Gastrointestinal Stromal Tumors: Retrospective Analysis of the Computer-Tomographic Aspects

Ioana G. Lupescu[1], Mugur Grasu[1], Mirela Boros[1], Cristian Gheorghe[2], Mihnea Ionescu[3], Irinel Popescu[3], Vlad Herlea[4], Serban A.Georgescu[1]

1) Radiology Department. 2) Gastroenterology Department. 3) General Surgery and Hepatic Transplantation Department. 4) Histopathology Department, Fundeni Hospital, University of Medicine and Pharmacy "Carol Davila", Bucharest

Abstract

Purpose. To describe the computer-tomographic (CT) aspects of gastrointestinal stromal tumors (GISTs) in correlation to their histology. **Material and methods.**The medical records of all patients at our hospital with a histologic diagnosis of GIST between January 2002 and June 2006, and investigated before surgery by CT, were reviewed. Two radiologists with knowledge of the diagnosis reviewed the CT findings. **Results.** Amongst 15 cases of GISTs, 9 cases involved the stomach and 4 cases the small intestine. Location of the primary tumor could not be determined for 2 of 15 tumors, because of the presence of extensive peritoneal metastases. Most primary tumors were predominantly extraluminal (13 cases) while two were clearly endoluminal. The mean diameter of the primary tumor was 8 cm. The tumor margin was well defined in 12 patients and irregular in 3 cases. Central fluid attenuation was present in 11 tumors, while central gas was seen in two cases. Metastases were seen in 2 cases at presentation and in another 2 patients during follow-up. Spread was exclusive to the liver or peritoneum. Visceral obstruction was absent even in extensive peritoneal metastatic disease. Ascites was an unusual finding. **Conclusions.** CT plays an important role not only in the detection and the localization but also in the evaluation of the extension and follow-up of theses tumors. Using only CT aspects, we can only suspect the diagnosis to GISTs. Often other soft-tissue tumors with gastrointestinal involvement can mimic GISTs. In all cases histological diagnosis is essential.

Key words

Gastrointestinal stromal tumors (GIST) - computer tomography (CT) - histopathology

J Gastrointestin Liver Dis
June 2007 Vol.16 No 2, 147-151

Address for correspondence: Ioana G. Lupescu, Ass Prof
Dept.Radiology, Fundeni Hospital
Sos.Fundeni, no.258
Bucharest, Romania
E-mail: ilupescu@gmail.com

Introduction

Gastrointestinal (GI) stromal tumors (GISTs) are rare and account for 0.1–3.0% of all GI neoplasms and for 5.7% of sarcomas (1). GISTs represent the most common mesenchymal neoplasms of the digestive tract (2). These tumors arise from Cajal interstitial cells (3). This definition excludes the gastrointestinal smooth-muscle tumors (leiomyomas/ leiomyoblastomas and leiomyosarcomas), as well as schwannomas and neurofibroma (1,4). Most GISTs (70–80%) are benign (1). The diameter of GISTs range from a few millimeters to more than 30 cm (5). Larger tumors have a higher rate of malignancy (6). Malignancy is characterized by local invasion and metastases. Computer tomography is ideal in defining the endoluminal and exophytic extent of tumor (7-9). The purpose of this study was to make a retrospective analysis of the CT aspects found in GISTs in correlation with the histopathological findings (malignant or benign GISTs).

Material and methods

We reviewed retrospectively from histological data to CT findings analysis, 15 cases (7 females and 8 men) of operated GISTs (between January 2002 and June 2006) amongst 44 cases of rare digestive tumors, in an attempt to better characterize and delineate this particular pathology. The age of the patients ranged from 29 to 72 years (mean: 53 years). CT examinations were performed in all patients, using a monoslice CT acquisition (Philips Aura), after oral administration of water or Gastrografin (500-750 ml) in association with intravenous administration of nonionic iodinated contrast material (100 ml; flow rate, 3 ml/sec; 370 mgI/ml) in late arterial phase (portal inflow) and hepatic venous phase, with a section thickness of 5-7 mm and a pitch of 1.5.

