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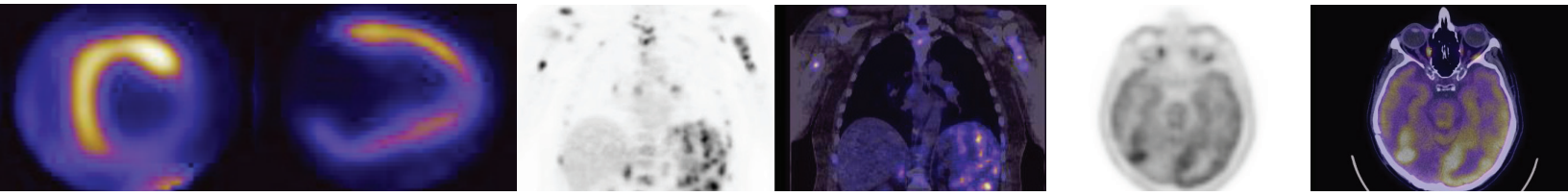

Lymphoma and Molecular Imaging: Get the Facts

About Lymphoma

Each year, approximately 75,000 new cases of lymphoma are diagnosed and more than 20,000 people die from lymphoma. New developments in molecular imaging technologies are dramatically improving the ways in which lymphoma is diagnosed and treated. Research in molecular imaging is also contributing to our understanding of lymphoma and helping to direct more effective care of patients with the disease.

What is lymphoma?

Lymphoma is a cancer of the lymphatic system—the body's main defense against infection—a complex series of lymph nodes encompassing the spleen, thymus and bone marrow. The two main types of lymphoma are Hodgkin lymphoma—which often strikes teens and young adults and is highly treatable—and non-Hodgkin lymphoma—which has many different forms and is the fifth most common cancer in the United States. Non-Hodgkin lymphoma, which can afflict individuals of any age, is classified as B-cell or T-cell—malignancies that bind to a specific molecular structure and can significantly impact the lymph nodes. About 85 percent of non-Hodgkin lymphomas in adults are B-cell in origin. B-cell non-Hodgkin lymphomas include Burkitt lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma and mantle cell lymphoma. The prognosis and treatment of lymphoma depend on the stage and type of disease.

What are molecular imaging procedures, and how can they help lymphoma patients?

Molecular imaging procedures are highly effective, safe and painless diagnostic imaging and treatment tools that present physicians with a detailed view of what's going on inside an individual's body at the cellular level. Most nuclear medicine procedures are molecular imaging procedures using radioactive substances. New and emerging molecular imaging therapies, such as radioimmunotherapy (RIT), continue to provide major breakthroughs for patients with non-Hodgkin lymphoma by allowing tailored treatments at the molecular level.

What types of MI technologies currently are available for lymphoma patients?

The most commonly used molecular imaging procedure for diagnosing or guiding treatment of lymphoma is Positron Emission Tomography (PET) scanning, which is often used in conjunction with Computed Tomography (CT) scanning. The National Oncologic PET Registry (NOPR)—a nationwide database documenting the use of PET and PET/CT in managing cancer—shows that in more than one out of three cases, PET/CT scan results prompt changes in a patient's treatment. The results, published in The Journal of Clinical Oncology, demonstrate the vital role that PET/CT can play to properly diagnose or verify the suspected recurrence. [For more information on PET/CT scanning, please read SNM's fact sheet "PET/CT Scans: Get the Facts" on SNM's Web site at http://interactive.snm.org/index.cfm?PageID=7988.] In addition, the National Comprehensive Cancer Network (NCCN) has incorporated ^{18}F-FDG PET and PET/CT in the practice guidelines and management algorithm of most types of lymphoma[1], [2].

PET/CT Scanning
How can PET/CT scanning help lymphoma patients?

Specifically, PET/CT scanning is a powerful tool for lymphoma for:

- Establishing how advanced the cancer is and whether it has spread to other parts of the body;
- Helping physicians and patients decide on courses of treatment that are tailored to patients' individual conditions and needs;
- Determining early on whether chemotherapy or other treatments are working as intended; and
- Detecting whether the disease is recurring after treatments are completed and assisting physicians in determining a site that is appropriate for biopsy, if necessary.

How does PET/CT scanning work?

