Imaging Evaluation of Pancreatic Cancer

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KEYWORDS

• Pancreatic cancer • Pancreatic imaging • Computed tomography • MRI
• Resectability • Structured radiologic reports

KEY POINTS

- Imaging techniques available for the diagnosis, staging, and management of pancreatic neoplasms include computed tomography (CT), PET-CT, MRI, and endoscopic ultrasound (EUS).
- Specialized imaging protocols tailored for evaluation of the pancreas are essential for optimal lesion detection and accurate staging and management of pancreatic neoplasms.
- Biphasic (or dual-phase) multidetector CT is the preferred imaging modality for staging and assessing the resectability of pancreatic adenocarcinoma.
- MRI is nonionizing, has a higher contrast resolution, and is used to evaluate pancreatic neoplasms if the primary tumor is not visible with CT or if patients have a contraindication to contrast-enhanced CT.
- Structured radiologic reporting with standardized terminology and format is critical to ensure that all information needed to stage and plan treatment of pancreatic adenocarcinoma is communicated to the multidisciplinary team.

INTRODUCTION

Pancreatic cancer is the tenth most common cancer in the United States, with an estimated 48,960 new cases reported in 2015. It is currently the fourth leading cause of cancer-related deaths in the United States.[1] The best hope for cure of pancreatic ductal adenocarcinoma (PDA), the most common form of pancreatic cancer, includes complete surgical resection as part of a multimodality treatment plan. However, it has been estimated that only 15% to 20% of patients present with resectable disease.[2] Patients with complete, incomplete, or margin-positive resection (R0, no residual disease; R1, residual microscopic disease; or R2, residual macroscopic disease, respectively) have progressively decreasing survival rates.[3]

Imaging studies are critical for the detection, characterization, initial staging, management, and monitoring of pancreatic cancer cases. Diagnostic imaging of the

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Surg Clin N Am 96 (2016) 1235–1256
http://dx.doi.org/10.1016/j.suc.2016.07.007 surgical.theclinics.com

pancreas has traditionally posed a challenge to the radiologist because of the subtle imaging appearance of some tumors, especially those that are smaller than 2 cm and those that do not cause a border deformity of the pancreas. Dedicated pancreatic imaging protocols tailored to optimize pancreatic lesion conspicuity and highlight the ductal and peripancreatic anatomy are crucial for accurate determination of resectability. As such, the National Comprehensive Cancer Network (NCCN) has established guidelines for the imaging modalities and imaging protocols used to evaluate PDA.[4]

Treatment of pancreatic cancer requires a multidisciplinary approach. Ideally, assessing resectablility with imaging and subsequent treatment decisions should be made at a high-volume center of excellence with a multidisciplinary team. Recently, a structured radiologic report using standardized nomenclature and formatting has been endorsed by radiologic and clinical specialties to appropriately communicate essential information required to accurately stage and manage pancreatic cancer. Although the use of this form of reporting is not yet universal, it has been shown to add significant value to the care of patients with PDA.[5]

This article reviews the major imaging modalities used to evaluate pancreatic neoplasms, with an emphasis on pancreatic imaging protocols. We describe the imaging appearance of solid pancreatic neoplasms, and the imaging criteria used to stage and determine resectability for PDA. An approach to standardized radiologic reporting is also reviewed.

IMAGING TECHNIQUES AND PROTOCOLS

Computed tomography (CT) and MRI are the first-line imaging modalities used to evaluate pancreatic neoplasms. The role of PET remains unclear, but this modality is most commonly used to assess for the presence of extrapancreatic metastatic disease. Endoscopic ultrasound (EUS) plays an important role in guiding fine-needle aspiration (FNA) or biopsy. Endoscopy in the evaluation of pancreatic cancer is covered in detail elsewhere in this issue. A summary of the indications, advantages, and disadvantages of each imaging modality is provided in **Table 1**.

Computed Tomography

Pancreatic protocol dual-phase CT is recommended by the NCCN guidelines as the preferred imaging study for the initial evaluation of PDA (**Table 2**).[4] CT is more widely available than MRI and is less costly. Furthermore, the spatial resolution of CT is much better than MRI allowing for more accurate assessment of subtle perivascular disease. A dual-phase study should be performed even if a single-phase standard CT scan is available, unless there is evidence of metastatic, nonresectable disease on the standard CT scan.[5] Dual-phase imaging is performed in the pancreatic (late arterial) and portal venous phases of contrast enhancement. Conspicuity of PDA is greatest in the pancreatic phase (**Fig. 1**); therefore, this phase is used to delineate the primary tumor and to evaluate arterial involvement by the tumor. The portal venous phase images are used to evaluate venous involvement by the tumor and to identify distant spread of disease.[6] Unenhanced imaging is not helpful in the initial staging of pancreatic cancer. Intravenous contrast should be injected via a power injector at a rate of at least 3.5 to 5 mL/s. The timing of imaging after contrast injection varies among scanners and is typically determined in one of two ways. Scans can be performed at a fixed time delay after contrast administration (typically 35–80 seconds for late arterial phase depending on scanner speed and 65–80 seconds for portal venous phase).[7] This method is plagued by suboptimal enhancement in some patients because of variations in circulation. Alternatively, automated bolus tracking software can trigger scans

Table 1
Imaging modalities for pancreatic cancer

Modality	Indications	Advantages	Disadvantages	Contraindications
CT	Preferred modality to stage PDA	High spatial resolution Widely available Lower cost than MRI	Tumors may not be visible because of poor contrast resolution	Intravenous contrast contraindicated in patients with severe allergy or poor renal function
MRI	Cases with high suspicion for pancreatic neoplasm and negative CT Preferred modality to evaluate pancreatic cystic lesions Alternative for those with CT contrast allergy or compromised renal function	Excellent contrast resolution Provides characterization of liver lesions (potential metastasis)	High cost Limited availability Image artifacts	Noncompatible implanted medical devices GFR <30 mL/min/1.73 m^2 (relative contraindication because of nephrogenic systemic fibrosis risk) Not suitable for patients who cannot lie still/hold breath or have claustrophobia
PET-CT	Role in pancreatic cancer evaluation is unclear; may be used for metastatic evaluation	Provides functional metabolic information	Poor spatial and contrast resolution High cost	Elevated glucose levels
EUS	Guide FNA for tissue sampling Cases with strong suspicion for pancreatic lesion and negative CT and MRI	Useful for cytohistopathologic sampling	Invasive Small field of view	Patient must be able to undergo conscious sedation

Abbreviations: CT, computed tomography; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; GFR, glomerular filtration rate; PDA, pancreatic ductal adenocarcinoma.

Table 2
CT protocol for pancreatic imaging

Parameter	Value
CT scanner specifications	Multidetector
Oral contrast	250 mL water (or neutral contrast) while waiting for scan and 250 mL water just before scan No iodinated or high-attenuation contrast
Intravenous contrast	150 mL Omnipaque 300 (or other high-concentration contrast) 60 mL saline flush 4-mL/s injection rate
Scan acquisition timing	Pancreatic (late arterial) phase: trigger with bolus tracking Portal venous phase: trigger with bolus tracking or 70–80 s (depending on speed of scanner)
Image acquisition and reconstruction	0.6-mm collimation (thinnest) 3-mm slice thickness 1 mm × 0.8 mm for reconstruction (smallest slice with overlap)
Reconstruction	3 mm × 3 mm coronal multiplanar reformat for both phases 3D, MIP, multiplanar reformat software available to radiologists during review

Abbreviations: 3D, three-dimensional, MIP, maximum intensity projection.

to be performed once a certain threshold of contrast attenuation is reached at a set location (typically the descending or upper abdominal aorta). This corrects for variance in circulation among patients and improves the conspicuity of PDA during the pancreatic phase.[8] At our institution, automatic bolus tracking is used to time the pancreatic phase, and venous-phase imaging is then performed at a fixed time (70–80 seconds).

