Seminars in ULTRASOUND CT and MRI

Dual-Energy CT of the Pancreas

Domenico Mastrodicasa, MD,* Andrea Delli Pizzi, MD,† and Bhavik Natvar Patel, MD, MBA*

This article explores the technical background of dual-energy CT (DECT) imaging along with its basic principles, before turning to a review of the various DECT applications specific to pancreatic imaging. In light of the most recent literature, we will review the constellation of DECT applications available for pancreatic imaging in both oncologic and non-oncologic applications. We emphasize the increased lesion conspicuity and the improved tissue characterization available with DECT post-processing tools. Finally, future clinical applications and opportunities for research will be overviewed.
Semin Ultrasound CT MRI 40:509-514

Introduction

The first description of dual-energy CT (DECT) was by Sir Godfrey Hounsfield, in 1973.[1] However, for several years the idea of scanning with two different energies was technically limited by an inadequate generation of CT scanners burdened by relevant spatial, and temporal mis-registration as well as a higher radiation exposure.[2,3]

With most of these limitations now largely surmounted, DECT has been gaining widespread acceptance in clinical practice as an innovative imaging tool, particularly in the abdominal imaging setting. In this article, we briefly discuss the basic principles of DECT imaging, followed by a review of the latest applications of DECT for pancreatic pathologies. Finally, we will discuss DECT future clinical applications and opportunities for research.

Abbreviations: DECT, dual-energy computed tomography; FOV, field of view; HU, Hounsfield Units; keV, kiloelectron Volt; kVp, kilovoltage peak; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuroendocrine tumor; VMI, virtual monochromatic image; VUE, virtual unenhanced images

*Division of Body Imaging, Department of Radiology, Stanford University School of Medicine, Stanford, CA.

†ITAB Institute for Advanced Biomedical Technologies, Department of Neuroscience, Imaging and Clinical Sciences, "G. d'Annunzio" University, Chieti, Italy.

Financial Disclosures: Dr. Patel receives research support from General Electric Healthcare and Siemens Healthcare. He is also on the speaker's bureau for GE Healthcare.

Address reprint requests to Domenico Mastrodicasa, MD, Department of Radiology, Stanford University School of Medicine, Stanford University, 300 Pasteur Drive, Stanford, CA 94305-5105. E-mail: mastro@stanford.edu

Basic Principles of DECT

In diagnostic imaging, there are two essential photon interactions with the human body at the basis of a CT image. One of them, Compton scattering, requires an incident photon ejecting an outer shell electron weakly bounded to the atomic nucleus.[1,4] This process results in a partial absorption of the incident photon. The photoelectric effect is the other mechanism, in which an incident photon ejects an innermost shell (K-shell) electron. The K-shell electrons are more tightly bounded than the aforementioned due to their closer proximity to the atomic nucleus, and as a consequence the incident photon is completely absorbed.

Both Compton scattering and the photoelectric effect are responsible for the total image attenuation.[4] However, the first depends on the electron density of the material and provides little contrast to the CT image. On the other hand, the photoelectric effect is highly dependent on the atomic number (Z), and on the K-shell electron binding energy. Notably, a spike in the photon's attenuation (K-edge) occurs when the photon's energy is just above the K-shell binding energy for the specific element. For instance, the K-edge of Iodine is 33.2 kiloelectron volt (keV).[1,4]

In conventional single-energy CT, a polychromatic X-ray beam with one kilovoltage peak (kVp) typically ranging from 70 to 150 kVp is used for image acquisition. A single kVp limits the differentiation of tissue types, as it is mostly a function of their photon attenuation expressed numerically as Hounsfield units (HU).[1,4,5] A common clinical example is when it is difficult to distinguish faint calcium from dense iodine, as can be in the case of calcified plaques and the iodinated blood within arterial vessels on angiographic

https://doi.org/10.1053/j.sult.2019.05.002
0887-2171/

studies. Calcium and iodine may be indistinguishable on single-energy CT, despite the difference in their atomic number.

