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Case Report

Innovative imaging approaches for neuroendocrine tumor characterization: Combined dual energy CT and perfusion protocol implementation☆,☆☆

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ABSTRACT

The article addresses the diagnostic value of the combined use of computed tomography (CT) perfusion and dual-energy CT (DECT) in patients with neuroendocrine tumors. It emphasizes the heterogeneity and complexity of these neoplasms, primarily affecting the gastrointestinal tract, bronchopulmonary system, and pancreas. While conventional CT is widely employed in their diagnosis, the combination of CT perfusion and dual-energy CT offers greater precision, particularly in detecting synchronous tumors and characterizing their vascularization. A clinical case of a patient with chronic abdominal symptoms, whose diagnosis was facilitated using both combined techniques, is presented. The discussion explores how CT perfusion assesses tumor vascularization and how dual-energy CT improves soft tissue differentiation, resulting in increased diagnostic accuracy. It is highlighted that this approach not only enhances detection rates but also positively impacts clinical management and healthcare costs. Therefore, the importance of considering these advanced tools in the diagnosis of neuroendocrine tumors to improve diagnostic precision and efficiency in patient care is underscored.

Introduction

Neuroendocrine neoplasms represent a diverse array of malignant tumors distinguished by unique histological traits and a complex classification. These tumors affect the neuroendocrine system, which encompasses endocrine glands like the pituitary, adrenal glands, and parathyroid glands, as well as endocrine tissue nestled within glandular structures (such as the thyroid or pancreas) and scattered cells within the ex-

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ocrine parenchyma, like the endocrine cells lining the digestive tract and respiratory passages [1].

Most neuroendocrine tumors arise within the gastrointestinal tract (55%-67%), the bronchopulmonary system (25%) [2], and the pancreas [3]. In the gastrointestinal realm, the most prevalent sites vary in the literature, with contention over the top spot between the small intestine, reported in up to 45% of cases [2], and the rectum, reported in up to 34% [3]. Other notable locations include the appendix (6%-16%), colon (8%-11%), stomach (7%-12%), duodenum (8%), and cecum (6%) [2,3].

Diagnostic imaging strategies for neuroendocrine neoplasms encompass ultrasound, contrast-enhanced computed tomography, magnetic resonance imaging, as well as functional assessments utilizing nuclear medicine [3,4]. Computed tomography stands out as the preferred modality for assessing vascular infiltration and proves invaluable in surgical strategizing; furthermore, it aids in discerning between benign and malignant pancreatic lesions [4,5]. Given the intricate nature and progression of these neoplasms, selecting the appropriate imaging protocol for diagnosis is paramount [4].

Though relatively underutilized, the combined employment of computed tomography with perfusion protocol and dual-energy computed tomography holds promise in accurately identifying such tumors [6]. This diagnostic imaging proves indispensable in characterizing, staging, and determining therapeutic courses of action [7].

Case presentation

A 37-year-old female patient presented to the emergency department with chronic epigastric abdominal pain, with acute exacerbations radiating to the right hypochondrium that worsened with food intake and had been occurring intermittently for months. In the initial assessment, an abdominal ultrasound revealed chronic cholecystitis, which required surgical management by general surgery.

Following the surgical procedure, the patient reported worsening of the initial symptoms, characterized by vomiting, persistent burning abdominal pain localized in the epigastrium, and loss of appetite. As a result, the patient was reassessed, and an endoscopic evaluation was performed without complications, revealing grade C esophagitis according to the Los Angeles classification, Hill type 1 diaphragmatic pinch, erosive gastropathy with extensive subepithelial hemorrhage (suspicion of H. pylori infection), and severe bulb duodenitis. Various random samples were taken during the procedure (from the body, antrum, and incisura of the stomach) as well as from a 1 cm sessile gastric polyp for histopathological study.

Biopsy results from the body, antrum, and incisura of the stomach were negative for H. pylori without dysplastic or metaplastic changes. However, they revealed the presence of inactive superficial and deep chronic gastritis, as well as reactive chronic gastropathy (chemical gastropathy). The polyp biopsy result indicated a well-differentiated G1 neuroendocrine tumor (positive immunohistochemical reactions with markers: CKAE1-AE3, Neuronal specific enolase, Synaptophysin, Chromogranin, and KI 67 of 1%).

