State-of-the-art Imaging of Pancreatic Neuroendocrine Tumors

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INTRODUCTION
Pancreatic neuroendocrine tumors (PNETs) account for only 3% of pancreatic malignancies, but have an increasing incidence, currently 0.3 to 0.4 per 100,000. They are notably more common in multiple endocrine neoplasia type I (MEN-I), von Hippel-Lindau syndrome, neurofibromatosis type I, and tuberous sclerosis. PNETs can be divided into 2 groups: functional tumors, usually subcentimeter, that manifest

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KEY POINTS
Knowledge of the type of functional tumor (eg, gastrinoma versus insulinoma) is important in choosing appropriate imaging strategies to identify primary lesions and their metastases.

Fluorodeoxyglucose PET/computed tomography (CT) has poor sensitivity for well-differentiated pancreatic neuroendocrine tumors but good sensitivity for poorly differentiated types, and therefore has a complementary role with octreotide scanning.

To optimize treatment planning, it is important to inspect all potential sites of disease, particularly with regard to the extent of liver and nodal involvement, and potential distant metastases to lung and bone.

Metastatic adenopathy can show enhancement similar to adjacent vasculature structures and can be difficult to detect on CT. MRI, particularly diffusion-weighted imaging, and nuclear medicine studies can be helpful.
because of the symptoms caused by the hormones they produce; and nonfunctional
tumors, usually several centimeters, that manifest secondary to mass effect.

State-of-the-art imaging plays a central role in the identification, diagnosis, and
staging of PNETs. Computed tomography (CT) and MRI are often used initially to
detect and stage these lesions, and evolving nuclear medicine techniques provide
improved specificity and whole-body assessments for distant disease. A multimodal-
ity approach may be necessary to identify potentially very small primary tumors and to
identify all sites of metastatic disease to optimize treatment planning.

**IMAGING TECHNIQUES**

*Computed Tomography*

CT is often used for the initial evaluation of patients with abdominal pain or to identify
suspected small functional PNETs because of its speed, resolution, and robustness.
Recent advances allow detailed multiplanar reconstructions, and new low-kilovoltage
imaging or multispectral imaging may improve the conspicuity of PNETs.

A typical abdominal multidetector CT examination for PNET is multiphasic (Figs. 1
and 2). Unenhanced images may be obtained to help identify calcifications or hem-
orrhage. At our institution, patients are then imaged following injection of iodinated
intravenous contrast at 4 to 5 mL per second for an injection duration of approximately
30 seconds, with abdominal imaging obtained first at 40 to 45 seconds after the start
of contrast injection for the late arterial phase of enhancement, and then 60 to 70 sec-
onds after the start of contrast injection for the portal venous phase (see Figs. 1 and 2).
Images are created at a slice thickness of 2 to 3 mm for diagnostic review, and at
0.625 mm for creating coronal and sagittal multiplanar reconstructions to facilitate
problem solving. CT was reported in a 2009 consensus statement to have a mean

![Fig. 1. Pancreatic tail neuroendocrine tumor (white arrows) on multiphasic CT is (A) hyper-
dense to background on the arterial phase and (B) isodense on the portal venous phase.](image-url)
Fig. 2. PNET liver metastases (white arrowheads) on multiphasic CT are classically hyperdense to background on (A) early and (B) late arterial phases and either isodense or hypodense on (C) portal venous phase, but they can be variable.
sensitivity of 73% and specificity of 96%. Sensitivities for small functional tumors, such as insulinomas, vary by phase: approximately 83% to 88% for the arterial phase versus 11% to 76% for portal venous phase imaging, although a small study of 13 patients evaluating the late arterial phase (pancreatic parenchymal phase) showed a sensitivity of 100% for that phase. Detection is optimized by close evaluation of all phases.

