 18 negative results for nodal disease on evaluable PET scans. These results are summarized in Table 2. The 13 true-positive results were confirmed with tissue sampling in 10 cases and by obvious clinical progression in three patients. Five results were judged to be false-positive, with three proved by biopsy and two by clinical follow-up (these patients were stable at 30 and 31 months, respectively). Seventeen of the 18 negative results were classified as true-negative by clinical follow-up in 16 patients (range, 6–24 months; average, 12 months) and by biopsy of a clinically suspicious area in one patient. One result was false-negative on the

FIG 2. 65-year-old man with a right-sided neck mass that yielded squamous cell carcinoma on fine-needle aspiration. A head and neck examination was unremarkable, but an endoscopic biopsy specimen of the right base of the tongue was positive for squamous cell carcinoma.

A, Axial T1-weighted baseline MR image (600/11/2) shows an enlarged right jugulodigastric lymph node (*arrow*).

B, After radiation therapy, the node is reduced in size on an axial T1-weighted (650/13/2) image (*arrows*).

C, The node has low signal intensity on an axial T2-weighted (4000/102$_{eff}$/2) image (*arrow*). It was not clear whether active tumor persisted within the node or whether this finding represented postradiation fibrosis, so an FDG-PET scan was ordered to investigate this site as well as the primary site and the other side of the neck.

D, FDG-PET scan shows intense tracer accumulation within the questionable lymph node. The remainder of the examination was unremarkable. A fine-needle aspirate of the right-sided jugulodigastric node yielded squamous cell carcinoma, and the patient was treated with modified right-sided radical neck dissection. The left side of the neck has remained negative over an 18-month follow-up period.
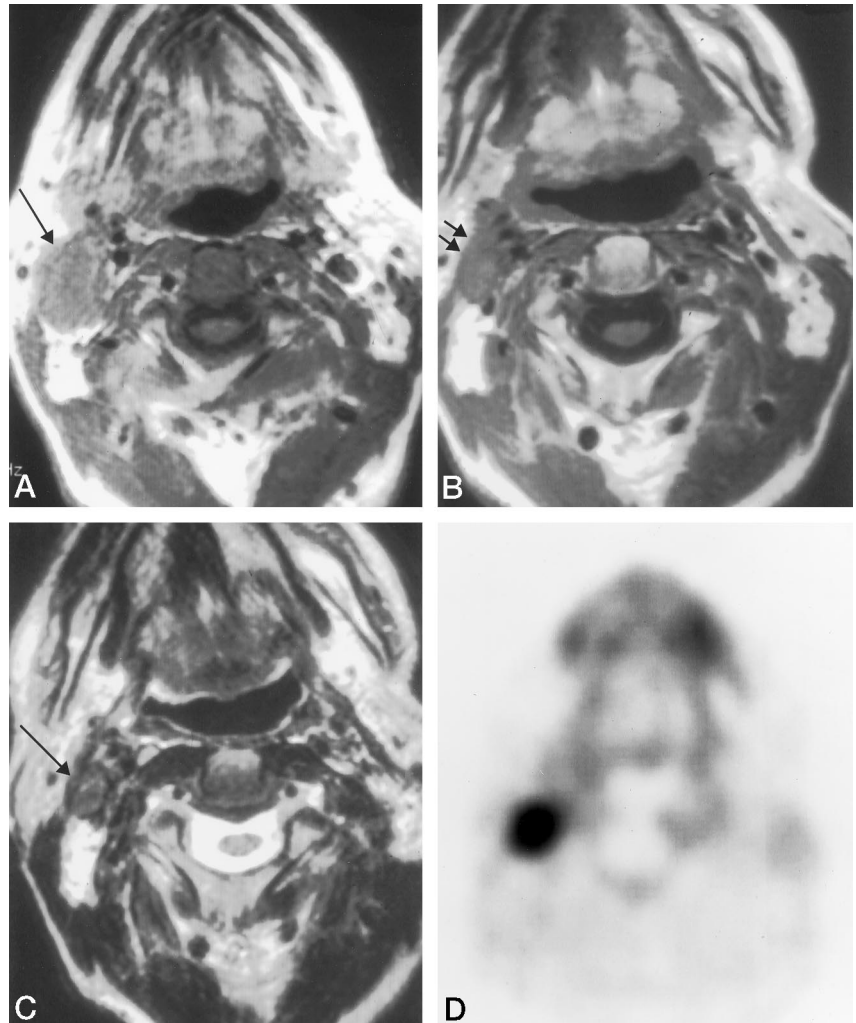
basis of findings at neck dissection performed for a clinically persistent mass. For detection of residual/recurrent disease at nodal sites, FDG-PET had a sensitivity of 93%, a specificity of 77%, a positive predictive value of 72%, a negative predictive value of 94%, and an overall accuracy of 83%.

