

Pancreatic Cancer Imaging: What the Surgeon Wants to Know?

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Abstract

Pancreatic cancer is rare but is one of the deadliest cancers. Complete surgical removal of the cancer with negative margins is the only potentially curative treatment. However, majority of the cases present with distant metastases and/or locally advanced disease, and only a limited subset (up to 20%) of patients are surgical candidates. Therefore, accurate staging of pancreatic cancer is very important for treatment planning. It is very important to distinguish between patients who are surgical candidates and those who would need palliative treatment. Imaging plays a crucial role in the detection of the primary tumor, vascular involvement and variants, metastasis, prediction of resectability, and monitoring treatment response. High-resolution multidetector computed tomography (CT) is the primary imaging modality of choice for diagnosing and staging pancreatic cancers. Nevertheless, integration of ultrasound, CT, and magnetic resonance imaging (MRI) may be needed for accurate determination of the tumor extent and optimal management. Herein, we aim to provide a radiological review for "what the surgeon wants to know about pancreatic cancer?" In this review, we highlight the main types of invasive pancreatic cancers and discuss the role of imaging in determining the resectability of pancreatic tumors and the role of neoadjuvant treatment in downstaging borderline or unresectable cases in addition to featuring significant postsurgical complications.

Keywords

- ► pancreatic cancer
- surgeons
- ► borderline resectable
- ► malignant IPMN
- malignant pancreatic neuroendocrine tumor

Introduction

Pancreatic cancer accounts for approximately only 3% of cancers in the United States (12th in incidence order); however, it is one of the deadliest cancers, with a 5-year survival rate of only 8%.¹ As per a European cancer epidemiology study in 2017, pancreatic cancer is the fourth most fatal cancer in both men and women.² Around 70% of patients die within the first year of diagnosis. About 56,770 new cases and 45,750 deaths are estimated to occur due to pancreatic cancer in the United States during 2019.¹ Complete surgical removal of the cancer with negative margins is the only potentially curative treatment.³ However, only a limited subset of patients with localized disease (up to 20%) are surgical candidates, as the majority of the patients have distant metastatic and/or locally invasive disease at presentation.^{4,5} Therefore, accurate staging of pancreatic cancer is very important for outlining its treatment approach.⁶

Besides the tumor, node, and metastasis (TNM) staging system (**- Table 1**), several staging systems and consensus meetings have discussed the staging criteria of pancreatic cancer.⁷⁻¹² Regardless of the specific details in every classification, the main concern for every medical oncologist and pancreatic surgeon is to distinguish between patients who would benefit from the surgical intervention and those who would better receive alternative palliative treatment

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		5					
M0							M1
M0		Tis	T1	T2	Т3	T4	Stage
	N0	Stage 0	Stage IA	Stage IB	Stage IIA	Stage III	IV
	N1		Stage IIB				
	N2		Stage III				
M1	Stag	e IV					

 Table 1
 Pathological classification of pancreatic cancer

Abbreviations: M0, no distant metastases; M1, distant organ metastasis; N0, no nodal metastases; N1, 1-3 regional nodal metastases; N2, \geq 4 nodal metastases; Tis, carcinoma in situ; T1, tumor \leq 2 cm; T2, tumor >2, \leq 4 cm; T3, tumor >4cm; T4, tumor involving celiac axis, CHA or SMA.

options. Radiological assessment plays a crucial role in the detection of the primary tumor, vascular involvement and variants, metastasis, prediction of resectability, and monitoring treatment response.¹³ High-resolution multidetector computed tomography (HR MDCT) is the primary imaging modality of choice for diagnosing and staging pancreatic cancers. Nevertheless, integration of ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) may be the mainstay for accurate determination of tumor extent for optimal management.¹⁴⁻¹⁶ Herein, we aim to provide a radiological review for "what the surgeon wants to know about pancreatic cancer?"

