difference between discovering a tumor of head and neck versus an adjacent tonsillar mass or a supraglottic versus a glottic lesion in the larynx, respectively.

These distinctions have important implications for therapy. The limitations of separate CT and PET imaging may be compensated for when the two modalities are used in a complementary fashion. High-resolution anatomic information produced by CT adds significant data to tissue characterization revealed by PET. Computerized corregistration of CT and PET can negate the shortcomings of PET and “marry” functional and anatomic imaging in a clinical setting which both are critically important.

Originally, this result was achieved with image fusion techniques involving studies performed at different times with different settings. Alignment settings when such scans are taken at different times have not been completely successful, however, especially when dealing with structures not fixed in a bony vault. Today, integration of separate PET and CT image sets into a single study can be achieved with software fusion, and several commercial packages have been developed for this purpose.

Integrated PET/CT provides physicians with additional information on staging of cancers, restaging of cancers, patient prognosis, and effectiveness of cancer therapies. Advantages include superior lesion localization from near-perfect anatomical/functional registration with fewer motion artifacts, better distinction between physiologic uptake and pathologic uptake, consolidation of patient’s imaging studies, and shorter scan time (average 30 minutes to complete versus 60 minutes with standard PET) by using CT for attenuation correction. The last aids in patient comfort and minimizes claustrophobia problems.

CONCLUSION

The diagnosis and follow-up of squamous cell carcinoma of the head and neck is traditionally based on clinical evaluation and anatomic imaging studies such as contrast-enhanced CT or MRI. Though enormously helpful in locating suspicious areas, these modalities cannot always differentiate persistent or recurrent tumor from inflammation or post-treatment changes.

FDG-PET has been shown to be useful in the detection and staging of primary and recurrent squamous cell carcinoma of the head and neck. PET has also demonstrated its utility in the diagnosis of the unknown primary and in surveillance and surgical treatment of head and neck cancer. The advent of combined PET/CT scanners has augmented the potential for valuable information to be provided by the imaging to the clinicians who treat head and neck cancers.

REFERENCES
in less accessible sites such as the larynx. The appropriate nodal drainage areas are examined by careful palpation. Information from diagnostic imaging studies is also used in staging the HNSC patient. MR and CT scans are typically used in the detection and localization of head and neck cancers and the distinction of lymph nodes from surrounding soft tissue and blood vessels.

Structural tomographic imaging such as CT or MRI can precisely differentiate malignant tissue from normal tissue and from nonviable remnants by direct visualization of metabolic activity in vivo. PET is a functional imaging tool that is increasingly being used in the staging, therapeutic monitoring, and restaging of many malignancies. FDG, an analog of glucose, has high uptake in a wide range of tumors relative to normal tissues. Glucose metabolism in growing squamous cell carcinomas accounts for the increased uptake on FDG-PET studies. The glucose analog 2-deoxy-D-glucose is transported into the cell and metabolized in the glycolytic cycle. After phosphorylation and conversion to 2-D-phosphate, the compound remains in the malignant cells, where it can be used for imaging. Neoplastic cells, because of their proliferation, incorporate more 2-fluorine-labeled deoxyglucose, needed for nucleic acid synthesis. Uptake of 2-fluorine-labeled deoxyglucose and other enzymatic systems may manifest as increased tracer uptake.

CLINICAL UTILITY OF PET

The use of FDG-PET has direct clinical benefits in several areas:

- Primary tumors. The treatment of primary squamous cell carcinoma of the head and neck is dependent on staging of the tumor. Detection of extension to adjacent tissues and structures is important, and this is done by physical examination as well as conventional anatomic imaging with CT and MRI, which are highly sensitive for primary disease (67% to 88%) but lack specificity (50% to 75%). FDG-PET has an equivalent sensitivity (71% to 95%) but is more specific (67% to 100%).
- Regional lymph node status. Lymph node involvement dramatically reduces survival, and treatment must change in these cases. Clinical palpation is inaccurate, with false-negative rates of 5% to 44% and false-positive rates of 13% to 25%. With conventional imaging, the sensitivity for detection of lymph node involvement ranges from 36% to 95%, and the specificity from 58% to 97%. The diagnosis of involved nodes on CT or MRI is often based on size, generally using a high end of normal (1 to 1.5 cm) to differentiate benign from malignant disease. This problem is pronounced when multiple or large lymph nodes may simply be reactive to the underlying disease process.

