Why Nearly All PET of Abdominal and Pelvic Cancers Will Be Performed as PET/CT

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Clinical experience at Johns Hopkins and published literature regarding PET/CT applications in the abdomen and pelvis are reviewed, and the strengths and limitations of this evolving technology are summarized. More than 2,700 whole-body PET/CT scans including the abdomen and pelvis were performed for clinical indications by our nuclear medicine service from June 2001 through September 2003. Indications for these studies are reviewed, and our clinical impressions of diagnostic advantages and limitations of PET/CT are reported. Of the >2,700 whole-body PET/CT scans performed at our institution, >90% were for known or suspected cancers. Primary abdominopelvic indications were second in frequency to thoracic indications. In addition, a comprehensive literature search was performed, and key articles related to PET/CT in the abdomen and pelvis were identified, reviewed, and summarized. Under the search term "PET/CT," 142 articles were identified under the National Library of Medicine Pub Med database, and a number of general findings are summarized. **Conclusion:** PET/CT allows for the accurate localization of foci of radiotracer uptake and their separation from normal structures. In our experience, the method is quantitatively accurate, rapid, and easily implemented, including contrast studies, in clinical practice in a wide range of abdominopelvic indications. Although artifacts can occur from a variety of causes, close attention to protocol details and patient immobilization reduces their frequency. Where systematically studied, PET/CT improves diagnostic accuracy compared with PET alone. It is anticipated that PET/CT will increasingly become the routine and preferred procedure for abdominopelvic evaluations with PET imaging. It has already become the preferred method at our center.

Key Words: oncology; PET; PET/CT; abdominopelvic imaging; ^{18}F-FDG; colorectal cancer

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More than a decade ago, it was recognized that the intense target-to-background-ratios observed in tumors imaged with ^{18}F-FDG PET were clearly a blessing but also a potential curse (*1*). The blessing was obviously the detection and characterization by ^{18}F-FDG PET of small tumors not seen by other noninvasive methods. The curse was that the abnormalities could sometimes be difficult to precisely locate when the target-to-background ratios were so very high. Thus, with a successful method of imaging that was purely functional, the target-to-background ratios could be so high that the target might be seen but be difficult to put it into an appropriate anatomic context.

Although PET images are functionally based and, with attenuation correction, substantially anatomically correct, we not infrequently knew only the general area or region of abnormally increased ^{18}F-FDG uptake—not the precise anatomic location. For that reason, we and others focused on the development and use of software-based fusion methods to locate tumors anatomically in a process referred to as "anatometabolic imaging," in which the anatomic detail of CT or MRI was fused with the functional information uniquely available from PET (*2*). Although this technique can be applied and used successfully in evaluating the chest, abdomen, and pelvis, it is logistically challenging in many circumstances, especially when attempting fusion directly between emission PET images and CT without the use of fiducial markers (*3*). Challenges in fusion imaging can include mundane but vexing issues of data transfer between various computer-based imaging systems or nonavailability of digital datasets for patients referred for imaging. However, a more important challenge is posed by differences in anatomic positions of the patient between PET and CT, either as a result of external position differences or internal differences in organ anatomy. The latter can be caused by differences in bowel gas distribution (e.g., interval defecation, eating, or changes in hydration or excretory status). Moreover, the methodology can be complicated when studies are performed at two different medical centers, which is often the case when patients are referred from a tertiary or quaternary care center and digital datasets are not available for fusion. We have found that fusion methods can be applied carefully and successfully without PET/CT, but the best approach is when the patient has a specially constructed bed or bed-insert used on both the PET and CT studies, which are performed in close temporal proximity (*4*). Because PET and CT tables may differ in bed configurations, these additional complexities make software-based fusion difficult.

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As is outlined elsewhere in the supplement by Townsend et al. (*5*), the development of dedicated PET/CT imaging at their institution and others has made robust, nearly real-time, anatometabolic imaging routine in centers that have the new technology (*6*). In the PET/CT approach, high-quality mechanically intrinsically-registered images of both PET and CT are generated and used either as independent images or are fused to evaluate both form and function in the abdomen, pelvis, other sites in the abdomen, or in the rest of the body.

PET with ^{18}F-FDG and likely PET with other radiotracers have considerable utility in assessing the abdomen and pelvis. For example, PET has been shown to be more accurate than CT in determining whether and where colorectal cancer has recurred (*7*). PET with ^{18}F-FDG is similarly useful (among other applications) in characterizing metastases in the liver and adrenals, assessing the spleen for lymphomatous infiltration, determining whether the pancreas or adjoining lymph nodes contain cancer, and searching for metastatic ovarian, cervical, endometrial, renal, and bladder cancers.

Although PET is highly accurate and generally superior to CT in abdominal tumor assessments, a major challenge in PET interpretation in the abdomen is determining the precise location of areas of increased ^{18}F-FDG uptake and separating abnormal foci of tracer uptake from normal variants that accumulate ^{18}F-FDG. As has been reviewed by Shreve et al. (*9*), normal variants and artifacts can be confusing on PET and sometimes can be mistaken for tumor. Abdominal, pelvic, and retroperitoneal anatomy can be variable with variations in liver size, renal size, renal deformities and variability in bowel uptake patterns. Ureters and the urethra can vary in apparent caliber on PET, because these structures can contain different amounts of radioactivity. Finally, the rectosigmoid bladder, prostate region, ovaries, and uterus can vary in sizes, locations, and orientation, making assessment of the pelvis challenging. It also can be challenging in some occasions to determine whether a lesion localized to the anatomic pelvis is in the pelvis, in the bony structure of the pelvis, or simply extra-pelvic. Differences of a centimeter in lesion location can make a large difference in whether a disease process is categorized as intraabdominal/pelvic or located in bone and thus systemic.

The purpose of this report is to describe our clinical experience at Johns Hopkins with PET/CT, review the published literature regarding PET/CT applications in the abdomen and pelvis, and summarize the strengths and limitations of this evolving technology in clinical applications in this anatomic region. We also will briefly describe technical considerations for performance of PET/CT as practiced in the author's institution. The use of oral contrast, the quality of image fusion, the effects of organ and bowel motion, the effect of intravenous contrast, and the comparison of quantitative values between CT and ^{68}Ge/^{68}Ga transmission images, and initial clinical results on a variety of illnesses will be discussed. We believe our experience to date supports the routine use of PET/CT in evaluation of the abdomen and pelvis.

EXPERIENCE WITH PET/CT IN THE ABDOMEN AND PELVIS

More than 2,700 whole-body PET/CT scans including the abdomen and pelvis were performed for clinical indications by our nuclear medicine service from June 2001 through September 2003. More than 90% of the these scans were performed for indications related to known or suspected malignancy. Thoracic indications predominated, and indications with suspected abdominopelvic foci were the second most common. Based on protocols in place during this time period, nearly all of the thoracic and abdominal disease-focused scans included imaging of the abdomen and pelvis with PET/CT.

The Johns Hopkins PET center currently has three human whole-body PET scanners, one of which is a PET/CT unit. With the introduction of PET/CT technology in mid 2001, our patterns of scanner utilization for clinical PET indications evolved from performing PET only to a distribution of scans across PET and PET/CT devices to today imaging almost all abdominal and pelvic indications with PET/CT.

PET/CT imaging is also currently our preferred methodology in most oncology patients, except in brain imaging and in patients who are claustrophobic. The brain is an exception, because software-based fusion or image assessment visually are considered sufficient in most patients with epilepsy or brain tumors. The rare patient who is claustrophobic in PET/CT may find a regular PET scanner to be more suitable because of the shorter bore length and a perception of scanner "openness."

The author of this article has reviewed many of the PET/CT scans performed at Johns Hopkins either primarily or in consultation. All scans were generated with a General Electric Discovery LS PET/CT system (GE Medical Systems) using a protocol described in the next section. Initial PET scans were performed with ^{68}Ge/^{68}Ga attenuation correction and CT attenuation correction, but later scans were performed using CT attenuation correction only. Reconstructions have been by iterative methods. Clinical indications for the studies were reviewed, and our clinical impressions of the diagnostic advantages and limitations of PET/CT in the abdomen are reported based on our experience.

In addition, a comprehensive literature search on PET/CT was performed using the National Library of Medicine PubMed database. We found 142 articles using PET/CT in the search, which was expanded to include author searches on individuals who gave presentations on PET/CT at the Society of Nuclear Medicine annual meetings in 2002 and 2003. Key completed articles related to PET/CT in the abdomen and pelvis were identified and reviewed, including studies reported from the nuclear medicine group at Johns Hopkins. Examples of major scan findings from this literature and from the experience of the Johns Hopkins group are

provided here to illustrate key points regarding the use of PET/CT in the abdomen and pelvis.

