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## Review Article

# Clinical Application of $^{18}$F-FDG PET and PET/CT in Patients with Head and Neck Cancers

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**Abstract.**

Fluorine-18 fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography (PET) and integrated PET/CT have been increasingly used in patients with head and neck cancers. $^{18}$F-FDG PET and PET/CT can provide valuable information during initial staging, especially in the nodal staging of the neck and in the detection of distant metastases or synchronous second primary malignancies. They are also helpful in identifying a primary tumor in patients with cervical lymph node metastases from an unknown primary tumor. PET and PET/CT are useful for the evaluation of treatment response in patients undergoing radiotherapy or chemoradiotherapy. PET and PET/CT are accurate in the detection of recurrent disease and can be used in patients at high risk or with clinically suspected recurrence. In addition, PET and PET/CT can provide independent prognostic information with regard to relapse-free survival and overall survival. The role of PET/CT in the radiotherapy planning has been under active investigation recently.

***Keywords*** **:** positron emission tomography, head and neck cancers

## 綜合評論

# 氟-18 氟化去氧葡萄糖正子斷層攝影及正子/電腦斷層攝影在頭頸部癌症病患之臨床應用

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**中文摘要**

氟-18 氟化去氧葡萄糖正子斷層攝影以及正子/電腦斷層攝影逐漸廣泛應用於頭頸部癌症病患。在疾病分期方面，正子斷層攝影以及正子/電腦斷層攝影可以提供有用的臨床資料，特別是關於頸部淋巴分期以及偵測遠端轉移和第二原發惡性腫瘤。對於原發腫瘤部位不明之頸部淋巴轉移病患，正子斷層攝影以及正子/電腦斷層攝影可以幫忙確定腫瘤部位。對於接受放射治療或合併化學與放射治療的病患，正子斷層攝影以及正子/電腦斷層攝影在治療效果評估方面很有幫助。同時，正子斷層攝影以及正子/電腦斷層攝影在偵測腫瘤復發方面準確性高，可以應用於高危險群及臨床懷疑復發的病患。另外，正子斷層攝影以及正子/電腦斷層攝影能夠提供關於存活率的相關預後資訊。至於正子/電腦斷層攝影在放射治療計劃應用方面，目前正在積極研究之中。

***關鍵字***: 正子斷層攝影、頭頸部癌症

# INTRODUCTION

Head and neck cancers are common and important tumors all over the world. Imaging studies, mainly computed tomography (CT) and magnetic resonance imaging (MRI), are helpful in the evaluation and management of patients with head and neck cancers. Fluorine-18 fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography (PET) can provide useful functional and metabolic information which is complementary to the anatomic imaging modalities. FDG-PET and integrated PET/CT have been increasingly used in patients with head and neck cancers in recent years [1-4]. In this article, we will briefly review the recent literature on the clinical application of $^{18}$F-FDG PET and PET/CT for head and neck cancers.

# INITIAL STAGING

## Tumor Staging (T staging)

The main purpose of imaging studies in tumor staging is to accurately delineate the extent of the primary tumor, particularly with regard to the involvement of adjacent structures, such as osseous, vascular, or peri-neural invasion. In this setting, CT or MRI is usually recommended as the initial imaging modality for head and neck cancers [5]. Previous studies have shown that PET has high sensitivity, at least as sensitive as CT or MRI, in detecting the primary tumors [6,7]. However, PET alone usually does not provide further anatomic information because of inadequate imaging resolution. Therefore, there is only a limited role for PET in the tumor staging of head and neck cancers. In contrast, $^{18}$F-FDG PET or PET/CT can be used in identifying the primary tumor sites in those patients who present with cervical lymph node metastases from unknown primary tumors (will be discussed in a later section).

