FDG—A significant development in nuclear medicine

BY PATRICK SINCO

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THE PET SCAN itself, imaged with an emerging nuclear scanning agent that has a number of medical practitioners gushing, looks like any other diagnostic image—grayish and fuzzy. This one, which nuclear physician Robert Henkin, M.D., points to on his computer, shows the skeletal system of an 11-year-old girl. What is extraordinary about the scan, however, is what is missing from it.

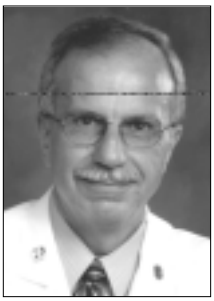
The girl had been diagnosed with non-Hodgkin's lymphoma and was thought to be in remission until a followup CT (computed tomography) scan indicated a mass growing in her chest. Her doctors grew more concerned as a gallium-67 scan—routinely used to specifically identify lymphoma—also revealed a mass in the same area of the girl's chest. Only a third image—the grayish PET (positron emission tomography) scan that was taken after injecting the girl with a sugar compound labeled with fluorine-18—showed no abnormalities.

Henkin

A biopsy finally determined that the mass in her chest was simply her thymus gland regenerating after being damaged by earlier cancer treatments. The PET image was correct: There was no recurrent disease.

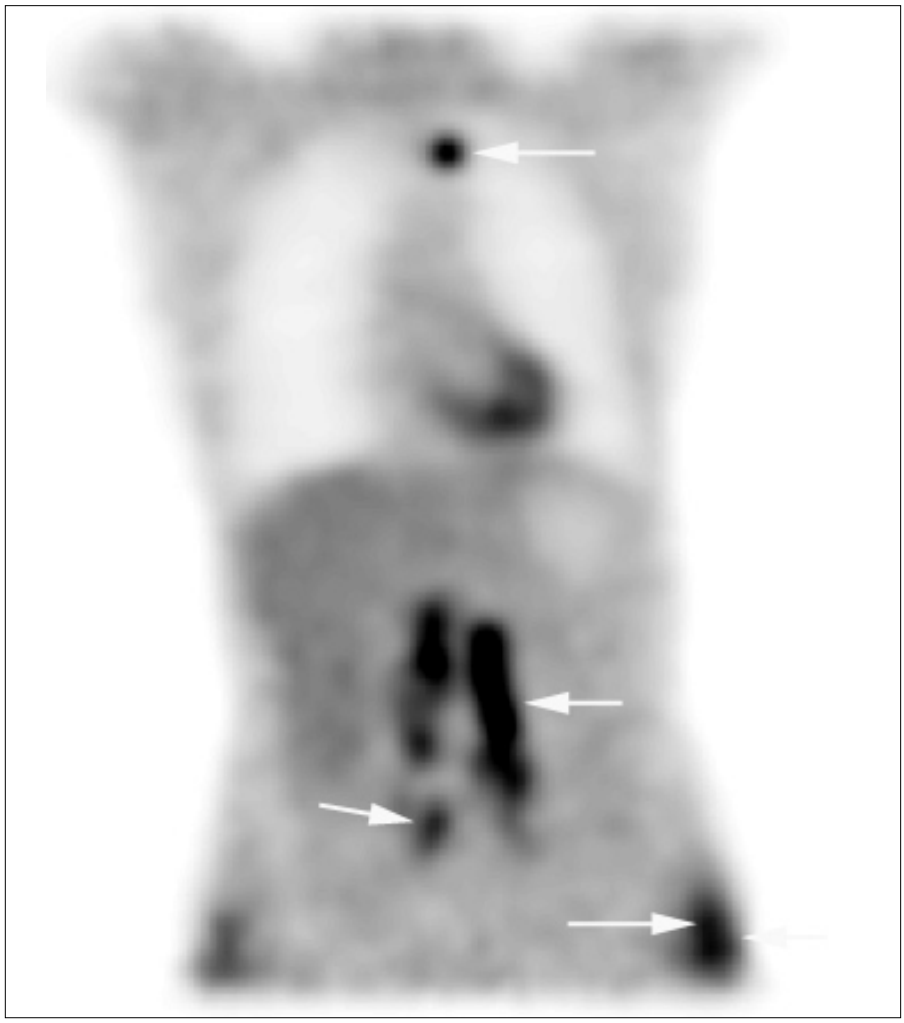
The example is one of many encountered by Henkin—professor of radiology at Loyola University Medical Center, in Maywood, Ill., and a past president of the American College of Nuclear Physicians (see *NN,* Feb. 1998, p. 30)—and his colleagues at Loyola that has excited them about the possibilities of a relatively new nuclear imaging agent, F-18 fluorodeoxyglucose, or FDG. They are not alone in their enthusiasm.

"I think that FDG will make the biggest impact [on nuclear medicine] of any molecule that was developed in the 20th century," predicted R. Edward Coleman, M.D., director of nuclear medicine in the Department of Radiology at Duke University Medical Center, in Durham, N.C. "The uses of this molecule are tremendous, and its use clinically has been shown to be very important in the management of patients. It's been shown to be extremely cost-effective in the management of patients. This molecule is going to make a huge impact on the practice of medicine."



