# Fluorodeoxyglucose Positron Emission Tomography in the Evaluation of Tumors of the Nasopharynx, Paranasal Sinuses, and Nasal Cavity

Brendan C. Stack, Jr, MD, FACS[*]
Val J. Lowe, MD[†]
Robert V. Lane, MD[‡]

[*]*Division of Otolaryngology-HNS, Penn State University Milton S. Hershey Medical Center, Hershey, Pennsylvania.*
[†]*Department of Nuclear Medicine and PET facility, Mayo Clinic Foundation, Rochester, Minnesota.*
[‡]*Department of Otolaryngology-HNS, University of Missouri Health Sciences Center, Columbia, Missouri.*

*This study was presented at the 5th International Conference on Head and Neck Cancer in San Francisco, California, July 29-August 2, 2000.*

**KEY WORDS:** Positron emission tomography, paranasal sinuses, nasopharynx, and skull base

## ABSTRACT

**Introduction:** The purpose of this study was to review the clinical utility of 2-[18F]-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) in the diagnostic evaluation of a series of patients with tumors of the nasopharynx, paranasal sinuses, and nasal cavity.

**Methods:** The study group included 16 patients from a single institution who underwent a total of 31 FDG-PET scans for the evaluation of various histologic types of masses of the nasopharynx, nasal cavity, and paranasal sinuses for diagnosis and or surveillance. A review of the patients' medical records was performed in order to obtain all data including tumor type and location, PET scan results, CT and MRI results, treatments performed, tumor recurrence, and clinical outcome. This data was analyzed to determine the utility of FDG-PET in the identification of primary tumors and/or recurrent disease.

**Results:** FDG-PET identified 100% of all primary tumors examined with initial diagnostic intent (n=8). In addition, 1 case of lymphoid hyperplasia was correctly identified as nonmalignant. Of 22 PET scans performed for tumor surveillance, 16 scans identified recurrent disease and 5 scans were correctly interpreted as negative. One scan showed an area of increased metabolism at the base of tongue suspicious for malignancy that later proved to be an inflammatory process (1 false positive).

**Conclusion:** FDG-PET was an effective imaging modality in the evaluation of

primary and recurrent tumors of the nasopharynx, paranasal sinuses, and nasal cavities in our series. As a functional scanning modality, FDG-PET is particularly useful in tumor surveillance where normal anatomy has been disrupted by prior surgery or radiation. Our series reaffirms the results of similar series with respect to the use of PET in these particular sub sites of the head and neck.

## INTRODUCTION

Positron emission tomography (PET) is a nuclear medicine scan, which allows for a physiologic examination of tissue glucose metabolism. PET images are computer generated from tomographic detection of radiation emitted from a source trapped within hyper metabolic tissues. These tissues exist physiologically (brain, cardiac muscle, etc.) but also exist with the rapid cell proliferation of malignancy.

18-fluoro-2-deoxy glucose (FDG), the positron source, is intravenously administered and taken intracellular as a potential energy source by tumor cells in higher concentrations than most non-malignant tissue and then is arrested in the second step of glucose metabolism because of the 2-deoxy modification to the glucose molecule. There it remains intracellular as a positron source until radioactive decay is completed. Positrons react with electrons, which result in the production of 2 photons at 180 degrees from each other. Coincident detection of photon pairs leaving the body by an array of crystals within the gantry allow for computer localization of the emission source (malignant tumor) and consequently image creation.

PET theoretically offers advantages in head and neck oncology (most of which is squamous cell carcinoma, HNSCC) for diagnosis of small primary tumors and early recurrences where changes in anatomy might escape detection by clinical exam, endoscopy, or conventional imaging (computerized tomography, [CT] or magnetic resonance imaging [MRI]). PET has been reported as greater than 90% sensitive and specific for HNSCC across heterogeneous sub sites and stages, both in diagnostic and surveillance settings.[1,2] Clinical examples of these situations in HNSCC include the unknown primary, occult cervical nodal metastasis which occur at a rate up to 30%, and surveillance of recurrent disease in the previously treated patient. Besides surveillance because of risk, PET is an especially helpful tool for diagnosis of the at risk patient with symptoms (dysphagia, otalgia, or head and neck pain) where physical and imaging findings are non-specific. Finally, when treatment is employed that does not extirpate the disease (chemotherapy with radiation), PET allows for post treatment assessment of tumor response.

