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Abstract

Head and neck cancers (HNC) include a variety of neoplasms that are traditionally associated with high morbidity and mortality. Patients with these malignancies, of which squamous cell cancer is the most common, require a multidisciplinary approach to determine optimal treatment and follow-up. Treatment depends on TNM staging, which is determined using a combination of objective findings including physical examination, endoscopies, and importantly cross-sectional imaging. CT and MR imaging are the mainstays of cross-sectional imaging and are used extensively to stage and characterize these tumors. The goals of appropriate imaging is to establish the extent and size of tumor, assess nodal disease in the neck, look for perineural spread, distinguish tumor recurrence from postoperative- or postradiation-related changes, and monitor response to treatment. Cross-sectional imaging supplements and complements anatomic and pathologic changes of the neck.

CT and MRI are both used to image HNC. They both have their own strengths and weaknesses, and these should be carefully considered before choosing the respective study. Other techniques such as MR perfusion, MR spectroscopy, and MR magnetization transfer have the ability to measure functional parameters such as tissue perfusion that can be integrated with other clinical and radiological information to assess disease progression. Imaging with ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography (PET) has been found to be superior to CT and MR alone. New applications including combined PET/CT and PET/MR provide additional anatomical localization detail to assess for tumor response to treatment, tumor progression, and distant metastasis as well as spot unknown primary carcinomas or synchronous second tumor. With the rise in HPV-related tumors, imaging techniques can be used to identify these patients. From methodological development, these morphologic investigations are making the critical transition to preclinical and clinical validating methods and eventually to widespread clinical tools.

Keywords

Head and neck cancer • Computed tomography • Perfusion CT • Perfusion-weighted MRI • Diffusion-weighted imaging • Apparent diffusion coefficient • Fluorine-18 fluorodeoxy-

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glucose (FDG) • Positron emission tomography (PET) • Squamous cell carcinoma • Head and neck neoplasms • MR • Staging • Magnetic resonance imaging • PET/CT • Unknown primary • PET/MR • Synchronous second tumor

13.1 Head and Neck Cancer

Cancers of the head and neck (HNC) are common neoplasms that account for about 5 % of malignancies worldwide. They are the fifth most common cancer condition [1]. HNC include squamous cell carcinoma (HNSCC), basal cell carcinoma, many sarcomas, melanoma, and other tumors arising from a variety of sites. The primary risk factors for HNSCC in American men and women include tobacco use, alcohol use, and more recently HPV infection.

In 2015, approximately 59,340 new diagnoses and 11,260 deaths are expected in the United States due to head and neck cancer [2]. Patients with HNSCC require a careful evaluation and a multidisciplinary team approach to determine optimal management. Treatment planning depends to a large extent on TNM staging, which is evaluated with physical examination, endoscopies, and cross-sectional imaging [3].

Radiologic imaging with CT and MR imaging is extensively utilized to evaluate soft-tissue masses of the head and neck. These masses are diagnosed and staged primarily on the basis of physical examination and CT and MRI findings [4–6]. Imaging has become a vital and integral tool in characterizing and staging of malignant tumors involving the head and neck. CT and MRI provide essential information about the deep extension of clinically detected masses and also delineate additional clinically unsuspected masses [7, 8]. Accurate staging at the time of diagnosis is critical for selection of appropriate treatment strategy. Precise prediction of the extent of primary tumors, cervical lymph node status, and distant metastatic spread is important for treatment planning and prognosis. The goals of imaging in patients with head and neck cancer are to establish tumor extent and size, to assess nodal disease, for possible perineural tumor spread, and to distinguish recurrent tumor from posttreatment changes [9]. Imaging is also essential to follow up the patients after various therapeutic options available for the treatment are exercised, including surgery with or without radical dissection, lymph node dissections of various severities, radiotherapy, chemotherapy, and various combinations of all these [10]. Accurate evaluation of all these factors prior to treatment helps guide surgical extent or radiation therapy, minimizing locoregional treatment failure.

CT and MRI are the most commonly utilized imaging modalities for assessment of primary malignant tumor, local extension, and lymph nodal involvement. They are also the first imaging modalities for monitoring the result and response of surgical intervention, radiation or chemotherapy, or combinations thereof. In this goal cross-sectional imaging

supplements and complements the physical examination by delineating the anatomy and pathological changes of the neck. Complex anatomic structures and regions, such as the orbit, skull base, paranasal sinuses, deep spaces of the suprahyoid and infrahyoid neck, larynx, and lymph nodes, require that the radiologist be familiar with the imaging modalities available and their appropriate applications.

CT and MRI complement each other; certain conditions are better studied with one than the other. Various strengths and weaknesses of each modality should be carefully considered when selecting them for tumor assessment and follow-up [11]. The interpretation of CT and MRI should be based on the patient's history, physical findings, comorbidities, and previous procedures that may influence the structures visualized. Comparison with previous imaging is also essential to reliably understand the present condition.

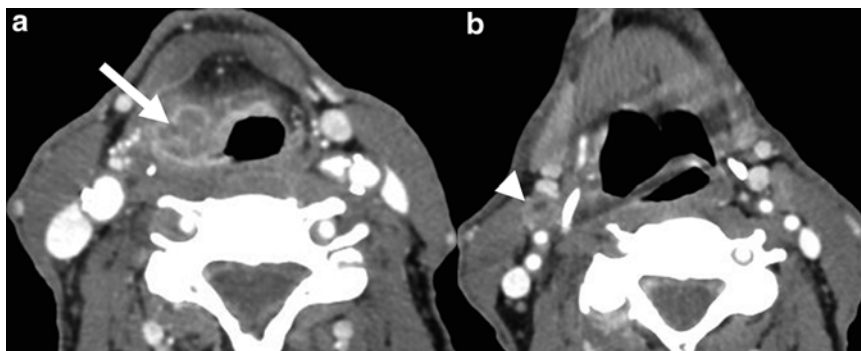
13.2 Anatomic CT

Computerized tomography (CT) was introduced about 40 years ago and has greatly enhanced clinical care. Its advantages include its speed, lower cost, and wide distribution in most medical centers. CT is excellent at delineating tumor extent and nodal disease. In head and neck tumors such as HNSCC, CT has helped in tumor staging, which dictated patient management and related to prognosis [8]. Helical multi-detector computerized tomography (MDCT) with 16 and now 64 detector rings has rapidly now become the new industry standard in CT imaging. This along with dynamic acquisition typically has resulted in reduced scan time, thinner sections, increased anatomic coverage, and better resolution of reformatted images and three-dimensional reconstruction. Section thickness as low as half an mm can be achieved along with acquisition of up to eight images per second [12, 13]. This has greatly enhanced the sensitivity and specificity of CT scan in head and neck cancer for primary staging as well as post-therapeutic follow-up (Fig. 13.1).

The anatomic coverage of a neck CT should include the base of the skull and should extend up to the medial end of the clavicles with 4 mm thick slices. Additionally, 2 mm slices and higher zoom factor may be employed at the region of interest using reconstructed spiral data. In patients with significant dental hardware, additional angulated images may also be obtained for better anatomic coverage avoiding streak artifacts.

CT has proved to be a modality of choice for initial work-up of a patient suspected of head and neck cancer and proved excellent for initial locoregional and lymph nodal staging and for post-therapeutic follow-up.

Fig. 13.1 Axial postcontrast CT scan showing T3 stage right aryepiglottic fold carcinoma (a) with transglottic extension (arrow) and metastatic right level 2 lymphadenopathy (b) consistent with N1 disease (arrowhead)



13.3 CT Perfusion

Computerized tomography perfusion (CTP) can be used to facilitate the evaluation of functional parameters such as tissue perfusion in many cancers. This can be integrated with morphologic information derived from conventional CT techniques. It is a dynamic contrast-enhanced technique which is used for quantitative assessment of tissue microcirculation [14], and it has recently been rediscovered as a promising noninvasive tool for evaluation of the microcirculatory changes associated with several neoplasms, including cancers of the head and neck [15–18]. CTP technique is based on the central volume principle, which relates blood flow, blood volume, and MTT as: $\text{blood flow (BF)} = \text{blood volume (BV)} / \text{MTT}$. Faggioni et al. have shown that BV, BF, and permeability-surface area product are significantly higher, whereas MTT is significantly reduced in head and neck tumor (both primary neoplasm and lymph node metastases, whenever present) compared with normal tissue and with muscle taken as a reference ($p < 0.01$); moreover, the alteration of CT perfusion parameters correlates with histopathologic diagnosis of adenocarcinoma in all cases [15]. Ash et al. have shown that CT perfusion parameters of the neck (BF and BV) correlate positively with microvessel density (MVD) of endoscopic biopsy specimens obtained from primary tumor sites of head and neck squamous cell carcinoma (HNSCC) [19]. Although, it seems unlikely that CT perfusion will replace biopsy for pretreatment assessment of MVD, CT perfusion has the potential to monitor treatment response by enabling noninvasive assessment of alterations in MVD and acting as a surrogate marker for tumor oxygenation (Fig. 13.2).

13.4 Anatomic Magnetic Resonance Imaging

Following the introduction of magnetic resonance imaging (MRI) 30 years ago, its use has enabled a quantum jump in diagnostic imaging of head and neck neoplasms. Early investigations highlighted the ability of MRI to differentiate neoplastic

from inflammatory lesions. MRI provides essential information about the deep extension of clinically detected masses and also delineates additional clinically unsuspected lesions [7]. It has added value for detection of soft-tissue extent, marrow involvement, and perineural spread [20]. The excellent tissue characterization and noninvasive multiplanar imaging capability of MR imaging result in more accurate diagnosis of neoplastic and benign tumors of the head and neck [21–25]. MRI is reported to be superior to CT in detecting tumor extensions, in separation of edema from the tumor, and in evaluation of possible bone marrow invasion. Dynamic MRI is also utilized to plan and evaluate radiotherapy of head and neck cancer [26].

MRI of the neck should be tailored for the anatomic region and processed under evaluation. A standard head coil usually suffices for relatively localized examinations of the suprahyoid region and base of the skull, whereas, the infrahyoid neck requires a neck coil. Axial, coronal, and sagittal sequences are essential. Unenhanced axial T1-weighted images display anatomic relationships and can detect lesions (e.g., lymph node lesions) embedded within fat. T1-weighted coronal images can define the false vocal cords, true vocal cords, laryngeal ventricle, and floor of the mouth [27, 28].