Pathological Classification

Pancreatic tumors constitute a heterogeneous group of malignant and benign neoplasms (**-Table 2**). Majority (~95%) occur from the exocrine cells and may arise from the ductal epithelium, acinar cells, or connective tissue.¹⁷ Pancreatic exocrine tumors include primary adenocarcinoma, cystic neoplasms, solid pseudopapillary tumor, pancreatoblastoma, lymphoma, and other rare tumors.¹⁸ Pancreatic cystic neoplasms account for about 10-15% of cystic pancreatic lesions and include most commonly intraductal papillary mucinous neoplasm (IPMN), serous cystadenoma, and mucinous cystic neoplasms ([MCNs] either cystadenoma or cystadenocarcinoma).¹⁹ Most of the exocrine pancreatic tumors are malignant (only 2% benign). The endocrine tumors (also called neuroendocrine tumors [NETs]) account for approximately 3 to 4% of the tumors and are the second most common type. Pancreatic NETs are mostly benign and include insulinoma, gastrinoma, glucagonoma, somatostatinoma, vasoactive intestinal peptide tumor (VIPoma), pancreatic polypeptide-secreting tumors, and nonfunctioning tumors.²⁰ Overall, the most common pancreatic malignancy is the pancreatic ductal adenocarcinoma (PDA), which accounts for approximately 85 to 96% of all pancreatic solid cancers. Some pancreatic cystic neoplasms including some IPMN and some MCNs (either cystadenoma or cystadenocarcinoma), as well as some NETs may be malignant.^{19,20}

 Table 2
 Pathological classification of pancreatic cancer

Malignant				
Ductal origin	PDAC Adenosquamous carcinoma Osteoclastic giant cell carcinoma Colloid carcinoma Medullary carcinoma Malignant IPMNs Malignant MCNs			
Nonductal origin	Acinar cell carcinoma Malignant PNETs Pancreatoblastoma Solid pseudopapillary neoplasm Lymphoma			
Secondary metastasis				
Benign				
Serous cystadenoma				
IPMNs				
MCNs				
PNETs				

Abbreviations: IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; PDAC, pancreatic ductal adenocarcinoma; PNET, primitive neuroectodermal tumor.

Clinical Presentation

Presenting symptoms of pancreatic cancer result from a mass effect based on location. Approximately, more than two-thirds (60–70%) of pancreatic cancers arise in the pancreatic head, with symptoms related to obstruction of the biliary tree and gastroduodenal tract, for example, abdominal pain, jaundice, pruritus, dark urine, and clay-colored stools. Nonspecific symptoms occur with cancers in the pancreatic body or tail (20–25%), including unexplained weight loss, anorexia, early satiety, dyspepsia, nausea, and depression.^{21,22} In addition, sudden onset of atypical diabetes mellitus in a thin patient older than 50 years is a suggestive criterion needing work-up to rule out pancreatic cancer.²³ In majority of the cases, these are symptoms of late presentation when curative measures are less likely to have a good effect.

Tumor Markers

Although discovered around 40 years ago, carbohydrate antigen (CA) 19-9 remains the gold standard serum marker for patients with pancreatic cancer and is still the only tumor marker approved by the U.S. Food and Drug Administration. However, it can also be elevated in other medical conditions such as acute cholangitis, liver cirrhosis, pancreatitis, and obstructive jaundice. Similarly, other tumor markers such as carcinoembryonic antigen and other CAs such as CA50, CA195, CA72-4, and CA125 also have limited accuracy. Therefore, in terms of diagnosis, these are considered poor biomarkers for early pancreatic cancer detection. On the other hand, CA 19-9 serum levels can provide valuable information concerning prognosis, overall survival, and treatment response, and predict postoperative recurrence. Recent studies have developed a large number of promising biomarkers including serum proteins and microRNAs, as well as genetic markers that might revolutionize the management approach for pancreatic cancer in future.²⁴

Imaging Modalities

While biopsy is needed to confirm the cancer diagnosis, cross-sectional imaging is essential to detect and narrow the differential diagnosis of a pancreatic mass.²⁵

