Dual-Energy CT in the Pancreas

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Abstract
Dual-energy computed tomography (DECT) is an evolving imaging technology that is gaining popularity, particularly in different abdominopelvic applications. Essentially, DECT uses two energy spectra simultaneously to acquire CT attenuation data which is used to distinguish among structures with different tissue composition. The wide variety of reconstructed image data sets makes DECT especially attractive in pancreatic imaging. This article reviews the current literature on DECT as it applies to imaging the pancreas, focusing on pancreatitis, trauma, pancreatic ductal adenocarcinoma, and other solid and cystic neoplasms. The advantages of DECT over conventional CT are highlighted, including improved lesion detection, radiation dose reduction, and enhanced image contrast. Additionally, data exploring the ideal protocol for pancreatic imaging using DECT is reviewed. Finally, limitations of DECT in pancreatic imaging as well as recommendations for future research are provided.

Keywords
► dual-energy CT
► pancreas
► pancreatic imaging

Introduction
Since its introduction 15 years ago, dual-energy computed tomography (DECT) has been increasingly adopted in clinical practice as a promising imaging tool with multiple clinical applications. Although originally described in the 1970s, technological limitations at the time such as the spatial resolution of early CT and prolonged scan duration resulting in motion artifacts prevented its clinical applicability.¹,² With these limitations now largely overcome, DECT has found increasing acceptance as an advanced CT technology for various applications. Abdominal applications of DECT have been extensively studied and its applications in various pancreatic pathologies have shown promising potential.³ This article reviews the current literature and clinical applications of DECT in various diseases of the pancreas.

Dual-Energy Computed Tomography: Principles
Tissues have different attenuation characteristics at varying energy levels. DECT makes use of this concept by acquiring CT attenuation data at two different energy levels simultaneously—typically low energy (80 or 100 kVp) and high energy (140 kVp).⁴ The principle of DECT can be explained by two primary mechanisms. The first mechanism, the photoelectric effect, consists of photon absorption resulting in electron emission, which rises with higher atomic numbers and at lower energy levels.⁴,⁵ The other mechanism is Compton scatter which is influenced significantly by the density of material and contributes the most to attenuation at higher energy levels. In DECT, two different energy levels are used to analyze how the photoelectric effect and Compton scatter affect attenuation, thus enabling improved...
characterization of tissue composition.\textsuperscript{4,5} Considering that single-energy CT can often be limited by its inability to distinguish among structures with different tissue composition, the energy-dependent attenuation employed in DECT allows radiologists to overcome this issue.\textsuperscript{4}

**Dual-Energy Computed Tomography: Scanner Technology**

DECT technology has undergone multiple advancements over the past decade and DECT imaging can be accomplished in several ways depending on the vendor platform. The three most common approaches include: (1) two X-ray tubes and corresponding detectors operating at two separate energy levels simultaneously, (2) single X-ray tube source and a corresponding detector with the capabilities for rapidly alternating between high/low energy X-ray output, and (3) a single X-ray tube source with a corresponding dual-layer detector with capabilities to absorb low energy X-rays on the superficial layer and high energy X-rays in the deep layers.\textsuperscript{4} Because of the differences in underlying technological approaches, each of these methods has distinct advantages and limitations.\textsuperscript{4} Each manufacturer also utilizes different postprocessing techniques to generate images. Irrespective of the type of technology or postprocessing technique, DECT enables the creation of a wide variety of reconstructed image data sets. The differentiation between various material types such as fat, calcium, iodine, and water using imaging at two different energy levels is enabled by the acquisition of distinct linear attenuation coefficients.\textsuperscript{6} Following detection, a specific material can be quantified or subtracted to obtain material-selective images such as iodine maps and virtual unenhanced (VUE) images. Additionally, information regarding tissue attenuation characteristics using the various polychromatic energy spectra enables the generation of monoenergetic images at multiple simulated energy levels (energy-selective images).\textsuperscript{7} Iodine maps, VUE images, and monoenergetic images are most relevant in pancreatic imaging.