DECT acquires images with two different kVp, usually corresponding to a high- and low-energy spectra (i.e., 80 and 140 kVp). Since the photoelectric effect is energy dependent, and the K-edge differs for each element, DECT has the potential to differentiate structures with similar density but different elemental composition (i.e., density) such as the aforementioned calcified plaque and iodinated blood.[1]

DECT Platforms: Strengths and Weaknesses

Over the past few years, dual-energy scanning has been performed with several hardware configurations. Currently, the three most commonly used dual-energy scanner configurations are a dual-source DECT scanner, a single-source DECT scanner with fast kVp switching, and a single-source DECT scanner with dual-layer detector.[1,4,5]

The dual-source DECT scanner was introduced by Siemens Healthineers in 2006. This system consists of two X-ray tubes allocated in one gantry with a 90°-95° offset, generating high- and low-energy photons, respectively, and with separated detector rows. The separated X-ray tubes and corresponding detectors give the advantage of optimizing spectral separation as well as increasing the signal-to-noise ratio. The second- and third-generation systems included a metallic tin (Sn) filter positioned in front of the high-energy X-ray tube. The Sn filter further improves the separation between the high- and low-energy photons. However, the field of view (FOV) of the two tubes is different. More specifically, the low-energy tube FOV is 50 cm, compared to the limited 25 cm of the high-energy tube of the first generation, currently increased to 35 cm with the third generation of CT scanners. The reduced FOV of the second tube can limit the evaluation of larger patients with abdominal structures located on the periphery and beyond the dual-energy FOV.

A single-source DECT scanner was developed by GE Healthcare.[4,5] In this configuration, a single X-ray tube switches rapidly between low- (80 kVp) and high-energy voltages (140 kVp). A clear advantage of this approach is the full 50 cm FOV for both high- and low-energy photons. On the other hand, since the same tube uses both energy spectra, the spectral separation is limited to these two energy levels and currently cannot be changed. Moreover, modulating tube current is not possible, thus limiting the dose reduction.

Finally, a single-source CT system equipped with dual-layer detectors was developed by Philips.[1,4,5] The detectors have a different composition, yttrium for the top layer that absorbs low-energy photons, and gadolinium-oxysulfide for the bottom layer detector absorbing the higher-energy photons. The opportunity to scan in dual energy virtually at any time is a major advantage of this system. Additionally, since the spectral separation focuses on the detector, automatic exposure control is also available which benefits radiation exposure. On the other hand, due to the proximity of the detector layers, spectral separation is potentially decreased in comparison with other systems.

DECT Post-processing Techniques Used in Pancreatic Imaging

As previously mentioned, DECT uses two different energy spectra. Therefore, complex DECT post-processing techniques are used in the daily clinical routine to obtain a variety of additional datasets: iodinated attenuation maps, monochromatic images virtually reconstructed at different energy levels (VMI), and virtual unenhanced or noncontrast images (VUE). Such tools have demonstrated promising results in the context of pancreatic imaging.

Pancreatic CT protocols have been discussed extensively elsewhere in the literature.[6] Though many institutions vary in which phase dual-energy is acquired in, most perform the arterial phase in dual-energy mode.[6] This leverages the advantages of increasing lesions conspicuity on iodine material density images and low-keV VMI. Moreover, arteries may also be better depicted because of the improved contrast thereby potentially allowing accurate assessment of vessel involvement for surgical staging. Most centers will reconstruct 70-keV or a blended image dataset that serve as the single-energy equivalent images.[6,7] Additionally, VUE, iodine material density, and 50-keV are the other common reconstructed datasets used.[6] True unenhanced acquisitions are no longer routinely obtained.[8] Because of the widespread benefits of dual energy (e.g., improved lesion conspicuity and characterization of incidental finings), some authors believe dual-energy should also be performed in the portal venous phase.[8] This could allow improved detection and characterization of metastatic lesions, such as those in the liver.[9]