High-attenuation oral contrast should not be administered when evaluating the pancreas because this type of contrast in the gastric body could cause beam attenuation artifact, compromising the evaluation of the adjacent pancreas and possibly obscuring ampullary pathology. Neutral oral contrast agents, such as those used in CT enterography (Breeza, Beekley Medical, Bristol, CT), water, or milk are usually administered to the patient before imaging to distend the duodenum, thereby improving conspicuity of lesions in this location (see **Fig. 1**C). At our institution, patients drink 250 mL of water 15 minutes before the study and again just before getting on the table. Some authors advocate using larger doses of neutral contrast agents to better distend the region when ampullary pathology is suspected. Some institutions also administer glucagon or effervescent crystals to reduce peristalsis and improve distention of the duodenum.[9]

Multidetector technology allows for rapid acquisition of high-resolution isotropic images that are reviewed in multiple planes via multiplanar reformat imaging. Studies have shown that reviewing multiplanar reformat CT data in the coronal and sagittal planes allows for improved detection and staging of tumors.[6,10] Curved planar reformatted images are used to view a specific structure of interest, such as a vessel, which may lie or course in a nonstandard plane (see **Fig. 1**D, E). At our institution, the pancreatic and portal venous image sets are reviewed in axial and coronal planes. Three-dimensional (3D) software is immediately available to the interpreting physician and is used to create additional sagittal or curved planar reformatted images for further evaluation.

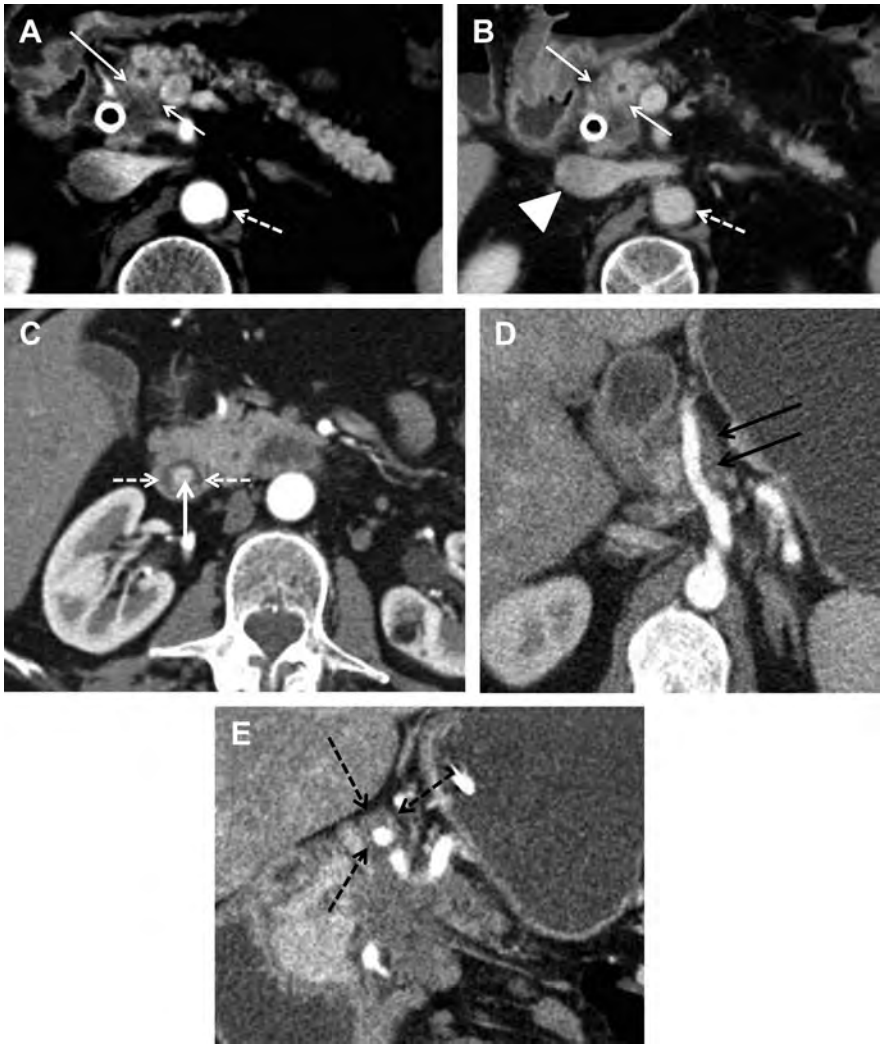

Fig. 1. Axial CT images through the pancreas obtained during the pancreatic or late arterial phase of contrast enhancement (*A*). This phase is recognized by the bright enhancement of the aorta (*dashed arrow*). The borders of the low-attenuation PDA (*solid arrows*) are well delineated in this phase compared with the background pancreatic parenchyma. A metal biliary stent is seen. Axial CT at the same level but obtained during the venous phase of contrast enhancement (*B*). The venous phase is identified by less dense enhancement of the aorta (*dashed arrow*) with similar attenuation to the inferior vena cava (*triangle*). The borders of the low-attenuation PDA (*solid arrows*) are less distinct on this phase. An axial CT image in a different patient obtained during the pancreatic phase of contrast enhancement shows a hypervascular duodenal carcinoid (*solid arrow*) (*C*). The lesion stands out against the surrounding lower-attenuation fluid (*dashed arrows*) within the duodenal lumen. An axial CT scan performed during the pancreatic phase shows soft tissue along 50% of the superior mesenteric artery (*arrows*) (*D*). The borders above and below the superior mesenteric artery are not visible in the axial plane. A coronal reformatted image obtained from the same arterial phase acquisition shows that the superior mesenteric artery is completely (100%) encased by soft tissue attenuation tumor (*dashed arrows*) (*E*).

Emerging CT technologies are also being explored for use in pancreatic imaging. Dual-energy CT scanners simultaneously image at two distinct energy levels. Dual-energy CT data can be processed to optimize images and to identify or quantify a certain material, such as iodine from contrast material. Although a thorough discussion of dual-energy CT imaging capabilities is beyond the scope of this article, studies have shown improved lesion detection, border definition, and lesion characterization, and improved evaluation of structures relevant to treatment planning with these techniques.[11] Additionally, the routine use of lower tube potential (kilovoltage) allows for better differentiation between enhancing normal parenchyma and the generally hypoenhancing pancreatic carcinoma.

MRI

Although CT is considered the first-line imaging modality for the evaluation of PDA, MRI can offer advantages over CT in specific clinical situations. MRI has superior contrast resolution compared with CT and is thus more sensitive for the detection of non-contour-deforming pancreatic tumors. However, because the spatial resolution of MRI is less than CT, subtle perivascular and peripancreatic changes are not as readily or accurately identified. MRI is used to characterize hepatic lesions as metastatic disease.[12] MRI combined with MR cholangiopancreatography (MRCP) offers better evaluation of the pancreatic duct and can better detect and classify pancreatic cystic lesions. MRI can also be used in patients with contraindications to CT, such as intravenous contrast allergy or renal insufficiency.

Most pancreatic MRI protocols use a combination of imaging sequences obtained in different planes; these sequences are designed to highlight pancreatic parenchymal and ductal anatomy. These protocols should include a T2-weighted single-shot fast-spin-echo sequence, T1-weighted in-phase and opposed-phase gradient echo sequences, a T2-weighted fat-suppressed sequence, heavily T2-weighted 3D MRCP sequences, and 3D gradient echo T1-weighted sequences with fat suppression obtained before contrast and with dynamic postcontrast imaging to include the pancreatic (arterial) and portal venous phases of contrast enhancement. Diffusion-weighed imaging (DWI) with apparent diffusion coefficient (ADC) mapping should also be included (**Table 3**).[5,12] A noncontrast MRCP scan is not sufficient to diagnose and stage PDA.[5]

T1-weighted in-phase and opposed-phase sequences are used to assess for intracellular fat. On these sequences, fat loses signal or appears darker on the opposed-phase set of images as compared with the in-phase set of images (**Fig. 2**A, B). The precontrast T1-weighted gradient echo sequence with fat suppression is used to assess for the presence of extracellular or macroscopic fat (**Fig. 2**C). Fat-suppression imaging is important in pancreatic imaging, because prominent or asymmetric areas of pancreatic fat can be mistaken for a mass. Images from this sequence are also compared against postcontrast images. T1-weighted images are used to assess for the presence of hemorrhage, which appears as T1 hyperintense (white).[13]

All MRI protocols to evaluate pancreatic cancers should include 3D gradient echo T1-weighted dynamic postcontrast imaging through the pancreas, peripancreatic tissues, and liver. MRI contrast agents taken up by biologic tissues appear as T1 hyperintense (white). This series of postcontrast scans is crucial for detecting lesions, evaluating the vascular anatomy, and assessing metastatic disease (**Fig. 2**D).

T2-weighted sequences, sometimes referred to as “fluid-sensitive” sequences, are used to assess for the presence of fluid. Simple fluid is T2 hyperintense (white) on these sequences (**Fig. 2**E). Many tumors, including hepatic metastases, demonstrate T2 intermediate signal, making this sequence helpful for lesion detection.