In the 13 patients with true-positive findings, four had anatomic imaging studies that showed questionable cervical lymph nodes. Two of these studies were considered equivocal for residual/recurrent tumor (Fig 2) and two were considered suggestive of tumor. The CT scans of the patient with the false-negative PET scan showed a small cystic mass, which at surgery correlated with a completely necrotic node.

Clinical Question

When the PET findings were looked at in terms of the clinical question being asked, 26 results were positive and 11 were negative. These findings are summarized in Table 3. Of the nine cases that were considered false-positive, five had directed biopsies performed on the basis of PET findings. Four patients were followed up clinically despite the positive PET result and have shown no evidence of recurrence

during an average follow-up period of 25 months (range, 10–33 months). Surgery had involved the paranasal sinuses in two of these patients, and the PET result was believed to be false-positive by the referring physician, since both patients had considerable mucosal inflammation. In the other two cases the area in question was readily accessible to physical examination, and the clinician elected to follow the patient closely with serial examinations.

Of the 11 negative results, 10 were judged to be true-negative on the basis of clinical follow-up to an average of 18 months (range, 6–32 months), and the one false-negative result was confirmed histologically, as mentioned above. This patient had received radiation therapy for squamous cell carcinoma involving the tonsil and neck on the right side. A PET scan obtained to evaluate residual disease 2 months after the completion of radiation therapy was unremarkable. However, because of clinical persistence of a neck mass, laryngoscopy and a right-sided modified radical neck dissection were performed 2 weeks later. The primary site was negative, but two necrotic nodes harboring carcinoma were identified in zone II.

With regard to the accuracy of PET in providing answers to the referring clinician's question, we cal-

TABLE 3: Performance of PET in addressing the clinical question

	Biopsy	Clinical Follow-up	Total
True-positive	14	3	17
True-negative	0	10	10
False-positive	5	4	9
False-negative	1	0	1

Note.—The main clinical questions posed included the following: Could neck dissection potentially be avoided in a previously irradiated patient without definite clinical evidence of active disease? Could surgical treatment of a primary site potentially be avoided in a previously irradiated patient without definite clinical evidence of active disease? Was a previously treated primary site still active in a patient presenting with a new primary lesion? and, Was there active disease at either the primary or nodal sites in a previously treated patient with a new clinical symptom, such as pain or increased swelling, but inconclusive clinical and conventional imaging examinations? In some cases, PET scans were prompted by confusing and/or worrisome findings on CT and/or MR studies.

culated a sensitivity of 94%, a specificity of 53%, a positive predictive value of 65%, and a negative predictive value of 91%. Overall accuracy was 73%.

Time to PET Scanning

The average time to PET scanning after completion of primary therapy was 16 months (range, 2–120 months; median, 8 months). One patient was scanned 2 months after primary therapy, and this study accounts for our only false-negative finding. Five scans were performed 3 months after primary therapy, and all other patients were scanned 4 or more months after primary therapy.

