

REVIEW

Malignant Small Bowel Neoplasms : a review of post-contrast multiphasic multidetector computed tomography

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Abstract : Small bowel neoplasms are rare and account for 3-6% of all gastrointestinal neoplasms. For the diagnosis of small bowel neoplasms, differentiating normal bowel tissue from tumor is critical and depends on imaging modality and scanning techniques. The detection and characterization of small bowel neoplasms have recently improved with the advance of computed tomography (CT) technology. Post-contrast multiphasic CT is an aid to detection and recognition of the vascular nature of small bowel neoplasms. Understanding the typical post-contrast multiphasic CT features of small bowel neoplasms is important because of overlapping features and the necessity of evaluating associated complications and metastases to lymph node and other organs. However, accurate classification of pathologies is still challenging in clinical practice. Texture analysis can quantify complex mathematical patterns within the gray-level distribution of the pixels and voxels of digital images, and texture analysis of the post-contrast multidetector CT data of various tumors has been attracting attention in recent years. The aim of this article is to provide a comprehensive guide to the relevant imaging features for different types of malignant small bowel neoplasms. *J. Med. Invest.* 69:19-24, February, 2022

Keywords : *malignant small bowel neoplasm, post-contrast multiphasic multidetector computed tomography (CT), neuroendocrine tumor (NET), malignant lymphoma*

INTRODUCTION

Small bowel neoplasms are rare, accounting for only 3-6% of all gastrointestinal neoplasms and 1-3% of all gastrointestinal malignancies (1). Diagnosis is often delayed because patients may remain asymptomatic until the late stages and the clinical symptoms are non-specific (2, 3). Early diagnosis, preferably with non-invasive methods, is important for the management of patients with small bowel neoplasms.

Barium small bowel examination was previously considered the most accurate radiological modality to detect small bowel malignancies. Small bowel neoplasms were traditionally diagnosed with small bowel follow-through study and fluoroscopic enteroclysis (4-6). Compared with small bowel follow-through study and fluoroscopic enteroclysis, cross-sectional imaging studies, including CT, have the advantage of identification and characterization of mural or extraluminal lesions as well as the assessment of the extramural structures and abdominal organs. The increased speed and improved temporal resolution of late-generation multidetector row CT (MDCT) scanners made CT the most frequent primary imaging option for small bowel lesions. Progressed bolus-tracking techniques further improved the radiologic detectability of enhancing small bowel lesions. These advantages made MDCT an optimal modality for the diagnosis of small bowel neoplasms.

This article reviews the typical CT imaging features of malignant small bowel neoplasms and presents the imaging appearance on post-contrast multiphasic MDCT with discussion of the

future analysis methods.

IMAGING TECHNIQUES

Advances in MDCT provide high-resolution imaging and more accurate depiction of small bowel neoplasms. Data sets with isotropic voxels can be obtained with the currently available 16-640 detector row MDCT machines. The increased speed and improved spatial resolution of late-generation MDCT has made CT scan capable of rapid acquisition of volumetric data and the first-line modality for the examination of suspected small bowel neoplasms.

Suggested CT parameters for a MDCT scanner are : 120 kV, 300 mAs, or auto mA mode, and a section thickness of 1.0-3.0 mm and a reconstruction interval of 1.0-3.0 mm, depending on the protocol used (3, 7-9). The unenhanced CT scan was performed and the images were acquired from the diaphragm to the perineum. Bolus tracking techniques with measurements performed in the abdominal aorta can be used to adapt the delay between contrast agent administration and scan initiation to the cardiac output of the individual patient. Non-ionic contrast material (100-150 mL) containing 300 mg I/mL can be injected at 3-5 mL/s for a triphasic scan in the bolus-triggered arterial, enteric, and venous (delayed) phase. Enteric phase is typically acquired at 35-50 s after the injection of intravenous contrast media and provides optimal small bowel mural enhancement (3, 7-11). However, multiphase studies are not routinely acquired on clinical practice, given the added radiation exposure (especially in younger patients). If a small bowel neoplasm is highly suspected and liver staging is sought, a triphasic scan may be advantageous. In patients with a suspected malignant small bowel neoplasm, MDCT enterography with a negative oral contrast agent composed of low density barium sulfate suspension is typically requested for adequate distention of the small bowel lumen (3, 7, 8).