New multispectral CT may improve detection of subtle differences in enhancement between lesions and background. Conventional multidetector CT uses a single polychromatic energy beam (eg, 120 kV peak [kVp]). Multispectral imaging uses either 2 polychromatic beams of high and low strengths (eg, 80 kVp and 140 kVp) or a dual-layer detector that can discriminate between photons of high and low energy. Multispectral imaging uses these additional data to mathematically create new types of images (Figs. 3 and 4), two of the most common being monochromatic energy images (the equivalent of theoretically being scanned at a discrete single energy level), and material density or material decomposition images (semiquantitative images based on decomposing image data into representative amounts of just 2 or more materials to mimic the actual behavior at each image voxel). The precise makeup of material decomposition images varies between vendors.

Low-energy monochromatic images (ie, 40–50 keV) improve the conspicuity of contrast enhancement. A small study investigating the detection of insulinoma compared 16 patients scanned with conventional dual-phase multidetector CT with 23 patients scanned with rapid switching single-source dual-energy dual-phase multidetector CT. A sensitivity of 95.7% was obtained when a combination of low-energy monochromatic energy images and iodine (minus water) material decomposition images were used, compared with a sensitivity of 68.8% for conventional dual-phase multidetector CT.

Another related approach has been the use of a low polychromatic kVp (ie, 80 kVp) technique, which improved contrast to noise results compared with conventional 140-kVp imaging for overall pancreatic tumor imaging but did not statistically improve tumor detection. To our knowledge, no assessment has been published of this technique for PNETs.

**MRI**

MRI offers several advantages for the imaging of PNETs, including multiple different sequences that provide opportunities to differentiate tumor from normal pancreas. A typical abdominal protocol at our institution includes fat-suppressed T2-weighted; fat-suppressed precontrast and post-contrast dynamically obtained T1-weighted, in-phase and out-of-phase T1-weighted images; diffusion-weighted images with multiple b values and apparent diffusion coefficient (ADC) maps; and fat-suppressed true fast imaging with steady-state precession (FISP) or fast imaging employing steady-state acquisition (FIESTA) images (Fig. 5). An effective slice thickness of 3 to 6 mm is used to minimize volume averaging artifact and improve sensitivity. The overall sensitivity of MRI published in a consensus report was 93%, with specificity of 88%. Limitations of MRI include greater frequency of motion-related artifacts and a longer imaging time compared with CT. Benefits include good sensitivity even in the absence of administration of an intravenous contrast agent (making it a useful alternative for patients with renal impairment or allergy to iodine-based CT contrast agents) and the absence of ionizing radiation, which is of particular concern in young patients who may require surveillance. Recent studies of advances in diffusion-weighted imaging suggest potential for improving detection, differentiating accessory spleen from small islet cell tumors, differentiating near-solid serous cystadenomas from neuroendocrine tumors, Tamm et al.
Fig. 3. Pancreatic tail neuroendocrine tumor (white arrows) seen on late arterial phase CT, as seen (A) conventionally at 140 kVp, and more conspicuously at dual-energy CT (DECT) (B), low-energy 50-keV, and (C) iodine (minus water) material density images.
Fig. 4. PNET metastases to liver (white arrows) and nodes (thick white arrow) seen on DECT late arterial phase at (A) 70 keV and (B) more conspicuously on iodine (minus water) material density images. Uptake in these sites on (C) octreotide images is highly specific to neuroendocrine tumors.
Fig. 5. Nonfunctioning tail PNET (white arrows) seen on MRI on dynamic (A) arterial phase, (B) T2, and (C) diffusion-weighted imaging. Diffusion imaging improves contrast, although resolution is less than in other series.
and potentially in evaluating tumor grade.\textsuperscript{19,20} MRI also offers potential advantages compared with CT in the detection of liver metastases, which is discussed later.