High-Resolution Multidetector Computed Tomography

Contrast-enhanced HR MDCT is the most validated imaging modality for the diagnosis and staging of pancreatic cancer.14,15,26,27 For optimal detection and staging, using an injection rate of 3 to 4 mL/second of 350 mg/mL of iodinated contrast, the scan is performed during three phases: arterial phase, which occurs around 20 to 25 seconds postinjection, pancreatic (early portal) phase, which occurs at 35 to 40 seconds, and late venous phase, which occurs at 70 seconds. The main goal is to increase tumor visualization by maximizing enhancement difference from the surrounding parenchyma during the arterial phase and to detect the hepatic metastasis during peak hepatic enhancement in the portal venous phase in addition to an assessment of the vascular invasion through the best possible opacification of peripancreatic vessels.^{26,28} Depending on the tumor size, sensitivity of CT for tumor detection is approximately 89 to 97% for large tumors²⁶ and around 77% for masses < 2 cm.²⁹

PDA usually enhances poorly compared with the surrounding pancreas, appears as a hypoattenuating area (\neg Fig. 1) in the early phase of dynamic CT, and gradually enhances more on delayed images. However, sometimes this may be isoattenuating or isoenhancing compared with the normal parenchyma and may be difficult to detect. In such cases, secondary signs such as distal pancreatic atrophy and pancreatic ductal dilatation point to the presence of pancreatic mass (\neg Fig. 2).

Granata et al discussed the importance of the parenchymal pancreatic phase using the dual-energy MDCT and the perfusion CT in visualizing the undetected tumors due to lack of attenuation gradient between the tumor and the surrounding parenchyma.³⁰ CT images can be viewed at multiple energy levels on dual-energy CT, which also allows the generation of iodine images and virtual noncontrast (water only) CT images. Iodine images increase lesion conspicuity, improve pancreatic cancer detection (Fig. 3), and can, sometimes, be especially useful in the detection of small and isoattenuating cancers. Low energy or iodine datasets can also be used to create CT angiogram images to improve the staging of pancreatic cancer. Moreover, adding the multiplanar reconstructed images in coronal and sagittal views to the axial images in these novel CT techniques increases the sensitivity for tumor detection and evaluation of local extension.31



Fig. 1 A 43-year-old male with worsening left flank pain. Axial contrastenhanced computed tomography shows a hypoenhancing mass (arrow) in the pancreatic tail compared with the adjacent enhancing pancreatic parenchyma (short arrow). This was proven to be pancreatic adenocarcinoma.

MRI may be used as a problem-solving tool and to detect the isoattenuating pancreatic masses not seen on CT (**Fig. 4**).^{32,33}

Magnetic Resonance Imaging

MRI is very useful in the detection and staging of pancreatic cancers, particularly when CT findings are equivocal.³⁴ It has particularly superior diagnostic value for pancreatic cystic lesions and may be more accurate in detecting small hepatic lesions and metastases.³⁵ However, there is no significant diagnostic advantage of MRI over contrast-enhanced CT (CECT) (sensitivity of 86% on CT vs. 84% on MRI), and combining the two tests does not give more advantage when compared with one test alone.³⁶⁻³⁸ Typically, the most used MRI protocol is pre- and postgadolinium-enhanced T1-weighted images (T1-WI) with and without fat suppression, along with T2-weighted spin-echo sequences.³⁷

Pancreatic cancer is hypointense on gadolinium-enhanced T1-WI in the pancreatic and venous phases because it is hypovascular compared with the normal pancreas, and it may become isointense on delayed images due to slow contrast wash-in.³⁹ Double duct sign with a dilated common bile duct and pancreatic duct with an abrupt cutoff is classically seen on MR cholangiopancreatography (MRCP) due to pancreatic head masses (**~ Fig. 5**).

The choice between MRI and CT depends on the institutional resources, availability of expertise, and clinician's preference. MRI can also be used in patients with allergy to iodinated contrasts and impaired renal function, whereas MRI may be contraindicated in patients with active pacemakers or in case of incompatible metal or implants in the body.^{34,37-39}

In addition, diffusion-weighted imaging (DWI) offers functional tissue evaluation by mapping the restriction of



Fig. 2 A 45-year-old male with biliary stent placement for obstructive jaundice. Coronal contrast-enhanced computed tomography shows mild atrophy of the pancreatic body and tail, with underlying dilatation of the pancreatic duct (arrow), which shows an abrupt cutoff in the region of the bulky pancreatic head (short arrow) suspicious for an isoattenuating or isoenhancing mass. Endoscopic ultrasound-guided fine needle aspiration (not shown) revealed pancreatic adenocarcinoma involving the head.

