

Recent advances in imaging of the pancreas

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Abstract: Pancreatic diseases benefit from early and appropriate diagnosis and therapeutic intervention. Variety of imaging technologies give clinicians an unparalleled set of tools to help in every day clinical practice and decision-making. The basal techniques include computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), radionuclide imaging, optical coherence tomography (OCT) and endoscopic retrograde cholangiopancreatography (ERCP) in selected patients. Advances in all these technologies and development of molecular-based imaging could enable clinicians to identify diseases at an earlier stage and, thereby, improve patient outcomes. CT is introduced in late 1970s. Since then there has been dramatic improvement in pancreatic imaging.

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I. Introduction

Pancreatic diseases including acute and chronic pancreatitis, pancreatic cancer and diabetes mellitus are observed in 10% of the world's population. A wide spectrum of anomalies of pancreas and the pancreatic duct system are commonly encountered at diagnostic imaging examinations. Pancreatic diseases benefit from early and appropriate diagnosis and therapeutic intervention. Variety of imaging technologies give clinicians an unparalleled set of tools to help in every day clinical practice and decision-making. The basal techniques include computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), radionuclide imaging, optical coherence tomography (OCT) and endoscopic retrograde cholangiopancreatography (ERCP) in selected patients. Advances in all these technologies and development of molecular-based imaging could enable clinicians to identify diseases at an earlier stage and, thereby, improve patient outcomes.

II. Computed tomography

At the end of the 1980s, spiral CT scanners were introduced. Their technology allows much faster data acquisition with a layer thickness of 1-2 mm and a set of data for 3D imaging. In addition, today's power injectors are used to allow bolus contrast administration for fast dynamic scanning. Spiral scanning provides better spatial resolution and allows use of dual-phase CT protocol with pancreatic and portovenous phases. Dynamic scanning increases the tumor conspicuity and allows better detection and staging of pancreatic neoplasms. Despite the progress, at this stage the multiplanar imaging still suffers from stair-stepping artifacts. With the introduction of multidetector computed tomography (MDCT) in late 1990s this drawback is overcome. These scanners in contrast to single-detector helical CT scanners, use multiple detector rows. They are 10 times faster, and can obtain 16-64-320 slices per rotation at a slice thickness of 0.4 mm. In daily clinical practice, CT scanners with 16-64 slices per rotation are most commonly used. Comparison of 320-detector volumetric and 64-detector helical CT images of the pancreas revealed no significant difference in CT imaging of pancreas. MDCT has improved volume coverage, speed and spatial resolution along z-axis.

This new technology allows three-dimensional reformatting due to isotropic voxels and detailed multiplanar reconstruction of pancreatic anatomy. Because of high speed of data acquisition MDCT allows organ imaging in clearly defined perfusion phase. MDCT permits the acquisition in the early arterial phase, pancreatic (parenchymal) phase and portal venous (hepatic) phase with a delay of 20, 40 and 70 sec, using 100-120 ml of injected intravenously iodinated contrast medium. Images obtained in the arterial phase are useful for a good visualization of arterial delivery. For tumor detection, particularly adenocarcinoma, pancreatic and portal venous phases are superior to those obtained in the arterial phase. Multiphase protocol allows to increase the differences in density of the hypovascular tumor and normal perfusion is surrounding parenchyma and this is most pronounced in the pancreatic parenchymal phase. It occurs 40 seconds after the onset of the venous bolus, which is administered at a high injection rate of 3-5-8 ml / sec. Evaluation of vascular invasion and hepatic metastasis is better on the images obtained in the portal vein phase, than those obtained in the pancreatic and arterial phases. The use of a special multiphase protocol for pancreatic diseases makes possible to diagnose and characterize a small lesion of the pancreas (less than 2 cm in diameter) the level of vascular invasion and the

detection of liver metastases. Multiphase protocol increases the accuracy of adenocarcinoma detection to over 90%.