PET versus Anatomic Imaging (CT/MR)

All patients had CT or MR examinations within 4 weeks of PET scanning, most within 2 weeks, and either the scan itself or a report was available at the time the PET study was performed. Reports of imaging findings were reviewed to determine how the PET results correlated with imaging findings. Nineteen of the CT or MR examinations were reported to show posttherapeutic changes (edema, anatomic distortion, fibrosis/scarring) that were considered indeterminate for the presence of residual or recurrent tumor. PET scans in these 19 patients were interpreted as positive in 13 cases and negative in six cases. Of the positive results, eight were true-positive and five were false-positive. All six negative findings were true-negative. In 12 cases, a mass (primary site or nodal) was identified on anatomic images; among these, eight PET scans were true-positive, three were false-positive, and one was false-negative. Five patients had unremarkable CT or MR studies: two patients had PET scanning because of persistent pain and clinical concern for recurrent cancer, while three were scanned to assess for residual disease to help determine whether a postradiation therapy neck dissection should be performed. In this group, one PET scan was true-positive and four were true-negative.

Discussion

The timely diagnosis of residual or recurrent disease after primary therapy for squamous cell carcinoma of the head and neck is critical if salvage therapy is to be effective. Surgery and radiation therapy result in a variety of acute and chronic tissue changes, including edema, scarring and fibrosis, and necrosis, which obliterate and distort normal fascial planes on anatomic imaging studies (7, 8). Flap reconstruction also results in considerable anatomic distortion. These factors limit the sensitivity and specificity of the clinician's physical examination and of the radiologist's interpretation of anatomic imaging studies, such as CT and MR images. Biopsy of previously irradiated tissues to screen for disease recurrence cannot be done with impunity as it carries a significant risk of complications, including bleeding, infection, and, in the larynx, chondronecrosis (9) (Fig 3). A diagnostic tool such as FDG-PET, which assesses abnormal metabolic activity of tumor rather than anatomic features associated with tumor growth, avoids some of the difficulties inherent in examining the posttreatment head and neck.

FDG-PET imaging has been applied extensively to the evaluation of squamous cell carcinoma of the head and neck, with uptake in both primary and metastatic tumor deposits shown consistently (13, 17, 20–22). Several groups have addressed the role of PET in the diagnosis of residual and/or recurrent disease after primary therapy in small groups of patients with squamous cell carcinoma of the head and neck. In studies that included 10 to 15 patients, sensitivity for detection of residual/recurrent disease ranged from 0.88 to 1.00, while specificity ranged from 0.43 to 1.00 (14–16, 18, 19). Most of these studies did not distinguish between the performance of the technique at primary and nodal sites of disease. In one study (19), sensitivity and specificity were 1.00 and 0.64, respectively, at the primary site and 1.00 and 0.94, respectively, at nodal sites, although the length of the follow-up period for nodal disease was not noted. Our results showed a high sensitivity at both primary and nodal sites for residual/recurrent disease in a large cohort of patients with squamous cell carcinoma of the head and neck. Our specificity was lower than the 1.00 reported by Anzai et al (14) but comparable to the 0.43 reported by Lapela et al (15) when both "clearly malignant" and "suspicious" lesions (equivalent to our grades 1 and 2) were considered positive. When we analyzed our data with only grade-2 scans considered as positive, then sensitivity decreased and specificity increased, as would be expected. These differences in results among investigators are most likely related to the varying criteria by which a study is designated positive, and such differences will most likely persist until a reliable indicator of tumor versus inflammation exists. The distinction between tumor and inflammation may not be achievable with FDG and may require the development of alternative markers for the presence of tumor. Given the potentially significant consequences of delayed

Fig 3. 72-year-old man who had radiation therapy for a T3N0M0 squamous cell carcinoma of the larynx reported throat pain and poor voice at follow-up. Clinical examination was limited by severe mucosal edema.

A, Axial T1-weighted (600/13/2) MR image shows severe laryngeal edema consistent with postradiation change, but tumor cannot be excluded.

