Nuclear Medicine in Head and Neck Oncology: Reality and Perspectives*

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The extracranial head and neck together comprise a region of complex anatomy that challenges imaging techniques. Moreover, because biopsy and surgical treatment are often indicated and readily performed in this accessible region, the extent and nature of the various diseases encountered in the head and neck yield valuable information.

A priori in a region of such anatomic complexity, MRI, CT and ultrasonography (US) should leave little scope for radionuclide studies. However, because CT and MR diagnostic criteria depend exclusively on structural alterations, these imaging techniques have certain limitations especially in oncology, such as the early detection of tumors before any anatomic distortion occurs and in the postoperative setting. Nuclear medicine and in particular PET imaging, which depend not only on morphologic criteria but on the metabolic activity of the constituent tissue, can therefore be expected to have a significant clinical impact on the diagnosis and management of head and neck cancers (*1*). Is this so? The question can be best answered by a quantitative assessment of nuclear medicine diagnostic and therapeutic impact in head and neck oncology, which would require a comprehensive evaluative framework. This kind of assessment has been done for other imaging modalities (*2*) but not for nuclear medicine procedures in the head and neck. However, that is beyond the scope of this article. The following considerations are based on published results and personal experience.

Most nuclear medicine applications in head and neck oncology are not therapeutic but concern tumor diagnosis and surveillance (*1*). Most head and neck malignancies are—excluding skin cancer and melanomas—mucous squamous cell carcinomas (SCCs) of the oral cavity, pharynx and larynx (90%). Thyroid cancers constitute the second most common group (*2*), followed by the less frequent malignancies such as salivary gland tumors, lymphomas, sarcomas and rare tumors (e.g., paragangliomas).

Nuclear medicine has a traditional role in thyroid and parathyroid diseases; indeed ^{131}I scintigraphy, like US, continues to be a major imaging modality in the assessment of differentiated thyroid cancer (DTC) (*3,4*). Whole-body scanning with ^{131}I or nonspecific radionuclides (*5*) is an indispensable tool for the detection of metastases. However, patients with less well-differentiated carcinomas have more limited abilities to concentrate radioiodine and can benefit from combined whole-body ^{131}I and ^{18}F-fluorodeoxyglucose (FDG) PET whole-body scanning, with a reported sensitivity of 95% (*6*). The rationale of this approach, concisely formulated by Davis et al. (*7*), is that "some metastases are best demonstrated by PET, others by ^{131}I scanning, the difference largely being determined by the degree of differentiation within the tumor." FDG PET seems to be the method of choice in attempting to resolve the DTC follow-up dilemma, which is characterized by the presence of elevated thyroglobulin levels and a normal whole-body ^{131}I scan (*6*). For the difficult task of detecting minimal residual or metastatic disease from the less-common medullary carcinoma of the thyroid, somatostatin receptor scintigraphy may serve as a guide to subsequent selective venous catheterization (*8*). In postoperative parathyroid carcinoma—a rare cause of primary hyperparathyroidism—FDG PET provided the most accurate information, compared with the misleading findings of CT, MRI and ^{99m}Tc-sestamibi (*9*).

Direct scintigraphic assessment of the common SCC is generally performed using two categories of radiopharmaceuticals: (a) positron emitters such as FDG (with PET or non-PET dedicated systems) or ^{11}C-labeled amino acids and (b) ^{201}Tl or ^{99m}Tc-sestamibi. In addition, the evaluation of SCC osseous extension benefits from the use of bone scintigraphy. In detecting primary tumor and initial nodal disease in the neck, FDG PET performs as well as or marginally better than conventional investigations (CT and/or MRI and/or US) (*7,10*). However, MRI and CT are the imaging modalities of choice at initial staging because of

