



Role of Dual-Energy Computed Tomography in Gallbladder Disease: A Review

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Abstract

Gallbladder diseases are common and include a spectrum ranging from benign to cancer. Imaging plays an integral role in the diagnosis and in guiding appropriate management. While most patients with gallstone (GS) diseases can be evaluated with ultrasound, those with complicated GS disease, suspicion of cancer, or staging of cancer need additional cross-sectional imaging. Computed tomography (CT) is widely available and is often the imaging test of choice following an equivocal ultrasound or negative ultrasound in patients with unexplained symptoms. Conventional CT has limited sensitivity in detecting GS or common bile duct stones. In other scenarios, including diagnosis of acute cholecystitis (AC) and characterization of gallbladder wall thickening, an increase in accuracy using novel techniques is desirable. Dual-energy computed tomography (DECT) is increasingly incorporated into clinical practice. DECT has shown promising results in the detection of cholesterol stones that otherwise go unnoticed on conventional CT. However, its role beyond GS disease has largely been unexplored. In this review, we discuss the available literature on the DECT in biliary diseases and discuss the potential applications of this technique.

Keywords

- ▶ gallbladder
- ▶ cancer
- ▶ dual-energy CT
- ▶ CT

Introduction

There is a spectrum of pathologies affecting the gallbladder (GB), ranging from benign to malignant. Among these conditions, gallstone (GS) disease is the commonest.¹ Therefore, imaging plays an essential role in investigating patients suspected to have biliary diseases. Imaging modalities that are frequently utilized to evaluate biliary tract disease include ultrasonography (USG), computed tomography (CT), magnetic resonance cholangiopancreatography, and hepatobiliary scintigraphy. USG is a cost-effective and readily available technique for evaluating biliary diseases with esti-

mated sensitivity and specificity for acute cholecystitis (AC) being 88 to 94% and 78 to 80%, respectively.² CT also plays an essential role in diagnosing GB diseases especially complicated AC and suspected malignancy, although it is less sensitive than USG for the detection of GS.³ Dual-energy computed tomography (DECT) is a technical advancement that has been exploited for clinical applications in various organ systems and pathologies, including biliary diseases. In this article, we review the role of DECT in the evaluation of biliary disease.

DECT can overcome some of the limitations of conventional CT in the evaluation of GB diseases. DECT is based on

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the concept of scan acquisition with the help of different X-ray energy levels: one acquired at higher kVp (usually 140 kVp) and the other at lower kVp (usually 80–100 kVp). We can extract the composition of a substance if we know how it interacts at different energy levels. The interaction that is most important for DECT application is the photoelectric effect. The increase in photoelectric absorption of X-ray photon, which is seen at energy levels higher than k-shell binding energy, is termed K-edge and forms the basis of dual-energy techniques.⁴ The most common methods for acquisition of DECT include dual source, single-source rapid kilovoltage switching, and dual-layer DECT (sandwich). Postprocessing techniques can be used to differentiate various structures based on their different X-ray absorption behavior as a function of X-ray energy.⁵ Virtual noncontrast (VNC) images can be generated when the iodine content is subtracted. Quantitative assessments, including the amount of iodine uptake and degree of enhancement, can be achieved from single CT image acquisition with the help of pure iodine map or overlay maps, where iodine content is superimposed. Atomic number map (Rho/Z) is a newly developed application of DECT that helps calculate the atomic number values in the lesion, thus allowing the separation of various materials.

Role of DECT in Various Disease

Cholelithiasis

GS disease affects ~10 to 15% of the adult population, thus constituting a significant health problem.¹ Individuals may remain asymptomatic throughout their life. The most common presentation is biliary colic that occurs due to obstruction by calculus at the cystic duct. Complications of GS include AC (ranging in severity from mild to severe, uncomplicated, or complicated), GS ileus, acute pancreatitis, and Mirizzi syndrome. Association of GS with GB cancer has also been reported in a few studies. Although USG is accurate in the diagnosis of GS, a CT scan is frequently utilized for routine

