The Application of PET in Radiation Treatment Planning for Head and Neck Cancer

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KEYWORDS

• PET • Head and neck cancer • Treatment planning

The American Cancer Society estimates that in 2009 there were more than 48,000 new cases of head and neck cancers and more than 11,000 deaths due to head and neck cancer.[1] While the majority of these cancers are squamous cell carcinoma (SCCA), head and neck cancers represent a diverse group of histologies that occur in sites that can have vastly different anatomic environments. Over the past two decades landmark studies have led to improved treatments for head and neck cancers and a focus on organ preservation.[2–4] Advances have also been made using chemoradiation postoperatively in locally advanced disease.[5,6] These studies have led to a multidisciplinary approach in the management of head and neck cancers, and radiation treatment is playing a more important role in the management of head and neck cancer.

Although improvements in survival and locoregional control have been made, the early and late side effects from head and neck radiation treatment are often significant. Advances in imaging and computing have allowed radiation oncologists to design more complex radiation treatments. Treatments have moved from 2-dimensional (2-D) plans to 3-dimensional (3-D) conformal planning, and now intensity-modulated radiation therapy (IMRT) is commonly used in the treatment of head and neck malignancies.[7] IMRT using inverse planning produces steep dose gradients that allow for highly conformal treatment of tumors while minimizing dose to adjacent normal structures uninvolved by tumor.[8,9] In head and neck cancer treatment, the use of IMRT has led to a reduction in xerostomia and improvements in quality of life following treatment.[10–12] However, highly conformal treatments can lead to microscopic disease not being included in the high-dose radiation fields, resulting in locoregional failures. On the other hand, overdrawing the target volumes can result in high-dose radiation delivered to the critical structures that may lead to increased toxicities. Therefore, in head and neck cancer IMRT planning it is critical to accurately delineate the target volumes.

Advances in computed tomography (CT) and magnetic resonance (MR) imaging have coincided with advances in radiation treatments, and are commonly used in the design of radiation treatment plans. While these advances in anatomic imaging have improved the delineation of radiation targets, they give limited information regarding the metabolic activities of the tumor. More recently ^{18}F-fluoro-deoxy-D-glucose (FDG)-PET has been used increasingly in oncologic imaging. Malignant cells have a higher incorporation of the glucose

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analogue, FDG, relative to most nonmalignant cells. Thus this difference can be exploited to obtain metabolic or biologic information about the tumor and surrounding area. However, FDG-PET has limitations. PET has an inherent lower limit of resolution because the positron that is produced during positron decay must travel a distance away from the nucleus from where it was produced before undergoing annihilation with an electron. Also, normal tissues (brain, lymphoid tissue) and physiologic processes (muscle activity, inflammation) can lead to the accumulation of FDG by these cells, making it difficult to differentiate them from malignancy (**Fig. 1**).

Despite these limitations, FDG-PET has proved to be a useful tool in the management of head and neck cancers. Integrated PET/CT scans are able to provide both functional and anatomic imaging. Initial staging can be accomplished with a single scan that covers most of the body, thus simultaneously providing information about the primary tumor, lymph nodes, and potentially metastatic or synchronous diseases. PET is now routinely used in the staging of head and neck cancer because of its improved accuracy over CT and MR. Roh and colleagues[13] reported an improved accuracy by PET or PET/CT compared with CT/MR at detecting primary tumor in head and neck cancer patients (98%–97% vs 86%–88%). Ng and colleagues[14] reported improved sensitivity with PET over CT/MR at detecting nodal metastases in 124 oral cavity cancer patients (74.7% vs 52.6%). Sensitivity was similar between the two methods at detecting primary tumor. In a meta-analysis by Al-Ibraheem and colleagues,[15] FDG-PET or PET/CT was able to detect distant metastases or a second primary in 113 of 722 patients (16%). Patients can also present with cervical nodal metastases with an unknown primary. In another meta-analysis of 8 studies, FDG-PET or PET/CT was able to detect the primary site in 51 of 180 patients (28%) with an unknown primary who had a negative initial workup.[15]

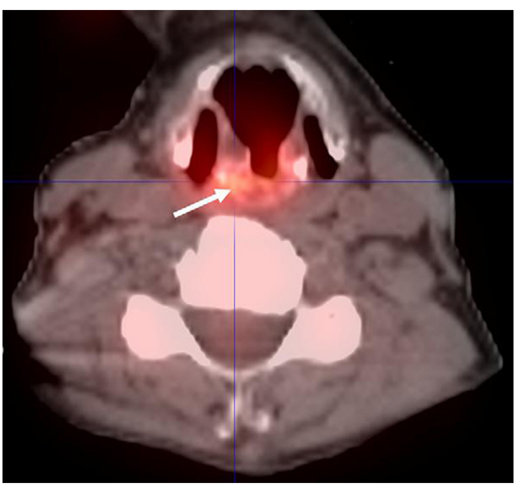

Fig. 1. Physiologic uptake of FDG by the arytenoid musculature (*arrow*).

FDG-PET can also be used to evaluate response to treatment. McCollum and colleagues[16] reported on using FDG-PET to assess response to induction chemotherapy (ICT). FDG-PET had a 100% sensitivity and 100% negative predictive value (NPV) in detecting residual disease when compared with the gold standard of endoscopic examination and biopsy under anesthesia following ICT. Yen and colleagues[17] reported that FDG-PET after ICT can be predictive of outcome in patients with nasopharyngeal carcinoma (NPC). Patients with locally advanced disease were treated with ICT and restaged by PET. Patients who were downstaged by PET were found to have a significantly improved overall survival compared with the nonresponder group (33.7 months and 44.7 months, $P = .0024$). When assessing tumor response following radiation therapy, Yao and colleagues[18] reported that FDG-PET had an NPV of 98.7% and 99% at the primary tumor site and cervical nodal sites, respectively.

PET imaging can also be a powerful tool for target delineation of tumors in treatment planning for radiotherapy. PET images have obvious advantages in target delineation when the tumor density in CT images is difficult to differentiate from that of the surrounding normal tissue such as in cancer of the base of tongue, when there is significant dental artifact, and in identifying small lymph nodes that may be missed in CT images. PET images have been increasingly incorporated into daily practice by radiation oncologists. In a random survey of radiation oncologists conducted by Simpson and colleagues,[19] 95% of respondents reported using advanced imaging for target delineation, with FDG-PET being the most commonly used (76%). The goal of this article is to explore how PET is currently being used in radiation treatment planning and to highlight areas that may benefit from further study.

IMAGE REGISTRATION

Before determining target volumes for IMRT planning, treatment planning CT and PET data must be coregistered accurately. Ideally, a dedicated PET/treatment planning CT would be obtained at the same time, in the treatment position with the patient immobilized with a thermoplastic mask so as to minimize patient movement. However, most radiation oncology facilities do not have a dedicated PET/CT scanner, and patients often