SUGGESTED ABDOMINOPELVIC IMAGING PROTOCOL

Our clinical protocol for the abdomen and pelvis has evolved over the past 2 y based on logic, trial, and error, with the latter of disproportionate importance. Given the rapid evolution of PET/CT technology, it is important to note that current protocols continue to evolve as new information becomes available. We are aware that our protocol differs to some extent from those in use at other centers.

Patient preparation for an oncologic ^{18}F-FDG PET/CT scan is similar to that for a standard oncologic ^{18}F-FDG PET scan. Patients fast for at least 4 h before imaging in our protocol. If the glucose in the serum is $<$200 mg/dL, the patient is injected intravenously with ^{18}F-FDG. An injected dose of 0.22 mCi/kg is used with our 2-dimensional PET imaging and bismuth germanate orthosilicate. We have found that this dose of ^{18}F-FDG provides satisfactory true count density across a wide range of patient body weights when using acquisition times of 5 min per PET scanning level. Lower doses of ^{18}F-FDG are certainly feasible, but with the 5-min imaging duration these could result in low count density studies that can be of statistically lower quality and less "optimal" in image quality on our 2-dimensional PET system (*9*). It is not established that this dose is required to achieve diagnostic accuracy, but it is effective for achieving uniformly high image quality across a wide range of body weights and sizes (*9*). With 3-dimensional PET systems and more sensitive 2-dimensional systems, lower doses of ^{18}F-FDG or shorter acquisitions might produce similar diagnostic results but may have challenges in larger patients due to scatter.

In our current protocol for abdominal and thoracic imaging, we perform the CT scan immediately before the PET scan. In our initial assessment of the PET/CT device, we determined the type of CT protocol we would use. The group from the University of Zurich (*10,11*) has explored several different milliamperage settings for the x-ray tube used in PET/CT, including settings for the multidetector spiral that is similar to the one in our scanner (4-detector spiral CT unit). They showed that an x-ray tube energy as low as 10 mA was sufficient for attenuation correction but that such a method provided little diagnostic information. They reported that the 40-mA tube current is generally adequate for PET/CT and allows for suitable image localization. We also have found that a relatively low-energy setting is quite adequate for image acquisition in most patients. Thus, in general, we use an 80-mA tube current and 140-kVp x-ray energy for our CT images of the abdomen and pelvis. In very small patients, we adjust the tube current downward to 40 or 60 mA and, in very large patients, up to 120 or even 160 mA. Our subjective impression is that this somewhat higher tube current is sufficient to produce CT images of diagnostic quality and is obviously more than adequate to allow for the generation of attenuation correction maps. We vary the tube current in an effort to optimize image quality yet minimize radiation dose to the patient.

Before PET/CT imaging, our patients change into gowns. All loose metallic objects are removed, because these can cause hot-spot artifacts on PET/CT as a result of attenuation correction errors (*12*). A technical consideration in the performance of the CT scan is whether the arms are placed at the patient's side or above the head. In the authors' past experience, the duration of traditional PET image acquisitions was such that the arms were usually placed at the patient's side both for comfort and to reduce the likelihood of motion during the lengthy acquisition of ^{68}Ge/^{68}Ga attenuation correction images and emission PET images. Our initial studies with the PET/CT system were also performed with arms at patients' sides. We found, however, that although this position minimized patient motion, the beam-hardening artifact and possible arm motion degraded the quality of CT images of the upper abdomen. These artifacts were noticeably propagated into the attenuation-corrected emission PET images. For this reason, we have attempted, whenever possible, to have the arms immobilized above the patient's head for the acquisition of abdominal and pelvic PET images. With this protocol and cooperative patients, beam-hardening artifact frequency across the liver appears to have been reduced on CT-corrected emission PET images and higher quality CT images also resulted.

For abdominal imaging, we initially did not use oral contrast to enhance visualization of the bowel but have more recently moved to using oral contrast quite routinely. At present we administer two bottles or approximately 2 L of barium sulfate, (approximately 1.3% weight/volume) by mouth before the CT. About half the volume is administered before the ^{18}F-FDG is injected, and the other half is administered starting about 30 min after the FDG injection. This dilute oral CT contrast is given in a nonglucose-containing medium to minimize the possibility of ^{18}F-FDG uptake changes resulting from insulin release induced by increasing glucose levels. The uptake period of ^{18}F-FDG is typically approximately 1 h before the initiation of PET imaging. During this period, the patient sits quietly without reading or talking and then drinks additional oral contrast about 10 min before imaging. Whether or not oral contrast is used depends on the specific question being addressed in imaging. In general, oral contrast is well tolerated. The precise volume of oral contrast that should be administered varies with patient size. High-density oral contrast can cause significant artifacts as a result of over-attenuation correction. Cohade et al. (*13*), however, have demonstrated that oral contrast of a low density is generally unlikely to cause significant artifacts. Other groups have shown similar results with only modest alterations in absolute quantitation resulting from the oral contrast (*14,15*). An example of an oral contrast-induced artifact is shown in Figure 1.

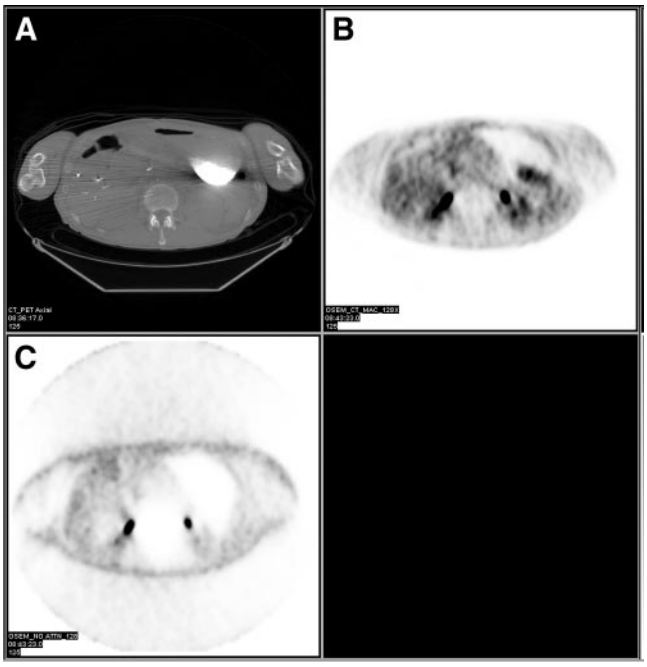

FIGURE 1. (B) PET image (emission image, CT-corrected for attenuation) showed intense tracer activity in posterior stomach region. (A) CT showed very dense contrast (CTHU >3,000) in same area as result of high-grade partial gastric outlet obstruction. Patient had ingested barium several days before. (C) Nonattenuation-corrected image did not show this "gastric tracer uptake." Uptake in stomach was artifactual from inaccurate attenuation correction in presence of very dense barium. Nonattenuation-corrected images can help resolve such a case. (Reprinted with permission from [*13*]).

Our CT protocol for abdominal and pelvic imaging generally is performed so that the chest and abdomen are included. We usually begin our CT scan from the external auditory meatus and continue caudally to the midthigh for a typical whole-body acquisition. A key issue in CT is the choice of respiratory status during the scan to optimize fusion with PET. For many CT scans not including PET, full inspiration is held to maximize lung volume and minimize respiratory artifacts. However, the roughly 30-s CT scan performed in our PET/CT system may make it difficult for some cancer patients to hold their breath during the entire acquisition. In addition, although holding nearly mid expiration is probably the best position in which to achieve the most accurate image fusion between PET and CT, as reported by Goerres et al. (*16*), our patients are allowed to breath quietly during the CT scan because many are ill and unable to hold their breath for the full time of the CT acquisition (*17*). Thus, quiet tidal breathing is the norm for our protocol for imaging the abdomen with our 4-slice multidetector scanner. Immediately before the PET/CT is begun, the patient is asked to urinate and fully empty the bladder. The patient then lies on the imaging table in a supine position and is lightly immobilized, especially around the head and neck.

As indicated previously, the protocol for CT involves placing the patient's arms above the head. For the body images, a helical scan is obtained with the 4-detector scanner at high speed with a pitch of 6, 22.5 mm/s table speed, 8-s rotations, and 5-mm slices, with tube settings most commonly at 140 kVp and 80 mA. The field of view is 50 cm, and the matrix size is 512 × 512 for the CT. These images are rapidly reconstructed and are then available for comparison with the PET images. The datasets can be transformed into attenuation maps by published algorithms (*18*).