workup. As the majority of GS are of cholesterol type (70%), these may not be visible on CT as they are isoattenuating to surrounding bile. Dual-energy postprocessing techniques such as virtual monochromatic imaging (VMI) and VNC have shown positive results in improved detection of GS on DECT.^{6–11} Kim et al found that VNC images were of equivalent quality as true unenhanced images.⁷ VNC images showed increased contrast to noise ratio for the cholesterol GS compared with true unenhanced images. However, the visibility of calcified GS and smaller GS (<9mm) was negatively affected due to the inaccurate decomposition of calcium and iodine. Thus, calcified GS are better visualized on true unenhanced images.⁷ In a study by Uyeda et al, VMI was useful in distinguishing GS from surrounding bile.⁸ The GS, which are of similar attenuation to bile on conventional CT (120 kVp), becomes more discernible on higher (200 keV) and lower (40 keV) keV VMI. The reason for better visualization is that GS has an energy-dependent X-ray attenuation curve different from surrounding bile.⁹ Noncalcified GS has lower attenuation than bile on low keV images and higher attenuation on high keV images. Low keV images have been found better in the detection of GS as the contrast difference among noncalcified GS, and surrounding bile is maximum compared with that at high keV images. Recently, Soesbe et al found that dual-layer DECT generation of the two-dimensional histogram of Compton and photoelectric attenuation was even more helpful in differentiating small (<9mm) isoattenuating GS from the bile.¹⁰ Most materials have a different position in the two-dimensional histogram based upon their Compton and photoelectric ordered pairs. Thus, we can differentiate isoattenuating GS from bile (→Fig. 1). Atomic number map (Rho/Z) is another important application of DECT, which can help identify GS from surrounding fluid in the small bowel in cases of GS ileus.¹¹

Acute Cholecystitis

In most cases, AC is caused by GS. Few cases occur secondary to stasis.¹² USG is the initial imaging of choice for diagnosing

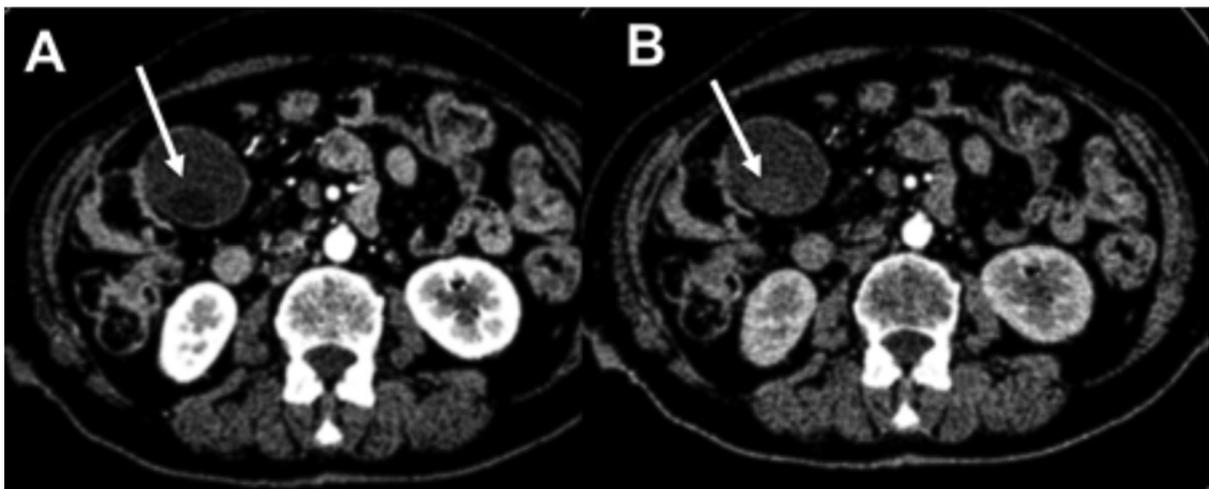


Fig. 1 Dual-energy computed tomography (DECT) in gallstone disease: (A, B) 80 keV, 140 keV DECT images show hypoattenuating calculus in gall bladder on 80 keV images (arrow) and hyperattenuating calculus on 140 keV images (arrow).