Table 3
MRI protocol for pancreatic imaging

Sequence	Plane	Slice Thickness	Purpose
T2-weighted single-shot FSE or HASTE	Axial, coronal, sagittal (optional)	4 mm	Evaluate overall anatomy
T1-weighted in-phase and opposed-phase gradient echo	Axial	4 mm	Evaluate intracellular fat
T2-weighted with fat suppression	Axial	7–9 mm	Lesion detection Evaluate for fluid signal
Heavily T2-weighted 3D MRCP	Coronal, MIP reconstruction (optional)	1.1 mm 3D	Evaluate duct and cystic structures
T1-weighted 3D gradient echo with fat saturation before and after contrast to include arterial, portal venous, delayed venous, and 4-min delayed phases	Axial, coronal (optional)	2.3 mm 3D	Detect and characterize lesions, evaluate vascular involvement
DWI with ADC mapping	Axial	6 mm	Detect lesions
Offline 3D reconstructions	—	—	Characterize duct anatomy and relationship of cysts to ducts

Abbreviations: FSE, fast spin echo; HASTE, half-Fourier acquisition single-shot turbo spin echo; MIP, maximum intensity projection.

MRCP is a special type of sequence that is heavily T2 weighted so that only fluid signal is imaged. MRCP images are obtained using two-dimensional or 3D techniques. The 3D technique produces thin-slice images, which can more effectively evaluate small side branches and filling defects. These sequences are used to evaluate the pancreatic and biliary duct anatomy. MRCP imaging is also helpful for evaluating pancreatic cystic lesions (**Fig. 2**F).[13]

DWI is a functional MRI technique that assesses water motion in biologic tissues (called Brownian motion). Brownian motion is affected by tissue cellularity, viscosity of fluids, and the presence of intact cell membranes. Increased cellular density with many intact cellular membranes, a finding in many neoplastic tissues, is associated with restricted water motion. On DWI, tissues with restricted diffusion appear bright (white). The generation of ADC maps allows for quantitative assessment of this diffusion.[14] In the setting of pancreatic cancer, DWI is used to detect primary tumor and metastatic disease. Both PDA and pancreatic neuroendocrine tumors (PNET) typically demonstrate higher signal intensity than the background pancreas on DWI, along with lower ADC values (**Fig. 2**G, H). Studies have shown that adding DWI to MRI protocols increases the sensitivity for lesion detection, particularly for lesions smaller than 2 cm.[15,16] However, DWI cannot be used alone to characterize lesions, because more necrotic or less fibrous tumors may not show restricted diffusion. Additionally, benign processes, such as infection and pancreatitis, can demonstrate restricted diffusion. Current research is evaluating the use of DWI and ADC values as predictors of tumor aggressiveness and response to therapy.[17]

Newer techniques, such as MRI perfusion imaging, are also being evaluated for use in pancreatic tumor characterization and therapy monitoring.[14,18]

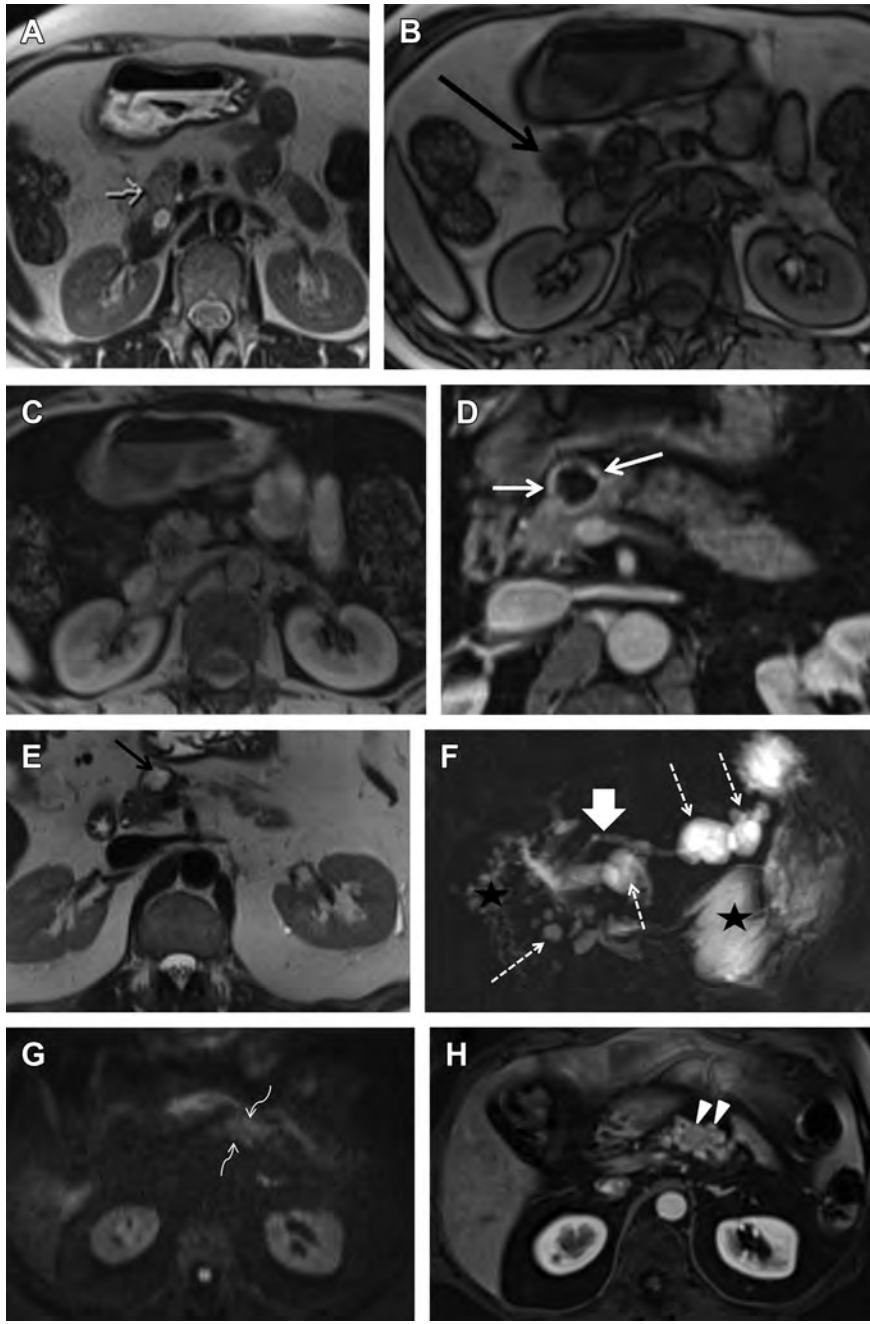

Fig. 2. Axial T2-weighted image without fat suppression shows focal T2 hyperintense lesion (*arrow*) in the pancreatic head (*A*). Subcutaneous and mesenteric fat is also hyperintense on this image. On the axial T1-weighted opposed-phase image, the pancreatic head lesion shows blooming T2 hypointense signal (*arrow*) (*B*). Axial T1 gradient echo precontrast image with fat suppression shows that the pancreatic head lesion is hypointense compared with the background pancreas (*C*). Fat in the mesentery is also hypointense.

Not every patient can undergo MRI. These studies take much longer to perform than CT examinations and thus require greater patient cooperation, with patients being required to lie still and maintain longer breath holds. Some patients cannot tolerate the examinations because of claustrophobia. Others may not be suited for MRI because of the presence of incompatible implanted devices. Finally, patients may not be eligible for the use of intravenous gadolinium-based contrast because of allergy or poor renal function (glomerular filtration rate <30 mL/min/1.73 m^2), which could lead to nephrogenic systemic fibrosis in the presence of gadolinium-based contrast.