Our PET images are reconstructed by iterative methods as previously described. The PET and CT images are fused on a workstation (GE Entegra). In addition to the fused images, the CT and PET images can be viewed independently. Thus, several potential datasets are available from the workstation. It is possible to view both the 512 × 512 transverse CT images and the 128 × 128 matrix images in coronal, sagittal, and transverse views using this software. Both attenuation-corrected (generally based on the CT dataset) and nonattenuation-corrected images are available for assessment. Maximum intensity projection images of the emission PET datasets are available as well a CT scanogram. Thus multiple methods are available to examine the CT images and the PET. Multiple presets are available to examine the CT images and a variety of windows (lung, soft tissue, and bone are the most commonly used). We also use the brain window to look for liver metastases on CT that may be relatively subtle on noncontrast studies.

QUANTITATIVE DATA FROM EMISSION PET IMAGES PROCESSED USING CT ATTENUATION CORRECTION

One of the key advantages of PET over other imaging methods is that it is functional in nature and that the functional information provided is quantitative. Quantitative information has been the hallmark of PET imaging. Using CT to correct for attenuation potentially could result in errors because of the much lower energy of the CT X-ray beam compared with the 511-keV photons from a $^{68}Ge/^{68}Ga$ source. Our PET/CT scanner is equipped so that it has both $^{68}Ge/^{68}Ga$ and CT attenuation sources. Nakamoto et al. (*19*) closely examined the quantitative characteristics of PET and CT in a study of 28 patients with known or suspected cancer who underwent whole-body PET scanning for clinical diagnostic purposes. In these patients, attenuation-correction maps from both the CT and $^{68}Ge/^{68}Ga$ transmission data for the two different attenuation-correction emission datasets were produced. Activity was then measured for identical regions of interest in normal organs and in pathologic foci of uptake. In general, excellent agreement between the $^{68}Ge/^{68}Ga$- and CT-corrected emission datasets was seen. Using our scanner and software, the median and average radioactivity concentrations were minimally, about 4%–15%, higher for the CT corrected images than for $^{68}Ge/^{68}Ga$-corrected images. Osseous lesion standard uptake values (SUVs) were higher on CT-corrected images, as were activity levels in lesions in the pelvis. Overall, however, SUV

levels for abdominal lesions were comparable between the two methodologies. Thus, CT attenuation-correction measurements are quite satisfactory for accurate quantitation of lesions in the abdomen and elsewhere.

A modest correlation was observed between the CT Hounsfield units (HU) and the percentage difference in the measured activity between the CT-corrected PET images and the ^{68}Ge/^{68}Ga-corrected images. However, these data indicate that the quantitative data from PET/CT are quite comparable with those of traditional ^{68}Ge/^{68}Ga attenuation sources. One advantage of using CT attenuation, in addition to precise anatomic detail, is that the images can be obtained in approximately 30 s, faster than the approximately 20 min needed in some traditional attenuation-correction algorithms. One consideration for sequential studies is that switching between varying PET/CT systems can be problematic. One probably would not want to use a traditional PET system and then PET/CT for longitudinal follow-up studies in a single patient because of these slight differences in quantitation. The CT approach has now been reported by other groups (*10*,*20*–*22*).

Given that quantitative data are generally quite comparable between PET/CT and traditional PET, another issue is the accuracy of image registration. Cohade et al. (*23*) established that image registrations between PET and CT for lesions in the thorax were generally quite good, with error magnitudes commonly 6–8 mm for lung nodules even with the imaging during tidal respiration. Similar results were seen by the Zurich group (*24*) with best fusion accuracy in moderate expiration or tidal breathing. As the lungs move, so do the upper abdominal organs. We were thus concerned that PET/CT fusion imaging in the abdomen might be complicated by differences in organ size between PET and CT. Our expectation was that abdominal organs would generally appear larger on PET than they did on CT, because respiration during PET distributes organs over a larger volume than on a single breath-hold CT. It can be difficult to determine precise lesion size in PET, because edge definition can be problematic. For evaluation of the abdomen, the quality of organ registrations is important. Poor registrations could cause artifacts.

Nakamoto et al. (*25*) studied 26 consecutive patients who underwent clinical PET/CT scans for suspected cancer. Image attenuation correction of PET was by both CT and germanium transmission images. The locations of organs, including the liver, spleen, and bilateral kidneys, were independently defined on emission PET (with both CT and ^{68}Ge/^{68}Ga transmission correction) and on CT. He observed that between the CT and PET images >10% of image pairs showed a discrepancy in position of >2 cm between the CT-based and the germanium-corrected PET and the CT, particularly at the upper margin of the liver and lower margin of the spleen, although the differences in the position of the edges were <10 mm in most cases. The center of the liver on PET tended to be located cephalad and to the right and the spleen tended to be cephalad and posterior compared with their relative positions on CT. Subtle differences were observed in organ size. The liver appeared approximately 6 mm thicker and 2–3 mm wider on PET than on CT. The spleen appeared slightly smaller in height (by about 7 mm) on PET than on CT. This also tended to be the case in the kidneys, which appeared to be smaller on PET than CT. The differences were small but statistically significant. Although these differences were minor, the sometimes >2-cm mismatch between PET and CT in the upper margin of the liver and the lower margin of the spleen indicate that this technique, although probably mechanically nearly perfect, is perfect only in fusing organs in cadavers or phantoms. In a living, breathing patient, some minor mismatches in organ location and size are currently to be expected between PET and CT images as a result of physiologic respiratory motion. Thus, absolute dependence on PET and CT for accurate image registration in this location with maximal respiratory motion could be challenging. The differences in organ size between PET and CT of the spleen and kidneys may be the result of fat that contributes to the size of the organs on CT but is not ^{18}F-FDG avid on PET. If the organs are not of identical size on the two imaging methods, it is obvious that one cannot achieve precise fusion of the centroids of the organs and edges without image warping or scaling. Thus, although the quality of image fusion in the abdomen is excellent, it is not perfect (*25*).

Because of misregistration between the location of the upper liver and differences in the size of the liver and spleen, it is apparent that mismatches between PET and CT in location of lesions could occur in this region. We have observed two findings of clinical relevance in this area. Respiratory artifacts using the free-breathing approach are not uncommon. We examined 50 consecutive patients who underwent PET/CT scans including the abdomen (*17*). Both CT and ^{68}Ge/^{68}Ga attenuation-correction maps were obtained during free tidal breathing. "Cold" curvilinear artifacts at the interface between the lungs and diaphragm that were the result of respiratory motion were seen on the CT attenuation-corrected emission PET images but not on ^{68}Ge-corrected emission images. These artifacts were rated on a 4-point scale from 0 (no artifact) to 3 (severe artifact). Curvilinear cold artifacts paralleling the diaphragm at the lung–diaphragm interface were noted in 84% of patient images performed with PET/CT but were not seen on the ^{68}Ge/^{68}Ga-corrected images. Thus, this curvilinear artifact is unique to PET/CT (Fig. 2). This artifact probably can be avoided, in part, by suspending the respiratory cycle in moderate but not full expiration to more closely match the respiratory volume of the lungs between PET and CT, but this requires a high degree of cooperation from the patient (*16*). However, in many patients, artifacts can occur in this area "above" the liver, and attention to these must be noted to avoid mislocalizations and misidentification as disease in this region.

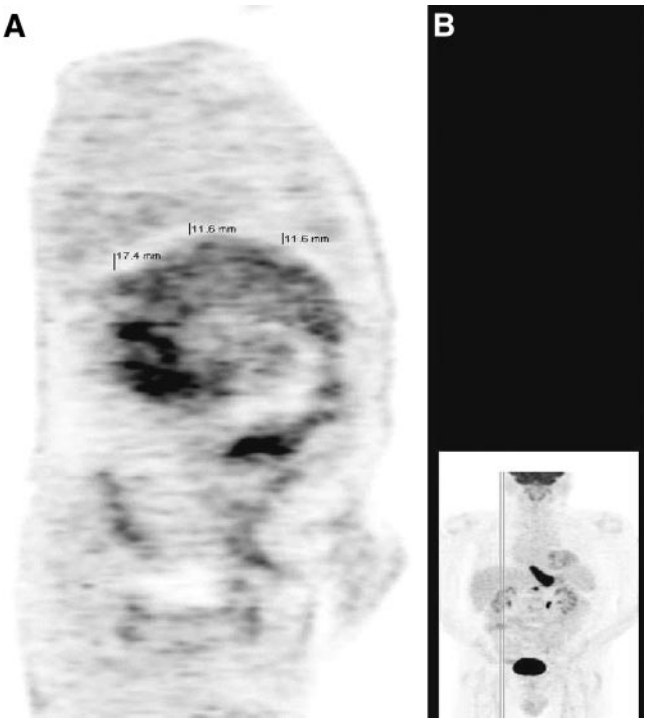

FIGURE 2. (A) Example of respiratory artifact that can be seen on PET/CT images obtained when patients breathe quietly. Moderate-sized "cold" area (above liver) was curvilinear and resulted from mismatch of top of liver on PET (free tidal breathing) (B) and CT (more full inspiration in this case). Cold area was actually part of liver, not lung. (Image courtesy of M. Olman).