Considering these findings, serum gastrin levels were measured, resulting in 4699 pg/mL, and imaging studies were conducted for the staging of the neuroendocrine tumor. Contrast-enhanced nonionic iodinated computed tomography with a protocol for upper abdomen perfusion, including a venous phase extension of the chest and abdomen with dual-energy, was performed.

During the dynamic perfusion phase of the upper abdomen, seven lesions with hyper vascular behavior were identified, with arterial phase densities of up to 340 HU, demonstrating synchronous peak enhancement in all identified lesions, consistent with the histopathological report of well-differentiated tumors, localized in the pancreas, stomach, and duodenum, without evidence of lymphadenopathy or distant lesions. Nodular lesions were identified in the posterior aspect of both thyroid lobes, smaller than 1 cm, consistent with parathyroid adenomas, during the venous phase extension. Therefore, it was recommended to consider brain MRI to rule out pituitary adenoma as part of MEN-1 spectrum (Figs. 1, 2 and 3, Table 1).

The importance of imaging acquisition with perfusion protocol is highlighted due to its high spatial resolution, with high sensitivity for detecting multiple synchronous lesions within and outside the Passaro triangle, which would have been limited with another imaging method. The suspicion of Multiple Endocrine Neoplasia type 1 association was raised due to the multicentricity of the lesions, confirmed by the presence of parathyroid adenomas.

Discussion

Computed tomography perfusion is a minimally invasive technique that allows for qualitative and quantitative evaluation of tissue perfusion by injecting iodinated contrast agent and performing dynamic tomography to estimate time enhancement curves within organs and tissues [8]. During the study, tissue attenuation is measured after the intravenous contrast agent is administered within the scanned volume. Consequently, the total volume of the organ or tumor is scanned at different points over time. Subsequently, density in 2 different regions of interest (ROIs), in an afferent artery and in the desired tissue, is compared through mathematical analysis [9].

Thus, by repeatedly scanning a tissue volume after contrast injection (i.e., multiple scans within a short interval) [9,10], computed tomography perfusion allows for the measurement of functional parameters of tumor vascularization, such as blood flow (BF), blood volume (BV), capillary permeability (permeability surface area product or k-trans) and provides information on contrast agent transit (such as mean transit time and time to peak) [8–10].

Computed tomography perfusion has been proposed as a promising option in oncology, with potential uses not only in the evaluation of tissues and masses but also in monitoring and assessing patient response to chemotherapy and radiotherapy. This is particularly relevant considering that some of the newer anticancer medications focus on intervening in the blood supply and metabolic pathways of tumors [10,11].

Fig. 1 – Pancreatic and lesions perfusion curves. This graphic illustrates the synchronous peak enhancement observed in identified lesions (18 seconds from the start of the scan, 34 seconds from contrast injection) in relation to the normal pancreatic parenchyma.

Table 1 – List of identified lesions.

Lesion	Topography	Dimensions
1	Posterior and inferior aspect of the pancreatic head	27 mm Vol 5.9 mL
2	Posterior aspect of the uncinate process	16 mm Vol 1.1 mL
3	Upper and posterior wall of the duodenal loop	16 mm Vol 0.8 mL
4	Anterior aspect of the ampulla of Vater	6 mm Vol 0.07 mL
5	Antimesenteric border of the second portion of the duodenum	5 mm Vol. 0.04 mL
6	Superior and distal aspect of the pancreatic tail	11 mm Vol 0.3 mL
7	Inferior aspect of the proximal portion of the pancreatic tail	6 mm Vol 0.05 mL

In the pancreas, computed tomography with perfusion protocol is considered a novel and debated technique. However, it has demonstrated greater diagnostic accuracy in cases of neuroendocrine tumors compared to traditional contrast-enhanced computed tomography, achieving a detection rate of up to 89.1% [12]. Additionally, the technique has shown good results in the diagnosis of pancreatic adenocarcinoma [13]. Its utility has also been described in cases suspected of serous cystic neoplasms, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, suspected metastases, acinar cell carcinomas, acute and chronic pancreatitis, as well as inflammatory pseudo tumors [9].