DECT in Oncologic Pancreatic Lesions

Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer death in the United States, burdened by a poor prognosis and a high mortality rate.[10-12] PDAC is characterized by a late onset of clinical symptoms along with a rapid growth pattern; therefore, early diagnosis is of paramount importance to improve survival rates. Additionally, in light of the absence of a pancreatic capsule, PDAC has a tendency for vascular invasion, consequently the number of patients suitable for resectability is low at the time of diagnosis.[13]

CT is the modality of choice to detect and stage PDAC, as well as for surgical planning and follow-up.[13] PDAC CT appearance usually ranges from mildly hypodense to isodense to the normal pancreatic parenchyma; however, the subtle CT appearance makes PDAC a potential diagnostic challenge (Figs. 1-3). Notwithstanding the optimal scanning

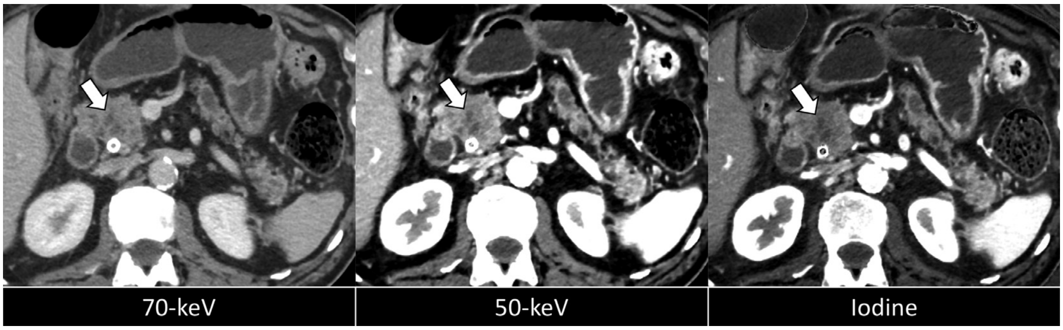

Figure 1 48-year-old male with biopsy proven pancreatic adenocarcinoma. Single-energy equivalent 70-keV image shows a subtle hypodense mass (arrow) in the pancreatic head with an adjacent CBD stent. Note the increased lesion conspicuity (arrows) on 50-keV and iodine material density images; CBD, common bile duct.

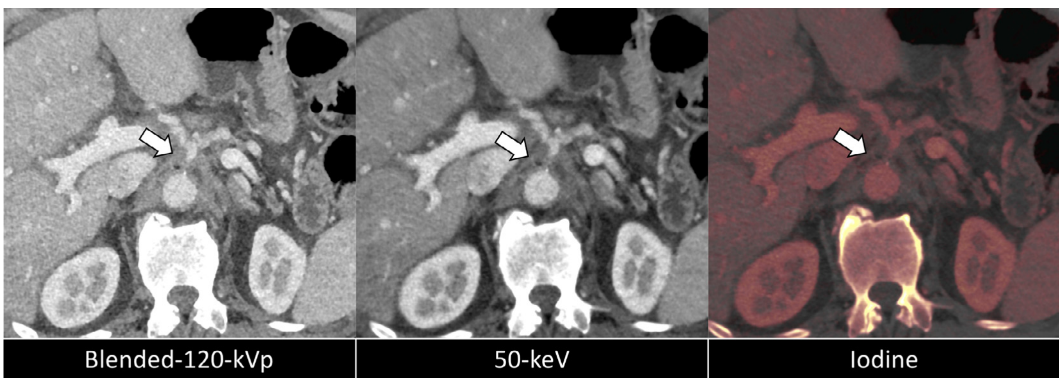

Figure 2 54-year-old female status post-Whipple for pancreatic adenocarcinoma. Blended-120-kVp (single-energy equivalent) image shows an increased soft tissue around the celiac artery and its branches (arrow). Note the increased conspicuity (arrows) on 50-keV and iodine overlay images, showing soft tissue attenuation and vascularity, respectively. These findings are consistent with tumor recurrence with perineural invasion.