Patient characteristics

The most common symptom was abdominal pain present in 10 patients (66.6%). The other presenting symptoms were a palpable abdominal mass in 8 patients (53.3%), weight

Table I Location and CT aspects of primary GISTs

Location	No. of cases	CT features	
Stomach	9 cases	Giant heterogeneous and irregular extraluminal mass (6 cases)	Polypoid form - axial diameter > 5 cm (1 case) - axial diameter < 5 cm (2 cases)
Small bowel - duodenum - jejunum	4 cases 1 case 3 cases	Heterogeneous tumoral extraluminal mass - axial diameter > 5 cm (2 cases)	Homogeneous mass - axial diameter < 5 cm (1 case at the duodenum, 1 case- at the jejunum)
Unknown origin	2 cases	Multiple and confluent intraperitoneal spherical tumors	

loss in 5 patients (33.3%), and gastro-intestinal beleeding in 3 patients (20%).

Review of imaging. Two radiologists with knowledge of the GIST diagnosis reviewed the CT findings. The presence of necrosis, hemorrhage (density more than 60-70 UH), invasion of adjacent structures, omental thickening, and ascites was noted. Necrosis was determined if the center of the mass had a Hounsfield density of less than 25 units on contrast-enhanced study. In all cases, transverse dimensions of the two largest (if more than one present) liver and peritoneal metastases were recorded. The dynamic enhancement characteristics of the center and periphery of the masses were recorded. Masses that enhanced, at least in part, to a greater degree than normal liver on arterial phase contrast study were appreciated as hypervascular. All the CT criteria used in the analysis of GISTs were compared with the intraoperatory and histological findings.

Results

Image analysis

The CT features of the primary tumors are given in Tables I and II. Amongst 15 cases of GISTs, 9 cases involved the stomach and 4 part of the small intestine (jejunum - 3 cases and 1 case the third duodenum). Location of the primary tumor could not be determined for 2 of 15 tumors, because of the presence of extensive peritoneal metastases. Most primary tumors were predominantly extraluminal (13 cases) while two were clearly endoluminal. The mean diameter of the primary tumor was 8 cm (range: 3–18 cm). The tumor margin was well defined (smooth or lobular) in 12 patients and irregular in 3 cases. Central fluid attenuation was present in 10 tumors, while central gas was seen in 2 cases.

Table II CT findings of primary GISTs

CT findings	No. patients(%)
Heterogeneous enhancement	11 (66.6)
Exophytic growth	13 (86.6)
Larger than 5 cm	11(53.3)
Necrotic center areas	10 (66.6)
Hypovascular tumors	8 (73.3)
Hypervascular tumors	4 (26.6)
Cystic tumors	3 (20.0)
Mucosal ulceration	3 (20.0)
Central gas	2 (13.3)
Hemorrhage	1 (6.6)
Extension into nearby structures	3 (20.0)
Bowel obstruction	0
Hepatic metastasis	2 (13.3)
Peritoneal metastasis	2 (13.3)
Lymph node involvement	0

No tumor at presentation showed calcification. Smaller GISTs (4 cases - less than 5 cm in axial diameter) appeared as: smooth, sharply defined intramural masses with uniform, homogeneous attenuation (Figs.1,2). Smaller GISTs involved in 2 cases the stomach, in one case the third part of the duodenum and in one case the proximal part of the jejunum.

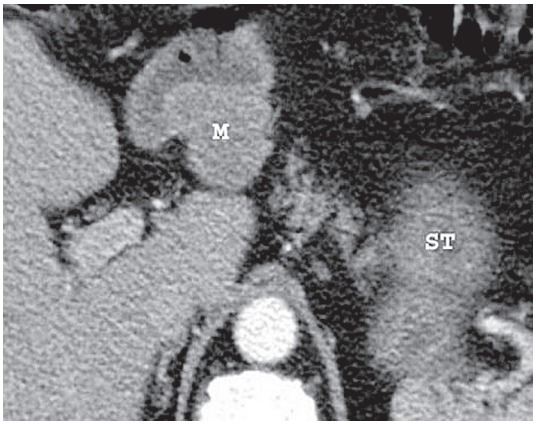

Fig.1 Sharply defined intra-/ extramural mass with homogeneous attenuation in axial CT section. Histological diagnosis: gastric benign GIST.

