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**Imaging diagnosis of pancreatic cancer: A state-of-the-art review**

Lee ES *et al*. Imaging diagnosis of pancreatic cancer

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**Abstract**

Pancreatic cancer (PC) remains one of the deadliest cancers worldwide, and has a poor, five-year survival rate of 5%. Although complete surgical resection is the only curative therapy for pancreatic cancer, less than 20% of the patients newly diagnosed with pancreatic cancer undergo surgical resection with a curative intent. Due to the lack of early symptoms and the tendency of pancreatic adenocarcinoma to invade adjacent structures or to metastasize at an early stage, many patients with pancreatic cancer already have advanced disease at the time of their diagnosis and, therefore, there is a high mortality rate. To improve the patient survival rate, early detection of PC is critical. The diagnosis of PC relies on computed tomography (CT) and/or magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP), or biopsy or fine-needle aspiration using endoscopic ultrasound (EUS). Although multi-detector row computed tomography currently has a major role in the evaluation of PC, MRI with MRCP facilitates better detection of tumors at an early stage by allowing a comprehensive analysis of the morphological changes of the pancreas parenchyma as well as the pancreatic duct. The diagnosis could be improved using positron emission tomography techniques in special conditions in which CT and EUS are not completely diagnostic. It is essential for clinicians to understand the advantages and disadvantages of the various pancreatic imaging modalities in order to be able to make optimal treatment management decisions. Our study investigates the current role and innovative techniques of pancreatic imaging focused on the detection of pancreatic cancer.

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**Key words:** Pancreatic neoplasms;Multidetector computed tomography;Magnetic resononce imaging;Ultrasonography; Endoscopic ultrasound-guided fine needle aspiration;Positron-emission tomography

**Core tip:** To improve the survival rate of pancreatic cancer, early detection and optimal treatment with various imaging modalities is essential. Our study investigates the current role of pancreatic imaging including computed tomography (CT), magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography, or biopsy/fine-needle aspiration using endoscopic ultrasound, focused on the pancreatic cancer. And this study introduces rapidly developing novel imaging techniques, including dual energy, low-tube-voltage CT techniques, iterative reconstruction CT algorithms, functional MRI methods, and hybrid positron emission tomography/MR, are expected to become widely used and to show excellent performance for pancreatic cancer imaging in the near future.

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**INTRODUCTION**

Pancreatic cancer is the fourth most common cause of cancer-related mortality worldwide and with its incidence equaling the mortality rate[[1-3](#_ENREF_1)]. Whereas there have been great advances in the early detection and treatment of other malignancies such as colorectal cancer, breast cancer, and prostate cancer, the prognosis of pancreatic cancer is still bleak as the five-year survival rate is less than 5% and the mortality rate has not declined over the last decades[[4](#_ENREF_4),[5](#_ENREF_5)]. Therefore, pancreatic cancer seems to remain one of the greatest challenges in the fight against cancer in the 21st century[[6](#_ENREF_6)]. One of the main causes of the poor prognosis of pancreatic cancer is the difficulty of its early diagnosis. Because pancreatic cancer typically develops with few symptoms in the early stage and there are not many specific, well-known risk factors except smoking and a family history, the appropriate screening and early diagnosis of pancreatic cancer are quite challenging[[7](#_ENREF_7)]. Therefore, only 10% to 20% of the diagnosed patients have a chance of successful resection and a possible cure, and even in patients with resectable disease, the survival rate is only 23%[[3](#_ENREF_3)].

Despite the numerous obstacles detailed above, there is a continued effort to achieve early detection and to make the appropriate selection of surgical candidates with pancreatic cancer[[8-12](#_ENREF_8)]. Furthermore, the currently available pancreatic imaging has a key role in the characterization of pancreatic focal lesions, the initial staging, surgical and therapeutic planning, and assessment of the treatment response using various imaging modalities, including ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and endoscopic ultrasonography (EUS)[[8-18](#_ENREF_8)]. Multi-detector row computed tomography (MDCT) has a major role in the diagnosis and staging of pancreatic malignancies. And MDCT of the pancreas is favorably complemented by EUS which is more sensitive for the early detection of lesions, allows relatively easy access to the pancreas for tissue diagnosis using fine-needle aspiration (FNA), and provides further important information for use in the tumor staging[[19](#_ENREF_19)].

MRI with magnetic resonance cholangiopancreatography (MRCP) and PET scanning can also have a successful role as a secondary imaging modality under special circumstances when CT and EUS are not diagnostic. Our study provides an overview of the current role and innovative techniques of pancreatic imaging for the detection and treatment of pancreatic cancer.