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their more accurate anatomic delineation of the primary tumor, metastases and patterns of local spread, particularly vascular invasion. The rates of FDG PET success in identifying unknown primary cancers in patients who present with nodal disease have been diversely reported (10%–60%) (*7,10*), and it is unclear whether it improves on the low yield of conventional techniques, not withstanding its whole-body scanning capacity. Although the problem of unknown primary cancer occurs in only 1%–5% of cases (*2*), a major validation effort through more studies should be made to avoid the "shotgun" blind treatment that is otherwise applied in these patients, namely surgery, radiation therapy or both. According to Keyes et al. (*10*), whole-body FDG PET proved disappointing in addressing the special problem of synchronous primary tumors, which have a high association with SCC arising below the level of the nasopharynx. However, FDG PET in the post-therapy setting seems to be more effective and reliable than anatomic imaging techniques (CT, MRI) (*6,10*). The anatomic distortion and scarring caused by surgery and radiotherapy—particularly in the larynx, base of tongue and oropharynx—often make it difficult to detect recurrent or residual disease using clinical examination and anatomic imaging techniques, especially when these are performed within 1 y of treatment completion. Moreover, a blind biopsy at an edematous or fibrotic site suspected of recurrence is often nondiagnostic. The sensitivity of FDG PET in detecting residual or recurrent disease at the primary site (*7*) is comparable with that of MRI and/or CT (88%–100% versus 70%–92%), but its specificity is superior (75%–100% versus 50%–57%). FDG PET has been suggested as a first study when no recurrent lesion is found on physical examination (*11,12*). Despite the reported better "statistical" accuracy with PET (*12*), because of the usual availability of previous MR and CT images and the cost-related lack of previous PET images, CT or MRI and FDG PET are generally used as complementary rather than alternative imaging methods. The detection of recurrence is particularly crucial in the larynx to allow salvage total laryngectomy. FDG PET is more accurate than CT or MRI in differentiating recurrent laryngeal cancer from postirradiation soft tissue sequelae (85% versus 42%) (*13*). PET performed at least 3–4 mo after irradiation can be the only helpful noninvasive test when laryngoscopic evaluation, CT and MRI are inconclusive (*10*). Moreover, surgeons are reluctant to obtain multiple or deep biopsy specimens for fear of initiating or aggravating radionecrosis (*13*) that might necessitate a laryngectomy. PET was also reported to successfully resolve the same diagnostic dilemma of tumor recurrence versus radiation necrosis in the irradiated mandible (*14*). Still, in the postoperative setting, FDG PET has an edge in that it provides metabolic information necessary for monitoring response to chemotherapy and radiotherapy. It can assess early effects of chemotherapy in locally advanced unresectable malignancies, because there is a linear relationship between FDG accumulation and growth rate during therapy (*15*), an increase in FDG uptake being consistently associated with treatment failure. This enables identification of nonresponders and, as a result, avoidance of the severe effects of useless therapy or a possible change in therapy. After radiation therapy, FDG uptake in the tumor can decrease dramatically, indicating local control (*7*), while it is unchanged in normal structures. As for malignancies in other regions, PET should not be performed earlier than 4 mo after completion of radiotherapy (*16*) to avoid potential early false-positive and later false-negative results (*12*). As already reported regarding PET monitoring of chemotherapy (*15*), FDG PET provides a noninvasive parameter of tumor aggressiveness that is not always predicted by pathohistology (*17*). Thus FDG PET contributes unique biological information with potential therapeutic implications. In a carefully designed study, Minn et al. (*18*) showed a poor risk of survival in head and neck patients with high tumor FDG uptake, concordantly quantified by standardized uptake value (SUV) lean and FDG metabolic rate. According to these authors, these patients should be considered for intensive treatment protocols including hyperfractionated radiotherapy and chemotherapy. They believe that the impact of FDG PET on therapy in a selected group of high-risk patients justifies its routine incorporation in their pretreatment evaluation.