**Dual-Energy Computed Tomography: Postprocessed Images**

Iodine-specific images and VUE images are generated through material decomposition-based iodine extraction. The iodine-specific images permit qualitative and quantitative determination of iodine content within tissues and therefore could be used for detection and characterization of vascular structures, parenchymal organ evaluation, sites of bleeding, and identification of perfusional abnormalities including ischemia.\textsuperscript{8,9} McNamara et al reported that iodine images enhanced reader confidence in the detection of small pancreatic adenocarcinomas.\textsuperscript{10}

The subtraction of iodine can be used to create VUE images, enabling the avoidance of a true unenhanced acquisition and reducing radiation dose exposure by around 21%.\textsuperscript{11} Although unenhanced images are not routinely obtained for pancreatic imaging, studies examining the quality of VUE images in the pancreas have reported excellent image quality comparable in quality to true noncontrast imaging.\textsuperscript{12} Differences noted between VUE and true unenhanced images included smoother appearance of VUE images with blurred organ margins.\textsuperscript{11,13} However, VUE remains an acceptable substitute for true noncontrast images with good correlation between pancreatic Hounsfield unit measurements.\textsuperscript{11–13}

The monoenergetic images are simulated image data sets resembling images which could be generated through scanning with monoenergetic X-ray beams. Monoenergetic images in the low energy range (40–55 keV) provide higher attenuation of iodine enhancing structures as they are close to the k-edge of iodine (33.2 keV).\textsuperscript{4} In comparison to conventional polychromatic images acquired at 120 kVp, monoenergetic images at 70 keV were found to be superior in quality.\textsuperscript{14} In parenchymal organs with limited tissue contrast such as the pancreas, this technique improves the detection of both hyperenhancing and hypoenhancing lesions as the lower energy levels highlight subtle variations in contrast enhancement.\textsuperscript{15} Additionally, DECT enables image quality adjustments to be performed after image acquisition, hence possibly avoiding a repeat examination. This is a significant benefit over conventional CT, where image quality optimization need to be ensured before acquisition.\textsuperscript{16}

**Dual-Energy Computed Tomography: Pancreatic Protocols**

Pancreatic DECT protocols are still under debate, with most institutions performing a pancreatic phase acquisition in the DE mode.\textsuperscript{17} This leverages the advantages of improved lesion conspicuity of hypoattenuating tumors such as pancreatic adenocarcinoma as pancreatic parenchymal attenuation increases with low-energy monoenergetic images (40–55 keV).\textsuperscript{18} Additionally, the higher iodine attenuation on low-energy monoenergetic images raises the possibility of decreasing oral and intravenous contrast doses, subsequently reducing beam-hardening and streak artifacts with no effect on diagnostic performance.\textsuperscript{19} Patel et al reported that DECT for the pancreas during the portal venous phase is not indicated nor is it being performed by centers across the U.S. True unenhanced acquisitions in addition to DECT images are no longer routinely obtained.\textsuperscript{17} Noda et al found that a pancreatic protocol CT generated from a single portal venous phase DECT acquisition was a feasible alternative to the standard dual-phase acquisition in the pancreatic and portal venous phase. The proposed portal venous phase protocol with a single DECT acquisition was found to have comparable diagnostic performance and the added benefit of radiation dose reduction.\textsuperscript{20}

**Dual-Energy Computed Tomography: Clinical Applications in Pancreas**

**Pancreatitis**

CT is a preferred modality for imaging evaluation in patients with acute pancreatitis. DECT has been demonstrated to have a role in early pancreatitis and in diagnosing the etiology and
complications of pancreatitis such as necrosis, vascular injury, as well as pancreatic and peripancreatic fluid collections.