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MALIGNANT NEOPLASMS OF THE SMALL INTESTINE

Adenocarcinoma

Adenocarcinoma is documented to be the most common primary malignant neoplasm of the small bowel, and it represents 25-40% of primary malignant small bowel tumors (3, 12). The predominant location is the duodenum, followed by the jejunum, primarily within the first 30 cm beyond the ligament of Treitz (13-15). Exceptions to this rule occur in patients with Crohn's disease, in which over 66% of cases originate from the ileum (16). The clinical presentation of adenocarcinoma may include vague symptoms such as abdominal pain, nausea, vomiting, weight loss, anemia, and jaundice. Adenocarcinoma typically appears as an asymmetric wall thickening involving a short segment that can cause luminal stenosis and small bowel obstruction on CT (Figure 1). It may also appear as an ulcerated lesion or an annular "apple core" lesion with luminal narrowing. Post-contrast CT typically demonstrates heterogeneous attenuation and moderate contrast enhancement. A recent study reported that peak enhancement occurred in the enteric phase with a relatively low threshold level in adenocarcinoma on post-contrast multiphase CT (11). In addition, post-contrast multiphase MDCT may

reveal other CT findings including vascular invasion, lymphadenopathy, distant metastases, and peritoneal dissemination.

Neuroendocrine tumor

Neuroendocrine tumor (NET), formerly known as carcinoids, originate from the enterochromaffin cells within the gastro-entero-pancreatic and bronchopulmonary systems (17). Gastrointestinal neuroendocrine tumors (GI NET) originate from enterochromaffin cells at the base of the Lieberkuhn crypts within the bowel wall and represent approximately 20-25% of malignant small bowel neoplasms (9, 18). Approximately 30% of GI NET can be found in the small bowel with a predilection for the ileum (19). In early stage, clinical symptoms are rare and a typical CT finding is a solitary enhancing mass within the small bowel mucosa. The tumor rarely appears as an ulcerating mass in the small bowel. There was rapid enhancement in the arterial and enteric phases followed by washout in the venous phase (11). It resembles a mural contrast-enhancing mass extending into the adjacent mesentery, causing a soft tissue density mass in later stages (Figure 2). The mesenteric mass may contain calcifications often with spiculated margins due to the desmoplastic reaction, and may stimulate a fibrotic reaction in the

1A



1B

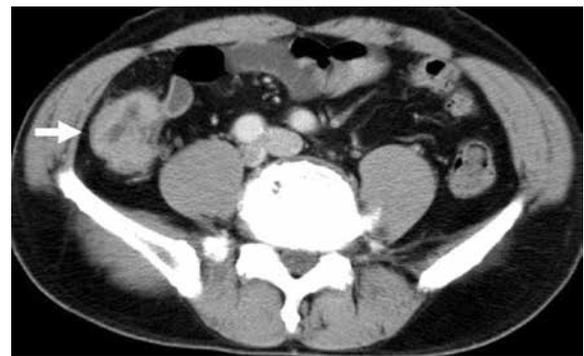


Figure 1. A 66-year-old man with an ileal adenocarcinoma.

Axial CT images in the unenhanced CT (A) and the enteric phase (B) demonstrate a large enhancing mass arising from the ileal wall (arrow) and focal narrowing of the ileum.

2A



2B

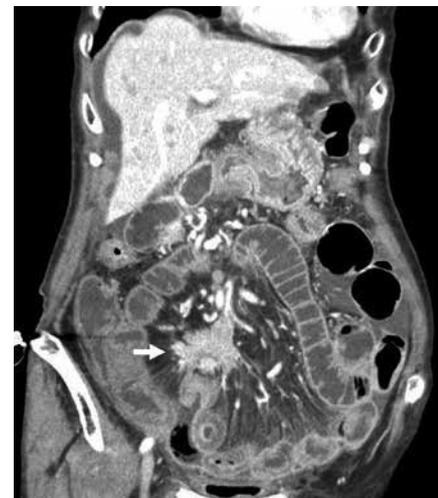


Figure 2. An 83-year-old woman with ileal neuroendocrine tumor (G2) with liver metastases.