PET can also be used with radiopharmaceuticals other than FDG for evaluating head and neck SCC. Although ^{11}C-methionine PET is as effective as FDG in tumor detection and in assessing response to radiotherapy (*19*), it is still unresolved whether it has a higher potential for early tumor monitoring than FDG (*20*). Moreover, in contrast to FDG, the amount of tumor ^{11}C-methionine uptake does not seem to predict the final outcome (*21*). For the assessment of neck metastases, ^{11}C-tyrosine has a better specificity than FDG (*22*), allowing differentiation between cancerous and reactive inflammatory palpable lymph nodes. Thus, it can be used to guide fine needle aspiration. A drawback of these PET-labeled amino acids is their high uptake in the salivary glands, which impairs image analysis, especially when metastases are localized close to these structures, the submandibular nodes being among the first nodal echelons infested with micrometastases from carcinomas of the oral cavity.

Although further prospective series are necessary to reach definite conclusions regarding the routine clinical value of PET for the diagnosis and management of head and neck tumors, there is agreement in the literature regarding the strength of PET in two areas: (a) post-therapy evaluation, in particular earlier detection of persistent or recurrent tumor, and (b) in vivo assessment of tumor aggressiveness and prediction of survival. However, Keyes et al. (*10*), in the largest published study on FDG PET in head and neck cancer, evoke the "seeming paradox of a technique of high accuracy but of limited usefulness." They give as main reasons the lack of required high anatomic resolution that is easily provided by competing imaging techniques and the high cost of FDG PET. These two points merit consideration.

The lack of high anatomic resolution limits both tumor

detection and accurate identification of tumor site. Limited resolution casts doubts on the possibility of detecting small tumors; although 4-mm tumors reportedly have been detected (*23*), the "minimum tumor burden" (*24*) detectable with FDG PET by the various systems remains to be determined. Precise tumor localization also poses a particular problem in view of the anatomic complexity of the head and neck. However, both tumor detection and localization can be improved by quantification of PET studies and by co-registration of the PET images with CT or MR images. Quantification by calculation of SUV or glucose metabolic rate can be helpful, especially in cases that are borderline on visual analysis. Lapela et al. (*11*) did not find a clear advantage in the more arduous dynamic studies over the calculated SUVs corrected for the lean body mass or for the body surface area. However, to compare SUVs obtained at different institutions, they should be calculated under the same conditions (*25*), with at least standardization of the measurement times after injection and strict adherence to fasting conditions. Even then, SUVs should be used with caution because they are subject to other sources of variability, such as the effect of the lesion size on tissue activity. An SUV of more than 7 can be considered as suspicious of malignancy (*11,12*); however, it should be kept in mind that optimal cutoff values between benign and malignant lesions are difficult to determine because of increased FDG uptake in inflammatory tissue (*11*). Co-registration can also help distinguish between abnormal and normal structures. Although co-registration is more crucial here than in any other part of the body because of the anatomic complexity of the head and neck, the registration method must account for the deformation that results from different neck positions (*26*), because the neck is mobile and affected by patient positioning. To minimize this problem, Wong et al. (*27*) used a radiotherapy-type immobilization device to accurately reproduce neck positions for the various imaging procedures undergone by patients with laryngeal malignancy. In assessing the accuracy of CT/MRI co-registration with FDG PET in head and neck SCCs against pathological findings, Wong et al. (*27*) showed additional and relevant clinical information compared with that obtained from clinical evaluation, CT or MRI, which resulted in management alterations in 7 of 30 patients. In 4 of them in whom disease had been assessed as incurable, it enabled surgical resection followed by histological confirmation of the co-registered tumor delineation. Further validation of the registration technique's accuracy, as well as further refinement with reduction in the time required for the procedure in a clinical setting (*28*), will facilitate its incorporation in clinical practice and will in turn increase the clinical utilization of PET. Co-registration of PET emission and transmission images can also be useful.

Concerning the issue of FDG imaging costs, it is expected that expenses will decline and availability increase with regional distribution of FDG and with more scanning options, including SPECT equipped with 511-keV collimators or dual coincidence imaging devices. The scarce and small series published on these devices (*29,30*) show inferior sensitivity and spatial resolution compared with FDG PET, a major problem in oncologic applications. Stokkel et al. (*30*) were able to detect local relapse in six patients with previously irradiated laryngeal carcinomas, tumor size range 1.4–5 cm. Another obstacle to wider clinical use of FDG PET is the long duration of the test. PET head and neck tumor imaging necessitates two or even three contiguous bed positions with transmission and emission scans to cover the distance from the midcranial level to about the arch of the aorta, which requires that the patient lie for a long period (1–2 h), a significant drawback in those patients whose airway is sometimes compromised by the lesion. This prompted Lauberbacher et al. (*31*) to propose an abbreviated protocol using only emission scans and without the possibility of quantification.