## Nodal Staging (N staging)

Accurate nodal staging of cervical lymph nodes is critical not only for determination of the optimal treatment but is also an important prognostic factor for survival in patients with head and neck cancers. Numerous studies have assessed the accuracy of $^{18}$F-FDG PET in the detection of cervical node metastases during initial staging [5-8]. In a recent review, Schoder and Yeung reported an average sensitivity of 87%-90% and a specificity of 80%-93% from several earlier studies. Moreover, recent studies which compared the accuracy of anatomic imaging modalities and FDG-PET have shown that $^{18}$F-FDG PET is comparable or superior to conventional imaging in detecting regional lymph node metastases (sensitivity 70%-100% and specificity 82%-94% for PET versus sensitivity 58%-88% and specificity 41-100% for CT/MR/US) [1]. More recent studies using integrated $^{18}$F-FDG PET/CT showed that combined PET/CT images were more accurate than PET or CT alone. Jeong et al. demonstrated the combined PET/CT images provided additional information over PET for the anatomical localization and lesion characterization of 18 sites (19.8%) in 17 patients (36.2%) [9].

Patients with head and neck cancer and clinically negative neck (N0 stage) remain a medical dilemma. About 25% to 30% of these patients are found to have neck node metastases. Therefore, the majority of patients are unlikely to have a therapeutic benefit from neck dissection. Several studies have evaluated the usefulness of $^{18}$F-FDG PET and PET/CT in this clinical setting [10,11]. Schoder el al., in a prospective study of 31 patients, reported the sensitivity and

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specificity of $^{18}$F-FDG PET/CT were 67% and 85% on the basis of neck sides and 67% and 95% on the basis of number of nodal levels, respectively. The authors concluded that the clinical application of PET/CT in N0 neck may be limited by the combination of limited sensitivity for small metastatic deposits and a relatively high number of false-positive findings [10]. Sentinel lymph node biopsy with elective neck dissection, if positive of sentinel lymph node, provided a highly accurate staging of N0 necks [11].

### Distant Metastases (M staging) and Second Primary Malignancies

The frequency of distant metastases increases with higher T stage and N stage of patients. In addition, patients with head and neck cancers have increased risk of second primary malignancies. $^{18}$F-FDG PET and PET/CT, with the advantage of whole-body coverage, will play an important role in this setting. Many studies have demonstrated that PET may detect occult distant metastatic disease in patients with locoregionally advanced disease [12-15]. Schwartz et al. demonstrated 7 (21%) out of 33 patients had evidence of distant disease by extended-field FDG PET, including 4 with metastases and 3 with synchronous primary cancers of the aero-digestive tract [12]. Teknos et al. also showed that FDG PET detected mediastinal disease, that was not identified with conventional imaging techniques, in 2/12 patients (17%) with advanced-stage head and neck cancer [13]. Wax et al. reported the sensitivity, accuracy, and positive predictive value of PET were, respectively, 100%, 80%, and 80% in the detection of synchronous lung lesions in a retrospective review of 59 previously untreated patients [14]. Schmid et al. demonstrated $^{18}$F-FDG PET led to a change of treatment in approximately 8% of patients [16]. A similar result was also reported by Sigg et al [17].

## CERVICAL LYMPH NODE METASTASIS FROM UNKNOWN PRIMARY TUMORS

Occasionally, patients will present with cervical lymph node metastases without clear evidence of a primary tumor site. It is a great challenge from both the diagnosis and treatment viewpoints. Identification of the primary tumor site is critical because it may lead to surgical resection or more precise radiotherapy and therefore better treatment results and few side effects.

$^{18}$F-FDG PET has been used for evaluation of patients with cervical lymph node metastasis from unknown primary tumors for many years [18-22]. Schoder and Yeung, after reviewed 11 studies comprising 253 patients, reported a tumor detection rate of 30% (range: 5 - 60%). As the authors indicated, this wide range of results was largely related to varying inclusion criteria and methods of verification [1]. Another review made by Rusthoven et al., involving 16 studies with a total of 302 patients, showed FDG-PET detected primary tumors that went undetected by other modalities in approximately 25% of cases and was sensitive in the detection of previously unrecognized regional or distant metastases in 27% of cases [22]. Menda and Graham also reviewed 7 studies in which PET was performed after a negative endoscopy and negative CT and/or MRI and demonstrated 27% detection rate in 150 patients [4]. Recent studies using FDG PET/CT also demonstrated it was a useful diagnostic tool in the detection of a potential primary tumor [23,24]. Gutzeit et al., in a retrospective study, demonstrated that PET/CT depicted the primary tumor in 15 (33%) of 45 patients while PET and CT side-by-side evaluation, PET alone, and CT alone depicted 13 (29%), 11 (24%), and 8 (18%), respectively [24].