An enhancing ileal lesion (arrow in A) with mass-forming desmoplastic reaction within the adjacent mesenteric fat. Coronal CT imaging in the enteric phase visualizes a spiculated mesenteric mass (arrow in B) with stellate appearance tethering small bowel loops.

surrounding tissues leading to bowel obstruction, ischemia, or vascular compromise (20). The desmoplastic reaction may also occur with mesentery lymph node metastasis. Liver metastasis may lead to carcinoid syndrome, with typical symptoms that include watery diarrhea, flushing, sweating, endocardial fibrosis, and sudden crisis.

Lymphoma

Lymphoma represents 15-20% of malignant small bowel tumors, with more than 60% found in the ileum (21-23). Most lymphomas involving the small bowel are non-Hodgkin B-cell lymphoma. T-cell lymphoma has a high association with celiac disease and commonly occurs in the jejunum (24). Patients complain about non-specific symptoms such as weight loss, fever, nausea, diarrhea, and abdominal pain. Small bowel lymphomas have a variety of radiological appearances. In early cases, lymphoma may manifest as plaque-like mucosal expansions. On the other hand, in advanced cases, infiltrative lesions may cause full mural thickening and even mucosal ulcers. Lymphomas are mostly soft and maintain the lumen of small bowel. The lumen may maintain dilatation (aneurysmal dilatation) in advanced cases. In the differentiation from adenocarcinoma on CT, lymphoma may be suggested in the presence of significant homogeneous wall thickening (> 2 cm), eccentric stenosis, and coexistent lymphadenopathy (25). Lymphoma tends to have multifocal involvement compared with adenocarcinoma (6). Distant lymphadenopathy and splenomegaly help distinguish lymphoma from other small bowel neoplasms (Figure 3). On post-contrast

multiphasic CT, lymphoma mostly shows homogeneous and mild enhancement with peak enhancement occurring in the enteric phase (11).

Malignant gastrointestinal stromal tumor

Malignant gastrointestinal stromal tumor (GIST) arises from the smooth muscle pacemaker interstitial cells of Cajal, or similar cells, within the small bowel wall and is mostly located in the jejunum (9, 26). Malignant GIST is less common than benign GIST. Malignant GIST arises mainly in the distal ileum (3). GISTs of small bowel can grow to a large size before causing symptoms. Patients commonly present with non-specific abdominal symptoms such as abdominal pain and nausea. They can also be found with clinical presentations including bowel obstruction and intraluminal GI bleeding. The CT features of small bowel GIST vary depending on the tumor size and aggressiveness. GIST typically shows large, hyperenhancing, and exophytic tumors on post-contrast CT, although GIST can exhibit hypo-enhancement and be located endoluminally (Figure 4). On post-contrast multiphasic CT, GIST typically shows intense peak enhancement on arterial phase followed by washout on the venous phase (11). GIST may have a heterogeneous appearance secondary to necrosis or intra-tumoral hemorrhage and may ulcerate, cavitate, and fistulize to adjacent structures (27). Moreover, GIST may cause obstruction by mass effect or mechanical obstruction due to kinking and compression of the intestine. Malignant GIST is suggested by tumor that is larger than 5 cm, cavitation, exophytic growth, invasion of adjacent structures,

3A



3B



3C



Figure 3. A 63-year-old man with ileal diffuse large B-cell lymphoma. Axial images in the unenhanced CT (A) and the arterial phase (B) show near-circumferential thickening of an ileal bowel loop in the lower abdomen (arrow). Coronal image (C) in the venous phase shows a thickening of ileal bowel wall (arrow) and multiple lymphadenopathies (curved arrows) in the mesentery.

metastasis, and peritoneal seeding (6, 28). Bulky lymphadenopathy is uncommon and favors the diagnosis of other neoplasms.

Metastases

The small bowel is the main site of metastatic tumor in the GI tract. Metastases can reach the small intestine by intraperitoneal seeding, direct invasion from adjacent tumors, or a hematogenous route (29). The most frequent causes of hematogenous metastases are lung carcinoma, breast cancer, melanoma (Figure 5), and renal cell carcinoma. Metastases show solitary or multiple polypoid intraluminal lesions or focal bowel wall thickening. The tumors have a variety of CT features such as luminal narrowing, central ulceration, cavitation, invasion to adjacent organs, and intraperitoneal spread. The enhancement patterns of metastases may vary depending on the vascularity of the primary tumor (11). Metastases to small intestine may cause ileus and intussusception. In addition, metastases to small intestine may be ulcerated and perforated, especially in metastasis from bronchogenic carcinoma (6, 30).