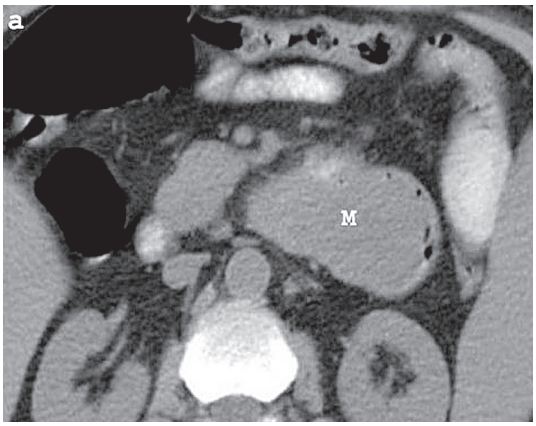

Fig.2 Dense, homogeneous jejunal mass in axial CT section. Histological diagnosis : jejunal benign GIST.

Larger GISTs (11 cases - larger than 5 cm in axial diameter) appeared as heterogeneous masses with enhancing borders of variable thickness and irregular central areas of fluid, air,

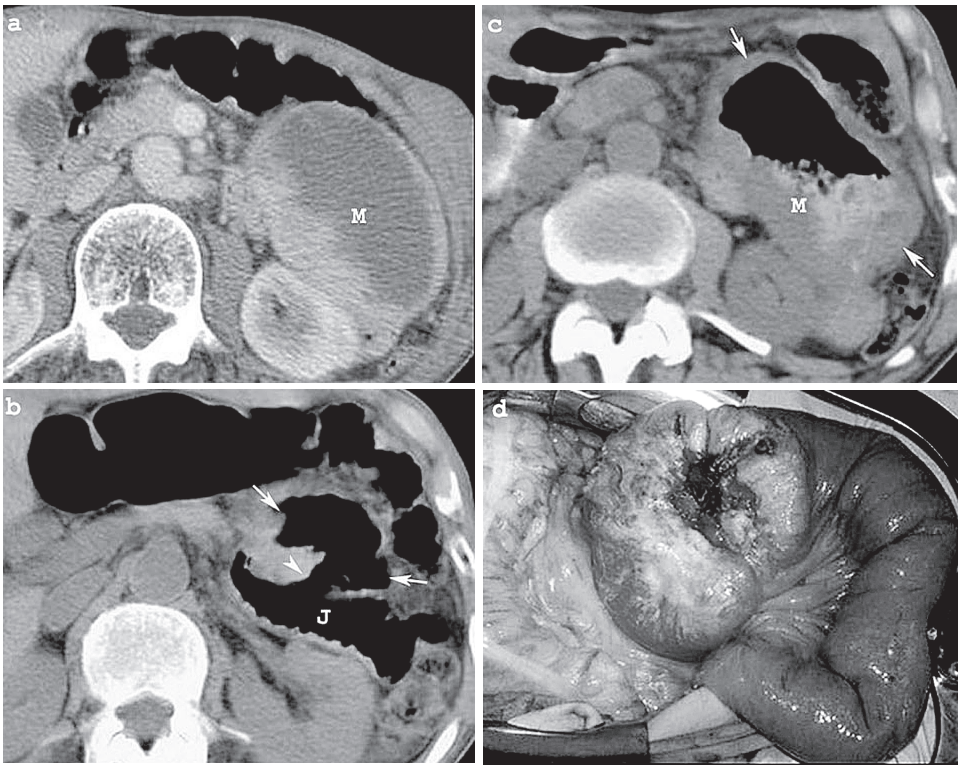

Fig.3.a First CT: heterogeneous mass with enhancing borders of variable thickness and irregular central areas of fluid located in dorsal and caudal position from the tail of the pancreas; b, c - second CT (after 1 year) mass with central cavitation (white arrows); that communicate with the jejunal lumen (short arrow). d - macroscopic view of the jejunal tumor after surgical resection. Histological diagnosis - malignant jejunal GIST.

