Hybrid Technologies Explode Onto the Scene

Hybrid imaging systems have long been useful for staging in early phases of disease, but are also quickly gaining recognition as a valuable option for monitoring treatment response.

By Joanna Downer, PhD

In many ways, the hybrid systems combining computed tomography (CT) with positron emission tomography (PET) and with single photon emission computed tomography (SPECT) are but children. But because their component technologies have been around much longer, machines coupling anatomic and functional imaging have exploded onto the scene at medical centers around the world – and their applications are growing.

Just two years ago, Siemens introduced its hybrid TruePoint™ SPECT·CT scanner at the Society of Nuclear Medicine meeting in Philadelphia (July 2004). Just eight years ago (1998), the first prototype PET·CT scanner, partially funded by an NIH grant from 1995, was built in Knoxville, Tennessee, and put into clinical use at the University of Pittsburgh Medical Center. Even one of the prototype's developers, David Townsend, PhD, is surprised at how hybrid technologies have been adopted into clinical practice.

"Building a prototype PET·CT scanner was a state-of-the-art research project when we got funded in 1995," says Townsend, now Director of the Cancer Imaging and Tracer Development Research Program at the University of Tennessee Medical Center in Knoxville. "It took three years to build, a year of reporting our results to get it appreciated, and then it just took off when commercial machines became available. It has made a lot more progress than I expected."

In part, Townsend says, hybrid PET·CT technology has benefited greatly from good timing. As the prototype entered clinical service in May 1998, the United States Center for Medicare and Medicaid Services announced they would authorize reimbursement of PET scans for patients with certain cancers. Approval of reimbursement for Medicare patients in turn led other insurers to reimburse for PET scans in certain cases, too.

"The two things went together," says Townsend. "People would probably not have bought hybrid PET·CT scanners if there hadn't been reimbursement of PET scans. Think of it this way: PET would have expanded without

hybrid technology, but PET·CT wouldn't have expanded without reimbursement for PET."

Now there is no going back. PET·CT and SPECT·CT have been proving their value in improving patient throughput, retaining or improving image quality, and increasing interpretation confidence. Initially used for staging to uncover distant metastases that might preclude surgical intervention, hybrid scans have lived up to the expectation that they would impact treatment decisions when used for staging cancers.

"In the 'old' days, ten years ago, PET was used as a problem-solving tool," says Homer Macapinlac, MD, Director of the PET Center at The University of Texas M. D. Anderson Cancer Center in Houston. "But with the advent of PET·CT, it is one of the first studies – if not *the* first study – ordered for staging patients with thoracic tumors, such as small-cell lung cancer. It is so useful at directing appropriate treatment options. There's a lot of data showing that for this purpose, PET·CT is better than PET alone or CT alone. When the PET is negative, the CT can be used to direct the biopsy to enlarged nodes that might harbor microscopic disease that can't be detected by PET."

Plus Points: Fast, Accurate, and Compatible

Another advantage of hybrid systems is that they take a fraction of the time of doing two separate scans. For one, the patient only has to be positioned once. And unlike single-modality scanners, the hybrid systems do not require a lengthy rotating-source transmission scan for attenuation correction because the CT data serves double duty, saving time.

Moreover, physicians familiar with PET·CT and SPECT·CT hybrid systems would not give up the extra confidence they have when evaluating images in which the anatomic and functional information is perfectly co-registered. "There are, of course, still PET scanners out there doing good work, but the added value of the PET·CT is extremely important," says Townsend. "PET·CT improves the readability and interpretation of a lot of studies."

BIOGRAPH™ TruePoint PET·CT (above) and Symbia TruePoint SPECT·CT (below) are the flagships of Siemens hybrid imaging product portfolio.

Because the value of PET·CT and SPECT·CT is in the combination of the studies, images should be interpreted together, say both Macapinlac and Townsend. As a result, PET·CT has helped blur the line between the traditional fields of radiology (home to CT) and

Homer A. Macapinlac, MD

Homer A. Macapinlac, MD, is an Associate Professor of Nuclear Medicine at The University of Texas M. D. Anderson Cancer Center in Houston, TX. He is also the Center's Chairman ad interim of the Department of Nuclear Medicine, Chief of Clinical Nuclear Medicine, Director of the PET facility, Chief of Positron Emission Tomography (PET), and Chief of Clinical Translational Imaging for the Department of Experimental Diagnostic Imaging. He received his BSc in Biology from the University of the Philippines and did his internship at the Ramon Magsaysay Memorial Medical Center and the Philippine Ministry of Health's Rural Health Practice Program. Fellowships at the University of California School of Medicine in San Francisco and the Memorial Sloan-Kettering Cancer Center in New York followed. His association with Sloan-Kettering also included positions as Chief Resident in Nuclear Medicine Service, Assistant (and later Associate) Attending Physician and Clinical Director of the PET facility, and various administrative appointments and responsibilities associated with the Center's Nuclear Medicine Division. A respected international lecturer and trainer on PET, Macapinlac is also an expert consultant for the International Atomic Energy Agency in Vienna, Austria.

nuclear medicine (home to PET and SPECT). Turf battles aside, the two specialties are meeting the challenge.