**Nuclear Medicine**

The primary nuclear medicine imaging tool for PNET is somatostatin receptor scintigraphy performed with a radiolabeled somatostatin analogue. Somatostatin is a peptide hormone for which 5 types of receptors have been identified. Octreotide, a somatostatin analogue, binds to receptors type 2 and 5.\textsuperscript{21} Octreotide is typically labeled with indium-111, administered intravenously, and patients are then imaged 4 hours and 24 hours after tracer administration using both planar imaging and single-photon emission CT (SPECT).\textsuperscript{22} At our institution, and in many centers, a CT study is performed concurrently with SPECT on a dedicated hybrid SPECT/CT camera, allowing more precise anatomic localization of octreotide uptake (Figs. 6–8).\textsuperscript{22} Overall sensitivity for $^{111}$In-octreotide for

![Fig. 6. Patient with increased gastrin levels and large pancreatic gastrinoma (white arrowheads) on multiphasic CT in (A) arterial phase with invasion and marked distention of the portal vein (curved black arrow) and (B) multiple liver metastases (white arrows). Octreotide scan (C) projection images show intense uptake in primary gastrinoma (black arrowhead), and liver metastases (black arrows).](image)
Fig. 7. PNET (thick white arrow), adenopathy (long white arrow), liver metastases (white arrow), and tumor thrombus in vein (black arrowhead) as seen on arterial phase (A) 70 keV, (B) iodine material density, and (C) portal venous phase imaging, the last showing metastases and portal vein thrombus. Octreotide fused SPECT CT (D), as a whole-body study, identifies distant metastatic left supraclavicular node. Note the similarity of some adenopathy to adjacent vessels.
PNET is approximately 70% to 90% but varies with tumor type and diminishes particularly for subcentimeter lesions.\(^{22,23}\) Sensitivity for insulinoma, which typically expresses receptor type 3, is notably limited (Fig. 9), at 50% to 70%.\(^{24}\)

Although fluorodeoxyglucose (FDG)-PET/CT would offer potentially greater precision, PNET’s don’t typically demonstrate sufficient uptake unless they are poorly differentiated. FDG-PET/CT is therefore used as a complementary technique (Fig. 10) to SPECT/CT octreotide, which shows poor uptake in poorly differentiated tumors.\(^{22}\) New PET/CT agents that have been developed include gallium labeled somatostatin analogs such as DOTA-tyrosine-3-octreotide (DOTA-TOC), which has a higher affinity for somatostatin receptor type 2, and DOTA-1-Nal-octreotide (DOTA-NOC), which demonstrates a higher affinity for subtypes 2, 3, and 5 (Fig. 11).\(^{24}\) Although these PET somatostatin radiotracers have faced many regulator barriers in the United States, the somatostatin analogue, DOTA-octreotate (DOTA-TATE, GaTate), has recently been given orphan drug status by the US Food and Drug Administration (FDA). Somatostatin receptor imaging using positron-emitting isotopes is attractive because of the improved spatial resolution of PET imaging compared with SPECT.\(^{25}\) A recent meta-analysis of 22 studies of the broad category of somatostatin receptor PET/CT, including more than 2100 patients, showed a sensitivity of 93% and specificity of 95%.\(^{26}\) The radiation dose to the patient is often lower with PET agents compared with conventional \(^{111}\)In-labeled radiotracers. Although Ga-68 has been used extensively, other radioisotopes are under investigation for imaging of neuroendocrine tumors, including Cu-64 and F-18. Using the approach of theranostics, a therapeutic radioisotope (such as Y-90 or Lu-177) can be paired to the somatostatin-binding pharmaceuticals to deliver a high-dose radioisotope therapy to eligible patients, and trials are currently underway in the

![Fig. 8. Metastatic PNET on whole-body fused octreotide SPECT/CT with uptake in metastatic nodal disease (white arrows) in (A) mediastinum, (B) retroperitoneum, and (C) liver metastasis (thick white arrow).](image-url)
Fig. 9. Small pancreatic insulinoma on multiphasic CT and octreotide scan. (A) Insulinoma (white arrow) here is uniformly hyperdense on late arterial phase but (B) near isodense to background on portal venous phase. On octreotide scan (C), it is not seen (normal uptake in liver, spleen, and kidneys).
Fig. 10. Nonfunctioning poorly differentiated pancreatic body PNET (white arrows) on (A) axial late arterial phase CT, and (B) showing intense uptake on PET/CT fused image, as is (C) a liver metastasis.
United States to achieve regulatory approval. In addition, metabolic pathways are being explored as a means to image PNET tumors, including PET imaging with amino acid precursors such as F-18 dihydroxyphenylalanine (DOPA), and C-11–labeled hydroxytryptophan (5-HTP).

