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PET/CT in Surgical Planning for Head and Neck Cancer

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Fluorine-18 (^{18}F)-fluorodeoxyglucose (FDG) positron emission tomography fused with computed tomography (PET/CT) is a valuable tool in surgical planning for head and neck squamous cell carcinoma (HNSCC). If performed prior to biopsy or other surgical intervention, FDG-PET/CT has high sensitivity for the detection of the primary site in patients with cervical lymph node metastases from unknown primary origin and can be used to direct the surgical workup. FDG-PET/CT is superior to CT alone for detection of nodal metastases outside the expected pattern or distant metastases or second primary cancers and can greatly affect determination of appropriate management including surgical eligibility. Prior to the advent of PET/CT, many patients undergoing (chemo)radiation-based therapy had planned post-treatment neck dissection; FDG-PET/CT now has a proven role in the evaluation of recurrent or persistent disease amenable to salvage surgery and enables safe avoidance of planned postradiation neck dissection with a high negative predictive value. Specifically for this important application, two standardized reporting metrics may be used in the head and neck anatomic region: the "Hopkins criteria" and the "Neck Imaging Reporting and Data System"; both systems produce a formalized evaluation and recommendation based on PET/CT findings. The role of PET/CT as a replacement for elective neck dissection or examination under anesthesia remains controversial but deserves further study. FDG-PET/CT has a wide-ranging impact on the surgical management of patients with HNSCC and should be used routinely in patients with unknown primary nodal disease and those presenting with advanced-stage cancers at initial staging and to assess treatment response.
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Introduction

Treatment of head and neck squamous cell carcinoma (HNSCC) is multidisciplinary, and the choice of therapy is directed by anatomic site and extent of disease. Imaging plays a critical role in accurate evaluation and staging of head and neck cancer patients in order to determine the appropriate treatment strategy, and in particular, the role and extent of surgery. Conventional imaging modalities such as contrast-enhanced magnetic resonance imaging (MRI) and computed tomography imaging (CT) are critical in delineating the extent of local disease; however, these studies can be suboptimal in detecting regional and distant metastases that affect management and prognosis. Another imaging modality, fluorine-18 (^{18}F)-fluorodeoxyglucose (FDG) positron emission tomography fused with computed tomography (PET/CT) provides not only anatomic but complementary physiological information about a patient's disease status and has greater sensitivity for small-volume (nodal) disease. FDG-PET/CT is the only form of PET/CT in routine clinical use and the term PET/CT is typically thought to refer to the most commonly used FDG radiotracer.

PET/CT thus provides essential information for the surgeon to make decisions about the needed extent or necessity of surgery. This review addresses numerous particular

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situations in which PET/CT can be helpful with surgical planning for head and neck cancer patients. These include detection of the primary site in patients with cervical lymph node metastases of unknown origin, determining management of nodal disease in the neck, detection of distant metastases or second primary cancers, assessing response after completion of therapy, evaluation for recurrent or persistent disease amenable to salvage surgery, and restaging at the time of recurrence or metastasis in follow-up.

FDG-PET/CT in the Head and Neck

FDG-PET/CT is routinely used in the initial evaluation and follow up for patients with HNSCC.[1] F18-fluorodeoxyglucose is a radiolabeled glucose analogue that serves as surrogate marker for increased glucose metabolism. Cancer cells with increased glucose metabolism preferentially accumulate ^{18}F-FDG, and therefore PET allows for the visualization of metabolically active cancer tissue.[2-5] While other agents have been previously described to detect HNSCC, including ^{68}Ga-FAPI[6], ^{68}Ga-PSMA-11[7], and ^{18}F-fluciclovine[8], ^{18}F-FDG remains the standard of care due to its high sensitivity and specificity for detection of occult, recurrent, and metastatic disease.[3]

FDG-PET can be used for initial staging, localizing unknown primary tumors, identifying regional and distant metastases, and detecting recurrence. However, FDG-PET alone lacks the precise anatomic detail needed for treatment planning and needs correlation with high quality contrast-enhanced cross-sectional imaging.[1,2] The addition of a contrast-enhanced diagnostic-quality CT, at least through the area of the body in question (e.g., the neck), is critical to assess morphologic imaging features including nodal size, presence of nodal necrosis or cystic change (which is often not FDG-avid), and imaging features of extracapsular extension.[1,4] When acquired as a combined fused study incorporating PET and CT, FDG-PET/CT allows for simultaneous image acquisition and correlation of CT with functional metabolic data to aid in treatment planning.