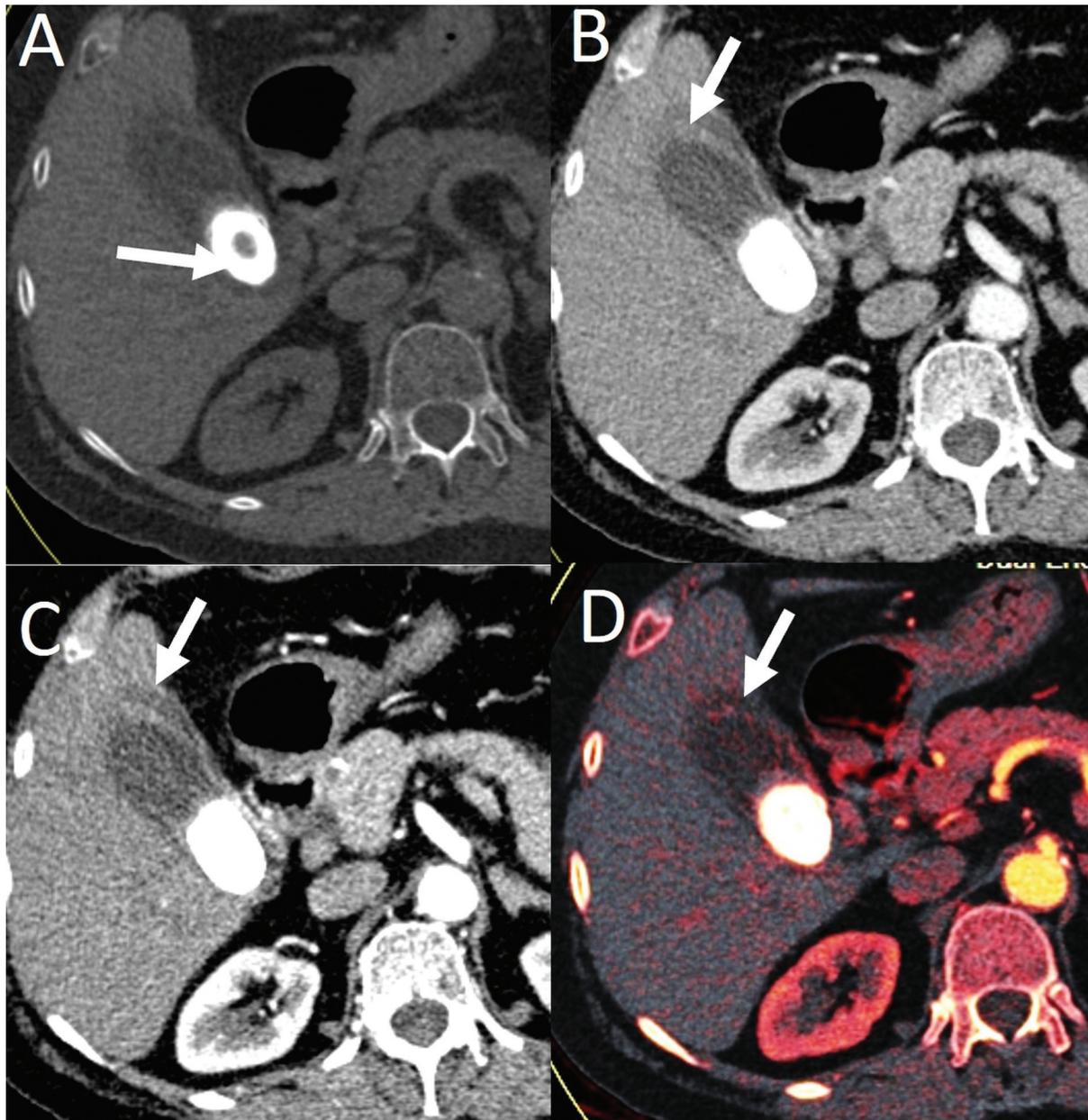


Fig. 2 Dual-energy computed tomography (CT) in acute cholecystitis. (A) Virtual nonenhanced CT image shows a large calculus impacted at the gallbladder neck (*arrow*). (B, C) 80 keV and 140 keV images show mural thickening and continuous mural enhancement (*arrow*). (D) Iodine overlap image depicts the discontinuity of mural enhancement better (*arrow*). This may be a predictor of gallbladder perforation.