T1-weighted sagittal images provide helpful information about the preepiglottic space and nasopharynx. T2-weighted transaxial images characterize tissue, detect tumor within the muscle, demonstrate cysts, and assist differentiation of post-therapy fibrosis from recurrent tumor [29].

Gradient moment nulling, flow compensation, cardiac gating, and presaturation pulses are some techniques used to minimize motion artifacts [27]. Gadolinium (Gd)-enhanced images improve delineation of margins in many lesions. Fat-suppression techniques, such as short tau inversion recovery (STIR) and frequency-selected fat suppression, may improve the conspicuity of soft-tissue lesions embedded in fatty tissue by selectively diminishing the hyperintensity of fat on T1-weighted images [30] (Fig. 13.3). Postcontrast T1-weighted images usually best delineate the tumor margins [31], and this may be further improved with fat saturation (fat-sat), which, however, frequently results in artifacts and image degradation [32]. However, the normal enhancement of the aerodigestive mucosa may conceal small mucosal tumors.

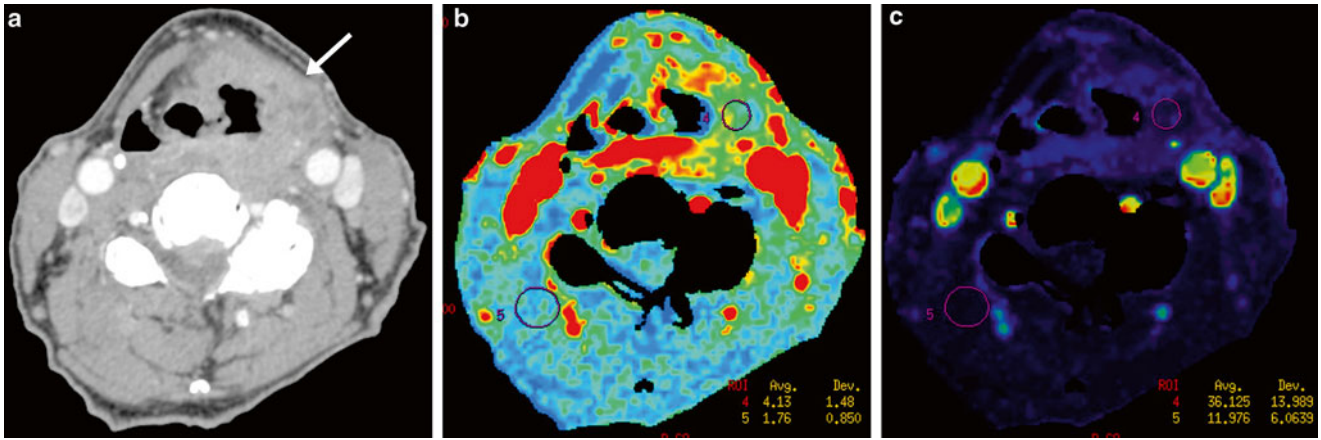


Fig. 13.2 (a) Contrast-enhanced neck CT image in a 69-year-old woman with history of previous surgery and chemoradiation for supra-glottic and hypopharyngeal carcinoma. A patchily enhancing soft tissue is seen at the right-left anterior neck, involving the strap muscle

(arrow), involving the lateral wall of left pyriform sinus and left aryepiglottic fold, and extending on to prevertebral spaces. (b, c) CT perfusion map shows increased blood volume and blood flow, suggestive of hyperperfusing malignant mass

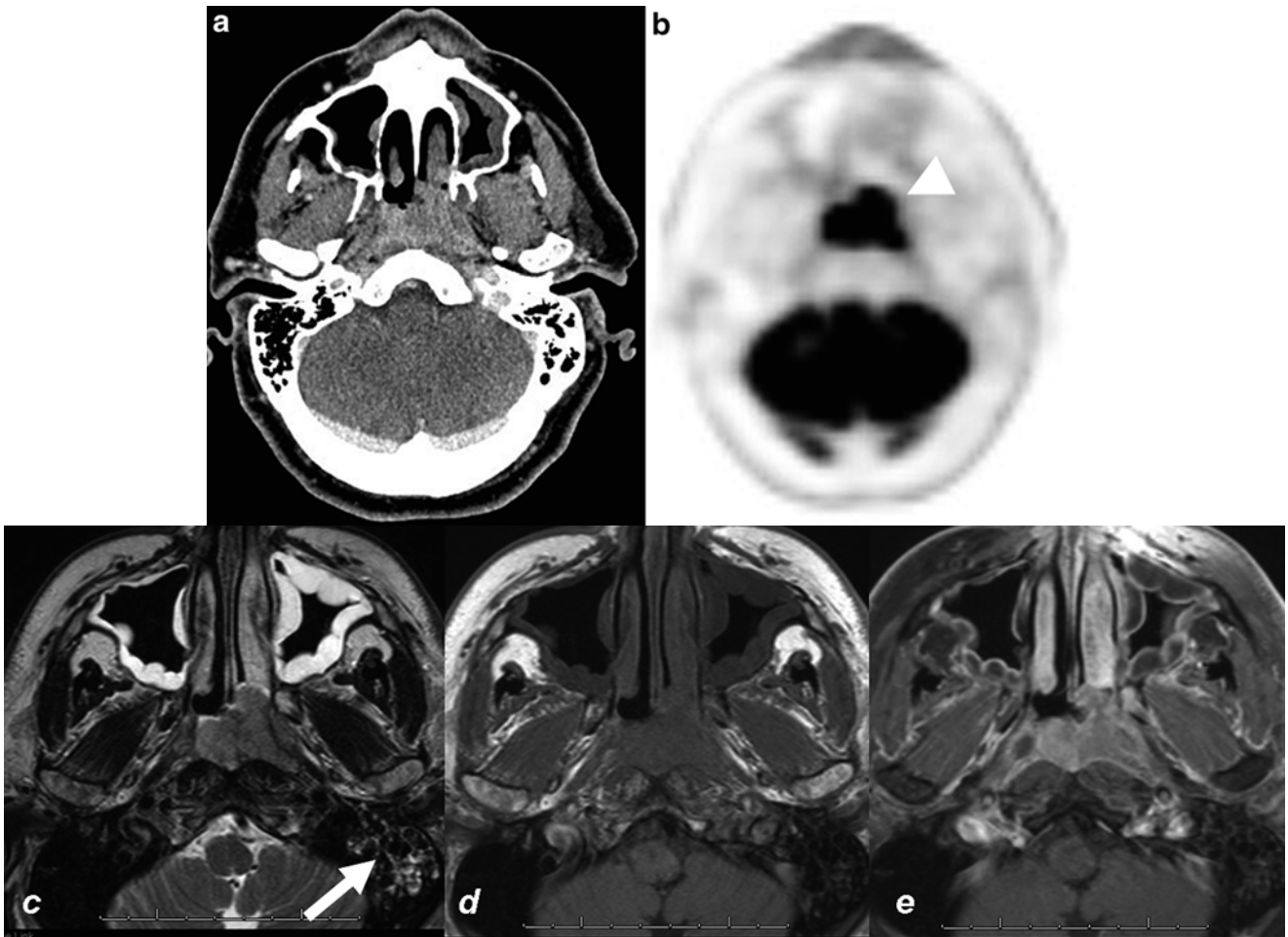


Fig. 13.3 PET/CT (a and b) images showing FDG-avid nasopharyngeal mass (arrow head). Axial T2W (c) and pre- and postcontrast fat-suppressed T1W images (d and e) showing enhancing mass

within the left posterior nasopharynx crossing to the right side. Fluid in the right mastoid air cells (arrow) secondary to Eustachian tube dysfunction

Early investigators credited MR imaging with greater precision in head and neck imaging than was warranted [33]. Conventional MR imaging did not have the last word in histological specificity, early detection of primary malignancy, and differentiating neoplastic from inflammatory lymph nodes. In spite of early enthusiasm, MR imaging did not eliminate the need for biopsies or aspirations of lesions. Spin echo imaging is still the mainstay of MR imaging, but now various new techniques hold promise for the future of head and neck imaging [34].

13.5 MR Diffusion

MR diffusion-weighted imaging (DWI) has been traditionally used to evaluate ischemia of the brain parenchyma. Its utility in evaluating pathologies outside the calvarium has recently been recognized, specifically, extracranial neoplastic disease. Hypercellular tissue within malignant tumors will show low ADC values [35, 36], while tissue changes such as edema, inflammation, fibrosis, and necrosis show low cellularity and hence higher ADC values [34] (Fig. 13.4). Diffusion-weighted imaging of oropharynx can easily be performed at the time of MR conventional imaging and adds approximately only 1–2 min of additional time to the examination. Localization and extent of primary squamous cell cancer, one of the commonest malignant neoplasms of head and neck, is usually well defined by CT or conventional MRI. High sensitivities and specificities, better than CT or conventional MRI, are also reported in staging of neck lymph nodes in squamous cell carcinoma [37, 38]. Whole-body DWI at high b-values with ADC mapping is technically feasible and improves assessment of metastatic spread in routine MR examinations. The characterization of neck lymph nodes remains a difficult issue with anatomy-based imaging methods, and DWI may be useful in this regard [39, 40]. DW imaging performed with ADC (b_0 –1000) values had higher accuracy than turbo spin-echo MR imaging in nodal staging, providing added value in the detection of subcentimeter nodal metastases [40].

13.6 MR Perfusion

MR perfusion is used to evaluate dynamic microscopic blood flow changes through a region of interest. The change in tissue signal intensity on MRI can be measured during a dynamic contrast infusion. This is used to generate blood flow, blood volume, and transit time parameters within areas of interest. Perfusion characteristics of tissue demonstrate changes in blood flow or volume of the head and neck lesions depending on underlying pathologic processes [34]. This technique has been

previously studied in characterizing brain ischemia, particularly in identifying infarcted tissue versus tissue at risk [41]. Changes in perfusion characteristics are also demonstrated in neoplastic tissue (Fig. 13.5). Generally, these findings may not add substantial additional information regarding tumor extent at the diagnosis. However, such imaging may be of benefit in qualitative analysis of tumor tissue. Specifically, additional recent studies have demonstrated that squamous cell carcinomas of the upper aerodigestive tract with increased blood volume/flow are more chemosensitive than other lesions with relative decreased perfusion parameters. This is likely due to relative increased oxygenation and metabolism of such lesions [17]. Such perfusion techniques could be particularly useful in determining which patients would benefit from such medical treatment, as opposed to surgical therapies which may not always preserve organ function.

