high negative predictive value. Our study also showed this to be so for PET/CT colonography—indeed, by combining the attributes of CT colonography and PET, PET/CT colonography would seem to be a highly reliable test for classifying higher-risk symptomatic patients into those with or without significant colorectal neoplasia.

REFERENCES

1. Taylor SA, Bomanji JB, Manpanzure L, et al. Nonlaxative PET/CT colonography: feasibility, acceptability, and pilot performance in patients at higher risk of colonic neoplasia. *J Nucl Med.* 2010;51:854–861.
2. Mandel JE, Lichtenstein GR, Metz DC, Ginsberg GG, Kochman ML. A prospective, randomized, comparative trial evaluating respiratory depression during patient-controlled versus anesthesiologist-administered propofol-remifentanil sedation for elective colonoscopy. *Gastrointest Endosc*. May 19, 2010.
3. von Wagner C, Halligan S, Atkin WS, Lilford RJ, Morton D, Wardle J. Choosing between CT colonography and colonoscopy in the diagnostic context: a qualitative study of influences on patient preferences. *Health Expect.* 2009;12:18–26.

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VQ/SPECT

TO THE EDITOR: In the December 2009 issue of *The Journal of Nuclear Medicine,* an invited perspective (*1*), a study (*2*), a continuing education paper on ventilation–perfusion (V/Q) SPECT (*3*), and a lung SPECT/CT image on the front cover can be found. These appeared shortly after the June (*4*) and July (*5*) 2009 publication of guidelines by the European Association of Nuclear Medicine detailing V/Q SPECT interpretation criteria. This amount of information seems to indicate that V/Q SPECT has gained much interest.

Several years ago, we compared V/Q SPECT with planar lung scanning in 95 patients who were suspected of recent pulmonary embolism but in whom planar lung scans had been nondiagnostic (*6*). CT angiography and lower-limb ultrasonography were used as independent reference standards. Using our own V/Q SPECT diagnosis criterion—that even a single subsegmental mismatch defect indicates pulmonary embolism—we found a negative predictive value of 0.94, which is similar to normal D-dimer plasma levels. Sensitivity, specificity, and accuracy were 0.79, 0.83, and 0.80, respectively. All discrepancies with final diagnosis were related to single subsegmental or nonoccluding segmental thrombi.

The tomographic mode enables more precise assessment of the shape of defects, and V/Q SPECT interpretation must overcome the simplistic criterion that a mismatch defect is always related to an underlying thrombus. Because a mismatch defect is not specific to pulmonary embolism, a careful visual analysis is mandatory. At the time that we submitted our manuscript, the topic of V/Q SPECT was considered of low priority and led us to publish our results (*6*) in a free-access journal (http://www.bentham.org/open/tomij/).

In their study, Gutte et al. (*2*) use low-dose CT in an elegant way to improve V/Q SPECT performance. There is no doubt that CT will greatly aid in the interpretation of V/Q studies. However, not all nuclear medicine departments have a hybrid γ-camera available to perform V/Q lung SPECT combined with CT.

According to our experience, a precise analysis of V/Q SPECT mismatch defects (location, shape, extent to fissure, presence and location of hot spots when using Technegas [Cyclopharm]) enables a diagnosis in 99% of patients without the use of CT. Illustrations given by Gutte et al. confirm this point.

In daily practice, V/Q lung scanning is used as the first imaging test in a few situations. This trend could be reversed if nuclear medicine physicians would routinely use tomographic instead of planar imaging. The addition of low-dose CT when feasible will probably help to shorten the learning curve for V/Q SPECT abnormalities significantly.

REFERENCES

1. Parker JA. Improving lung scintigraphy. *J Nucl Med.* 2009;50:1919–1920.
2. Gutte H, Mortensen J, Jensen CV, et al. Detection of pulmonary embolism with combined ventilation-perfusion SPECT and low-dose CT: head-to-head comparison with multidetector CT angiography. *J Nucl Med.* 2009;50:1987–1992.
3. Stein PD, Freeman LM, Sostman HD, et al. SPECT in acute pulmonary embolism. *J Nucl Med.* 2009;50:1999–2007.
4. Bajc M, Neilly JB, Miniati M, Schuemichen C, Meignan M, Jonson B. EANM guidelines for ventilation/perfusion scintigraphy. Part 1. *Eur J Nucl Med Mol Imaging.* 2009;36:1356–1370.
5. Bajc M, Neilly JB, Miniati M, Schuemichen C, Meignan M, Jonson B. EANM guidelines for ventilation/perfusion scintigraphy. Part 2. *Eur J Nucl Med Mol Imaging.* 2009;36:1528–1538.
6. Weinmann P, Moretti JL, Brauner MW. Usefulness of tomographic versus planar lung scintigraphy in suspected pulmonary embolism in a daily practice. *Open Med Imaging J.* 2008;2:49–55.