AC because of its high sensitivity.¹³ Patients whose diagnosis remains unclear on USG due to limitations of scanning or impacted stone in the neck or patients with complicated AC may undergo CT.¹⁴ DECT has the potential to be the single best imaging test for patients presenting with biliary colic because of its ability to identify GS and better visualization of findings of AC.¹⁵ Iodine maps generated from DECT can easily detect mural hyperemia and hypervascularity of the adjacent liver parenchyma (hot rim sign). Also, complications such as GB perforation may be better visualized using VMI and color-coded iodine maps where a nonenhancing defect in the GB wall can be easily detected (► Fig. 2).

GB Polyp

GB polyps are of many types, some of them have malignant potential, and others are generally benign, thus can be grouped into neoplastic (adenomatous) and nonneoplastic (cholesterol, inflammatory). USG has a high sensitivity for detecting polyps but cannot differentiate the histological type of GB polyps. Risk factors that help predict malignancy are size, female sex, elderly patient, number, and shape of the lesion.¹⁶ Based on previous studies, size >1 cm of the lesion is the most important criteria for the likelihood of malignant polyp, but a lesion of size <1cm may also turn out to be adenomatous.¹⁷ Therefore, size cannot be reliably used as the only criteria to differentiate benign from malignant polyps.

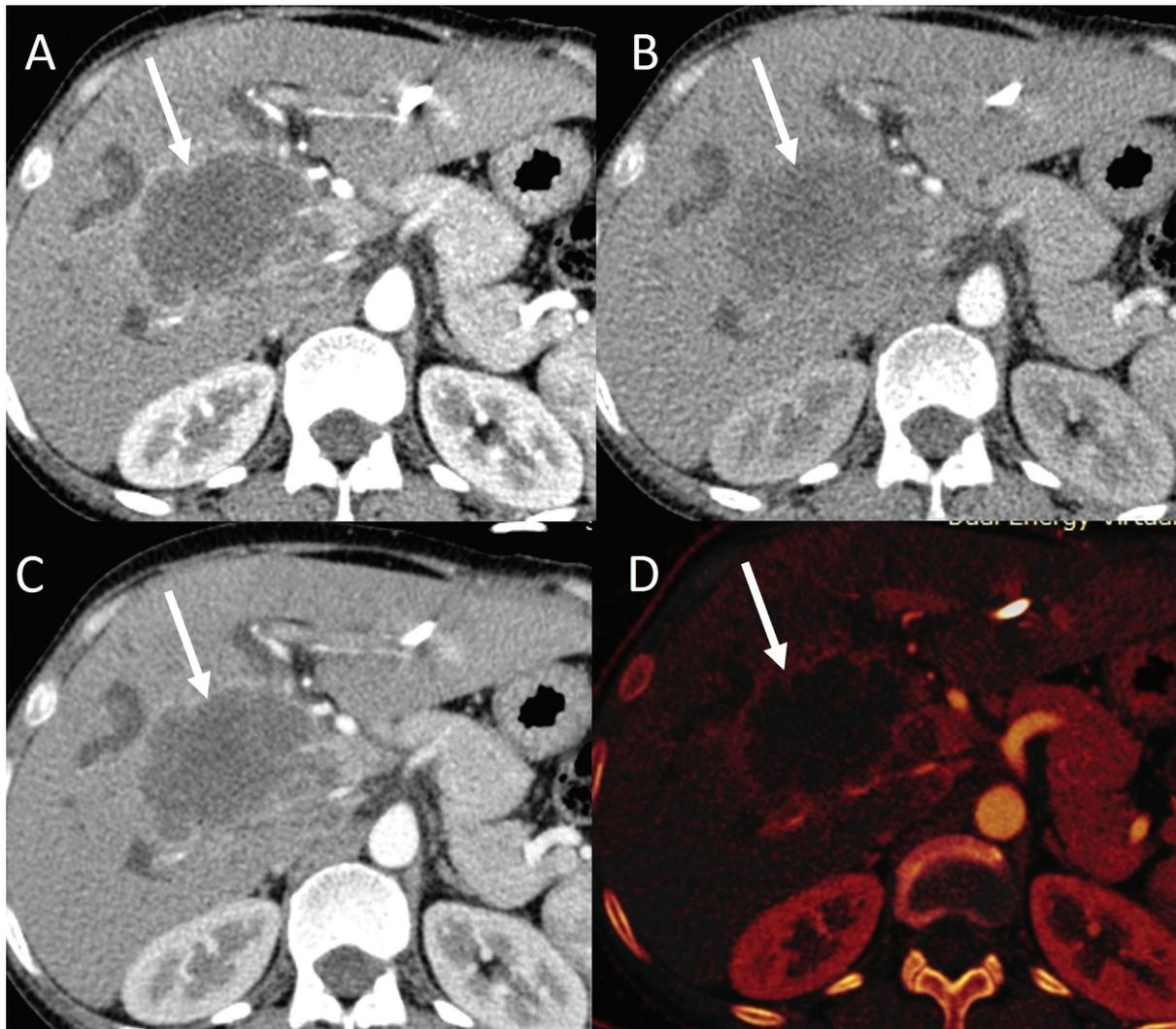


Fig. 3 Dual-energy computed tomography (DECT) in gallbladder cancer: mass replacing gallbladder. (A–C) 80 keV, 140 keV, and mixed (representative of conventional CT) DECT images show a large mass replacing the gallbladder. The mass is necrotic and shows peripheral enhancement (arrow). (D) Iodine overlay image (D) shows the peripheral iodine uptake (arrow).