Brownian water molecule motion. Tumors usually show an increase in diffusion restriction as a marker of cellularity and pathologic characteristics of cellular barriers. Calculating and mapping of the apparent diffusion coefficient (ADC) allows for a quantitative assessment of restrictive diffusion. DWI with ADC maps are now been widely studied to estimate the tumor response with encouraging results.⁴⁰

Endoscopic Ultrasound-Guided Fine Needle Aspiration

Endoscopic ultrasound (EUS) and fine needle aspiration (FNA) may be used in the preoperative assessment of pancreatic cancers and to detect lesions not seen on MDCT and MRI in suspected cases.⁴¹ The sensitivity of EUS-FNA in diagnosing pancreatic cancer is 80 to 95%42-44; however, its diagnostic accuracy may be lower in cases of obstructive jaundice and chronic pancreatitis.45 An absence of a visualized mass lesion on EUS almost certainly rules out pancreatic cancer.⁴⁶ Sometimes, EUS may be planned preoperatively to assess tumor resectability, as it accurately visualizes portal vein, splenic vein, and peripancreatic lymph nodes invasion. However, involvement of the superior mesenteric artery and the superior mesenteric vein can be better visualized by MDCT.43,44,47,48 The main limitations of EUS is its high dependence on operator experience and the limited availability of skilled experts.³⁴

Positron Emission Tomography and Positron Emission Tomography–Computed Tomography

Positron emission tomography (PET)-CT utilizes the combined functional assessment of PET with anatomical

aspect and spatial resolution of CT. However, the superiority of this technique over MDCT in detecting pancreatic cancers is still a controversial issue, as some studies have proven a higher value of PET-CT over MDCT^{49,50} and some studies have shown no equivalent results.⁵¹ PET-CT is inferior to CT in evaluating regional lymph nodes and vascular involvement, but it is superior to CT in detecting distant metastases (**-Fig. 6**).^{49,52} Focused research may be needed to evaluate the role of PET-CT for the diagnosis and staging of pancreatic cancer, particularly in patients with a negative or indeterminate MDCT.

Staging and Assessment of Resectability

The TNM staging system is the most commonly used staging method to assess the tumor status (T), lymph nodes (N), and metastasis $(M)^{53}$ (**-Table 2**). The most desired result of staging is to segregate the resectable, borderline resectable, locally advanced, and metastatic tumors. Stages I and II are evidently resectable (**Figs. 3–5**). Stage IV is defined by distant metastasis (>Fig. 6); consequently, these will not benefit from resection and are directed to palliative treatment. Stage III tumor gets more targeted attention from the surgeons and radiologists, as they are localized tumors with major vessel involvement and need subcategorization into locally advanced unresectable tumors (Fig. 7) and borderline resectable tumors (>Fig. 8). Furthermore, the borderline resectable pancreatic cancer may benefit from resection, especially if preceded by neoadjuvant treatment.54





Fig. 3 A 49-year-old female presented with abdominal pain, nausea, and jaundice. Axial images of the pancreatic postcontrast phase of (**A**) dual-energy computed tomography (DECT) shows a vague hypodense pancreatic head mass (long arrows), which is better seen and more conspicuous on the (**B**) iodine map images of the DECT. The superior mesenteric artery and vein (short arrows) as well the adjacent aortic bifurcation (arrowheads) were separate from the mass, with clear fat planes suggestive of a resectable tumor. This was proven to be periampullary pancreatic adenocarcinoma following Whipple surgery.

Despite the multiple staging systems and consensus meetings, there is no agreement on the exact criteria of tumor resectability. The MD Anderson Cancer Center (MDACC) and the National Comprehensive Cancer Network established the two most commonly used definitions for local staging to categorize borderline resectable cancers.^{7,8} **- Table 3** presents a comparison of the two most commonly cited definitions of borderline resectable pancreatic cancers. **- Table 4**⁵⁵ shows the imaging criteria adopted by the AHPBA/SSO/SSAT (Americas Hepato-Pancreato-Biliary Association/Society of Surgical Oncology/Society for Surgery of the Alimentary Tract) versus the MDACC criteria^{8,27,56} for potentially resectable, borderline resectable, and locally advanced/ unresectable pancreatic cancers.