According to Olmos et al. (*32*), who evaluated 69 patients, thallium SPECT in head and neck SCC compares favorably with PET and is likewise useful in detecting occult tumors, especially naso- and oropharyngeal carcinomas and tumor recurrences (accuracy of 87% versus 64% for CT or MRI). Olmos et al. (*32*) also reported a much higher specificity than with CT or MRI in differentiating metastases from reactive neck lymph nodes (90% versus 30%). In patients with nasopharyngeal carcinoma (NPC) (*33*), sestamibi and ^{201}Tl are reported to have higher accuracy (85% and 82%, respectively) than CT/MRI (61%) in the post-therapeutic course, justifying the incorporation of sestamibi scintigraphy into the initial work-up for NPC to obtain a baseline study. However, the minimal detectable lesion size was 1.6 cm with both radiopharmaceuticals. In addition, as with ^{11}C-labeled amino acids, tumor detection with both ^{201}Tl and sestamibi is hindered by high normal uptake within the salivary and thyroid glands. Only SPECT/CT or MRI co-registration and superimposition of the matched images might help to avoid false-negative results, because pretreatment with potassium perchlorate is unsuccessful in suppressing the physiological uptake of ^{201}Tl and sestamibi in the salivary glands (*32,33*). Notwithstanding these limitations, ^{201}Tl and sestamibi SPECT are practical scintigraphic techniques that are underused in head and neck oncology. Together with CT and/or MRI, they can reach a high specificity in detecting recurrence of NPC. They represent real alternatives in the most common situation: when PET tracers are not available.

The clinical and subclinical extension of head and neck SCC to the numerous bony structures of the face and skull base can be evaluated by bone SPECT, alone or associated with other scintigraphic techniques of direct tumor imaging. This information is not always provided by CT and MRI and is crucial because of its surgical implications. It is particularly relevant for oral cavity carcinomas, especially those of the retromolar trigone and the floor of the mouth, because the mandible is frequently involved subclinically. When the mandible is documented to be free of tumor, mandibular continuity can usually be preserved by the surgeon. Accord-

ing to Chan et al. (*34*), bone SPECT not only excludes bony invasion but reliably differentiates periosteal reaction from bone invasion by intraoral SCCs by semiquantitative analysis, allowing the surgeon to strip only the periosteum. The detection of bone involvement can be refined by adding sestamibi SPECT of the primary tumor to bone SPECT and by superimposing images from both studies, excluding in some cases osseous tumor spread despite positive bone SPECT. Leitha et al. (*35*) have validated their conclusions for SCCs with histopathological confirmation of nonspecific periosteal reaction as the explanation of the positive bone scan and reported a more accurate detection of bone involvement than with CT. Likewise, skull-base invasion, which significantly affects a patient's prognosis, could be detected early (*36*) by simultaneous bone and tumor dual-isotope SPECT with ^{99m}Tc-hydroxymethylene diphosphonate (HMDP) and ^{201}Tl. As for the traditional role of the whole-body bone scan in the metastatic work-up of head and neck malignant tumors, Ampil et al. (37) question this routine indication in asymptomatic patients with locally advanced head and neck cancer because the positive yield of this test is low.