Fig 1a.: Pancreatic carcinoma. Non-contrast CT image; There is a deformation of the contour of the head of the pancreas, without a visible tumor.

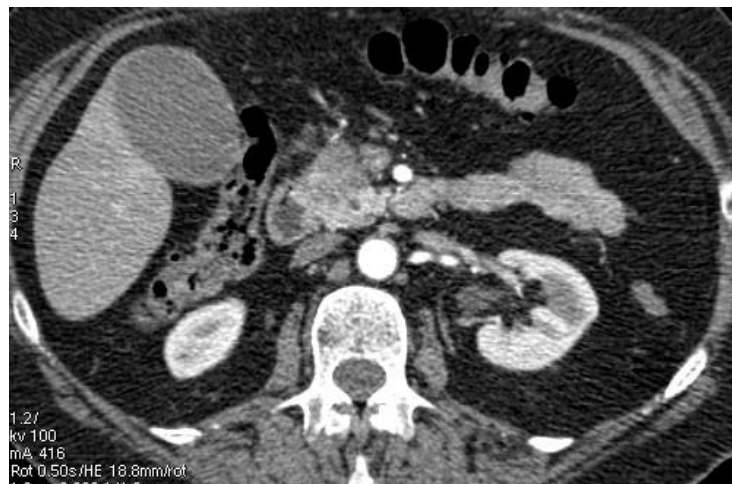


Fig 1b.: Pancreatic carcinoma. Pancreatic phase image allows clear delineation of the hypovascular tumor against the background of normally perfused pancreatic parenchyma.



Fig 1c.: In the portal phase the tumor is depicted worse due to penetration of contrast material into the interstitium.



Fig 1d.:In the late phase the tumor equates its density with that of the surrounding parenchyma.

Most pancreatic neuroendocrine tumors are small, well - vascularized and are best seen in arterial phase images, but in some cases, portal venous phase imaging best demonstrates the formations. That's why dual-phase MDCT protocol, at 20 and 70 sec following intravenous contrast injection, is recommended for optimal detection of both the primary tumor and liver metastases.

MDCT is the method of choice for the diagnosis and staging of acute pancreatitis. CT has high sensitivity in detecting the necrosis, signs of severe acute pancreatitis and peripancreatic fluid collections. CT is the best imaging modality in detecting calcifications, a specific hallmark of advanced chronic pancreatitis, and its complications such as intraductal calculi, pseudocysts, inflammatory masses or pseudoaneurysms. MDCT has poor sensitivity in detecting early stage chronic pancreatitis. Pancreatic tissue replaced by fat has a negative attenuation value on unenhanced CT images. Therefore CT can reliably diagnose diffuse fatty changes involving the pancreas. CT is also the noninvasive modality of choice for characterization of pancreatic cystic lesions.

CT increases sensitivity in detecting late stage chronic pancreatitis, but may provide normal findings in the early stages. One of the most frequent abnormalities in chronic pancreatitis includes an irregularly expanded main pancreatic duct (MPD), pancreatic atrophy, calcifications, and pseudocysts. Intraductal calcifications are the most specific deviation, but intraductal localization is not always easily detectable, especially in non-expanded channels. The uneven dilation of MPD is a common sign, but it's not the only characteristic of this disease. It also occurs in ductal and pancreatic carcinomas. Less common CT features include enlargement of the gland, involvement of peripancreas fatty layers and fascia, and chronic fluid collections. CT with contrast enhancement demonstrates delayed enhancement due to fibrosis. On a few occasions the pancreas is locally enlarged and mimics neoplasm. Such inflammatory formation may affect the head of the pancreas and cause obstruction of extrahepatic bile duct.

III. Magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP)

Although CT remains the most used imaging modality for examination of the pancreas, magnetic resonance imaging (MRI) is increasingly used for further identification and characterization of pancreatic disorders. The magnetic resonance has a number of advantages: lack of invasiveness, safety, excellent soft tissue resolution and possibility for functional evaluation of exocrine function. Technical progress in MRI allows improved spatial resolution and faster T1- and T2- weighted sequences for imaging the entire upper abdomen in a single breathhold and providing cross-sectional images of pancreatic parenchyma similar to CT images. The normal pancreas has high signal on T1-weighted sequences with or without fat saturation. It is the most T1 hyperintense structure in abdomen excluding fatty liver. This is due to content of proteinaceous secretion into the gland. T1 fat saturated images are very sensitive for identification of any focal lesion within the pancreas as many of the focal lesions have low signal and are easily recognised. The usage of fat saturation and dynamic sequences following gadolinium contrast injection improves the sensitivity of MR in detecting pancreatic lesions. MR angiography (MRA) is useful tool for noninvasive examination of splanchnic blood vessels.



Fig 2: MRCP in chronic pancreatitis. There is uneven dilatation of the main pancreatic canal and cysts.

MRCP replaces ERCP for the diagnostic imaging of pancreatic and biliary ducts. It is a dedicated MR technique in which heavily T2 weighted sequences are used to image fluid filled structures without a need for contrast agent. Thus, immobile and slow moving fluids, such as pancreatic juice and bile, are displayed with a bright signal while other surrounding tissues show a low signal intensity.

During the last decade, magnetic resonance cholangiopancreatography has become more widely used in aiding the diagnosis of pancreatic diseases. MRCP allows delineation of pancreatic duct and side branch and detection of anatomic variants such as pancreatic divisum and pancreaticobiliary maljunctions. The ductal changes are better visualised on MRCP as compared to CT. Administration of secretin improves the visualization of the ductal system and allows monitoring of pancreatic flow dynamics. Secretin enhanced MRCP helps in evaluation of pancreatic exocrine function, and planning surgery or therapeutic endoscopic procedure.

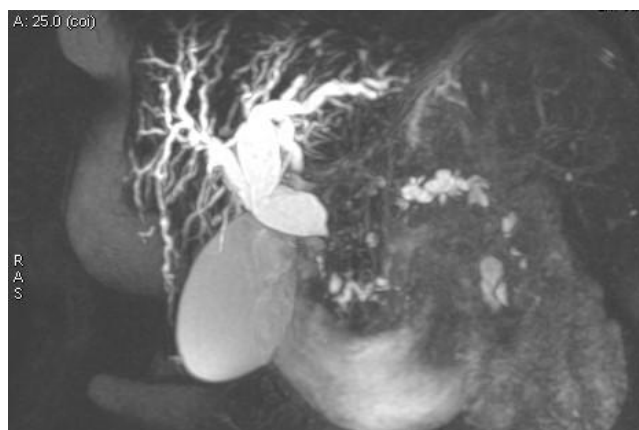


Fig 3: MRCP in pancreatic head carcinoma. There is dilatation of the intra- and extrahepatic bile ducts and the pancreatic duct above the tumor level.

Because of high soft tissue contrast resolution MRI has very good accuracy in local staging of the pancreatic malignancies, for assessment of peripancreatic fat infiltration, for evaluation of vascular infiltration, peritoneal deposits and lymph node involvement. For identifying the liver metastases MRI has higher sensitivity and specificity compared to CT. The use of liver-specific contrast agents (gadobenatodimeglumine -Gd-BOPTA and gadoxetic acid -Gd-EOB-DTPA) further improves the diagnostic value of MRI for detecting liver metastases. MRI has a role in diagnosis of focal fatty replacement of pancreas using dual-echo (in-phase and opposed phase) chemical shift imaging technique and avoids invasive diagnostic procedures or surgery for histologic verification. Diffusion-weighted MRI (DWI) can help to differentiate different subtypes of pancreatic endocrine tumors on the basis of tumor cellularity and/or extracellular fibrosis that may account for various apparent diffusion coefficient (ADC) values in these neoplasms.