Recently, few studies have shown DECT to be a promising modality that helps in diagnosis and differentiates the polyp types. In a study by Yin et al., different energy spectral curves were identified for cholesterol and adenomatous polyp.¹⁷ Cholesterol polyps showed positive mean attenuation value change, whereas adenomatous polyps had negative mean attenuation value change between 80–140 keV or 40–140 keV VMI.

GB Cancer

GB cancer is the most common malignancy of the biliary system with a predilection for specific geographic regions of the world.¹⁸ The presentation is nonspecific. Most patients are diagnosed at an advanced stage with metastasis and have a poor prognosis.¹⁹ For the diagnosis and staging of GB cancer, imaging plays a crucial role. USG is the initial investigation of choice as it is cost-effective and readily available. However, CT and magnetic resonance imaging remain the preferred modalities for accurate diagnosis and

staging. Morphologically, GB cancer has three main patterns; the most typical pattern is mass occupying or completely replacing the GB lumen (40–65%), followed by focal or diffuse asymmetric GB wall thickening (20–30%) and polypoid lesion (15–20%)²⁰ (→ Fig. 3). Additional imaging findings such as associated lymphadenopathy, invasion of surrounding structures, and distant metastasis help in the diagnosis of wall thickening type of GB cancer.

Benign Gallbladder Wall Thickening

Benign conditions like adenomyomatosis, xanthogranulomatous cholecystitis, and cholecystitis may have similar findings on conventional CT. It is often difficult to accurately diagnose GB wall thickening.^{21–23} Hence, we require advanced imaging modalities to characterize GB wall thickening. DECT is a potential tool for this problem that has not been investigated. It may show the mural characteristics, including enhancement pattern and intramural cyst/hypodense nodules, better than conventional CT,