The head and neck is a challenging region for interpretation of PET/CT due to dense cross-sectional anatomy, dynamic patterns of biomechanical activity, and complex appearance of post-treatment changes. In recognition of these difficulties, standardized reporting metrics have been developed for reporting PET/CT (Table 1). The first system is called the "Hopkins criteria."[9] In this response assessment method, areas are graded according to a 5-point scale, where 1 is no uptake, defined as less than that of the internal jugular vein (IJV); 2 is focal uptake, greater than that of IJV but less than that of liver; 3 is diffuse uptake greater than that of the IJV or liver; 4 is focal uptake greater than that of the liver; and 5 is focal and intense uptake. Both of these latter ratings of 4 and 5 are considered likely to represent residual or recurrent disease. Importantly, in an external validation study, a high degree of interobserver reliability was found, with sensitivity and specificity of 67% and 87% for residual disease detection and a negative predictive value of 97% in determining the overall response to therapy assessment.[10]

An additional standardized response assessment tool, termed "Neck Imaging Reporting and Data System," named NI-RADS by analogy to the widely used BI-RADS system in breast cancer), has been developed.[11] In contrast to the Hopkins criteria, NI-RADS uses a four category system − 1 meaning no evidence of recurrence, 2 meaning low suspicion of recurrence, 3 meaning high suspicion of recurrence, and 4 meaning definite recurrence. NI-RADS 0 signifies that the radiologist's assessment is incomplete at present, usually due to unavailability of prior imaging for comparison. In keeping with the BI-RADS system, a standardized "lexicon" is proposed, and different categories have specific management

Table 1 Standardized Reporting Systems for FDG-PET/CT to Improve Communication Between Radiologists, Clinicians, and Patients

Hopkins Criteria[9]	Neck Imaging Reporting and Data System (NI-RADS)[11]
• Utilizes ^{18}F-FDG-PET/CT • 5-point scoring system • Hopkins score 1 represents a complete metabolic response with resolution of ^{18}F-FDG uptake at the primary site and nodes at a level less than that of the internal jugular vein • Hopkins score 5 shows focal and intense ^{18}F-FDG uptake at the primary site or nodes, highly predictive of residual tumor • The sensitivity, specificity, positive predictive value, and negative predictive value of the overall therapy assessment were 66.7%, 87.3%, 33%, 96.5% respectively[10]	• Utilizes cross-sectional imaging (CT or MRI) with or without ^{18}F-FDG-PET/CT • 4-tier classification (NI-RADS 0 through NI-RADS 4) • NI-RADS 0 refers to a new baseline study for which prior comparison imaging is unavailable at the time of interpretation • NI-RADS 1 indicates no evidence of recurrence • NI-RADS 4 refers to known recurrence that is either proven pathologically or considered definite by imaging or clinical criteria • NI-RADs categories 1, 2 and 3 show positive rates of disease of 4%, 17% and 59.4%, respectively[82]

Both the Hopkins criteria and the Neck Imaging Reporting and Data System (NI-RADS) were developed as qualitative systems of interpretation of imaging for evidence of tumor recurrence.