**Endoscopic Ultrasonography**

Endoscopic ultrasonography (EUS) reportedly has a mean detection rate for neuroendocrine tumors of 90%. EUS-guided fine-needle aspiration (FNA) has been reported to result in overall diagnostic accuracy of 90.1%. Endoscopic ultrasonography (Fig. 12) is particularly helpful for gastrinomas because many are located within bowel, a region that is poorly evaluated by both CT and MRI. The primary limitations of EUS are that it depends on the skill and experience of the operator, requires sedation, and the technique is invasive.

A recent development is that of intravenous contrast agents, namely blood-pool contrast agents (microbubbles) for ultrasonography imaging, currently approved in the United States by the FDA for cardiac imaging but not abdominal imaging, although they have been approved for use more widely in other parts of the world. A study of 37 insulinomas, using one such microbubble agent, sulfur hexafluoride lipid-type A microspheres, reportedly showed an improvement from a sensitivity of 24% for transabdominal unenhanced ultrasonography to 87% to 89% following the administration of intravenous contrast. To our knowledge, only limited information is available regarding its use in the setting of pancreatic EUS. The already high sensitivity of EUS and the high specificity of EUS-guided FNA likely account for contrast enhancement not being more widely used.

**IMAGING FINDINGS**

The appearance of PNETs can vary considerably, even within the same patient, and differs markedly between functional tumors, which are typically small, and nonfunctional tumors, which are typically several centimeters in size.

**Functional Pancreatic Neuroendocrine Tumors**

Because they manifest with systemic symptoms, functional pancreatic tumors are usually 1 to 2 cm in diameter at the time of imaging but can be smaller. The most common types are insulinoma (see Fig. 9) and gastrinoma (see Figs. 6 and 11; Fig. 13).
Incidentally identified pancreatic tail mass (white arrows) on CT (A) similar to spleen (black asterisk) on multiphasic imaging, showed (B) no uptake of technetium sulfur colloid (therefore not an accessory spleen). (C) EUS with FNA showed well-defined slightly hypoechoic mass and PNET on histopathology.
Their incidence is increased in syndromes such as the autosomal dominant MEN-I, and von Hippel-Lindau disease.\textsuperscript{4,5} Their classic appearance is of a uniformly hypervascular, well-defined lesion (see Figs. 9 and 11) that is most notably prominent on arterial phases of contrast enhancement.\textsuperscript{8,31,33} Studies that have evaluated phases of contrast enhancement have shown a sensitivity of 83\% to 88\% for arterial phase imaging versus 11\% to 76\% for later portal venous phase imaging.\textsuperscript{8,9,34,35} However, lesions may be seen on only 1 of these 2 phases.

Cystic changes are typically seen with larger lesions,\textsuperscript{33} but even marked cystic transformation can occur with smaller lesions (Fig. 14). The presence of a hypervascular rim, sometimes very subtle, can be helpful in suggesting the diagnosis of PNET.\textsuperscript{36} Features such as heterogeneity, calcifications, and necrosis become more notable with increasing tumor size.\textsuperscript{33}

**Insulinomas**

Knowledge of the suspected tumor type (eg, insulinoma or gastrinoma) is important to guide assessment of the images. Insulinomas are typically solitary, 97\% occur within the pancreas, are typically smaller than other functioning tumors at initial evaluation (40\% are <1 cm), and only 10\% are malignant, with malignancy usually seen in lesions larger than 3 cm.\textsuperscript{32,37,38} Insulinomas are much more likely to be multiple in the setting of syndromes, notably MEN-I.\textsuperscript{37,39} CT and MRI are often used initially in this setting given their good sensitivity for intrapancreatic lesions and lack of invasiveness, and the poor sensitivity of octreotide as well as PET/CT.