The scintigraphic methods used in SCC are applicable to other head and neck malignancies. It is particularly true for malignant tumors of the parotid glands and their bony extension to the mandible and skull base. With regard to salivary gland malignant tumors, the clinical contribution of nuclear medicine including PET is not significant at this time (*38*). However, other radionuclide procedures can make a difference in certain cases, such as the management of cutaneous melanomas. Here, the nuclear medicine armamentarium includes not only the cost-effective screening FDG whole-body scan but lymphoscintigraphy, which is unrivaled in anatomically defining tumor lymphatic drainage to one or more sentinel nodes (SN) and designating them for biopsy (*39*). Although this SN concept is more difficult to implement in the anatomically dense head and neck region than in other parts of the body, it might avoid regional neck dissection in patients who do not have metastatic disease. An additional bold management step would be to spare the patient the biopsy when the SN does not accumulate FDG, but this has yet to be validated by large correlative studies. In the clinical evaluation and surveillance of head and neck lymphoma, ^{67}Ga SPECT still retains its tandem role with CT, although FDG PET might be just as effective (*40*). In the rare paragangliomas of the head and neck, a scintigraphic test that depicts specific endocrine activity, such as ^{111}In-octeotride, complements MRI or CT in differentiating a glomus tumor of the skull base from a neuroma and a postoperative scar from a recurrence. Likewise, ^{123}I-metaiodobenzylguanidine (MIBG) confirms the functional character of the lesion before potentially dangerous intraoperative manipulations. These tests also have the advantage of screening the entire patient for second primary and occult metastatic disease even when one lesion has already been localized by CT or MRI (*41,42*).

CONCLUSION

Radionuclide imaging has a definite clinical impact in the management of thyroid cancers and cutaneous malignant melanomas. For other head and neck malignancies, although more large prospective studies are warranted for further validation, FDG imaging has already fulfilled its promises (*43*) in the post-therapy setting. It is already a valuable tool for optimal patient management in head and neck oncology, assisting in important therapeutic decisions. This confirms the need to perform a nuclear medicine procedure in addition to anatomic imaging in this field. However, the wide incorporation of FDG imaging in clinical routine depends on economic solutions to cost availability issues and on possible technological and clinical progress of dual coincidence imaging in the head and neck. When PET tracers are not available, ^{201}Tl or ^{99m}Tc-sestamibi SPECT should be integrated in the decision-making process, especially in patients with NPC.

Another prerequisite to wider clinical use of PET and SPECT in head and neck oncology is the systematic use of correlative imaging with CT or MRI, including precise co-registration. Although recognized as conventional wisdom, this is not always implemented in clinical reality because of the limited user friendliness of registration techniques for the physician. Such an integrated imaging approach will permit a true and rewarding multidisciplinary collaboration in head and neck oncology between specialists of the imaging profession, surgeons, radiotherapists and oncologists, with a consequent beneficial impact on patient care.

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REFERENCES

1. Chisin R, Noyek AM, Israel O, Witterick IJ, Kirsh JC, Front D. Contribution of nuclear medicine to the diagnosis and management of extracranial head and neck diseases (excluding thyroid and parathyroid). *Isr J Med Sci.* 1992;28:254–261.
2. Vokes EE, Weichselbaum RR, Lippman SM, Kikong W. Head and neck cancer. *N Engl J Med.* 1993;328:184–194.
3. Boudreau RJ, Remley KB. Advances in imaging the thyroid and parathyroid glands: nuclear scintigraphy, computed tomography, and magnetic resonance imaging. *Thyroid Today.* 1996;19:1–16.
4. Gharib H. Management of thyroid nodules: another look. *Thyroid Today.* 1997;20:1–11.
5. Klain M, Maurea S, Cuocolo A, et al. Tc-99m tetrafosmin imaging in thyroid diseases. Comparison with Tc-99m pertechnetate, thallium-201 and Tc-99m methoxyisobutyl isonitrile scans. *Eur J Nucl Med.* 1996;23:1568–1574.
6. Grunwald F, Schomburg A, Bender H, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in the follow-up of differentiated thyroid cancer. *Eur J Nucl Med.* 1996;23:312–319.
7. Davis JP, Maisey NM, Chevreton EB. Positron emission tomography: a useful imaging technique for otolaryngology, head and neck surgery? *J Laryngol Otol.* 1998;112:125–127.
8. Dorr U, Sautter-Bihl ML, Bihl H. The contribution of somatostatin-receptor scintigraphy to the diagnosis of recurrent medullary carcinoma of the thyroid. *Semin Oncol.* 1994;21:42–45.