Fig. 4 A 63-year-old male presented with weight loss and pulmonary metastases. (**A**) Axial contrast-enhanced computed tomography revealed mild dilatation of the pancreatic duct (arrow) in the tail, with an abrupt cutoff in the region of the pancreatic body. No obvious pancreatic mass was seen on CT. As the isoattenuating mass was suspected, magnetic resonance imaging (MRI) was performed, which clearly shows a hypointense potentially resectable mass (short arrow) in the pancreatic body compared with a normal hyperintense signal of the adjacent pancreatic parenchyma (long arrow) on T1-weighted image **(B)**, with no involvement of the adjacent vasculature.

Preoperative Planning Based on Imaging

Tumor location, pathology, and relation to adjacent structures (e.g., pancreatic duct and vascular supply) are the main determining factors for the choice of the surgical technique. The main goal of the treatment is to achieve a negative margin status (R0 resection).⁵⁷ The main two surgeries for PDA are pancreaticoduodenectomy (PD)⁵⁸ and distal pancreatectomy (DP) with splenectomy. PD (Whipple procedure) is a major surgery performed for the pancreatic head and neck cancers and involves en bloc resection of the pancreatic head with the uncinate process, distal stomach, duodenum, proximal jejunum, gallbladder, distal common bile duct, and regional lymphadenectomy.⁵⁹



Fig. 5 A 60-year-old female presented with pancreatic head cancer, who underwent pancreaticoduodenectomy (Whipple surgery). (**A**) Presurgical magnetic resonance cholangiopancreatography shows dilated common bile duct (short arrow) and the main pancreatic duct (long arrow), with classic double duct sign and an abrupt cutoff in the region of the pancreatic head. This was because of the pancreatic adenocarcinoma that corresponded to the locally confined isoenhancing mass in the pancreatic head (arrow) seen on contrast-enhanced computed tomography (CT) (**B**) with no involvement of the adjacent vasculature and hence a resectable tumor.

DP is performed for distal pancreatic cancers through open procedure or by laparoscopy, depending on the location, size, and involvement of the surroundings. En bloc splenectomy is usually performed in cases of distal pancreatic cancer to achieve the targeted R0.^{60,61} These procedures and the potential postsurgical complications are described in detail elsewhere in this issue.

Role of Neoadjuvant Therapy

Patients with a borderline resectable tumor should receive neoadjuvant chemotherapy or combined chemoradiotherapy to categorize it as a resectable (downstage) tumor, which will benefit from surgery, or an unresectable tumor, which will receive palliative chemotherapy.⁶² Neoadjuvant therapies such as FOLFIRINOX (folinic acid, fluorouracil, irinotecan, oxaliplatin combination) and gemcitabine-based regimens have shown promising results in the downstaging of pancreatic cancers,62-64 and further improved therapies and clinical trials are needed. It is important to mention that the response (downstaging) of borderline resectable pancreatic cancer by neoadjuvant therapy may not be reflected on imaging using the Response Evaluation Criteria in Solid Tumors (RECIST) or modified RECIST (RECIST 1.1),⁵⁵ as these are conventional anatomical imaging-based criteria and have limitations in metabolic assessment. The fluorine-18 fluorodeoxyglucose PET-based criteria (PERCIST [PET response criteria in solid tumors]) seem to be more valuable in such cases. In a recent study, Dalah et al compared both RECIST 1.1 and PERCIST 1.0 criteria to assess the tumor treatment response and found that PERCIST may increase the chance to detect treatment response and is more informative due to its ability to assess tumor viability compared with RECIST 1.1 criteria.65

Malignant Cystic Neoplasia of the Pancreas

IPMNs and MCNs are the main cystic pancreatic lesions, which are found to be precursor lesions with premalignant potential in adenocarcinoma sequences.⁶⁶