PET scanning is a molecular imaging procedure that allows physicians to obtain three-dimensional images of what is happening in a patient's body at the molecular and cellular level. For a PET scan, a patient is injected with a very small amount of a radiotracer such as fluorodeoxyglucose (FDG), which contains both a sugar and a radioactive element. The radiotracer travels through the body and is absorbed by tumors or cancer cells. The patient then lies down on an examining table and is moved to the center of a PET/CT scanner. The PET/CT scanner contains a PET scanner and a CT scanner next to each other. The CT scan and the PET scan are obtained one after the other. The PET scanner is composed of an array of detectors that receive signals emitted by the radiotracer. Using these signals, the PET scanner detects the amount of metabolic activity while a computer reassembles the signals into images. [For more information on PET/CT scans and how they work, visit PET/CT Scanning: Get the Facts.]

How can PET/CT scanning help in the long-term management of lymphoma?

PET/CT scanning can help physicians gain a clear understanding of where the disease is occurring and how aggressive it is. Armed with this knowledge, physicians and patients can decide together on the best courses of treatment. PET/CT scanning can help determine how effective treatments are as soon as one cycle of treatment is completed. It may also eliminate the need for unnecessary surgeries after treatments are finished because PET/CT can determine whether any suspicious tissue masses are active tumors or residual masses.

How many PET/CT scans will patients require?

Depending on the course of treatment selected by physicians and patients, lymphoma patients may require several PET/CT scans during the course of their disease to make an accurate diagnosis and determine whether courses of chemotherapy or radiation are working as intended and ensure that patients are cancer-free after treatments have ended.

How long does it take to get PET/CT scan results?

A trained radiologist or nuclear medicine physician will interpret the results and write a report for the physician who ordered the tests. A verbal report is available the day of the PET/CT scan and the written report is usually delivered to the physician within two or three days.

Will insurance reimburse for PET/CT scans?

Insurance companies will cover the cost of most PET/CT scans. Because of the mounting evidence of the effectiveness of PET/CT scanning for the diagnosis and treatment of a wide range of cancers, coverage levels continue to expand. For the most updated figures, check with your insurance carrier or physician as the levels at which Medicare reimburses for PET/CT are under review with the Centers for Medicare and Medicaid Services (CMS) and subject to change.

What is radioimmunotherapy (RIT) and how does it work?

RIT is a relatively new personalized cancer treatment that combines the cancer-killing ability of radiation therapy with the precise targeting capacity of immunotherapy. A tumor-killing dose of a radioactive substance is linked to a specific kind of cell called a monoclonal antibody that, when injected into a patient, hones in on and attaches to cancerous tumor cells. The ability of the antibody to bind to a tumor-associated antigen—a molecule that can stimulate an immune response—ensures that the tumor gets a high dose of radiation, which kills the targeted cancer cells and nearby cancer cells. RIT is a more highly targeted therapy than traditional treatments because molecular imaging techniques and therapies can pinpoint the exact location of disease. One of the most promising areas for RIT is in the treatment of relapsed or refractory B-cell non-Hodgkin's lymphoma. Two RIT agents—yttrium-90-ibritumomab tiuxetan (Zevalin) and iodine131-tositumomab (Bexxar)—are currently approved by the Food and Drug Administration to treat these types of non-Hodgkin lymphoma and are used after conventional chemotherapies have failed.

What advantages can RIT treatments offer over traditional lymphoma treatments?

When lymphoma is first diagnosed, treatment choices depend on the cell type, extent of disease and rate of progression. Traditional management may include a 'watch and wait' approach or include a combination of external radiation, chemotherapy and monoclonal antibody therapy. Although patients usually respond to initial treatment, many patients with slow-growing lymphoma relapse and require additional treatments; these individuals often experience progressively shorter remissions and ultimately die.