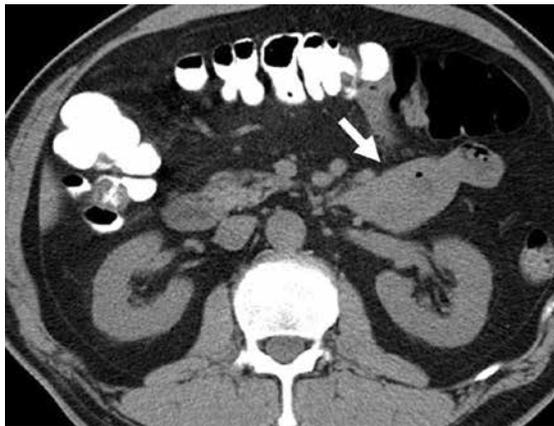
FUTURE DIRECTIONS

Recent advances in CT texture analysis have improved the capacity for processing tumor heterogeneity on imaging and provide indirect information on the tumor microenvironment within

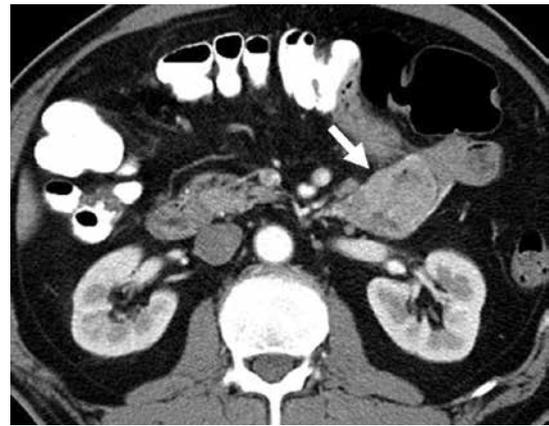
a certain range of quantitative parameters (31). CT texture analysis reflects the distribution and relationship of pixels in CT images. This reveals the subtle differences that are unrecognizable with the human eyes and compensate for the shortcomings of conventional CT imaging.

A recent study reported that volumetric CT texture analyses, especially entropy, may serve as biomarkers for risk stratification for small bowel GIST. Entropy in the venous phase reached high accuracy (AUC = 0.830) for differentiating low-risk from intermediate- to high-risk small bowel GISTs with a sensitivity of 82.4% and the specificity of 74.4% (32). For the differentiation of malignant small bowel neoplasms, a recent study reported that the texture model on arterial phase had an excellent diagnostic capacity in differentiating lymphoma from GIST and adenocarcinoma with a sensitivity of 83.3% and a specificity of 89.3% (33). Another study for gastric tumors reported that CT texture-based classification had a high diagnostic capacity in classification among adenocarcinoma, lymphoma, and GIST (34). These results demonstrated that classification based on texture analyses may be useful for radiologists in establishing the correct diagnosis of small bowel tumors on post-contrast multiphase CT. However, the diagnostic capacity of CT texture analysis has not yet been fully explored in differential diagnosis in patients with small bowel neoplasm. The texture analysis model in small bowel neoplasms deserves further investigations on post-contrast multiphase CT.

4A



4B



4C

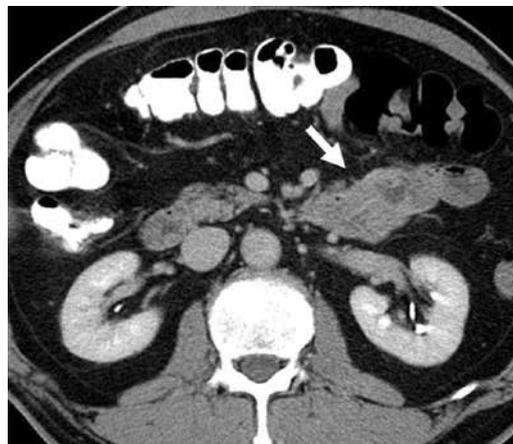


Figure 4. A 68-year-old man with ileal malignant gastrointestinal stromal tumor. Axial CT image in the unenhanced CT (A), the arterial phase (B), and the venous phase (C) show an intraluminal hypervascular mass in the jejunum in the abdomen (arrow).