## EVALUATION OF TREATMENT RESPONSE

Patients with locally advanced disease (stages III-IV) may undergo combined chemotherapy and ra-

diotherapy with curative intent. In addition, combined chemotherapy and radiotherapy are also used in some patients with organ preservation treatment protocols. In these clinical situations, early assessment of treatment response is critically important because prompt salvage surgery can be performed to improve local control of the disease if residual or recurrent disease exists [1].

Numerous studies have assessed the value of $^{18}$F-FDG PET and PET/CT in the monitoring of treatment response [25-32]. With regard to early follow-up evaluation, some investigators demonstrated good sensitivity and specificity but others did not. For instance, Nam et al. found that FDG PET performed 1 month after completion of definitive radiotherapy had 100% sensitivity and 87% specificity in evaluating residual tumors [25]. Similarly, Goerres et al. reported the sensitivity and specificity for follow-up PET scan performed approximately 6 weeks after the end of combined radiation and chemotherapy were 90.9% and 93.3%, respectively [26]. In contrast, Ryan et al. reported that PET scans of the head and neck region performed more than 1 month after the completion of radiation had a significantly higher sensitivity (95% versus 55%) and negative predictive value (99% versus 90%) when compared with scans performed within 1 month [27]. Similar results were also obtained by Greven et al., who concluded that one-month post-radiotherapy scans were inaccurate for predicting the presence of cancer and four-month post-radiotherapy scans were a better predictor [28]. Therefore, most investigators considered FDG PET and PET/CT were more accurate when performed at 2-3 months after the completion of radiation therapy than at earlier time points [2,3].

In a recent study of 108 patients, Ryan et al. demonstrated that PET/CT detected locoregional persistent or recurrent tumors with a sensitivity of 82%, specificity of 92%, positive predictive value (PPV) of 64%, negative predictive value (NPV) of 97%, and overall accuracy of 90% [27]. Similar results were also obtained by Yao et al. in the post-treatment assessment of patients treated with intensity-modulated radiation therapy (IMRT). The authors concluded that FDG PET was highly accurate in the detection of persistent and recurrent disease after treatment and allowed salvage treatment to be initiated in a timely manner [32]. In addition, Ryan et al. reported PET scan had a sensitivity of 89%, specificity of 97%, PPV of 85%, NPV of 98%, and overall accuracy of 96% for the detection of distant metastases [27].

The utility of FDG PET and PET/CT for the detection of disease in the residual neck nodes after radiotherapy or chemoradiotherapy was studied by several investigators [33-37]. Most studies demonstrated a very high negative predictive value. For instance, Porceddu et al. reported that the NPV of PET for viable disease in a residual anatomic abnormality was 97% [34]. Similarly, Yao et al. used SUVmax of less than 3.0 as the criterion for a negative FDG PET study and demonstrated NPV was 100% and PPV was 80% [35]. These authors suggested neck dissection might not be necessary for regional control if the post-radiotherapy FDG PET scan was negative [34-36]. However, Rogers et al. cautioned that a positive PET 1 month after definitive radiation therapy accurately indicated the presence of residual disease in all cases but a negative PET indicated absence of disease in only 14% [37].

## DETECTION OF RECURRENCE

The early detection of recurrent cancer is very important because prompt salvage surgery can improve the clinical outcome of these patients. Lowe et al. performed serial post-therapy FDG-PET, in addition to physical examination and correlative imaging, in 30 patients with complete response after therapy during the first year (at 2 and 10 months after therapy) and thereafter as clinically needed. Only PET detected all 16 recurrences in the first year, and 5 of these 16 patients had recurrence detected by PET only [38]. In symptomatic patients suspected of having cancer re-

currence, Lonneux et al. demonstrated the diagnostic accuracy was higher for PET than for combined CT + MRI (sensitivity 96% to 73%, specificity 61% to 50%, and accuracy 81% to 64%, respectively). In addition, the accuracy of FDG-PET was the highest (94%) in patients included more than 12 weeks after the end of therapy [39]. Similar results were also reported by other investigators [40-44].