An additional area of interest is in regard to tumor recurrence or regression. Conventional MRI or CT may simply demonstrate increased contrast enhancement within the treated neck. However, morphologic changes in tissue appearance (such as increase in size or nodularity) may not be well demonstrated on early posttreatment conventional imaging. Recent studies have concluded that for recurrent oral cavity and oropharyngeal carcinomas, perfusion parameters are altered. Specifically, BV and BF within recurrent tumor tissue are elevated in comparison to therapy-altered tissue, with corresponding decreases in transit time [42]. Perfusion imaging, like diffusion imaging, adds little time to either conventional MRI or CT examinations and can also be obtained noninvasively [43].

13.7 MR Magnetization Transfer

MR Magnetization transfer (MT) technique is based on the principle that the selective magnetization of protons associated with macromolecules may be transferred to the water protons that constitutes the MT image. A strong MT effect is observed where an efficient transfer mechanism exists between the two proton populations. It may be a useful technique for differentiating enhancing lesions from background tissue and defining poorly enhancing lesions. This is exploited to improve contrast between mass lesions that demonstrate an MT effect and background tissue like fat that does not [44]. Use of MT can improve contrast between head and neck lesions and background tissues. MT is shown to improve depiction of enhancing lesions adjacent to tissues with a strong MT effect [45]. MT can also aid unenhanced MR imaging in the delineation of tumors or lymph nodes in the parotid gland. MT is not indicated for cystic lesions, because they are generally well shown on a T2-weighted image or for cervical lymphadenopathy within

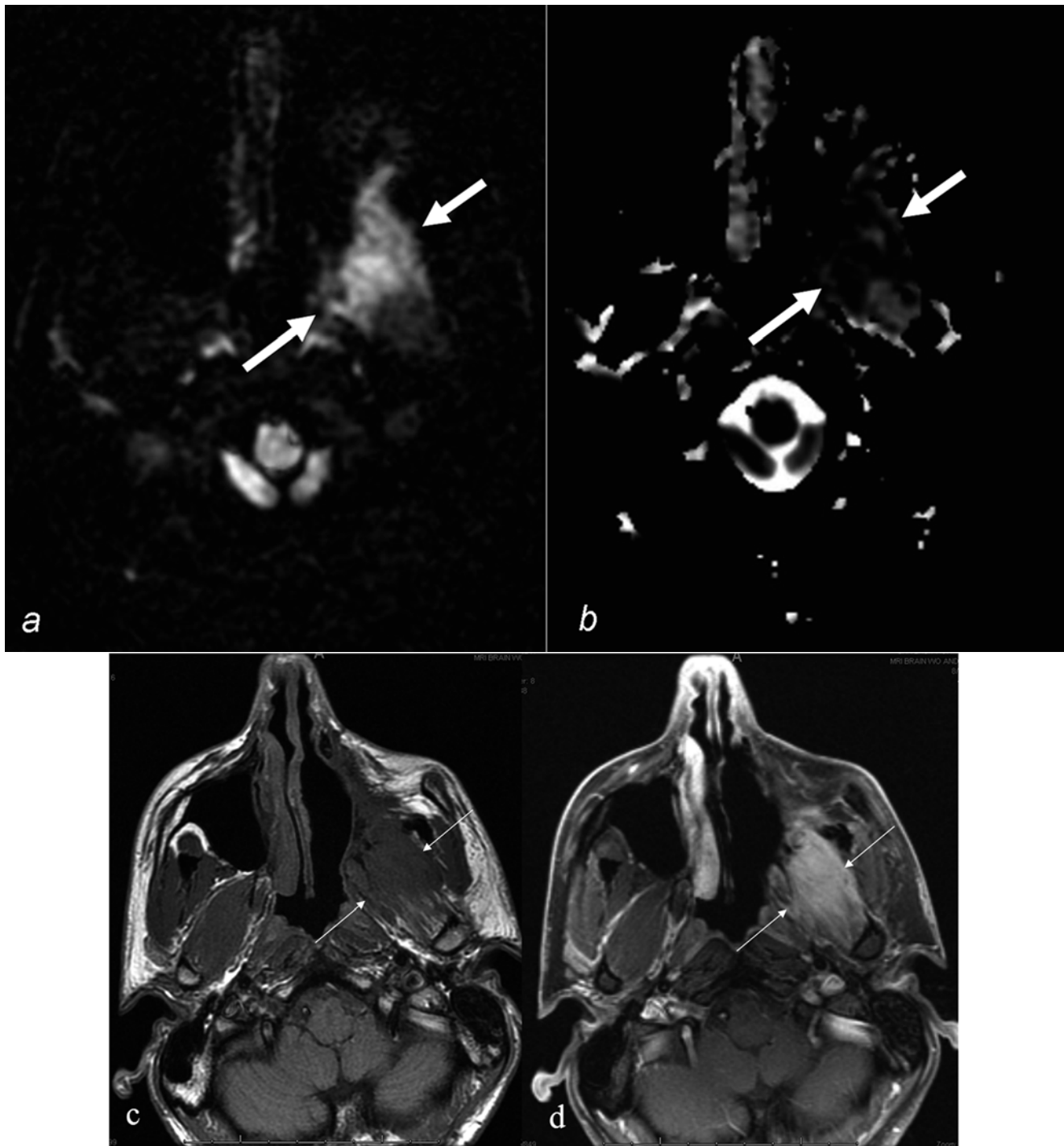


Fig. 13.4 Axial DWI (a) showing restricted diffusion in a left masticator space adenoid cystic cancer (arrows) with low ADC values (b) as seen on corresponding ADC maps (c and d, arrows)

lipoid tissue, because that has natural tissue contrast on conventional MRI [45].

However, MT has not enjoyed widespread application in head and neck imaging, partly because conventional imaging usually provides sufficient delineation of most primary lesions and lymphadenopathy.

13.8 MR Spectroscopy

Magnetic resonance spectroscopy (MRS) provides a noninvasive method for evaluation of various diseases of head and neck independent of the anatomic information provided by magnetic resonance imaging (MRI) [46]. 1H-MR

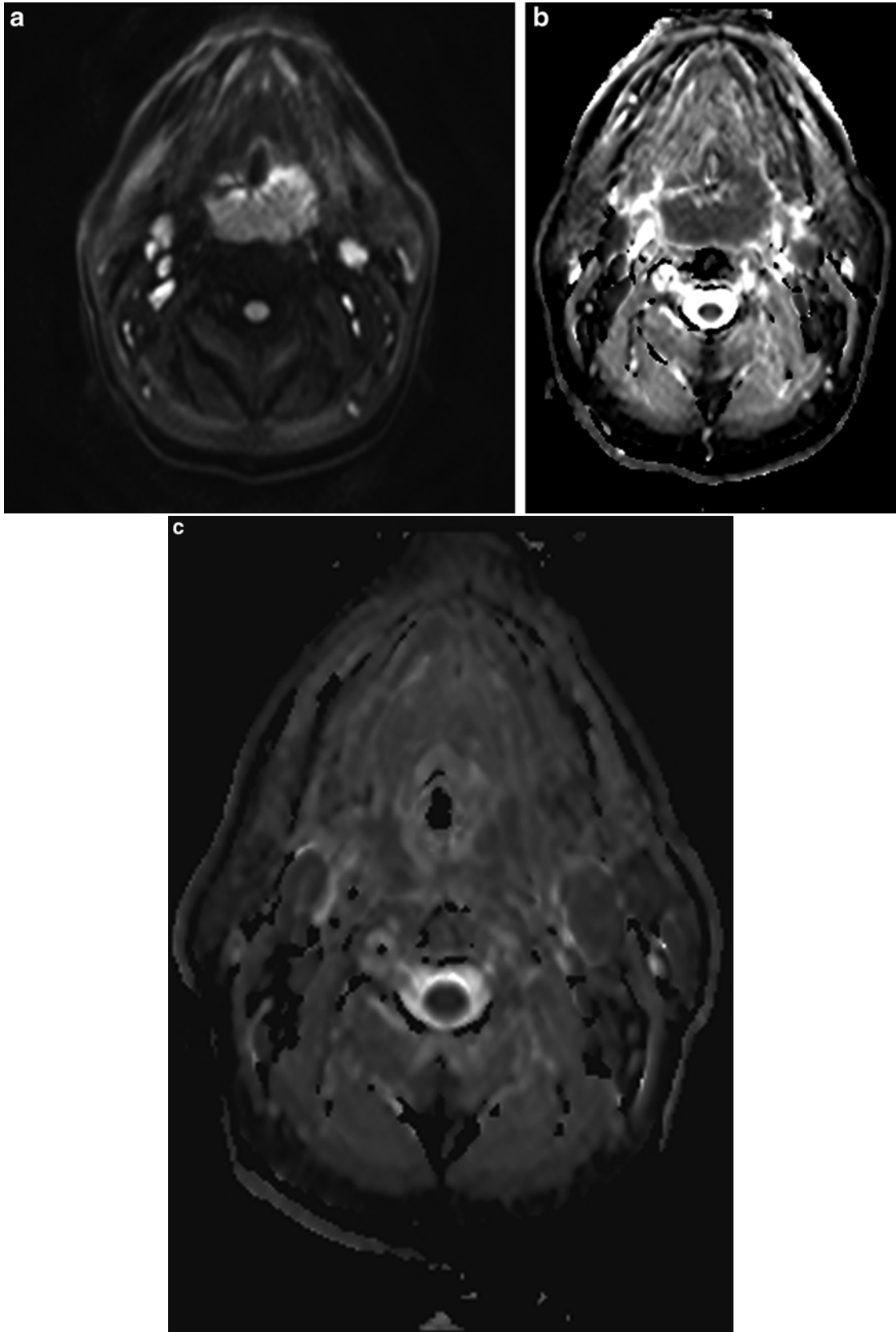


Fig. 13.5 (a, b, c) Large posterior oropharyngeal wall squamous cell carcinoma demonstrates increased DWI (a) and decreased ADC (b) signal intensity at presentation. Post-therapy, the lesion has decreased greatly in size (c). (d) Blood volume map of the same patient as in images (a–c) demonstrates increased perfusion values

of the lesion (*circled*) in comparison to the adjacent tissues at presentation (Reprinted from Shah GV, Wesolowski JR, Ansari SA, Mukherji SK. New directions in head and neck imaging. *J Surg Oncol.* Jun 15 2008;97(8):644–648. With permission from John Wiley & Sons)