Table 2 Summary Status of PET/CT in Surgical Planning for Head and Neck Cancer

Take-Home Points
• Two standardized reporting systems have been developed for reporting 18-FDG-PET/CT in the head and neck anatomic region: the "Hopkins criteria"[9] and the "Neck Imaging Reporting and Data System" (NI-RADS)[11]
• PET/CT for detection of the primary site in patients with cervical lymph node metastases of unknown primary origin has a sensitivity of 88.3 to 97% and specificity of 68-74.9%
○ PET/CT should be done prior to examination under anesthesia and/or biopsy in the operating room in order to cleanly identify sites that deserve close inspection
• PET/CT has a high negative predictive value in patients with clinically N0 neck disease among patients with T2-T4 HNSCC
○ Further trials are needed to determine if PET/CT can replace the need for elective dissection in a clinically N0 neck
• PET/CT has been shown to be more accurate than CT alone in detecting unexpected metastases
○ For patients with locally advanced disease, surgical treatment of the primary site can be extensive and require extensive reconstruction; in this patient population, detecting distant metastases is a means of preventing unnecessarily aggressive surgical treatment
• Prior to the widespread utilization of PET for post-treatment surveillance, patients often routinely underwent salvage neck dissection after definitive chemoradiation treatment regardless of status of persistent disease
○ Now, PET/CT is used to assess for the need for salvage surgery after completion of radiation, and salvage surgery is avoided if PET/CT is negative

recommendations – 1 being standard follow-up, 2 being short-term imaging follow up, 3 being biopsy, and 4 being management of a proven recurrence. While neither the Hopkins nor the NI-RADS system has been universally adopted as of the time of writing, they both represent important conceptual frameworks for interpreting and reporting ^{18}F-FDG-FDG PET/CT studies in HNSCC.

Workup of Cervical Nodal Metastases from Unknown Primary Site

Approximately 5%-10% of patients with carcinoma of the head and neck present with a cervical lymph node metastasis without identification of primary site on diagnostic examination.[12-14] The majority of unknown primary cervical lymph node carcinomas are squamous cell carcinomas, many of which are human papilloma virus (HPV)-related; however, skin, thyroid, and salivary gland cancers can also present with cervical lymphadenopathy and an undetectable primary site.[12] As such, localization of the primary site is critical for determining the overall treatment plan and directing surgical therapy.

A patient presenting with a cervical lymph node carcinoma of unknown primary site should first be assessed with a complete history and physical exam by a head and neck surgeon. If unrevealing, the patient should then undergo imaging prior to evaluation under anesthesia in the operating room. Pan-endoscopy, including direct laryngoscopy, esophagoscopy, and bronchoscopy used to be the gold standard in identifying potential primary sites. However, PET/CT has now become a standard imaging study done prior to biopsy; the PET/CT findings can facilitate identification of sites that deserve close inspection. A biopsy done prior to PET/CT risks creating false-positive inflammation at the manipulated sites and ideally should be avoided. Whether PET/CT can replace an examination and biopsy in the operating room and preclude the need for general anesthesia remains controversial although this less invasive option can be considered for patients with medical contraindications or risks.

In most cases, given that the reported specificities of PET/CT for unknown primary are sub-optimal, most unknown primary patients should undergo a traditional step-wise approach to diagnosis.[15] An attempt should be made to confirm suspicious PET/CT findings with biopsy, and if there is a negative PET/CT but continued suspicion for a mucosally-based primary site, pan-endoscopy should be performed. When pan-endoscopy is negative, the addition of palatine tonsillectomy and transoral robotic surgery lingual tonsillectomy can aid in the identification of the primary site.[15-18] Primary tumor detection from ipsilateral palatine tonsillectomy ranges between 18% and 45%,[15,19] with rates of tumor detection in contralateral palatine tonsillectomy ranging between 10% and 23%.[16,17] Lingual tonsillectomy by transoral robotic surgery or transoral laser microsurgery increases detection, with primary site identification rates of 63%-90%.[18,20-23]

