PET/CT Scanners: A Hardware Approach to Image Fusion

David W. Townsend, Thomas Beyer, and Todd M. Blodgett

New technology that combines positron tomography with x-ray computed tomography (PET/CT) is available from all major vendors of PET imaging equipment: CTI, Siemens, GE, Philips. Although not all vendors have made the same design choices as those described in this review all have in common that their high performance design places a commercial CT scanner in tandem with a commercial PET scanner. The level of physical integration is actually less than that of the original prototype design where the CT and PET components were mounted on the same rotating support. There will undoubtedly be a demand for PET/CT technology with a greater level of integration, and at a reduced cost. This may be achieved through the design of a scanner specifically for combined anatomical and functional imaging, rather than a design combining separate CT and PET scanners, as in the current approaches. By avoiding the duplication of data acquisition and image reconstruction functions, for example, a more integrated design should also allow cost savings over current commercial PET/CT scanners. The goal is then to design and build a device specifically for imaging the function and anatomy of cancer in the most optimal and effective way, without conceptualizing it as combined PET and CT. The development of devices specifically for imaging a particular disease (eg, cancer) differs from the conventional approach of, for example, an all-purpose anatomical imaging device such as a CT scanner. This new concept targets more of a disease management approach rather than the usual division into the medical specialties of radiology (anatomical imaging) and nuclear medicine (functional imaging).

Until recently, imaging technologies have primarily focused on a single aspect of a disease process, for example, the anatomical structure or a functional change. Some technologies, such as magnetic resonance (MR), can go further and image both anatomy (proton density) and other, more physiological aspects of tissue, such as nuclear spin relaxation times. However, combining an anatomical technique, such as computed tomography (CT), with a nuclear medicine-based functional technique, such as single photon (SPECT) or positron tomography (PET), has traditionally required computer software to align the images from the two modalities. Accurate image registration for body regions other than the brain is known to be a challenge owing to the variability of patient positioning and the involuntary movement of internal organs. Despite significant progress in software alignment techniques, they remain of limited accuracy, labour-intensive, and somewhat impractical to apply on a patient-by-patient basis.

The advantages of combining anatomy with function on a routine basis for every patient scanned may be debatable. PET, for example, is a functional imaging technique with a sensitivity and specificity in excess of 90% for many malignant diseases.[1] The incremental advantage of an accurately aligned CT scan may be marginal, particularly as many physicians habitually perform visual registration by reading the scans in parallel on adjacent displays. An incremental improvement in sensitivity from say 90% to 93%, cannot in general justify labour-intensive image registration for all patients, even though accurate anatomical and functional image alignment is obviously an advantage and provides precise localization of regions of increased tracer uptake within a morphological framework. Traditionally, such localization accuracy has not been expected from—or achieved with—low-resolution functional imaging. Instead, the relatively poor anatomical resolution has been mitigated by a functional specificity that cannot be achieved by CT or MR. Furthermore, the use of tracers, such as ^{18}F-fluorodeoxyglucose (FDG) that image glucose use and are not specific to cancer, actually provide a low-resolution anatomical framework because of the variable uptake in all tissues metabolizing glucose. Thus, brain, heart, liver, certain muscles, and soft tissues can be identified in an FDG image, as well as the renal collecting systems and the bladder due to the excretion of FDG through the urinary tract. Non-specific and variable FDG uptake in the gastrointestinal tract and colon may, nevertheless, complicate the interpretation of the images owing to the difficulty of distinguishing normal physiological accumulation from uptake in tumor. However, with experience, many of these ambiguities related to FDG uptake are recognizable, and an abnormal focus of tracer accumulation can be identified and approximately localized.

Most software registration techniques have been developed specifically for applications to the brain.[2-4] The effectiveness of these techniques when applied to image

From the Department of Medicine, University of Tennessee, Knoxville, TN; Department of Nuclear Medicine, University of Essen, Essen, Germany; and Department of Radiology, University of Pittsburgh, Pittsburgh, PA.

Address reprint requests to David W. Townsend, PhD, Department of Medicine, University of Tennessee, 1924 Alcoa Highway, Knoxville, TN 37920-6999.

Supported by National Cancer Institute Grant CA 65856.

0001-2998/03/3303-0005$30.00/0

doi:10.1053/snuc.2003.127314

registration for parts of the body other than the brain is much reduced due to problems of patient positioning and internal organ movement. However, the difficulties and advantages of image registration in whole-body imaging have been recognized for over a decade.[5] The problems encountered by the software approach can alternatively be addressed by a hardware approach that fuses the technologies, such as PET and CT, rather than the more conventional post hoc fusing by software of images acquired on separate scanners. The first technological design of a combined PET/CT scanner was introduced into the clinical arena in 1998, following 3 years of National Cancer Institute (NCI) funded development.[6] The motivation behind the design was to obtain clinical-quality CT and PET scans, accurately aligned, from a single imaging device. The availability of the CT scan to correct the PET emission data for attenuation and scatter is a secondary, but important, advantage offered by this approach. The PET/CT prototype was then operated as an investigational device at the University of Pittsburgh Medical Center for a period of 3 years following its installation in May 1998. The 300 or so patients who were scanned on the device during the clinical evaluation period were the first ever to benefit from this combined imaging approach. Although not directly part of the accepted standard of care, the combined studies nevertheless provided useful supplementary information for many patients, impacting management compared to PET alone in approximately 30% of those studied. Above all, however, these initial studies generated significant interest in PET/CT among radiologists and nuclear medicine physicians, even though the latter were somewhat more cautious to embrace the new approach than were radiologists and referring physicians.

Manufacturers of medical imaging equipment responded to the demand from the medical community by proposing combined PET/CT scanner designs that offered, above all, improved PET and CT performance compared with the prototype. The question as to the level of CT and PET performance that is actually required for such a device led to considerable debate, much of it fuelled by marketing rather than by technical, scientific, or clinical considerations. The issues have still to be resolved, with current commercial designs under evaluation in the field for less than 2 years. As more of these devices become operational for routine clinical applications at major medical centers, prospective studies must be performed to identify the areas in which combined PET/CT imaging offers added value over CT and PET scans acquired separately. The retrospective studies performed with the prototype[7-10] and at some of the early commercial installations[11-19] showed considerable promise, particularly in the areas of disease staging and therapy planning and monitoring. These results and other recent publications suggest that combined PET/CT scanning has initiated a new imaging modality that could have a major impact on health care in the oncology field. From the perspective of the physician, combined PET/CT imaging clearly offers accurate localization of pathology, greater confidence in reading the scans, and the convenience of scheduling a single examination that covers both modalities for the patient. This same convenience extends to the patient, because only a single visit is required for the complete study and, by demanding clinical-quality imaging for PET and CT, under most conditions both modalities can be billed and cost-savings are possible.

In little over 2 years since the Food and Drug Administration (FDA) cleared the first commercial dedicated PET/CT scanner, all major vendors of medical imaging equipment have offered some type of PET/CT design. These include the biograph scanners from Siemens Medical Solutions (Hoffman Estates, Chicago, IL), the Discovery LS and ST from GE Medical Systems (Milwaukee, WI), the Reveal series from CTI (Knoxville, TN), and the Gemini from Philips Medical (Milpitas, CA). All systems incorporate top performance PET components, combined with a range of CT scanner performance that includes multi-slice CT with 2, 4, 8, and 16 slices. Of particular note with these new designs is the significant reduction in whole-body scan time, from 45-60 min for PET alone to 10-20 min for PET/CT. In the coming months and years, the appropriate choice of CT and PET performance for effective imaging in oncology will doubtless be defined by the clinical demands. It is likely that different configurations may be more appropriate for cardiology and neurology, as opposed to a single design for all PET/CT applications.