PET

In PET, the radiotracer 18 F-fluorodeoxyglucose (FDG) is injected intravenously. In general, neoplastic cells take up proportionally more glucose than nonneoplastic tissue. FDG is trapped in the cells, because it cannot be metabolized by the usual glycolytic pathways. The radiolabeled FDG thus accumulates in neoplastic tissues and emits positrons, which are detected by the PET scanner. Radiologists use qualitative and semiquantitative data when interpreting PET studies. The quantitative standard uptake value represents the metabolic activity of an area of interest corrected for the dose of radiotracer administered and the weight of the patient.[19]

Hybrid PET-CT scanners combine low-dose CT imaging with standard PET imaging. In these studies, data from the CT scan are used for attenuation correction and radiotracer localization. The CT data are typically acquired during free respiration without oral or intravenous contrast. This results in CT images with decreased spatial resolution because of respiration motion artifact and suboptimal tissue contrast because of the lack of intravenous contrast. However, modern PET-CT scanners are now able to combine PET imaging with full-dose CT imaging and more sophisticated CT protocols, such as the dual-phase contrast-enhanced pancreas protocol described previously. This results in CT images with resolution and anatomic detail similar to those of standard CT scans with the added metabolic information provided by the PET data.

Interpreting studies on the use of PET and PET-CT in pancreatic tumors is confounded by discrepancies among protocols used in the past and those available on modern equipment. The NCCN guidelines state that the role of PET-CT in the management of PDA remains unclear but that it can be used particularly in high-risk patients, such as those with borderline resectable disease, markedly elevated tumor markers, and large tumors or lymph nodes.[5] This modality is currently most widely used for initial staging and treatment planning (**Fig. 3**). Research has demonstrated

Axial T1-weighted postcontrast image shows a cystic pancreatic neuroendocrine tumors (PNET) (*D*). The peripheral rim of solid tissue enhances more than the background pancreas (*arrows*), an imaging feature characteristic of neuroendocrine tumors. Axial T2-weighted image from the same location shows that the cystic component of the tumor is T2 hyperintense (*arrow*) (*E*). Maximum intensity projection image acquired from 3D heavily T2-weighted MRCP sequence shows multiple pancreatic cystic lesions (*dashed arrows*) that communicate with the main pancreatic duct (*thick arrow*), compatible with intraductal papillary mucinous neoplasms (*F*). Fluid signal is also present within the duodenal and gastric lumen (*asterisks*). Axial DWI in patient with increasing CA19-9 and negative CT 3 years after distal pancreatectomy for PDA (*G*). The recurrent hyperintense mass in the pancreatic body along the resection margin (*arrows*) is obvious on the DWI series (*G*) and subtle on the axial T1 gradient echo contrast-enhanced pancreatic phase images (*arrowheads*) (*H*).

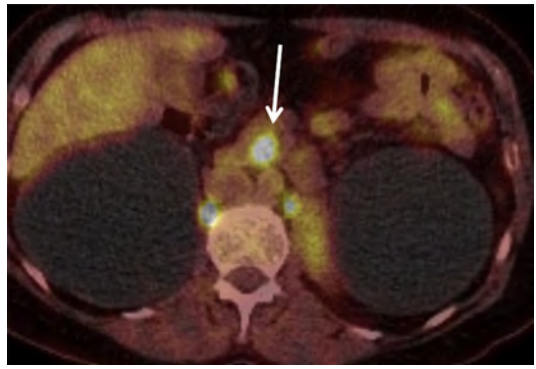

Fig. 3. Axial fused PET-CT image in a patient with newly diagnosed PDA shows FDG-avid uncinate process mass (*arrow*). PET-CT was ordered in this case because the patient had a history of lymphoma, breast cancer, and primary lung cancer.

that PET-CT also shows promise for predicting prognosis, planning radiotherapy, monitoring treatment response, and evaluating recurrent disease.[20,21]

PET-CT is generally not performed in patients with hyperglycemia (glucose levels >200 mg/100 mL) because this could cause decreased FDG uptake and thus lead to false-negative results. Contraindications for contrast agents with PET-CT are the same as those for standard CT.

PET-MRI is an emerging technology that uses MRI data for attenuation correction and spatial localization. The potential use of this modality in pancreatic cancer is yet to be determined.[22]

Endoscopic Ultrasound

EUS has become more widely available and accepted in the management of pancreatic cancer over the past decade. This modality uses a high-resolution EUS probe that is advanced to the stomach and duodenum in close proximity to the pancreas. As with all forms of ultrasound, image quality is user dependent. When performed by an expert practitioner, EUS is the most sensitive test available to evaluate for a pancreatic mass. This modality is particularly useful for lesion detection when the primary lesion is not seen by CT or MRI and when the lesion measures less than 2 cm.[23]

The main value of EUS imaging is that it is possible to introduce an FNA or core biopsy device under EUS guidance. This allows for preoperative tissue sampling, which in some cases is valuable for establishing a definitive diagnosis. EUS with FNA is an invasive procedure with inherent risks of bleeding and pancreatitis. The risk of these EUS-associated adverse effects has been estimated at 0.5% to 2%. Although very uncommon, tumor seeding has also been reported after EUS FNA.[23,24]

The American Society for Gastrointestinal Endoscopy advises the use of EUS with FNA in all cases of suspected resectable PDA.[23] The NCCN guidelines state that although EUS is not recommended as a routine staging tool, in patients with resectable disease, EUS with FNA is preferred over CT-guided biopsy because of a lower risk of tumor seeding.[5]

EUS can also be used to guide fiducial placement for use in radiation therapy, and EUS-guided fine-needle tattooing may be useful in patients with lesions that are not well visualized by other forms of abdominal imaging.[23]

IMAGING FEATURES OF SOLID PANCREATIC NEOPLASMS

PDA and PNET are the most common solid pancreatic neoplasms and are the focus of this discussion. Other solid pancreatic neoplasms include lymphoma, metastatic disease, and solid pseudopapillary tumor. Imaging features of solid pancreatic neoplasms are summarized in Table 4. Pancreatic cystic neoplasms are not discussed in this article because their evaluation generally follows a separate diagnostic algorithm.

Pancreatic Ductal Adenocarcinoma

Most PDA tumors are located in the pancreatic head, followed by the body and tail. On MRI, PDA tumors are hypointense to the background pancreas on T1- and T2-weighted images. PDA tumors typically restrict diffusion and appear hyperintense on DWI and hypointense on ADC maps.

On contrast-enhanced CT and contrast-enhanced MRI, PDA lesions typically enhance less than the background pancreas (Fig. 4A). This hypoenhancement is most evident on pancreatic phase images. Up to 10% of lesions may be isoattenuating to the background pancreas on CT, making these lesions difficult to detect.[25] However, when the primary mass cannot be identified, its presence may be inferred by the identification of ancillary imaging features including pancreatic or common bile duct obstruction, convex border deformity, or peripancreatic soft tissue infiltration. Obstruction and dilation of the pancreatic duct with abrupt duct cutoff at the level of the tumor is a commonly seen ancillary imaging feature. The "double duct sign" occurs when both the pancreatic and common bile ducts are obstructed by a pancreatic head mass. Atrophy of the pancreas proximal to the lesion may also be seen

Table 4
Imaging features of solid pancreatic neoplasms

Lesion	Imaging Modality	Imaging Findings
PDA	Pancreatic CT preferred for staging; pancreatic MRI if CT is contraindicated	Mass hypovascular compared with pancreas on pancreatic phase, heterogeneous enhancement on venous phase Pancreatic atrophy beyond mass Pancreatic duct dilated with cutoff at mass Common bile duct and hepatic ducts dilated if mass is in periampullary location Convex border deformity
PNET	Pancreatic CT; pancreatic MRI; octreotide scan for detection	Hypervascular T1 hypointense and T2 hyperintense Cystic change or calcifications may be present
Pancreatic lymphoma	Standard CT	Solid discrete mass or infiltrative Variable enhancement Tumor may not respect anatomic boundaries
Pancreatic parenchymal metastasis	CT or MRI	Hypervascular (renal cell carcinoma) or hypovascular Single, multifocal, or diffuse