Malignant Intraductal Papillary Mucinous Neoplasms

Majority of the IPMNs involve the pancreatic ductal side branches, but they may also affect the main pancreatic duct (MPD) or both. IPNMs of the ductal side branches show less aggressive behavior as compared with those involving the main duct as the prevalence of invasive cancer is higher in the main duct IPMN (23-57%)67,68; therefore, the location of the tumor is crucial for the prognosis (**Fig. 9**).⁶⁶ IPMNs are subdivided into four types-gastric, intestinal, pancreatobiliary, and oncocytic-based on the histopathological features⁶⁹; the pancreatobiliary subtype has the highest malignant potential among the first three, whereas the prognosis of the oncocytic subtype is not yet well studied compared with the other IPMNs.⁷⁰ Branch duct (BD) IPMNs have less malignant potential than MPD and combined-type IPMNs, with a prevalence of 6 to 46% for invasive carcinoma, 67,71,72 and they usually occur in the uncinate process as a small cyst. When the IPMN involves both the side branches and MPD, it is classified as a combined-type IPMN. It is diagnosed by visualizing the dilatation of the MPD and the side branches in the setting of IPMN.⁷³

Staging of all malignant IPMNs is similar to that of PDA. However, imaging features and management differ slightly from that of PDA. MRI has more value than MDCT because





Fig. 6 A 58-year-old female presented with stage IV metastatic pancreatic head cancer on chemotherapy, with a recurrent elevation of CA (carbohydrate antigen) 19-9 following earlier treatment response. (**A**) Axial fused color fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) image shows a hypermetabolic mass in the pancreatic head (arrow) consistent with viable pancreatic cancer. (**B**) Coronal fused PET-CT image shows multiple hypermetabolic hepatic metastases (long arrows). It also revealed new hypermetabolic nodules along the periserosal aspect of the sigmoid colon consistent with peritoneal metastases (short arrows), which were not seen on contrast-enhanced CT (not shown).

of its ability to detect ductal communication, and that is why MRCP is considered more accurate for the diagnosis of IPMNs.⁷⁴ The main features that suggest malignancy on imaging include MPD dilatation of more than 1.5 cm in diameter, the presence of enhancing mural nodules or focal hypoenhancing soft tissue mass, and bile duct obstruction.⁷⁵ All MPD lesions are managed by resection because of their high malignant potential.⁶⁷ The main imaging feature in BD IMPNs is the dilatation of the side ductal branches with the communication to the MPD. Enhancing soft tissue nodularity within it suggests malignancy, and tumors >3 cm in size have a higher risk of malignancy.⁷⁶ If the patient has an asymptomatic BD IPMN without any suggestive features of malignancy, conservative treatment and follow-up are the best approaches to adopt.⁷⁷

Malignant Mucinous Cystic Neoplasms

This usually occurs in the pancreatic body and tail. Patients usually present with vague abdominal pain and discomfort, with classic symptoms of pancreatitis in rare cases.⁷⁸ Staging is similar to that for PDA. It is usually visualized as large (> 6 cm) cystic masses, thick septae, and/or enhancing soft tissue (**~ Fig. 10**).



Fig. 7 A 67-year-old female presented with locally advanced pancreatic cancer. Contrast-enhanced computed tomography shows a large irregular hypoenhancing mass involving the pancreatic head and uncinated process. It completely (360-degree circumference) encases the proximal superior mesenteric artery (long arrow) and branch (short arrow) of the superior mesenteric vein but partially (180-degree circumference) encases the superior mesenteric vein (arrowhead).



Fig. 8 A 66-year-old male presented with abdominal pain and a weight loss of 15 lb. over 1 month. Contrast-enhanced computed tomography revealed a pancreatic body mass extending in the peripancreatic region and focally abutting (<180-degree circumference) the superior mesenteric artery (long arrow) and portomesenteric venous confluence (short arrow) without encasement. This was proven to be pancreatic adenocarcinoma and classified as borderline resectable based on imaging. On neoadjuvant chemotherapy, the tumor decreased in size. Unfortunately, chemotherapy was stopped for a while due to chemotoxicity, and cancer started growing again. The patient subsequently developed liver metastases, which were deemed unresectable.

