INVITED COMMENTARY

FDG PET Imaging in Patients with Lymphoma: A Clinical Perspective

With their article in this issue of *The Journal of Nuclear Medicine*, Tatsumi et al. (*1*) add to the growing body of literature that indicates PET with FDG detects more disease sites than does conventional imaging with CT and gallium scintigraphy. The authors have extended that body of information to include PET imaging with a gamma camera. Dedicated PET detected 20 more abnormal regions than were detected by gamma camera PET (abnormalities in 18/20 of these regions were <1.5 cm), but concordant staging information was obtained for 28 of 30 patients. What is the relevance of this information to medical and radiation oncologists?

Non-Hodgkin's lymphoma (NHL) is the sixth most common malignancy in the United States, with an annual incidence of 55,000–60,000 cases per year and 24,000 deaths. The incidence of NHL has been increasing for unknown reasons approximately 3%–4% per year for the past three decades. NHL is a diverse collection of approximately 40 entities with different clinical, immunopathologic, and cytogenetic characteristics. Unlike Hodgkin's disease (HD) treatment, which is based predominantly on stage, treatment for NHL also takes into consideration the untreated natural history of the various entities that are broadly grouped into low-, intermediate-, and high-grade disease.

Low-grade NHL accounts for 40% of new cases. These lymphomas have an indolent course with a median survival of 10–12 y but are generally considered incurable. The patients usually present with advanced-stage disease that is evident by CT and physical examination. PET and other imaging studies have a limited role in low-grade NHL because therapeutic options include watching and waiting or single-agent chemotherapy. PET may be useful in confirming limited disease in the few patients with early stage I disease, because these patients may be treated with local radiation. PET may not be important for evaluating residual disease after treatment, because this type of lymphoma has no cure and is generally indolent. Approximately 10%–20% of low-grade lymphomas will eventually transform to a higher grade at one or more sites. Whether PET will have a role to play in detecting transformation is uncertain.

High-grade NHL accounts for 5%–10% of new cases. If the disease is untreated, survival is measured in weeks, although approximately 60% of patients will achieve a complete remission. PET has little role in this group because all patients receive aggressive combination chemotherapy. Radiation is not a routine part of treatment. Relapses or incomplete responses are usually clinically evident and usually do not require PET for detection or confirmation.

PET has an important role in determining the treatment of patients with intermediate-grade NHL, who compose 40% of new cases. About one third of these patients will have early-stage disease. Standard treatment consists of combination chemotherapy. In addition, involved-field radiation is used in patients with bulky disease and patients with early-stage nonbulky disease. PET may confirm early-stage disease in patients with nonbulky disease, who are then treated with an abbreviated course of chemotherapy and radiation. PET may also help define the radiation field. PET findings of advanced nonbulky disease would result in a longer course of chemotherapy without radiation. PET may detect extranodal disease and small abnormal lymph nodes missed by CT.

Although not covered in the article by Tatsumi et al. (*1*), PET may have a larger role in patients with HD, because treatment is almost entirely based on stage. HD is much less common than NHL. Approximately 7,500 new cases occur each year in the United States. HD usually spreads in an orderly fashion from one lymph node group to a contiguous lymph node group. Extranodal disease is less common than in NHL. A few reports have appeared on the usefulness of PET specifically in patients with HD (*2–4*), and several other reports have appeared on PET in mixed populations of HD and NHL (*5–14*).

Asymptomatic patients with nonbulky disease above the diaphragm and who have no more than one extranodal site are considered to have a favorable prognosis and are typically treated with an abbreviated course of chemotherapy and involved-field radiation. Young patients with nodular sclerosis or the lymphocyte-predominant subtype and a low erythrocyte sedimentation rate are considered to have a very favorable prognosis and may occasionally be treated with radiation alone. Patients who have more advanced disease are usually treated with a longer course of chemotherapy without radiation, because the advantages of combined-modality treatment are unproven. PET, therefore, has an important role to play in the accurate staging of HD because the results may determine

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whether radiation is to be used; if radiation is used, PET can accurately define the radiation field. PET may also have a role in determining whether residual disease is present after initial therapy, because survival is improved with salvage therapy. Chemotherapy may be used in patients who were initially treated with radiation, whereas high-dose chemotherapy with stem cell support may be used in patients initially treated with chemotherapy. PET may also be useful in evaluating the extent of disease after achieving complete remission with chemotherapy, because patients with relapse in one site above the diaphragm may be treated with radiation alone.

The variety of treatment options in patients with NHL and HD makes it imperative to study the role of PET in subsets of patients for whom treatment may be altered by additional imaging information. Including patients for whom the additional information has little clinical value will not be useful to medical or radiation oncologists.

Histologic confirmation of imaging results is impossible in NHL and HD, because surgery is rarely indicated. The lack of acceptable alternative criteria has impeded the adoption of PET by clinicians because the true sensitivity and specificity of PET is unknown. The approach of Tatsumi et al. (*1*), as well as other investigators, has been to establish final stage on the basis of all available data, including PET. This approach heavily biases results in favor of the least specific test, deceptively making it appear to be more accurate. The solution to this vexing problem is important not only in determining the comparative accuracy of dedicated PET versus gamma camera PET but also in determining the comparative accuracy of PET versus CT.

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