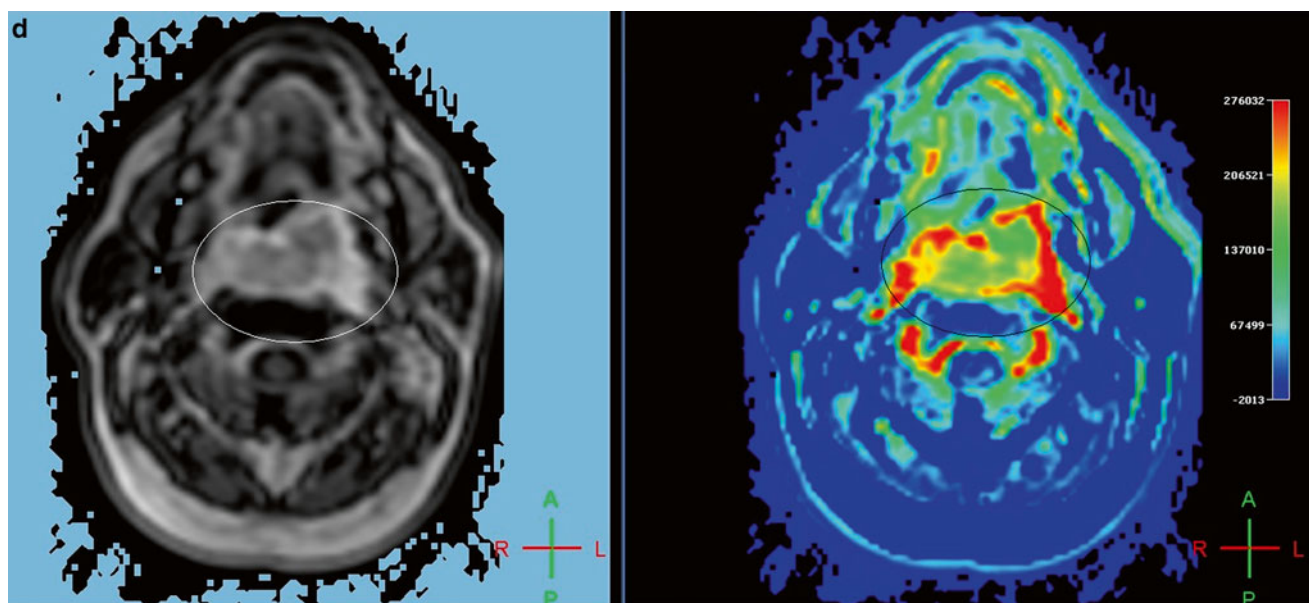


Fig. 13.5 (continued)

spectroscopy has the potential to assess biochemical composition and hence identify characteristics that could indicate malignant progression. It is widely accepted that cancer progression is accompanied by intracellular biochemical changes. It has the unique ability to analyze the tissue at the molecular level by evaluating the presence of specific metabolites. This is especially helpful to characterize lesions that have equivocal features on standard anatomic imaging. Early metastatic infiltration of nonenlarged lymph nodes or residual malignant disease in patients undergoing treatment for malignant process may also have normal or ambiguous appearance on routine anatomic CT or MR imaging [47].

In the case of HNSCC, it has been shown that 1H-MR spectroscopy has the potential to differentiate between normal and malignant tissue with a high degree of sensitivity and specificity [46, 48–51] (Fig. 13.6). MR spectroscopy of head and neck cancer and lymph nodes helps to differentiate nonmalignant from malignant tumors and lymph nodes and also helps to differentiate between residual malignancies from postradiation changes. Elevation of the Cho/Cr ratio appears to be a consistent finding for HNSCCA and has also been identified in analysis of various SCCA cell cultures and SCCA containing cervical metastatic lymph nodes [48]. Higher levels of choline metabolites in tumors are believed to be due to increased cell proliferation and biosynthesis, while reduced creatine resonance likely reflects increased energy metabolism within tumors [52].

For prognostication, MR spectroscopy has the potential to contribute to an accurate and early prediction of tumor behavior and response to treatment in squamous cell carcinoma of the head and neck region. Using the choline-to-creatine (3.2/3.0 ppm) and the 1.3/0.9 ppm spectral intensity

ratios (signal due to lipid or lactic acid), a sensitivity of 83 % and a specificity of 82 % were obtained in predicting which head and neck cancer patients would fail treatment [53].

Tumor hypoxia is a common phenomenon in solid tumors and has been shown to adversely affect the treatment outcomes in patients with head and neck (HN) squamous cell carcinoma treated with conventional therapy [54–56]. Resonance from lactate (Lac, 1.3 ppm) may be a marker for tumor oxygenation and may help staging and was thought to have potential for staging and monitoring the treatment [57]. However, in a recent work, the lactate SI did not correlate with tumor pO_2 , treatment response, or locoregional control in a series of 62 patients with resectable stage IV HN squamous cell carcinoma undergoing induction chemotherapy [58]. Additional research is needed to refine this technique.

13.9 Positron Emission Tomography

^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET) is a technique that has been found to be superior to conventional imaging work-ups such as CT and MRI, which were previously the mainstay work-up for diagnosis, staging, and post-therapeutic follow-up in patients with head and neck cancer [59–61]. ^{18}F FDG-PET has higher sensitivity and specificity for detecting lymph node metastases than CT or MRI. It improves detection of occult cervical lymphatic disease and distant metastasis and assists in localization of unknown primary carcinoma of the head and neck region [62–66]. ^{18}F FDG-PET is considered superior to CT and MRI for local staging and detection of malignant characteristics in cervical lymph nodal enlargements [59, 60, 67–70]. It has a

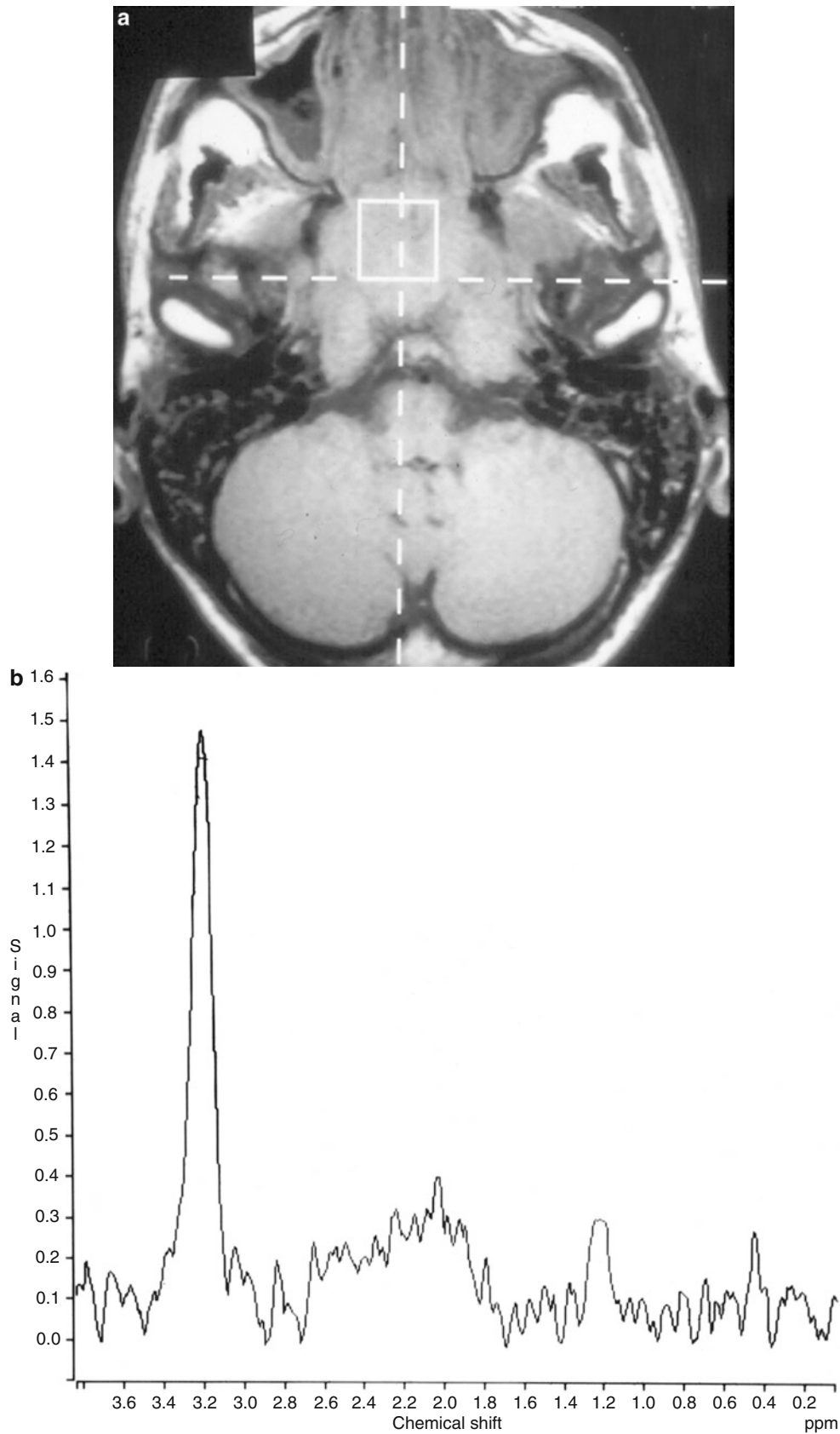


Fig. 13.6 Patient with throat pain and dry cough exhibits a nasopharyngeal mass on MR imaging. (a) T1 axial images show a large nasopharyngeal midline soft-tissue mass with nonspecific features and without frank aggression. (b) 1H-MRS reveals attenuation of *N*-acetyl aspartate peak, elevation of choline peak, and increased choline-to-

creatine ratio compatible with malignant mass. This lesion was proved on biopsy to be a squamous cell carcinoma (Reprinted from Shah GV, Fischbein NJ, Patel R, Mukherji SK. Newer MR imaging techniques for head and neck. *Magn Reson Imaging Clin N Am.* Aug 2003;11(3):449–469. With permission from Elsevier)

high negative predictive value (NPV) of approximately 90 %, which is more than any other imaging modality. There is growing evidence that ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging is increasingly accepted as a valuable imaging tool in evaluation of patients with head and neck carcinomas [62–65, 71–74]. The potential clinical applications include pretreatment staging, treatment monitoring, and evaluation of the previously treated patients [75] (Fig. 13.7).