Numerous studies have assessed the performance of PET and PET/CT in the detection of unknown primary cancer of the head and neck. PET/CT detection rates of a primary site range from 5% to 73%.[3] In a 2004 meta-analysis of 16 studies with 302 patients, Rusthoven et al. showed an added detection rate of 25% for primary tumors with the use of PET/CT over a conventional work-up (physical exam and pan-endoscopy). In this same study, the overall sensitivity and specificity of FDG-PET for detecting an unknown primary site were 88.3% and 74.9%, respectively. There was a higher rate of false-positive results in the palatine tonsils and reduced sensitivity for base of tongue tumors.[24] In a 2013 meta-analysis including a total of seven selected studies including 246 patients, Zhu et al. found FDG-PET/CT to have a sensitivity of 97% and a specificity of 68% for the detection of primary sites.[25] Figure 1 shows an example of utilization of PET/CT for detection of an unknown primary tumor.

Detection of the primary site has important prognostic and treatment implications. For oral cavity, skin, thyroid, and

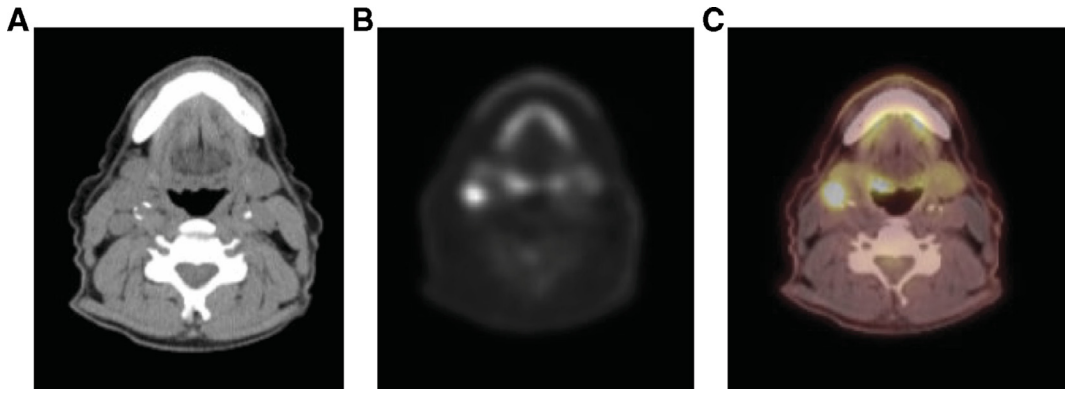

Figure 1 Detection of unknown primary tumor with ^{18}F-FDG-PET/CT. A 63-year-old man presented with a right neck mass that was biopsied and returned as squamous cell carcinoma. Physical exam, including flexible laryngoscopy, was unrevealing for a possible primary source. He underwent a FDG-PET/CT which showed asymmetric radiotracer uptake in the right base of tongue and right level II lymphadenopathy. A right lingual tonsillectomy was performed and pathology confirmed p16+ squamous cell carcinoma. (A) Axial CT image (non-contrast CT scan was obtained prior to presentation at our institution). (B) Transaxial PET image. (C) Fused ^{18}F-FDG-PET/CT axial image shows focal ^{18}F-FDG-updake in the right base of tongue region and right level II lymphadenopathy.

salivary gland cancers, directed surgical therapy to the primary site as well as neck dissection followed by indicated adjuvant therapy is typically the first line of treatment.[12] For HPV-related HNSCC, detection of the primary site leads to more precisely directed surgical or nonsurgical treatment options.[26] Patients with small primary site tumors and low-stage nodal disease may be candidates for upfront surgical treatment, with the possibility of avoiding adjuvant therapy if there are no adverse features. Alternatively, identification of the primary site as well as involved lymph nodes can allow for a more targeted radiation field as upfront therapy.[27]