There are many small lymph nodes that may contain cancer cells. It has been shown that many of these small nodes are actually found in lymph nodes smaller than 1 cm. These are often misdiagnosed as benign.

Because PET is a metabolic tool, it can define disease in small nodes and exclude large ones. Many studies have confirmed this ability. Overall, the data show that FDG-PET is both more sensitive (70% to 100%) and more specific (84% to 100%) than conventional imaging for detecting regional lymph node involvement.
- Unknown primary. The diagnosis of an occult primary tumor is made only if no primary tumor is detected after careful search and the primary tumor fails to appear during extended efforts to locate the primary tumor. PET is both more sensitive (70% to 100%) and more specific (84% to 100%) than conventional imaging for detecting primary tumors.

The high sensitivity of PET makes it very valuable for specifically investigating these patients. Several studies have shown that PET identifies the site of the tumor in about 40% to 60% of cases (Figures 1 and 2).13,14
- Second primary tumor and synchronous cancers. Unfortunately, despite progress in radiation therapy, chemotheraphy, and surgical reconstruction, the overall survival rate for squamous cell carcinoma of the head and neck has not improved appreciably in the last two decades.12 One factor that may significantly affect survival is the development of a second primary cancer within the head and neck. The risk of developing a second primary tumor translates to a lifetime incidence of 30% or more of patients who survive their initial HNSC.13 As many as 10% of patients with a primary HNSC may have a second primary head and neck cancer when they present for diagnosis. These tumors, as well as distant metastases, have important implications for management.
- Restaging of many malignancies. FDG-PET is both more sensitive (70% to 100%) and more specific (84% to 100%) than conventional imaging for restaging of many malignancies. One advantage of FDG-PET imaging over other imaging modalities is its ability to scan the entire body for disease activity, which may be neither feasible or practical with other techniques. Using FDG-PET as a whole-body imaging modality allows detection of ongoing second primary tumors and metastases to other organs. Stokkel et al reported that FDG-PET detected a second primary tumor in 12 of 68 patients with squamous cell carcinoma of the head and neck cancers. Among these 12 patients, only five had these tumors detected by clinical or radiological exami-inations.14 Goeres et al noted that in five of 34 patients with squamous cell cancer of the oral cavity, additional findings revealed by the body-wide PET resulted in a change of treatment plan.15
- Treatment assessment and recurrence. The assess-ment of patients after treatment of cancer of the head and neck is more difficult than assessment before treatment. Treatment itself—surgery, radiotherapy, or chemotherapy—leads to distortion of the anatomy, which can interfere with the clinical and radiological assessment of the region.

Differential relation between recurrence and post-treatment changes and scarring often requires surgical biopsy. Biopsy of the treated region is invasive, however, and can lead to wound complications. Metabolic imaging with FDG-PET is highly accurate in differentiating between post-treatment changes and recurrent disease.15 Collins et al demonstrated that if the results from both fine-needle biopsy and FDG-PET are combined, a sensitivity of 94% for detecting recurrent head and neck cancer can be achieved.16 Others, however, reported a sensitivity of over 90% with FDG-PET alone in the evaluation of recurrent head and neck cancers.15

INTEGRATED PET/CT

Although it is highly sensitive, PET suffers from imprecise anatomic localization of radiotracer uptake. FDG is also taken up by muscles and inflammatory processes as well as certain metabolically active organs such as the tonsils and salivary glands. Thus PET may provide inaccurate information on the exact location of focal abnormalities. In the head and neck region, this range of error may mean the
in less accessible sites such as the larynx. The appropriate nodal drainage areas are examined by careful palpation. Information from diagnostic imaging studies is also used in staging the HNSC patient. MR and CT scans are typically used in the detection and localization of head and neck cancers and the distinction of lymph nodes from surrounding soft tissue and blood vessels. Structural tomographic imaging such as CT or MRI can precisely delineate gross disease. Neither technique, however, can adequately rule out persistent or recurrent cancer. Early detection of a recurrence of head and neck cancer following definitive treatment may lead to less radical surgical intervention and a better outcome for the patient. Accurate initial evaluation of the primary head and neck tumor is paramount. Until recently, this evaluation relied solely on a combination of clinical evaluation coupled with anatomic imaging studies such as CT or MRI. PET technology is now being used as an adjunct to clinical and anatomic radiographic methods. Its role in staging and surveillance in HNSC continues to be elucidated.