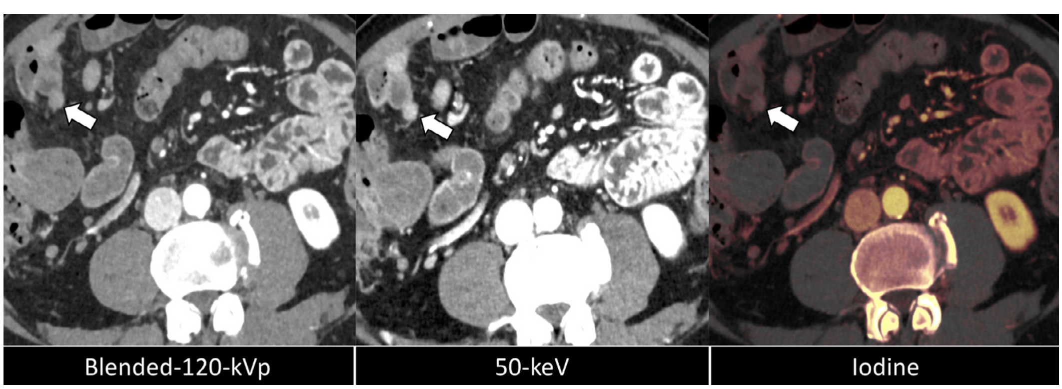

Figure 3 61-year-old male with known pancreatic adenocarcinoma. Blended-120-kVp (single-energy equivalent) image shows subtle nodularity along the right omentum (arrow). Note the increased conspicuity (arrow) on 50-keV and iodine overlay images, showing clear enhancement and vascularity, respectively. These findings are consistent with peritoneal carcinomatosis.

parameters adopted to improve the attenuation differences between the pancreatic tumor and the surrounding parenchyma, around 10% of all PDAC remains undetected.[14] Prokesch et al reported that those patients had PDAC visually isodense to the normal pancreatic parenchyma in both pancreatic and portal venous phase. In this regard DECT offers some advantages.

For instance, Macari et al reported that at 80-kVp the difference in attenuation between tumor and normal pancreas improves lesions conspicuity, otherwise undiagnosed at 120 kVp.[7] An increased lesion conspicuity using lower keV has been later demonstrated also for small PDAC (<3 cm) using DECT datasets reconstructed from the pancreatic phase.[15-17] Recently, Beer et al retrospectively evaluated the objective and subjective image quality of monoenergetic images using a noise-optimized algorithm, in 45 patients with PDAC. Their results indicated that 40- and 50-keV VMI resulted in better objective and subjective image quality, and should be the reconstruction technique of choice for the diagnostic workup of PDAC.[18]

Patients with PDAC might develop malignant biliary strictures that require a metallic bile duct stent.[19] Surgical clips are also frequently encountered during follow-up. Beam hardening artifacts from metal devices can degrade the image quality and hamper the evaluation of the pancreatic region (Fig. 1). DECT improves the image quality using metal artifact reduction algorithms or via monochromatic images virtually reconstructed from higher energy photons (ie, 140 keV).[20]

The hypothesis of CT perfusion as a tool to enhance the attenuation difference between the healthy portion of pancreas and PDAC has been previously advocated.[21,22] DECT perfusion is considered one of the new promising applications of DECT. Although still at its preliminary stage, there is evidence of potential for improving the delineation of PDAC. Klauss et al demonstrated that DECT perfusion could improve the visualization of PDAC via increased iodine contrast enhancement available at 80 kVp, and in combination with the noise reduction at 140 kVp.[23]

Pancreatic Neuroendocrine Tumors

Pancreatic neuroendocrine tumors (PNETs) represent only a small portion of pancreatic malignancies.[24] DECT might improve the conspicuity of PNET by enhancing subtle differences in attenuation between tumors and background.