Of course, PET/CT for the use of detection of unknown primary has limitations. The addition of CT to FDG-PET scans allows for better visualization of anatomic detail to correlate with physiologic findings. However, a nondiagnostic or noncontrast-enhanced CT may be limited in being able to accurately assess the site, extent of tumor spread and relationship between the tumor and adjacent structures.[28,29] Therefore, a cross-sectional contrast-enhanced MRI or CT remains standard for evaluation of the extent of primary site disease and has been shown to increase the efficiency and cost-effectiveness of diagnosis.[30] Furthermore, in the detection of unknown primary disease, FDG-PET/CT can still suffer from a relatively high background physiological uptake at common sites of occult primary squamous cell carcinoma such as the palatine tonsil and base of tongue tissue, creating some uncertainty in exact delineation of the primary extent.[3] There also may be limited value in detecting occult microscopic tumor deposits which lie below the level of PET detection.[4] Finally, it should be noted that for patients in which the primary site remains unknown despite work-up including PET/CT, there are multiple routes of treatment. Low-dose prophylactic radiation therapy to the likely mucosal sites of origin combined with definitive-intent high-dose radiation or chemoradiation to all sites of gross disease has been shown to provide effective cancer control.[27,31-34] Primary surgery, often followed by adjuvant therapy based on the pathologic results, is also an option.[35-37] Treatment choice is ultimately a multidisciplinary discussion and directed by patient factors.

Presurgical Assessment of Planned Primary Operative Site

There are certain situations where PET/CT can direct surgical planning in patients with known primary site HNSCC. PET/CT can be particularly helpful in delineating extent of tumor in a primary oral cavity cancer when dental artifact is present. In a 2014 study, Hong et al. showed that in 59% of patients with oral cavity squamous cell carcinoma and dental artifact on MRI, PET/CT was superior to MRI in accurate tumor sizing and staging as determined by final surgical pathology.[38] Additionally, PET/CT has been shown to be helpful in determining mandibular involvement. FDG-PET has been shown to have a high specificity (97%-100%) and sensitivity (85%) for detection of mandibular invasion.[39,40] As such, PET/CT may aid in evaluation of the extent of bony involvement when anatomic changes are questionable on CT or MRI. This is particularly critical for surgical decision-making in the oral cavity, with implications in determining the extent of resection and reconstructive options.

Presurgical Identification of Unappreciated Occult Nodal Metastasis

For a newly diagnosed HNSCC, FDG-PET/CT plays an important role in detecting the presence and extent of cervical lymph node involvement. There are a number of clinical scenarios where the PET/CT can alter or change surgical management. This includes detection of occult disease in a

clinically N0 neck, detection of nodes outside the expected lymphatic drainage basin for the primary site (aberrant or contralateral nodes), and detection of multiple nodes leading to upstaging of disease.

The main limitation of conventional imaging (MRI or CT) is a high rate of false-negative results, where a patient is staged as clinically N0 when occult neck disease is present. Historically, elective neck dissection is recommended for patients with HNSCC when the risk of occult metastases in the draining lymph node basins is determined to be greater than 20%.[41-43] The utility of elective neck dissection for early stage oral cavity squamous cell carcinoma was confirmed by D'Cruz et al.'s 2015 study, in which patients with stage I and II oral cavity squamous cell carcinoma with clinically N0 necks were randomized to elective neck dissection versus observation. This study showed a 12.5% overall survival benefit at 3 years and an improvement in disease-free survival in the elective neck dissection group.[42]

Neck dissection does carry a risk of morbidity, including damage to cranial nerves, sensory dysfunction, shoulder dysfunction, and cervical scars.[44,45] Therefore, the utility of PET/CT as a possible replacement for elective neck dissection in a clinically N0 neck has been investigated in a number of retrospective and prospective reviews.[46] Functional imaging has the advantage of detecting changes in cell metabolism even without changes in the size or structure of the lymph nodes. In 2006, Ng et al. prospectively evaluated the accuracy of FDG-PET, CT, and MRI in staging the neck in 134 patients with clinically N0 oral cavity cancer. The level-by-level sensitivity for detecting regional nodal metastasis was 41.2%, which was double the sensitivity of conventional imaging. The probability of a positive PET/CT findings in a clinically N0 neck was T-stage dependent.[47] Kyzas et al.'s 2008 meta-analysis of 32 studies including 1236 patients with HNSCC evaluated the accuracy of FDG-PET compared with CT, MRI, and ultrasound-guided fine needle aspiration. In studies where both FDG-PET and conventional tests were performed, the sensitivity and specificity of FDG-PET were 80% and 86%, compared with 75% and 79% of conventional tests. In the clinically N0 neck, the sensitivity of FDG-PET was only 50%.[48]