Inevitably, there are certain difficulties and challenges related to successful combined PET/CT imaging. In particular, the cost of the technology may be prohibitive for smaller medical centers, although this situation will doubtless improve in the future with appropriate cost-savings. The low level of integration of current systems—they are essentially two devices placed in tandem—imposes significant installation constraints because the already sizeable footprint is made even larger by the necessity to physically separate the modalities for servicing purposes. The usual patient bed travel for whole-body imaging is increased by the separation between the CT and PET imaging fields that may be as much as 80 cm, necessitating a scanning room that can accommodate a bed movement of up to 2 m without sag or vertical deflection. From an operational viewpoint, combined PET/CT scanning challenges the conventional approach of separately trained CT and nuclear technologists. A similar situation arises with the usual medical specialization into either anatomical or functional imaging, although this is more of an issue in Europe than in the US where a significant fraction of radiologists are also board-certified in nuclear medicine.

This article will cover a brief review of the development of combined PET/CT scanners, from prototype to current commercial devices, and offer an assessment of

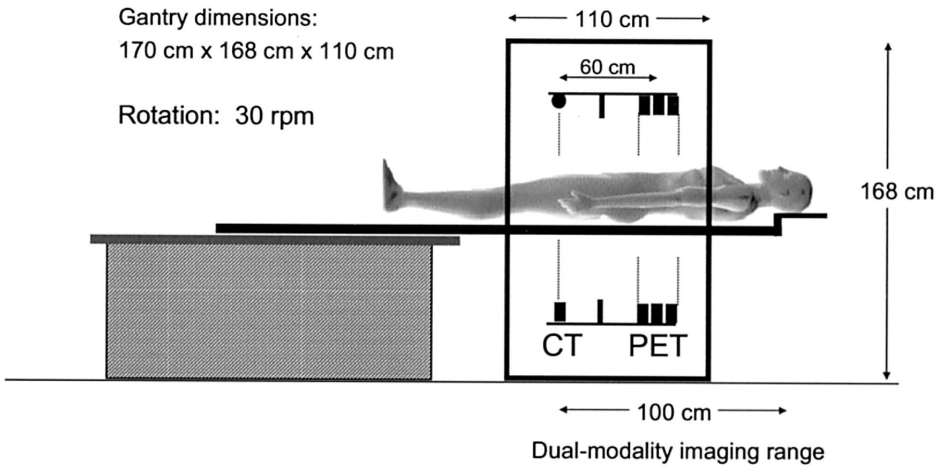

Fig 1. A schematic of the combined PET/CT showing the PET components mounted on the rear of the CT support. The axial separation of the two imaging fields is 60 cm. The entire assembly within the gantry rotates at 30 rpm. The co-scan range for acquiring both PET and CT is 100 cm (maximum).

the future of this technology, particularly for imaging cancer.

HISTORICAL ASPECTS OF PET/CT DEVELOPMENT

Historically, one of the first dual-modality devices was a combination of CT and SPECT. Hasegawa, Lang et al. at the University of San Francisco[20-21] combined anatomical (CT) and functional imaging (SPECT) by using a single material, high purity germanium, as the detector for both modalities. The x-ray CT images were also used to provide attenuation factors for correction of the SPECT data.[22] Operating the device with two different energy windows allowed simultaneous emission-transmission acquisitions to be performed. This early work of Hasegawa et al. is important because it highlights the potential of a single device that can perform both anatomical and functional imaging. However, the difficulty of achieving an adequate level of performance with the same detector material and without compromise for both SPECT and CT convinced the group to explore instead a combination of SPECT and CT using different, dedicated imaging systems for each modality—a clinical SPECT camera (GE 600 XR/T) in tandem with a clinical CT scanner (GE 9800).[23] With this design, Hasegawa et al. demonstrated significant improvements in attenuation correction and partial volume correction for SPECT imaging, in addition to intrinsic SPECT/CT image alignment, thereby further promoting the concept of dual-modality imaging.

Although a proposal to combine PET with CT dates back to 1994,[24] the first dedicated PET/CT scanner did not become operational for patient studies until 1998 when a prototype was installed at the University of Pittsburgh Medical Center.[6] The prototype was developed in collaboration with CTI PET Systems (Knoxville, TN) and funded by the National Cancer Institute (NCI). The design objective was to provide clinical CT and clinical PET imaging capability within a single, integrated scanner.[25] The short CT scan duration compared with a typical whole-body PET acquisition time essentially eliminated the requirement for simultaneous CT and PET acquisitions. The integration of the two modalities within a single gantry is more straightforward when simultaneous acquisition of CT and PET is not required. As shown in Fig. 1, in this design the PET and CT components were mounted on the same aluminium support with the CT at the front, and the PET at the rear.[6] The PET components were those of an ECAT ART scanner (CPS Innovations, Knoxville, TN)[26] and the CT a third generation spiral CT, the Somatom AR:SP (Siemens Medical Solutions) that incorporated a 25 kW x-ray tube and 512 xenon-filled detectors. The entire assembly rotated at 30 rpm and was housed within a single gantry of dimensions 170 cm wide and 168 cm high (Fig. 1). The patient port was 60 cm in diameter with an overall tunnel length of 110 cm and a 60 cm axial displacement between the center of the CT and the center of the PET imaging fields. A single patient bed was used for both modalities with an axial travel sufficient to cover 100 cm of combined CT and PET imaging. The acquisition and reconstruction paths were not integrated, with CT and PET scanning controlled from separate consoles. Once acquired and reconstructed, the CT images were transferred to the PET computer to provide the attenuation correction factors for the PET emission data. Final PET reconstruction and CT and PET fused image display was performed on the PET computer console.

In total, over a period of some 3 yr, from 1998-2001, more than 300 cancer patients were scanned on the PET/CT prototype, and retrospective reviews summariz-

ing the significant findings have been published.[7,8,27] Coincidentally, the timing of the clinical evaluation program for the PET/CT corresponded to the emergence of PET as a major imaging modality for cancer, with reimbursement for a limited number of indications beginning in July 1999. Thus, with the growing importance of PET for diagnosis, staging, and eventually therapy monitoring,[1] the combination of PET with CT came at an opportune moment for the technology. Because CT is still the primary anatomical imaging modality for many malignant diseases, the PET/CT scanner clearly has an important role to play in oncology, putting on hold, at least for the time being, a demand for the more technically challenging combination of PET with MR.[28]

Although the number of patients studied in each disease category was relatively small, the clinical evaluation program with the prototype clearly demonstrated performance superior to PET for head and neck cancer and abdominal and pelvic malignancy. The non-specificity of ^{18}FDG as an imaging agent for cancer becomes less of an issue with PET/CT because of the ability to distinguish normal uptake in the gastro-intestinal tract and bowel from tumor, and the accurate localization of abnormal uptake to specific anatomical structures. Overall, the PET/CT images were easier to read than PET alone, and increasingly, physicians requested a PET/CT scan rather than PET alone even though studies acquired on an investigational device are not eligible for reimbursement. The interest generated by this original work led to a number of awards, including the 1999 Image of the Year at the Society of Nuclear Medicine meeting in Los Angeles, California, the TIME Medical Invention of the Year 2000,[29] and the most Outstanding Basic Science paper appearing in the *Journal of Nuclear Medicine* in 2001.[6] Historically, therefore, the PET/CT scanner at the University of Pittsburgh was the first to combine dedicated PET with spiral CT in a single exam. Vendors and customers (physicians) alike recognized the advantages of PET/CT for oncology imaging, and the demand grew rapidly for a commercial device.