13.10 PET/CT

The use of PET alone provides poor quality of anatomical localization of the primary tumor, and metastases on ^{18}F FDG-PET can have negative impact on staging and management [76]. The poor spatial resolution of ^{18}F FDG-PET is a limiting factor, especially within the intricate anatomy of the head and neck [69]. Combined PET/CT scanners overcome these limitations by fusing the anatomic data of CT with functional data of ^{18}F FDG-PET [77–79]. In PET/CT, the most relevant additional effect is that the CT data adds specificity to ^{18}F FDG-PET data [80, 81]. The utility of PET/CT has been evaluated extensively in head and neck neoplasms. Several of these studies showed that the integrated combination of CT and ^{18}F FDG-PET is more accurate than either of the modalities alone for detection and anatomic localization of head and neck cancer, thus enhancing the patient care [82–87]. PET/CT has been shown to have high NPV but poor PPV following treatment [88, 89]. Recently, the Hopkins Interpretation system was introduced as a five-point qualitative scale for evaluation of PET/CT and was found to predict overall survival [90]. The accuracy of integrated PET/CT is also more than ^{18}F FDG-PET and CT images viewed side by side [83, 91–94]. In one study, CT data improved the specificity of the images in approximately two-thirds of patients with lesions seen on ^{18}F FDG-PET images [95]. In some situations, such as very small disseminated pulmonary metastases, addition of CT is able to increase the specificity and also the sensitivity of PET/CT examination [81].

PET/CT can detect unknown primary tumors of the upper aerodigestive tract [96, 97]. PET/CT can detect primary squamous cell carcinoma in 30–50 % of patients presenting with an unknown primary tumor. PET/CT is generally performed after confirming the presence of metastatic squamous cell carcinoma. It is usually performed before endoscopic biopsies to improve the tissue yield. This diagnostic yield can increase with PET/CT as it improves the anatomic localization of areas of abnormal FDG uptake [98, 99]. PET/CT is also utilized for determining response to chemotherapy and/or radiation. Comparison of pretreatment standard uptake values (SUVs) to SUVs 2 weeks into treatment can allow

measurement of the speed of response and also the sensitivity of the tumor to the treatment technique [100]. Poorly responsive tumors can then be treated to higher effective tumor doses of radiation, or surgery can be performed. Initial results suggest that PET/CT can be used to assist in defining primary site and nodal tumor targets for radiation therapy approaches. PET/CT is useful adjuvant to clinical staging of squamous cell carcinoma, and its utilization will increase with advancement of technology.

13.11 PET/MR

PET/MR is a new modality that has started to become more widely distributed and allows for increased anatomical localization of lesions like PET/CT. It may provide a number of advantages over PET/CT including simultaneous imaging, decreased radiation, and better soft-tissue resolution including perineural spread and infiltration of fascia and vessels [101, 102]. These characteristics have been demonstrated when imaging the head and neck region [103]. The disadvantages of PET/MR are few but include difficulty with attenuation correction. In addition, disadvantages that broadly apply to MRI such as missing small lung metastasis are also applicable to PET/MR [104].

Several centers are beginning to develop protocols and are exploring application for PET/MR in head and neck cancers. One study retrospectively compared PET/MRI fusion with PET and MRI alone and found increased sensitivity and specificity for tumor staging [105]. However, others have found no advantages in TNM staging as compared to PET/CT or MR alone [106–109]. It remains to be seen if PET/MR will become standard of care for diagnosing and tracking neoplasms in the head and neck.

13.12 Local Tumor Detection and Staging

The most important information required before surgery for proper therapeutic planning is the accurate knowledge of location, size, extent, the depth of invasion of the primary tumor, and its relation to the surrounding structures [69, 110]. Large primary tumors of the oral cavity or the oropharynx can be detected easily by clinical examination. The sensitivity of FDG-PET was considered even higher than CT or MRI for detection of primary tumors [111]. The sensitivity of FDG-PET for detection of primary carcinoma ranged from 88 to 100 % [61, 63, 112, 113]. Both MRI and CT can provide additional information about tumor extension into the deep spaces, the relationship to adjacent structures, and bone infiltration needed for treatment planning. Sensitivity of MRI earlier was thought to be less than that of CT [62, 112]. However, with increased

Fig. 13.7 Mantle cell lymphoma showing FDG avidity (a) in a nonenlarged left level 1 lymph node (arrows) in the neck (b)

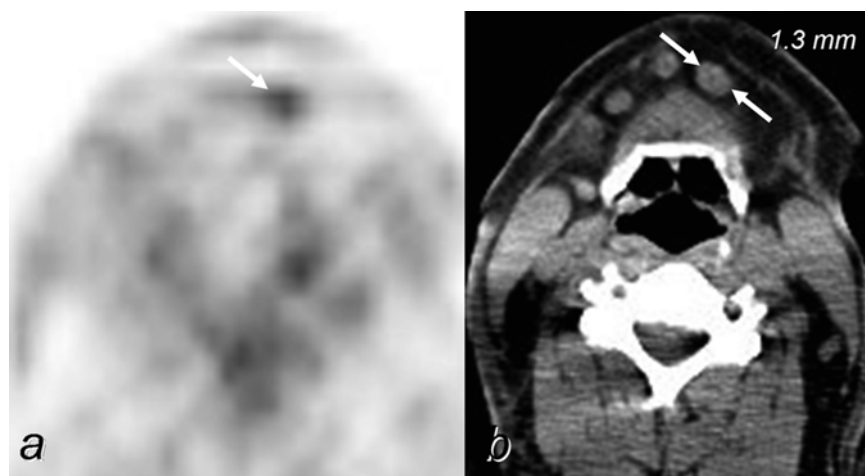
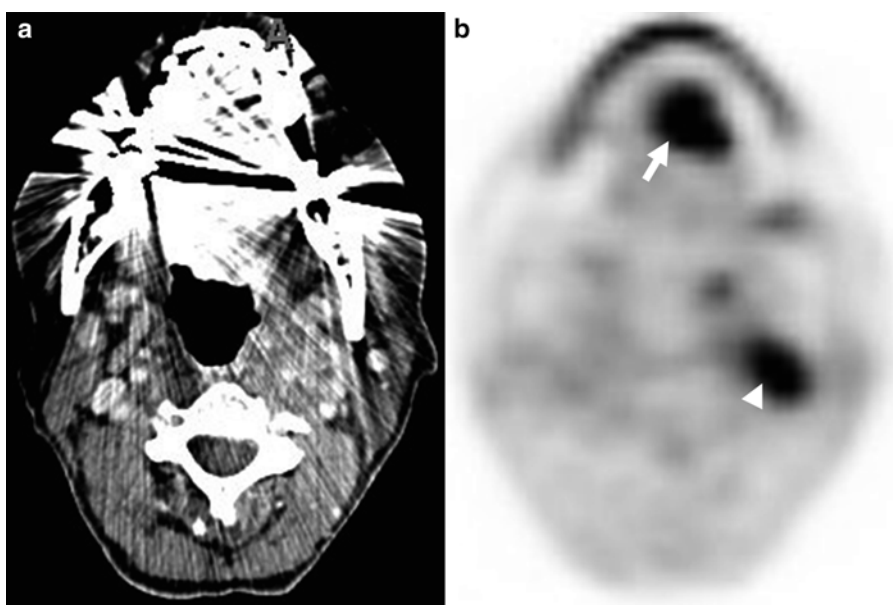


Fig. 13.8 Axial postcontrast CT scan (a) showing dense streak artifacts from unmovable dental hardware obscuring FDG-avid squamous cell cancer in the oral tongue (arrow) with metastatic left level 2 lymph node (arrow head) as seen on PET scan (b)



technical improvements, it is thought to be comparable to CT [114]. Scattering of focal uptake in primary oropharyngeal tumors can lead to overestimation of the extent of primary disease, and physiologic uptake in oropharynx may obscure small primary tumors in oropharynx [115]. Thus FDG-PET alone cannot provide the detailed information needed for planning of tumor resection, but fusion of FDG-PET data with CT data in PET/CT can overcome this limitation.

Sensitivity of CT, especially in oropharynx, can be compromised by streak artifacts from dental hardware, especially if the size of the tumor is small [114]. However, high metabolism on FDG-PET would indicate the possibility of an underlying mass (Figs. 13.8, 13.9, and 13.10). Earlier, the sensitivity of MRI was thought to be less than that of CT [62, 112], but with increased technical improvements, it is thought to be comparable to CT [114]. Some of the earlier reports showed that FDG-PET was more accurate than CT or

MRI for local detection of smaller tumors [62, 112, 113]. But some more recent studies have shown that CT and FDG-PET are equivalent in local staging [61, 116].