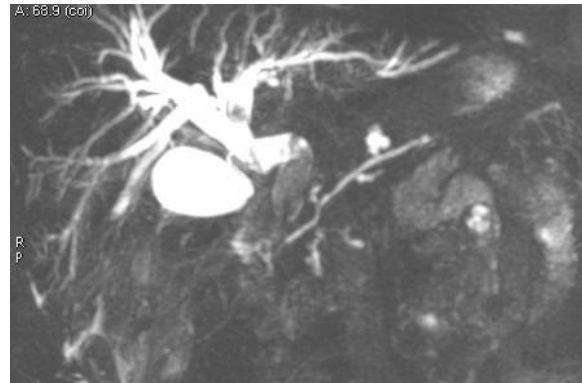


Fig 4: MRCP in side branch duct IPMN;

MRI have similar sensitivity as CT for the depiction of peripancreatic fluid collections and necrosis in the case of acute pancreatitis, but is less sensitive than CT for detection of calcifications in chronic pancreatitis. Fat-suppressed T1-weighted MRI is more sensitive for the detection of early chronic pancreatitis before to the development of calcifications. MRI can be useful in differentiating pancreatic cystic neoplasms from pseudocysts. Presence of internal debris is a highly specific MRI sign for pseudopancreatic cyst. In MRCP the ductal findings of early chronic pancreatitis can range from normal looking MPD to mild irregularity of MPD and side branches. With progression of disease, there is an increasing atrophy of pancreatic parenchyma and decreasing enhancement in pancreatic and portal venous phase and rising enhancement in delayed phase. Severe ductal changes include irregular dilatation of both MPD and side branches along with "chain of lakes" appearance on MRCP. MRCP can depict the associated complications such as fistula and pseudocysts. Intraductal calcifications are depicted as filling defects in the hyperintense background of fluid.

A major limitation of MRCP in the evaluation of chronic pancreatitis is the lack of functional information and incapacity to image the ductal system in distended state. This disadvantage is overcome by using secretin and acquiring serial MR images, known as secretin enhanced MRCP. Secretin acts primarily on pancreas and it causes transient increase in the tone of sphincter of Oddi and increased secretion of bicarbonate rich fluid. Thus, MRI in combination with secretin enhanced MRCP and MRA are useful tools in the diagnosis and management of pancreatic malignancies.



Fig 5a: Secretin enhanced MRCP; before applying secretin.



Fig 5b: Secretin enhanced MRCP; 4 minutes after applying secretin.



Fig 5c: Secretin enhanced MRCP; 10 minutes after applying secretin.

IV. Ultrasonography (US) and endoscopic ultrasound (EUS)

US is still the first line modality for the evaluation of pancreas, because of its easy availability, lower cost and lack of radiation. Pancreatic evaluation is done in fasting state to avoid small bowel and colon gas collections. Thus in some cases ultrasound (US) has a limited role in pancreatic examination as the overlying gas from the transverse colon and stomach makes visualizing pancreatic parenchyma difficult or even impossible. It is also dependent on the skill of the operator and the body habitus of the patient. Different maneuvers such as changing the patient's position, using the spleen as a window to visualize the pancreatic tail and expanding the stomach with water, may be necessary to depict the entire gland. US can identify gallstones as an etiology in patients with pancreatitis and biliary ductal dilation in patients with a pancreatic head mass. Most focal lesions are hypoechoic compared to normal pancreatic parenchyma. It can also show pseudocysts or collections around the pancreas.

Endoscopic ultrasound (EUS) announces a new dimension as it provides extremely distinctive images and exquisite details of pancreatic lesions. EUS also allows simultaneous tissue sampling of pancreatic mass with EUS-guided fine needle aspiration (FNA). Elastography is a new technique for evaluation of the tissue hardness. Elastography can be used with transabdominal and endoscopic ultrasound probes. There are two main types of elastography available. The first is strain imaging. It evaluates qualitatively the tissue strain in response to an exogenous acoustic pulse. The second type is shearwave elastography. It evaluates quantitatively the tissue hardness based on the velocity of shear waves into the tissues. The elastogram in both cases is represented as a color map superimposed over the B-mode images. It can be used for evaluation the extent of involvement in chronic pancreatitis and the extent of fibrosis.