According to previous studies, the sensitivity of FDG PET for the detection of recurrent head and neck cancer was usually high, but specificity in the treated postsurgical area was lower than elsewhere in the neck or at remote sites. The negative predictive value was consistently high among most studies. Therefore, it was suggested that patients with suspected recurrence but negative PET scan did not require further evaluation, however, a positive PET scan required biopsy for further confirmation [1].

## PREDICTION OF OUTCOME

Previous studies suggested that the intensity of FDG uptake in the tumor appeared to predict the clinical outcome after therapy. Allal et al. studied 120 patients prospectively with measurement of standardized uptake value (SUV) of tumor FDG uptake and found the median SUV was higher in patients who failed treatment than in the controlled patients. The authors suggested that pretreatment tumor FDG uptake represented an independent prognostic factor in patients with head-and-neck cancer, whatever the primary treatment modality [45]. Moreover, the same authors demonstrated that FDG uptake, as measured by the SUV, had potential value in predicting local control and disease-free survival in head and neck carcinomas treated by radiotherapy in another study [46]. Wong et al. also demonstrated that PET interpretation, SUV, and physical examination were independent predictors of relapse-free and over-all survival [43]. Similar results were also reported by other investigators [44-47].

## RADIOTHERAPY PLANNING

The role of $^{18}$F-FDG PET and PET/CT in the radiotherapy planning is an attractive topic under active investigation in recent years [48,49]. PET/CT can be used in cases with normal-sized but increased metabolic activity lymph node metastases and in cases when the borders of primary tumors are difficult to distinguish by anatomic imaging alone [2]. Several studies showed the hybrid PET/CT simulation was feasible and provided valuable information that resulted in greater delineation of normal tissues from tumor bearing areas at high risk for recurrence [50-52]. Moreover, Vernon et al. reported that a high level of disease control combined with favorable toxicity profiles was achieved in a cohort of head and neck cancer patients receiving PET/CT fusion guided radiotherapy with or without chemotherapy [53]. However, many questions remain that need to be addressed in this clinical application.

## CONCLUSIONS

$^{18}$F-FDG PET and PET/CT can provide valuable information during initial staging, especially in the nodal staging of the neck and in the detection of distant metastases or synchronous second primary malignancies. They are also helpful in identifying a primary tumor in patients with cervical lymph node metastases from an unknown primary tumor. PET and PET/CT are useful for the evaluation of treatment response in patients undergoing radiotherapy or chemoradiotherapy. PET and PET/CT are accurate in the detection of recurrent disease and can be used in patients at high risk or with clinically suspected recurrence. In addition, PET and PET/CT can provide independent prognostic information with regard to relapse-free survival and overall survival. The role of PET/CT in the radiotherapy planning has been under active investigation recently. In summary, $^{18}$F-FDG PET and PET/CT may play an important role in the management of patients with head and neck cancers and lead to change in staging, change in radiotherapy planning

and/or dose, and altered treatment response assessment in a significant percentage of patients [54,55].