In a retrospective study, Martin et al reported that the iodine density values varied significantly between normal and inflammatory pancreatic parenchyma suggesting a higher sensitivity for DECT in diagnosing early acute pancreatitis compared with standard imaging.21 Similarly, improved assessment and delineation of inflamed areas of the pancreas was provided by low monoenergetic images (specifically at 50 keV). Additionally, these images were shown to allow improved characterization of the degree of parenchymal necrosis, thus providing a better classification of DECT for acute pancreatitis (Fig. 1). This translates into a more reliable predictor of severe clinical outcomes such as hospitalization, intensive care unit admission, and drainage.22 By using low keV images to accentuate contrast enhancement, DECT is also able to better portray pancreatitis-related vascular complications, including lumen thrombosis and pseudoeuromys.3,5

In evaluating necrosis, Yuan et al looked at differences in attenuation between normal and necrotic pancreatic tissue using DECT and found that at 80 kVp the differences between areas of necrosis and normal pancreas is better accentuated.23 Using low keV images, DECT could allow improved evaluation of complex pancreatic and peripancreatic collections to discriminate necrotic debris, hematomas, or residual parenchyma with preserved enhancement (Fig. 2).3,24

Gallstone disease is among the most common causative factors for acute pancreatitis.25 DECT with monoenergetic images at low keV is helpful in detecting noncalcified gallstones in the gallbladder.26,27 The identification of iso-attenuating cholesterol stones in the biliary ducts including cystic ducts is made easier through the use of DECT, as the stones demonstrate higher attenuation values at high keV and lower attenuation values at low keV in comparison to the surrounding bile.26,28

Mass-forming chronic pancreatitis resembles pancreatic ductal adenocarcinoma (PDAC) on conventional CT and DECT has been reported to be useful in their differentiation. On iodine maps, mass-forming pancreatitis is found to have higher iodine concentration in contrast to ductal adenocarcinoma. Thus, Yin et al reported that iodine quantification is highly sensitive (up to 93.3%) and specific (up to 89.5%) for discriminating between the two.29

Trauma
Pancreatic trauma has significant morbidity and mortality.30 However, pancreatic injury is difficult to detect on imaging since the pancreas is not imaged at its peak parenchymal enhancement in most trauma CT protocols as image acquisition is performed in portal venous phase as compared with pancreatic phase.31 This has important implications on management and prognosis since treatment mostly relies on whether the main pancreatic duct is involved, a complication which is difficult to assess unless the pancreas is scanned at peak enhancement.32

In a retrospective study assessing pancreatic lacerations, Sugrue et al found that low-energy monoenergetic images (specifically at 40 keV) maximize the contrast-to-noise ratio (CNR), increase laceration conspicuity, and improves diagnostic confidence.33 The CNR is higher at lower energy levels as it is close to the $k$-edge of iodine. Accordingly, this amplifies the contrast between pancreatic lacerations which are hypodense compared with the enhancing uninjured parenchyma.33,34 This finding is in agreement with an earlier study by Sun et al that found 40 keV to be the ideal energy level for assessing lacerations of the liver and spleen.8

DECT iodine-selective images also play a role in trauma management through differentiating between parenchymal hematomas and organ lacerations, especially in cases with significant overlap in appearances with conventional CT. VUE

Fig. 1 Acute pancreatitis in an 80-year-old female presenting with epigastric abdominal pain and vomiting. The pancreas is enlarged and edematous with adjacent inflammatory stranding and prominent fluid in the peripancreatic space (arrow). The low energy monoenergetic images at 65 keV and iodine image allow better assessment of the pancreatic parenchyma for detection of hypoenhancement and therefore early diagnosis of pancreatic necrosis.