**ROLE OF PANCREATIC IMAGING**

Although the average survival time of the patients resected for PC is approximately 12 to 20 mo, and there is a high probability of relapse due to the highly adverse and aggressive nature of the evolving disease, the primary treatment offering the greatest potential for cure is the complete, curative, surgical resectioning of the primary carcinoma[[20](#_ENREF_20),[21](#_ENREF_21)]. As surgical and oncological treatments for pancreatic cancer have continually become more aggressive and sophisticated, the role of imaging has become more important not only for the initial diagnosis and staging, but also for determining both the resectability and the optimal treatment monitoring of pancreatic cancer[[16](#_ENREF_16),[17](#_ENREF_17),[22](#_ENREF_22)]. MDCT is currently the worldwide imaging modality of choice for evaluation of pancreatic cancer, although ultrasonography, endoscopic US, contrast-enhanced US, and MRI with MRCP provide complementary, sometimes even more detailed information[[10](#_ENREF_10)]. Each imaging modality has both its advantages and disadvantages according to the four, different aspects regarding pancreatic cancer imaging evaluation: (1) identification of the primary tumor; (2) local tumor resectability; (3) distant metastasis; and (4) treatment monitoring.

***Ultrasonography***

Ultrasonography is frequently the first-line diagnostic tool for patients presenting with jaundice or abdominal pain, as it is a non-invasive and cost-effective modality. A hypoechoic mass, dilatation of the pancreatic duct, and dilatation of the bile duct are typical imaging features of pancreatic head tumor when seen on US. However, in cases of pancreatic body and tail cancers, tumor detection is quite difficult due to the lack of biliary dilatation and the presence of gas bubbles in the stomach and transverse colon, and thus causing a posterior shadowing. In this situation, oral administration of water or other contrast agents may help to delineate the entire organ. The sensitivity and accuracy of pancreatic US are also highly dependent on the operator’s experience and the degree of disease progression as well as body habitus of patients. For these reasons, the US sensitivity for detecting pancreatic cancer is controversial and has been reported as anywhere between 50%-90%[[9](#_ENREF_9),[15](#_ENREF_15),[23-25](#_ENREF_23)]. Using US without contrast media, it is difficult to differentiate pancreatic cancer from other focal lesions, such as neuroendocrine tumor or chronic pancreatitis, as they show the same imaging features on conventional US. Overall, transabdominal US is an acceptable first-imaging method, although not a reliable method for the confident diagnosis or exclusion of small pancreatic tumors which are the only ones with even a slight chance for a cure[[26](#_ENREF_26)].

***Computed tomography***

In many medical institutions, MDCT is routinely used as the most important pre-operative examination in patients with suspected pancreatic cancer as it has good spatial and temporal resolution with wide anatomic coverage and thus permits both comprehensive local and distant disease assessment during a single session[[10](#_ENREF_10)]. In particular, among the cross-sectional imaging modalities, MDCT has shown the best performance for the evaluation of vascular involvement, which is the most important factor for predicting the tumor resectability[[27-33](#_ENREF_27)]. The reported positive predictive value, sensitivity, and specificity for predicting the resectability of pancreatic cancer were 89%, 100%, and 72%, respectively[[34](#_ENREF_34)]. In terms of the treatment monitoring following chemotherapy or surgery, MDCT is the primary imaging modality and is used in conjunction to PET/CT[[14](#_ENREF_14),[18](#_ENREF_18)]. However, MDCT may not depict small metastases to the liver or peritoneum[[30](#_ENREF_30)] or even a primary pancreatic tumor showing iso-attenuation[[35](#_ENREF_35)].

***Endoscopic ultrasonography and fine-needle aspiration***

As EUS offers excellent visualization of the pancreas from the duodenum or stomach and can produce high-resolution images of the pancreas, it has been considered one of the most accurate methods for the detection of pancreatic focal lesions, especially in patients with small tumors of 3 cm or less)[[36](#_ENREF_36),[37](#_ENREF_37)]. EUS also has the unique ability to obtain specimens for histopathological diagnosis using EUS-guided, FNA. Since its early introduction in the early 1990s, EUS-FNA has emerged as a safe and accurate imaging technique for tissue diagnosis in patients with pancreaticobiliary disorders and, particularly, in those with diagnosed pancreatic cancer. Furthermore, EUS-FNA has replaced endoscopic retrograde cholangiopancreatography (ERCP) with brush cytology as the endoscopic test of choice for tissue acquisition due to its higher success rates and decreased risk of post-procedural complications, especially in patients without obstructive jaundice[[38](#_ENREF_38)]. Although EUS alone has shown slightly disappointing accuracy for differentiating pancreatic cancer from chronic pancreatitis, *i.e.* 76% for malignancy and 46% for focal inflammation[[37](#_ENREF_37)], the reported sensitivity and accuracy of conjoined EUS-FNA for detecting pancreatic malignancy usually exceeds 90%[[39-44](#_ENREF_39)]. According to a recent meta-analysis, the pooled sensitivity and specificity of EUS-FNA were 86.8% and 95.8%, respectively, for diagnosing a solid pancreatic mass, during the time period between 1995 and 2008[[38](#_ENREF_38)].

