PET/CT Imaging: Facts, Opinions, Hopes, and Questions

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Dual-modality PET/CT, as the most comprehensive diagnostic tool in oncologic imaging, has invigorated nuclear medicine and attracted radiology's interest. The nuclear medicine physician can now precisely localize metabolic findings, and the radiologist can more accurately characterize structural alterations. PET/CT accounts for more than 65% of all current PET sales, and its share is anticipated to grow to more than 95% over the next years. Although many new PET/CT devices go to nuclear medicine services, even more are being delivered to diagnostic radiology services. PET/CT has become accepted in clinical practice despite the fact that experience is still limited and evidence of its effectiveness remains sparse. Facts are still few, as "hopes" and "opinions" drive the dissemination and acceptance of PET/CT. Questions remain and serve as the motivation for this special issue on PET/CT as a supplement to *The Journal of Nuclear Medicine*. The supplement is intended fill an educational void by presenting the current state of this new dual-modality approach. Because literature-based scientific documentation is still limited and, when available, mostly preliminary, much of the information presented reflects the personal experiences of the authors and their perceptions of the issues that need to be addressed.

PET imaging with ^{18}F-FDG diagnoses, stages, and restages many cancers with accuracies ranging from 80% to 90% (*1*). Responses to therapy can be identified earlier and with greater accuracy than is possible with anatomic imaging modalities. Prognostic information available through ^{18}F-FDG PET is superior to that of conventional imaging for many cancers. Given the already high performance of current ^{18}F-FDG PET, what accounts for the attractiveness of combined PET/CT and its almost universal clinical acceptance within only a few years? There are several answers. The concept of merging anatomic with molecular image information is intuitively correct and clinically meaningful. Molecular imaging benefits from anatomic landmarks, whereas anatomic imaging without molecular information remains incomplete and unsatisfactory. PET/CT has introduced radiologists to the importance of molecular imaging and helps to conceptualize the inherent limitations of size criteria for identifying anatomic abnormalities as malignant or benign. The molecular information available through PET enables radiologists to identify the functional content of anatomic abnormalities and to categorize them as malignant or benign. Conversely, molecular imaging benefits from the anatomic framework provided by CT. Hypermetabolic lesions can be assigned to specific normal or abnormal anatomic structures.

Townsend et al. (*2–4*) pioneered the concept of near-simultaneous imaging of molecular and anatomic information. The concept resulted in the first PET/CT system, consisting of a half-ring PET and single-slice CT system installed in 1999 at the University of Pittsburgh. Early studies of this device in patients with head-and-neck and other cancers not only proved the feasibility of PET/CT but also presented evidence for its potential clinical utility. The subsequent rapid clinical acceptance of this novel hybrid imaging system appeared to be driven mostly by the attractiveness of the concept of merging anatomic with functional information rather than by clinical evidence. Thus far, only a few investigations that conclusively prove PET/CT's clinical efficacy have been published in peer-reviewed scientific journals. It seems therefore that hopes, opinions, and questions have largely driven the initial dissemination of the technology.

Nevertheless, PET/CT offers indisputable advantages. These include shorter image acquisition times resulting in greater patient throughput and thus more efficient instrument utilization (*1*); improved lesion localization and identification (*2*); and more accurate tumor staging (*3*).

IMAGE ACQUISITION

PET/CT reduces image acquisition times, resulting in increased patient throughput. Conventional PET employs transmission images for photon attenuation correction using an external radiation source. Completion of the transmission scan requires 3–4 min per bed position and thus up to 30 min for whole-body PET studies. PET emission data traditionally have been acquired for 4 min per bed position.

Received Dec. 2, 2003; revision accepted Dec. 3, 2003.

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Thus, a conventional whole-body PET scan covering 6–8 bed positions requires about 1 h for completion. PET/CT imaging differs in that it utilizes whole-body CT data for attenuation correction. Depending on the number of CT detectors used, attenuation correction is achieved within seconds to slightly >1 min. Thus, the whole-body imaging time is reduced by 50%. With 3-dimensional imaging and lutetium oxyorthosilicate detectors, image acquisition times can be further shortened to <10 min in some patients (*5*). Shorter imaging protocols offer several advantages. Almost all patients can be studied in the "arms up" position, thereby reducing CT beam-hardening artifacts. Patient motion, a source of problems associated with image coregistration, is reduced. Higher patient throughput improves equipment utilization and is economically desirable. Finally, shorter image acquisition protocols are convenient for patients. Even with the addition of high-resolution and contrast CT studies, image acquisition times are <1 h.