In the context of neuroendocrine tumors, following the administration of intravenous contrast material, functioning pancreatic neuroendocrine tumors (typically highly vascularized) tend to enhance during the arterial phase and exhibit slow washout, appearing hyperdense or isodense compared to the surrounding parenchyma during the portal phase [12,14].

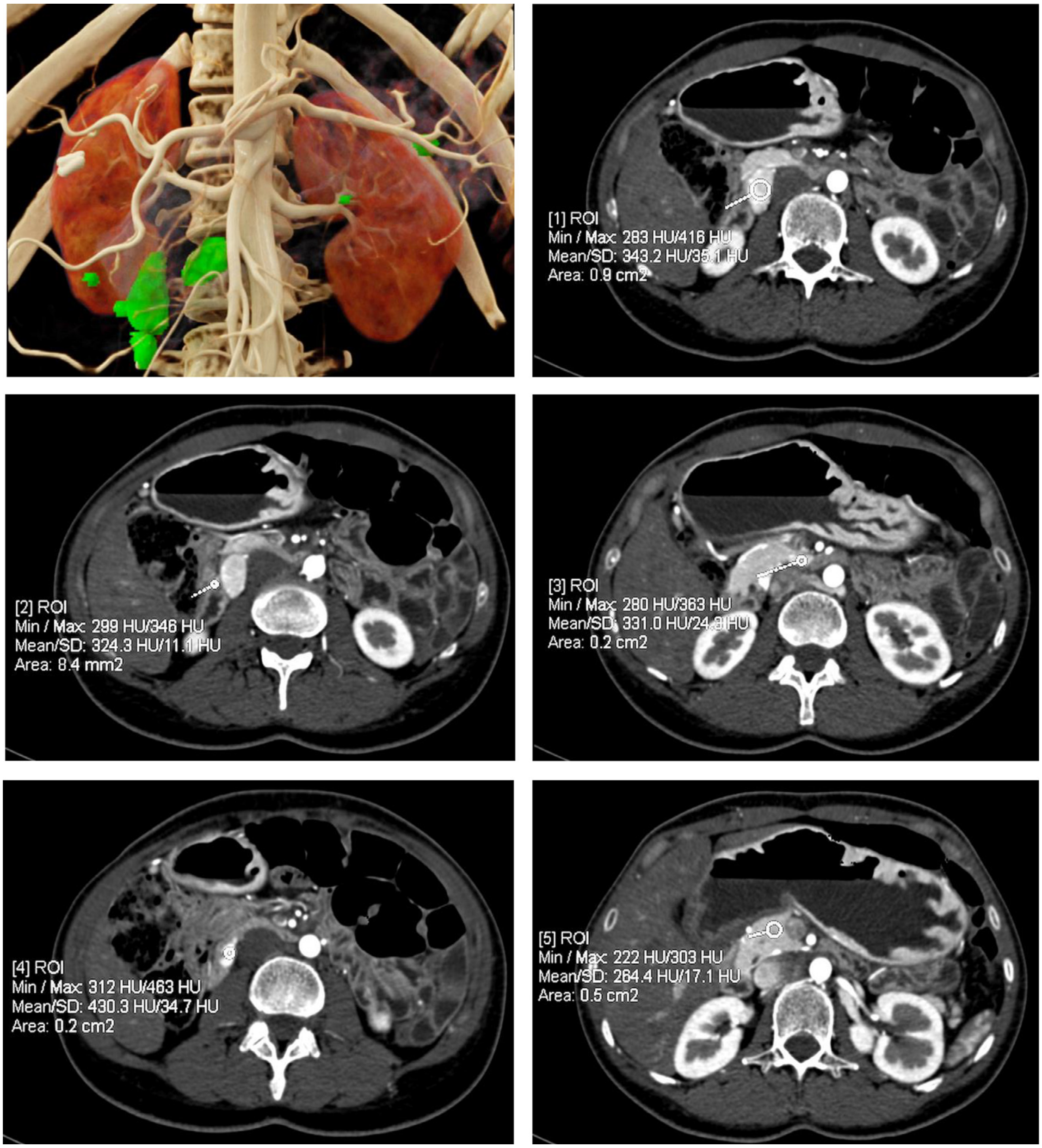

Fig. 2 – Dual-energy computed tomography of the abdomen with nonionic iodinated intravenous contrast, acquired with a superior abdomen perfusion protocol. In the postprocessing of the phases of perfusion of the superior abdomen, multiple lesions with hyper vascular behavior are identified when compared with the pancreatic healthy parenchyma, with densities in the arterial phase of up to 340 Hounsfield Units (HU).

On the other hand, non-functioning neuroendocrine tumors (primarily large ones) often present with atypical appearance (low enhancement); it is noteworthy that such atypical appearance is associated with a poorer prognosis [14].

Despite its utilities, the role of computed tomography perfusion has been found limited in clinical practice due to the need for standardizing protocols [15] and the high radiation dose it entails [12]. Hence, the combination of this technique with dual-energy computed tomography has been proposed as a viable alternative at the healthcare level, as it has proven useful in diagnosing neuroendocrine tumors while reducing radiation exposure by at least 10% compared to traditional computed tomography with classic perfusion protocol, among other advantages [6].

To understand how dual-energy works, it's important to clarify that while traditional computed tomography is an excellent diagnostic method for detecting complications associated with gastroenteropancreatic neuroendocrine tumors, such as intestinal obstruction, intussusception, or desmoplastic reaction [16], it presents a significant limitation in soft tissue differentiation because the pixel value depends entirely on the linear attenuation coefficient, which has considerable overlap between different body materials [17]. This linear attenuation coefficient results from 2 physical interactions