CT detects lytic foci of cortical mandibular invasion, which are best accomplished with a dedicated dental protocol. The reported sensitivity and specificity for standard neck CT in detection of mandibular involvement are 96 % and 87 %, respectively [117] (Fig. 13.11). However, a later study demonstrated a 93 % accuracy of MRI in detecting mandibular involvement in patients with oral and oropharyngeal cancer [118], indicating that CT may not be necessary to evaluate for cortical invasion. MRI with contrast-enhanced T1-weighted fat-sat images provides satisfactory accuracy of tumor thickness. The presence of malignant neoplasm adjacent to the neurovascular bundle is highly concerning for invasion. Tumors larger than 2 cm with aggressive margins and deep sublingual extension probably involve the neurovascular bundle [31]. Oral malignancies, especially of buccal

Fig. 13.9 Axial postcontrast CT scan (a) showing large necrotic left level 2 lymph node (*large arrow*) and necrotic left level 5 lymph node (*small arrow*), with FDG avidity on the corresponding PET scan (b)

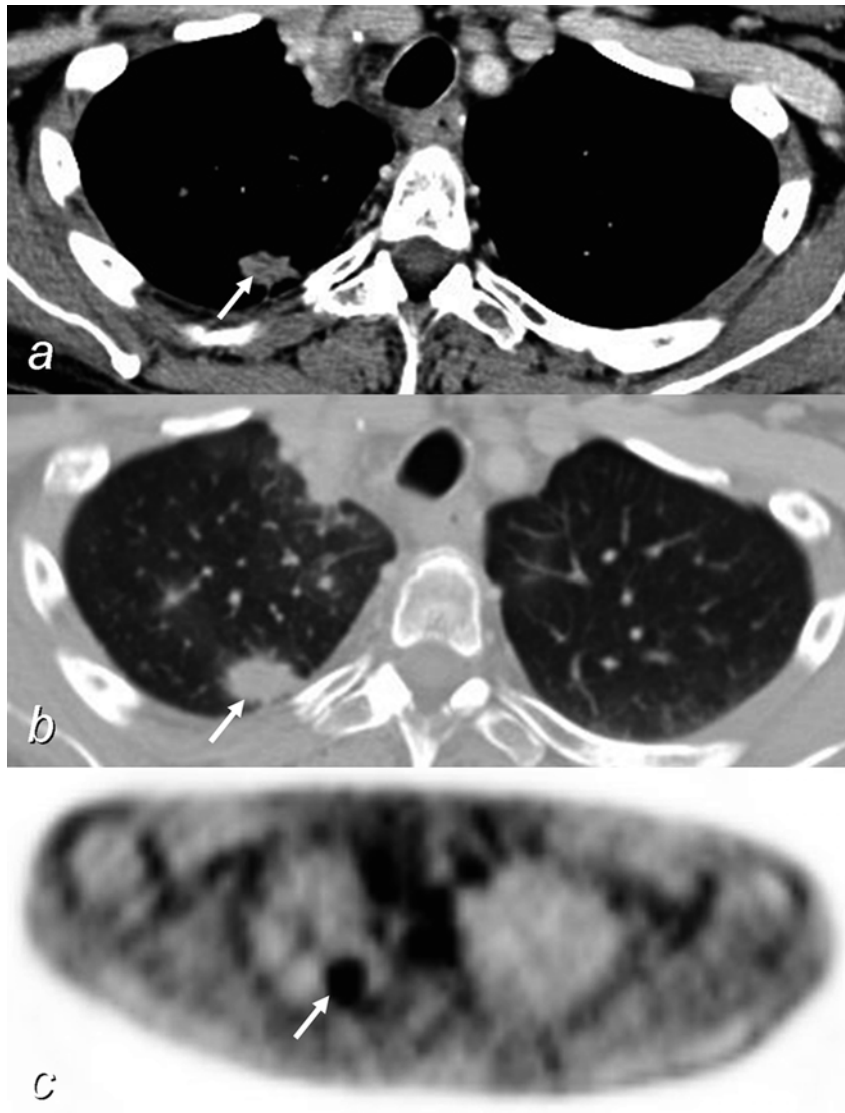
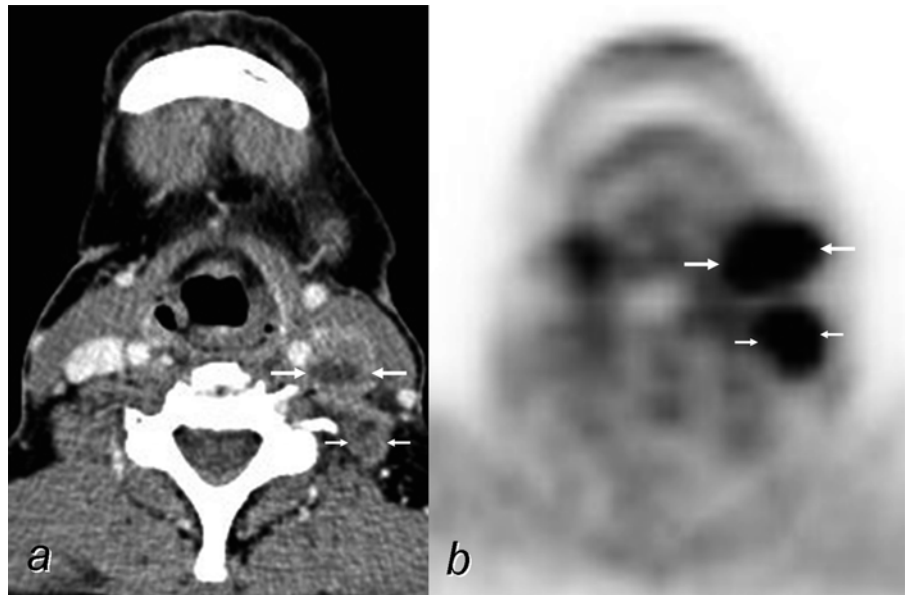
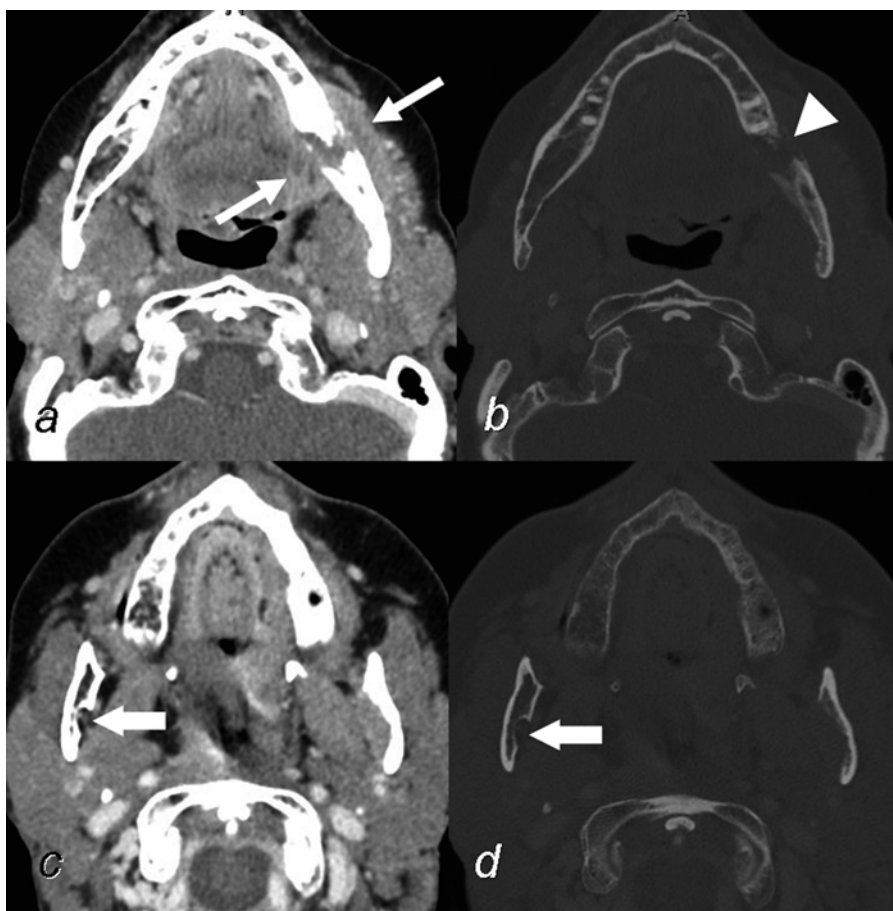


Fig. 13.10 CT thorax in mediastinal windows (a) and lung windows (b) showing a metachronous lung cancer (*arrow*) with increased FDG uptake on PET scan (c)

Fig. 13.11 Axial postcontrast CT scan (a) showing stage T4 left retromolar trigone cancer (arrow) with destruction of left mandibular ramus (arrow head) on bone windows (b). Perineural spread along left inferior alveolar nerve with loss of normal fat in the alveolar foramen on the left (d), compare with normal right side (c) (arrowhead)



spaces and retromolar trigone, are better visualized using the “puffed-cheek” CT technique, in which the patients perform a modified Valsalva maneuver during the scan distending the oral cavity by air [119].

Deep extension of nasopharyngeal cancer including the presence of skull base invasion, and intracranial spread is better evaluated with MRI than CT [120, 121]. Skull base invasion may occur through the neural foramina by perineural tumor spread, which primarily occurs after invasion of the pterygopalatine fossa, foramen ovale, and hypoglossal canal [122] (Fig. 13.12). Nonenhanced T1-weighted images are very well suited to evaluate perineural extension, revealing homogeneous gray mass of tumor against natural tissue contrast of T1 bright fat planes and bone marrow. Pre- and post-contrast T1-weighted MRI is very accurate in detection of subtle perineural tumor extension. Evaluation of possible perineural spread should be performed in all patients with facial paralysis and facial pain or numbness, because these symptoms may be the initial presentation of a head and neck malignancy [123, 124] (Fig. 13.13). Complementary direct coronal CT images with bone algorithm are recommended to evaluate subtle bone erosion which may escape detection by MRI.

Cartilage invasion by laryngeal and hypopharyngeal tumors is an important imaging finding because it automati-

cally leads to a T4 stage [9]. The overall sensitivity is 82 %, overall specificity is 79 %, and overall negative predictive value of cartilage erosion on CT overall is 91 % [125]. Cartilage invasion on MRI shows high T2 signal intensity, a low-to-intermediate T1 signal, and postcontrast enhancement. However, due to frequent reactive inflammation, edema, and fibrosis, the MRI findings of cartilage invasion may frequently be false positive, resulting in a positive predictive value of only 68–71 % [126]. However, the advantages of MRI over CT for soft-tissue differentiation may be outweighed by motion artifacts. CT remains a valuable and frequently used screening modality for the larynx as it is fast and readily available.