**Fig. 13.** Peripancreatic adenopathy as site of gastrinoma. Portal venous phase CT shows enhancing adenopathy (white arrow) (A) anterior to transverse duodenum and (B) near the aortocaval space, similar to aorta and opacified bowel loops.
Invasive techniques such as arterial stimulation and venous sampling, and transhepatic portal venous sampling, can be used to increase the likelihood of detection but may be controversial because intraoperative assessment has been reported to have high sensitivity. Noninvasive techniques such as CT and MRI, when able to localize lesions, can provide information that may be helpful in guiding decisions regarding surgery, such as the extent of primary tumor, potential metastatic nodal involvement, or the identification of liver metastases.

Gastrinomas

Gastrinomas (see Figs. 6, 11, and 13) have a very different pattern of presentation from insulinomas. Only 60% are located within the pancreas, with the remainder most commonly located in the duodenum or peripancreatic nodes; overall about 90% are identified within the so-called gastrinoma triangle bounded by the cystic duct junction with the common bile duct, the pancreatic neck, and the junction of the second and third portions of the duodenum. Rarely, lesions have been reported in the stomach and jejunum. Although gastrinomas within the pancreas are typically 3 to 4 cm and usually within the head, those within the duodenum are usually within the wall, multiple, and subcentimeter in size, making assessment by CT and MRI difficult. For this reason, EUS is particularly useful for identifying gastrinomas preoperatively and to biopsy suspicious nodes. Because of the nature

![Cystic pancreatic tail lesion (white arrows) on CT shows subtle peripheral enhancement. EUS FNA confirmed PNET.](image-url)
and high concentration of their somatostatin receptor expression, these lesions are more amenable to evaluation with nuclear medicine octreotide scanning. Unlike insulinomas, 60% of gastrinomas show malignant behavior at presentation, requiring careful inspection for all sites of disease and close evaluation for potential liver metastases. Gastrinomas are the most common functioning PNET in the MEN-I syndrome, in which they are most likely to manifest with multifocal duodenal involvement.

NONFUNCTIONING PANCREATIC NEUROENDOCRINE TUMORS

Nonfunctioning PNETs (see Fig. 5; Fig. 15), typically manifest because of symptoms caused by mass effect, such as pain and weight loss, and as such typically present at a larger size. These nonfunctioning tumors often secrete hormones, such as pancreatic polypeptide, but without causing an apparent clinical syndrome. Being larger, these lesions also more commonly manifest as heterogeneously enhancing lesions, may contain areas of necrosis/cystic change that can be markedly extensive, and can contain foci of calcification. They are also more likely to be metastatic (see Fig. 3) at presentation (60%–80% of cases), most often to liver and lymph nodes (see Fig. 7). The presence of calcifications is a useful indicator for potential malignancy. Duct obstruction can be seen secondary to mass effect, and occasionally tumor can be seen to have spread within a distended duct. In a study of 88 patients with nonfunctioning tumors, 33% had venous tumor thrombus (see Fig. 15), identification of which can alter

Fig. 15. Large nonfunctioning pancreatic head PNET on CT. (A) Late arterial phase shows tumor (white arrows) extending anterior to a metallic biliary stent (black arrow), and (B) infiltrating (black arrowhead) the superior mesenteric vein.
surgical planning, and is a useful distinguishing feature from pancreatic ductal adenocarcinoma.44

Although most often solitary, nonfunctional PNET can be multiple in familial syndromes, and is the most common pancreatic endocrine tumor in patients with MEN-I and von Hippel-Lindau disease.8 With the growing use generally of cross-sectional imaging, up to 35% of nonfunctional PNETs are now found incidentally, which often portends a better prognosis.43

POORLY DIFFERENTIATED PANCREATIC ENDOCRINE TUMORS

An important criterion is poorly versus well-differentiated PNETs. The former are more likely associated with nodal and/or liver metastases, have few somatostatin receptors, and are therefore poorly visualized on octreotide studies, but are more likely to be visualized (see Fig. 10) on FDG-PET/CT studies.8,44,45