Now, clinical trials are showing that patients treated with Zevalin and Bexxar after a relapse have some significant advantages. While it won't be known for a few more years whether patients have been completely cured, initial results indicate that Zevalin and Bexxar can provide:

- Prolonged remission: Virtually all non-Hodgkin lymphoma patients who receive RIT live longer because of their treatments. For example, according to one clinical trial, patients with follicular lymphoma who received standard treatment achieved remission 36 percent of the time. Yet when Zevalin was added, the remission rate soared to 89 percent. Disease-free survival was prolonged by two years using Zevalin in a recent randomized trial of over 400 patients. In a separate study, Bexxar produced at least some response in 97 percent of patients. Another clinical trial that examined the use of Bexxar in treating primary cutaneous B-cell lymphoma indicated that patients had a median of 47 months of remission after Bexxar, compared with 6 months

after chemotherapy. These results indicate that patients who receive Zevalin or Bexxar can enjoy years of disease-free survival, which is not commonly the case with any other form of therapy.

- Short, targeted outpatient treatments: RIT treatments take about two weeks to administer on an outpatient basis and there is only one infusion of the treatment dose. This is much shorter than most courses of standard treatments for lymphoma, which can include daily radiation therapy for six weeks and four to six courses of chemotherapy administered over three or four weeks. In addition, RIT minimizes toxicity to normal tissues because it kills targeted and nearby cancer cells, while normal tissue gets only a minimal dose. Chemotherapy, on the other hand, destroys any rapidly dividing cells, which often include non-cancerous cells as well as cancer cells. Because some cells tend to be especially sensitive to the effects of chemotherapy, they are often damaged or destroyed along with the cancer cells. Damage of these non-cancerous cells by intensive chemotherapy may lead to side effects such as a decreased blood cell counts, which can cause bleeding or infections; damage to the gastrointestinal tract and resulting nausea, vomiting and diarrhea; and hair loss.

What are the side effects of RIT?

RIT is generally well tolerated. Typical side effects are short-term and include fever, chills, reduced blood cell counts, low blood pressure, diarrhea and rash. Occasionally, side effects such as infection can be more severe.

How is RIT administered?

The treatment is given in one or two doses. Treatments are administered intravenously by a team of medical professionals—an oncologist, a nuclear medicine physician and a radiation safety officer—and tailored specifically for each patient. In preparation, the patient first receives an infusion of a non-radioactive antibody that attaches to non-malignant cells to protect them from the radioactive antibody used for treatment. This infusion may take up to two hours. The patient also receives a test dose of the radiotracer the same day to take pictures of the body. Over the course of the next week, a series of scans are taken to determine where the radiotracer has traveled in the body and how long it remains. Based on these scans, physicians can decide if the patient is a candidate for the therapy and calculate the appropriate dose of radiation needed for treatment. The therapy consists of a similar procedure performed one or two weeks later with a stronger radiation dose that targets the lymphoma.

How should patients prepare for the treatments?

Patients can eat and drink as usual. Patients may be asked to stop medications that could interfere with blood coagulation such as aspirin, nonsteroidal analgesics and blood thinners. Patients taking Bexxar will be asked to take a medication that helps protect their thyroid gland.

How many patients are currently receiving RIT?

It is estimated that only 5–10 percent of patients who are eligible for RIT are actually receiving it. Some experts speculate that RIT is being under-prescribed because some doctors are uncomfortable with the idea of radioactive drugs. In addition, the drugs can't be given to patients with cancer that has spread extensively to the bone marrow, and there are concerns about causing secondary malignancies or precluding later treatments if the bone marrow is destroyed. However, fewer than half of follicular lymphoma patients have clinically significant bone marrow involvement, and fears of high secondary malignancy risk and marrow destruction have so far not been borne out by clinical trial follow up.

How expensive is RIT for non-Hodgkin lymphoma and is it reimbursed by health insurance?

Bexxar and Zevalin are FDA-approved radiommunotherapies for the treatment of non-Hodgkin lymphoma. Estimates suggest that RIT is no more expensive than chemotherapy plus rituximab, the current standard of care for newly diagnosed non-Hodgkin lymphoma patients. Nonprofit medical organizations such as SNM are working with CMS to ensure that these life-extending therapies are appropriately classified as well as to expand coverage for other highly effective compounds.

Where can I get more information about lymphoma and molecular imaging?

To learn more about lymphoma, visit www.snm.org/facts. To learn more about PET/CT scanning or other nuclear medicine procedures, visit the SNM Molecular Imaging Center of Excellence.

(Endnotes)
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2 http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

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1. Witzig TE, Gordon LI, Cabanillas F, et al. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. J Clin Oncol. 2002;20:2453-63.

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