Although generally hypervascular, insulinomas can be difficult to localize because of their typical small size. Moreover, insulinomas can be mildly hypodense to isodense on CT images compared to the normal pancreatic parenchyma. Lin et al showed that hypoattenuating insulinomas are better visualized in iodine maps, which provided higher contrast-to-noise ratio, and lower image noise.[25] On the other hand, isoattenuating insulinomas show subtle enhancement on both monochromatic images and iodine maps. Nonetheless, when iodine maps are used in combination with monochromatic images the sensitivity of insulinoma detection significantly improved from 68.8% to 95.7%, for both hypo- and isoattenuating insulinomas.[25]

In a more recent investigation, Hardie et al retrospectively evaluated 24 patients with a focal pancreatic mass, including 5 neuroendocrine tumors, and using an advanced image-based virtual monoenergetic reconstruction. The authors found that among the focal mass masses, 55-keV VMI were preferred for all neuroendocrine tumors.[26]

Pancreatic Cystic Lesions

The characterization of pancreatic cystic lesions is a challenging task for Radiologists. Chu et al retrospectively evaluated 44 patients with suspected pancreatic solid or cystic tumors, and found that a DECT approach was helpful in determining the heterogeneity of cystic masses.[27] More in detail, DECT provided high-quality VUE images successfully replacing true noncontrast images in more than 90% of the study population. Moreover, iodine maps improved the distinction between the cystic or solid nature of the lesions (Fig. 4).[27] Two other studies demonstrated the differentiation between serous oligocystic adenomas and mucinous cystic neoplasms based on DECT.[28,29]

DECT of Pancreas: Non-oncologic Applications

CT represents the gold standard imaging technique to diagnose pancreatitis.[30] DECT might have a role in the detection of early pancreatitis and complications, such as necrosis, extrapancreatic complications, and vascular injuries.

Yuan et al investigated the difference in attenuation between necrotic and normal pancreatic parenchyma (Fig. 5). Such difference was accentuated using an 80 kVp tube setting.[31] DECT has also the potential to better define pancreatitis-related vascular complication, such a as lumen thrombosis or pseudoaneurysms, using low keV images. In low keV images, the higher contrast of the normal pancreatic parenchyma might help the Radiologist in ruling out the presence of pancreatic or peripancreatic fluid collections

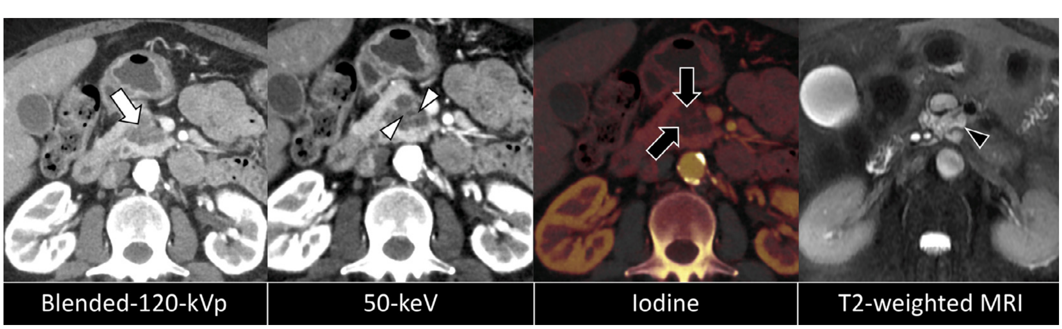

Figure 4 76-year-old female with a cystic pancreatic lesion. Blended-120-kVp (single-energy equivalent) image shows a lobulated hypodense lesion in the uncinate (white arrow). Note the increased conspicuity of enhancing septae (white arrowheads) on 50-keV and obvious cystic space (ie, no solid enhancement) on the iodine overlay image (black arrow). These findings are consistent with a serous cystadenoma, confirmed on T2-weighted MRI (black arrowheads).