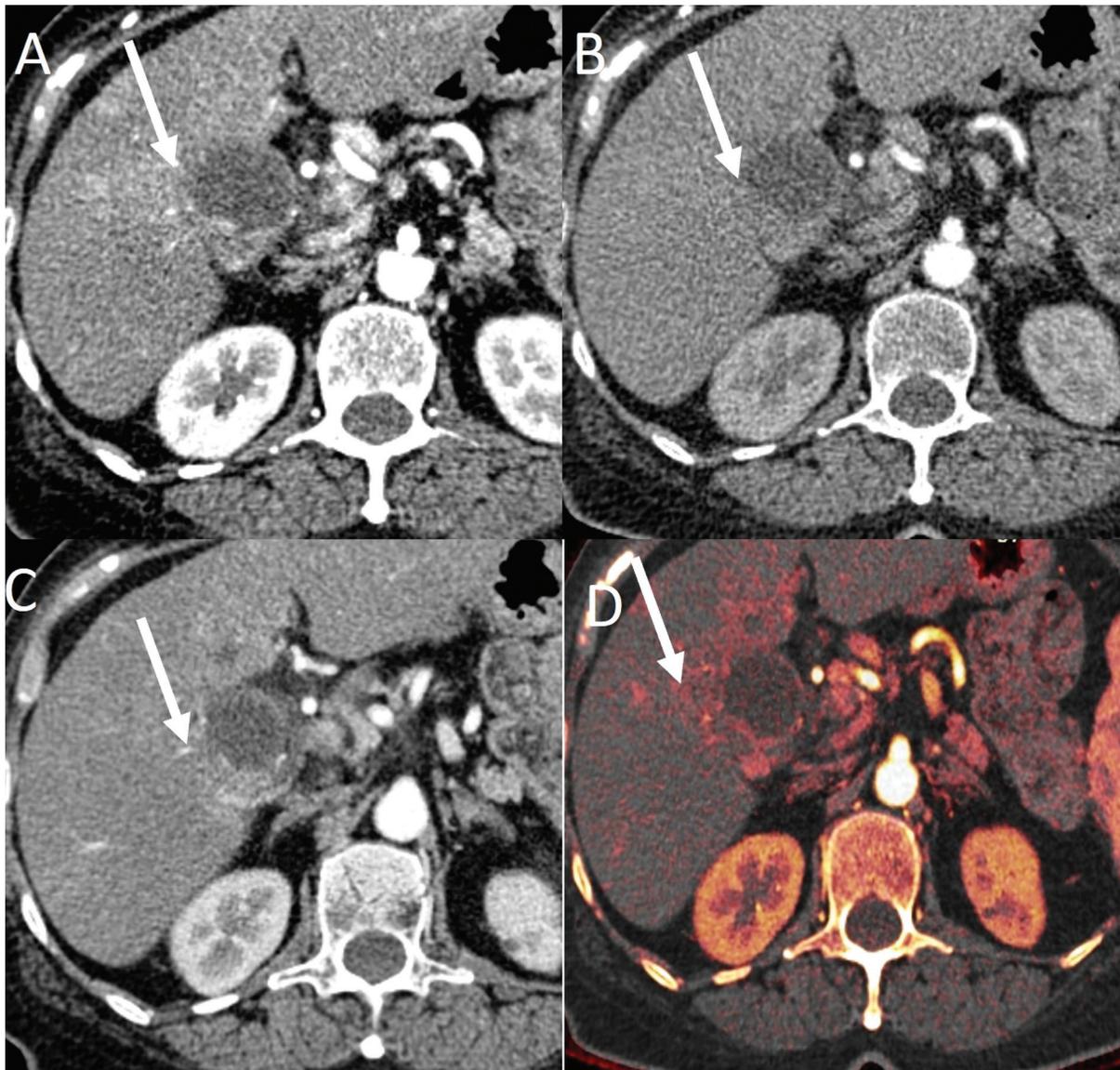


Fig. 4 Dual-energy computed tomography (DECT) in gallbladder cancer: wall thickening type. (A–C) 80 keV, 140 keV, and mixed (representative of conventional CT) DECT images show mural thickening of the gallbladder body (arrow). Note that the enhancement characteristics are better seen at 80 keV images. (D) Iodine overlap image shows that the enhancement is asymmetric and heterogeneous (arrow) features favoring malignant nature.

especially on iodine maps. The presence of intramural cysts/Rokitansky–Aschoff sinuses is diagnostic for adenomyomatosis. The intactness of mucosa is critical for the diagnosis of benign GB wall thickening and is better assessed on iodine overlay maps. Finally, adjacent liver infiltration will be better seen on the iodine overlay images (► Fig. 4).