EUS-FNA is highly accurate technique for preoperative staging of pancreatic cancer, because it has the ability to obtain the tissue confirmation and permit accurate nodal staging without relying only on lymph node size. The intraoperative ultrasound (IOUS) and laparoscopic ultrasound (LUS) are another diagnostic options. Both techniques are highly sensitive for assessment of tumor resectability during surgery. They permit accurate evaluation of number and location of lesions, locoregional tumor expansion, vascular involvement and liver or lymph node metastases. Intraductal endoscopic ultrasound (IDUS), can accurately localize the pancreatic endocrine tumors, especially those which are too small to be distinguish by MRI or CT. Color Doppler- EUS improves the finding of adenocarcinomas and small pancreatic endocrine tumors. Endocrine tumors exhibit plentiful color Doppler signal and have pulsatory or continuous waveform pattern. The vast majority of adenocarcinomas demonstrate low vascularisation. Contrast-enhanced EUS use microbubbles and also show improved detection and delineation of pancreatic tumors and liver metastasis. EUS-FNA aids the differential diagnosis of cystic lesions of pancreas that are indeterminate at cross-sectional imaging by using cytology and cyst fluid analysis. EUS may also be used therapeutically in pancreatic pseudocyst for image-guided drainage such as gastrocystostomy and for pain control in patients of pancreatic cancer or pancreatitis for celiac plexus neurolysis.

V. Positron emission tomography computed tomography (PET-CT)

Positron emission tomography (PET) is a functional imaging modality using 2-(18F)-fluoro-2-deoxy-D glucose (FDG) to characterize metabolism of cells. PET images do not contain high-resolution anatomy information. CT imaging delivers a precise localization of lesions seen on PET imaging. In 1998 was introduced first integrated PET-CT scanner. PET-CT can be applied in preoperative diagnosis, staging and in post-therapeutic monitoring of ductal adenocarcinoma. PET/CT is a useful supporting imaging technique when conventional cross-sectional imaging is non-diagnostic, when there is pancreatic carcinoma accompanying with chronic pancreatitis, and in the cases of cystic or complex lesions. PET/CT has high rates of sensitivity (85-

100%) and specificity (67-99%) for differentiation between malignant from benign pancreatic masses. PET-CT is more accurate than CT for M-staging because it allows better detection of distant metastasis. PET-CT provides greater ability of differentiating benign from malignant behavior of equivocal lesions on conventional CT. About 1/3 of metastases <1 cm in the liver and peritoneum are missed by MRI and CT. PET-CT has the highest sensitivity (up to 91%) in detecting peritoneal metastases when compared to MRI and CT. The accuracy of PET-CT for primary pancreatic lesions is 91%, for loco-regional staging - 85%, and for restaging of pancreatic cancer -92%. PET-CT provides a more accurate staging of pancreatic cancer and changes care management of patients. PET-CT is useful to differentiate residual/recurrent hypermetabolic malignancy from post-surgical changes/fibrosis. PET-CT can also characterize the metabolic behavior of non-specific hepatic lesions too small or not accessible for biopsy. The modality is helpful to restage cases presenting with elevated tumor marker levels and negative CT examination and to estimate the tumor response to neoadjuvant therapy. The sensitivity of FDG PET-CT for detecting lymph node metastasis in patients with pancreatic cancer and differentiating pancreatic cancer from chronic pancreatitis is more than that of MRI or CT. PET-CT has some limitations. It depends on the target-to-background activity ratio of the tumor. The latter can be limited by various factors. A small lesion size, like ampullary carcinoma, a necrotic tumor or a neoplasm with low metabolic activity (mucinous adenocarcinoma or neuroendocrine tumor) can cause false-negative results. The hyperglycemic status, which is often seen in patients with pancreatic pathology, may also lead to a decrease in the absorption of glucose due to competitive inhibition. Some benign conditions, such as inflammation, post-operative changes, infection, iatrogenic acute pancreatitis, and adjacent bowel activity, can resemble malignancies.