In a 2019 study, Lowe et al. showed that FDG-PET/CT had a high negative predictive value of 0.942 in patients with clinically N0 neck disease among patients with T2-T4 HNSCC. On the basis of PET/CT findings, the planned surgical treatment prior to PET/CT was changed in 51 (21%) of 234 patients, including planned dissection of additional nodal levels in 29 patients (12%) and fewer planned dissected nodal levels in 12 patients (5%). A negative PET/CT in the clinically N0 neck was a true negative in 87% and false negative in 13%.[49,50]

The detection of occult contralateral or aberrant lymph nodes on PET/CT would lead to alterations in surgical planning. For example, for oral cavity squamous cell carcinoma, the presence of a concerning lymph node contralateral to the primary lesion would mean a bilateral neck dissection should be performed. In 2015, Park et al. published a prospective study on 160 patients with untreated HNSCC comparing PET/CT with CT/MRI imaging for detection of contralateral neck metastasis. The use of FDG-PET/CT was significantly more sensitive (85.0% vs 45.0%, $P = 0.008$) and accurate (91.6% vs 80.3%, $P = 0.008$) than conventional CT/MRI imaging when evaluating the contralateral neck for metastatic disease in these patients.[51] However, a previous meta-analysis from 2012 showed equal diagnostic accuracy between CT, MRI, PET and ultrasound to detect clinically N0 disease.[52]

For patients with HPV-related oropharyngeal squamous cell carcinoma, the presence of a contralateral lymph node or multiple lymph nodes would lead to upstaging of disease. This may lead to an alteration in the treatment plan in order to minimize the possible need for triple therapy (surgery, radiation, and chemotherapy).[31] Furthermore, PET/CT has been shown to be helpful in detecting occult retropharyngeal nodes in patients with HPV-related oropharyngeal cancer.[53] Such nodes would be missed by conventional neck dissection as usually carried out in this population, and might lead one to recommend radiation or chemoradiation rather than surgery as upfront therapy.[54]

PET/CT may miss very small lymph node lesions of a volume less than 5 mm (possible false-negative results), and may be confounded by local infections where inflamed lymph nodes have increased FDG-avidity (possible false-positive results).[4] Therefore, clinical judgment and knowledge of patterns of spread must be brought to bear in interpreting the PET/CT and determining the final surgical plan. Furthermore, the multidisciplinary team should be aware that the timing of PET/CT should be carefully considered in interpreting potential nodal spread. For example, a PET/CT obtained after any surgical manipulation rather than in the pre-surgical setting could show false-positive, inflammatory lymph nodes or a primary site healing inflammatory response which would be the result of surgery rather than residual cancer. If a postsurgical PET/CT were to show such evidence of potential residual disease, the recommended best practice would be to confirm the finding with fine-needle aspiration biopsy.

Presurgical Screening for Distant Metastatic Spread

Screening for distant metastatic disease is important in patients with presenting with locally advanced carcinoma of the head and neck. It is the most important predictor of survival in several cancers. The overall incidence of distant metastasis in head and neck cancer is low (ranging from 2% to 18%), but this critical finding has important implications for surgical treatment strategy.[55-58] The National Comprehensive Cancer Network (NCCN) guidelines recommend that all patients presenting with stage III/IV HNSCC have FDG-PET/CT as part of their initial diagnostic workup.[52] For patients with locally advanced disease, surgical treatment of the primary site can be extensive and require large-scale reconstruction; in this patient population, detecting distant metastases is a means of preventing unnecessarily aggressive surgical treatment.