In order to improve diagnostic accuracy of EUS, contrast-enhanced EUS and EUS elastography are valuable new techniques to be considered. By administrating micro-bubble agents, the diagnostic accuracy of EUS can be as high as 82% for pancreatic adenocarcinoma[[45](#_ENREF_45)]. EUS elastography, one of the most recent advances in gastrointestinal endoscopy, is a noninvasive technique that measures tissue elasticity in real time using a dedicated probe and system. A number of recent investigations have shown promising results of EUS elastography for diagnosing pancreatic focal lesions[[46-49](#_ENREF_46)].

***Magnetic resonance imaging***

Over the past few years, MRI scanners and imaging techniques have become more sophisticated and much improved, thus resulting in improvements in both the imaging quality and diagnostic accuracy. Therefore, MRI with MRCP is currently used as a problem-solving tool for patients with pancreatic disease[[50](#_ENREF_50)]. Given the greater soft-tissue contrast of MRI compared with that of CT, there are several specific advantages of and situations in which MRI is superior to CT, *i.e.* small tumors, hypertrophied pancreatic head, iso-attenuating pancreatic cancer, and focal fatty infiltration of the parenchyma[[17](#_ENREF_17)]. Therefore, MRI has been proven to be outstanding for characterizing pancreatic masses. Magnetic resonance cholangiopancreatography (MRCP) is also a very successful and classical MR technique for noninvasively delineating the pancreatic ductal system as well as a valuable alternative to ERCP[[51](#_ENREF_51)]. MRCP is also very useful for detecting subtle ductal narrowing that may suggest the presence of a small mass. Moreover, MRCP is very useful for delineating the presence of stones as an alternative cause of biliary or pancreatic ductal dilatation[[17](#_ENREF_17),[52](#_ENREF_52),[53](#_ENREF_53)]. Although MDCT currently has a major role in the evaluation of PC, MRI with MRCP allows more successful tumor detection at an early stage by allowing a comprehensive analysis of the morphological changes of the pancreas parenchyma as well as that of the pancreatic duct[[20](#_ENREF_20)].

***Positron emission tomography***

PET/CT is an established molecular imaging modality, and fluorine 18-fluorodeoxyglucose (FDG), a glucose analogue, is the most widely used radiotracer[[14](#_ENREF_14),[54](#_ENREF_54)]. The reported sensitivity and specificity of FDG-PET for the depiction of pancreatic cancer are 46%-71% and 63%-100%, respectively[[55](#_ENREF_55)]. However, FDG-PET is more sensitive for treatment monitoring following chemoradiotherapy and for depicting tumor recurrence after resection than is MDCT[[22](#_ENREF_22),[56-59](#_ENREF_56)]. Its wide anatomic coverage which allows the depiction of all possible evidence of metastasis in the entire body, is one of the advantages of PET/CT[[18](#_ENREF_18)]. However, its inherent low spatial resolution and false-positive results caused by normal physiologic FDG uptake are well-known limitations of PET/CT[[60](#_ENREF_60),[61](#_ENREF_61)].

**STANDARD PROTOCOL FOR PANCREATIC CANCER EVALUATION**

In our institution, EUS and PET/CT are not performed by radiologists. Therefore, we do not deal with technical protocols of EUS and PET/CT in this section.

***Ultrasonography***

US examination of the pancreas is performed following a minimum fast of 6 h. The purposes of the fast are to improve visualization of the pancreas, limit bowel gas, and ensure an empty stomach. US scan plans include transvers, longitudinal, and oblique scans along the pancreatic duct. Bowel gas can be displaced by moving the transducer and applying compression when necessary. To obtain complete visualization of all the portions of the pancreatic gland it is possible and sometimes convenient to employ different scanning techniques, such as filling the stomach with water, examining the patient with suspended inspiration or expiration, and changing the patient’s position to erect, supine, and left and right decubitus. If the pancreas is poorly visualized, the water technique with 100 to 300 mL of water through straw would be helpful[[62](#_ENREF_62)].