IMPROVED LESION LOCALIZATION

PET/CT facilitates the precise localization of molecular alterations of cancer tissue, which is difficult if not impossible with PET alone. For example, the level of mediastinal lymph node involvement in lung cancer patients cannot be determined reliably with PET alone. Appropriate localization of hypermetabolic foci to chest wall versus lung, base of the lung versus liver, neck versus superior mediastinum, and in other areas may significantly affect patient management. Judging from our own experience, accurate lesion localization with PET/CT also reduces the number of false-positive and false-negative PET findings. The question of how frequently such improved lesion localization results in changes in patient management awaits clarification.

TUMOR STAGING AND RESTAGING

Numerous abstracts but few peer-reviewed and published research studies have examined the incremental value of PET/CT over PET alone for staging and restaging of cancer. Preliminary data suggest significant increments in diagnostic and staging accuracy, significant reductions in the number of false-positive and false-negative findings, and an increased reader confidence in PET findings. A recent prospective study published in the *New England Journal of Medicine* assessed the diagnostic accuracy of integrated PET/CT in patients with non–small cell lung cancer (*6*). In 50 patients, the staging accuracy of PET/CT was compared with visually correlated PET and CT as well as with PET and CT individually. PET/CT had a significantly lower number of incorrectly assigned tumor stages than did CT or PET alone. The accuracy of PET/CT was superior to that of "visual" image fusion. However, with regard to lymph nodes, PET had the lowest number of incorrectly assigned stages. As expected, the number of equivocal nodes by PET alone was higher than that with combined PET/CT. Moreover, PET/CT provided additional important information in 41% of patients, including localization of lymph nodes (n = 9), precise identification of chest wall infiltration (n = 3), correct differentiation between tumor and inflammation (n = 7), and localization of distant metastases (n = 2). In a surprising result, the accuracy of PET alone for staging of lung cancer appeared to be considerably lower than previously reported. This is probably explained by the introduction of an additional category for classifying metabolic lesions termed "correct classification but equivocal." It is important to note that this study did not examine prospectively whether the "additional important information" led to significant changes in patient management. More clinical trials with greater patient numbers will be required to firmly establish possible advantages of PET/CT over PET or CT alone for each type of cancer.

Widespread opinions and hopes pertain to significant gains in lesion detection, localization, and characterization and thus to improvement in cancer detection, staging, and restaging and accurate therapy monitoring. Clinical trials clearly are needed to substantiate these opinions in order for these hopes to materialize. Hopes and opinions also relate to PET/CT as a tool for planning more accurate radiation treatment that could improve tumor treatment at a lower radiation burden. Needs for better radiation treatment planning arise from a discrepancy between total anatomic mass and the mass of viable tumor. Tumor "masses" as determined by CT can encompass various tissue types, including inflammation, necrosis, scar, and viable tumor. Exact localization of viable tumor components with ^{18}F-FDG PET can affect radiation target volumes and might alter radiation doses. Whether PET/CT-based radiation planning will improve outcomes or quality of life for cancer patients is unknown and will be difficult to establish, because many end-stage cancer patients receive palliative radiation when the aggressiveness of the underlying malignancy might outweigh the benefits of better-targeted radiation treatment. Moreover, large areas of "necrosis" appearing as hypometabolic tumor masses may contain isolated islands of tumor cells that would remain untreated if the radiation target included only viable (i.e., hypermetabolic) tumor sections.

Opinions, hopes, and questions also surround future developments. For example, should PET/CT combinations be designed to stand on their own as the cancer imaging modality of choice? How many CT detectors are necessary for comprehensive metabolic and anatomic evaluation of cancer patients? Does the combination with PET really provide the optimum utilization of 16-slice CT scanners? Should combinations of 16-slice CT and PET be reserved or specifically developed for cardiac applications? Can a comprehensive cardiac evaluation, including myocardial perfusion, coronary calcification, wall motion, and noninvasive coronary angiography, be provided in a single study session? Most vendors offer various combinations of PET and CT, ranging from dual- to 16-slice CT combined with state-of-the-art PET. However, we believe that PET combined with 16-slice CT may not be necessary for obtaining

all relevant information in a largely oncologic patient population.