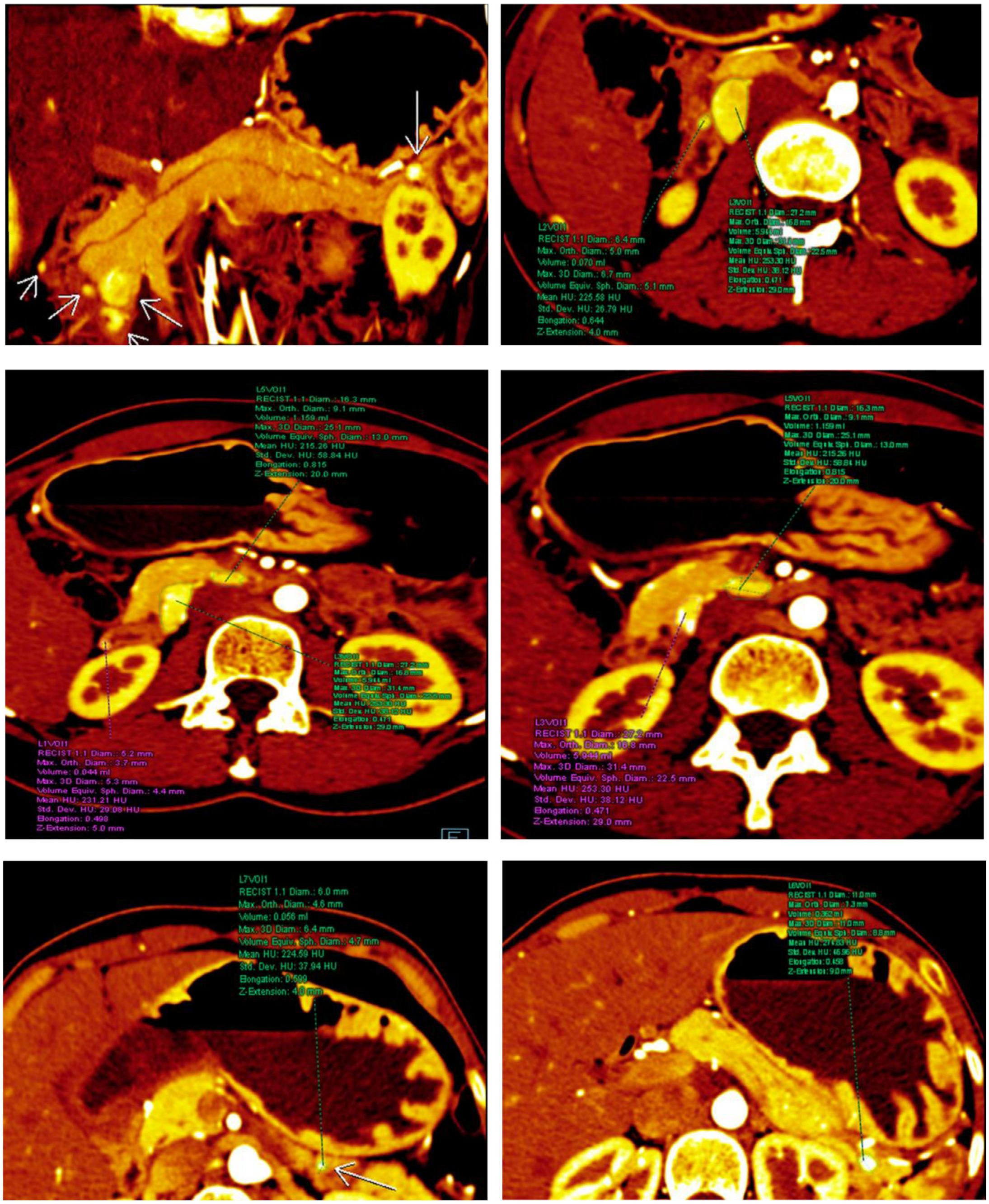

Fig. 3 – Dual-energy computed tomography of the abdomen with nonionic iodinated intravenous contrast, acquired with a superior abdomen perfusion protocol. Pancreatic multiplanar reconstruction and axial images of the upper abdomen post-processed in an iodine map.

between X-ray photons. There are few atoms in the body, such as calcium and iodine, whose strong photoelectric effect can be easily differentiated from tissues with weak photoelectric effect [17]. In diagnostic images, the photoelectric effect is the most important mechanism by which X-ray photons interact with matter [18].

In dual-energy computed tomography, 2 different X-ray spectra are used to obtain images of the same anatomical region, allowing for the analysis of energy-dependent changes in the attenuation of different materials [18]. Matter exhibits a relatively specific change in attenuation between images obtained with high and low-energy spectra; this differentiation in attenuation allows for better tissue characterization [17–19].

In clinical practice, the information obtained from dual-energy computed tomography is primarily utilized in areas such as the detection of low-contrast splenic, pancreatic, and hepatic lesions; identification of noncalcified gallstones; differentiation of uric acid; distinguishing between pancreatitis and pancreatic necrosis; characterization of kidney stone composition; differentiation of intracranial calcium from intracranial hemorrhages; identification of bone marrow edema; bone removal in angiography; iodine maps, among others [18,20].

Dual-energy computed tomography can aid in identifying tumors by enhancing iodine uptake in parenchymal tissues and by quantifying materials such as fat and blood [21]. Additionally, through the creation of iodine maps, it can assist in quantifying and evaluating tumor viability using data such as the level of local invasion, extension to adjacent tissues, and peripheral metastases [21].

In the diagnosis of neuroendocrine neoplasms, the use of images obtained through dual-energy computed tomography is still considered a rare practice [4]. However, the use of iodine maps has been suggested as a parameter that reduces the need for follow-up studies such as magnetic resonance imaging and subsequently increases radiologists' confidence, thus indirectly impacting by reducing costs associated with imaging healthcare [22].

In reviews, dual-energy computed tomography has also shown promising results in significantly reducing metal artifacts and helping to decrease the contrast agent dose (thus being useful in patients at risk of contrast-induced nephropathy) [23]. In this regard, its combination with perfusion computed tomography has likewise been shown to decrease noise and artifacts [6].