The most common sites of metastasis for head and neck cancers are the lungs, bone and liver, although other rare sites such as the adrenal glands have been picked up on PET.[59] FDG-PET has been shown to be more accurate than CT alone in detecting unexpected metastases, particularly subtle bone metastases that are not detectable on routine CT.[5,60-62] Various retrospective studies have shown that the detection of distant metastatic disease has changed management in up to 30% of head and neck cancer patients.[5,60,62-65]

Presurgical Detection of Second Primary Cancers

Secondary primary cancers can occur in up to 5%-10% of patients presenting with HNSCC particularly in patients that are smokers or presenting with HPV-negative disease.[66-70] Second primaries are often found in the head and neck, esophagus, and lungs.[71,72] The detection of a second primary has important implications for treatment. The reported rate of synchronous second primary tumors ranges from 1% to 18% and is due to the high prevalence of risk factors such as smoking and alcohol use in this population leading to field cancerization.[56,73-75]

Prior to the widespread use of PET/CT, patients with a new diagnosis of head and neck cancer were recommended to undergo pan-endoscopy to evaluate for secondary head and neck primaries.[75] However, FDG-PET/CT has shown to be an accurate method of screening for second primary that may be able to replace this function of pan-endoscopy.[68,69] Haerle et al. evaluated 311 patients with advanced-stage HNSCC who underwent pan-endoscopy and PET/CT for initial staging for synchronous primary tumors. They found that the prevalence of second primary tumors detected by pan-endoscopy was 4.5%, compared with 6.1% detected by PET/CT, and that the negative predictive value of PET/CT was 100%.[69]

PET/CT also has the added value of detecting second primary cancers outside the coverage of pan-endoscopy.[69,72] In a study of 1912 patients with known or suspected malignancies of all types, Ishimori et al. found that whole body PET/CT detected new, unexpected FDG-avid primary malignant tumors in at least 1.2% of patients.[72] Second primary sites included lung, thyroid, colon, breast, esophagus, bile duct, and prostate. Figure 2 shows examples of two patients who were found to have suspected second primary cancer on PET/CT.

The pre-surgical detection of a second primary cancer has important implications, as the surgery plan may need to altered in order to encompass treatment of the second primary, or alternatively, the head and neck surgery may need to be coordinated or temporized in accordance with appropriate treatment of the other cancer. Detection of a second primary cancer typically leads to complex multidisciplinary management requiring extensive coordination with other medical teams.

Detection of Persistent or Recurrent Disease in Follow-up

FDG-PET/CT has increasingly been used to evaluate treatment response and surveillance in patients with head and neck cancer. Up to 40% of patients with HNSCC develop recurrent or second primary disease.[76,77] Typically, regardless of recurrence stage or site, salvage surgery is the major first-line choice