***Computed tomography***

A pancreas-specific protocol for pancreatic cancer typically utilizes a thin-section, multi-phase technique with precontrast images and early arterial phase (CT angiography phase) images of the aorta and the superior mesenteric artery (17-25 s after the start of contrast injection), pancreatic phase (35–50 s after the start of contrast injection) and portal venous phase images (55–70 s after the start of contrast injection). Pancreatic phase images show peak pancreatic parenchymal enhancement, and therefore, provide the best lesion to pancreas contrast. Portal phase images are helpful to assess the extent of the venous involvement and to identify possible liver metastases[[34](#_ENREF_34),[63-66](#_ENREF_63)]. The bolus tracking technique is currently routinely used to adjust for variations in the cardiac circulation time[[34](#_ENREF_34)]. With regard to post-processing, a variety of post-processing techniques have been described for pancreatic imaging. The most commonly used techniques are multiplanar reformations (MPR), curved multiplanar reformations (CMPR), and minimum intensity projections (MinIP)[[65](#_ENREF_65),[67](#_ENREF_67)]. Oblique coronal or sagittal MPR and CMPR along the pancreatic duct can clearly demonstrate the relationship between tumors and the pancreatic duct or adjacent major structures. MinIP images use the lowest density values along each ray and clearly show low-density structures such as pancreatic and bile ducts. The recommended MinIP slab thickness is 3 mm for the pancreatic duct[[65](#_ENREF_65),[66](#_ENREF_66),[68](#_ENREF_68)]. Maximum intensity projections (MIP) are also often used to evaluate the relationship between tumors and adjacent, enhanced vessels.

In our medical institution at the time of our study, quadruple-phase CT images were obtained according to our biliary-pancreas protocol. First, a baseline, unenhanced scan was obtained from the hepatic dome to the third portion of the duodenum. After unenhanced scanning, patients received 1.5 mL/kg of iopromide (Ultravist 370; Schering, Berlin, Germany) intravenously for 30 s using a power injector and at a rate of 3–5 mL/s. Triple-phase, dynamic CT scans were then obtained. The scanning delay for the arterial, pancreatic, and portal-venous phases was approximately 25 s, 40 s, and 70 s, respectively, after the initiation of the contrast injection. For MDCT scanners, a bolus-tracking method was used. After reaching an enhancement of up to 100 Hounsfield units in the descending aorta, as measured using the bolus-tracking technique, the scanning delay for the arterial phase was 5–6 s for all MDCT scanners. The scanning delay for the pancreatic phase was 19 s-22 s and that for the portal-venous phase was 52 s-65 s following contrast injection. The time required to reach 100 Hounsfield units in the descending aorta ranged from 18 to 23 s. For the clinical interpretation, the CT images were reconstructed with a slice thickness of 2.5–3.0 mm and a reconstruction interval of 1.5–2 mm for MDCT[[69](#_ENREF_69)]. The minimum technical specifications for MDCT of the pancreas are summarized in Table 1.

***Magnetic resonance imaging***

In many medical institutions, patients fast for four to six hours before their MRI examination so that the gallbladder is distended and the signal from the overlying stomach and duodenum is decreased. For full evaluation of the pancreatic parenchyma and the pancreaticobiliary ductal system, obtaining the following MR sequences is recommended[[50](#_ENREF_50)]: T1-weighted gradient-echo; T2-weighted axial and coronal sequences, usually turbo spin-echo (TSE); two dimensional(2D) and three dimensional (3D) MRCP; and T1-weighted 3D gradient-echo (GRE) before and after intravenous administration of gadolinium. Diffusion-weighted imaging (DWI) is currently becoming an increasingly used, optional sequence for the detection and characterization of pancreatic lesions[[70](#_ENREF_70)]. The minimum technical specifications for MRI of the pancreas are summarized in Table 2. In our clinical practice at the time of our study, unenhanced T2-weighted images are usually obtained using a single-shot, fast SE sequence or a half-Fourier rapid acquisition with relaxation enhancement sequence. Unenhanced T1-weighted images are commonly acquired using in-phase and opposed-phase, spoiled GRE (T1-weighted, dual-echo GRE) techniques. In addition, the following three MR cholangiographic methods were used to evaluate the biliary anatomy: (1) the breath-hold, single-section, rapid acquisition with relaxation enhancement technique with fast or turbo SE sequences, (2) the breath-hold, multisection, single-shot, fast SE or half-Fourier rapid acquisition with relaxation enhancement technique, and (3) the respiratory-triggered, 3D, fast SE technique. Dynamic images were obtained using one of two fat-suppressed, 3D GRE sequences, *i.e.* LAVA [liver acquisition with volume acceleration], GE Medical Systems and VIBE [volume interpolation with breath-hold examination], Siemens Medical Solutions) before and following the administration of gadolinium-based contrast agents (Gd-BT-DO3A, Gadovist, Bayer Schering Pharma AG, Berlin, Germany) at a dose of 0.1 mmol per kilogram of body weight and with an injection rate of 1.5-2 mL/s (injection duration approximately 5-8 s). The arterial phase images were obtained five seconds after the gadolinium-containing bolus was detected in the abdominal aorta. Acquisition of 3D LAVA or VIBE data for each phase was completed during a single breath-hold at the end of expiration (mean time, 20 s; range, 18–21 s). Arterial, portal venous, and equilibrium phase images were obtained approximately 20–40 s, 45–65 s, and 3–5 min, respectively, after injection of the contrast agent. An additional, fat-suppressed LAVA or VIBE sequence was performed two minutes after the contrast-agent injection (between the portal venous phase and the equilibrium phase) on the coronal plane and parallel to the portal vein bifurcation[[71](#_ENREF_71),[72](#_ENREF_72)].