Figure 5 44-year-old male with autoimmune pancreatitis. Blended-120-kVp (single-energy equivalent) image (A) shows subtle peripancreatic halo of fat stranding (arrow). Note the increased conspicuity (arrows) on 50-keV (B) and relatively more clear delineation of normal enhancing pancreatic parenchyma.

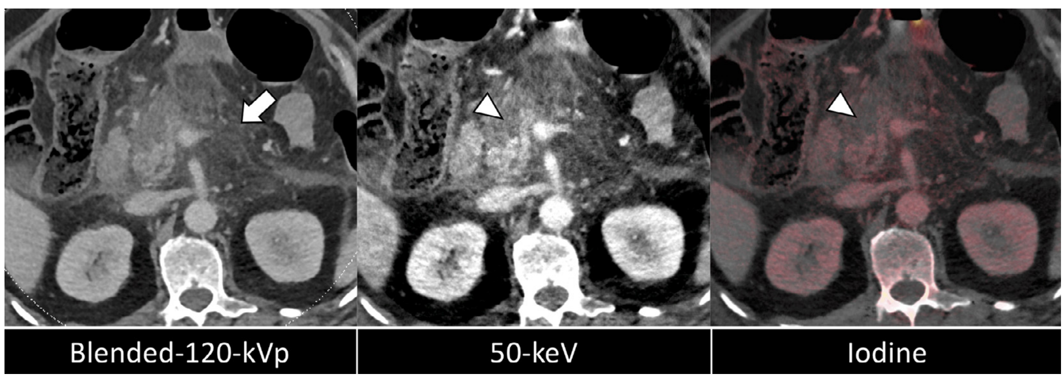

Figure 6 47-year-old female with pancreatitis. Blended-120-kVp (single-energy equivalent) image shows peripancreatic fat stranding and fluid (arrow). Note the area of pancreatic parenchymal nonenhancement (arrowheads) on 50-keV and iodine overlay images showing necrosis.

(Fig. 6). Moreover, noncalcified stones can be identified as the cause of the inflammatory disease using VMI.[32,33]

In a recent study, Martin et al retrospectively investigated the value of iodine maps in 45 patients with early acute pancreatitis.[34] The authors showed that iodine quantification differentiates between normal and inflammatory pancreatic parenchyma, thus diagnosing early acute pancreatitis with a significant higher sensitivity (0.855) in comparison to the image-based evaluation (0.797) and attenuation-based analysis (0.834).

Chronic mass-forming pancreatitis is a focal pancreatic enlargement occurring in 30% of chronic pancreatitis.[35] It resembles the appearance of PDAC on CT. Interestingly, such similarity is found on histopathology as well. Therefore, a correct diagnosis is essential to avoid unnecessary surgical approaches.[36] According to Yin et al, DECT showed an improved diagnostic accuracy in differentiating chronic mass-forming pancreatitis and PDAC. Based on iodine maps, the authors found a significantly higher concentration of iodine in chronic mass-forming pancreatitis compared with PDAC.[37]

Future Applications

In light of the many advantages over conventional polychromatic images, DECT keeps expanding its role in pancreatic imaging in both oncologic and non-oncologic applications. DECT, in particular low-keV monochromatic images and iodine maps, provides a better contrast resolution leading to a higher lesion conspicuity, better delineation of margins, as well as vascular and peripancreatic overall assessment. Moreover, with VUE image available, a true noncontrast phase is not necessary, thus allowing a reduction in the radiation dose.

In a recent White Paper published by the Society of Computed Body Tomography and Magnetic Resonance, DECT with lower energy VMI and iodine maps are suggested as appropriate for routine clinical use in patients with known or suspected pancreas neoplasms, including PDAC and PNETs.[38] On the other hand, the evaluation of cysts' content is considered experimental, although promising since cystic lesions are well detected with DECT. DECT perfusion is another promising tool of DECT, but barely explored so far. More studies are needed to further establish the role of DECT in patients' pancreatic disease.

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