DESIGN CONCEPTS FOR PET/CT SCANNERS

The demand for combined PET/CT imaging technology met with a positive response from a number of major vendors of medical imaging equipment. The first device to become commercially available was a dual-head coincidence system with anatomical imaging capability[30] marketed by GE and now distributed as the Discovery VH. However, given the range of possible options and choices, a number of designs had to be considered and reviewed before an appropriate configuration emerged. Important decisions, include the appropriate level of CT and PET performance, the extent of integration, the flexibility of the configuration and protocols, the potential for upgrades, the targeted users and applications, and of course, the cost.[25] Specifically, some of the main design issues are:

- The choice of the PET and CT components and the level of performance of each
- The provision, or not, of standard PET transmission sources
- The extent of the hardware integration of the components
- The design of the patient bed to maximize the co-scan range for PET and CT
- The level of software integration and the choice of display features

Experience gained with the prototype influenced some of these decisions, particularly for the design developed by CPC Innovations and currently distributed through CTI, Inc. as the Reveal and through Siemens Medical Solutions as the biograph.™ Comparable high performance PET/CT designs from other vendors include the Discovery from GE Medical Systems and the Gemini from Philips Medical. The current PET/CT designs from the major vendors are shown in Fig. 2.

The appropriate level of CT and PET performance depends to some extent on the applications envisaged. As with the prototype, the commercial designs described here are targeted primarily at whole-body oncology, although potential applications in cardiology and neurology should not be excluded. Because the PET scanner performance is the limiting factor in terms of statistical image quality, spatial resolution, and scan duration, the highest possible PET performance is generally indicated. The appropriate choice for the CT performance has been more controversial, ranging from mid to top-of-the-line. The main differences are in the number of axial detectors (CT slices) and the rotation speed. In CT, the current trend is to multi-slice detectors and sub second rotation times. The most rapid CT scan protocols are obviously targeted primarily at cardiac applications, although from the perspective of the patient a short scan time is to be preferred when breath-holding is required. However, for oncology purposes, such high performance CT may not be necessary, particularly when the patient is allowed to breathe shallowly throughout the CT scan to more closely match the PET acquisition protocol. A mid-range CT, such as a 2 or 4 slice system, may indeed be sufficient for most oncology studies. Early designs from the major vendors combined a high-end PET scanner with a 2 or 4 slice CT, while more recent designs have incorporated improved PET performance and an 8 or 16 slice CT. PET/CT is still in its infancy and more experience from patient imaging at the major medical centers is needed before a definitive design will emerge.

A commercial PET/CT design with which the authors have some experience is that distributed by Siemens as the biograph and by CTI as the Reveal, shown in Fig. 2a and schematically in Fig. 3. The scanner comprises a Siemens Somatom Emotion dual-slice spiral CT (Siemens Medical Solutions, Erlangen, Germany) with a CPS Innovations ECAT PET scanner. The PET scanner can be either a bismuth germi-

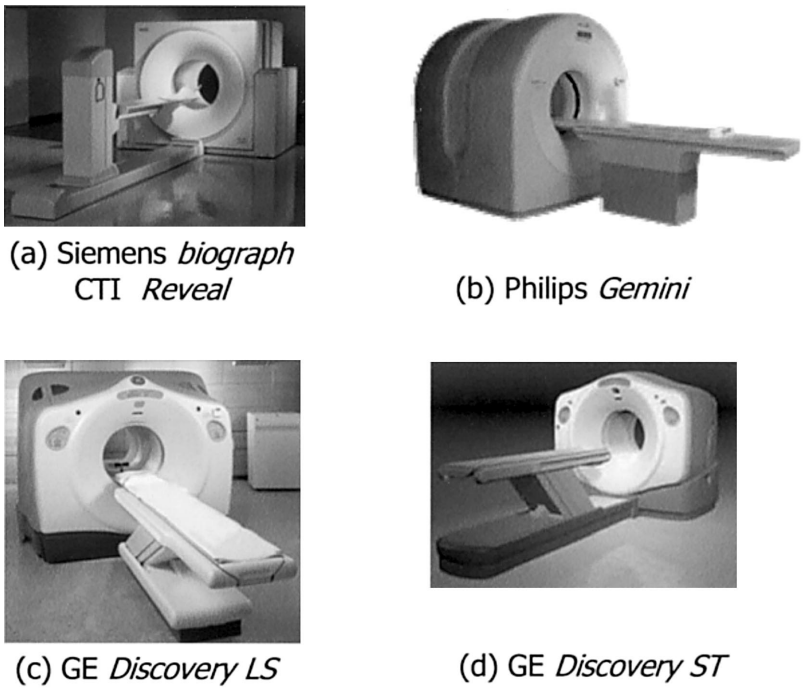

Fig 2. Current commercial PET/CT scanners from the four major vendors of PET imaging equipment.

nate-based ECAT HR+ or a lutetium oxyorthosilicate (LSO)-based ECAT ACCEL (CPS Innovations). Of note in this design is the minimal level of actual hardware integration. The two scanners are essentially placed in tandem within the gantry housing. The gantry is 188 cm high and 228 cm in width. The overall length is 158 cm, although with the front and rear contouring, the effective tunnel length is 110 cm. The axial separation of the centers of the CT and PET fields-of-view is about 80 cm. The patient port diameter is 70 cm throughout the length of the tunnel, which is an important feature when scanning patients for radiation therapy and which also reduces claustrophobic effects despite the 110 cm tunnel length. For servicing, the gantries can be separated by moving the PET scanner backwards on rails for up to 1 m. Access to the rear of the CT and the front of the PET scanner is then possible. No service procedures on either device have been significantly modified as a consequence of integration into the PET/CT.

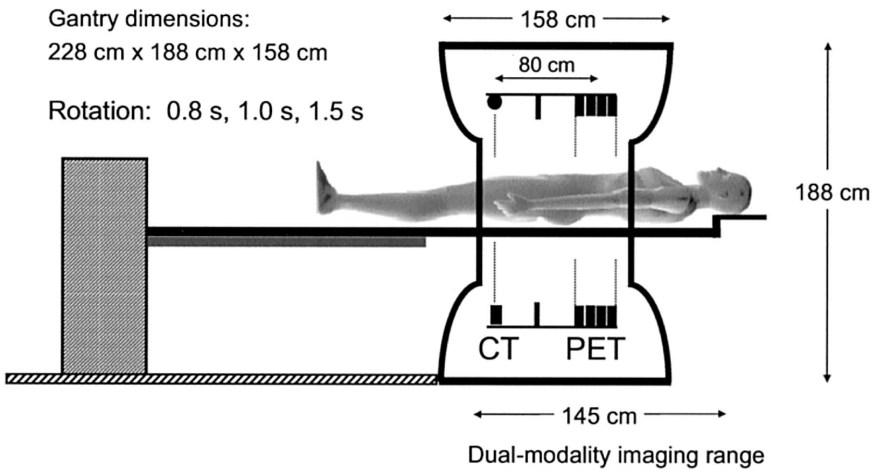

Fig 3. A schematic of the biograph PET/CT scanner. The axial separation of the two imaging fields is 80 cm. The co-scan range for acquiring both PET and CT is 145 cm maximum.