Recent studies have attempted to identify imaging biomarkers of aggressiveness. A study of 60 PNETs showed on dual-phase imaging (arterial/portal venous) that atypical enhancement, namely persistent enhancement on portal venous phase imaging or increasing enhancement on later phase compared with typical early enhancement followed by washout on portal venous phase (Fig. 16), was more likely to be carcinoma on histopathologic examination.46 A study that evaluated similar characteristics and diffusion-weighted imaging on MRI also showed that malignant features were more likely to be hypovascular on the arterial phase of imaging, and also showed lower ADC values.18 In one study, the presence of multiple factors, such as poorly defined margin, upstream pancreatic duct dilatation, vascular invasion, tumor size, and enhancement features, were significant in predicting histopathologic grading of tumors,47 whereas another study found that only identification of ill-defined boundaries between tumor and peripancreatic tissues or vessels was significantly associated with World Health Organization 2010 pathologic classification.48

STAGING

The 2 most commonly used staging systems are the European Neuroendocrine Tumor Society system (ENETS, 2006) and the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) 2009 system. Their differences are primarily in T staging, as shown in Table 1.
Primary Tumor

As noted earlier, the type of tumor being considered (ie, insulinoma vs gastrinoma) and differentiation (well vs poorly differentiated) can have significant implications regarding the imaging modalities being chosen (nuclear medicine octreotide study, FDG-PET/CT, EUS/CT/MRI).

The 2 primary modalities for assessing local extent of disease, including involvement of adjacent organs and vasculature, are MRI and CT. CT has the advantages of relative insensitivity to motion and submillimeter slice thickness, and therefore can produce detailed reconstructions useful for evaluating the relationship of tumors to adjacent structures (Fig. 17). MRI can image directly in multiple planes with good soft tissue contrast even when intravenous contrast agents cannot be administered.

Disease Beyond the Pancreas: Nodal and Distant Metastatic

Nodal disease

It is important to identify potential metastatic nodal sites of PNET preoperatively to improve the likelihood of resecting all sites of disease. The most commonly used techniques are CT, MRI, and octreotide scanning (see Figs. 7 and 8; Fig. 18), with octreotide scanning being the most specific. However, only limited information is available on nodal staging. As noted previously, CT provides high-resolution imaging with few artifacts. A recent study of 181 patients undergoing pancreatic resection with curative intent showed a sensitivity and specificity of CT for detecting nodal metastases of 35% and 91% respectively. PNET nodal metastases can be prominently hypervascular and therefore more conspicuous on the arterial phase of dynamic imaging. In our experience, such enhancement can also be similar to, and therefore difficult to distinguish from, adjacent vasculature. In this context, T2-weighted and diffusion-weighted MR imaging can be helpful, because vessels are typically black on images obtained with these techniques because of flow phenomena, whereas nodes (both metastatic and benign) are characteristically bright on both T2-weighted and diffusion imaging (see Fig. 18). However, both CT and MRI are insensitive for micrometastases. Using size criteria of greater than 1 cm in short axis to identify adenopathy is fairly insensitive but somewhat specific. Octreotide scanning with SPECT with fusion with unenhanced CT images can be helpful for identifying small, avid liver, node, and bone metastases but is also insensitive for micrometastases. A very recent study of Ga-DOTA-TOC

Table 1

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<th>Stage</th>
<th>AJCC/UICC 2009</th>
<th>ENETS 2006</th>
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<tbody>
<tr>
<td>T1</td>
<td>Pancreatic confined primary tumor &lt;2 cm</td>
<td>Pancreatic confined primary tumor &lt;2 cm</td>
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<tr>
<td>T2</td>
<td>Pancreatic tumor extending beyond</td>
<td>Pancreatic tumor &gt;4 cm in size or extending</td>
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<td></td>
<td>pancreas without major vessel involvement</td>
<td>beyond pancreas with invasion limited to</td>
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<td></td>
<td></td>
<td>duodenum or bile duct</td>
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<tr>
<td>T3</td>
<td>Pancreatic tumor extending to involve</td>
<td>Pancreatic tumor invading major vessels or</td>
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<td></td>
<td>major vessels such as celiac or superior</td>
<td>invasion of adjacent organs other than</td>
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<td>mesenteric artery</td>
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Fig. 17. Staging of pancreatic head NET (white arrowheads) showing superior mesenteric vein (SMV) abutment on late arterial phase CT (A). Although PNET is not as well seen on (B) portal venous phase images, the SMV is clearly free of thrombus, and coronal reconstruction (C) shows PNET not involving the portal vein (PV) and separate from the superior mesenteric artery (SMA).
PET/MRI with gadoxetate disodium compared with Ga-DOTA-TOC PET/CT showed an advantage for PET/CT for evaluation of involved lymph nodes. As noted previously, conventional FDG-PET/CT may be advantageous compared with octreotide scanning for identifying metastatic sites for poorly differentiated PNET.