The critical characteristics of DECT studies evaluating biliary diseases are summarized in ►Table 1.

Future Directions

DECT may provide quantitative data for texture analysis and radiogenomics in GB cancer. A recent study showed the incremental value of the radiomics model for detecting

serosal invasion in preoperative restaging for locally advanced gastric cancer.²⁴ Another study reported a DECT-based nomogram for detecting HER 2 status in gastric cancer.²⁵ Furthermore, DECT may allow accurate differentiation of metastases from cholangitic abscess in the setting of GB cancer. This has enormous prognostic and therapeutic implications as metastatic GB cancer has a dismal prognosis and receives the best supportive care. In a recent study comprising 28 patients with multiple malignancies (GB cancer) and 23 patients with liver abscesses, DECT had sensitivity and specificity of 89.3 and 93.3% and area under the curve of 0.963 for differentiating liver abscess from metastases.²⁶ The comparative performance of different DECT scanners/techniques needs full exploration before confident clinical applications.

Table 1 Studies highlighting the role of DECT in the evaluation of biliary diseases

Authors	Year	Country	Scanner	Technique of DECT	Aim	Key results
Kim et al ⁷	2011	Korea	Somatom definition, Siemens Healthcare	Dual-source DECT scanner	To assess whether VNC images are equally good as nonenhanced images for evaluation of biliary stones and compare VNC images obtained during LAP and PVP with true nonenhanced images	VNC images have moderate accuracy for detection of biliary stone. However, limited role in detection of smaller GS (<9mm) and relatively radiolucent CBD stones of attenuation <78HU
Lee et al ⁶	2015	Korea	Somatom definition Flash, Siemens Healthcare	Dual-source DECT scanner	To compare GS on VNC and true unenhanced images acquired with DECT	VNC images allow better visualization of cholesterol GS, but calcium and small GS are better seen on true unenhanced images
Yang et al ⁹	2016	China	Discovery CT750 HD scanner	Single tube, dual-energy fast-switching spectral imaging mode	To investigate whether spectral CT can differentiate cholesterol GS from surrounding bile	VMI images at lower and higher keV provide significant attenuation difference between cholesterol GS and surrounding bile
Uyeda et al ⁸	2017	USA	Siemens FLASH, Forchheim Germany	Dual-source 128 × 2 slice scanner	To assess whether VMI allow better detectability of noncalcified GS on DECT in comparison with conventional CT imaging	Noncalcified stones are better visualized on low keV VMI images
Soesbe et al ¹⁰	2019	USA	IQon; Philips Healthcare, Best, the Netherlands	Dual-Hayer DECT	To develop a dual-energy technique for differentiation of iso-attenuating GS from bile	Segmented images improved the detection of isoattenuating GS from bile with good accuracy even for smaller GS (<9mm)
Yin et al ¹⁷	2020	China	Somatom definition Flash, Siemens, Erlangen, Germany	Dual-source DECT	To investigate whether DECT can differentiate between cholesterol and adenomatous polyp	DECT scans with their unique energy spectrum information can differentiate cholesterol and adenomatous polyps 1.0–2.0 cm in size

Abbreviations: CBD, common bile duct; DECT, dual-energy computed tomography; GS, gallstones; HU, Hounsfield unit; keV, kiloelectron voltage; LAP, late arterial phase; PVP, portal venous phase; VMI, virtual monoenergetic images; VNC, virtual noncontrast.

Conclusion

DECT is a promising tool for the evaluation of biliary diseases. It has the potential to provide a one-stop solution to the detection of intraluminal and intramural pathologies, including differentiation of benign and malignant pathologies. However, there is limited data available on individual biliary tract pathologies. Therefore, future research must focus on knowing the potential of this application of CT scan.

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Conflict of Interest

None declared.

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