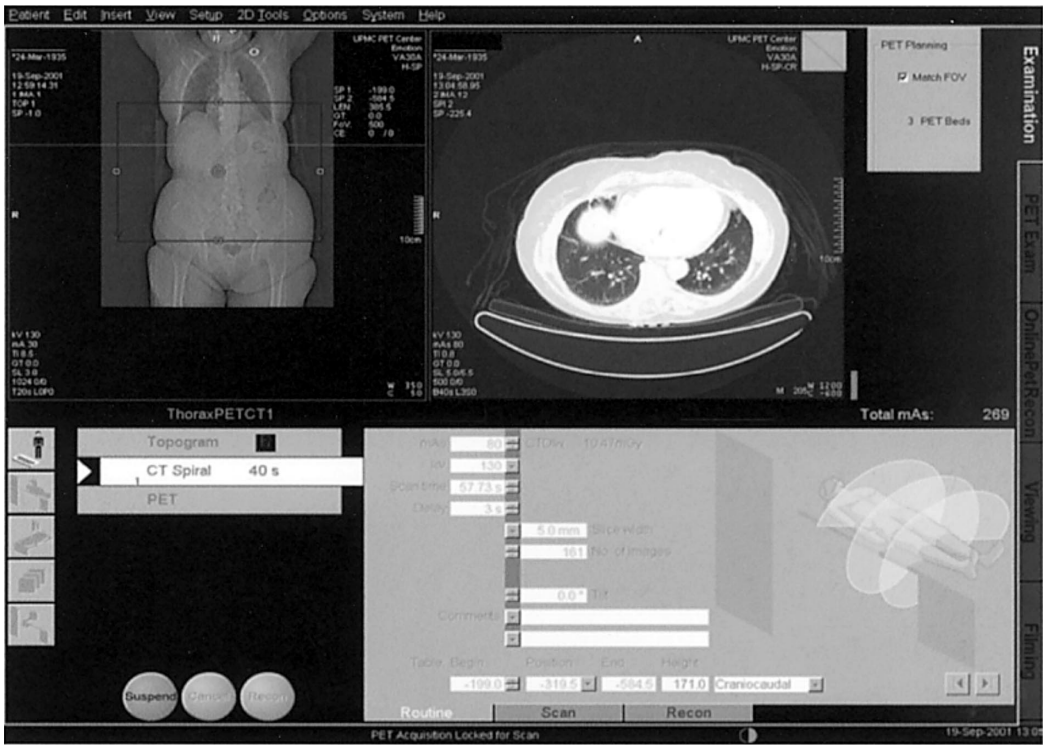

Fig 4. The syngo-based user interface for the biograph PET/CT displaying the CT examination task card and showing the topogram (top, left) with a single reconstructed transverse CT section (center). Scanner controls are in the bottom left of the screen.

To ensure accurate image registration, it is important that any vertical bed deflection is minimized as the pallet extends into the field of view. A conventional CT or PET bed does not meet this requirement and, therefore, a complete redesign of the patient handling system (PHS) is necessary. The problem with a standard bed arises because the cantilever point of the pallet changes as it moves into the scanner. A design that essentially eliminates the vertical deflection is shown in Fig. 3. A carbon fibre pallet is supported at one end by a pedestal that moves horizontally on floor-mounted rails driven by a linear motor. Because the cantilever point does not change, the vertical deflection is fixed to a few millimetres once the patient is aligned on the bed, allowing sub-millimeter intrinsic registration accuracy to be achieved between the CT and the PET, independently of the patient weight. In this design, a total length, including the head holder, of 145 cm can be scanned with both CT and PET. A flat pallet option is available for use with the PHS when scanning patients undergoing PET/CT for radiation therapy treatment planning. A second approach that also addresses the vertical deflection problem is a two-position pallet support pedestal, one position for the CT scan and the second position for the PET scan. The pedestal is advanced from one position to the other between the CT and PET scans, thus ensuring a similar deflection in the two fields of view. This approach has been adopted by GE in the Discovery PET/CT design (Fig. 2c).

Integration of the PET and CT control, processing, and display software is obviously a key feature of a unified PET/CT operation. For the design shown in Fig. 3, this integration was achieved through the use of the Siemens modality-independent software environment syngo® (Siemens Medical Solutions). Different task cards are provided for CT and PET operation selectable from a single console. An example of a task card for the CT operation is shown in Fig. 4. Reconstruction software includes CT-based attenuation correction, Fourier rebinning, and an attenuation-weighted ordered-subset expectation-maximization (OSEM) algorithm.[31] The complete whole-body, attenuation-corrected PET images are available within a few minutes of the completion of the scan, and all image formats are DICOM standard compliant to facilitate transfer to Picture Archiving and Communication System or radiation therapy planning systems. Features of the syngo image viewer include transverse, coronal, and sagittal displays of CT, PET, and fused images using an alpha-blending fusion algorithm. Each modality has the usual set of specific features, such as preset windows and measurement

tools for CT, and region-of-interest (ROI) manipulation and standardized uptake value (SUV) calculations for PET.

For the design shown in Fig. 3, the only modification to the Emotion CT scanner is suppression of the tilt option. The performance characteristics are, therefore, identical to a standard Emotion CT scanner. The PET scanner was modified to accommodate a 70-cm patient port to match that of the CT scanner. This change involves reducing the side shielding thereby exposing the PET detectors to increased levels of activity from outside the field-of-view. However, by making adjustments to the operating characteristics of the PET scanner, such as reducing the signal integration time and shortening the coincidence window, and implementing a variance-reduction technique in the correction of randoms, the PET performance in this design is comparable to that of the scanner with the standard, 60 cm patient port.

CT-BASED ATTENUATION CORRECTION

In addition to acquiring co-registered anatomical and functional images, a further advantage of the combined PET/CT scanner is the potential to use the CT images for attenuation correction of the PET emission data, eliminating the need for a separate, lengthy PET transmission scan. The use of the CT scan for attenuation correction not only reduces whole-body scan times by at least 40%, but also provides essentially noiseless attenuation correction factors compared to those from a standard PET transmission scan. Kinahan et al in this issue (page 166) provide a rather complete discussion of the use of the CT images for attenuation correction of the PET data and the problems associated with scaling the attenuation coefficients from CT energies to 511 keV. Nevertheless, a number of practical aspects unique to the use of CT-based attenuation correction need to be addressed, including patient respiration, truncation of the CT field-of-view, the use of intravenous and oral CT contrast media, and the presence in the patient of catheters and other metal objects that could potentially generate artifacts.

The scaling algorithms typically use a bilinear function to transform with different scaling factors the attenuation values above and below a given threshold. One such algorithm[32] scales pixels above and below 300 HU with different factors since pixels above 300 HU are assumed to be bone-related (spongiosa or cortical). Other algorithms set the change in scale factor at 0 Hounsfield units (HU) assuming that pixels >0 HU can be represented by a mixture of water and bone, whereas pixels <0 HU, are represented by a mixture of water and air. Because there is no unique transformation, different approaches may be equally valid and hopefully will lead to only small differences in the transformed coefficients. More serious effects potentially arise from the mismatch between the CT and PET images caused by patient respiration. This mismatch is generally a maximum when the clinical CT is acquired with breath-hold on full inspiration (maximum expansion of the thorax) while the PET is acquired with the patient breathing normally (Fig. 5a). Alternative protocols that incorporate breath holding at partial inspiration for the CT acquisition, or allow shallow breathing throughout both the CT and PET scans, are also being explored.[6] The anatomical regions most affected by breathing artifacts include the diaphragm, base of lung, and upper part of the liver, as shown in Fig. 5b where the dome of the liver appears localized in the lung. The use of multi-slice CT and shorter scanning times may help to reduce the frequency of such artifacts. A recent publication[33] noted that, in 300 patients with proven liver lesions, approximately 2% appeared to have the lesion localized in the lung due to respiratory motion. Care must, therefore, be exercised when interpreting studies on patients with disease in the region of the base of lung, diaphragm, and upper pole of the liver where breathing is allowed during the CT scan.