Liver metastases
Multiphasic imaging on CT is also useful for liver metastases, which have a variable appearance requiring careful inspection of all dynamic phases. The classic appearance (see Fig. 2) is of a hypervascular metastasis seen best on the arterial phase of imaging. However, metastases can also be hypoenhancing on all phases, portending a worse prognosis. A study of 64 patients in 2005 compared SPECT octreotide scanning, spiral CT, and MRI. SPECT octreotide identified 200 liver metastases, CT identified 325, and MRI identified 394 lesions. Newer developments since then include MRI diffusion-weighted imaging, and the development of liver-specific agents. A study of MRI in 59 patients, 41 patients with 162 liver metastases from neuroendocrine tumors and 18 control subjects with no liver metastases, showed sensitivities of 72% for diffusion-weighted, 57.2% for T2-weighted, and 48% for conventional intravenous gadolinium dynamic multiphasic imaging with decreasing sensitivities for decreasing size of metastases. Gadoxetate disodium, a liver-specific agent retained by normal liver parenchyma, washes out of liver metastases, making them notably conspicuous on 20-minute delayed images (Fig. 19). Although very limited information is available regarding PNET liver metastases, a study has shown greater detection of colorectal liver metastases with gadoxetate disodium MRI than triphasic CT. An interesting recent development has been combined Ga-DOTA-TOC PET/MRI with gadoxetate disodium.

Other Distant Metastases
PNET can also metastasize to bone and lung. Although CT has excellent sensitivity for assessing lung metastases, it is less capable at assessing bone metastases. MRI is useful for characterizing and assessing limited regions of the skeleton, whereas nuclear medicine studies provide the benefit of a whole-body assessment.
Fig. 19. PNET liver metastases (white arrows) on MRI on (A) arterial phase of dynamic, (B) portal venous phase, (C) 20-minute delayed post–gadoxetate disodium, and (D) diffusion-weighted imaging. Conspicuity of liver metastases can vary greatly between arterial/portal venous images but, because they lack hepatocytes, metastases are usually distinctly dark and well defined on (C) delayed gadobenate dimeglumine images. Diffusion-weighted imaging also shows lesions well.
SUMMARY

State-of-the-art imaging for PNET continues to evolve with developments such as dual-energy CT, new MRI techniques such as diffusion-weighted imaging, the increasing use of EUS for solid pancreatic lesions, and the evolving use of PET/CT, including the role of FDG-PET for poorly differentiated tumors and new PET agents that promise greater utility than conventional octreotide nuclear medicine imaging. Optimal use of imaging techniques (focused abdominal imaging and complementary whole-body imaging) depends on such issues as functional versus nonfunctional tumors and well versus poorly differentiated tumors. Insulinomas, which are almost always confined to the pancreas, are typically best imaged by a combination of cross-sectional imaging techniques, such as CT or MRI, with cautious use of whole-body nuclear medicine conventional octreotide imaging, given the often poor uptake of octreotide by this tumor. In contrast, gastrinomas, which are frequently extrapancreatic and octreotide avid, are best managed by a combination of CT or MRI, whole-body octreotide imaging, and EUS to evaluate for pancreatic and intraluminal lesions. In contrast, the typically large size of nonfunctional tumors is such that these are often best managed by cross-sectional imaging, CT or MRI, to provide detail with regard to staging with the type of whole-body imaging depending on whether tumor is well differentiated (in which case whole-body octreotide is used and FDG-PET/CT has only limited utility) versus poorly differentiated (in which case octreotide scanning often performs poorly, but FDG-PET can provide a useful whole-body assessment).

REFERENCES