The nose, paranasal sinuses, nasopharynx, and skull base are areas with limited accessibility by physical exam. Office endoscopy has aided in their examination but its interpretation can be confounded by mucus, inflammation, and cicatrix. Conventional imaging of these areas is limited for the same reasons. PET imaging may be a helpful adjunct for diagnosis and/or surveillance of these areas of the head and neck, especially when other clinical data is ambiguous.

## MATERIALS AND METHODS

The study group included 16 consecutive patients who underwent a total of 31 FDG-PET scans for the evaluation of various histologic types of masses of the nasopharynx, nasal cavity, and paranasal sinuses. All patients reviewed were diagnosed and/or treated at the St. Louis University Health Sciences Center, St. Louis, Missouri from 1995 to 1998 (Tables 1 and 2). Demographic description of the study population includes 6 males, 10 females mean age of 58.4

**Table 1.** Patient Characteristics

| Site | No. | Path | Stage |
|---|---|---|---|
| Maxillary | 3 | SCC (2) | III (2) |
| | | Lymph | IV |
| Nasopharynx | 9 | WHO I (5) | III (4) |
| | | WHO II (2) | IV (4) |
| | | WHO III (2) | N/A |
| Ethmoid | 1 | SCC | IV |
| Frontal | 1 | Small | III |
| | | Cell Ca | |
| Nasal Cavity | 2 | SCC | II |
| | | Melanoma | N/A |

*SCC indicates squamous cell carcinoma; WHO, World Health Organization; NA, not available; and Lymph, lymphoma. Roman numerals are AJCC Staging SCC of the head and neck.

**Table 2.** Outcomes of Patients Studied by PET at Last Follow-Up

| | |
|---|---|
| No evidence of disease | 6 |
| Alive with recurrence | 8 |
| Dead of disease | 2 |

years. A retrospective review of the patients' medical records was performed in order to obtain all data including tumor type and location, PET scan results, CT and MRI results, treatments performed, disease status, and clinical outcome. These data were analyzed to determine the utility of FDG-PET in the identification of primary tumors and/or recurrent disease. Of the 16 patients studied, follow-up ranged from 18 months to 4 years (Table 1) and between 1 to 4 scans were evaluated per patient.

## RESULTS

PET had 100% sensitivity (n=8) of all primary tumors investigated prior to treatment in our small series. Our experience demonstrated PET specificity by correctly imaging one nasopharynx mass as normal uptake (SUV-standard uptake values) that turned out to be benign lymphoid hyperplasia on permanent pathology.

Twenty two scans were performed for post treatment tumor surveillance. Sixteen scans demonstrated recurrent tumor and 5 scans showed no evidence of recurrence. One false positive scan was noted at the tongue base, which was biopsy negative and never developed into a clinical tumor on further surveillance examinations (specificity 97%) (Table 2). Several cases below demonstrate various scenarios when PET may be useful for diagnosis or surveillance of sinonasal, nasopharyngeal, and skull base malignancies.

### Case 1

A patient with a history of extensive sinus exenteration for ethmoid sinus cancer underwent routine imaging of the skull base with CT and MRI and was judged to have recurrent maxillary sinus neoplastic disease and postoperative changes elsewhere in the operative field. PET indicated a recurrence in the ethmoid sinus, not in the maxillary (Figure 1). The patient successfully underwent a second resection of recurrence, which was localized to the ethmoid sinuses without maxillary sinus extension.

### Case 2

A patient with nasopharynx cancer was treated with chemotherapy and radiation and had a complete clinical response. The patient complained of ear pain 2 months following completion of treatment, which was evaluated, by CT and PET (Figure 2). The CT scan was read as negative, as was the PET. Persistence of symptoms prompted repeat CT and PET imaging 10 months following the completion of treatment. Again the CT was reported as negative.