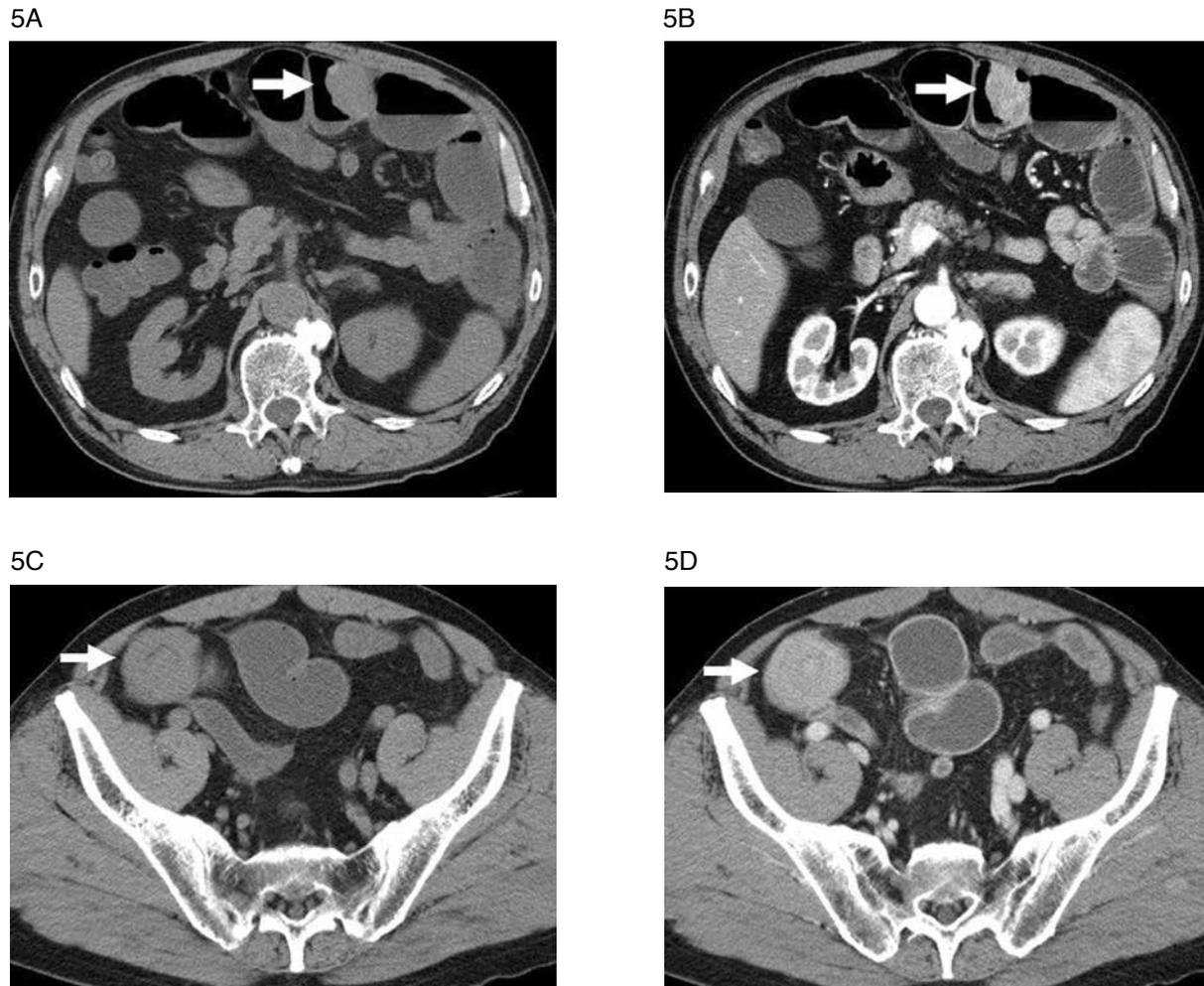


Figure 5. A 71-year-old man with metastatic small bowel tumors from malignant melanoma. Axial images in the unenhanced CT (A) and the enteric phase (B) show an intraluminal polypoid mass with inhomogeneous enhancement in the jejunum (arrow). Axial images in the unenhanced CT (C) and the venous phase (D) shows another large ileal mass (arrow).