## REFERENCES


1. Schoder H, Yeung HWD. Positron emission imaging of head and neck cancer, including thyroid carcinoma. **Semin Nucl Med 34:** 180-197, 2004.
2. Quon A, Fischbein NJ, McDougall IR, et al. Clinical role of $^{18}$F-FDG PET/CT in the management of squamous cell carcinoma of the head and neck and thyroid carcinoma. **J Nucl Med 48:** 58S-67S, 2007.
3. Zimmer LA, Branstetter BF, Nayak JV, et al. Current use of $^{18}$F-fluorodeoxyglucose positron emission tomography and combined positron emission tomography and computed tomography in squamous cell carcinoma of the head and neck. **Laryngoscope 115:** 2029-2034, 2005.
4. Menda Y, Graham MM. Update on $^{18}$F-fluorodeoxyglucose positron emission tomography and positron emission tomography/computed tomography imaging of squamous head and neck cancers. **Semin Nucl Med 35:** 214-219, 2005.
5. Dammann F, Horger M, Mueller-Berg M, et al. Rational diagnosis of squamous cell carcinoma of the head and neck region: comparative evaluation of CT, MRI, and $^{18}$F-FDG PET. **AJR 184:** 1326-1331, 2005.
6. Hannah A, Scott AM, Tochon-Danguy H, et al. Evaluation of $^{18}$F-fluorodeoxyglucose positron emission tomography and computed tomography with histopathologic correlation in the initial staging of head and neck cancer. **Ann Surg 236:** 208-217, 2002.
7. 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 126:** 1457-1461, 2000.
8. Schwartz DL, Ford E, Rajendran J, et al. FDG PET-CT imaging for preradiotherapy staging of head-and-neck squamous cell carcinoma. **Int J Radiat Oncol Biol Phys 61:** 129-136, 2005.
9. Jeong HS, Baek CH, Son YI, et al. Use of integrated $^{18}$F-FDG PET/CT to improve the accuracy of initial cervical nodal evaluation in patients with head and neck squamous cell carcinoma. **Head Neck 29:** 203-210, 2007.
10. Schoder H, Carlson DL, Kraus DH, et al. $^{18}$F-FDG PET/CT for detecting nodal metastases in patients with oral cancer staged N0 by clinical examination and CT/MRI. **J Nucl Med 47:** 755-762, 2006.
11. Stoeckli SJ, Steinert H, Pfaltz M, et al. Is there a role for positron emission tomography with $^{18}$F-fluorodeoxyglucose in the initial staging of nodal negative oral and oropharyngeal squamous cell carcinoma? **Head Neck 24:** 345-349, 2002.
12. Schwartz DL, Rajendran J, Yueh B, et al. Staging of head and neck squamous cell cancer with extended-field FDG-PET. **Arch Otolaryngol Head Neck Surg 129:** 1173-1178, 2003.
13. Teknos TN, Rosenthal EL, Lee D, et al. Positron emission tomography in the evaluation of stage III and IV head and neck cancer. **Head Neck 23:** 1056-1060, 2001.
14. Wax MK, Myers LL, Gabalski EC, et al. Positron emission tomography in the evaluation of synchronous lung lesions in patients with untreated head and neck cancer. **Arch Otolaryngol Head Neck Surg 128:** 703-707, 2002.
15. Nishiyama Y, YamamotoY, Yokoe K, et al. FDG PET as a procedure for detecting simultaneous tumours in head and neck cancer patients. **Nucl Med Commun 26:** 239-244, 2005.
16. Schmid DT, Stoeckli SJ, Bandhauer F, et al. Impact of positron emission tomography on the initial staging and therapy in locoregional advanced squamous cell carcinoma of the head and neck. **Laryngoscope 113:** 888-891, 2003.