Because radiological distinction between benign and malignant lesions is often difficult, all mucinous lesions are managed as premalignant and surgically resected.⁷⁹

Malignant Pancreatic Neuroendocrine Neoplasia

Gastroenteropancreatic NETs, also called carcinoids, can be nonfunctional (NF-PNETs) or functional (F-PNETs). In practice, they are also known as nonsyndromic PNETs or syndromic PNETs, with the latter being named according to the predominant hormone secreted by the tumor, for example, insulinomas, gastrinomas, VIPomas, glucagonomas, and so on.⁸⁰ Most of PNETs are benign. The malignant PNETs represent around 1.3% of pancreatic malignancies, and the incidence is growing because of the advancements in imaging techniques that lead to increased detection.⁸¹ Although extremely rare in children, they can occur at any adult age, with equal gender frequency. Per the World Health Organization classification, PNETs are classified as grade 1 or grade 2 or as neuroendocrine carcinoma based on the mitotic count and K1-67 index. Morphological or imaging criteria of malignancy include metastases to the regional lymph nodes, invasion of adjacent organs, and size more than 2 cm.⁸² Preoperative imaging is important in the management and prediction of prognosis. Research linking malignant potential of these tumors using morphological criteria with MDCT and MRI modalities is underway.^{83,84} Per one of the pathological classifications, nonsimple nodular PNET is more associated with morphologic features and malignant potential than simple nodular type.85

Imaging and Management

MDCT plays the main role in evaluating PNETs, with a diagnostic sensitivity of >80% (**Fig. 11**). Most F-PNETs are less than 3 cm in size, hyperenhancing, and therefore better seen in the portal venous or pancreatic phase. Syndromic PNETs can be homogeneous, heterogeneous, or cystic in appearance. Cystic degeneration, calcification, and necrosis are more common in NF-PNETs, which are commonly larger than F-PNETs.⁸⁶

MRI is preferred in patients with allergy to iodinated contrast and renal impairment and has the advantage of lack of radiation compared with CT. Furthermore, MRI is superior to CT in detecting smaller pancreatic lesions and liver metastases.⁸⁷ Sensitivity and specificity of MRI in detecting small islets cell tumors are around 85%.⁸⁸ Other helpful imaging techniques for evaluation of PNETs include EUS, OctreoScan, and other functional imaging such as somatostatin receptor imaging and PET scan labeled with somatostatin analogues. Gallium-68 DOTA-TATE PET-CT scan, which shows the highest affinity for somatostatin receptor 2 tissues, is found to have higher accuracy and detection rate.^{89,90}

Based on the location, resectable lesions in the pancreatic tail can be treated with DP, whereas lesions in the head require Whipple surgery. Patients with oligometastatic disease in the liver may benefit from surgical resection

	MDACC	NCCN
Arterial	 SMA Tumor abutment ≤180 degrees (one half or less) of the circumference of the artery; periarterial stranding and tumor points of contact forming a convexity against the vessel improve chances of resection CA/CHA Short-segment encasement/abutment of the CHA (typically at the gastroduodenal origin); the surgeon should be prepared for vascular resection/interposition grafting 	 Pancreatic head/uncinate process Tumor adjacent to CHA, not passing into CA and CHA branch, conditions for safe and radical resection with reconstruction Tumor adhering to the SMA at ≤180 degrees of its circumference The presence of a vascular anatomical variant in the arterial system (e.g., an additional right HA) and its position relative to the tumor and/or infiltration by the tumor should be taken into account during the planning of the surgical technique Body/tail Adherence of the tumor to CA at ≤180 degrees of its circumference Adherence of the tumor to the CA at >180 degrees of its circumference Adherence of the tumor to the CA at >180 degrees of its circumference Adherence of the tumor to the CA at >180 degrees of its circumference Adherence of the tumor to the cat >180 degrees of its circumference without the features of pulling the wall of this vessel into the tumor, provided that the lesion is not in contact with the aorta or the gastroduodenal artery (some experts believe that this criterion qualifies the case as inoperative)
Venous	 SMV/PV Short-segment occlusion with suitable vessel above and below; segmental venous occlusion alone without SMA involvement is rare and should be apparent on CT images 	 Tumor adhering to SMV or PV at ≤180 degrees of circumference, changing the shape of the vessel Presence of venous thrombosis with preserved normal vessels on the proximal and distal parts of the infiltration site conditions for safe and radical venous resection with subsequent reconstruction The tumor adheres to the IVC

Table 3 Definition of borderline resectable pancreatic cancer according to both MDACC and NCCN criteria

Abbreviations: CA, celiac axis; CHA, common hepatic artery; CT, computed tomography; HA, hepatic artery; IVC, inferior vena cava; MDACC, MD Anderson Cancer Center; NCCN, National Comprehensive Cancer Network; PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric vein.