"We have tried to use faculty members of each specialty to help train other physicians and fellows, and to train them to interpret the images in an integrated fashion," says Macapinlac. "We need to describe functional and anatomic findings in a single report. It will be much more efficient and useful if it's possible."

Already, many radiologists are seeking additional training in PET and SPECT image evaluation, and many nuclear medicine specialists are being trained to interpret CTs. The American College of Radiology and the Society of Nuclear Medicine have published guidelines for PET·CT certification, although no guidelines are available yet for SPECT·CT. Similarly, individuals are becoming certified as both radiology and nuclear medicine technologists, so a single person can run a hybrid scanner.

Versatility Expands Application Options

Hybrid systems are also affecting other specialties as the power of hybrid images becomes clear. In some cases, hybrid images are actually being used to help direct surgery – not just whether to perform surgery, but how to do the surgery, particularly in the neck and abdomen.

For example, in the neck, a surgeon might use the anatomic and functional data to determine where to make an incision and at what angle to approach a parathyroid adenoma for a minimally invasive parathyroid resection. Such applications are likely to become more common if images are available in a volumetric – rather than slice-by-slice – presentation, says Macapinlac, whose team is working on just such a project.

Another new application of hybrid technologies' combination of function and form is SPECT·CT's use to image infection and inflammation, a common result of cancer patients' immunocompromised status. By using gallium^{-67}, technetium^{-99m}, or indium^{-111} labeled white blood cells with SPECT, physicians have been able to detect areas of infection or inflammation, but using the hybrid system is proving to be even better.

"Having SPECT with CT allows us to better localize the infection and even determine what type of infection is present," says Macapinlac, adding that these preliminary findings are being prepared for presentation. "The activity from the SPECT tells us where to look on the CT, and the CT might reveal a pattern of infection indicative of a particular type of infection – say pneumonia caused by tuberculosis. This could be helpful for infectious disease specialists, too."

Because of its utility for inflammation, SPECT·CT can also be used to distinguish between recurrence in the bone and a benign cause of bone pain – severe osteoarthritis for example – in cancer patients with rising tumor markers but no pain, or perhaps with pain and no elevated markers.

"If you have a bland-looking SPECT but the patient has pain, the CT allows us to look very closely," says Macapinlac, whose facility has five Symbia® TruePoint SPECT·CT systems. "Having two studies together allows us to make a more accurate assessment. We can't say yet that SPECT·CT should be the first method for screening for osseous metastases, but we hope to have recommendations soon."

Hybrid technology also is being used to evaluate response to treatment much earlier than in years past, so that a failing treatment can be changed or important prognostic information can be uncovered.

"The best example of this is PET·CT and lymphoma," says Macapinlac. "We usually do a baseline PET·CT study and then another one after just two cycles of therapy, instead of at the end of treatment. The data show that patients who do well long-term have an early demonstrable drop in FDG activity. PET·CT demonstrates this metabolic response."

Future Potential: Screening for Disease

Studies of treatment response in multi-center studies should be eased by the recent (June 2006) publication in the *Journal of Nuclear Medicine* of consensus recommendations for

»We can't say yet that SPECT·CT should be the first method for screening for osseous metastases, but we hope to have recommendations soon.«

Homer Macapinlac, MD,
Associate Professor
of Nuclear Medicine,
The University of Texas
M. D. Anderson Cancer Center,
Houston, TX, USA

David W. Townsend, PhD

David W. Townsend, PhD, was honored by *Time* magazine in 2000 with the Invention of the Year Award for the PET·CT scanner. His paper on PET·CT is the third most frequently cited *Journal of Nuclear Medicine* publication of all time. In 2004, he received the Distinguished Clinical Scientist Award from the Academy of Molecular Imaging. Currently Director of the Cancer Imaging and Tracer Development Program at the University of Tennessee Graduate School of Medicine, Townsend has a BSc in Physics from the University of Bristol, a PhD in Experimental High Energy Physics from the University of London, and a Docent in Medical Imaging from the University of Geneva. A former staff member at CERN in Geneva and later a Co-Director of the University of Pittsburgh PET Facility, he has served as a visiting scientist, consultant, and analyst to numerous hospitals, laboratories, corporations, and universities around the world during his more than 25-year career. He has lectured extensively on PET instrumentation, applications, and the development of the PET·CT scanner.

FDG-PET in National Cancer Institute-sponsored trials. These recommendations cover every aspect of imaging, from preparing the patient to image acquisition to attenuation corrections to image construction and even when to re-image, and they should make inter-institution comparison simpler.