If the organs are in different locations on PET and CT, mislocalization of lesions is a possibility. Clinically significant inaccurate location of lesions with PET/CT has been described by our group. Osman et al. (*26*) examined 300 clinical patients with PET/CT. Both CT and germanium scans were used to correct the PET emission data. When CT was used for attenuation correction or fusion, lesion mislocalization occurred in images of 6 of the 300 patients. The most serious artifact was in two separate liver dome lesion localizations to what appeared to be the lung base on PET/CT, probably because the liver was higher on PET than on CT performed at full inspiration (Fig. 3). True liver metastases in this area of crescentic cold activity on PET must not be confused with lung metastases. This is a very serious potential artifact and must be recognized in evaluations of the upper abdomen for appropriate interpretation of PET/CT images. It is also possible that through examination of the nonattenuation-corrected images it will be possible to determine whether a lesion is in the lung base or liver. Examination of anatomic images is also important to confirm that a lesion thought to be in the lung is actually in the lung and not in the liver. With a sufficient difference in position between CT and PET at the time of image acquisition, the same sort of artifact can occur with lesions located immediately below the liver that might appear to be within the liver. Again, PET requires a slow acquisition over several minutes (in our study, 5 min per level), whereas CT is obtained over just a few seconds, leaving the potential for mislocalization on the fused images as a result of differences in respiratory phase.

THE USE OF CONTRAST IN PET/CT IN THE ABDOMEN AND PELVIS

Oral Contrast

Utilization of contrast in the abdomen is often diagnostically important, and we now use oral contrast whenever feasible in the evaluation of the abdomen and pelvis. Cohade et al. (*13*) examined 91 clinical patients who received oral contrast per the protocol described previously. They also performed a phantom study with varying concentra-

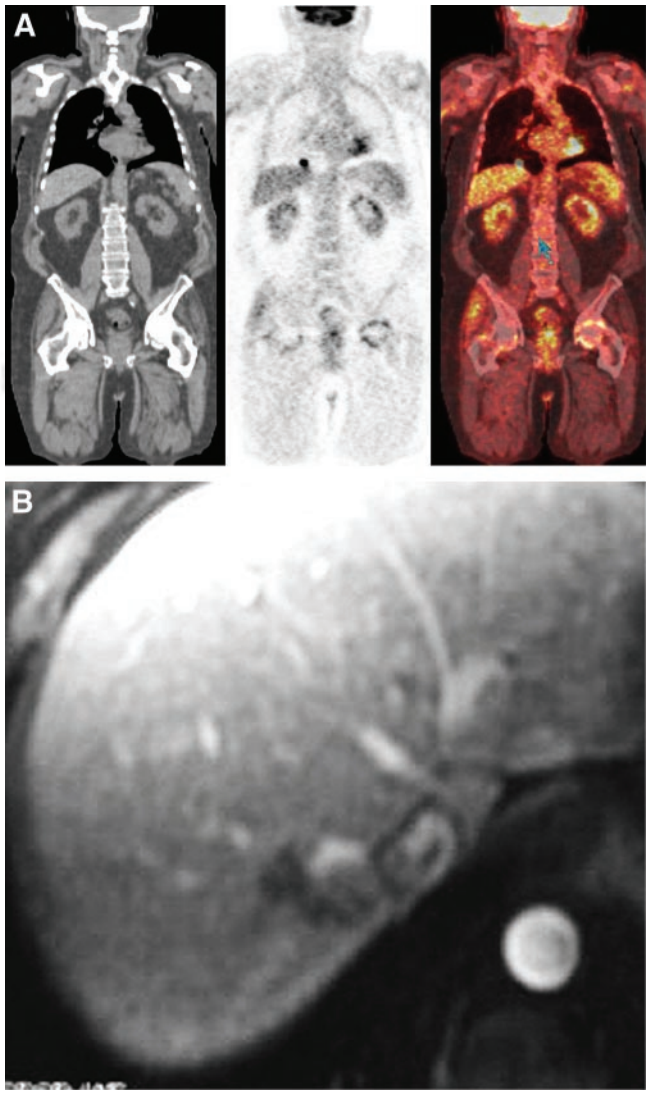

FIGURE 3. Mislocalization of liver metastasis. (B) Focal intense area on emission PET image appeared to be in right lung but, in fact, was liver metastasis. This artifact resulted from vigorous inspiration during CT scan (A) and from tidal breathing during PET. Lesion was clearly hepatic on MRI (C). (Reprinted with permission from (*26*)).

tions of diluted high-density barium (98% weight per volume), which resulted in artifactual foci of intense apparent activity on PET at the sites of dense barium. They also found in a clinical study that the same hot-spot artifact could occur in areas of high-density barium in patients. In the 91 clinical patients who were administered the 1.3%-weight-per-volume barium, the maximum measured contrast in the gut was 239 HU, a level not expected to cause substantial hot-spot artifacts. Dilute oral contrast is used routinely in our studies. High-density barium should be avoided, because it can cause significant artifacts. Although low-density barium may cause minimal distortion in quantitative assessments of ^{18}F-FDG uptake in PET images performed with CT attenuation, the quantitative distortions are typically minimal. Another concern with low-density barium is possible interference in imaging of patients schedule for 3-dimensional CT contrast angiography. Nevertheless, in abdominal imaging, visualization of the bowel and separation of bowel activity from peritoneal metastases and other processes are important and can be enhanced with oral contrast (Fig. 4).

Intravenous Contrast

Intravenous contrast has a major role in the evaluation of the abdomen in traditional CT imaging. Multiphase contrast studies have been used to evaluate liver lesions, because these may enhance at differing times after intravenous injections. Intravenous contrast can be extremely useful in CT angiographic procedures in which CT vascular anatomy is exquisitely displayed using multidetector systems. Oral contrast can interfere with the quality of CT angiography performed with intravenous contrast. If CT angiography is planned, oral contrast should be avoided or the procedures should be scheduled on different days. As with oral contrast, we have found that intravenous contrast can cause artifacts on PET/CT. Nakamoto et al. (*27*) evaluated nonionic intravenous contrast agents in PET/CT imaging in phantom and canine studies. The studies in phantoms showed that the presence of dense intravenous contrast (using our software and scanner) resulted in an overestimation of emission data and apparent radioactivity concentrations. CT Hounsfield unit numbers were strongly positively correlated with the percentage of overestimation of activity. These effects were not the result of attenuation of the ^{18}F-FDG signal by contrast but of overestimation of CT attenuation values in the presence of contrast compared with those determined using ^{68}Ge/^{68}Ga sources (*27*). In the canine model, the presence of a vascular contrast agent also increased apparent emission activity, but the percentage bias was generally $<$15% in the liver and smaller in all other organs except the kidney, which was 26%. High concentrations of contrast agents can cause considerable overestimation of apparent tracer activity in phantom studies and smaller overestimates in animal studies. Highly concentrated intravenous contrast, particularly in the arterial phase, could result in significant alterations in quantitation, especially in large vessels. However, delayed intravenous contrast administration with lower enhancement levels is likely to cause lesser problems.