Table 4 AHPBA/SSO/SSAT and MDACC classifications of lo	ocalized pancreatic cancer
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	AHPBA	A/SSO/SSAT classif	ication ²⁷	MDACC classification ^{8,56}			
Localization	Potentially resectable	Borderline resectable	Locally advanced	Potentially resectable	Borderline resectable	Locally advanced	
SMV/PV	No abut- mentª or encasement ^b	Abutment, encasement, or occlusion	Not reconstructible	Abutment or encasement without occlusion	Short-segment occlusion	Not reconstructible	
SMA	No abutment or encasement	Abutment	Encasement	No abut- ment or encasement	Abutment	Encasement	
СНА	No abutment or encasement	Abutment or short-segment encasement	Long-segment encasement	No abut- ment or encasement	Abutment or short-segment encasement	Long-segment encasement	
Celiac trunk	No abutment or encasement	No abutment or encasement	Abutment	No abut- ment or encasement	Abutment	Encasement	

Abbreviations: AHPBA, Americas Hepato-Pancreato-Biliary Association; CHA, common hepatic artery; MDACC, MD Anderson Cancer Center; PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SSO, Society of Surgical Oncology; SSAT, Society for Surgery of the Alimentary Tract.

Source: adapted from Katz et al.55

^aLess than 180 degrees of vascular circumference. ^bAt least 180 degrees of vascular circumference.



Fig. 9 A 72-year-old female presented with epigastric pain and weight loss. Axial contrast-enhanced computed tomography showed the dilated main pancreatic duct (long arrow) in the tail, with a large heterogeneously enhancing soft tissue component (short arrow) along its posteromedial aspect suspicious for malignant intraductal mucinous neoplasm. Endoscopic ultrasound-guided fine needle aspiration confirmed the diagnosis.



Fig. 10 An 85-year-old female presented with abdominal pain. Axial contrast-enhanced computed tomography showed a complex lobulated cystic mass involving the pancreatic tail, with eccentric solid contents (arrows) suspicious for malignant cystic pancreatic neoplasm. Endoscopic ultrasound-guided fine needle aspiration confirmed the diagnosis of mucinous cystadenocarcinoma. Although distal pancreatectomy was considered in view of the location of the mass, the patient underwent radiotherapy due to comorbidities.

or hepatic artery chemoembolization. Syndromic PNETs cases should undergo endocrinological review to search for other neoplasms depending on the syndrome affecting them, such as multiple endocrine neoplasia-1 (Wermer's syndrome), von Hippel Lindau's disease, neurofibromatosis-1 (von Recklinghausen's disease), and tuberous sclerosis complex.^{91,92}



Fig. 11 A 64-year-old female presented with persistent back pain. Axial contrast-enhanced computed tomography showed a large hypoenhancing mass in the pancreatic tail (long arrow), with multiple rim-enhancing liver nodules and masses (small arrows) suspicious for liver metastases. Liver mass biopsy revealed dedifferentiated neuroendocrine cancer. Pancreatic mass was presumed to be the primary neuroendocrine carcinoma.

Conclusion

Pancreatic cancers constitute a heterogeneous group of neoplasms, including mainly adenocarcinoma, malignant cystic neoplasms, and PNETs. With the recent advances in cancer management, radiologists and surgeons should always be on the same page to provide the best quality of care in these cases. In this review, we highlight the main types of invasive pancreatic cancers and discuss the role of imaging in determining the resectability of pancreatic tumors and the role of neoadjuvant treatment in downstaging borderline or unresectable cases in addition to featuring significant postsurgical complications.

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Conflict of Interest

None declared.

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