**TYPICAL IMAGING FEATURES OF PANCREATIC CANCER**

Pancreatic adenocarcinoma occurs most common in the pancreatic head (65%) and usually presents on US as a hypoechoic solid mass with ill-defined margins (Figure 1). Masses in the head of the pancreas cause ductal obstruction with secondary dilatation of both the common bile duct and the pancreatic duct, and resulting in the so-called double-duct sign[[62](#_ENREF_62)]. On Doppler studies, pancreatic ductal adenocarcinoma shows poor vascularity[[73](#_ENREF_73)] as well as poor enhancement on all phases of contrast-enhanced US[[74](#_ENREF_74)]. This may be caused by the marked desmoplasia, low mean vascular density, as well as with the possible presence of necrosis and mucin[[75](#_ENREF_75)].

On CT, pancreatic adenocarcinomas most often appear as hypoattenuating masses (Figure 2)[[76](#_ENREF_76)]. However, approximately 10% of pancreatic adenocarcinomas are isoattenuating relative to the background pancreatic parenchyma[[35](#_ENREF_35)], especially in small tumors 2 cm or less[[77](#_ENREF_77)], and thus making diagnosis more difficult. In these situations, indirect (secondary) signs such as upstream pancreatic duct dilation or the double-duct sign caused by pancreatic and common bile duct obstruction, are helpful for the diagnosis[[76](#_ENREF_76),[77](#_ENREF_77)]. In addition, the pancreas distal to the tumor also usually appears atrophic. As the tumor grows, it typically infiltrates the peripancreatic structures and may result in encasement of adjacent vasculature and in some cases adjacent organs. Pancreatic cancers can occasionally appear to be cystic or necrotic, and in rare cases they can contain calcium[[78](#_ENREF_78)].

On MRI, pancreatic cancer typically appears hypointense on fat–suppressed, T1-weighted imaging (Figure 3) and on pancreatic parenchymal phase, dynamically enhanced, fat–suppressed, T1-weighted sequences, whereas it has a variable appearance on T2-weighted images[[79](#_ENREF_79)]. Pancreatic cancer also has a variable appearance on diffusion-weighted images. In a recent study of 80 patients, 38 pancreatic cancers appeared hyperintense, 12 isointense, and four hypointense[[80](#_ENREF_80)].

Pancreatic adenocarcinoma usually manifests as an area of increased uptake on PET/CT and appears as a “hot spot” within the pancreas. On the basis of tumor biology and the degree of desmoplastic response, pancreatic ductal adenocarcinoma may demonstrate a low level of or no FDG uptake[[14](#_ENREF_14)]. The reported SUV (standardized uptake value) of pancreatic adenocarcinoma (3.5–5.1 ± 1.6–2.6) was found to be higher than that of benign lesions (1.9–0.8 ± 0.6–1.7) and of the normal pancreas[[81](#_ENREF_81)]. In a recent study of patients with suspected pancreatic cancer, the FDG uptake of malignant tumors was also distinctly higher than that of benign lesions and in patients with chronic pancreatitis[[55](#_ENREF_55),[82](#_ENREF_82)].