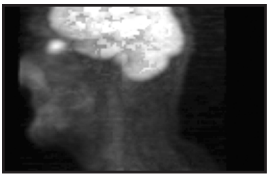

**Figure 1** Ethmoid sinus recurrence detected by PET surveillance.

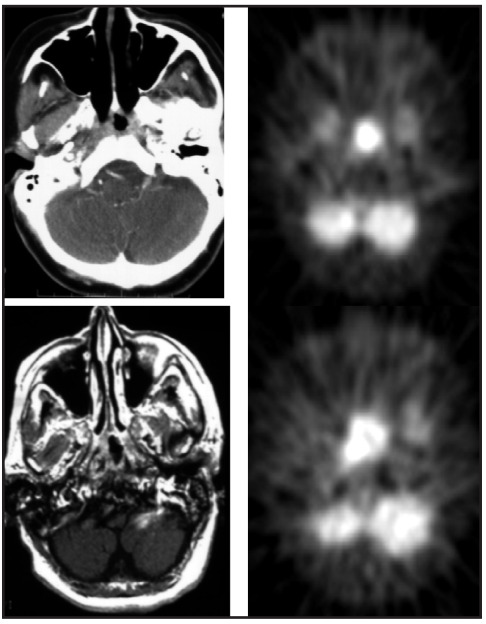

**Figure 3** Recurrent nasopharyngeal cancer detected by PET and not CT (top). Recurrent nasopharyngeal cancer detected by PET and MRI (bottom).

The PET was read as positive in the nasopharynx and these results were confirmed by a biopsy shortly thereafter.

**Case 3**

A patient with nasopharynx tumor under went a surveillance exam by CT and PET, 15 months following treatment. The CT was read as negative, the PET as positive but no biopsy confirmed the recurrence. Three months later, an MRI showed evidence of recurrence. Repeat PET at this time showed local progression of disease and then biopsy confirmed recurrence (Figure 3).

## DISCUSSION

The diagnosis of HNSCC is imperfect and is limited by current technology. Initial assessment is often initiated by complaints of pain, throat obstruction,

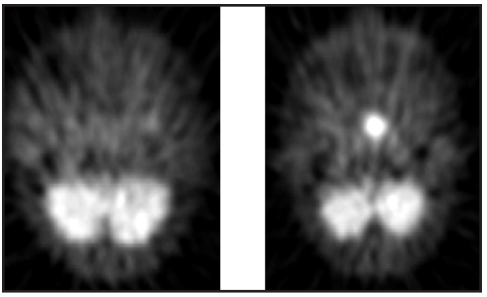

**Figure 2** Recurrent nasopharyngeal cancer detected by PET surveillance.

or the development of a neck mass. Once a biopsy confirms the diagnosis of HNSCC, a staging work up ensues which can include imaging and endoscopy. Imaging most often utilizes CT but may also involve MRI. This imaging usually encompasses the primary site and the neck but may also assess the brain, skull base, and lungs. Endoscopy may be performed in the office or may require an operative procedure depending on primary location, patient cooperation, and adequacy of airway. Imaging, biopsies, and endoscopy produce the data necessary to stage the patient's cancer for the purposes of prognostication and clinical decision-making.

**Primary and Secondary Tumors**

PET has some value in detecting primary tumors but may not be a preferred method for initial screening, diagnosis, and staging. By the time there is enough clinical or symptomatic evidence for suspicion of head and neck cancer, primary tumors are often advanced enough to be detected by palpation or physical examination with the exception of some skull base tumors. In these obvious cases, routine PET would be an unnecessary expense. Di Martino et al compared PET to CT and color-coded sonography for detecting primary head and neck lesions and found PET to be the most reliable method, although panendoscopy had a similar sensitivity and specificity.[3] PET is less expensive than panendoscopy and requires no risk associated

with general anesthesia. Stokkel et al studied the use of PET in detecting second primary neoplasms and found PET to significantly increase the rate of detection of second primaries than by conventional imaging.[3] The significance is that a synchronous second primary may be small and escape detection and a metachronous second primary occurs in a treated field where physical exam, endoscopy, and conventional imaging may yield ambiguous.