Coleman

The compound has been studied for decades, but only in the past few years has it caught the attention of referring physicians and nuclear medicine departments around the country. Aside from important uses in cardiology and neurology, FDG has shown an ability to identify cancerous tissue undetectable by conventional means or, as in the case of the young girl, identify false indications of disease. And, unlike imaging agents that seek



This FDG study shows a 49-year-old woman with recurrent colon cancer who was a candidate for further surgery. A CT scan showed only one recurrence in the abdomen; the FDG study showed a diffuse involvement of lymph nodes in the abdomen and even in the chest (as shown by the arrows)—saving the woman from a surgical procedure that would not have benefited her. FDG is about 94 percent accurate in finding recurrent colon cancer, while CT is only about 65 percent accurate, Henkin said. (Source: Robert Henkin, M.D.)

only certain cancers in the body, FDG isn't so particular about which tumors it will concentrate in.

"The holy grail of nuclear medicine has been a tumor scanning agent that is nonspecific—a radioactive drug that is picked up by lots of tumors," Henkin explained. "In the last 30 years, there have been a lot of drugs that people have tried with mixed success. The best success to date has been had with fluorine-18 FDG."

FDG, which uses F-18 that was produced in a cyclotron by proton bombardment of oxygen-18 enriched water, works well to detect tumors because it can avidly concentrate in cancerous tissue. FDG exploits a fundamental change that occurs in cells when they become malignant: Cancer cells lose the ability to efficiently convert glucose into energy. Consequently, they require much more glucose—up to 20 to 50 times more, according to Michael Phelps, chief of nuclear medicine at the UCLA School of Medicine, in Los Angeles, Calif., and chair of the Department of Molecular and Medical Pharmacology.


Phelps

"That's a very unusual and very fundamental issue—that cancer cells turn to enormous increases . . . in their use of glucose—and all cancer cells seem to do that," said Phelps, who in 1973 developed the first PET scanner. Therefore, he explained, "FDG is incredibly important" for cancer detection. "In fact, you can see even very small tumors because their use of glucose is so amplified."

"FDG looks like sugar to the tumor, so it tends to gobble it up," Henkin added. "Because it isn't the sugar the tumor is used to, it really can't use it; it gets stuck there, and you have a chance to image it. Basically, you're fooling the tumor into thinking that it's taking up something that it needs."

FDG is most often used in PET procedures, in which a compound is labeled with a radioisotope tracer and injected into a patient. In a typical procedure, a patient is injected with FDG—a dose of 5–10 millicuries—after not eating for four hours. After a 60–120-minute wait, during which time the patient is asked to remain still and quiet while the compound travels through the body, he or she lies down under the camera system and is imaged. The scanner reads the 511-keV gamma photons resulting from the interaction of the FDG-emitted positrons with electrons in the body at locations where the FDG has become concentrated. A computer then converts the data to images for physicians to examine.

The procedure can last anywhere from six minutes for a brain scan to more than an hour for a whole body scan. Because the half-life of the F-18 radioisotope is short, 109.8 minutes, and because the compound is also excreted in urine, there is no need for the patient to take extra precautions due to the radiation—most of the compound is gone by the time the examination is over and the patient is free to leave.

"I think the era of diagnostic antibodies may be over," Henkin said. "The quality of the image is so good from FDG, it's hard to make a strong argument for continuing to use antibodies unless FDG doesn't work in that disease—and in some diseases FDG doesn't work well."

Although almost all tumors concentrate FDG to some level, Henkin said, some cancers are better suited to FDG imaging than others. Lung cancer, colorectal cancer, breast cancer, lymphoma, and melanoma are among the common cancers that avidly concentrate FDG.

Prostate cancer, however, is still being tested. "There's a lot of argument about prostate cancer right now, and we are not routinely imaging prostate cancer with FDG," Henkin said. "It was about 80 to 85 percent accurate, which is actually more accurate than the antibodies are. But, right now there's not enough data to justify switching to FDG for prostate cancer."

In studies of lung cancer, colorectal cancer, melanoma, and lymphoma, FDG has improved the accuracy of detection and staging in 8 to 43 percent of the cases compared to conventional diagnostics—which include plain films, CT scans, magnetic resonance imaging, and fiberoptic exams—Phelps said. And it changed disease management in 20 to 40 percent of the cases, depending on the clinical question, he said. "That's incredible. I mean, to step into such an important disease and make such a dramatic difference is really quite incredible."

Phelps said that in those cases in which disease management changed after an FDG-PET study, about 65 percent of them were upstaged—meaning disease was identified that was not detected by other techniques. That tends to eliminate surgeries because they won't help the patient, he said. About 30 percent of the patients were downstaged, and their treatment became simpler and their prognosis better following an FDG study.

"We actually are changing the therapy of patients," Henkin concurred. "We have one patient here who we studied who had only evidence of disease in his neck, clinically. If he was treated based on that, he would've gotten radiation therapy plus chemotherapy—but only half a dose of chemotherapy. When we scanned him [using FDG] we found other disease they didn't know about in the pelvis. So, his treatment was changed to six courses of chemotherapy and no radiation, because that's the appropriate treatment to that stage of disease."

The impact of FDG is just beginning to reverberate through healthcare systems. "The reason you don't hear as much about it [FDG] as you should hear about it is right now there are only between 200 and 300 machines in the country that are capable of imaging it," Henkin said. That number is still a nearly fivefold increase from four years ago, when there were only about 60 machines in the United States capable of imaging FDG, he noted.

At St. Louis University Hospital, in St. Louis, Mo., chief technologist Penny Yost said the number of FDG scans has increased from one study per day a few years ago to eight studies per day now. And at Duke University Medical Center, Coleman estimated that the facility is performing 12–14 FDG studies per day—an increase of 40 percent over last year. "We need a second PET scanner now—we're looking to get that," Coleman said. "And a lot of places are seeing this big growth and [are] needing more imaging devices. The institutions that didn't have imaging devices before are getting them and learning how to use them and use this molecule." NN