**PERFORMANCE OF CT AND MR FOR DIAGNOSIS, STAGING, AND RESECTABILITY**

With the continuing, substantial improvements in CT technology, the capacity of MDCT for the detection, diagnosis, and local staging of pancreatic cancer has increased. MDCT is very effective for detecting and staging adenocarcinoma, with a sensitivity of up to 90% for the detection and an accuracy of 80%–90% for the staging[[26](#_ENREF_26)]. Determination of the extent of vascular involvement is usually made by identifying the extent to which the tumor involves the cross-sectional circumference of a vessel. This can be done by identifying with regard to the circular cross-section of a vessel the degrees of circumferential involvement, as described by Lu *et al*[[31](#_ENREF_31)]. Since their study was published in 1997, the terms “abutment” and “encasement” have also been used, abutment referring to 180° or less involvement of a vessel’s circumference and encasement referring to greater than 180° of vascular circumferential involvement[[79](#_ENREF_79)]. As described above, as MDCT has shown the best performance for evaluating vascular involvement[[27-33](#_ENREF_27)] (Figure 4), it is the most important factor for predicting tumor resectability. For example, four-section CT has been reported to have 100% negative predictive value for vascular invasion and 87% negative predictive value for overall tumor resectability[[30](#_ENREF_30),[83](#_ENREF_83)]. Therefore, MDCT is still the modality of choice for the diagnosis as well as the local staging of patients with pancreatic cancer.

Recently, distinct advances in MR technology have caused great improvement in pancreatic cancer imaging. At the same time, several literature reports have been published describing the comparable diagnostic performance of MDCT and MR[[84-88](#_ENREF_84)]. According to the recent report of Koelblinger *et al*[[85](#_ENREF_85)], the mean sensitivity and specificity of 64–detector row CT and 3.0-T MR imaging for the detection of pancreatic cancer (mean sensitivity, 95% *vs* 96%, respectively; mean specificity, 96% for both) do not differ significantly.

**NEW TECHNIQUES IN PANCREATIC IMAGING**

***Dual-energy CT and low-tube-voltage techniques***

Although MDCT has become the modality of choice for pancreatic cancer imaging and shows excellent performance regarding its diagnosis and staging, the detection of small pancreatic cancers < 2 cm in diameter, or of iso-attenuating tumors, and which accounts for approximately 10% of all pancreatic adenocarcinomas, still remains challenging[[35](#_ENREF_35),[77](#_ENREF_77)]. For those cases, we can improve the contrast-to-noise ratio between pancreatic cancer and normal parenchyma using the dual-energy or low-tube-voltage techniques[[89](#_ENREF_89)]. A low-tube-voltage CT technique increases the x-ray absorption of iodine by increasing the gap between the mean effective energy of the x-ray spectrum and the k edge of iodine[[90](#_ENREF_90)]. Clinically, this phenomenon results in improved contrast enhancement of normal pancreatic parenchyma in order to maximize the contrast to typically poorly vascularized pancreatic cancers[[90](#_ENREF_90),[91](#_ENREF_91)]. Therefore, dual-energy CT and low-tube-voltage techniques offer increased detection rates for small or otherwise iso-attenuating pancreatic tumors[[89-93](#_ENREF_89)].

***Iterative reconstruction algorithm on MDCT***

A new method for CT noise reduction based on iterative reconstruction (IR) algorithms has recently been developed. Because the medical radiation exposure is, in general, currently increasing and has been one of the greatest concerns for radiologists, the use of this novel technique has recently been increasing due to its potential to preserve and enhance the diagnostic capability of CT with reduced radiation doses[[94](#_ENREF_94)]. Currently, several IR methods have been proposed and are being commercially used for reducing the radiation dose by decreasing the image noise during the reconstruction process, *i.e.* adaptive statistical iterative reconstruction (ASiR, GE Health-care), model-based iterative reconstruction (MBIR, GE Healthcare), iterative reconstruction in image space (IRIS, Siemens Healthcare), sinogram-affirmed iterative reconstruction (SAFIRE, Siemens Healthcare), and iDose (Philips Healthcare)[[95](#_ENREF_95)]. Based on its development, many studies have continuously revealed the superiority of IR, compared with routine filtered back projection, across the whole body[[94-107](#_ENREF_94)]. Regarding the variety of reconstructing algorithms, each method may show a detailed difference in image quality and also provides abnormal features such as a plastic, waxy, blotchy or pixilated texture[[104](#_ENREF_104),[107](#_ENREF_107)]. Considering the effects of IR techniques on reducing image noise, these techniques could be used for high spatial resolution, pancreatic CT imaging which may provide high quality, 1-2 mm, thin-slice CT images. Optimizing the IR technique using a study protocol is necessary to balance imaging distortion and radiation reduction and to balance image quality and high spatial resolution along the z-axis.