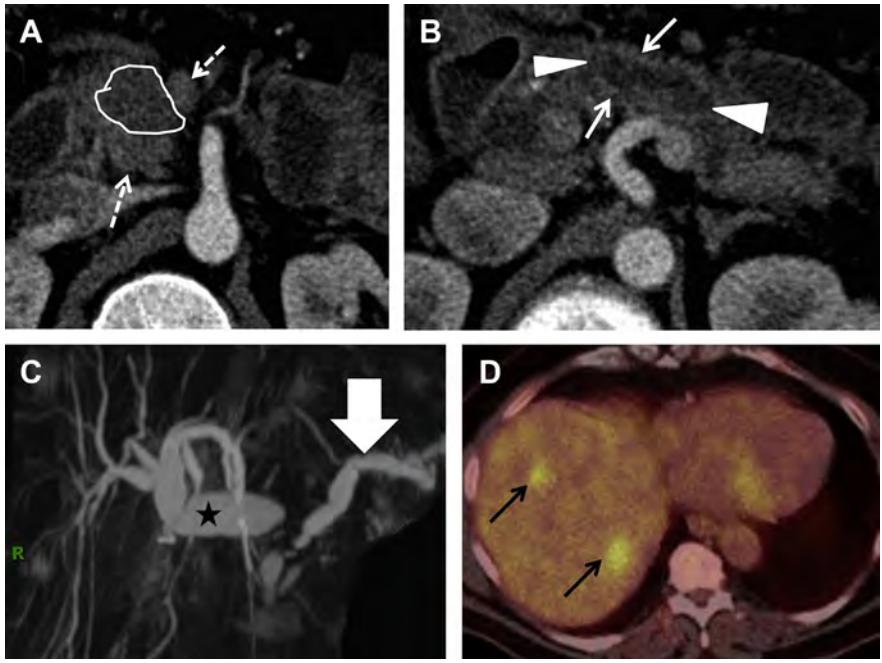

Fig. 4. Pancreatic phase axial CT scan through the level of the pancreatic head shows a mass that is hypodense (*outline*) compared with the background pancreas (*dashed arrows*) (*A*). Axial image from the same patient at a different level shows markedly dilated pancreatic duct (*arrowheads*) and atrophic pancreatic parenchyma in the body and tail (*arrows*) (*B*). Maximum intensity projection image from MRCP shows the "double duct sign," with markedly dilated common bile duct (*asterisk*), intrahepatic ducts, and pancreatic duct (*arrow*) (*C*). Axial PET-CT image from a different patient with pancreatic cancer shows FDG-avid liver metastasis (*arrows*) (*D*).

(Fig. 4B, C).[26,27] Vascular invasion is identified when soft tissue surrounds vessels with loss of the expected perivascular fat plane. Vessels, especially venous structures, may be effaced or displaced by surrounding soft tissue tumor. Filling defects or thrombus within vessels can also be seen. Distant metastatic disease is most commonly identified in the liver and peritoneum.

On EUS, PDA lesions are hypoechoic compared with the normal pancreas and tend to be ill defined. The field of view with EUS is narrow, limiting the evaluation of metastatic spread to locoregional lymph nodes and adjacent vessels.

PDA lesions and metastatic disease are hypermetabolic on PET (Fig. 4D). However, small lesions and lesions with necrosis may not be detected on this imaging modality.

Pancreatic Neuroendocrine Tumors

PNET account for 1% to 2% of all pancreatic neoplasms. They may occur at any age but are most common in the fourth to sixth decades of life. There is no sex predilection with these tumors. Although there is increased risk for PNET with some genetic syndromes, most cases of PNET occur sporadically. PNET is either benign or malignant and functioning or nonfunctioning.[28]

PNET have a varied imaging appearance. Functioning tumors that secrete peptides that cause symptoms typically present earlier than nonfunctioning tumors

and are thus often smaller at presentation. On CT and MRI, functioning tumors demonstrate uniform precontrast attenuation or signal and homogeneous postcontrast enhancement (Fig. 5A). Nonfunctioning tumors may not be clinically diagnosed until they cause symptoms from mass effect or metastatic disease; therefore, these lesions are often larger at presentation. Nonfunctioning tumors may have areas of cystic degeneration or internal calcifications resulting in mixed attenuation or signal on precontrast images. These lesions demonstrate heterogeneous enhancement (Fig. 5B). Unlike PDA, PNET are typically hypervascular compared with the background pancreas.[26,28]

On MRI, PNET tend to be T1 hypointense. T2 signal is variable, with most tumors showing T2 hyperintense signal compared with the background pancreas and others showing intermediate T2 signal. As on CT, PNET typically enhance more than the background pancreas.

IN-111 octreotide scans can be used to detect suspected PNET. In these studies, radiolabeled octreotide is picked up by PNET with somatostatin receptors (Fig. 5C, D). This modality is not sensitive for insulinomas.[28] In PNET, PET-CT is mainly used to evaluate metastatic lesions, which appear as FDG avid.

Pancreatic Lymphoma

Pancreatic lymphoma is typically a B-cell, non-Hodgkin type of disease. Primary pancreatic lymphoma is rare, comprising less than 2% of all extranodal lymphomas.

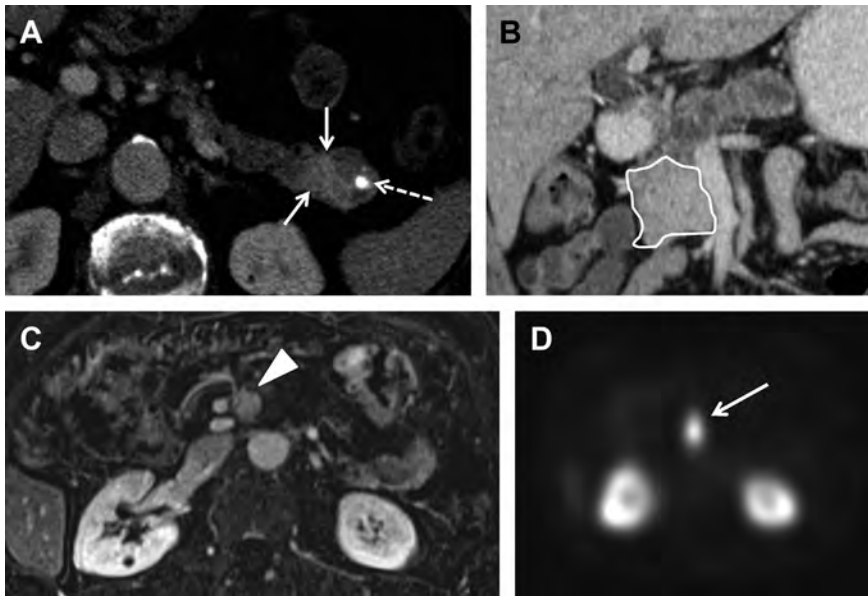

Fig. 5. Axial contrast-enhanced CT scan shows pancreatic tail PNET that is hypervascular (*solid arrows*) compared with the background pancreas (*A*). The mass contains a calcification (*dashed arrow*). Axial contrast-enhanced CT scan in another patient with pancreatic head PNET enhancing more than the background pancreas (*outline*) (*B*). Axial T1 contrast-enhanced MRI in a patient who had undergone pancreaticoduodenectomy for pancreatic head PNET with new enhancing soft tissue nodule adjacent to the superior mesenteric artery (*arrowhead*) (*C*). Axial image from IN-111 octreotide study in the same patient at the same level shows that the nodule takes up octreotide (*arrow*), compatible with recurrent/metastatic disease (*D*).

Secondary lymphoma with spread from adjacent lymph nodes is the most common form to involve the pancreas. Pancreatic lymphoma can appear as a well-circumscribed discrete mass or as infiltrative disease with enlargement of the gland. Lymphomatous masses generally enhance to the same degree of the pancreas although the enhancement pattern is variable. Untreated lymphoma does not contain calcifications. Pancreatic lymphoma does not respect anatomic boundaries, and disease may be seen in the intraperitoneal abdomen with nodal disease below the level of the renal arteries. Lymphoma can surround vasculature, as in PDA; however, the vasculature is typically not occluded by lymphoma.[29] One important feature of lymphoma is that when the pancreatic head is involved the degree of biliary and pancreatic ductal dilation is much less than one would expect for the size of the mass (**Fig. 6**).