Fig. 2 Necrotizing pancreatitis in a 33-year-old male presenting with severe epigastric pain. The pancreas is edematous with extensive peripancreatic fat stranding suggesting pancreatitis. Axial iodine overlay accentuates the lack of enhancement of the pancreatic body and tail indicating necrosis (arrow).
images are helpful in these challenging cases as they allow depiction of hemorrhagic products in hematomas as hyperattenuating material.\textsuperscript{35}

DECT has potential for use in various vascular applications, although studies for its use in pancreatic vascular injury are scarce. For visceral vascular imaging in general, iodine-selective or bone-masked angiographic visualization of the vasculature can be used with low-kVp imaging in cases of poor vascular opacification or to examine smaller more peripheral vasculature.\textsuperscript{36} In instances of suspected gastrointestinal bleeding, VUE differentiation of high attenuating hematomas from actively extravasating iodine eliminates the need for unenhanced or delayed imaging to show progressive enhancement.\textsuperscript{36} A study on penetrating abdominopelvic trauma using animal models found that in comparison to conventional CT, dual-contrast DECT considerably improved reader accuracy in the determination of vascular versus enteric extravasated contrast material.\textsuperscript{37}

**Solid and Cystic Neoplasms**

**Pancreatic Ductal Adenocarcinoma**

PDAC is the most common pancreatic malignancy and the fourth leading cause of cancer deaths worldwide.\textsuperscript{38} It is characterized by rapid growth, early vascular invasion, and late symptom onset which together confer a poor prognosis and a high mortality rate. Consequently, early diagnosis and intervention are crucial to improving survival rates.\textsuperscript{39}

On CT, the most common imaging manifestation of PDAC is a hypodense infiltrative mass, primarily due to the presence of desmoplastic tissue and fibrosis within the tumor.\textsuperscript{1} Dual-phase pancreatic protocol CT acquired in the pancreatic and portal venous phase is the recommended imaging technique for diagnosis and staging of PDAC.\textsuperscript{40} Prokesch et al reported that PDAC is isoattenuating in 11% of both those phases due to tissue composition and similar vascularization compared with the normal pancreas or as a result of inadequate contrast timing.\textsuperscript{40}

In this respect, DECT offers some advantages: low-energy monoenergetic images and iodine maps improve tumor conspicuity, provide higher CNR, and enhance radiologist confidence in PDAC identification.\textsuperscript{1,10,41} Macari and colleagues reported in their 2010 study that while cases of PDAC went undiagnosed using 120 kVp, the use of 80-kVp instead provided a significant improvement in attenuation between the normal pancreas and the tumor.

Recently, Noda et al found that 40 keV monoenergetic images significantly increased signal-to-noise ratio (SNR) of the pancreas, CNR, and lesion conspicuity and had a high reproducibility in measuring tumor size compared with higher energy levels.\textsuperscript{18} In a different study, Noda et al showed that 40 keV portal venous phase images could be a substitute for the pancreatic phase images. This finding advocates the creation of a simulated twin-phase pancreatic protocol CT from a single DECT acquisition in the portal venous phase with radiation dose benefits of 44%, especially given that radiation dose reduction is appealing in the surveillance and screening for pancreatic diseases.\textsuperscript{42}

Iodine images provide high CNR and SNR for PDAC compared with monoenergetic and 120-kVp images. Qualitatively, iodine images have been rated highly for lesion conspicuity, differentiation of solid/cystic lesions, and improve reader confidence.\textsuperscript{10,43} They have demonstrated value in the evaluation of pancreatic tumors in around 50% of cases. The hypovascular nature of pancreatic cancer has been suggested to be the reason behind the increased conspicuity as this results in an even lower attenuation in comparison to normal pancreatic parenchyma on iodine maps (Fig. 3).\textsuperscript{44} Lastly, variations in iodine uptake displayed positive potential in evaluating chemotherapeutic treatment response of PDAC.\textsuperscript{45}