9. Neumann DR, Esselstyn CB, Kim EY. Recurrent postoperative parathyroid carcinoma: FDG PET and sestamibi SPECT findings. *J Nucl Med.* 1996;37:2000–2001.
10. Keyes JW Jr, Watson NE, Williams DW, et al. FDG PET in head and neck cancer. *AJR* 1997;169:1663–1669.
11. Lapela M, Grenman R, Kurki T, et al. Head and neck cancer: detection of recurrence with PET and 2-(F-18)fluoro-2-deoxy-D-glucose. *Radiology.* 1995;197: 205–211.
12. Anzai Y, Carroll WR, Quint DJ, et al. Recurrence of head and neck cancer after surgery or irradiation: prospective comparison of 2-deoxy-2(F18)fluoro-deoxyglucose PET and MR imaging diagnoses. *Radiology.* 1996;200:135–141.
13. McGuirt WF, Greven KM, Keyes JW Jr, et al. Positron emission tomography in the evaluation of laryngeal carcinoma. *Ann Otol Rhinol Laryngo.* 1995;104:274–278.
14. Minn H, Aitasalo K, Happonen RP. Detection of cancer recurrence in irradiated mandible using positron emission tomography. *Eur Arch Otorhinolaryngol.* 1993;250:312–315.
15. Reisser C, Haberkorn U, Dimitrakopoulou-Strauss A, Seifert E, Strauss LG. Chemotherapeutic management of head and neck malignancies with positron emission tomography. *Arch Otolaryngol Head Neck Surg.* 1995;121:272–276.
16. Greven KM, Williams DW 3rd, Keyes JW Jr, et al. Positron emission tomography of patients with head and neck carcinoma before and after high dose irradiation. *Cancer.* 1994;74:1355–1359.
17. Kado H, Ogawa T, Okudera T, Kanno I, Hatazawa J, Uemura K. Parapharyngeal meningioma extending from the intracranial space evaluated by FDG PET. *J Nucl Med.* 1998;39:302–304.
18. Minn H, Lapela M, Klemi PJ, et al. Prediction of survival with fluorine-18-fluorodeoxyglucose and PET in head and neck cancer. *J Nucl Med.* 1997;38:1907–1911.
19. Lindholm P, Leskinen-Kallio S, Grenman R, et al. Evaluation of response to radiotherapy in head and neck cancer by positron emission tomography and (^{11}C) methionine. *Int J Radiat Oncol Biol Phys.* 1995;32:787–794.
20. Higashi K, Clavo AC, Wahl RL. In vitro assessment of 2-fluoro-2-deoxy-D-glucose, L-methionine and thymidine as agents to monitor the early response of a human adenocarcinoma cell line to radiotherapy. *J Nucl Med.* 1993;34:773–779.
21. Lindholm P, Leskinen S, Lapela M. Is tumor carbon-11-methionine uptake of prognosis value in squamous cell head and neck cancer? *J Nucl Med.* 1998;39: 1393–1397.
22. Braams JW, Pruim J, Nikkels PGJ, Roodenburg JLN, Vaalburg W, Vermey A. Nodal spread of squamous cell carcinoma of the oral cavity detected with PET-tyrosine, MRI and CT. *J Nucl Med.* 1996;37:897–901.
23. Braams JW, Pruim J, Kole AC, et al. Detection of unknown primary head and neck tumors by positron emission tomography. *Int J Oral Maxillofac Surg.* 1997;26: 112–115.
24. Wong WL, Chevretton EB, McGurk M, et al. A prospective study of PET-FDG imaging for the assessment of head and neck squamous cell carcinoma. *Clin Otolaryngol.* 1997;22:209–214.
25. Keyes JW Jr. SUV: standard uptake or silly useless value? *J Nucl Med.* 1995;36:1836–1839.
26. Uematsu H, Sadato N, Yonekura Y, et al. Coregistration of FDG PET and MRI of the head and neck using normal distribution of FDG. *J Nucl Med.* 1998;39:2121–2127.