Pancreatic Parenchymal Metastases

Metastatic disease to the pancreas is rare. Renal cell carcinoma and lung cancer are the most common neoplasms associated with pancreatic metastasis; metastatic disease from breast cancer, gastrointestinal tract malignancies, melanoma, osteosarcoma, and thyroid cancer have also been described. Metastatic disease to the pancreas can be solitary, multifocal, or diffuse. Enhancement patterns with metastases are variable. Although most metastatic lesions show peripheral or homogeneous contrast enhancement greater than the background pancreas, metastatic lesions from colon, lung, or breast cancers can be hypovascular. Renal cell carcinoma metastases are often hypervascular. Cystic degeneration and necrosis can also be seen (**Fig. 7**).[26,30]

Miscellaneous Solid Pancreatic Neoplasms

Solid pseudopapillary tumor accounts for 1% to 2% of all pancreatic tumors. This tumor exhibits a strong female predilection (9:1) and occurs in younger patients, typically occurring in the second decade of life. These lesions are well encapsulated and slow growing and thus tend to be large at presentation. The capsule is low attenuation on CT and shows hypointense signal on T1- and T2-weighted images. The center of the tumor is characterized by cystic degeneration and hemorrhage, causing a

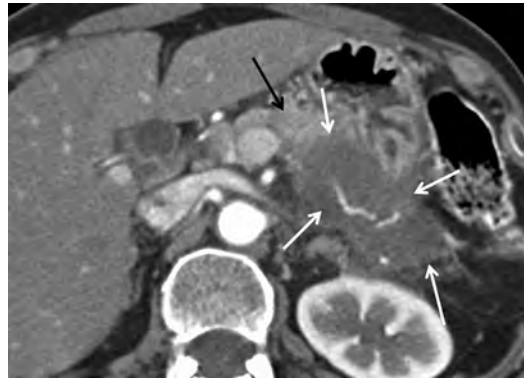

Fig. 6. In a 72-year-old woman with a history of lymphoma, contrast-enhanced CT scan shows an infiltrative pancreatic body/tail hypodense mass (*white arrows*) enhancing less than the pancreas (*black arrow*) that encases but does not occlude the splenic artery. A biopsy demonstrated B-cell lymphoma.

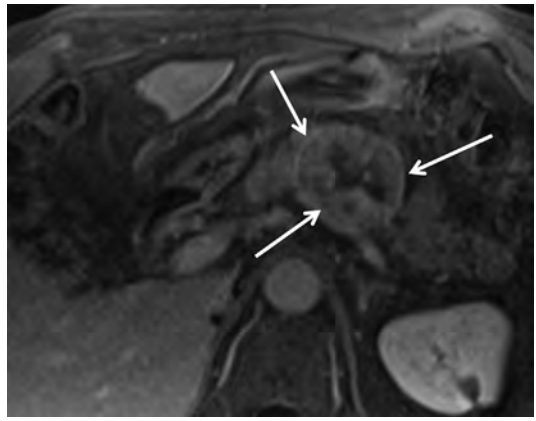

Fig. 7. In a 62-year-old man with a history of renal cell carcinoma who had undergone a right nephrectomy, MRI shows a heterogeneously enhancing pancreatic body/tail (*arrows*), indicating renal cell carcinoma metastasis.

heterogeneous appearance on MRI and CT. Postcontrast imaging shows early enhancement of the capsule with heterogeneous progressive enhancement of the center of the lesion.[31]

Other rare tumors, including pancreatoblastoma, epithelial tumors, mesenchymal tumors, and mixed tumors, can occur in the pancreas but are rare and beyond the scope of this article.

CLASSIFICATION OF RESECTABLE, BORDERLINE RESECTABLE, AND LOCALLY ADVANCED/NONRESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA

PDA treatment guidelines published by the NCCN classify PDA as resectable, borderline resectable, or locally advanced/nonresectable.[5,32,33] Assessment of tumor resectability is based on tumor location, vascular involvement, and metastasis as determined by imaging (**Table 5**). For nonmetastatic PDA, decisions regarding resectability should be made by a multidisciplinary team after acquisition of dedicated pancreatic protocol imaging and staging studies.[5]

PDA is considered resectable when there is no distant metastatic disease or lymphadenopathy. In addition, there must be a clear fat plane with no tumor contact with the surrounding arteries and either no tumor contact or less than 180° tumor contact with the superior mesenteric vein (SMV) and portal vein with no contour deformity (**Figs. 8** and **9**). A staging laparoscopy should be selectively considered based on clinical predictors that optimize yield. These predictors include pancreatic head tumors larger than 3 cm, tumors of the pancreas body and tail, equivocal findings on CT scan, and high CA 19-9 levels (>100 U/mL).[33]

Borderline resectable pancreatic cancer represents a tumor that is confined locoregionally with no imaging or laparoscopic evidence of metastatic disease; additionally, the tumor is deemed not imminently resectable to a negative margin but potentially resectable to a negative margin by surgical criteria after trial of neoadjuvant therapy. **Table 6** summarizes the current various definitions of borderline resectable tumors used by different groups based on vascular involvement.[5,33–35] A multidisciplinary approach that can arrive at a consensus recommendation is highly recommended in the treatment of borderline resectable pancreatic cancer (**Fig. 10**).

Table 5
PDA resectability based on NCCN 2015 guidelines

Resectability Status	Arterial Involvement	Venous Involvement
Resectable	No contact with CA, SMA, or CHA	No or <180° tumor contact with SMV/PV with no contour deformity
Borderline resectable	Pancreatic head/uncinate • Solid tumor contact with CHA, which does not extend to hepatic bifurcation or celiac axis • Solid tumor contact <180° • Solid tumor contact with variant arterial anatomy (eg, replaced SMA) Pancreatic body/tail • Solid tumor contact with CA <180° • Solid tumor contact with CA >180° with no involvement of aorta and intact GDA	• Solid tumor contact with SMV >180° but reconstructable • Solid tumor contact with IVC
Unresectable	Pancreatic head/uncinate • Solid tumor contact with SMA or CA >180° • Solid tumor contact with first jejunal branch of SMA Pancreatic body/tail • Solid tumor contact with SMA or CA >180° • Aortic involvement	• Unreconstructable venous involvement of SMV or PV • Contact with most proximal jejunal draining vein of SMV

Abbreviations: CA, celiac artery; CHA, common hepatic artery; GDA, gastroduodenal artery; IVC, inferior vena cava; PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric artery.

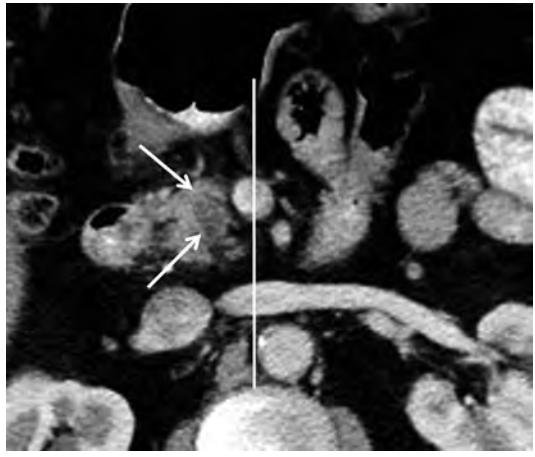

Fig. 8. In a 59-year-old man with abdominal pain, CT scan in the late arterial phase shows a hypodense pancreatic head/uncinate mass (*arrows*) to the right of the superior mesenteric vein (SMV) (*vertical line*) with no involvement of the SMV or superior mesenteric artery. This case was resectable.

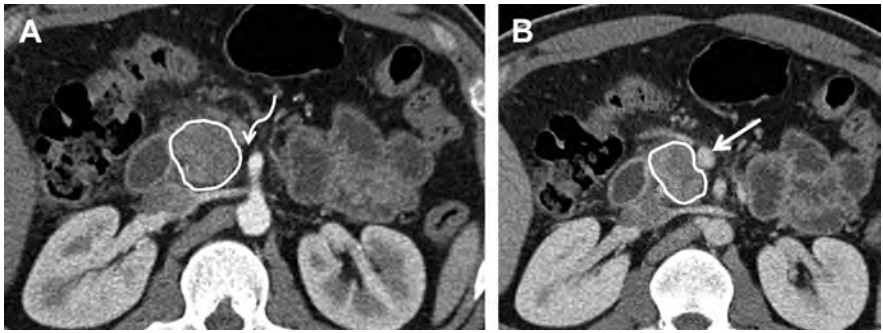

Fig. 9. In a 35-year-old man with abdominal pain, CT scan in the pancreatic parenchymal phase (*A*) and portal venous phase (*B*) shows a 3-cm pancreatic head/uncinate mass (*outlined*) abutting (<180°) the SMV (*straight arrow*) with no involvement of the superior mesenteric artery, as shown by the preserved fat plane (*curved arrow*). There were no metastasis, and this case was resectable.

PDA is considered nonresectable when metastatic disease is present, including distant metastases and nonregional nodal metastases. Common sites of distant metastatic disease from PDA are the liver and peritoneum (Fig. 11). PDA is also considered nonresectable when there is more than 180° solid tumor contact with the superior mesenteric artery or celiac axis or solid tumor contact with the first jejunal branch of the superior mesenteric artery. For body/tail PDA, cases of solid tumor contact greater than 180° with the celiac artery and contact with the aorta are considered nonresectable. Cases involving unreconstructable SMV/portal vein involvement and contact with the most proximal draining jejunal branch of the SMV are also nonresectable.