Imaging studies cannot reliably distinguish benign from malignant salivary gland masses. MRI is the modality of choice for evaluation of parotid masses [21]. The real advantage of cross-sectional imaging is the ability to accurately reveal the location and extension of a tumor and to assess for perineural tumor spread. Magnetization transfer, dynamic imaging, and especially, diffusion imaging have shown promising results in detection of parotid malignancies [127].

The relationship of a tumor to the facial nerve is difficult to determine on MRI. However, the lateral margin of the retromandibular vein on cross-sectional imaging as a marker

Fig. 13.12 Coronal fat-suppressed postcontrast T1W images showing large infiltrating soft-tissue attenuation mass in the left masticator space (*bold arrow*) extending into the pterygopalatine fossa (**a**). There is associated abnormal enhancement along the second and third divisions of the left trigeminal nerves and left Vidian canal (*small arrows*) (**a, b, d**). There is infiltration of the left orbital floor with enhancing soft tissue and thickening of the left inferior rectus muscle (*small arrow*) (**c**)

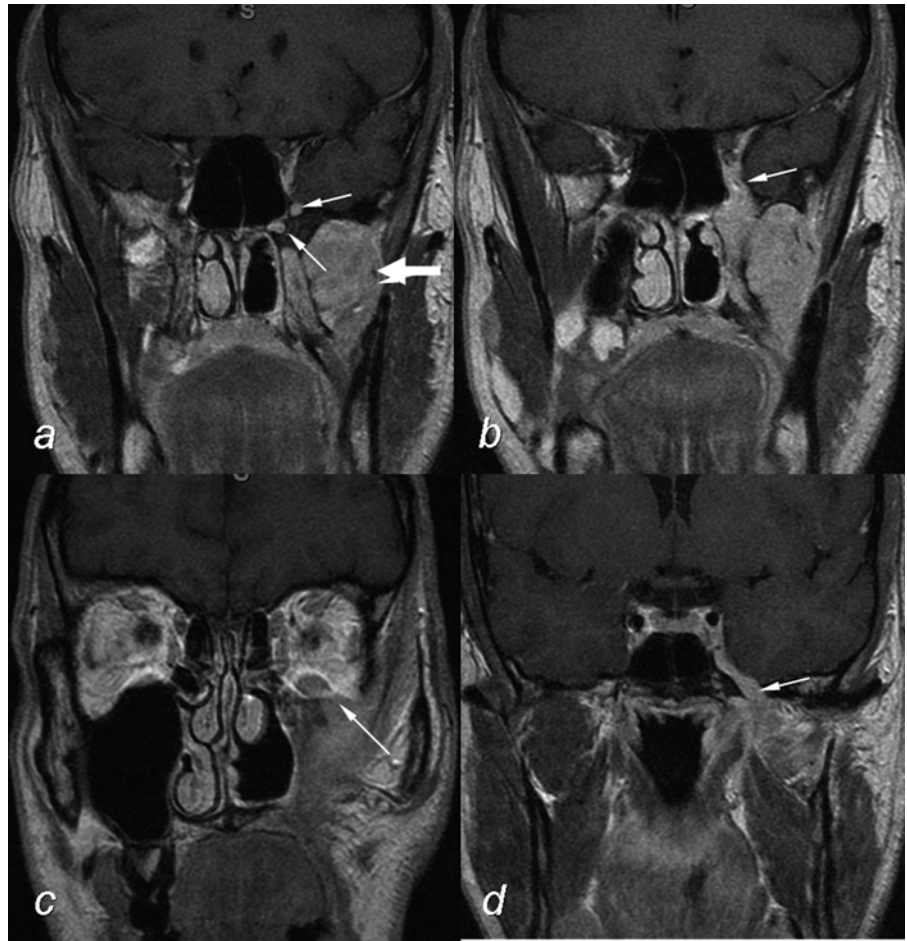
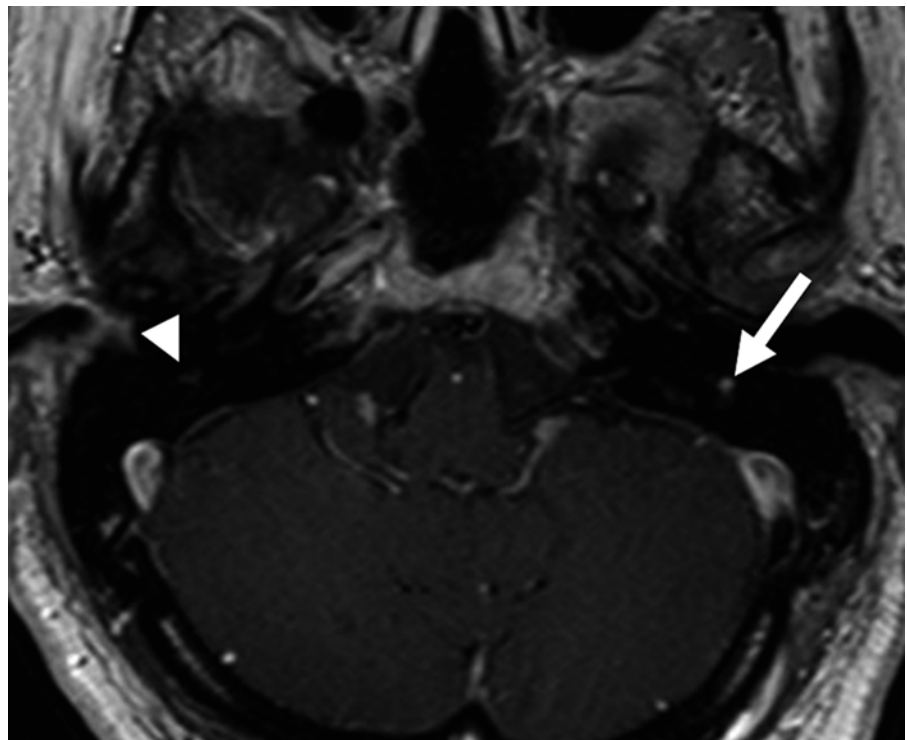


Fig. 13.13 Postradiotherapy “facial neuritis.” Axial (3 mm section) postcontrast, fat-suppressed T1W image showing increased enhancement of the tympanic segment of the left facial nerve (*arrow*), compared to normal right-sided facial nerve (*arrow head*)



for the facial nerve has an accuracy of approximately 90 % [128]. A careful search for perineural tumor spread along the facial, auriculotemporal, and mandibular (V3) nerves should be undertaken on MRI scans in all patients with parotid masses [129].

Multiple series have been reported evaluating FDG-PET or PET/CT for patient with newly diagnosed HNSCC in the preoperative setting [60, 63, 130]. Sensitivity of FDG-PET was reported to be 98 % and of PET/CT 97 % for detection of primary tumors in patients with newly diagnosed HNSCC in a large series with 167 patients [69], higher than sensitivity of CT (86 %) and MRI (88 %) in the same patient set. Similar results were reported in numerous previous studies [59, 60, 63, 82, 85, 86, 130]. Even as sensitivity of PET/CT is considered higher than any morphological imaging for primary detection of HNSCC, the detailed anatomic information like depth of invasion and relationship of tumor to surrounding structures could not be provided only by the CT data of PET/CT. This may be due to inherent technical limitations of CT data set. With availability of multi-slice and multi-detector scanner capability in future with PET/CT, this situation may improve.

13.13 Lymph Node Staging

As most primary head and neck malignant neoplasm have a relatively high incidence of nodal metastasis, the staging of the neck is most important before a therapeutic plan is evolved. Staging can be done by a combination of clinical palpation and anatomic imaging. Nearly 40 % of all lymph nodes in the body are located above the clavicles. Lymph nodes are usually embedded within the fat planes that surround the vessels and separate major cervical muscles. Therefore, the fat of the neck provides an excellent natural contrast with the nodes on T1-weighted MR images [11]. Lymph nodes are divided into ten major groups [131] named for the structures in proximity to nodal location.

Patients with limited nodal spread of head and neck cancer are often treated surgically with radical neck dissection, while more extensive disease may additionally require adjuvant radiation therapy. Complete removal of all metastasis lymph nodes is essential for curative treatment. Lymph node metastases are common in patients with head and neck cancers. In up to 20–30 % of patients, lymph nodal spread of the disease is found, even though it may not be apparent on physical exam [132, 133]. The prognosis for these patients is strongly influenced by the presence of lymph node metastases [112]. Metastatic lymph node disease was found in approximately 50 % of the patients at the time of diagnosis [71, 114].

The imaging recommendations are mixed regarding an appropriate modality for evaluating lymphadenopathy [5,

134, 135]. CT is preferred because of its availability, speed, and excellent spatial resolution. Lymph nodes are usually embedded within fat, and fat is well portrayed by CT (Fig. 13.7). MRI has superior soft-tissue contrast and multi-planar capabilities. CT and MRI have a high rate of false-negative diagnoses, which can be explained by micrometastases within otherwise normal lymph nodes [32, 136]. The reported sensitivity for CT in detection of metastatic lymph nodes is from 67 to 90 % [32, 71, 136–138] and for MRI is from 71 to 91 % [32, 65, 71, 112, 114, 136]. The reported sensitivities of PET for nodal disease range from 67 to 91 % [62, 65, 71, 72, 113, 114, 116, 137, 138]. Both FDG-PET and PET/CT have technical resolution limitations of 4–5 mm and were unable to detect lymph metastases smaller than 4–5 mm, contributing to false-negative results [139–141]. The reported specificity of FDG-PET ranges from 88 to 100 % [65, 71, 72, 84, 113, 137]. The specificity value for CT is 38–97 % and for MRI is 48–94 % [32, 71, 137, 142]. False-positive FDG-PET findings may be primarily due to its inability to discriminate between inflammatory process and tumor infiltration [111]. This is because FDG is not a tumor-specific tracer but a metabolic marker, and hence various inflammatory processes can lead to increased FDG uptake, potentially returning false-positive results [143]. However, a practical benefit of employing PET/CT in presurgical evaluation for lymph node staging in patient with HNSCC is improved imaging staging for the expert and also a nonexpert interpreter [84]. PET/CT imaging is also reported to reduce equivocal head and neck image interpretations and increase evaluator confidence [144]. Combining structural information with morphological imaging like CT and metabolic information with functional imaging like FDG-PET with coregistered PET/CT is a method of choice for lymph node imaging in the future.

