PET–Computed Tomography in Head and Neck Cancer

Current Evidence and Future Directions

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KEYWORDS

• Head and neck • Squamous cell carcinoma • HNSCC • FDG • PET • PET-CT

KEY POINTS

- ^{18}F-fluorodeoxyglucose (FDG) PET–computed tomography (CT) provides more accurate staging in head and neck cancers (HNCs) and is critical for treatment planning.
- FDG PET-CT is more useful than conventional imaging in detection of unknown primary HNC and secondary primary malignancies, which affects therapy.
- FDG PET-CT has tremendous value for staging in advanced HNC, prognostication, assessing treatment response, as well as for long-term surveillance.
- Novel non-FDG PET tracers are under investigation and have great potential in improving personalized care for HNC in the future.

INTRODUCTION

According to the American Cancer Society, almost 50,000 new cases of head and neck cancer (HNC) occur each year in the United States, with approximately 10,000 attributable deaths.[1] HNC most commonly arises in the oral cavity, oropharynx, and larynx; followed by nasopharynx and nasal cavity, and other less common sites. From a histopathologic perspective, squamous cell carcinoma (SCC) accounts for more than 90% to 95% of HNC; therefore, head and neck SCC (HNSCC) is the focus of this article.[2] Over recent years, although there has been decreasing incidence of HNC associated with the carcinogens tobacco and alcohol, there has been increasing incidence of HNC related to human papillomavirus (HPV).[3]

The tumor-node-metastasis (TNM) staging system of the American Joint Committee on Cancer is most commonly used to predict prognosis and guide therapy for HNSCC.[4] Early-stage HNSCC may be managed by radiation or surgery alone, whereas locally advanced HNSCC may require a combination of surgery, radiation, and chemotherapy or targeted-therapy. Accurate staging at initial diagnosis, as well as posttherapy assessment, is of vital importance in optimizing outcomes. Although contrast-enhanced computed

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tomography (CT) and MR imaging remain critical in the management of HNSCC, recently, PET with ^{18}F-fluorodeoxyglucose (FDG) has become increasingly important in the care of patients with HNSCC.[5] This article focuses on the utility of FDG PET–CT in HNSCC at initial diagnosis and treatment, assessing therapeutic response, and long-term surveillance. This is followed by an overview of novel non-FDG PET tracers for HNSCC as the future direction of molecular imaging and personalized medicine.

BASICS OF 18F-FLUORODEOXYGLUCOSE PET–COMPUTED TOMOGRAPHY

PET can provide quantitative evaluation of physiologic processes by combining positron-emitting radioisotopes with ligands that target the biochemical processes of interest. PET radioisotopes emit a positron that travels a short distance of a few millimeters in tissue before colliding with an electron, leading to an annihilation event and emission of 2 511 keV photons, 180° apart, detectable by the PET scanner. FDG is the most commonly used PET tracer clinically and is vital to the management of many solid malignancies.[6] FDG is an analogue of glucose that becomes irreversibly trapped in a cell after phosphorylation and is, therefore, a measure of glycolysis, which tends to be higher in tumors. Increased FDG uptake is not specific for malignancy. Benign processes, including inflammation, can also be FDG-avid. In clinical practice, FDG PET is generally combined with CT. The CT can be low-dose used for attenuation correction and anatomic localization. Alternatively, if the appropriate workflow is in place, the CT portion can be done similar to diagnostic CTs with inclusion of intravenous contrast, which can be especially useful in necrotic tumors.[7] For HNSCC, FDG PET-CT is commonly acquired from skull base or vertex of the skull to the proximal thighs. Some institutions also acquire separate dedicated head and neck images with longer bed time and smaller field of view, which may offer better assessment of locoregional disease, although the incremental utility of these dedicated head and neck images has been questioned. For example, Yamamoto and colleagues[8] showed that, although the dedicated head and neck PET-CT was more sensitive than whole body imaging, the findings did not reach statistical significance. Recent advancements in PET-CT scanners, including time of flight, has led to improved lesion detection and further research may be warranted to assess the added utility of dedicated head and neck PET-CT in current clinical practice.

Tumor metabolism can be measured semiquantitatively on FDG PET-CT using standard uptake value (SUV), which normalizes the photon counts in a region of interest to the administered radiotracer dose and patient's weight (or, alternatively, lean body mass or body surface area). Clinically, the most commonly used SUV measure is the maximal SUV value (SUVmax) value, which can be sensitive to noise, reconstruction algorithms, and other acquisition parameters. Therefore, changes in SUVmax should be interpreted with caution when 2 PET-CT studies are acquired from different scanners without cross-calibration, and strict cutoffs in SUVmax should not be used given the variability in tumor FDG uptake and technical parameters. Another measure is the metabolic tumor volume (MTV) more commonly seen in the radiation oncology literature, which measures tumor volume using a percentage of SUVmax to define boundaries. Total lesion glycolysis (TLG) is also commonly encountered and defined as mean SUV multiplied by MTV. Despite its shortcomings, SUVmax remains the predominantly used measure of FDG uptake by tumors clinically due to its ease of use.

UTILITY OF 18F-FLUORODEOXYGLUCOSE PET–COMPUTED TOMOGRAPHY IN INITIAL DIAGNOSIS AND TREATMENT

Initial Staging

Accurate staging of HNSCC has significant impact on prognosis and treatment planning.[4] The T component in the TNM staging system is based on primary tumor size and extent of local disease involvement, which differs for various regions in head and neck, and is beyond the scope of this article. Although PET has inferior resolution and anatomic details compared with CT and MR imaging, studies have shown that FDG PET-CT has higher sensitivity in depicting primary HNSCC.[9,10] One example in which FDG PET-CT is more useful in demonstrating the primary tumor is in the oral cavity adjacent to dental hardware, an area that remains obscured from streak artifacts on CT and susceptibility artifacts on MR imaging (**Fig. 1**). Combining FDG PET with contrast-enhanced CT, Krabbe and colleagues[9] reported sensitivity and specificity of FDG PET-CT for detecting primary tumor of greater than 90%. Due to the spatial resolution of PET, small lesions of a few millimeters may not be detected, especially along superficial mucosal surfaces.[11] This limitation in spatial resolution is compounded by physiologic FDG uptake in the head and neck, such as lymphoid tissues in Waldeyer ring, vocal cords, and muscles. In addition, necrotic primary tumors may not exhibit

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