Iodinated contrast is used in CT to enhance attenuation values in the vessels (intravenous administration) and gastrointestinal tract (oral administration). Contrast-enhanced pixels that are incorrectly scaled to 511 keV can potentially generate focal artifacts in the PET image. This would be an undesirable outcome, particularly for tumor imaging. Of course avoiding the administration of contrast would eliminate the problem. However, standard-of-care CT scanning generally dictates the use of either intravenous or oral contrast, or both as in the case of the abdominal and pelvic studies. One obvious way to avoid such problems is to perform two CT scans, a clinical CT with appropriate contrast administration, and a low-dose, non-contrast CT for attenuation correction and co-registration. The two scans could even be acquired with different breathing protocols. This would, however, further increase the radiation exposure to the patient. Recent results[34] have shown that the presence of intravenous contrast at normal concentrations actually has little effect on the CT-based attenuation correction factors. Unfortunately, this is not the case for oral contrast where the larger intestinal volumes and wide range of concentrations can lead to over-correction of the PET data. However, Carney et al[35] have shown that a modification can be made to the original algorithm of Kinahan et al[32] to separate contrast-enhanced CT pixels from those of bone. Since at 511 keV the presence of iodinated contrast has a negligible effect ($<2\%$) on photon attenuation, the CT image pixels identified as oral contrast can be set to a tissue-equivalent value, thus ensuring accurate attenuation correction factors for the PET data. This modified algorithm can, to a large extent, also reduce artifacts caused by catheters and metallic objects in the patient.

In early PET/CT studies, particularly with the

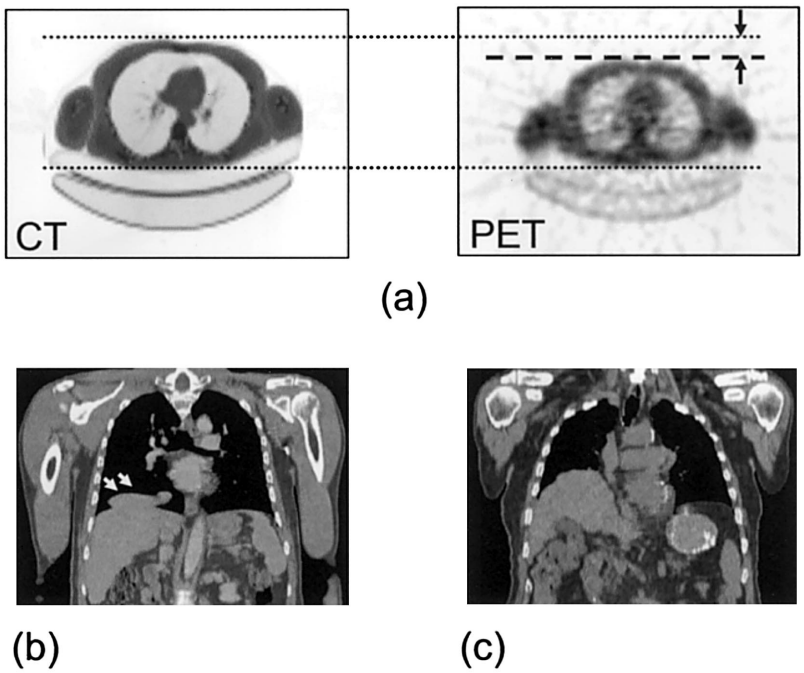

Fig 5. The effect of patient respiration on the CT-based attenuation procedure. (a) CT scan acquired with inspiration breath-hold (left) is not matched with the PET image that is acquired with regular breathing (right). (b) CT acquired with normal breathing showing artifacts near the base of the lung (arrows), and (c) with shallow breathing, the artifacts at the lung base can be greatly reduced.

prototype, all scans were acquired with the arms of the patient inside the field-of-view. This was necessary because the length of time of the PET scan created difficulties for patients to keep their arms up for the duration of the study. The procedure frequently resulted in truncation of the CT images at the edge of the limited, 45 cm diameter, transverse field-of-view, and reduced the signal-to-noise for the lines-of-response passing through the arms. Because the PET imaging field-of-view is 60 cm, the truncation artifacts resulted in inaccurate CT-based attenuation correction factors. However, recently, the PET imaging time has been significantly reduced to a level at which most patients can now, if required, maintain their arms raised for the entire duration of the PET/CT scan. This protocol then completely eliminates artifacts due to truncation and decreased signal-to-noise in all but the very large patients.

CT-based attenuation correction continues to be an area of active development. Nevertheless, the benefits of low statistical noise and rapid transmission imaging far outweigh potential problems of scaling bias, respiration artifacts, and contrast. Consequently, while some PET/CT designs come equipped with standard PET transmission sources, few, if any centers actually use them for routine transmission scanning. Using CT-based attenuation correction, fully quantitative whole-body scans can now be acquired in as little as 10 min, which is very convenient for the patient and ensures rapid throughput.

CLINICAL PROTOCOLS FOR PET/CT SCANNING

The clinical protocols for the newer generation PET/CT scanners are similar to those used with the prototype PET/CT. After injection of approximately 370 MBq (10 mCi) of FDG and a 1-hr uptake period, the patient is positioned in the scanner and a topogram or scout scan, is acquired. The total range to be scanned by both PET and CT is selected by the physician based on the particular indication for the study (ie, skull base to abdomen for head and neck malignancies, and neck through pelvis for most other malignancies). To minimize the mismatch between the CT and PET images, the patient is instructed to breathe shallowly during the spiral CT acquisition, rather than holding his or her breath. The spiral CT is then followed by a PET acquisition covering the same axial extent. The reconstruction of the CT images occurs in parallel with the acquisition of the PET data, allowing the calculation of the attenuation correction factors to be performed during the PET acquisition. Once the first bed position is completed, PET reconstruction can commence. The CT-based attenuation correction factors are calculated according to the algorithm of Kinahan et al[32] and 3D reconstruction is