13.14 Distant Metastases

Distant metastasis to other organs and distant lymph nodes from HNSCC is generally a late event and usually represents an incurable disease [145]. The lung is the most common site of distant spread; however, distant bone metastasis can also occur in case of other widespread metastatic disease [146, 147] and can cause severe local morbidity at the metastatic site [148]. The reported incidence for distant bone metastases in HNSCC ranges from 17 to 31 % [149–151]. Apart from the lungs, screening for distant metastases is routinely not performed in initial staging of patients with HNSCC [146, 152]. However, some studies have shown FD-PET to be valuable in detecting distant metastasis in advanced HNSCC, suggesting a role for whole-body FDG-PET scanning, including lungs and bones for initial staging [153–155].

PET/CT may be performed in squamous cell carcinoma to evaluate for possible occult distant metastases to the lungs or bones [137] (Figs. 13.8, 13.9, and 13.10). The presence of pulmonary metastases upstages a patient from M0 to M1 and alters treatment regimen. Routine imaging work-up for patient with squamous cell carcinoma pulmonary includes conventional radiography of the chest at most institutions. Chest CT is performed in patients with advanced stage disease. A solitary nodule on CT scan may represent a metastasis or a granuloma. PET would be helpful in this evaluation as a FDG-positive nodule would likely be metastatic and may require biopsy. An FDG-negative nodule may likely indicate a granuloma.

13.15 Unknown Primary Tumor

The incidence of unknown primary tumors in the head and neck region ranges overall from 3 to 7 % of all head and neck cancers including HNSCC [64, 67, 142, 156–162]. Apart from the routine physical examination, the evaluation includes fiber-optic laryngoscopy/nasopharyngoscopy, pan-endoscopy, and morphological imaging including CT and MRI and directed biopsy [156, 160, 161]. More recently, transcervical and intra-oral ultrasound has shown promise in detecting the primary lesion [163, 164]. The areas most likely to harbor an occult primary, such as the tonsil, tongue, base, piriform fossa, and postnasal space, should be thoroughly evaluated with physical examination and office-based endoscopies [161]. Focused morphological imaging with CT and MRI looking for evidence of primary as well as additional areas of lymphadenopathy is also performed. Further management is often a combination of surgery and radiotherapy; however, this depends on the primary site of the disease as well as the treating center [165, 166]. In spite of thorough clinical, endoscopic, and morphological imaging, 1–2 % of head and neck cancer patients will not have a primary site detected [167, 168].

An important application of PET imaging may be in patients with nodal disease and unknown primary tumor—the primary site has been found in 10–60 % of cases when conventional imaging and clinical investigations have failed [9]. FDG-PET is generally more sensitive than morphological imaging in patients with unknown sites of the primary carcinoma [169, 170]. However, it is also associated with false-positive findings in up to 11 % of these cases [169, 171]. Tumors of oral cavity account for a majority of cases with unknown primary and can generally be detected by clinical examination. However, in the head and neck regions with lower sensitivity for clinical examinations and morphological imaging, the role of FDG-PET and PET/CT becomes more evident [114].

Tumor detection rate of about 31 % of primary tumors is reported in patients presenting with unknown primary [162]. A few retrospective studies suggest FDG-PET detection rates of 24–27 % for an occult head and neck primary carcinoma [64, 172]. Another study reported a low rate of true-positive scan (33 %) but a high rate of true-negative scans (88 %) [173], suggesting that negative FDG-PET or PET/CT helps to rule out a primary site (Fig. 13.14). This is complicated by the fact that false-positive reports are reported in large lymph nodes up to 20 mm in size [136, 137] or in necrotic lymph nodes. PET/CT serves as a valuable clinical tool for occult metastatic disease of the head and neck, most commonly HNSCC and synchronous primary tumors.

13.16 Synchronous Second Tumor

Patients with head and neck tumors also have a high incidence of secondary tumors of the aerodigestive tract (estimated at approximately 8 %), and PET identifies synchronous primary neoplasms that are missed on conventional imaging. The incidence for metastatic spread to lungs in patients with HNSCC is low, but there is also a high incidence of second primary tumor in patients with head and neck cancer, with detectable lung lesion [174]. A few previous studies have shown a high sensitivity of 100 % and positive predictive value of 85 % for FDG-PET to differentiate a malignant from a benign pulmonary lesion [153, 175]. Due to its ability to conduct whole-body imaging, PET/CT can be useful for detection of distant metastases and second primary cancer (Figs. 13.8, 13.9, and 13.10) [176, 177]. PET/CT can serve as an excellent screening tool for distant metastatic disease or a synchronous primary tumor in the lungs [162].

13.17 HPV

The recent rise of head and neck cancers related to the HPV has resulted in investigations to identify these patients. They are more likely to be younger, male, nonsmokers, and non-drinkers [178]. HPV-associated cancers also carry a better prognosis. Imaging findings have been studied in this population to better identify this subset of patients. HPV+ tumors have more likely to have lower tumor volumes and glycolytic indices on PET/CT [13, 179–181]. These have been found to be predictive of tumor recurrence and overall survival [182–186]. HPV status in combination with posttreatment PET/CT further increases the negative predictive value for recurrence and may allow for less frequent surveillance [187–190].

In conclusion, morphological imaging techniques are crucial for therapy planning in head and neck neoplasms. The highest sensitivity and optimal anatomic information of the

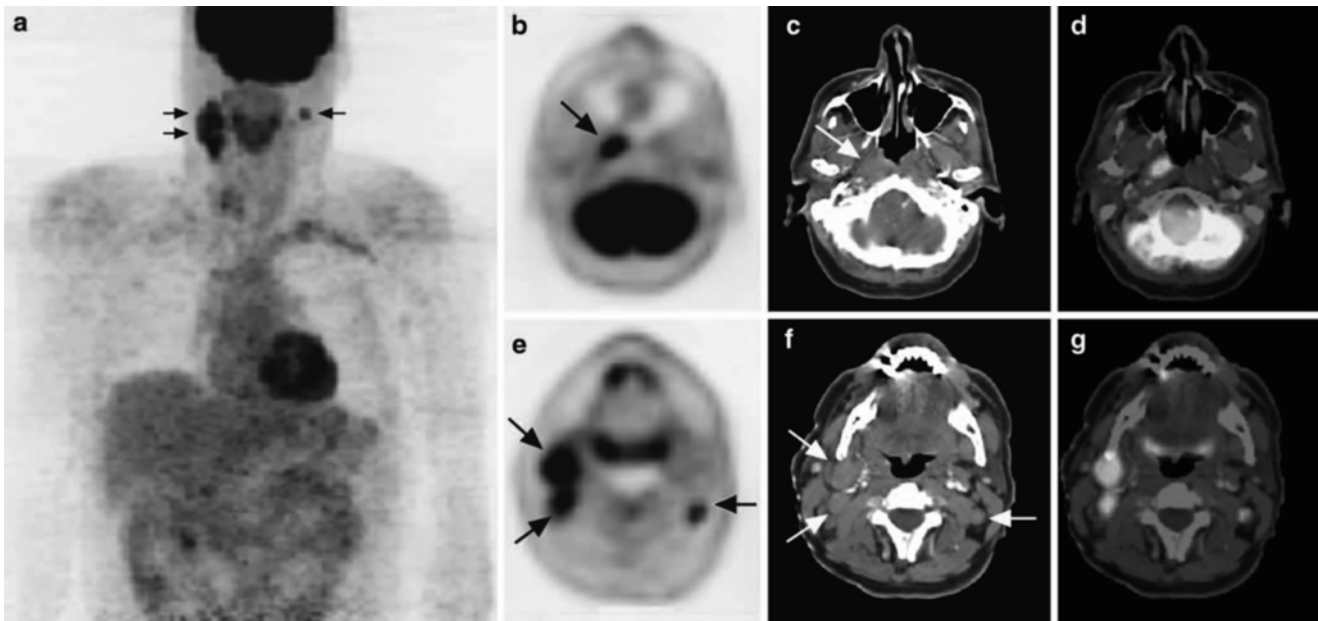


Fig. 13.14 Patient presented with bilateral lymph nodal neck masses. PET/CT reveals unknown primary neoplasm of nasopharyngeal squamous cell carcinoma. (a) MIP PET image demonstrates bilateral increased abnormal FDG uptake in the neck (*black arrows*). (b) Axial PET in the region of nasopharynx shows focal abnormal FDG uptake in the region of the right torus tubarius (*black arrow*). (c) Axial CT of nasopharynx shows mild soft-tissue fullness in the same region (*white arrow*). (d) Axial PET/CT demonstrates increased abnormal FDG uptake in the region of mild soft-tissue fullness representing primary

unsuspected squamous cell carcinoma of nasopharynx. (e) Axial PET of the neck at the level of mandibular angle demonstrates FDG uptake in bilateral level 2 cervical lymph nodes (*black arrows*). (f) Axial CT shows enlarged bilateral level 2 lymph nodes (*white arrows*). (g) Axial PET/CT demonstrates fusion imaging signifying malignant nature of enlarged lymph nodes (Reprinted from Shah GV, Wong KK, Gandhi D, Parmar H, Mukherji SK. Squamous Cell carcinoma: Initial Diagnosis and Staging with PET/CT. *PET Clinics* 2007;2(4):469–480. With permission from Elsevier)

local tumor site for local staging are provided by MRI. MRI, CT, and PET are similar for detection of abnormal and pathologic lymph nodes. However, in case of equivocal findings by MRI or CT, PET provides relevant information for determining the extent of surgical neck dissection. FDG-PET and CT complement each of the strengths, providing additional accuracy for staging head and neck cancer and make a notable impact on clinical decision-making. The application of ultrasonography and PET/MR may further assist clinicians in staging of tumors as these technologies are further developed and studied.

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