Advances in PET Scanning

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PET/CT, PET/MR and radiotracers all pushing PET into new applications

While PET scans are well established in diagnosing and staging cancer, researchers say the technology’s potential is untapped, with exciting advances on the horizon. Researchers are looking for different applications for PET scanning, testing new radiotracer agents for organs and disease processes not well visualized with FDG, and monitoring treatment effectiveness.

Before 2000, PET scans were just that, PET scans, according to Vivek Bhatt, General Manager of GE Healthcare’s PET division. The scans showed the level of radiotracer uptake, pinpointing activity levels of cancer cells, but without an understanding of the involved organs or anatomical features. Were you looking at a lymph node? An organ? That’s where PET/CT came in, superimposing the CT’s anatomical details onto the PET-provided cellular activity level.

According to Bhatt, using MR for that anatomical detail was considered as early as 2002, since it’s better at differentiating soft tissue in the brain, liver and spine than CT.

“A major thing right now in our field is getting into some other applications of PET,” said Abass Alavi, MD, professor in the department of radiology at University of Pennsylvania’s School of Medicine. Alavi noted that cancer has been PET’s main focus over the past 20 years. “It can be used for diagnosis, but it’s mostly used for staging, seeing the extent of the disease, response to treatment, and looking for follow-up recurrence. It’s been revolutionary. We see the extent of the disease much more because it’s at least 20% more sensitive than CT.”

New Radiotracers

While the FDG radiotracer agent is still the gold standard, researchers are working on new tracers that would allow PET scans for different uses. “We have barely touched the ground even with the drug like FDG,” said Alavi. There is also a lot of interest in developing more targeted tracers for liver, prostate and cardiac imaging, angiogenesis, Alzheimer’s disease and Parkinson’s disease. “These are situations in which FDG is not the ideal tracer to use,” said Bhatt.

Alzheimer’s disease is one of the hottest areas. JAMA published a study in January, 2011 by Christopher Clark, MD of Avid Radiopharmaceuticals, showing promise that their biomarker was able to detect beta amyloid in the brains of living patients. Being able to confirm Alzheimer’s disease in living patients, especially before dementia or other symptoms appear, could help researchers develop and test medications to treat the disease.

“One of the areas that’s exciting is in amyloid imaging for Alzheimer’s disease,” said Carolyn Cicis Meltzer, MD, chair of radiology at Emory University School of Medicine. “Agents like the f18 AV-45 are particularly promising, for binding to amyloid.”

Researchers have looked at amino acids as one approach to developing more specific tumor markers, as well as receptors that could be tumor markers, such as estrogen receptors in breast cancer, said Meltzer. Other proteins may be markers for disease processes, like amyloid is for Alzheimer’s disease. “The idea is to get as specific as possible with the markers that we target,” said Meltzer.

Within the cancer realm, researchers are looking at markers of hypoxia, since tumors outgrowing their blood supply rely on anaerobic metabolism. Meltzer said that while the agents developed the past for hypoxia weren’t very sensitive, newer agents are showing greater promise.

Hybrid PET/MR Machines

Three companies have introduced some form of hybrid PET/MR technology (see sidebar). “The great advantage of MR/PET will be simultaneous functional imaging which you don’t have from PET/CT, which is sequential,” said Meltzer. Her department was one of two U.S. sites to have an early prototype of Siemens’ PET/MR machine.

Siemens Healthcare Biograph mMR is the most advanced of hybrid technologies, and actually scans the patient only once, taking about 30 minutes. It just received its CE mark in early June, so European customers can use it for routine clinical use. In the U.S., it’s being used for clinical research at Massachusetts General Hospital. (Siemens recieved FDA approval in the US post-publication.)
Philips Ingenuity TF system places the PET scanner and MRI scanner at opposite ends of the patient table. The table is rotated between exams, to allow scanning from the same position. This scanner received its CE Mark in January of this year. The only PET/MR technology available in the United States is GE’s Tri-Modality Imaging PET/CT + MRI. It’s not a true hybrid, because the machines are not only separate, but in different rooms. However GE’s software merges data from the two scans and the machines can be used independently.

While software fusing PET and MR images has been available for a number of years, “GE’s very elaborate and complicated system is unique in its design,” said Alavi.

Alavi said that PET/CT has established itself as an important and in many ways a required modality to practice PET, however “PET-MRI is still considered experimental at this stage and it will take a while before we will realize how important its contribution will be. The excitement from PET/CT cannot be translated to PET-MRI at this time.”

Meltzer had similar thoughts. “Certainly I don’t think it’s going to be as big a mainstream hit as PET/CT, though we didn’t foresee at that time that PET/CT would be the unifying modality that it’s become. MR/PET is still searching for the right clinical application, and working out the bugs in terms of the technical aspects.”

Part of the research is to find out where PET/CT is superior to PET/MR, and vice versa. “Just having a PET/MR system doesn’t necessarily mean that it will be better than PET/CT in all cases,” said Bhatt, noting that CT is currently a better technology for lung imaging than MR. He added that a PET/MR combination, along with new tracers, could potentially create tools that are not available today. The technical aspects have been challenging for developers. Alavi said that the main issue with PET/MR is correcting for attenuation of gamma rays emitted from positron emitting isotopes. “X-ray from CT is ideally suited for this purpose. This is an extremely serious problem with MRI and it may never become solvable. Therefore, the use of PET-MRI is mostly confined to brain disorders where attenuation correction is a minor issue.”

Bhatt noted that the challenge in developing a PET/MR machine is that a standard PET detector, an analog photomultiplier tube technology, won’t work in a hybrid PET/MR machine. Instead, what’s needed is a digital technology like the more mature avalanche photodiode detector or the newer, better performing silicon (solid-state) photomultiplier, which is more capable of the latest reconstruction techniques. Bhatt said that GE wants to have both a solid-state photomultiplier and Time-of-Flight capability in a PET/MR machine, but he was not able to comment on when a machine like this would be available.

**PET for Monitoring**

While researchers know the value of PET for diagnosing and staging cancer, Bhatt says the future of PET imaging is therapy monitoring. Rather than just imaging the patient at the beginning and end of chemotherapy, he said physicians will be monitoring patients more frequently to determine how well the treatment is working. “Clinicians want to reduce variability and make quantification repeatable enough so they know whether the tumor trends are going down or up,” Bhatt said. He noted that pharmaceutical companies are working on developing quantitative biomarkers for this.

Another type of quantification, said Alavi, is being able to quantify the extent of the disease with a number. “We think that with new, modern quantification, which we can’t do with CT or MRI, we can see the extent of the disease. These are valuable pieces of information you cannot get with other modalities.”

PET scanning is helping monitor the therapy of patients with tuberculosis. The Journal of Nuclear Medicine published a study in May, with patients who underwent tuberculosis treatment, with scanning before and then four months after treatment began. They found the maximum standardized uptake value, the lymph nodes involved, and which patients responded to treatment. “Therapeutic evidence can be seen early on with PET scanning, whereas those changes won’t show on CT for a long time,” said Alavi.