Moreover, in oncology, dual-energy computed tomography has shown good results in diagnosing tumors located in tissues such as the adrenal glands, pancreas, thymus, ovaries, parathyroid glands, thyroid, breast gland, salivary glands, kidneys, and liver [5,23,24]. It also aids in differentiating pancreatic neuroendocrine tumors from neuroendocrine carcinomas [25] and facilitating the visibility of neuroendocrine tumors in the small intestine [3], as well as insulinomas [26], among others.

Indeed, the combination of both techniques (computed tomography perfusion and dual-energy computed tomography) achieves a detection rate in neuroendocrine tumors of up to 96.6%, which is higher than the detection rate reported solely with conventional pancreatic computed tomography perfusion. It is worth mentioning that when combined, the detection rate reaches 96.6% during the arterial phase and 84.6% in the venous phase, still maintaining overall superior results compared to traditional pancreatic perfusion computed tomography [6].

Therefore, although the combination of these techniques is not commonly used in daily clinical practice for the diagnosis of neuroendocrine tumors, both individual [3,9,25–27] and combined [6] results pave the way for their application to be included in diagnostic algorithms when suspicions or clinical needs involving these pathologies arise [6,25].

Conclusion

Images obtained through the combination of computed tomography perfusion and dual-energy computed tomography represent an available and highly useful tool in the diagnostic processes of clinical cases suspected of single or multiple neuroendocrine tumors, providing, among other benefits, reduced radiation doses, decreased artifacts, fewer additional imaging studies, and lower costs in the diagnostic process.

Patient consent

Informed consent was obtained from the patient for the preparation of this case report. Confidentiality of personal information will be respected according to ethical standards.

REFERENCES

[1] Oronsky B, Ma PC, Morgensztern D, Carter CA. Nothing but NET: a review of neuroendocrine tumors and carcinomas. Neoplasia 2017;19(12):991–1002.
[2] Ahmed M. Gastrointestinal neuroendocrine tumors in 2020. World J Gastrointest Oncol 2020;12(8):791–807.
[3] Malla S, Kumar P, Madhusudhan KS. Radiology of the neuroendocrine neoplasms of the gastrointestinal tract: a comprehensive review. Abdomin Radiol 2021;46(3):919–35.
[4] Półtorak-Szymczak G, Budlewski T, Furmanek MI, Wierzba W, Sklinda K, Walecki J, et al. Radiological imaging of gastro-entero-pancreatic neuroendocrine tumors. the review of current literature emphasizing the diagnostic value of chosen imaging methods. Front Oncol 2021;11:670233.
[5] Agrawal MD, Pinho DF, Kulkarni NM, Hahn PF, Guimaraes AR, Sahani DV. Oncologic applications of dual-energy CT in the abdomen. Radiographics 2014;34(3):589–612.
[6] Wan Y, Hao H, Chen Y, Zhang Y, Yue Q, Li Z. Application of spectral CT combined with perfusion scan in diagnosis of pancreatic neuroendocrine tumors. Insights Imaging 2022;13(1):145.
[7] Sahani DV, Bonaffini PA, Fernández–Del Castillo C, Blake MA. Gastroenteropancreatic neuroendocrine tumors: role of imaging in diagnosis and management. Radiology 2013;266(1):38–61.
[8] Garbino N, Brancato V, Salvatore M, Cavaliere C. A systematic review on the role of the perfusion computed tomography in abdominal cancer. Dose-Response 2021;19(4):155932582110561.
[9] Grözinger G, Grözinger A, Horger M. The role of volume perfusion CT in the diagnosis of pathologies of the pancreas. RöFo - Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren 2014;186(12):1082–93.
[10] Schneeweiß S, Horger M, Grözinger A, Nikolaou K, Ketelsen D, Syha R, et al. CT-perfusion measurements in pancreatic carcinoma with different kinetic models: is there a chance for tumour grading based on functional parameters? Cancer Imaging 2016;16(1):43.
[11] Sinitsyn V. Analysis and interpretation of perfusion CT in oncology: type of cancer matters. Radiology 2019;292(3):636–7.
[12] Wan Y, Hao H, Meng S, Li Z, Yu F, chi Meng, et al. Application of low dose pancreas perfusion CT combined with enhancement scanning in diagnosis of pancreatic neuroendocrine tumors. Pancreatology 2021;21(1):240–5.
[13] Zaborienė I, Barauskas G, Gulbinas A, Ignatavičius P, Lukoševičius S, Žvinienė K. Dynamic perfusion CT: a promising tool to diagnose pancreatic ductal adenocarcinoma. Open Med 2021;16(1):284–92.
[14] Chiti G, Grazzini G, Cozzi D, Danti G, Matteuzzi B, Granata V, et al. Imaging of pancreatic neuroendocrine neoplasms. Int J Environ Res Public Health 2021;18(17):8895.