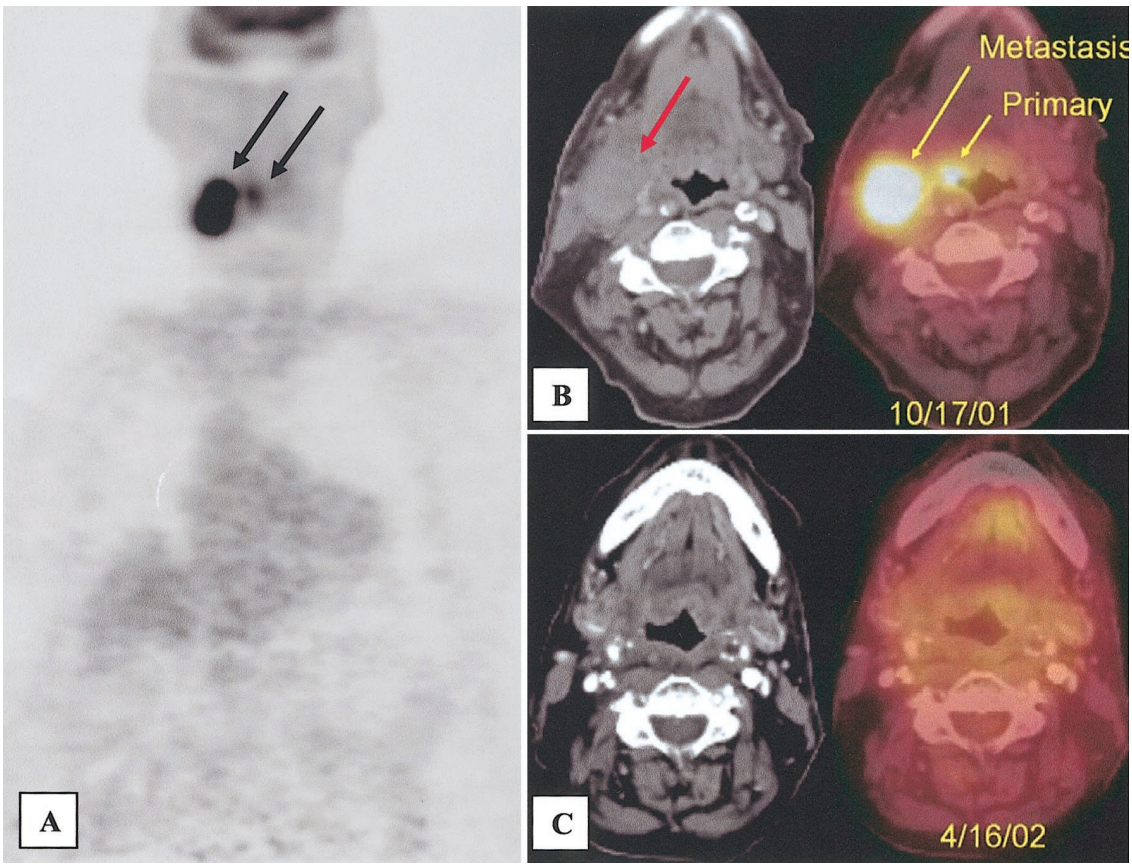

Fig 6. (A) Coronal PET. (B) Pre-surgical axial CT and PET/CT images. (C) Post-surgical axial CT and PET/CT. This patient was diagnosed with metastatic squamous cell carcinoma of the head and neck by fine needle biopsy of a large right neck mass. CT (not shown) prior to combined PET/CT could not identify a mucosal primary. Coronal PET shows intense uptake in a large right neck mass with an adjacent focus of uptake (black arrows). Pre-surgical CT shows the large mass (red arrow) but does not show the primary mucosal lesion. Only the fused image demonstrates the exact location of the mucosal primary (small yellow arrow). Follow-up images after surgery and radiation demonstrate no evidence for recurrence.

performed by using Fourier rebinning and an attenuation-weighted ordered-subset EM algorithm.[31] Within a few minutes of the conclusion of the final PET bed position, the attenuation-corrected and reconstructed PET images are available for viewing, co-registered with the CT scan. Depending on the model of PET/CT scanner used, the total time of scanning and reconstruction can range from 10-30 min for a whole body scan. Following reconstruction, the images are transferred to an off-line viewing station and the data are archived.

Because many oncology patients today undergo both CT and PET scans as part of their workup, fusing CT (anatomy) with PET (function) consolidates the imaging studies and, as mentioned, is more convenient for the patient. Although patient convenience is an important factor in the conceptual design, the real utility of a combined PET/CT scanner is in the additional information obtained that can not be extracted from PET and CT scans acquired separately. Three illustrative cases are presented below that demonstrate this synergy and illustrate the types of additional information that likely would not have been obtained by performing PET and CT separately.

Case 1: Head and Neck Cancer-Detecting Mucosal Primary Lesions

To detect malignancy, anatomical imaging modalities rely on either architectural distortion or enhancing characteristics that are suggestive of, or consistent with, cancer. On the other hand, the ability of functional imaging to identify pathology depends on the avidity of a tumor for the injected tracer, such as FDG, and the size of the abnormality. Case 1 (Fig. 6) illustrates how a combined in-line PET/CT scanner provides additional information through the perfect, or near-perfect, registration of the images. The PET scan identifies the large metastasis in the right neck, as well as a focus adjacent to the metastasis and more medial. It is difficult, or impossible, to determine whether this represents a second metastasis or a primary mucosal lesion. Normally,

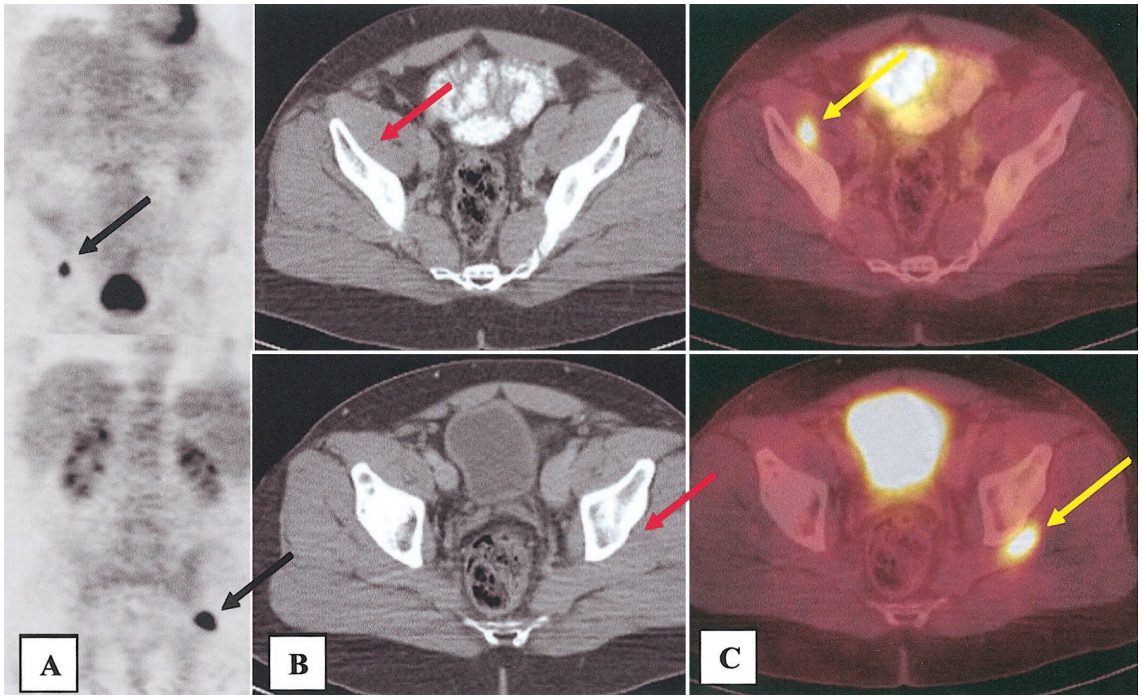

Fig 7. (A) Coronal PET. (B) Axial CT. (C) Axial PET/CT. Patient had a history of non-Hodgkin's lymphoma in remission and had recent complaints of pelvic pain. Coronal PET images demonstrate multiple foci of intense FDG uptake in the pelvic area initially thought to represent abnormal foci within the osseous structures. CT images do not demonstrate any abnormalities. PET/CT images localize lesions to soft tissue (yellow arrows) rather than bone.

the interpreting physician would try to correlate visually the abnormality seen on PET with the CT scan. As this case illustrates, there is often no corresponding anatomical abnormality, or the functional change may precede any anatomical change that could be detected on a CT scan. However, with the fused PET/CT images, precise localization to the right lateral tongue base can be diagnosed with confidence. A directed biopsy of this area based on the images confirmed a primary mucosal squamous cell carcinoma. Without the identification of this primary lesion, it is likely that additional metastases would have occured from seeding of the primary lesion.