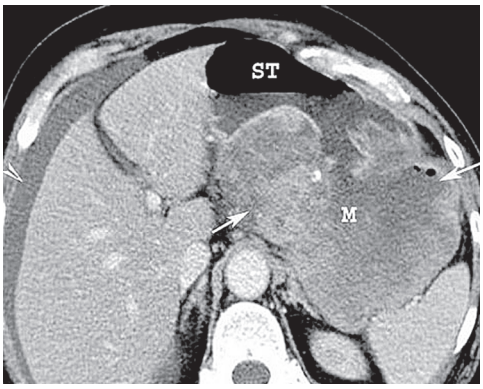

Fig.4 Giant heterogeneous gastric and retrogastric mass with solid portions, central necrosis and small air bubles. Histological diagnosis - malignant gastric GIST.

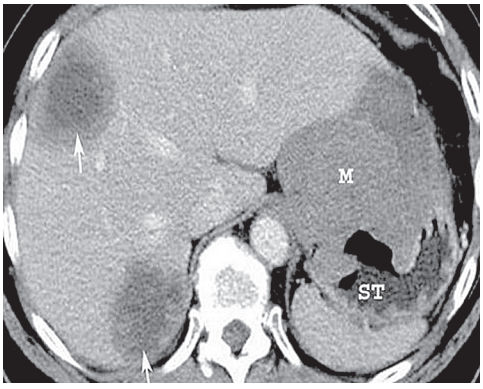

Fig.5 Large gastric and extragastric tumor (M) involving the small gastric curvature, with hepatic metastasis. Ascites (small arrow). Histological diagnosis - malignant GIST.

or oral contrast attenuation that reflect necrosis, cavitations that communicate with GI lumen (Figs.3,4); mucosal ulcerations were present in 3 cases and extension into nearby structures also present in 3 cases. Intratumoral hemorrhage was present in one case. Hypervascular tumors were found in 4 cases in comparison with hypovascular tumors present in 8 cases. Cystic tumors were found in 3 cases. Liver metastases were present in 2 patients who underwent CT at presentation and in another 2 patients during follow-up. Peritoneal metastases were present in 2 cases. Hepatic (Fig.5) and peritoneal metastases (Fig.6) presented central fluid attenuation. The mean number of hepatic metastases was 4 (ranges: 1 to 7). We did not evidence abdominal lymphadenopathies. One patient had ascites. There were no cases of visceral obstruction as determined on CT scans in the 15 patients who underwent CT at presentation.

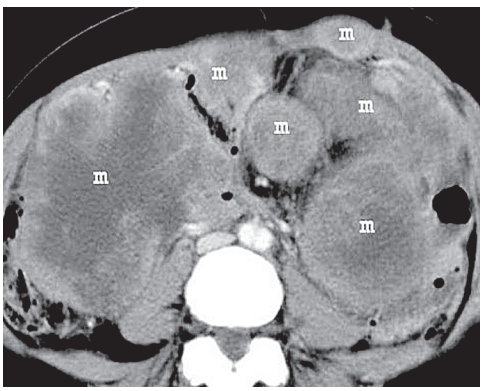

Fig.6 Multiple peritoneal tumoral masses (m-metastases). Histological diagnosis- peritoneal metastasis from malignant GISTs.

All cases selected in this study were operated on the basis of CT findings. There was a concordance between the CT description and the intra-operatory aspects and there was a histological confirmation of GISTs in 86.6% of the cases. The two cases (13.3%) with multiple heterogeneous and bulky peritoneal tumors with unkonwn origin at CT, had in fact at intraoperatory evaluation and histological examination, a diagnosis of advanced jejunal GIST with multiple peritoneal metastases.