B, FDG-PET scan shows minimal diffuse symmetric tracer accumulation in the larynx and was considered negative; biopsy was therefore not performed. The patient has improved clinically and has had no evidence of disease recurrence over 11 months of follow-up.
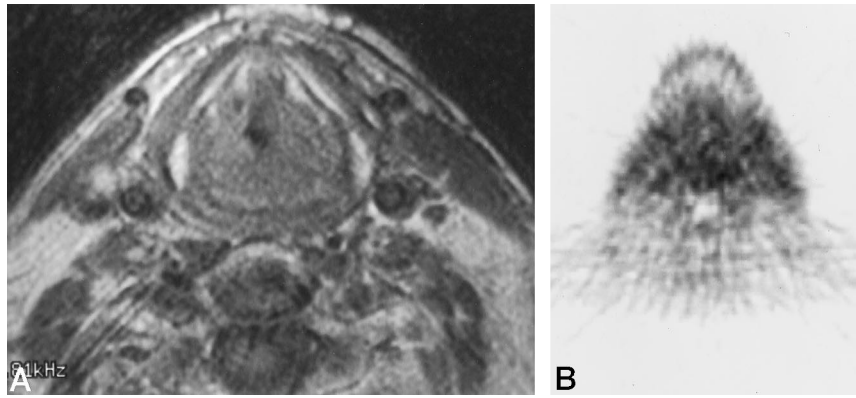
therapy if a suspicious lesion is not pursued, we are willing to accept a relatively lower specificity in the interest of being highly sensitive.

Visual Analysis

Our studies were interpreted visually, without quantification. It has been suggested that visual analysis of FDG-PET images performed by experienced observers is sufficiently sensitive and specific for detection of recurrent head and neck cancer (15). The fact that squamous cell carcinoma generally has a high FDG uptake, as measured by the standardized uptake value (SUV) and by other quantitation methods, supports the use of visual analysis, since foci of recurrent disease should be readily detectable. Quantitative methods may also not be as accurate as they seem at the present time. Both Lapela et al (15) and Anzai et al (14) observed modest overlap of SUVs between recurrent tumor and inflammatory lesions. Additionally, small lesions may show artificially low activity, especially on lower-resolution scanners. Finally, Hamberg et al (23) pointed out that SUV measurements should be made when the concentration of tracer has reached a plateau, but that the time to plateau cannot be identified from a single static acquisition and may be as long as 5 or 6 hours. Therefore, SUVs may vary widely with the time of measurement, must be interpreted with caution, and are unlikely to be comparable among institutions. In the future, the use of dynamic imaging studies and extremely delayed imaging with more robust PET cameras may make quantitation more reliable and more absolute (23).

Because the referring clinician must deal with all results that raise a question of active tumor, we considered all abnormal focal and asymmetric activity to be suggestive of tumor. This policy most likely contributed to our relatively low specificity. However, we also analyzed our data in terms of counting only PET scores of 2 as positive. This generally improved specificity but at the cost of sensitivity, which is in general agreement with the experience of Lapela et al (15), who found that lesions that were only "visually suspicious" rather than "clearly positive for malignancy" could be either neoplastic or inflammatory.

False-Positive and Negative Results

False results limit both the sensitivity and specificity of FDG-PET. In general, the avidity of squamous cell carcinoma for FDG makes false-negative findings a less significant clinical problem than false-positive findings except under specific circumstances, as discussed below.