***DCE-MR, DWI, and gadoxetic-acid-enhanced liver MR for evaluation of liver metastasis***

Although there is still technical complexity and room for improvement in terms of imaging resolutions regarding dynamic, contrast–enhanced (DCE) MR imaging, in previously published studies the quantitative analysis of the enhancement patterns and perfusion parameters using DCE-MR imaging has been shown to be both objective and helpful for the evaluation of malignant diseases regarding both their diagnosis and treatment monitoring[[108-110](#_ENREF_108)]. In our preliminary data, the K(trans), K(ep), and iAUC values in patients with pancreatic cancer were significantly lower than those seen in patients with a normal pancreas (*P* < 0.05), and they were, therefore, useful for differentiating pancreatic cancer from pancreatic neuroendocrine tumors[[110](#_ENREF_110)].

DWI has also been used to characterize pancreatic lesions of various pathologic entities such as cystic lesions, pancreatitis and malignant tumors[[70](#_ENREF_70),[111-113](#_ENREF_111)]. Although MR has the great advantage of excellent soft-tissue contrast for focal lesion detection, small or non-contour-deforming pancreatic adenocarcinomas may lack classic imaging features and may, thus, not be detected on conventional MRI. The use of diffusion-weighted imaging may allow earlier detection of pancreatic adenocarcinoma as these neoplasms have increased signal intensity on diffusion-weighted images with high b values (b > 500 s/mm2) as well as relatively low ADC values because of their restricted diffusion associated with fibrosis[[70](#_ENREF_70)]. The intravoxel incoherent motion (IVIM) model takes these two sources of signal decay into account, thus providing a theoretical framework from which to derive diffusion and perfusion parameters from DWI[[114](#_ENREF_114)]. Recently, the IVIM-approach with multiple b-values has been applied to pancreatic imaging and there have been several reports showing promising results regarding the differentiation of pancreatic cancer from normal pancreas[[112](#_ENREF_112),[115](#_ENREF_115)]. DWI may also show small metastases that are not as well seen using other sequences and which, therefore, suggest to radiologists, on the basis of the high-signal-intensity lesion seen on diffusion-weighted imaging, to more closely examine the images obtained on other sequences[[70](#_ENREF_70),[116](#_ENREF_116)]. Gadoxetic acid-enhanced liver MR imaging is also regarded as one of the best imaging tools for detecting liver metastasis in patients with pancreatic cancer. The reported sensitivity of gadoxetic acid-enhanced liver MR is 85% for detecting liver metastasis in pancreatic cancer, and which is significantly higher compared with that of CT which is 69%[[117](#_ENREF_117)].

***Hybrid PET/MR***

Integrated PET and MR (PET/MR) scanners have recently available for use in humans. As MR has the inherent strength of superior soft-tissue contrast resolution, multiplanar imaging acquisition, and functional imaging capability such as that seen in DCE-MR, DWI, MR spectroscopy or elastography, PET/MR may exhibit superior diagnostic performance compared with that of PET/CT[[118](#_ENREF_118)]. In our medical institution, PET/MR imaging is now being used for evaluation of staging in patients with locally advanced pancreatic cancers, and also for evaluation of tumor response in patients with pancreatic cancer undergoing neoadjuvant chemoradiotherapy before and after treatment (Figure 5).

**CONCLUSION**

There have recently been notable improvements in pancreatic imaging using the multi-modality approach, although each imaging modality has its own role, advantages, and disadvantages not only for diagnosis but also for the treatment of and follow-up of pancreatic cancer. Not only radiologists, but also clinicians should be familiar with those characteristics of imaging modalities and should apply them whenever possible. Rapidly developing, novel imaging techniques, including dual energy, low-tube-voltage CT techniques, IR algorithms, functional MR imaging methods, and hybrid PET/MR, are expected to become widely used and to show excellent performance for pancreatic cancer imaging in the near future.