17. Sigg MB, Steinert H, Gratz K, et al. Staging of head and neck tumors: [18F]fluorodeoxyglucose positron emission tomography compared with physical examination and conventional imaging modalities. **J Oral Maxillofac Surg 61:** 1022-1029, 2003.
18. Nieder C, Gregoire V, Ang KK. Cervical lymph node metastases from occult squamous cell carcinoma: Cut down a tree to get an apple? **Int J Radiat Oncol Biol Phys 50:** 727-733, 2001.
19. Regelink G, Brouwer J, de Bree R, et al. Detection of unknown primary tumours and distant metastases in patients with cervical metastases: value of FDG-PET versus conventional modalities. **Eur J Nucl Med Mol Imaging 29:** 1024-1030, 2002.
20. Fogarty GB, Peters LJ, Stewart J, et al. The usefulness of fluorine 18-labelled deoxyglucose positron emission tomography in the investigation of patients with cervical lymphadenopathy from an unknown primary tumor. **Head Neck 25:** 138-145, 2003.
21. Miller FR, Hussey D, Beeram M, et al. Positron emission Tomography in the management of unknown primary head and neck carcinoma. **Arch Otolaryngol Head Neck Surg 131:** 626-629, 2005.
22. Rusthoven KE, Koshy M, Paulino AC. The role of fluorodeoxyglucose positron emission tomography in cervical lymph node metastases from an unknown primary tumor. **Cancer 101:** 2641-2649, 2004.
23. Wartski M, Stanc EL, Gontier E, et al. In search of an unknown primary tumour presenting with cervical metastases: performance of hybrid FDG-PET-CT. **Nucl Med Commun 28:** 365-371, 2007.
24. Gutzeit A, Antoch G, Kuhl H, et al. Unknown primary tumors: detection with dual-modality PET/CT – initial experience. **Radiology 234:** 227-234, 2005.
25. Nam SY, Lee SW, Im KC, et al. Early evaluation of the response to radiotherapy of patients with squamous cell carcinoma of the head and neck using $^{18}$FDG-PET. **Oral Oncol 41:** 390-395, 2005.
26. Goerres GW, Schmid DT, Bandhauer F, et al. Positron emission tomography in the early follow-up of advanced head and neck cancer. **Arch Otolaryngol Head Neck Surg 130:** 105-109, 2004.
27. Ryan WR, Fee WE Jr, Le QT, et al. Positron-emission tomography for surveillance of head and neck cancer. **Laryngoscope 115:** 645-650, 2005.
28. 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 23:** 942-946, 2001.
29. Chan SC, Yen TC, Ng SH, et al. Differential roles of $^{18}$F-FDG-PET in patients with locoregional advanced nasopharyngeal carcinoma after primary curative therapy: response evaluation and impact on management. **J Nucl Med 47:** 1447-1454, 2006.
30. McCollum AD, Burrell SC, Haddad RI, et al. Positron emission tomography with $^{18}$F-fluorodeoxyglucose to predict pathologic response after induction chemotherapy and definitive chemoradiotherapy in head and neck cancer. **Head Neck 26:** 890-896, 2004.
31. Kitagawa Y, Nishizawa S, Sano K, et al. Prospective comparison of $^{18}$F-FDG-PET with conventional imaging modalities (MRI, CT, and $^{67}$Ga scintigraphy) in assessment of combined intraarterial chemotherapy and radiotherapy for head and neck carcinoma. **J Nucl Med 44:** 198-206, 2003.
32. Yao M, Graham MM, Smith RB, et al. Value of FDG PET in assessment of treatment response and surveillance in head-and-neck cancer patients after intensity modulated radiation treatment: a preliminary report. **Int J Radiat Oncol Biol Phys 60:** 1410-1418, 2004.
33. Ware RE, Matthews JP, Hicks RJ, et al. Usefulness of fluorine-18 fluorodeoxyglucose positron

emission tomography in patients with a residual structural abnormality after definitive treatment for squamous cell carcinoma of the head and neck. **Head Neck 26:** 1008-1017, 2004.