Table 6
Various definitions of borderline resectable PDA

VESSEL	NCCN 2015[5]	MD Anderson[35]	AHPBA/SSAT/SSO[33]	Intergroup Trial[34]
SMV-PV	Abutment[a]	Occlusion	Abutment, encasement[b]	Tumor-vessel interface >180° and/or reconstructable[c] occlusion
SMA	Abutment	Abutment	Abutment	Tumor-vessel interface <180°
CHA	Abutment or short-segment encasement	Abutment or short-segment encasement	Abutment or short-segment encasement	Reconstructable short-segment interface tumor-vessel interface
Celiac trunk	No abutment or encasement	Abutment	No abutment or encasement	Tumor-vessel interface <180°

Abbreviations: AHPBA, american hepato-pancreato-biliary association; SSAT, society for surgery of the alimentary tract; SSO, society of surgical oncology.

[a] Abutment: tumor-vessel interface less than 180° circumference.

[b] Encasement: tumor-vessel interface greater than 180° circumference.

[c] Normal vein or artery proximal and distal to the site of tumor vessel involvement suitable for vascular reconstruction.

Data from Refs.[5,33–35]

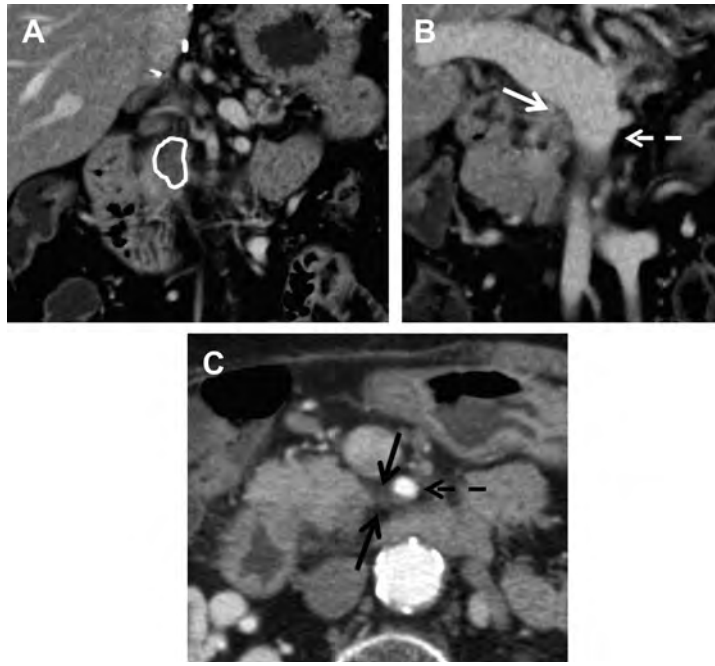

Fig. 10. In a 69-year-old woman with abdominal pain, contrast-enhanced CT scan in coronal reformats (*A*, *B*) and axial (*C*) shows a hypodense pancreatic head/uncinate mass (*outlined*) with less than 180° abutment (*white straight arrow*) of the SMV (*white dashed arrow*) and less than 180° abutment (*black straight arrows*) of the superior mesenteric artery (*black dashed arrow*). This case was considered borderline resectable by the multidisciplinary tumor board.

STANDARDIZATION OF RADIOLOGIC REPORTING FOR PANCREATIC DUCTAL ADENOCARCINOMA

Because imaging plays an essential role in the staging and assessment of resectability for PDA, it is imperative that radiologic reports include all information necessary to determine resectability and that this information is communicated in a clear and consistent format. Structured radiologic reports include a checklist of findings to be reported and use a standardized lexicon. This form of reporting facilitates management of PDA and allows for assessment of eligibility for clinical trials and decreases the need for repeat imaging studies. Various societies and institutions have proposed unique standardized templates and lexicons for reporting imaging findings for PDA.[36,37] The Society of Abdominal Radiology has collaborated with the American Pancreatic Association and developed a standardized structured reporting template for PDA[36]; this template has been adopted by our institution and is described next (**Tables 7–9**).

The term "head/uncinate" is defined by its location with respect to the SMV. Tumors to the right of the SMV are in the head/uncinate and if resectable, are amenable to pancreatoduodenectomy. Tumors to the left of the SMV are in the body/tail and are potentially amenable to distal pancreatectomy.

In descriptions of vascular involvement, the term "abutment" is used when there is less than 180° of contact between the solid tumor and a vessel, whereas the term

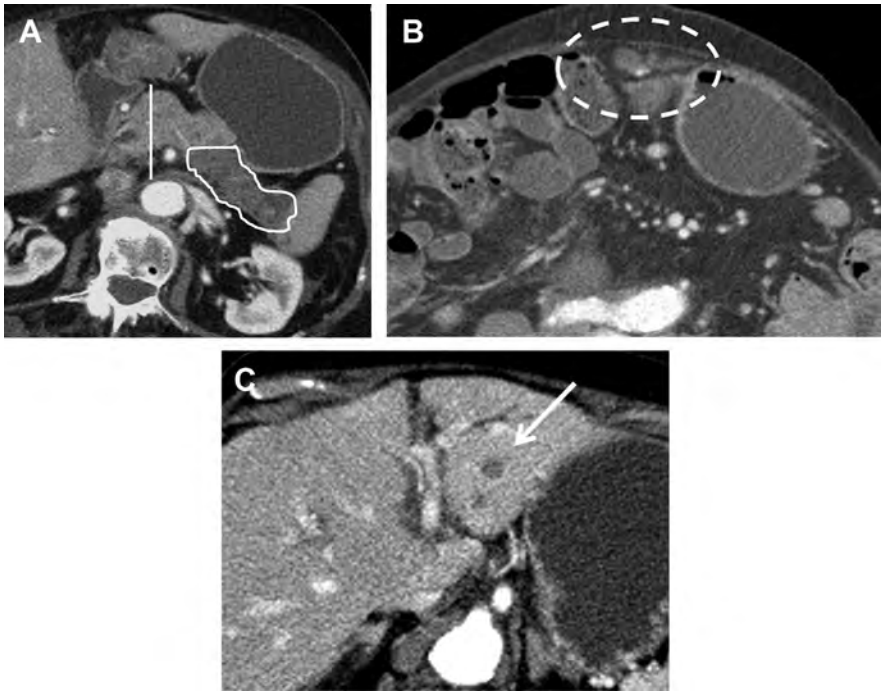

Fig. 11. In an 80-year-old woman with diarrhea, contrast-enhanced CT scan (*A*) shows a pancreatic body/tail hypoenhancing mass (left of SMV, *vertical line; outline*) (*B*). There is peritoneal carcinomatosis (*dashed circle*) and (*C*) liver metastasis (*arrow*). This case was non-resectable. With such a presentation, dual-phase CT is not needed.

"encasement" is used when there is more than 180° of contact between the solid tumor and a vessel. The presence of hazy stranding in the perivascular fat should be mentioned, because this could indicate tumor infiltration, posttreatment change (after chemoradiotherapy), or pancreatitis, especially in cases of recent FNA or biopsy.

The celiac axis, common hepatic artery and its variants, and superior mesenteric artery should be specifically evaluated and reported in all cases. Any change in contour deformity or thrombosis should also be recorded. If pertinent, the length of the vascular segment involved, the proximity of involved vascular segments to

Table 7
Structured reporting template for PDA: morphology

Characteristic	Description
Morphology (pancreatic parenchymal phase)	Hypodense/isodense
Size	Measurable disease >1 cm (give dimensions)
Location	Head/uncinate: right of SMV Body/tail: left of SMV
Pancreatic duct narrowing/cutoff	Present or absent
Biliary duct narrowing/cutoff	Present or absent

Table 8
Structured reporting template for PDA: vascular evaluation

Artery Characteristic	Description
SMA	
Degrees of solid soft tissue contact	Present or absent; <180° or >180°
Degrees of hazy attenuation/stranding	Present or absent; <180° or >180°
Focal vessel narrowing or contour deformity	Present or absent
Involvement of first jejunal branch	Present or absent
CHA	Similar to SMA
Celiac	Similar to SMA
Splenic	Similar to SMA
Variant anatomy (if present)	Similar to SMA
Veins Characteristic	**Description**
SMV	
Degrees of solid soft tissue contact	Present or absent; <180° or >180°
Degrees of hazy attenuation/stranding	Present or absent; <180° or >180°
Focal vessel narrowing or contour deformity	Present or absent
Involvement of most proximal jejunal draining vein	Present or absent
Main PV	Similar to SMV

other landmarks (branch vessels), and the presence of arterial variants involved by the tumor should be noted. The presence of celiac and superior mesenteric artery stenosis should also be recorded, because this might affect surgical management.