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Additional Gains with Time-of-Flight PET at High Counting Rates: Lessons Learned from Early Time-of-Flight PET Systems

TO THE EDITOR: Recent publications on the new generation of time-of-flight (TOF) PET cameras by Lois at al (*1*), Surti et al. (*2*), and Karp et al. (*3*) very elegantly show the reduction in image noise and improvement in lesion detection with TOF PET positron cameras using phantoms and clinical studies. These new TOF PET cameras are optimized for high-resolution tumor detection using ^{18}F-FDG as the tracer and show that the highest improvement in signal-to-noise ratio in the image is obtained when imaging large 35- to 40-cm-diameter objects. Their noise reduction results are consistent with the published result by Yamamoto et al. (*4*) in 1982 for 35-cm-diameter objects scanned at low counting rates using the early Super PETT I TOF PET camera built at Washington University, Saint Louis, Missouri. However, Yamamoto et al. (*4*) also showed that, at high counting rates, there is an additional gain with TOF PET due to the way random coincidences are

treated with TOF PET. Therefore, there is the possibility of even better performance capabilities with TOF PET when imaging at higher counting rates.

The early TOF PET systems (*4–6*) were designed for fast imaging with short-lived isotopes. Experience with these systems showed that there are 3 areas of PET in which the TOF information obtained with fast detectors can significantly improve image quality over non-TOF PET. The first is the low-counting-rate mode of imaging whereby only the true counts are taken into consideration and the improvement in image signal-to-noise ratio is expressed as the square root of D/d, where D is the diameter of the object and d is the TOF resolution measured as the full width at half maximum in centimeters. The mathematics of TOF PET signal-to-noise ratio is elegantly described in a teaching editorial by Budinger (*7*). The gains obtained by TOF PET were simulated by Wong et al. (*8*) for different-sized objects and different TOF resolutions. Basically, in lay terms, the use of TOF information helps place the detected positron closer to the real location of the radioactivity during the image reconstruction process, thus improving the image quality. And the larger the object, the greater the improvement.

The second area in which TOF PET can improve image quality is in the reduction of random coincidences during dynamic imaging at high counting rates. When one is imaging organs such as the brain and the heart with short-lived isotopes such as ^{15}O, ^{11}C, ^{13}N, and ^{82}Rb, random coincidences can degrade image quality. Using the Super PETT I, Yamamoto et al. (*4*) measured the signal-to-noise gain at higher counting rates to be as high as 2.8, compared with 1.7 at lower counting rates. This experimental observation was subsequently confirmed by Holmes et al. (*9*) using a mathematic model of the effects of accidental coincidences in TOF PET systems.

The third area of image quality improvement in TOF PET systems is in the reduction of dead-time losses in the system at high counting rates. The data acquired during a typical scan comprise true counts, scattered counts, and random counts. Randoms increase as the square of the radioactivity in the field of view, whereas true and scattered counts increase linearly with the activity. Therefore, at higher counting rates, randoms can be higher than true counts and compete with true counts for transfer to the computer. As randoms increase at higher counting rates, true counts are disproportionately reduced because of dead-time losses in the system. The combination of randoms and dead-time losses can reduce the noise equivalent counts, the equivalent of good counts, for large objects such as the abdomen at higher counting rates as shown by Surti et al. (*2*). Their data show that randoms and scatter counts are equal to true counts at a much lower counting rate for a 35-cm-diameter object than for a 20-cm-diameter object. Thus, any increase in injected dose to the patient beyond this point will yield reduced improvement in signal-to-noise ratio in the image while increasing the radiation dose to the patient.

