Proponents: PET Imaging Could Expand Role in Diagnosing Infections

When it comes to imaging otherwise hidden infections, “MRI is not even close to PET; that’s the message for today,” says Ronald Walker of Vanderbilt University Medical Center in Nashville, Tennessee. He chaired the symposium “New Imaging Modalities for Diagnosing Occult Infections,” convened as part of the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held during September 2009 in San Francisco, Calif.

Walker was comparing magnetic resonance imaging (MRI), which is widely used in clinical medicine, to positron emission tomography (PET), another imaging technology whose clinical use is generally limited to cancer patients and for viewing central nervous system functions. However, some researchers consider its broad biochemical range advantageous and potentially applicable to many infectious diseases.

Walker and a small cohort of clinicians using PET experimentally for distinguishing infectious diseases from cancers would like to see these applications expand. “PET is very cost-effective, and its cost will go down,” says Abass Alavi, another participant in the ICAAC symposium, who is from the University of Pennsylvania Medical Center in Philadelphia. “We’re trying to convince Medicare to pay for this. We’re really in bad shape with regard to reimbursement.” Medicare is the U.S. national health insurance program for individuals who are 65 or older (and for the disabled), and its reimbursement policies can determine whether experimental technologies such as PET scans for diagnosing infectious diseases will be widely adopted.

PET, as its name implies, depends on molecules that are labeled with positron-emitting nuclides. When injected into individuals, those labeled molecules travel to particular cells or tissues, from where positrons are emitted, and then detected and recorded either by film or electronic sensors. As with X-rays in the case of computerized tomography (CT), PET signals can be used to construct three-dimensional (3D) images, based on input data coming from many different angles and positions.

At some facilities, CT X-rays and PET scans are done with single instruments that take separate but nearly simultaneous scans, yielding anatomic and metabolic-based images, respectively, of the individual being examined, according to Walker. The separate images then can be overlaid to generate a composite image. Unlike purely X-ray-based CT scans, however, PET can draw on a variety of nuclide-labeled biochemical molecules to detect distinct metabolic activities or molecular interactions. Thus, for example, labeled deoxyglucose is used to focus on simple sugar metabolism within cells, while labeled versions of antimicrobial peptides are being developed to bind and detect bacterial pathogens.

“Ultimately, we’d like [PET] to be more specific,” Walker says. Nonetheless, it is a “clear winner for osteomyelitis.” For example, when fluoro-deoxyglucose (FDG) is used when trying to distinguish a tumor mass from an infection, FDG localizes and is trapped in infected cells but not in...
tumor cells because the latter typically lack the enzyme glucose-6-phosphatase, he says. Adds Alavi, “There is increased glycolysis where there is an infection and inflammation, and increased glucose uptake by such cells.”

A combined CT-PET reading “can tell the difference between an infection and tumor, which is useful even when a patient is immunocompromised,” Walker says. This difference tends to be masked when patients are examined via CT or MRI, particularly for those patients receiving high doses of steroid drugs, he points out. “PET did very well even where other infection-imaging [methods] would be dismal.”

The list of different anatomic sites and infections for which PET has proved useful continues to grow, according to Walker. “A myeloma patient had liver lesions that turned out to be a fungal infection that we detected with PET,” he says. “Another patient with multiple myeloma and a hip replacement turned out to have osteomyelitis.” Knowing that an infection has developed at a deep-seated site can prove critical when deciding how to treat patients.

Altogether, U.S. doctors do about 1 million hip replacement procedures per year, with a rate of prosthesis infection following surgery as high as 4%, according to Alavi. “PET can determine whether there is an abscess versus an infection along the prosthesis itself,” he says. Abscesses typically are more readily treatable and, for instance, can be drained without damaging or replacing the prosthesis. However, if a biofilm infection forms along such a prosthetic device, antibiotic treatments typically fail, and replacement surgery may be required. PET scans provide “very high sensitivity and specificity” for distinguishing between infection and inflammation in cases affecting prosthetic hips, and are “even better for knee prostheses,” he says. PET scans are also more rapid, give better images, and appear to be more cost-effective than another imaging procedure that depends on labeled white blood cells, he adds. However, to gain wider acceptance for PET, “we need a multicenter clinical trial, and we have to do it for the sake of our patients because a lot of them are suffering.”

Meanwhile, considerable effort goes into developing markers for PET that will be even better at detecting infectious agents. For example, several technetium-labeled, chemical derivatives of ubiquicidin, which is a 59-amino acid peptide with antimicrobial activity, “preferentially bind to microorganisms instead of the host” and give “very high accuracy compared to FDG” when used to distinguish pathogens from leukocytes, says Mick Welling of Leiden University Medical Center in Leiden, the Netherlands, who also spoke during this ICAAC symposium. In the first series of clinical studies, the use of these semisynthetic peptides “improved images, gave high sensitivity and specificity, resulted in lower costs, and were well tolerated by patients.”

Taking yet another approach, a research group at the University of California, Los Angeles (UCLA) is evaluating a series of “nucleoside salvage probes,” says Evan Nair-Gill from UCLA. Some of the probes are “differentially sequestered in innate and adaptive immune-response cells.” Moreover, one compound within this group of experimental probes is being evaluated for its ability “to track CD8 T cells as they respond to tumors or chronic viral infections,” he adds. Although clinical findings are preliminary, this approach could prove “broadly applicable, including to [monitor and detect] infections and autoimmune diseases.”

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Ancient Endosymbionts May Have Led to Double-Membrane Bacteria

Ancient clostridia and actinobacteria formed an endosymbiosis that eventually led to the double-membranated, or