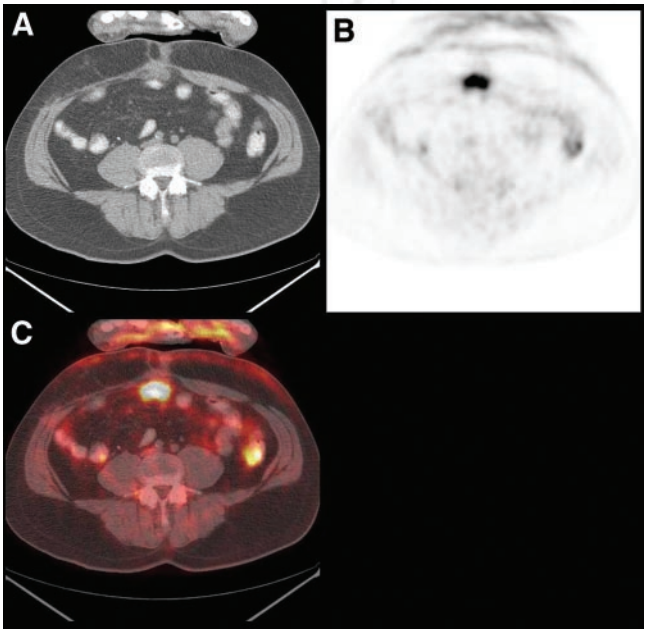

FIGURE 4. Recurrent colorectal cancer. (B) Intense focal uptake was seen in anterior abdomen on PET. It was unclear whether this was in bowel or peritoneum. CT (A) and fused image (C) showed bowel to be opacified by oral contrast and that focus of intense activity was just anterior to bowel. Focus was peritoneal metastasis and not atypical normal bowel uptake. Scar just anterior to focal uptake was normal in appearance and intensity of uptake. (Courtesy of C. Cohade, MD).

In view of the challenges associated with intravenous contrast use in PET/CT, our algorithms until recently have not included the use of intravenous contrast in the abdomen. If intravenous contrast is used, it must be used in an appropriate setting, realizing that quantitative values may be altered (Fig. 5). However, intravenous contrast may be perfectly suitable for PET/CT imaging and provide accurate attenuation correction. An alternative approach is to perform a noncontrast CT for attenuation correction and then the contrast CT only of a relevant area. This technique is in evolution, and some investigators are now using contrast at some point in their studies (*28*). Nonetheless, quantitative errors can occur, and caution must be used when this technology is applied.

FILTERED BACKPROJECTION VERSUS ITERATIVE RECONSTRUCTION

Another issue in the quantitative evaluation of tumor metabolism beyond using CT or ^{68}Ge/^{68}Ga attenuation correction is the effect of filtered backprojection versus iterative reconstruction with CT attenuation correction. Radioactivity concentrations in metastatic liver lesions in patients were examined by Chin et al. (*29*). Both the iterative-with-CT and germanium-with-filtered-backprojection methods were used, including segmented attenuation corrections with the ^{68}Ge/^{68}Ga sources. Iterative reconstructions re-

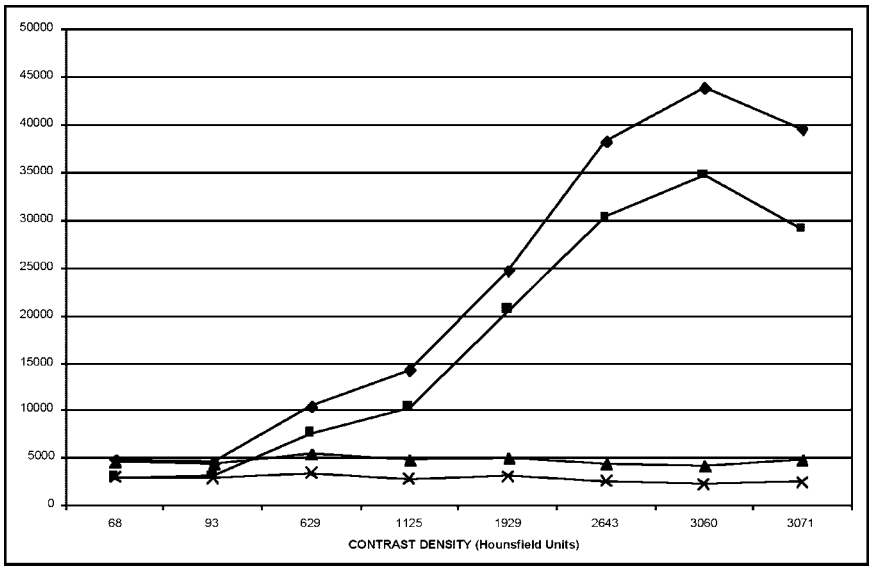

FIGURE 5. Relationship between HU on CT (x axis) and apparent radioactivity level (y axis) in phantoms filled with both iodinated contrast and ^{18}F-FDG. At low HU, CT (upper 2 curves) and ^{68}Ge attenuation maps gave identical results. At higher HU, CT results were markedly elevated. This indicated that high levels of iodinated contrast could result in miscorrection (overcorrection) of PET data and in hot spots. Thus, contrast must be used cautiously in patients to avoid this problem. (Reprinted with permission from (*13*)).

sulted in significantly lower metastatic tumor activity and slightly higher liver background activities, resulting in a slightly lower lesion-to-background ratio than the filtered backprojection method (*29*). However, these differences were quite small, although they were significant at about an 11% difference. Nonetheless, we and most users are using the iterative approaches because streak artifacts are minimized. This advantage is particularly important in the anatomic pelvis, where streak artifacts are common when intense bladder tracer activity is present and filtered back projection is used.

CLINICAL DATA SUPPORTING PET/CT IN THE ABDOMEN AND PELVIS

Clinical data supporting the use of PET/CT in the abdomen and pelvis are in rapid evolution. Only a limited number of studies of its use in illnesses have been reported, and these have included relatively small numbers of patients. Nevertheless, the key benefits of PET/CT over PET are particularly apparent in those studies dealing with the abdomen and pelvis and their substantially variable anatomy. The ability of PET/CT to localize tumor foci that may be hard to localize by PET alone and the ability of PET/CT to identify normal foci of uptake that might be confused with tumor are two major benefits. An additional benefit is the faster performance of the PET/CT scan compared with PET alone because of the addition of faster CT attenuation correction. In our experience, physician acceptance and understanding of the fused images have been greater than their understanding and appreciation of PET-only images. Presenting the still somewhat unfamiliar concept of functional imaging on PET in the familiar anatomical context of CT is a powerful tool in increasing physician understanding, acceptance, and referral. This observation is supported by the growth of clinical PET in the last 3 y at the author's PET center by approximately 900%, almost all of which can be attributed to growth in PET/CT.

Renal Cancers

Anatomic variants that can be characterized easily by PET/CT include radiotracer activity within the stomach that can be separated from the left lobe of the liver or splenic tumor, as can occur with lymphoma (Fig. 6). Tracer activity in the kidneys and their collecting systems can be separated from other structures. Renal masses that have low ^{18}F-FDG uptake can also be assessed. It should also be noted that

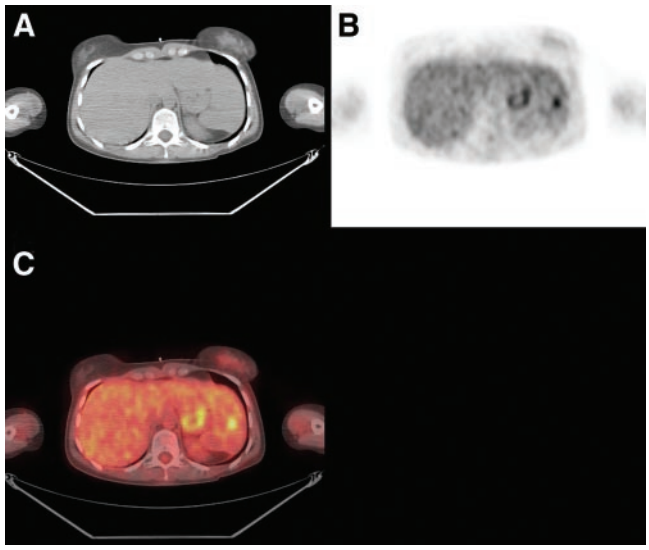

FIGURE 6. (B) PET image showed 2 foci of increased tracer uptake. It is not clear whether medial lesion was in left lobe of liver or left-most lesion in spleen or bowel. CT (A) and fused images (C) showed medial activity was normal stomach wall, whereas lesion in left upper abdomen was within spleen. Patient had non-Hodgkin's lymphoma, and lesion in spleen was consistent with recurrent tumor.

renal examination with ^{18}F-FDG has significant pitfalls. A recent study in the *European Journal of Nuclear Medicine* indicated that only 47% of renal cancers have increased ^{18}F-FDG uptake. ^{18}F-FDG PET/CT can detect renal masses that are not ^{18}F-FDG avid and help identify those patients whose renal cancers are visible on CT but not ^{18}F-FDG-avid. Our experience in this area is limited, but we have also observed renal cancers that are not ^{18}F-FDG avid on PET/CT.