Questions and opinions also center on optimal imaging protocols. One school of thought believes that CT image data should be used only for attenuation correction of PET and for localizing hypermetabolic lesions, whereas others advocate the need for elaborate contrast and high-resolution CT. Can "ultra-fast" PET imaging protocols be established to further reduce whole-body PET/CT imaging times without compromising diagnostic quality? Many of these debates have not yet produced a consensus. It therefore appears likely that, at least initially, the specific expertise of users and patient populations studied will lead to the development of institution-specific imaging protocols.

This supplement to *The Journal of Nuclear Medicine* offers an account of the current state of PET/CT. Townsend et al. (*7*) review the current state of imaging instrumentation and explore future developments. Beyer et al. (*8*) present technical and methodologic aspects of PET/CT. Slomka (*9*) discusses less expensive software image fusion approaches as an alternative to "in-line" PET/CT systems, and Ratib (*10*) highlights the need for clinically practical approaches allowing navigation of large sets of diagnostic image data. Goerres et al. (*11*) and Wahl (*12*) explore the diagnostic possibilities of PET/CT and present arguments as to why PET/CT will replace standard PET. Vogel et al. (*13*) present a more tempered view that sees PET/CT as needed only in more selected patients. Schöder et al. (*14*) examine the need for an interdisciplinary approach to PET/CT and its benefits for oncologic patients, and Antoch et al. (*15*) present the radiologist's perspective. Bradley et al. (*16*) discuss the potential of PET/CT for improved radiation planning and suggest areas of technologic improvement. With these contributions, conceived, prepared, and published within a time frame of $<$6 mo, the supplement presents the actual state of PET/CT and its complexity, along with its opportunities, future promise, clinical potential, and impact on patient care. The supplement is also intended to highlight questions, hopes, and opinions and, thus, to contribute to their resolution.

REFERENCES

1. Czernin J, Phelps ME. Positron emission tomography scanning: current and future applications. *Annu Rev Med.* 2002;53:89–112.
2. Townsend DW, Cherry SR. Combining anatomy and function: the path to true image fusion. *Eur Radiol.* 2001;11:1968–1974.
3. Kinahan PE, Townsend DW, Beyer T, Sashin D. Attenuation correction for a combined 3D PET/CT scanner. *Med Phys.* 1998;25:2046–2053.
4. Beyer T, Townsend DW, Brun T, et al. A combined PET/CT scanner for clinical oncology. *J Nucl Med.* 2000;41:1369–1379.
5. Halpern B, Dahlbom M, Vranjesevic D, et al. LSO-PET/CT whole-body imaging in 7 minutes. Is it feasible? *J Nucl Med.* 2003;44:A1355.
6. Lardinois D, Weder W, Hany TF, et al. Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. *N Engl J Med.* 2003;348:2500–2507.
7. Townsend DW, Carney J, Yap JT, Hall NC. PET/CT today and tomorrow. *J Nucl Med.* 2004;45(suppl):4S–14S.
8. Beyer T, Antoch G, Müller S, et al. Accquisition protocol considerations for combined PET/CT imaging. *J Nucl Med.* 2004;45(suppl):25S–35S.
9. Slomka P. Software approach to merging molecular with anatomical information. *J Nucl Med.* 2004;45(suppl):36S–45S.
10. Ratib O. PET/CT image navigation and communication. *J Nucl Med.* 2004; 45(suppl):46S–55S.
11. Goerres GW, von Schulthess GK, Steinert HC. Why most PET of head and neck and lung cancer will be PET/CT. *J Nucl Med.* 2004;45(suppl):66S–71S.
12. Wahl RL. Why nearly all PET of abdominal and pelvic cancers will be performed as PET/CT. *J Nucl Med.* 2004;45(suppl):82S–95S.
13. Vogel WV, Oyen W, Barentsz JO, Kaanders J, Corstens F. PET/CT: panacea, redundancy, or something in between? *J Nucl Med.* 2004;45(suppl):15S–21S.
14. Schöder H, Larson SM, Yeung H. PET/CT in oncology: Integration into clinical management of lymphoma, melanoma and gastrointestinal malignancies. *J Nucl Med.* 2004;45(suppl):72S–81S.
15. Antoch G, Freudenberg L, Beyer T, Bockisch A, Debatin J. To enhance or not to enhance? ^{18}F-FDG and CT contrast agents in dual-modality ^{18}F-FDG PET/CT. *J Nucl Med.* 2004;45(suppl):56S–65S.
16. Bradley JD, Perez CA, Dehdashti F, Siegel BA. Biological target volumes in radiation treatment planning for non-small cell lung cancer. *J Nucl Med.* 2004; 45(suppl):96S–101S.