False-Positive Results

FDG is known to accumulate in inflammatory tissue (24–26). Anzai et al (14) reported one false-positive finding in their series in which histopathologic examination showed chronic ulceration and granulation tissue without evidence of recurrence. Lapela et al (15) also reported false-positive findings due to inflammation, with the highest regional metabolic rates in benign lesions found in two patients with marked inflammatory changes. We had six false-positive results that had histopathologic correlation. In five cases, the tissue samples showed inflammatory changes; in one case, only the absence of tumor was reported. Lapela et al (15) investigated time-activity curves of malignant and benign lesions as a way to potentially differentiate inflammation from tumor, but no major differences could be detected. It is unlikely that a nonspecific marker of metabolic activity such as FDG will be able to differentiate tumor from inflammation with complete accuracy; we would anticipate that this will be possible only with tumor-specific markers or with significantly improved quantitative methods. PET scanning may also be somewhat less reliable when surgery has involved the paranasal sinuses, presumably because of inflammatory mucosal reaction. Among our cohort of patients, four had had a maxillectomy, and all had abnormal FDG accumulation in the maxillary region (two had true-positive findings, two had false-positive findings).

The occurrence of false-positive findings is more or less problematic clinically depending on the specific question being asked. If the referring clinician is concerned about nodal disease but gets a positive reading at a relatively accessible primary site in an informed patient who is reliable and will participate in close clinical follow-up, watchful waiting is an acceptable alternative (Fig 4). Patients who are at risk of being
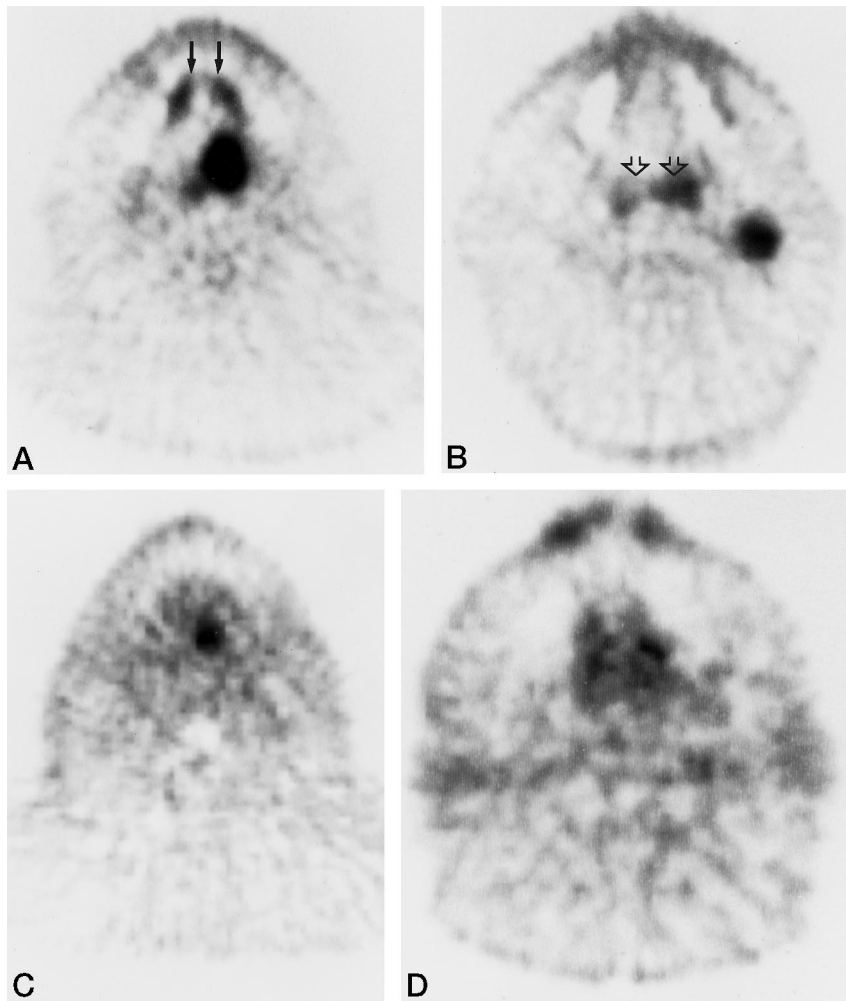
Fig 4. 61-year-old man with squamous cell carcinoma of the left base of the tongue.