Case 2: Lesion Localization

Prior to the availability of the combined PET/CT scanner, an abnormality seen on PET could not be confirmed by CT because either there was no obvious anatomical abnormality, or the abnormality developed in the interim period between the CT and PET scans. Consequently, the interpreting physician would have to make an informed guess as to the precise location based solely on the anatomical information from the PET scan. Case 2 (Fig. 7) demonstrates multiple abnormalities identified on the PET scan that appear to involve bony pelvic structures. The CT did not identify any bony or soft tissue abnormalities, which makes precise localization essentially impossible. The fused PET/CT images demonstrated that the abnormalities do not correspond to osseous structures, but in fact localize to the adjacent muscles. In some types of malignancies, the difference between osseous and soft tissue involvement could lead to a change in treatment.

Case 3: Accurate Biopsy Localization

It is not uncommon for a biopsy of a malignant lesion to return falsely negative. The reasons for a false-negative biopsy include sampling from a necrotic center, sampling of adjacent tissues, or inadequate sampling of malignant cells. PET has been used to help localize the most metabolically active portion of a tumor and guide the biopsy to this location. However, Case 3 (Fig. 8) demonstrates the power of combined PET/CT in guiding biopsies. Intense uptake in the presacral space, consistent with recurrent colorectal cancer, appears to correlate with the large presacral mass, which was interpreted as equivocal on CT alone. The combined PET/CT image illustrates that the majority of the mass is not metabolically active and likely represents post operative changes, and that there is only a small focus within this mass that is metabolically active. A directed biopsy of this focus using CT guidance, rather than random biopsy of the presacral mass, led to the confirmation of recurrent colorectal cancer rather than a false negative biopsy.

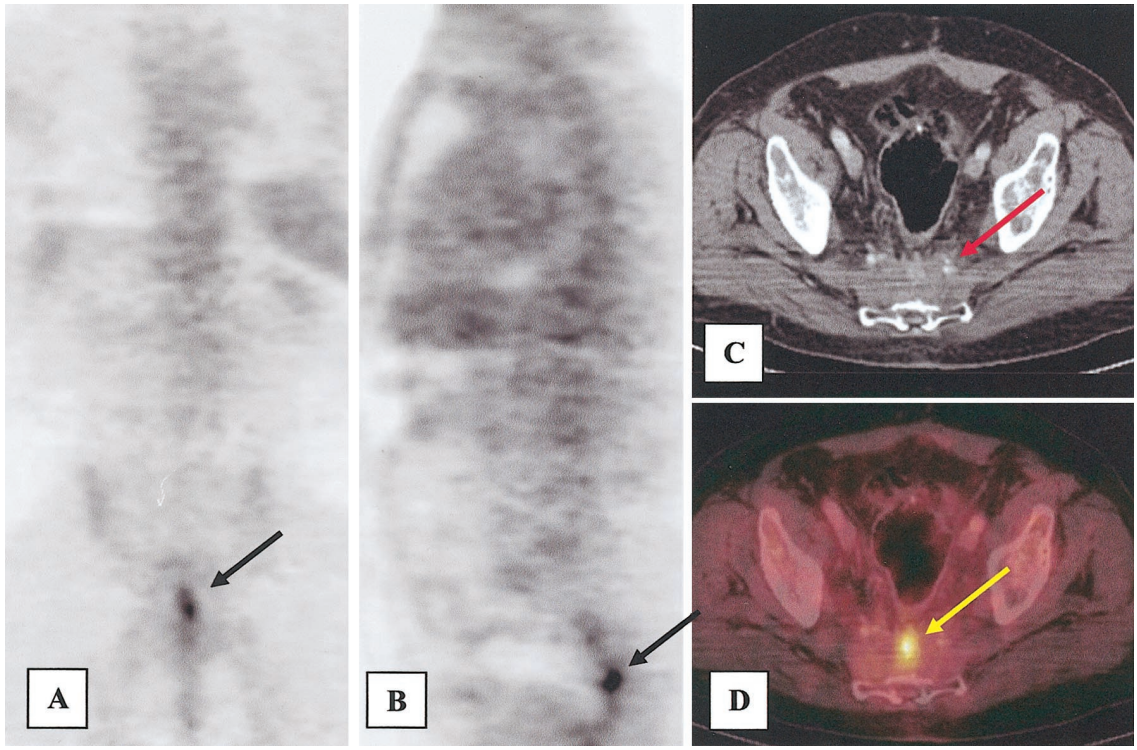

Fig 8. (A) Coronal PET. (B) Sagittal PET. (C) Axial CT. (D) Axial PET/CT. Patient with a history of colorectal cancer had undergone sigmoid resection and then presented with rising CEA levels. PET images demonstrate intense uptake in the presacral space that appears to correspond to the large presacral mass seen on the CT scan (red arrow). PET/CT image shows clearly that only a small part of the large presacral mass was involved. These fused images led to a directed biopsy of this area, which confirmed recurrent adenocarcinoma.

CURRENT STATUS AND FUTURE PROSPECTS

The rapidly increasing use of functional imaging in areas that have traditionally been dominated by anatomical imaging modalities will demand reliable and easy-to-use PET/CT scanners that can achieve high throughput. The recent introduction of the new fast scintillators LSO and gadolinium oxyorthosilicate as PET detectors has occurred at a timely moment for PET/CT because a reduction in the lengthy PET imaging time is essential to more closely match that of the CT scan duration. Although it is unlikely that whole-body PET imaging times will be reduced to the 30 to 60 seconds required for CT scanning, a scan time less than 10 minutes has already been achieved. Throughput will increase significantly, as will patient comfort and convenience. New applications, such as dynamic whole-body scans and the use of short-lived radioisotopes (eg, ^{11}C with a 20-minute half-life) will then be within reach.

As the installed base of PET/CT scanners increases, many of the problems and challenges discussed in this article will be addressed and solutions undoubtedly found. In particular, appropriate PET/CT protocols for different cancer types must be defined and further potential applications in cardiology and neurology identified. The role of PET/CT with tracers other than FDG will be explored, and as molecular probes are developed that are more disease-specific, the requirement for co-registered anatomy will become even more important. The use of CT-based attenuation correction factors will doubtless also be an area of further investigation, particularly for the definition of appropriate breathing protocols and for the use of CT contrast media.

Future developments in combined PET/CT scanners will be exciting, attaining a higher level of integration and of anatomical and functional imaging performance than ever before. By fulfilling an important role, not only in the diagnosis and staging of cancer, but in designing and monitoring appropriate therapies, the hardware approach to image fusion will undoubtedly have a significant impact on patient care strategies, patient survival, and ultimately, on the quality of life.