[15] Skornitzke S, Vats N, Mayer P, Kauczor HU, Stiller W. Pancreatic CT perfusion: quantitative meta-analysis of disease discrimination, protocol development, and effect of CT parameters. Insights Imaging 2023;14(1):132.

[16] Pellegrino F, Granata V, Fusco R, Grassi F, Tafuto S, Perrucci L, et al. Diagnostic management of gastroenteropancreatic neuroendocrine neoplasms: technique optimization and tips and tricks for radiologists. Tomography 2023;9(1):217–46.

[17] Goo HW, Goo JM. Dual-energy CT: new horizon in medical imaging. Korean J Radiol 2017;18(4):555–69.

[18] Sanghavi PS, Jankharia BG. Applications of dual energy CT in clinical practice: a pictorial essay. Indian J Radiol Imaging 2019;29(03):289–98.

[19] Agostini A, Borgheresi A, Mari A, Floridi C, Bruno F, Carotti M, et al. Dual-energy CT: theoretical principles and clinical applications. Radiol Med 2019;124(12):1281–95.

[20] Sodickson AD, Keraliya A, Czakowski B, Primak A, Wortman J, Uyeda JW. Dual energy CT in clinical routine: how it works and how it adds value. Emerg Radiol 2021;28(1):103–17.

[21] Cruz-Hernández E, Mahmood U, Golia Pernicka JS, Paroder V, Petkovska I, Gollub MJ, et al. Initial evaluation of dual-energy computed tomography as an imaging biomarker for hepatic metastases from neuroendocrine tumor of the gastrointestinal tract. Quant Imaging Med Surg 2021;11(5):2085–92.

[22] Atwi NE, Sabottke CF, Pitre DM, Smith DL, Danrad R, Dharaiya E, et al. Follow-up recommendation rates associated with spectral detector dual-energy CT of the abdomen and pelvis: a retrospective comparison to single-energy CT. J Am Coll Radiol 2020;17(7):940–50.

[23] Gentili F, Guerrini S, Mazzei FG, Monteleone I, Di Meglio N, Sansotta L, et al. Dual energy CT in gland tumors: a comprehensive narrative review and differential diagnosis. Gland Surg 2020;9(6):2269–82.

[24] Wang X, Liu D, Zeng X, Jiang S, Li L, Yu T, et al. Dual-energy CT quantitative parameters for evaluating immunohistochemical biomarkers of invasive breast cancer. Cancer Imaging 2021;21(1):4.

[25] Wang Y, Hu X, Shi S, Song C, Wang L, Yuan J, et al. Utility of quantitative metrics from dual-layer spectral-detector CT for differentiation of pancreatic neuroendocrine tumor and neuroendocrine carcinoma. Am J Roentgenol 2022;218(6):999–1009.

[26] Lin XZ, Wu ZY, Tao R, Guo Y, Li JY, Zhang J, et al. Dual energy spectral CT imaging of insulinoma—Value in preoperative diagnosis compared with conventional multi-detector CT. Eur J Radiol 2012;81(10):2487–94.

[27] Yuan J, Wang Y, Hu X, Shi S, Zhang N, Wang L, et al. Use of dual-layer spectral detector computed tomography in the diagnosis of pancreatic neuroendocrine neoplasms. Eur J Radiol 2023;159:110660.