Since the introduction of the early TOF PET systems in the 1980s, detectors, electronics, and computer performance have increased dramatically. Things that were not possible at that time can be implemented in the present TOF PET systems to further enhance the signal-to-noise ratio by reducing the effects of randoms and dead-time losses. One of these advances is the ability to dynamically change the coincidence acceptance window to fit the object being imaged. The coincidence timing windows in the early systems were fixed and controlled by the position of the attenuation ring at the periphery of the field of view. Today, it is possible to use the attenuation data to selectively shorten coincidence timing acceptance windows during data acquisition for different parts of the body. As an example, for brain imaging, the coincidence window can be reduced to accept only counts emitted from the brain by using the TOF information, thus reducing the randoms collected and reducing the dead-time losses for the system. So, although the paper by Lois et al. (*1*) shows a smaller improvement with TOF PET in imaging the head than in imaging the abdomen at lower counting rates, it may be possible to increase the signal-to-noise ratio when imaging the brain at higher counting rates with ^{15}O or ^{11}C. Even if only ^{18}F-FDG is used to do the imaging, the possibility of obtaining first-pass blood flow in tumors with ^{18}F-FDG during the first 2 min after injection of the ^{18}F-FDG bolus will result in significantly higher randoms and dead-time losses. Therefore, the anticipated gain with TOF PET in the future may be higher than published by Lois et al. (*1*) and Surti et al. (*2*) at higher counting rates as the new generations of TOF PET cameras are optimized to reduce randoms and dead-time losses.

One area of improvement that I have wished to pursue is selective-area data acquisition and reconstruction. From the first demonstration of TOF PET using a heart phantom (*10*), we showed that the TOF confidence-weighted back-projected image (without image reconstruction) clearly delineates the heart from the rest of the phantom. This finding suggests that, using the TOF information, it is possible to isolate the heart from the chest during data acquisition. If we can use the TOF information to limit the data acquisition to just over the heart, we may be able to selectively scan a smaller area in a larger object and reconstruct it with an even greater improvement in signal-to-noise ratio. So, even though the static mode of TOF PET did not show a significant gain by Lois et al. (*1*) in the heart, selective imaging of the heart in the future with ^{82}Rb, ^{11}C, or ^{13}N may produce even better results by using the full potential of TOF PET.

This is an exciting time for PET. The development of new and faster detectors has created the possibility that clinical imaging with PET will be faster, have higher resolution, and have better time-of-flight timing than currently. Reduction of TOF timing to one half of the current timing is now feasible, thus opening up new areas of research and development in clinical image improvement, reduction of radiation to patients and smarter imaging with PET. And in the future, as the timing resolution improves even further, we may be able to image selective areas to reduce the effects of randoms and dead-time losses and further enhance image quality.

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the introduction of the new detectors. He would be the first to congratulate the developers of the new generation of TOF PET cameras.

REFERENCES

1. Lois C, Jakoby BW, Long MJ, et al. An assessment of the impact of incorporating time-of-flight information into clinical PET/CT imaging. *J Nucl Med.* 2010; 51:237–245.
2. Surti S, Kuhn A, Werner ME, Perkins AE, Kolthammer J, Karp JS. Performance of Philips Gemini TF PET/CT scanner with special consideration for its time-of-flight imaging capabilities. *J Nucl Med.* 2007;48:471–480.
3. Karp JS, Surti S, Daube-Witherspoon ME, Muehllehner G. Benefit of time-of-flight in PET: experimental and clinical results. *J Nucl Med.* 2008;49:462–470.
4. Yamamoto M, Ficke DC, Ter-Pogossian MM. Experimental assessment of the gain achieved by the utilization of time-of-flight information in a positron emission tomograph (Super PETT I). *IEEE Trans Med Imaging.* 1982;1:187–192.
5. Trebossen R, Mazoyer B. Count rate performances of TTVO3: the CEA-LETI time-of-flight positron emission tomograph. *IEEE Trans Med Imaging.* 1991;10: 261–266.
6. Mullani NA, Wong WH, Hartz RK, Yerian K, Philippe EA, Gould KL. Design of TOFPET: a high resolution time-of-flight positron camera. In: *Proceedings of the International Workshop of Time of Flight Positron Tomography; St. Louis, Missouri; May 1981.* Washington, DC: IEEE Computer Society; 1982:31–36. Catalog no. CH1791-3.
7. Budinger TF. Time-of-flight positron emission tomography: status relative to conventional PET. *J Nucl Med.* 1983;24:73–78.
8. Wong WH, Mullani NA, Philippe EA, Hartz R, Gould KL. Image improvement and design optimization of the time-of-flight PET. *J Nucl Med.* 1983;24:52–60.
9. Holmes TJ, Snyder DL, Ficke DC. The effect of accidental coincidences in time-of-flight positron emission tomography. *IEEE Trans Med Imaging.* 1984;3:68–79.
10. Mullani NA, Markham J, Ter-Pogossian MM. Feasibility of time-of-flight reconstruction in positron emission tomography. *J Nucl Med.* 1980;21:1095–1097.

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