ACKNOWLEDGEMENT

The combined PET/CT project with which we are associated has involved many colleagues at the University of Pittsburgh, CPS Innovations in Knoxville, Tennessee, and Siemens CT division in Forchheim, Germany, over the last few years. In particular, we acknowledge the seminal contributions of Dr. Ron Nutt, CPS President, who led the PET/CT prototype development team at CPS, and Dr. Charles Watson, who led the commercial development of the PET/CT scanner for CPS. The

PET instrumentation and methodology group at the University of Pittsburgh made a major contribution to this project, in particular Drs. Paul Kinahan, Jonathan Carney, David Brasse, and Jeffery Yap. Finally, we thank the many physicians and technologists in the Pittsburgh PET Facility who contributed to the PET/CT clinical evaluation program, especially Drs. Charron, Meltzer, and McCook and technologists Denise Ratica, Stacey Mckenzie, Marsha Martinelli, and Donna Mason.

REFERENCES

1. Weber WA, Avril N, Schwaiger M: Relevance of positron emission tomography PET in oncology. Strahlenther Onkol 175:356-373, 1999

2. Pelizzari CA, Chen GTY, Spelbring DR, et al: Accurate three-dimensional registration of CT, PET and MR images of the brain. J Comp Assist Tomogr 13:20-26, 1989

3. Pietrzyk U, Herholtz K, Heiss W-D: Three-dimensional alignment of functional and morphological tomograms. J Comput Assist Tomogr 14:51-59, 1990

4. Woods RP, Mazziotta JC, Cherry SR: MRI-PET registration with an automated algorithm. J Comp Assist Tomogr 17:536-546, 1993

5. Wahl RL, Quint LE, Cieslak RD, et al: "Anatometabolic" tumor imaging: Fusion of FDG PET with CT or MRI to localize foci of increased activity. J Nucl Med 34:1190-1197, 1993

6. Beyer T, Townsend DW, Brun T, et al: A combined PET/CT scanner for clinical oncology. J Nucl Med 41:1369-1379, 2000

7. Charron M, Beyer T, Bohnen N, et al: Image analysis in patients with cancer: Studies with a combined PET and CT scanner. Clin Nucl Med 25:905-910, 2000

8. Kluetz PG, Meltzer CC, Villemagne, MD, et al: Combined PET/CT imaging in oncology: Impact on patient management. Clin Posit Imaging 3:1-8, 2001

9. Meltzer CC, Martinelli MA, Beyer T, et al: Whole-body FDG PET imaging in the abdomen: Value of combined PET/CT. J Nucl Med 42:35P, 2001a (abstr)

10. Meltzer CC, Snyderman CH, Fukui MB, et al: Combined FDG PET/CT imaging in head and neck cancer: Impact on patient management. J Nucl Med 42:36P, 2001b (abstr)

11. Blodgett TM, Meltzer CC, Townsend DW, et al: PET/CT in re-staging patients with ovarian cancer. J Nucl Med 45:310P, 2002a (abstr)

12. Blodgett TM, Meltzer CC, Townsend DW, et al: PET/CT in staging and re-staging patients with cervical cancer. J Nucl Med 45:310P, 2002b (abstr)

13. Bar-Shalom R, Keidar Z, Guralnik L, et al: Added value of fused PET/CT imaging with FDG in diagnostic imaging and management of cancer patients. J Nucl Med 43:32P, 2002 (abstr)

14. Dizendorf E, Ciernik IF, Baumert B, et al: Impact of integrated PET/CT scanning on external beam radiation treatment planning. J Nucl Med 43:33P, 2002 (abstr)

15. Freudenberg LS, Antoch G, Mueller SP, et al: Preliminary results of whole body FDG-PET/CT in lymphoma. J Nucl Med 43:30P, 2002 (abstr)

16. Yeung HW, Schoder H, Larson SM. Utility of PET/CT for assessing equivocal PET lesions in oncology—Initial experience. J Nucl Med 43:32P, 2002 (abstr)

17. Keidar Z, Bar-Shalom R, Guralnik L, et al: Hybrid imaging using PET/CT with ^{18}F-FDG in suspected recurrence of lung cancer. Diagnostic value and impact on patient management. J Nucl Med 43:32P, 2002 (abstr)

18. Steinert HC, Hany TF, Kamel E, et al: Impact of integrated PET/CT scanning on pre-operative staging of lung cancer. J Nucl Med 43:151P, 2002 (abstr)

19. Osman MM, Cohade C, Leal J, et al: Direct comparison of FDG-PET and PET-CT imaging in staging and re-staging patients with lung cancer. J Nucl Med 43:151P, 2002 (abstr)

20. Hasegawa BH, Stebler B, Rutt BK, et al: A prototype high-purity germanium detector system with fast photon-counting circuitry for medical imaging. Med Phys 18:900-909, 1991

21. Lang TF, Hasegawa BH, Soo Chin L, et al: Description of a prototype emission-transmission computed tomography imaging system. J Nucl Med 33:1881-1887, 1992

22. Hasegawa BH, Lang TF, Brown EL, et al: Object specific attenuation correction of SPECT with correlated dual-energy X-ray CT. IEEE Trans Nucl Sci NS-40:1242-1252, 1993

23. Blankespoor SC, Xu X, Kaiki K, et al: Attenuation correction of SPECT using X-ray CT on an emission-transmission CT system: myocardial perfusion assessment. IEEE Trans Nucl Sci 43:2263-2274, 1996

24. Townsend DW, Beyer T, Kinahan PE, et al: The SMART scanner: A combined PET/CT tomograph for clinical oncology. IEEE Nucl Sci Symp Conf Rec M5-1, 1998

25. Townsend DW: A combined PET/CT scanner. The choices. J Nucl Med 3:533-534, 2001a

26. Bailey DL, Young H, Bloomfield PM, et al: ECAT ART - a continuously rotating PET camera: Performance characteristics, initial clinical studies and installation considerations in a nuclear medicine department. Eur J Nuc Med 24:6-15, 1997

27. Townsend DW, Beyer T, Kinahan PE, et al: Recent studies with a combined PET/CT scanner: A synergistic approach to patient management, in Tamaki N, Tsukamoto E (eds): Positron Emission Tomography in the Millenium. Proceedings of the International PET Symposium, Hokkaido, Japan, 2000, pp 220-244

28. Townsend DW, Cherry SR: Combining anatomy with function. The path to true image fusion. Eur Radiol 11:1968-1974, 2001b

29. Jaroff L: A winning combination. Time 156(23), 72-74, 2000

30. Comtat C, Kinahan PE, Defrise M, et al: Fast reconstruction of 3D PET data with accurate statistical modeling. IEEE Trans Nucl Sci 45:1083-1089, 1998

31. Patton JA, Delbeke D, Sandler MP: Image fusion using an integrated dual-head coincidence camera with x-ray tube-based attenuation maps. J Nucl Med 41:1364-1368, 2000

32. Kinahan PE, Townsend DW, Beyer T, et al: Attenuation correction for a combined 3D PET/CT scanner. Med Phys 25:2046-2053, 1998

33. Osman MM, Cohade C, Nakamoto Y, et al: Clinically significant inaccurate localization of lesions with PET/CT: Frequency in 300 patients. J Nucl Med 44:240-243, 2003

34. Yau YY, Coel M, Chan WS, et al: Application of IV contrast in PET-CT: Does it really produce attenuation correction error. J Nucl Med 44:272P 2003 (abstr)

35. Carney JP, Beyer T, Brasse D, et al: Clinical PET/CT scanning using oral CT contrast agents. J Nucl Med 45:57P, 2002 (abstr)