CONCLUSIONS

Post-contrast multiphasic CT is a powerful tool in the detection and evaluation of small bowel neoplasms. An understanding of the typical CT imaging features of each pathology may limit the diagnostic possibility in differential diagnosis for small bowel neoplasms. However, the differential diagnosis with post-contrast CT is still challenging as malignant small bowel neoplasms are a rare disease and small in size in the early stage with or without non-specific symptoms. Further evaluation with texture analysis on post-contrast multiphasic CT could be a clue to provide a clearer imaging strategy in the differential diagnosis for malignant small bowel neoplasms.

DECLARATIONS OF INTEREST

None

REFERENCES

- Cheung DY, Choi MG : Current advance in small bowel tumors. *Clin Endosc* 44 : 13-21, 2011
- Maglinte DD, O'Connor K, Bessette J, Chernish SM, Kelvin FM : The role of the physician in the late diagnosis of primary malignant tumors of the small intestine. *Am J Gastroenterol* 86 : 304-308, 1991
- Anzidei M, Napoli A, Zini C, Kirchin MA, Catalano C, Passariello R : Malignant tumours of the small intestine : a review of histopathology, multidetector CT and MRI aspects. *Br J Radiol* 84(1004) : 677-690, 2011
- Nolan DJ, Traill ZC : The current role of the barium examination of the small intestine. *Clin Radiol* 52(11) : 809-820, 1997
- Maglinte DD, Lappas JC, Kelvin FM, Rex D, Chernish SM : Small bowel radiography : how, when, and why? *Radiology* 163(2) : 297-305, 1987
- Jasti R, Carucci LR : Small Bowel Neoplasms : A Pictorial Review. *Radiographics* 40(4) : 1020-1038, 2020
- Sokhandon F, Al-Katib S, Bahoura L, Copelan A, George D, Scola D : Multidetector CT enterography of focal small bowel lesions : a radiological-pathological correlation. *Abdom Radiol (NY)* 42(5) : 1319-1341, 2017
- Paulsen SR, Huprich JE, Fletcher JG, Booya F, Young BM, Fidler JL, Johnson CD, Barlow JM, Earnest 4th F : CT enterography as a diagnostic tool in evaluating small bowel disorders : review of clinical experience with over 700 cases.