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**Table 1 The minimum technical specifications for pancreas computed tomography**

|  |  |  |
| --- | --- | --- |
| **Feature** | **Specification** | **Comment** |
| Scanner type | Multidetector row scanner |  |
| Detector type | Minimum of four detector rows |  |
| Reconstructed slice thickness | Minimum of 5 mm | Thinner slices are preferable,  especially in multiplanar reconstructions (MPR) |
| Injector | Power injector, preferably dual-chamber | Bolus tracking desirable |
| Contrast injection rate | No less than 3 mL/s of contrast, 300 mg I/mL or a higher concentration, For a dose of 1.5 mL/kg of body weight | A saline flush desirable |
| Mandatory dynamic phases | 1. Early arterial phase 2. Pancreatic phase 3. Portal venous phase | MPR,  Curved MPR along the pancreatic duct,  Minimum intensity projections are helpful |

**Table 2 The minimum technical specifications for pancreas protocol magnetic resonance imaging**

|  |  |  |
| --- | --- | --- |
| **Feature** | **Specification** | **Comment** |
| Scanner type | 1.5-T or greater main magnetic field | Low-field magnets not suitable |
| Coil type | Phased-array, multichannel torso coil | Unless patient-related factors preclude the use |
| Gradient type | Current-generation, high-speed gradients (providing sufficient coverage of upper abdomen) |  |
| Slice thickness | 5 mm or less for dynamic series, 8 mm or less for other imaging |  |
| Breath holding and matrix | Approximately 20 s of breath hold  with a minimum matrix of 128 X 256 | Breath hold instructions are very important |
| Injector | Power injector, preferably dual-chamber | Bolus tracking/MR fluoroscopy desirable |
| Contrast injection rate | 1.5-2 mL/second of gadolinium chelate | Preferably resulting in the vendor-recommended total dose |
| Minimum sequences | T1-weighted, gradient echo (3D preferable) T2-weighted, turbo spin echo (axial, coronal) MRCP (both 2D and 3D preferable) Post-Gd, T1-weighted gradient echo |  |
| Mandatory dynamic phases | 1. Arterial 2. Portal-venous phase 3. Equilibrium phase |  |
| Dynamic timing | Arterial: 20-40 s Portal venous: 45-65 s Equilibrium: 3-5 min after contrast injection |  |

**Figure 1 A 58-year–old, male patient with pancreatic body cancer with typical imaging findings.** A, B: Endoscopic ultrasonography shows an approximately 3-cm, hypoechoic mass in the pancreatic body and with distal pancreatic duct dilatation; C, D: The mass shows hypointensity on portal-venous-phase, contrast enhanced MR and hypermetabolism on PET/CT, respectively. MR: Magnetic resonance; PET: Positron emission tomography; CT: Computed tomography.

**Figure 2 A 73-year-old make with pathologically proven pancreatic head cancer.** A: Approximately 3-cm low attenuating mass is noted at the pancreatic head on the CT scan; B: In precontrast T1-weighted gradient echo sequence of MR, this mass shows lower signal intensity, compared to the normal pancreatic parenchyma; C: After contrast media administration, the pancreatic head cancer has poor enhancement; D, E: DWI with 1000 of b-value and ADC map reveal the diffusion restriction of the pancreatic head cancer. CT: Computed tomography; MR: Magnetic resonance; DWI: Diffusion weighted imaging; ADC: Apparent diffusion coefficient.

**Figure 3 A 64-year-old male with biopsy-proven pancreatic adenocarcinoma with liver metastasis.** A, B: On MDCT, the pancreatic tail mass shows iso-attenuation causing distal parenchyma atrophy; C: On precontrast, T1–weighted, gradient-echo sequence MRI, the pancreatic tail mass is clearly depicted as well as the liver metastasis, owing to the increased soft-tissue contrast of MR compared with that of CT. MRI: Magnetic resonance imaging; MDCT: Multi-detector computed tomography.

**Figure 4 Post-process of multi-detector computed tomography for pancreatic cancer.** A: In the axial CT scan, an ill-defined pancreatic body cancer invading the celiac axis, is identified; B: On the curved MPR along the pancreatic duct, the relationship between the pancreatic duct and the cancer can be more easily understood; C, D: The extent and degree of major vascular involvement caused by the pancreatic cancer, can be comprehensively assessed using MPR and the maximum intensity projections. MDCT: Multi-detector computed tomography; MPR: Multiplanar reformations.

**Figure 5 Treatment monitoring of pancreatic cancer using positron emission tomography/magnetic resonance.** A, B: There is a 5-cm mass of biopsy–proven, adenosquamous carcinoma in the pancreatic head, as seen due to the strong FDG uptake; C, D: The mass shows a marked decrease in size and glucose metabolism (from 22.0 to 3.8 of mSUV) after six cycles of neoadjuvant concurrent chemoradiation treatment. The specimen obtained during the following surgery revealed complete remission; E: All tumor cells are replaced by a foamy histiocytes collection of cholesterol clefts and multinucleated giant cells. PET: Positron emission tomography; MR: Magnetic resonance; FDG: Fluorodeoxyglucose; mSUV: Maximum standardized uptake value.