Aortic Wall Uptake and Calcifications

Visualization of the aortic wall on PET/CT in the thorax and upper abdomen is common in many older patients (*30*). Records of 85 consecutive cancer patients who underwent ^{18}F-FDG PET/CT were evaluated retrospectively by Tatsumi et al. (*30*). Fifty patients had at least one area of ^{18}F-FDG uptake in the thoracic aortic wall, and 14 of these showed focal ^{18}F-FDG uptake. Intermediate-to-intense ^{18}F-FDG uptake tended to be observed in the descending aorta. Forty-five patients had at least one measurable aortic calcification. Thick calcification was observed most often at the aortic arch. Twelve patients had 13 uptake areas at the calcification site. Patients with positive findings were on average older ($P < 0.05$ for both increased uptake and calcification), and the older patient group had higher frequencies of both aortic wall uptake ($P < 0.005$) and calcification ($P < 0.001$). The calcification score correlated with age ($r = 0.60$; $P < 0.001$), but the ^{18}F-FDG uptake score did not. Women, patients with hyperlipidemia, and patients with histories of cardiovascular disease tended to show increased ^{18}F-FDG uptake ($P = 0.073$, 0.080, and 0.068, respectively), whereas patients with diabetes had significantly more calcifications ($P < 0.05$). Thus, PET/CT depicted ^{18}F-FDG uptake in the thoracic aortic wall. The ^{18}F-FDG uptake site was for the most part distinct from the calcification site and may possibly have been located in areas of metabolic activity of atherosclerotic changes. It is possible that this aortic uptake is related to inflammatory changes associated with atherosclerosis, but more study is needed. This type of aortic uptake should not be confused with the more diffuse uptake of ^{18}F-FDG in and around infected vessels that has been reported on PET/CT (*31*).

Colorectal Cancer

Colorectal cancer has been the second most common indication for clinical PET studies at our institution. These cancers can occur nearly anywhere in the pelvis and abdomen, as well as systemically. We recently assessed 45 patients with colorectal cancer referred for PET/CT (*7*). We used ^{68}Ge/^{68}Ga attenuation correction initially for our imaging assessments and fused these emission PET images with the CT images. Both PET and PET/CT images were then independently reviewed. A 5-point lesion-characterization scale was applied, ranging from 0 (definitely benign) to 4 (definitely malignant). Lesion location was scored on a 3-point scale, with 0 (uncertain) to 2 (definite localization). All available clinical information was assessed on follow-up to determine true status. PET/CT reduced clinically equivocal lesion characterization by 50%, from 50% to 25%, compared with PET. The frequency of definite lesion characterizations was increased by 30%, from 84 to 109 lesions with PET/CT (Table 1). The number of definite localizations of lesions was increased by 25%, from 92 to 115 localizations using PET/CT. Overall correct tumor staging increased from 78% to 89% with PET/CT on a patient-by-patient basis. PET/CT can also be helpful in the upper abdomen in separating brown fat uptake, which most commonly is supraclavicular but which can extend into the upper abdomen from adrenal metastases or liver metastases (*32*).

TABLE 1
PET and PET/CT in Lesion Localization in Colorectal Cancer*

Localization certainty	Number of lesions localized	
	PET	PET/CT
0 (unknown localization)	14	5
1 (probable localization)	28	14
2 (definite localization)	92	115

*Reproduced with permission from Cohade et al. (*6*).

PET/CT can be most informative in characterizing lesions in the anatomic pelvis, where separation between the uterus, bowel, and recurrent colorectal cancer can be challenging, such as when the uterus is retroverted (*33*). Another situation in which PET/CT is helpful in which there is low tumor uptake of ^{18}F-FDG but an abnormal mass is seen on CT. This can be the result of a mucinous cancer that is known to be an ^{18}F-FDG nonavid lesion or at least of low avidity. In some cases, the CT can be more informative than the PET for lesion detection or localization (*7*). Other instances in which PET/CT can be helpful in the abdomen include lesions located posterior to the liver near the adrenals. This is complex anatomy, and lesions in the posterior liver can be confused with the adrenal, upper pole of the kidney, or lung base, because they are in very close proximity (*26*,*34*). We have found PET/CT can help us considerably in such cases. Examples of such cases are shown in Figures 7 and 8. Improved separation of retroperitoneal nodes from the ureters is also possible with PET/CT (Fig. 9). Similarly, separation of nodes from tumor involvement of pelvic bones is feasible with PET/CT (Fig. 10).

False positives still occur with PET/CT and can occur in cases of inflammation and granuloma. False negatives can occur with small tumors and non-^{18}F-FDG avid lesions and after therapy. Peritoneal metastases from colorectal cancer can be seen extremely well with PET/CT. From our data, it seems reasonably clear that although PET is a very good technique in assessing colorectal cancer, PET/CT is better, improving our staging and restaging accuracies. PET/CT

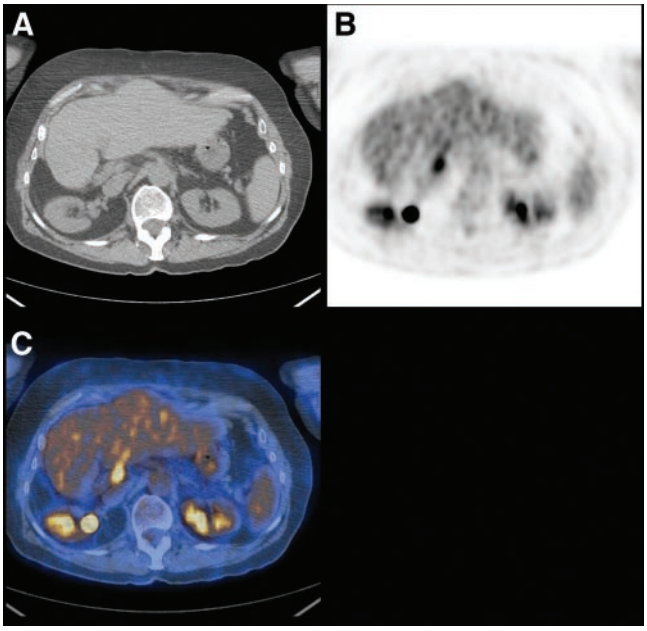

FIGURE 7. (B) PET image showed several foci of intense activity. Paired structures posteriorly were most consistent with renal activity, but it was difficult to pinpoint anterior lesion to determine if it was adrenal, nodal, or hepatic. (C) On fused images, it was apparent that lesion was extrahepatic and in lymph nodes in this case of metastatic colorectal cancer. Kidneys were also seen clearly. (Courtesy of C. Cohade, MD [*17*]).

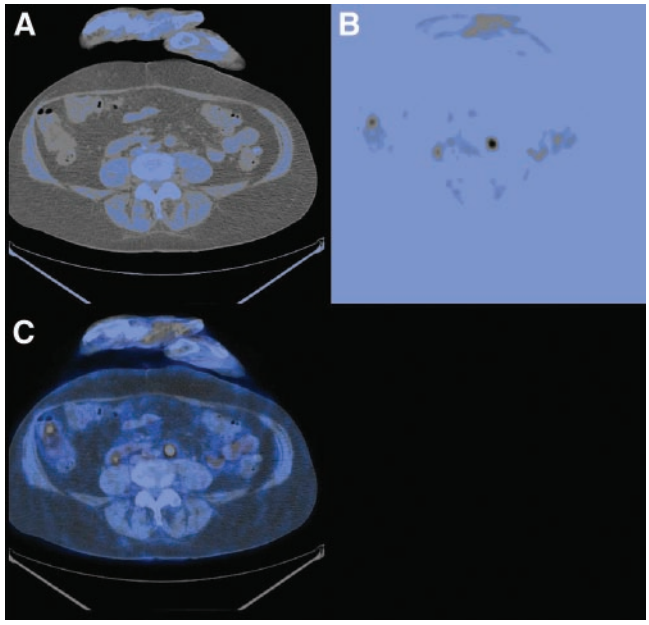

FIGURE 9. (B) PET image showed 2 foci of increased tracer uptake. In general, paired ^{18}F-FDG-containing structures in retroperitoneum are ureters. However, examinations of CT (B) and in particular fused PET/CT (C) images showed lesion on left to clearly medial to left ureter and corresponded to $<$1-cm lymph node (normal size). Right focus was ureter. Left focus was in metastatic lymph node from colorectal cancer, and only PET/CT resolved this finding. (Courtesy of C. Cohade, MD)