SMV and portal vein involvement is the most important determinant of resectability. The extent of circumferential involvement, thrombosis, and contour deformity should be described. As with arterial assessment, the extent of segmental involvement and its proximity to the nearest venous branch should also be described.

Information about invasion of adjacent structures, such as the stomach or duodenum, should also be included in the radiology report, because this may alter the surgical approach.

SUMMARY

Imaging plays an important role in the diagnosis and management of solid pancreatic neoplasms. Standardization of imaging algorithms, imaging protocols, and

Table 9
Structured reporting template for PDA: extrapancreatic evaluation

Extrapancreatic Characteristic	Description
Liver lesions	Present or absent; suspicious, indeterminate, or benign
Peritoneal/omental nodules	Present or absent
Ascites	Present or absent
Suspicious lymph nodes[a]	Present or absent; location
Invasion of adjacent structures	Present or absent

[a] Greater than 1 cm, round, heterogeneous.

radiologic reporting is important to ensure optimal patient care and disease management.

REFERENCES

1. American Cancer Society website. Cancer facts and figures 2015. Available at: www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2015/. Accessed March 9, 2016.
2. Li D, Xie K, Wolff R, et al. Pancreatic cancer. Lancet 2004;363(9414):1049–57.
3. Hernandez J, Mullinax J, Clark W, et al. Survival after pancreaticoduodenectomy is not improved by extending resections to achieve negative margins. Ann Surg 2009;250(1):76–80.
4. National Comprehensive Cancer Network website. NCCN Clinical Practice Guidelines in Oncology. Pancreatic adenocarcinoma, version 2.2015. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed March 9, 2016.
5. Brook OR, Brook A, Vollmer CM, et al. Structured reporting of multiphasic CT for pancreatic cancer: potential effect on staging and surgical planning. Radiology 2015;274(2):464–72.
6. Ichikawa T, Erturk SM, Sou H, et al. MDCT of pancreatic adenocarcinoma: optimal imaging phases and multiplanar reformatted imaging. AJR Am J Roentgenol 2006;187(6):1513–20.
7. Lall CG, Howard TJ, Skandarajah A, et al. New concepts in staging and treatment of locally advanced pancreatic head cancer. AJR Am J Roentgenol 2007;189(5):1044–50.
8. Fukukura Y, Takumi K, Kamiyama T, et al. Pancreatic adenocarcinoma: a comparison of automatic bolus tracking and empirical scan delay. Abdom Imaging 2010;35(5):548–55.
9. Alessandrino F, Souza D, Ivanovic AM, et al. MDCT and MRI of the ampulla of Vater. Part II: non-epithelial neoplasms, benign ampullary disorders, and pitfalls. Abdom Imaging 2015;40(8):292–312.
10. Brugel M, Link TM, Rummeny EJ, et al. Assessment of vascular invasion in pancreatic head cancer with multislice spiral CT: value of multiplanar reconstructions. Eur Radiol 2004;14(7):1188–95.
11. Agrawal MD, Pinho DF, Kulkarni NM, et al. Oncologic applications of dual-energy CT in the abdomen. Radiographics 2014;34(3):589–612.
12. Miller FH, Rini NJ, Keppke AL. MRI of adenocarcinoma of the pancreas. AJR Am J Roentgenol 2006;187(4):W365–74.
13. Sandrasegaran K, Lin C, Akisik FM, et al. State-of-the-art pancreatic MRI. AJR Am J Roentgenol 2010;195(1):42–53.
14. Luna A, Pahwa S, Bonini C, et al. Multiparametric MR imaging in abdominal malignancies. Magn Reson Imaging Clin N Am 2016;24(1):157–86.
15. Park MJ, Kim YK, Choi SY, et al. Preoperative detection of small pancreatic adenocarcinoma: value of adding diffusion-weighted imaging to conventional MR imaging for improving confidence level. Radiology 2014;273(2):433–43.
16. Matsuki M, Inada Y, Nakai G, et al. Diffusion-weighed MR imaging of pancreatic carcinoma. Abdom Imaging 2007;32(4):481–3.
17. Barral M, Taouli B, Guiu B, et al. Diffusion-weighted MR imaging of the pancreas: current status and recommendations. Radiology 2015;274(1):45–63.
18. Liu K, Xie P, Peng W, et al. Assessment of dynamic contrast-enhanced magnetic resonance imaging in the differentiation of pancreatic ductal

adenocarcinoma from other pancreatic solid lesions. J Comput Assist Tomogr 2014;38(5):681–6.
19. Kalra MK, Maher MM, Boland GW, et al. Correlation of positron emission tomography and CT in evaluating pancreatic tumors: technical and clinical implications. AJR Am J Roentgenol 2003;181(2):387–93.
20. Dibble EH, Karantanis D, Mercier G, et al. PET/CT of cancer patients: part 1, pancreatic neoplasms. AJR Am J Roentgenol 2012;199(5):952–67.
21. Chirindel A, Alluri KC, Chaudhry MA, et al. Prognostic value of FDG PET/CT-derived parameters in pancreatic adenocarcinoma at initial PET/CT staging. AJR Am J Roentgenol 2015;204(5):1093–9.
22. Huellner MW, Appenzeller P, Kuhn FP, et al. Whole-body nonenhanced PET/MR versus PET/CT in the staging and restaging of cancers: preliminary observations. Radiology 2014;273(3):859–69.
23. ASGE Standards of Practice Committee, Elobeidi MA, Decker GA, et al. The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia. Gastrointest Endosc 2016;83(1):17–28.
24. Mizuno N, Hara K, Hijioka S, et al. Current concept of endoscopic ultrasound-guided fine needle aspiration for pancreatic cancer. Pancreatology 2011; 11(Suppl 2):40–6.
25. Prokesch RW, Chow LC, Beaulieu CF, et al. Isoattenuating pancreatic adenocarcinoma at multi-detector row CT: secondary signs. Radiology 2002;224(3):764–8.
26. Low G, Panu A, Millo N, et al. Multimodality imaging of neoplastic and nonneoplastic solid lesions of the pancreas. Radiographics 2011;31(4):993–1015.
27. Schima W, Ba-Ssalamah A, Kolblinger C, et al. Pancreatic adenocarcinoma. Eur Radiol 2007;17(3):638–49.
28. Lewis RB, Lattin GE Jr, Paal E. Pancreatic endocrine tumors: radiologic-clinicopathologic correlation. Radiographics 2010;30(6):1445–64.
29. Merkle EM, Bender GN, Brambs HJ. Imaging findings in pancreatic lymphoma: differential aspects. AJR Am J Roentgenol 2000;174(3):671–5.
30. Scatarige JC, Horton KM, Sheth S, et al. Pancreatic parenchymal metastases: observations on helical CT. AJR Am J Roentgenol 2001;176(3):695–9.
31. Cantisani V, Mortele KJ, Levy A, et al. MR imaging features of solid pseudopapillary tumor of the pancreas in adult and pediatric patients. AJR Am J Roentgenol 2003;181(2):395–401.
32. Tempero MA, Arnoletti JP, Behrman SW, et al. National Comprehensive Cancer Networks. Pancreatic adenocarcinoma, version 2.2012: featured updates to the NCCN guidelines. J Natl Compr Canc Netw 2012;10(6):703–13.
33. Callery MP, Chang KJ, Fishman EK, et al. Pretreatment assessment of resectable and borderline resectable pancreatic cancer: expert consensus statement. Ann Surg Oncol 2009;16(7):1727–33.
34. Katz MH, Marsh R, Herman JM, et al. Borderline resectable pancreatic cancer: need for standardization and methods for optimal clinical trial design. Ann Surg Oncol 2013;20(8):2787–95.
35. Varadcharary GR, Tamm EP, Abbruzzese JL, et al. Borderline resectable pancreatic cancer: definitions, management, and role of preoperative therapy. Ann Surg Oncol 2006;13(8):1035–46.
36. Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology 2014;270(1):248–60.
37. CT pancreatic mass staging. radreport.org. Radiological Society of North America. 2015. Available at: www.radreport.org/template/0000135. Accessed March 9, 2016.