INVITED COMMENTARY

PET/CT in Colorectal Cancer

After the prototype PET/CT scanner was introduced by David Townsend and his team, dual-modality imaging has remained in the spotlight. Their device combined a PET scanner and a CT scanner, permitting subsequent mechanical fusion of the images separately acquired by each modality. They produced a fused head-and-neck scan that was selected as image of the year at the 1999 SNM congress (*1*). Later, improvements were introduced and devices built that combine SPECT or PET with CT. The marriage of nuclear medicine and MRI has been attempted, remains a challenge, and is still investigational (*2*).

In this issue of *The Journal of Nuclear Medicine,* Cohade et al. report their experience with an in-line PET/CT device in colorectal cancer (CRC) (*3*). They focused on 2 aspects of the lesions that were identified: the type (i.e., malignant or benign) and the anatomic location. For PET, the conventional technique of attenuation correction was applied, that is, measured with a positron-emitting transmission source (^{68}Ge). The duration of the transmission scan was 3 min per bed position, and a segmentation algorithm was used to calculate the attenuation map. The PET images were generated with iterative reconstruction techniques, yielding a standard upper body scan. CT images were reconstructed with filtered backprojection.

The criterion standard, or final diagnosis, was established by a consensus panel of 3 imaging experts; only a limited number of lesions were verified by pathology. The results of a single nuclear medicine reader with "moderate experience" were presented. The purpose of the CT was to help the physician in interpreting the study, localize the lesion in anatomic terms, and categorize the lesion in pathologic terms (benign vs. malignant). These results were contrasted with the interpretation of PET images alone. The advantage of this paradigm is clear: The PET-alone reading, which is the current clinical standard, with numerous reports in the literature, can be compared directly with this new PET/CT reading.

Two methods of data analysis were used: lesion based and patient based. For lesions, the certainty of anatomic location and lesion type were scored. After pooling of data in positive, negative, and equivocal categories, the obtained results were compared with the consensus evaluation. In this study setting, Cohade et al. found that the uncertainty in lesion location decreased by 55% and in lesion type by 50%. These differences did not translate into a different performance for PET alone versus PET/CT. There were no statistical differences in sensitivity, specificity, or accuracy. In addition, disease stage determined with PET alone was compared with that determined with PET/CT. The accuracy of staging CRC increased 11%.

There were several shortcomings in the Cohade study (*3*). It was retrospective, had relatively few patients, included patients with advanced disease, had a selection bias, and presented the results of a single inexperienced reader. The authors were able to demonstrate a decrease in uncertainty of about 50% in both lesion localization and lesion characterization. What was measured in this study? The authors evaluated how the inexperienced reader compared with the consensus panel of 3 experienced readers. In this respect, it is not warranted to conclude that the accuracy of staging increased by adding PET/CT. Verification of data by pathology or by outcome analysis was insufficient to establish the final diagnosis. The decrease in uncertainty of the inexperienced reader translated into an approximately 10% increase in correct assignments of the clinical stage, which is not the pathologic stage. Accuracy cannot be established with this study design.

As the authors point out, the gain by PET/CT is not "tremendously high" (*3*). One has to keep in mind that the sensitivity and specificity of ^{18}F-FDG PET for staging CRC is already quite high, as was established nearly a decade ago (*4,5*). In the early days, PET was compared with thin cross-sectional CT slices with gaps in between. Currently, helical CT acquires the entire volumetric dataset; there are no more gaps between the slices, improving CT performance. Although a significant advantage of PET over CT has been amply documented (*6,7*), PET has size limitations and frequently misses tumors smaller than 5 mm. The study of Cohade et al. demonstrated that an inexperienced reader benefits from registration and fusion of PET to CT. The certainty that an area of increased ^{18}F-FDG accumulation constitutes a lesion is clearly increased. Although this did not significantly increase PET/CT staging over staging with PET alone, Cohade et al. found an overall improvement of 11% in the staging of CRC. In a group of 169 patients referred for staging of a variety of neoplasms, our group found a 12% improvement by PET/CT (*8*).

Since the advent of clinical PET in the 1990s, nuclear medicine specialists are often confronted with a lack of identifiable structures and landmarks in the whole-body ^{18}F-FDG PET scan. The introduction of attenuation correction was a significant improvement; the images started to reflect a real patient body instead of a halo of hot skin around subcutaneous fat. However, attenuation cor-

Received Jun. 13, 2003; revision accepted Jul. 9, 2003.

For correspondence or reprints contact: Christiaan Schiepers, MD, PhD, Department of Molecular and Medical Pharmacology, Ahmanson Biological Imaging Clinic, UCLA School of Medicine, 10833 Le Conte Ave., AR-144 CHS, Los Angeles, CA 90095-6948.

E-mail: cschiepers@mednet.ucla.edu

rection did not solve all problems and created new ones by increasing and amplifying image noise. Software developments such as segmentation, attenuation-weighted and iterative reconstruction, and scatter correction are now routinely applied, furnishing high-quality images of the whole body. This can be achieved with PET/CT in less than 30 min of acquisition time and almost real-time processing.

The authors indicated that they would also evaluate the performance of more experienced readers and the different methods to correct for attenuation (*3*). These types of studies are necessary to sort out the contribution of every step in PET/CT that differs from standard dedicated PET.

Some main areas of contribution for PET/CT are precise localization of the bowel and lymph nodes, and association of physiologic ^{18}F-FDG uptake with gastrointestinal mucosa, which is quite variable. These areas are even more important for restaging and therapy monitoring after surgery, when the anatomy has been changed. The contribution of breathing is less important for the abdomen (*9*) than for the chest. Even the so-called "mushroom" effect of the liver does not seem to pose a real clinical problem in the staging of CRC. Non–attenuation-corrected tomograms and 2-dimensional projection images are always available to check for possible artifacts. To reduce bowel uptake, some use pharmacologic interventions that inhibit secretion and motility, but this step does not seem necessary routinely.