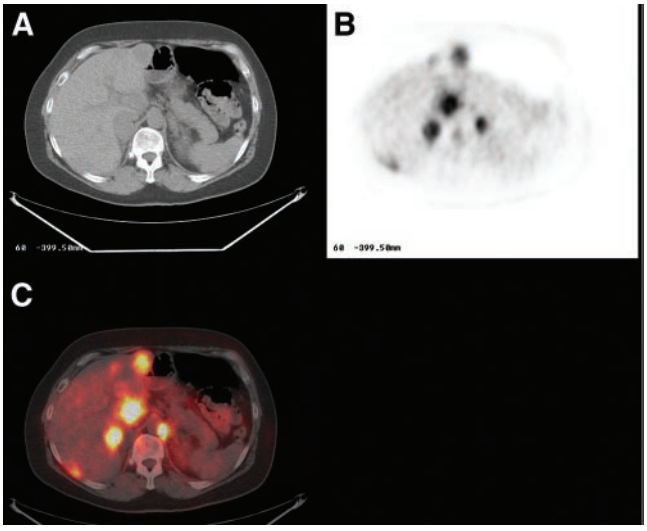

FIGURE 8. (B) Multiple FDG-avid foci were seen on PET image. Most anterior lesions appeared to be anterior to liver, whereas posterior lesions could be hepatic, adrenal, or nodal, based on PET only. With CT (A) and fusion (C), it was apparent that anterior lesion was in liver, as was posterior lesion. Two posterior foci, however, were adrenal metastases. These findings resulted from metastatic lung cancer to abdomen. Metastatic lung cancer is common cause of hepatic findings on PET. (Courtesy of P. Patel, MD)

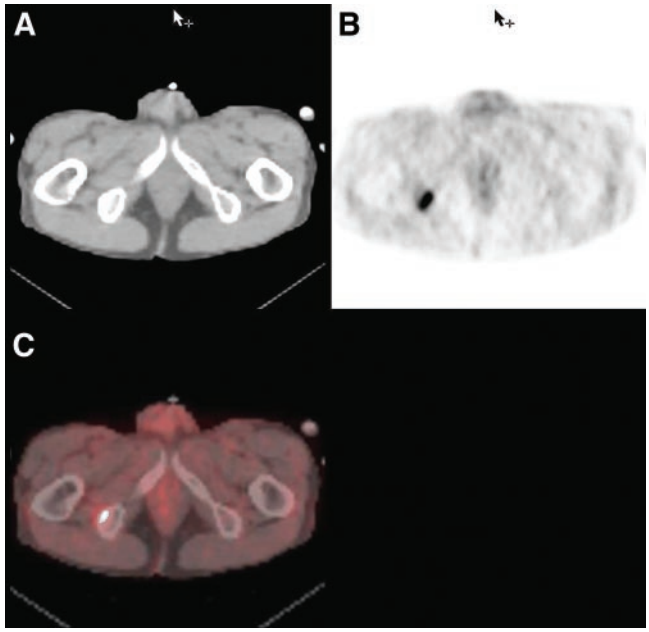

FIGURE 10. (B) Pelvic lesion imaged with PET. Pelvic lesion seen on PET could be intrapelvic, nodal, osseous, or extra pelvic. Implications for lesions in varying locations were considerable. (C) Fusion showed metastatic lesion to bone in patient with stage IV melanoma metastatic to pelvic bone.

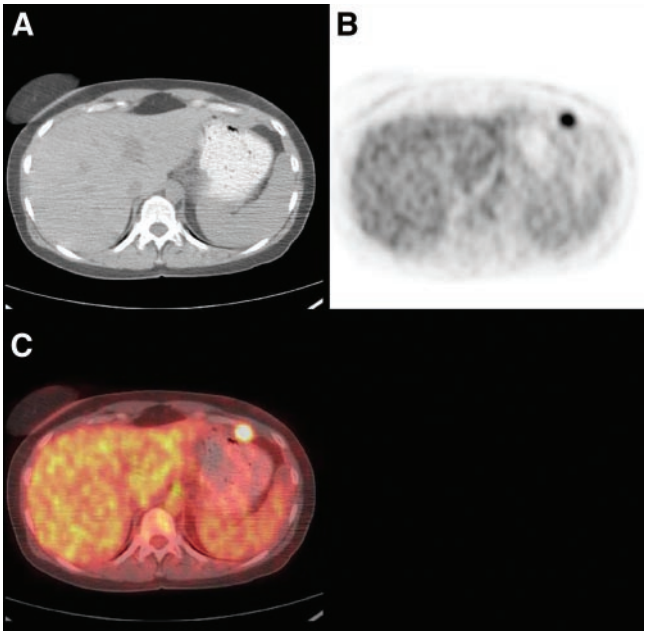

FIGURE 11. CT (A) was normal, but PET (B) and fused images (C) showed clear focus of intense tracer activity in left peritoneal cavity just anterior to stomach (on fused image but clearly not involving rib, as might be suspected from PET alone). This was focus of ovarian carcinoma. (Image courtesy C. Cohade and H. Pannu)

imaging with coincidence methods (TET imaging) has been evaluated in colorectal and several other types of tumors and has shown increased diagnostic certainty, changing interpretations of PET or CT in about half of cases (*35*). Similarly, experience from a >200-patient series, including many with abdominopelvic disease, has shown that PET/CT reduced the frequency of equivocal readings and localizations and changed management in about 14% of patients when compared with PET alone (*36*).

Ovarian Cancer

Ovarian cancer is another common indication for performing abdominal PET scans at our PET center We recently reviewed our early experience with PET/CT and ovarian cancer in 22 patients with epithelial ovarian cancer. The specific question in this group was whether we could identify tumor masses ≥1 cm in size in women with otherwise clinically occult recurrent disease. Such patients may benefit from in situ cytoreductive surgery. The 22 patients had rising CA125 levels, negative or equivocal CT imaging, and were imaged with PET/CT >6 mo after primary therapy. PET/CT imaging was followed by surgical reassessment of disease activity. We assessed the ability of PET to detect microscopic disease ≥1 cm in size. Of the patients, 91% had International Federation of Gynecology and Obstetrics (FIGO) stage 3 or 4 disease, with an average rise in cancer antigen 125 level of at least 24 units. Traditional CT was read as negative in 15 and equivocal in 7 patients. Eighteen patients were found at surgery to have recurrent ovarian cancers measuring >1 cm in diameter, with a median tumor diameter at 2.3 cm. On a patient-based assessment, PET/CT was 81% accurate for assessing the presence of recurrent ovarian carcinoma, with a sensitivity of 83.3% and a positive predictive value of 93.8%. Failure to detect small 1 cm tumor foci was not uncommon, as has been previously reported in ovarian carcinoma with PET. In 72% of our patients with recurrent ovarian cancer >1 cm in diameter, complete surgical cytoreduction with no gross residual tumor was achieved. Thus, in these patients in whom CT was negative or equivocal, PET/CT had a major role in identifying resectable tumors in 72% of the cases (*37*). The study did not systematically examine the incremental benefit of PET/CT over PET, but this is currently being studied. Preliminary assessments by Cohade et al. (presented, SNM 2003) a considerable advantage to PET/CT over PET. Examples of peritoneal metastases are shown in Figure 11. Ovarian carcinoma often has peritoneal metastases that can be invisible on CT, and this disease can metastasize outside of the pelvis and abdomen. Fallopian tube cancers also can be imaged with PET/CT (*38*,*39*). Differentiating tumors of the peritoneal cavity and pelvis from the nodes and bony pelvis can be challenging with PET alone but is aided by PET/CT (Fig. 12).

Pancreatic Cancer

Pancreatic cancer also can be imaged effectively with PET/CT in our limited experience (Tatsumi et al., presented, RSNA 2003). In pancreatic cancer, PET/CT is able

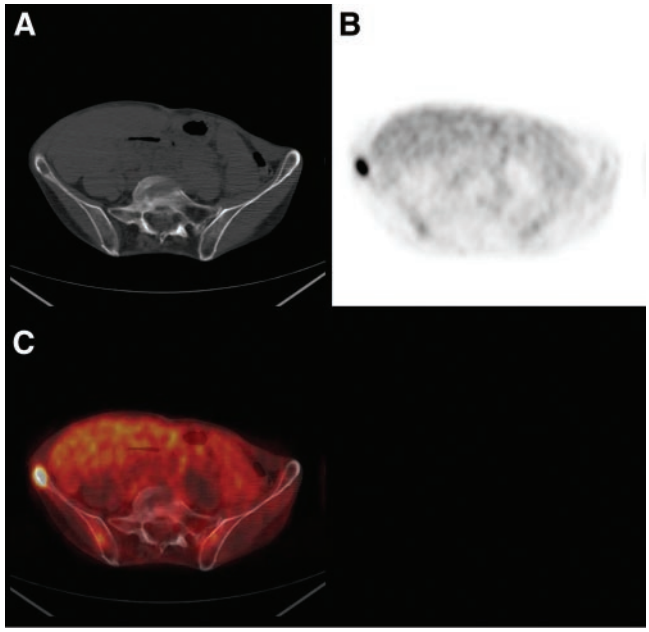

FIGURE 12. CT (A), PET (B), and fused images (C) in patient with history of cancer. On first examination of PET image alone, possibility of peritoneal or bowel metastasis existed. Examination of CT and fused image showed lesion was actually lytic bone metastasis, in this case from thyroid cancer. This example illustrates how PET/CT helped differentiate peritoneal or bowel disease from disease in bone of pelvis.