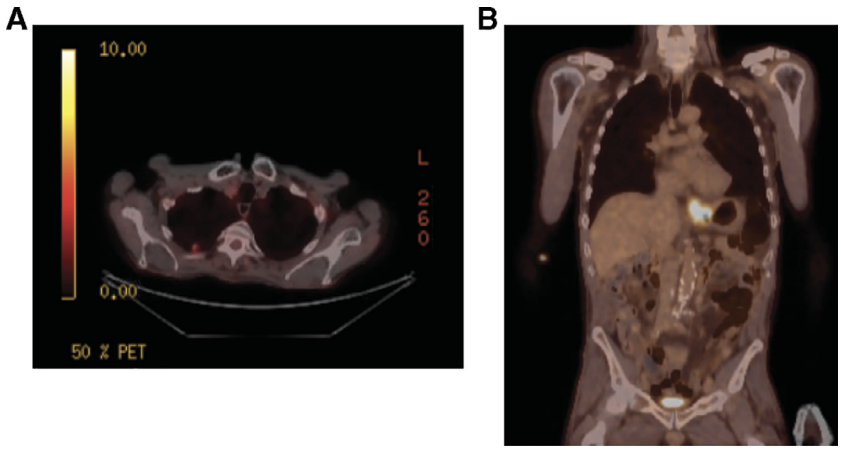

Figure 2 (A) Eighty-year-old-man with T1N2 HPV+ HNSCC of the left tonsil. Axial fused ^{18}F-FDG-PET/CT shows 1 cm solitary right upper lobe nodule. Based on appearance, the second primary lung finding was thought to represent a second primary. The patient declined biopsy of the lung lesion but was treated for both cancers. (B) Sixty-two-year-old man with a heavy smoking and drinking history who presented with a T2N0 oral tongue squamous cell carcinoma. Coronal fused ^{18}F-FDG-PET/CT shows focal hypermetabolic activity at the gastro-esophageal junction. On FDG-PET/CT, he was noted to have focal hypermetabolism and mucosal irregularity involving the gastroesophageal junction, concerning for esophagitis versus second primary. The patient underwent esophagoscopy and biopsy of the gastro-esophageal junction, which showed invasive adenocarcinoma. He underwent surgery for his oral tongue cancer, and subsequently was treated with chemoradiation for his esophageal cancer.

for a retreatment in the head and neck region, if it is feasible. In these scenarios, salvage surgery is likely of most value in patients with limited locoregional spread or situations in which negative surgical margins can be obtained.[78] Therefore, imaging is critical to delineate the extent of the new disease and determine the feasibility and utility of the proposed salvage surgery. In these patients, functional imaging is important because many of these patients have a history of prior neck radiation or surgery, which can complicate conventional imaging findings due to anatomic alteration or chronic treatment-related inflammation.

PET/CT has also been shown to be useful in determining the need for salvage neck dissection to address persistent disease after chemoradiation. Prior to the widespread utilization of PET for post-treatment surveillance, patients often routinely underwent salvage neck dissection after definitive chemoradiation treatment, regardless of the status of persistent disease. However, recent studies have shown that PET and PET/CT can help refine the decision-making around the need for salvage neck dissection.

In 2016, Mehanna et al. published results of 564 patients with HNSCC presenting with advanced nodal disease (clinical stage N2 or N3) who were treated with definitive chemoradiation and then were randomized to a planned neck dissection at 12 weeks after completion of therapy versus a FDG-PET/CT with a subsequent neck dissection if the imaging was deemed to be positive. Only 19% of patients in the PET/CT group went on to receive a neck dissection. At 2 years, both groups had similar survival (84.9% in the PET/CT group and 81.5% in the planned surgery group). The study authors concluded that surveillance with PET/CT reduces the need for salvage neck surgery without compromising survival.[79]

A 2018 meta-analysis of studies evaluating the diagnostic value of PET/CT in detecting nodal disease within 6 months of head and neck cancer treatment showed pooled estimates of sensitivity and specificity in detecting recurrent/persistent disease of 85% and 95%, respectively. Interestingly, in a subgroup analysis, FDG-PET/CT had a lower sensitivity and specificity in patients who had HPV-related tumors (75% and 87%, respectively).[80]

PET/CT can reveal the presence of synchronous distant disease when evaluating a patient suspected to have recurrence or second primary, which may then preclude surgical salvage treatment. In a 2019 retrospective study of 275 patients with suspected recurrent HNSCC, distant disease was revealed in 29.8% of the FDG-PET/CT scans.[81]

Conclusion

^{18}F-FDG-PET/CT is a valuable tool in surgical planning for HNSCC with numerous clinical applications. It can aid in detection of the primary site in patients with cervical lymph node metastases, nodal metastases outside the expected pattern, distant metastases, or second primary cancers. It can also be used in the evaluation of recurrent or persistent disease amenable to salvage surgery and for avoidance of planned post-radiation neck dissection for slowly resolving disease. The role of PET/CT as a replacement for elective neck dissection or examination under anesthesia remains controversial. PET/CT has a wide-ranging impact on the surgical management of patients with HNSCC and should be used routinely in patients with unknown primary nodal disease and those presenting with advanced-stage cancers.

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