**Recurrence**

PET has proven to be particularly valuable in the detection of recurrent disease when anatomic or fascial planes and fibrotic tissues have been distorted by, or resulted from previous treatment. The sensitivity of PET in detecting recurrent disease has been reported to be between 92% to 100% and the specificity has been reported between 61% to 96%. Several studies have examined the use of PET surveillance after radiotherapy[5-7] and that it is superior to CT[8] or MRI[9] in this context.

**Detection of Occult Primary Tumors**

Occult primary disease presents a particular problem in treatment decisions for head and neck cancer. At least one study suggested that PET was not effective in this context. Greven et al studied 13 patients with occult primary disease and found that PET provided an accurate localization in 1 case and provided false positives in 6 cases.[10] Several other studies, many using larger samples, have found PET to be effective in localizing primary tumors of unknown origin.[11-14] Overall, the current weight of evidence favors a role for PET in the localization of tumors of unknown origin. The nasopharynx is one of the classic locations of unknown primaries of the head and neck.

**Treatment Assessment**

Several studies have considered the use of PET in assessing patients' response to treatment, particularly after radiotherapy.[15-17] Treatment assessment is performed shortly following therapy (6 weeks to 6 months) and is to be distinguished from surveillance exams (at greater than 6 months). Greven et al found that while PET was useful for initial imaging of head and neck cancers, SUV's were not useful for predicting outcomes following primary radiation therapy.[18] Rege et al and others found that pretreatment PET was an independent predictor of which patients achieve long-term local control with primary radiation therapy.[19] Lowe et al reported 100% sensitivity and specificity for PET detection of recurrence in complete responding (CR) stage III/IV HNSCC patients with a greater sensitivity than conventional imaging ($P$=0.013) or physical exam ($P$=0.002).[20]

Our series demonstrates PET to be a useful modality to image the paranasal sinus, nasopharynx, and skull base. Admittedly, the size of this series makes the conclusion limited and somewhat anecdotal. These areas are difficult to assess under normal conditions. Post treatment changes including flaps, grafts, implants, retained mucus, and cicatrix are confounding elements on direct examination and imaging. PET allows for a reliable means to discern treatment artifact from recurrence and it can detect it earlier than conventional imaging. In order to determine the specific utility of PET for these subsites it will require a large, prospective, controlled study, which has yet to be done. For now, our series and the few others published for this particular PET application will serve to indicate the usefulness of PET for diagnosis and surveillance of sinonasal and nasopharyngeal cancers.

## CONCLUSION

With respect to diagnosis, evaluation of treatment, and surveillance for recur-

rence, PET offers diagnostic advantages to the unique and challenging area of head and neck anatomy, the paranasal sinuses, nasopharynx, and skull base. With an increased acceptance of PET for management of HNSCC (including coverage by the US Government Medicare program), PET should be routinely considered for evaluation and surveillance of HNSCC especially of the sinuses, nasopharynx, and skull base not clearly examined by physical exam, endoscopy, and conventional imaging.