A and *B*, Baseline FDG-PET study shows focal accumulation in left base of tongue (*A*) and a left-sided jugulodigastric lymph node (*B*). Some uptake is noted in the mylohyoid muscles (*arrows, A*) and in the prevertebral muscles (*arrows, B*), which is normal. After radiation therapy (78 Gy), the question arose as to whether a postradiation neck dissection should be performed.

C and *D*, Follow-up FDG-PET study shows persistent focal accumulation of FDG in the left base of the tongue (*C*), while the abnormal nodal accumulation has resolved (*D*). A mild generalized increase in background activity is attributable to postradiation therapy inflammatory changes. Note that pre- and posttherapeutic images were normalized by photographing them at the same brightness and contrast levels. The clinician elected to observe the tongue site and forgo neck dissection, and there has been no evidence of disease over a 2-year follow-up period.

lost to follow-up would be less favorable candidates for such an approach and would most likely need to undergo correlative biopsy.

False-Negative Results

False-negative results are generally a less significant problem because of the avid accumulation of FDG in tumor deposits (13, 17). However, false-negative results may occur when scans are performed earlier than 4 months after the completion of radiation therapy (22). False-negative findings may also occur when a tumor is largely necrotic, since there are fewer viable cells to accumulate tracer, or when a tumor deposit is very small. Our one false-negative result occurred in a patient who was scanned only 2 months after completion of radiation therapy and who had nodal necrosis at histopathologic examination. Both factors most likely contributed to the negative result in this case.

Future Directions

The role of FDG-PET imaging in the management of patients who have had therapy for primary squamous cell carcinoma of the head and neck remains to

be established. Our findings support the proposed management algorithm of Anzai et al (14), who suggested that the high sensitivity of PET makes it useful as the first step in assessing a patient with negative or equivocal findings on clinical examination in whom residual/recurrent disease is suspected. Even if disease is not suspected clinically, PET may have a role in noninvasive monitoring of patients at very high risk of recurrent disease. Additionally, when FDG-PET results are negative, our experience shows that patients who have no identifiable lesion on clinical examination may be safely monitored by close clinical follow-up.

We believe this strategy is cost-effective. FDG-PET is a relatively expensive diagnostic tool because of the high cost of the scanner and the radiopharmaceutical, with charges for a head and neck FDG-PET examination generally in the range of $2500 to $3000; however, the cost of a neck dissection is considerably greater, both in dollars and in potential morbidity for the patient. There is also a cost associated with random biopsies of potential sites of residual/recurrent disease, again both in dollars and in potential patient morbidity due to the risk of biopsy-associated soft-tissue necrosis or infection. A negative PET scan may obviate biopsy and/or neck dissection in a patient who

has no suspicious findings on clinical examination or on conventional imaging studies. Conversely, a positive PET scan can direct the clinician to the site most likely to yield tumor when a biopsy is performed, and intervention can be accomplished early, when the likelihood of successful salvage therapy is greatest. A false-positive scan may be associated with the additional cost of what proves to be an unnecessary biopsy if the clinician feels a biopsy is warranted. These costs, however, are more than balanced by the savings in dollars and morbidity resulting from the high negative predictive value of the technique.

Conclusion

Our results support the hypothesis that FDG-PET is sensitive but not specific in the detection of recurrent cancer, and that a negative FDG-PET scan reliably excludes disease. FDG-PET suffers in terms of specificity and positive predictive value for recurrent tumor because it is very sensitive to both tumor and inflammation, but it is likely to detect disease when it is present. This high sensitivity to residual and recurrent disease (94%) is very useful in terms of early detection, as it enables timely institution of salvage therapy. The high negative predictive value (91%) suggests that a negative FDG-PET result may obviate unnecessary diagnostic and surgical procedures that ensue from indeterminate clinical or imaging findings in patients who have been previously treated for squamous cell carcinoma of the head and neck.

Acknowledgment

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