34. Porceddu SV, Jarmolowski E, Hicks RJ, et al. Utility of positron emission tomography for the detection of disease in residual neck nodes after (chemo)-radiotherapy in head and neck cancer. **Head Neck 27:** 175-181, 2005.
35. Yao M, Graham MM, Hoffman HT, et al. The role of post-radiation therapy FDG PET in prediction of necessity for post-radiation therapy neck dissection in locally advanced head-and-neck squamous cell carcinoma. **Int J Radiat Oncol Biol Phys 59:** 1001-1010, 2004.
36. Ong SC, Schoder H, Lee NY, et al. Clinical utility of $^{18}$F-FDG PET/CT in assessing the neck after concurrent chemoradiotherapy for locoregional advanced head and neck cancer. **J Nucl Med 49:** 532-540, 2008.
37. Rogers JW, Greven KM, MCGuirt WF, et al. Can post-RT neck dissection be omitted for patients with head-and neck cancer who have a negative PET scan after definitive radiation therapy? **Int J Radiat Oncol Biol Phys 58:** 694-697, 2004.
38. Lowe VJ, Boyd JH, Dunphy FR, et al. Surveillance for recurrent head and neck cancer using positron emission tomography. **J Clin Onco l18:** 651-658, 2000.
39. Lonneux M, Lawson G, Ide C, et al. Positron emission tomography with fluorodeoxyglucose for suspected head and neck tumor recurrence in the symptomatic patient. **Laryngoscope 110:** 1493-1497, 2000.
40. Terhaard CH, Bongers V, van Rijk PP, et al. F-18-fluoro-deoxy-glucose positron-emission tomography scanning in detection of local recurrence after radiotherapy for laryngeal/pharyngeal cancer. **Head Neck 23:** 933-941, 2001.
41. Yen RF, Hung RL, Pan MH, et al. 18-fluoro-2-deoxyglucose positron emission tomography in detecting residual/recurrent nasopharyngeal carcinomas and comparison with magnetic resonance imaging. **Cancer 98:** 283-287, 2003.
42. Yen RF, Hong RL, Tzen KY, et al. Whole-body $^{18}$F-FDG PET in recurrent or metastatic nasopharyngeal carcinoma. **J Nucl Med 46:** 770-774, 2005.
43. Wong RJ, Lin DT, Schoder H, et al. Diagnostic and prognostic value of [$^{18}$F]fluorodeoxyglucose positron emission tomography for recurrent head and neck squamous cell carcinoma. **J Clin Oncol 20:** 4199-4208, 2002.
44. Kunkel M, Forster GJ, Reichert TE, et al. Detection of recurrent oral squamous cell carcinoma by [$^{18}$F]-2-fluorodeoxyglucose positron emission tomography: implications for prognosis and patient management. **Cancer 98:** 2257-2265, 2003.
45. Allal AS, Slosman DO, Kebdani T, et al. Prediction of outcome in head-and-neck cancer patients using the standardized uptake value of 2-[$^{18}$F]-fluoro-2-deoxy-D-glucose. **Int J Radiat Oncol Biol Phys 59:** 1295-1300, 2004.
46. Allal AS, Dulguerov P, Allaoua M, et al. Standardized uptake value of 2-[$^{18}$F]fluoro-2-deoxy-D-glucose in predicting outcome in head and neck carcinomas treated by radiotherapy with or without chemotherapy. **J Clin Oncol 20:** 1398-1404, 2002.
47. Brun E, Kjellen E, Tennvall J, et al. FDG-PET studies during treatment: prediction of therapy outcome in head and neck squamous cell carcinoma. **Head Neck 24:** 127-135, 2002.
48. Bujenovic S. The role of positron emission tomography in radiation treatment planning. **Semin Nucl Med 34:** 293-299, 2004.
49. Paulino AC, Thorstad WL, Fox T. Role of fusion in radiotherapy treatment planning. **Semin Nucl Med 33:** 238-243, 2003.
50. Heron DE, Andrade RS, Flickinger J, et al. Hybrid PET-CT simulation for radiation treatment planning in head-and-neck cancers: a brief technical

report. **Int J Radiat Oncol Biol Phys 60:** 1419-1424, 2004.

51. Schwartz DL, Ford EC, Rajendran J, et al. FDG-PET/CT-guided intensity modulated head and neck radiotherapy: a pilot investigation. **Head Neck 27:** 478-487, 2005.
52. Koshy M, Paulino AC, Howell R. F-18 FDG PET-CT fusion in radiotherapy treatment planning for head and neck cancer. **Head Neck 27:** 494-502, 2005.
53. Vernon MR, Maheshwari M, Schultz CJ, et al. Clinical outcomes of patients receiving integrated PET/CT-guided radiotherapy for head and neck carcinoma. **Int J Radiat Oncol Biol Phys 70:** 678-68, 2008.
54. Connell CA, Corry J, MilnerAD, et al. Clinical impact of, and prognostic stratification by, F-18 FDG PET/CT in head and neck mucosal squamous cell carcinoma. **Head Neck 29:** 986-995, 2007.
55. Ha PK, Hdeib A, Goldenberg D, et al. The role of positron emission tomography and computed tomography fusion in the management of early-stage and advanced-stage primary head and neck squamous cell carcinoma. **Arch Otolaryngol Head Neck Surg 132:** 12-16, 2006.