VI. Optical coherence tomography (OCT)

OCT is introduced in 1991. This optical imaging modality performs high-resolution, cross-sectional, subsurface tomographic imaging of the microstructure in biologic systems and materials. In the last decades, OCT technology has developed gradually from an experimental laboratory tool to a new diagnostic imaging technique. It has a wide spectrum of clinical applications in medical practice, including pancreaticobiliary ductal system. OCT studies in various organs have demonstrated the ability of OCT to differentiate between normal and pre-malignant conditions. It has a promising role in evaluating pancreaticobiliary ductal system, as it can recognize different patterns of the duct wall structure in neoplastic and non-neoplastic conditions. OCT has high diagnostic accuracy, better than brush cytology, for distinguishing neoplastic from a non-neoplastic MPD stricture. In summary, OCT provides high resolution images of the cyst morphology, enabling clinicians to accurately differentiate between serous and mucinous cysts. Unfortunately, the penetration depth for OCT is generally limited to about 2 mm, and thus only a small area of the cystic lesion can be evaluated at the time, for a given position of the OCT probe within the cyst.

VII. Endoscopic retrograde cholangiopancreatography (ERCP)

ERCP enables detection of pancreatic duct changes including ductal ectasia, stricture, abnormal side branches, communicating pseudocysts, pancreatic duct stones and pancreatic duct leaks. ERCP has sensitivity for the diagnosis of chronic pancreatitis of 71%-93% and a specificity of 89%-100%. The Cambridge classification, which assesses changes into the main pancreatic duct and side branches is a broadly approved system for scoring ductal findings seen on ERCP. When the diagnosis of chronic pancreatitis is being looked for, ERCP should be reserved for patients in whom the diagnosis is still indistinct after pancreatic function testing or other non-invasive (MRI and CT) or less invasive (EUS) imaging examinations have been performed. ERCP does not provide information regarding the surrounding pancreatic parenchyma. Over the last 15 years, endoscopic retrograde cholangiopancreatography (ERCP) has evolved from a diagnostic tool to one that is primarily used to provide therapy. This development occurred first for biliary disorders and subsequently to a lesser extent for pancreatic diseases. A selected number of patients with pancreatic diseases may benefit from pancreatic endotherapy and avoid complex surgery and chronic use of medications. Pancreatic sphincterotomy, pancreatic stenting and pancreatic cyst drainage are some of the most effective and challenging endoscopic pancreatic interventions and should be performed with caution by expert therapeutic endoscopists. Pancreatic duct leaks can be treated with endoscopic placement of transpapillary stents in a manner comparable to the use of biliary stents for closing bile duct leaks.

VIII. Conclusion

CT, MRI, EUS and PET-CT are excellent imaging techniques for detection and characterization of pancreatic diseases. Structural imaging modalities such as CT and MR provide information about local tumor invasion and surgical resectability, whereas FDG PET-CT provides a noninvasive and accurate method for early detection of pancreatic cancer, unsuspected metastases, differentiation between malignant and benign pancreatic lesions, and evaluation of pancreatic masses with ambiguous CT or MRI diagnosis. PET-CT has a

great impact on the posttherapeutic monitoring for recurrence, and on the response to adjuvant therapy. EUS-guided FNA biopsy is helpful in cases that are indefinable at cross-sectional imaging. OCT has occurred as a new modality that differentiates between non-neoplastic and neoplastic pancreatic duct strictures. ERCP is useful for the diagnosis of chronic pancreatitis but it should be reserved for patients in whom the diagnosis has not been established by non-invasive or minimally invasive procedures. ERCP is currently used mainly for therapeutic interventions.

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