Other applications of DECT in PDAC follow-up include the use of metal artifact reduction algorithms or monochromatic images at high keV (i.e., 140 keV) to reduce streaking artifacts in patients with biliary prostheses or surgical clips.\textsuperscript{46} Finally, DECT perfusion is a promising new technique in evaluating pancreatic cancer. On perfusion imaging, PDAC typically demonstrates low blood flow and volume compared with normal pancreatic tissue.\textsuperscript{47} Klauss et al thus showed that the combination of noise reduction at 140 kVp with increased iodine contrast enhancement at 80 kVp using DECT perfusion can improve the detection and delineation of PDAC.\textsuperscript{48}

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**Fig. 3** A 44-year-old male with known pancreatic ductal adenocarcinoma with liver metastases. Axial contrast enhanced 140 kVp image shows a subtle hypodense mass (arrow) in the pancreatic head with an adjacent common bile duct stent. Note the increased lesion conspicuity (red arrow) on the iodine material density image.

**Fig. 4** An 86-year-old female with pancreas divisum and a biopsy-proven cystic mucinous neoplasm in the pancreatic neck. Axial contrast enhanced pancreatic phase images at 140 kVp (A) and iodine image (B) shows a low attenuation lesion in the pancreatic head (arrow). There is improved depiction of the internal characteristics of the cyst on iodine images.
Pancreatic Cysts
DECT also has a role in the diagnosis and characterization of pancreatic cystic lesions (Fig. 4). In a retrospective study on 44 patients, Chu et al found that the ability of iodine maps to differentiate among cystic and solid components is useful in assessing the heterogeneity of cystic pancreatic masses.44 Li et al demonstrated that iodine concentration could allow differentiation of serous oligocystic adenomas and mucinous cystic neoplasms. In their study, a computer-aided diagnosis algorithm utilizing a set of conventional and DECT-based data was able to correctly classify 93% of serous and mucinous tumors.49 Further studies are required to compare DECT with other modalities such as magnetic resonance imaging (MRI) and endoscopic ultrasound to further elucidate its role in the characterization of pancreatic cysts.

Neuroendocrine Tumors
In patients with pancreatic neuroendocrine tumors (PNETs), DECT has been shown to improve lesion detection.50 A small study investigating the detection of insulinomas using DECT versus conventional dual-phase multidetector CT revealed a substantial increase in sensitivity from 69 to 96% using a combination of low keV monoenergetic and iodine images (Fig. 5).51 In a study on image quality, Hardie et al reported that 55-keV monoenergetic images were preferred for hypervascular neuroendocrine lesions.52 Finally, a recent study investigating the use of monoenergetic images in patients with hypervascularized abdominal tumors, including 9 PNETs, found that low-energy monoenergetic images improved diagnostic confidence with no associated increase in radiation dose. However, the authors noted decreased efficiency as a result of longer reading times.53

Future Directions
As DECT technology continues to evolve, its role as a reliable tool in pancreatic imaging will keep expanding. However, further research focused on studying the correlation between DECT findings with those of other well-established modalities (such as positron emission tomography, MRI, and endoscopic ultrasound) is required to definitively determine its diagnostic yield and accuracy in detecting pancreatic lesions. More work is also needed to determine the association between imaging features as depicted on DECT and patient outcome. This is particularly important for the detection, management, and follow-up of solid and cystic pancreatic lesions. Additionally, further studies are required to establish consensus on DECT protocols in pancreatic imaging and the ideal phases of acquisition, keeping the goal of radiation dose reduction in mind. DECT perfusion is another promising avenue that is yet to be properly explored in pancreatic imaging. Finally, the role and benefit of DECT in the early detection of acute pancreatitis needs to be further established. DECT provides several benefits over single energy CT in the evaluation of pancreatic disease; however, more research is necessary to recognize its full potential.

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Conflict of Interest
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References

Fig. 5 A 72-year-old female with an 8-mm hyperenhancing neuroendocrine tumor at the junction of the pancreatic body and tail (arrow). The low energy monoenergetic images are preferred for hypervascular neuroendocrine lesions.
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