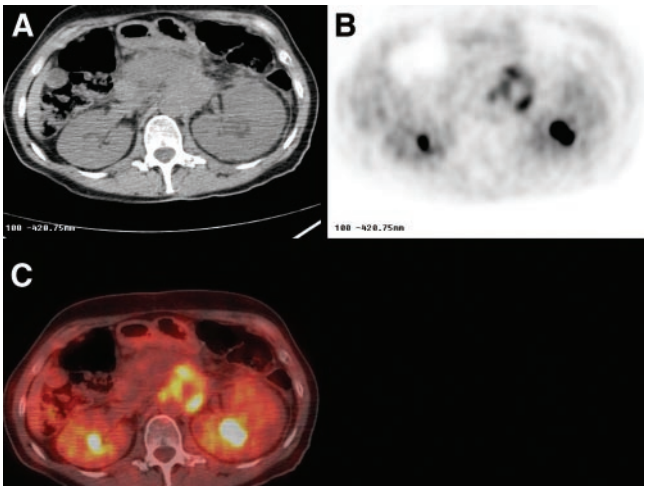

FIGURE 13. Primary pancreatic cancer on PET/CT. Image courtesy of M. Tatsumi.

to detect and localize primary and metastatic lesions. More than 20 patients have been studied, and the full study will be reported elsewhere. Separating primary pancreatic cancers from lymph nodes adjoining the pancreas can be challenging. If disseminated metastatic disease is present, diagnosis is helpful in avoiding unnecessarily aggressive surgical procedures. An example of a primary pancreatic cancer on PET/CT is shown in Figure 13.

PET/CT seems an ideal method for assessing the retroperitoneum, with its complex anatomy and the proximity of normally ^{18}F-FDG avid structures to potential sites of metastatic disease. Correlation of functional imaging with a mass is also very helpful in separating bowel and adrenal activity from masses in the adjoining pancreas. Similarly, lower in the retroperitoneum, focal ^{18}F-FDG retention in the ureters can mimic nodal disease.

Cervical, Endometrial, Bladder, and Prostate Carcinomas

Cervical and endometrial carcinomas can be assessed with ^{18}F-FDG PET. We and others have studied cervical carcinomas with PET (*40*). One of the challenges in cervical cancer assessment is in separating ^{18}F-FDG activity in normal bowel adjoining the cervix from cervical masses resulting from tumor and in separating retroperitoneal metastases from ureters. Our initial experience with PET/CT in cervical cancer is encouraging. Our experience with endometrial carcinoma assessment by PET/CT is also promising. The same challenges in dealing with variable pelvic anatomy are true for cervical and endometrial carcinoma. Assessment in this region is complex, because of varying patterns of tracers in bowel, myomas uterus, and urine. Recently, successful separation of a sarcoma of the labia from urinary contamination was achieved using PET/CT (*41*).

We have also had very promising initial results using PET/CT in bladder carcinoma. Comparison of PET alone to PET/CT anatomic and functional images should be superior to PET alone, but such a comparison in the same physiologic state is highly desirable. It must be emphasized for evaluation of the pelvis, full emptying of the bladder is essential before imaging. We have the patient void immediately before PET imaging. On occasion, we obtain delayed images after having the patient void further. It is rarely necessary, in our experience, to have the patient catheterized, although this may be necessary in selected cases.

At present, prostate cancer is not commonly studied with ^{18}F-FDG PET at our institution. Although prostate cancer can be visualized well with ^{18}F-FDG PET in aggressive prostate cancers, results are often negative. Pelvic anatomy can be complex, and it can be difficult to separate presacral masses from lesions in the sacrum itself. Even intense ^{18}F-FDG uptake in the sacrum is not always cancer, however. We recently observed several cases of stress fractures of the sacrum that were ^{18}F-FDG avid and that could be determined to be benign fractures and not tumor only through the use of GIST PET/CT (*42*).

Liver Tumors

Detection and localization of primary and metastatic liver tumors is well achieved with PET/CT, when these tumors are ^{18}F-FDG avid. Primary hepatomas can be false negative on FDG PET/CT in more than half of cases, based on an early report in the Chinese literature (*43*). Image localization artifacts can occur as described previously. Intense ^{18}F-FDG uptake can be seen in some hepatomas and in cases of primary cholangiocarcinoma. Tracers other than ^{18}F-FDG may have greater promise in heptoma evaluation.

GI stromal tumors (GIST) are rare, but in cases with a C-kit mutation can be treated with STI571 (imatinib mesylate). We have examined GISTs with PET/CT, and these have relatively characteristic large areas of high peripheral activity with central cold areas. GISTs and their response to therapy can be assessed quite accurately by PET/CT. Further assessment is necessary to know the incremental benefit of PET/CT over PET in this tumor. However, we have found the PET/CT study is particularly useful after treatment, when ^{18}F-FDG uptake is reduced markedly and warm lesions could otherwise be missed on PET alone.

CONCLUSION

Our initial published experience in colorectal and ovarian cancer supported the utility of PET/CT in image evaluation of the abdomen and pelvis. Our additional initial clinical experience in a wide variety of other abdominopelvic cancers, including pancreatic cancer, strongly supported PET/CT imaging as an appropriate technique for abdominal visualization. A review of the published literature in PET/CT in the abdomen and pelvis also showed PET/CT to be offering increased diagnostic value in comparison with PET alone, consistent with the first reports of clinical use of this method (*44*). Most studies, however, did not directly compare simultaneously examined but unfused nonconcur-

rent PET and CT with fused PET/CT. In at least two reports using computer-fused methods in the thorax, the addition of CT was clearly helpful to PET, but fusion (at least based on software) did not markedly improve diagnostic accuracy over visual fusion by an experienced reader of PET and CT datasets (*3*,*45*). This remains a critical test in assessing the very promising results consistently seen to date with PET/CT. This author's subjective impression is that visual fusion, although good in the hands of an experienced reader, is not as good as the high-quality, real-time, precise registrations possible from PET/CT on a consistent basis in each case. Visual fusion is also unlikely be useful in guiding radiation therapy, a process that is both feasible and extremely promising with PET/CT. PET/CT radiation treatment planning often has far different gross tumor volumes than traditional anatomy-based treatment plans (*46*).

Referring physician acceptance of PET/CT is also excellent. When our PET/CT scanner is down for maintenance, our referring physicians generally prefer not to order a PET scan in the interim but to have their patients wait to be scanned when the PET/CT is again operational. PET/CT is now the preferred method for abdominal and pelvic imaging at our institution. We believe that this technique will become the standard for abdominopelvic imaging with PET in the United States and elsewhere. Radiation dosimetry considerations obviously must be carefully considered, and attention must be given to minimizing the radiation dose from the CT portion of the PET/CT study while maintaining anatomic clarity (*3*,*47*). Although the radiation dose from CT is not a major concern in cancer patients, the promise of ^{18}F-FDG and PET/CT for imaging infections and other nonmalignant processes such as atherosclerosis indicate that it is important to attempt to minimize radiation dose from the procedure (*30*,*48*,*49*).

Careful continued, large studies are essential to more precisely determine the incremental benefit of PET/CT over PET and computer or visual fusion. However, logistically PET/CT is a very reproducible and rapid technique. The available data in our clinical experience support the use of PET/CT for routine evaluations of the abdomen and pelvis. All the protocols we have applied work reasonably well in routine clinical practice. They may be improved on, and there is no doubt that additional technical improvement in PET and CT scanners and radiotracers can only improve the accuracy of PET/CT imaging. PET/CT imaging of the abdomen and pelvis has a bright future in the diagnosis of disease, treatment monitoring, prognosis assessment, radiation treatment planning, and in drug development. We predict that this technique will prevail as the preferred PET method for evaluating the abdomen and pelvis.

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