Critics may remain unconvinced of the additional value of PET/CT in the diagnosis and staging of cancer (*10*). More studies will be needed to assess the additive value of PET/CT over PET alone in diagnostic imaging. For instance, evaluation of the effects of intravenous and oral CT contrast agents on the PET images has just started (*11*,*12*). Much more work is ahead. PET/CT also involves local politics and perhaps a turf issue, as was addressed in recent letters to the editor of the *European Journal of Nuclear Medicine and Molecular Imaging* (*10*,*13*).

PET/CT has, however, already influenced the way we read standard ^{18}F-FDG PET scans. Accurate localization of muscle and brown fat uptake by PET/CT has been demonstrated (*14*). These patterns are found in young, tense, skinny, or shivering patients and are physiologic variants, now recognized in PET-alone readings. Exchanging information and sharing experience with the PET/CT experts has led to this improvement in interpretation of routine ^{18}F-FDG PET studies.

It would be desirable to quantify the difference between mechanical-fusion images and fusion of separately acquired PET and CT images to answer the question of whether software fusion suffices in clinical practice. Such studies are extremely difficult to perform, since patients cannot be used as their own control. Many PET and CT scans would have to be performed in a short time. The other way, direct comparison of 2 groups of patients, implies a financially prohibitive trial that is randomized, multicenter, and matched for age, sex, and disease.

Therapy monitoring will become increasingly important and will have a major impact. PET/CT will soon play an important role in the planning of radiotherapy. This will be relevant for all types of cancer, including CRC.

Finally, we should not forget the reasons for doing these scans, that is, providing the referring physician, whether a surgical, medical, or radiation oncologist, with diagnostic information about the patient to whose care the physician is entrusted. From the patient's point of view, PET/CT is a tremendous plus with regard to preparation time and time in the imaging suite. In addition, modern technology produces high-quality images, reflecting anatomy and metabolism, and key pictures can be provided to the referring physician electronically. The physician, in turn, can share this information with and explain it to the patient. Therefore, the highest-quality images, corrected for all degrading effects such as nonuniformity, singles, randoms, depth of interaction, decay, attenuation, scatter, and motion, should be provided. Then, we will be able to provide optimal clinical service to both the patient and referring physician.

PET/CT is a technology in evolution and is here to stay. Faster detectors and multislice acquisitions will provide an even more patient-friendly device, offering a single-session diagnostic examination for managing the oncologic patient.

Christiaan Schiepers, MD, PhD
David Geffen School of Medicine at UCLA
Los Angeles, California

REFERENCES

1. Wagner HN Jr. SNM 1999: fused image tomography—an integrating force. *J Nucl Med.* 1999;40(8): 13N–14N, 17N–18N, 21N–22N.
2. Townsend DW, Cherry SR. Combining anatomy and function: the path to true image fusion. *Eur Radiol.* 2001;11:1968–1974.
3. Cohade C, Osman M, Leal J, Wahl RL. Direct comparison of ^{18}F-FDG PET and PET/CT in patients with colorectal carcinoma. *J Nucl Med.* 2003;44:1797–1803.
4. Beets G, Penninckx F, Schiepers C, et al. Clinical value of whole-body positron emission tomography with [^{18}F]fluorodeoxyglucose in recurrent colorectal cancer. *Br J Surg.* 1994;81:1666–1670.
5. Schiepers C, Penninckx F, De Vadder N, et al. Contribution of PET in the diagnosis of recurrent colorectal cancer: comparison with conventional imaging. *Eur J Surg Oncol.* 1995;21:517–522.
6. Delbeke D. Oncological applications of FDG PET imaging: brain tumors, colorectal cancer, lymphoma and melanoma. *J Nucl Med.* 1999;40:591–603.
7. Valk PE, Abella-Columna E, Haseman MK, et al. Whole-body PET imaging with [^{18}F]fluorodeoxyglucose in management of recurrent colorectal cancer. *Arch Surg.* 1999;134:503–511.
8. Schiepers C, Yap CS, Quon A, et al. Added value of PET-CT for cancer staging and lesion localization [abstract]. *Eur J Nucl Med Mol Imaging.* 2003; 30(suppl 2):S227.
9. Goerres GW, Burger C, Schwitter MW, Heidelberg TN, Seifert B, Von Schulthess GW. PET/CT of the abdomen: optimizing the patient breathing pattern. *Eur Radiol.* 2003;13:734–739.
10. Jager PL, Slart RH, Corstens F, Oyen WJ, Hoekstra O, Teule J. PET-CT: a matter of opinion? *Eur J Nucl Med Mol Imaging.* 2003;30:470–471.
11. Dizendorf E, Hany TF, Buck A, Von Schulthess GK, Burger C. Cause and magnitude of the error induced by oral CT contrast agent in CT-based attenuation correction of PET emission studies. *J Nucl Med.* 2003;44:732–738.
12. Cohade C, Osman M, Nakamoto Y, et al. Initial experience with oral contrast in PET/CT: phantom and clinical studies. *J Nucl Med.* 2003;44:412–416.
13. Ell PJ, Von Schulthess GK. Reply to letter. *Eur J Nucl Med Mol Imaging.* 2003;30:471.
14. Cohade C, Osman M, Pannu HK, Wahl RL. Uptake in supraclavicular area fat ("USA-Fat"): description on ^{18}F-FDG PET/CT. *J Nucl Med.* 2003;44:170–176.