But although hybrid technologies' applications are expanding – to different cancers and to different aspects of treatment planning – perhaps nothing is as tantalizing as the technologies' potential in screening for certain diseases. Although it is still just an idea, hybrid technologies could play important roles in screening for lung cancer in people at high risk and in detecting the earliest stages of heart disease, still the number-one killer in the United States.

"As I understand it, cardiologists think that some heart disease can begin as 'vulnerable plaque' that forms in the artery walls and doesn't occlude the blood vessel, and then it just bursts out causing heart failure," says Townsend. "If so, looking only for occlusions could miss subtle disease in the arterial wall. Detecting vulnerable plaque is therefore going to be a metabolic imaging problem, not an anatomic imaging problem. This is a huge opportunity for hybrid technology."

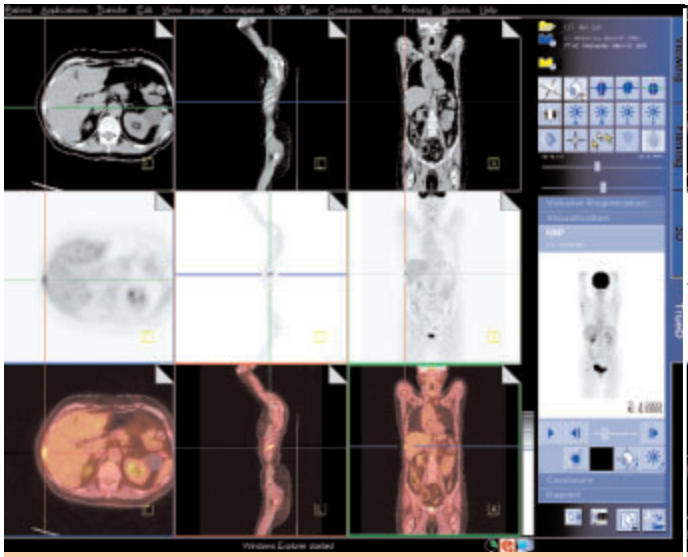
Similarly, lung cancer has only a 50% five-year survival rate for tumors caught at the earliest stage, and a survival rate near zero for anything more advanced. Given the disease's lack of noticeable symptoms, screening for early detection in individuals at very high risk of disease might improve survival more than anything else, short of global smoking cessation.

But while hybrid technologies must await new biomarkers and radiotracers – in addition to a better understanding of the disease process – before they are used in screening, they have already proven themselves invaluable in staging, directing treatment decisions, and increasingly in measuring response to treatment. Not bad for the new kids on the block.

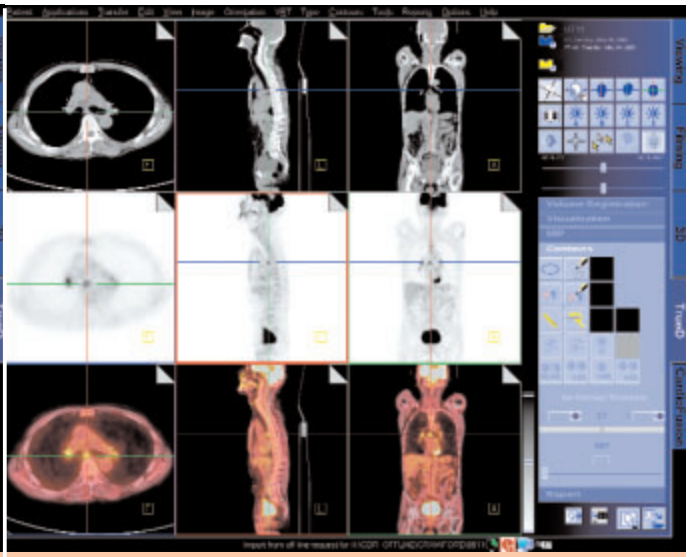
Author: *Joanna Downer is based in Durham, NC. She holds a doctorate in nuclear chemistry from Washington University in St. Louis, MO.*

»PET·CT improves the readability and interpretation of a lot of studies.«

David Townsend, PhD,
Director of Cancer Imaging and Tracer Development,
University of Tennessee Graduate School of Medicine,
Knoxville, TN, USA



CORONAL, SAGITTAL, AND TRANSVERSE PET·CT images of a 65 year-old patient with a six-year history of breast cancer. The patient was referred for a PET·CT scan following rising CEA levels over an eight-month period. The scan shows focal uptake in the ninth rib that is of concern for metastatic bone disease. The finding was subsequently confirmed from a bone biopsy.



CORONAL, SAGITTAL, AND TRANSVERSE PET·CT images of a 69 year-old male patient with right upper lobe lung nodules. The focal bilateral hilar activity is due to an inflammatory process, as is the low-level uptake in a speculated right apical nodule. The scan demonstrated no evidence of malignancy.