27. Wong WL, Hussain K, Chevretton E, et al. Validation and clinical application of computer-combined computed tomography and positron emission tomography with 2-(^{18}F)fluoro-2-deoxy-D-glucose head and neck images. *Am J Surg.* 1996;172: 628–632.
28. Chisin R, Pietrzyk U, Sichel JY, et al. Registration and display of multimodal images: applications in the extracranial head and neck region. *J Otolaryngol.* 1993;22:214–219.
29. Mukherji SK, Drane WE, Mancuso AA, Parsons JT, Mendenhall WM, Stringer S. Occult primary tumors of the head and neck: detection with 2-(F-18)fluoro-2-deoxy-D-glucose SPECT. *Radiology.* 1996;199:761–766.
30. Stokkel MP, Terhaard CH, Mertens IL, Hordijk G-J, Van Rijk PP. Fluorine-18-fluorodeoxyglucose detection of laryngeal cancer post radiotherapy using dual-head coincidence imaging. *J Nucl Med.* 1998;39:1385–1387.
31. Lauberbacher C, Saumweber D, Wagner-Manslau C, et al. Comparison of fluorine-18-fluorodeoxyglucose PET, MRI and endoscopy for staging head and neck squamous cell carcinomas. *J Nucl Med.* 1995;36:1747–1757.
32. Olmos RAV, Balm AJM, Hilgers FJM, et al. Thallium-201 SPECT in the diagnosis of head and neck cancer. *J Nucl Med* 1997;38:873–879.
33. Kostaglu L, Uysal U, Ozyar E, et al. Pre- and post-therapy thallium-201 and technetium-99m-sestamibi SPECT in nasopharyngeal carcinoma. *J Nucl Med.* 1996;37:1962–1964.
34. Chan KM, Merrick MV, Mitchell R. Bone SPECT to assess mandibular invasion by intraoral squamous cell carcinomas. *J Nucl* Med. 1996;37:42–45.
35. Leitha T, Glaser C, Pruckmayer M, et al. Technetium-99m-MIBI in primary and recurrent head and neck tumors: contribution of bone SPECT image fusion. *J Nucl Med.* 1998;39:1166–1171.
36. Fukomoto M, Yoshida S, Yoshida D, Kishimoto S. Dual-isotope SPECT of skull-base invasion of head and neck tumors. *J Nucl Med.* 1995;36:1740–1746.
37. Ampil FL, Wood MJ, Chin HW, Hoasjoe DK, Aarstad RF, Hilton DL. Screening bone scintigraphy in the staging of locally advanced head and neck cancer. *J Craniomaxillofac Surg.* 1995;23:115–118.
38. Keyes JW Jr, Harkness BA, Greven KM, Williams DW III, Watson NE Jr, McGuirt WF. Salivary gland tumors: pretherapy evaluation with PET. *Radiology.* 1994;192:99–102.
39. O'Brien CJ, Uren RF, Thompson JF, et al. Prediction of potential metastatic sites in cutaneous head and neck melanoma using lymphoscintigraphy. *Am J Surg.* 1995;170:461–466.
40. Walsh RM, Wong WL, Chevretton EB, et al. The use of PET-^{18}FDG imaging in the clinical evaluation of head and neck lymphoma. *Clin Oncol R Coll Radiol.* 1996;8:51–54.
41. Hansman Whiteman ML, Serafini AN, Telischi FF, Civantos JC, Falcone S. 111-In octreotide scintigraphy in the evaluation of head and neck lesions. *Am J Neuroradiol.* 1997;18:1073–1080.
42. Reuland P, Overkamp D, Aicher KP, Bien S, Müller-Schauenburg W, Feine U. Catecholamine secreting glomus tumor detected by iodine-123-MIBG scintigraphy. *J Nucl Med.* 1996;37:463–465.
43. Mancuso AA, Drane WE, Mukherji SK. The promise of FDG in diagnosis and surveillance of head and neck cancer. *Cancer.* 1994;74:1193–1195.