## REFERENCES


1. Kresnik E, Mikosch P, Gallowitsch HJ, et al. Evaluation of head and neck cancer with 18F-FDG PET: a comparison with conventional methods. *Eur J Nucl Med.* 2001;28:816-821.
2. Hollenbeak CS, Lowe VJ, Stack BC Jr. The cost-effectiveness of fluorodexyglucose 18-F positron emission tomography in the NO neck. *Cancer.* 2001;92:2341-2348.
3. Di Martino E, Nowak B, Hassan HA, et al. Diagnosis and staging of head and neck cancer: a comparison of modern imaging modalities (positron emission tomography, computed tomography, color-coded duplex sonography) with panendoscopic and histopathologic findings. *Arch Otolaryngol Head Neck Surg*. 2000;126:1457-1461.
4. Stokkel MP, Moons KG, ten Broek FW, van Rijk PP, Hordijk GJ. 18F-fluorodeoxyglucose dual-head positron emission tomography as a procedure for detecting simultaneous primary tumors in cases of head and neck cancer. *Cancer*. 1999;86:2370-2377.
5. Farber LA, Benard F, Machtay M, et al. Detection of recurrent head and neck squamous cell carcinomas after radiation therapy with 2-18F-fluoro-2-deoxy-D-glucose positron emission tomography. *Laryngoscope*. 1999;109:970-975.
6. Stokkel MP, ten Broek FW, van Rijk PP. Preoperative assessment of cervical lymph nodes in head and neck cancer with fluorine-18 fluorodeoxyglucose using a dual-head coincidence camera: a pilot study. *Eur J Nucl Med.* 1999;26:499-503.
7. Terhaard CH, Bongers V, van Rijk PP, Hordijk GJ. F-18-fluoro-deoxy-glucose positron-emission tomography scanning in detection of local recurrence after radiotherapy for laryngeal/ pharyngeal cancer. *Head Neck.* 2001;23:933-941.
8. Kao CH, ChangLai SP, Chieng PU, Yen RF, Yen TC. Detection of recurrent or persistent nasopharyngeal carcinomas after radiotherapy with 18-fluoro-2-deoxyglucose positron emission tomography and comparison with computed tomography. *J Clin Oncol*. 1998;16:3550-3555.
9. Tsai MH, Shiau YC, Kao CH, Shen YY, Lin CC, Lee CC. Detection of recurrent nasopharyngeal carcinomas with positron emission tomography using 18-fluoro-2-deoxyglucose in patients with indeterminate magnetic resonance imaging findings after radiotherapy. *J Cancer Res Clin Oncol.* 2002;128:279-282.
10. Greven KM, Keyes JWJr, Williams DW III, McGuirt WF, Joyce WT III. Occult primary tumors of the head and neck: lack of benefit from positron emission tomography imaging with 2-[F-18]fluoro-2-deoxy-D-glucose. *Cancer*. 1999;86:114-118.
11. Assar OS, Fischbein NJ, Caputo GR, et al. Metastatic head and neck cancer: role and usefulness of FDG PET in locating occult primary tumors. *Radiology.* 1999;210:177-181.
12. Jungehulsing M, Scheidhauer K, Damm M, et al. 2[F]-fluoro-2-deoxy-D-glucose positron emission tomography is a sensitive tool for the detection of occult primary cancer (carcinoma of unknown primary syndrome) with head and neck lymph node manifestation. *Otolaryngol Head Neck Surg*. 2000;123:294-301.
13. Safa AA, Tran LM, Rege S, et al. The role of positron emission tomography in occult primary head and neck cancers. *Cancer J Sci Am.* 1999;5:214-218.
14. Stokkel MP, Terhaard CH, Hordijk GJ, van Rijk PP. The detection of unknown primary tumors in patients with cervical metastases by dual-head positron emission tomography. *Oral Oncol*. 1999;35:390-394.
15. Greven KM, Williams DW, Keyes JW, et al. Positron emission tomography of patients with head and neck cancer after high dose irradiation. *Cancer.* 1994;74:1355-1359.
16. Mitsuhashi N, Huyakawa M, Hasegawa M, et al. Clinical PET in diagnosis and evaluation of radiation response of patients with nasopharyngeal tumors. *Anticancer Res*. 1998;18:2827-2832.
17. Greven KM, Williams DW III, McGuirt WF Sr, et al. Serial positron emission tomography scans following radiation therapy of patients with head and neck cancer. *Head Neck*. 2001;23:942-946.
18. Kao C-H, Shiau Y-C, Shen Y-Y, Yen R-F. Detection of recurrent or persistent nasopharyngeal carcinomas after radiotherapy with technetium-99m Methoxyisobutylisonitrile single photon emission computed tomography and computed tomography. *Cancer.* 2002;94;1981-1986.
19. Rege S, Safa AA, Chaiken L, Hoh C, Juillard G, Withers HR. Positron emission tomography: an independent indicator of radiocurability in head and neck carcinomas. *Am J Clin Oncol*. 2000;23:164-169.
20. Lowe VJ, Boyd JH, Dunphy FR, et al. Surveillance for recurrent head and neck cancer using positron emission tomography. *J Clin Oncol.* 2000;18:651-658.