- Radiographics 26(3) : 641-657, 2006
9. Sailer J, Zacherl J, Schima W : MDCT of small bowel tumours. *Cancer Imaging* 7(1) : 224-233, 2007
 10. Schindera ST, Nelson RC, DeLong DM, Jaffe TA, Merkle EM, Paulson EK, Thomas J : Multi-detector row CT of the small bowel : peak enhancement temporal window-initial experience. *Radiology* 243(2) : 438-444, 2007
 11. Shinya T, Inai R, Tanaka T, Akagi N, Sato S, Yoshino T, Kanazawa S : Small bowel neoplasms : enhancement patterns and differentiation using post-contrast multiphasic multidetector CT. *Abdom Radiol (NY)* 42(3) : 794-801, 2017
 12. Nelson RL : Adenocarcinoma of the small intestine. In : Nelson RL, Nyhus LM, eds. *Surgery of the small intestine*. Conn : Appleton & Lange, Norwalk, 1988, pp.223-230
 13. Lowenfels AB, Sonni A : Distribution of small bowel tumors. *Cancer Lett Jul 3* : 83-86, 1977
 14. Dabaja BS, Suki D, Pro B, Bonnen M, Ajani J : Adenocarcinoma of the small bowel : presentation, prognostic factors, and outcome of 217 patients. *Cancer* 101(3) : 518-526, 2004
 15. Gore RM, Mehta UK, Berlin JW, Rao V, Newmark GM : Diagnosis and staging of small bowel tumours. *Cancer imaging* 6(1) : 209-212, 2006
 16. Weber NK, Fletcher JG, Fidler JL, Barlow JM, Pruthi S, Loftus Jr EV, Pardi DS, Smyrk TC, Becker BD, Pasha SF, Bruining DH : Clinical characteristics and imaging features of small bowel adenocarcinomas in Crohn's disease. *Abdom Imaging* 40(5) : 1060-1067, 2015
 17. Pinchot SN, Hoen K, Sippel RS, Chen H : Carcinoid Tumors. *Oncologist* 13(12) : 1255-1269, 2008
 18. Anzidei M, Napoli A, Zini C, Kirchin MA, Catalano C, Passariello R : Malignant tumours of the small intestine : A review of histopathology, multidetector CT and MRI aspects. *Brit J Radiol* 84(1004) : 677-690, 2011
 19. Boudreaux JP, Klimstra DS, Hassan MM, Woltering EA, Jensen RT, Goldsmith SJ, Nutting C, Bushnell DL, Caplin ME, Yao JC, North American Neuroendocrine Tumor Society (NANETS) : The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors. *Pancreas* 39(6) : 753-766, 2010
 20. Paski SC, Semrad CE : Small bowel tumors. *Gastrointest Endosc Clin N Am* 19(3) : 461-479, 2009
 21. Cheung DY, Choi M : Current advance in small bowel tumors. *Clin Endosc* 44(1) : 13-21, 2011
 22. Bäck H, Gustavsson B, Ridell B, Rödger B, Westin J : Primary gastrointestinal lymphoma incidence, clinical presentation, and surgical approach. *J Surg Oncol* 33(4) : 234-238, 1986
 23. Ghimire P, Wu GY, Zhu L : Primary gastrointestinal lymphoma. *World J Gastroenterol* 17(6) : 697-707, 2011
 24. Mendelson RM, Fermoye S : Primary gastrointestinal lymphomas : a radiological-pathological review. Part 2 : Small intestine. *Australas Radiol* 50(2) : 102-113, 2006
 25. Lo Re G, Federica V, Midiri F, Picone D, Tona GL, Galia M, Casto AL, Lagalla R, Midiri M : Radiological features of gastrointestinal lymphoma. *Gastroenterol Res Pract* 2016 : 2498143, 2016
 26. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM : Gastrointestinal pacemaker cell tumor (GI-PACT) : Gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. *Am J Pathol* 152(5) : 1259-69, 1998
 27. Hong X, Choi H, Loyer EM, Benjamin RS, Trent JC, Charnsangavej C : Gastrointestinal stromal tumor : role of CT in diagnosis and in response evaluation and surveillance after treatment with imatinib. *Radiographics* 26(2) : 481-495, 2006
 28. Crosby JA, Catton CN, Davis A, Couture JC, O'Sullivan B, Kandel R, Swallow CJ : Malignant gastrointestinal stromal tumors of the small intestine : a review of 50 cases from a prospective database. *Ann Surg Oncol* 8(1) : 50-59, 2001
 29. Seth S, Horton KM, Garland MR, Fishman EK : Mesenteric neoplasms : CT appearance of primary and secondary tumors and differential diagnosis. *Radiographics* 10 : 985-998, 1990
 30. Ramachandran I, Sinha R, Rajesh A, Verma R, Maglente DDT : Multidetector row CT of small bowel tumours. *Clin Radiol* 62(7) : 607-614, 2007
 31. Lubner MG, Smith AD, Sandrasegaran K, Sahani DV, Pickhardt PJ : CT texture analysis : definitions, applications, biologic correlates, and challenges. *Radiographics* 37(5) : 1483-1503, 2017
 32. Feng C, Lu F, Shen Y, Li A, Yu H, Tang H, Li Z, Hu D : Tumor heterogeneity in gastrointestinal stromal tumors of the small bowel : volumetric CT texture analysis as a potential biomarker for risk stratification. *Cancer Imaging* 18(1) : 46. doi : 10.1186/s40644-018-0182-4, 2018
 33. Liu S, Zhang C, Liu R, Li S, Xu F, Liu X, Li Z, Hu Y, Ge Y, Chen J, Zhang Z : CT Texture Analysis for Preoperative Identification of Lymphoma from Other Types of Primary Small Bowel Malignancies. *Biomed Res Int Apr 2 ; 2021* : 5519144. doi : 10.1155/2021/5519144. eCollection 2021
 34. Ba-Ssalamah A, Muin D, Scherthaner R, Kulinna-Cosentini C, Bastati N, Stift J, Gore R, Mayerhoefer ME : Texture-based classification of different gastric tumors at contrast-enhanced CT. *European Journal of Radiology* 82(10) : e537-543. doi : 10.1016/j.ejrad.2013.06.024, 2013