**FUNCTIONAL IMAGING MECHANISM**

Functional PET imaging using fluorodeoxyglucose permits the differentiation of viable malignant tissue from normal tissue and from nonviable remnants by direct visualization of metabolic activity in vivo. PET is a functional imaging tool that is increasingly being used in the staging, therapeutic monitoring, and restaging of many malignancies. FDG, an analog of glucose, has high uptake in a wide range of tumors relative to surrounding normal tissues. Glucose metabolism in growing squamous cell carcinomas accounts for the increased uptake on FDG-PET studies. The glucose analog 2-deoxy-D-glucose is phosphorylated into the cell and metabolized in the glycolytic cycle. After phosphorylation of such an analog, 2-deoxy-D-glucose-6-phosphate is produced, and the compound remains in the malignant cells, where it can be used for imaging. Neoplastic cells, because of their proliferation, incorporate more fluorine-labeled deoxyglucose, needed for nucleic acid synthesis. Uptake of phosphorylated metabolites by FDG is also taken up by muscles and various metabolically active organs such as the tonsils and salivary glands. PET is also used to detect recurrent disease. PET identifies the site of the tumor in about 40% to 60% of cases (Figures 1 and 2).

**Histologic progression or recurrence or metastases to other organs.** PET identifies the site of the tumor in about 40% to 60% of cases (Figures 1 and 2).

**Second primary tumor and synchronous metastases.** Unfortunately, despite progress in radiation therapy, chemotherapy, and surgical resection, the overall survival rate for squamous cell carcinoma of the head and neck has not improved appreciably in the last two decades. One factor that may significantly affect survival is the development of a second primary cancer within the head and neck. The risk for developing a second primary tumor translates to a lifetime incidence of 30% or more of patients with a primary HNSC may be affected by this syndrome. Because PET is a metabolic tool, it can define disease in small nodes and small early-stage synchronous cancer. PET has been shown to be more sensitive than conventional imaging for detecting recurrent or metastatic disease. Biopsy of the treated region present as a malignant lymph node from a very small tonsil cancer.

**DISCUSSIONS IN PET IMAGING**

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The incidence of squamous cell carcinoma of the head and neck is approximately 50% of all malignancies, with squamous cell carcinoma being the most common histologic subtype. The five-year survival rate is approximately 60% without lymph node metastasis and 30% if metastatic nodes are present. The five-year survival rate for patients with locoregional spread of tumor that is undetected at presentation is 30% for all head and neck cancers. In addition to primary tumors being undetectable at the time of initial presentation, many patients also have anatomic limitations that prevent their complete staging including the presence of inflammatory processes and other benign disease processes. FDG-PET has been shown to be useful in the detection and staging of primary and recurrent squamous cell carcinoma of the head and neck. It has also demonstrated its utility in the diagnosis of the unknown primary and in surveillance and surgical treatment of head and neck cancer.

The advent of combined PET/CT scanners has augmented the potential for valuable information to be provided by the imaging to the clinicians who treat head and neck cancers.

Open completion of this activity, participants should be able to:

• Describe issues in staging and managing head and neck squamous cell carcinoma.
• Explain the utility of PET and PET/CT in staging primary head and neck malignancies.
• Summarize the difficulty in accessing treatment effect versus recurrent tumor with conventional imaging and the role of PET/CT in this scenario.
• List the advantages of PET/CT versus PET alone in evaluations of head and neck squamous cell carcinomas.

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Dr. Goldberg and Dr. Tufano have no significant financial arrangements or relationships with any pharmaceutical or medical device and are not affiliated in any manner with any pharmaceutical or medical device and are not affiliated in any manner with any pharmaceutical or medical device or any provider of any commercial medical or healthcare professional service.