From the histological point of view, 8 cases had a diagnosis of malignant GISTs and 7 cases a diagnosis of benign GISTs.

Discussion

GISTs are now defined as spindle cell, epithelioid, or occasionally pleomorphic mesenchymal tumors of the gastrointestinal tract, which express the KIT protein (CD117, stem cell factor receptor) detected at immunohistochemistry (1). Many tumors previously diagnosed as leiomyomas, leiomyoblastomas, or leiomyosarcomas have been found to be positive for CD117 and are now considered GISTs. Schwannomas, true leiomyomas, and true leiomyosarcomas are not GISTs because they are not derived from the GIST precursor cell and do not meet the specific immunohistochemical criteria (1,3).

The tumors occur equally in both sexes and have a unimodal peak incidence in persons aged 40-70 years (3). In our study, patients with GIST were similar to the literature findings concerning age, gender, peak of incidence, morphopathology and clinical manifestations.

Regarding *location,* 50-70% of GISTs occur in the stomach; 33% in the small bowel; 5-15% in the rectocolon, and only 1-5% in the esophagus. Uncommonly, they may occur in the peritoneal cavity. Retroperitoneal GISTs are extremely rare (4).

The *clinical manifestations* of GISTs depend on the location and size of the tumors and are often nonspecific. Patients may present with pain, dysphagia, weight loss, gastrointestinal bleeding, bowel obstruction, or a palpable abdominal mass (10). The most frequent symptom in our study was abdominal pain, followed by palpable abdominal mass.

Concerning *mortality and morbidity,* 10–30% of GISTs are malignant. The risk of malignancy increases with the extragastric location, a size greater than 5 cm, extension into the adjacent organs, and more than one mitosis per 50 high-power fields (1).

Survival rates in case of malignant GISTs are 69% at 1 year, 38-44% at 3 years, and 29-35% at 5 years. Of the patients who had malignant primary disease and who underwent complete gross resection of the tumor, 40% had recurrence (6).

Macroscopic aspects. GISTs are well-delineated spherical masses. They often project exophytically and extraluminally (Fig.7). They may have overlying mucosal ulceration. Size does not predict benignity (11).

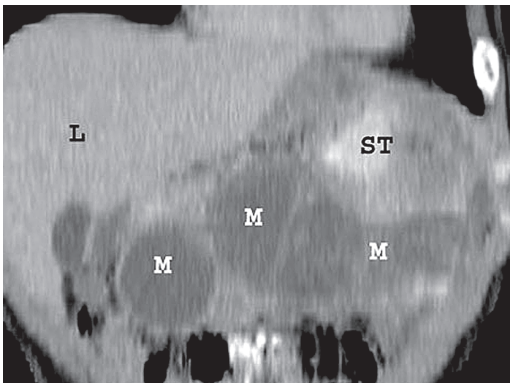

Fig.7 Giant extragastric cystic tumors (M) with compression on the large curvature of the stomach and extension into the splenic hilum - coronal CT reconstruction. Histological diagnosis - malignant gastric GIST.

In our patients, GIST tumors were predominantly extraluminal (n=13), only two were endoluminal. The relationship of the primary tumor to the GI wall could not be categorized in 2 cases. The predominance of large primary tumor size, heterogeneous enhancement and central necrosis reflects the tendency toward malignant GISTs in our series.

Imaging studies. An abdominal CT scan must be done before surgery in order to exclude liver or peritoneal metastases and to evaluate the extension of the primary tumor. As most GISTs have an exophytic growth CT is more useful than endoscopy and barium studies to evaluate the real size of the tumor and its extension (18,19). The CT aspects of GIST (description and tumoral extension) were similar to the intraoperatory findings, with a concordance between the CT features and macroscopic aspects of resecated GIST in 86.6% of cases.

CT is also sensitive for the detection of metastatic liver, peritoneal, lung, and bone lesions. Liver metastases can be: hypervascular, cystic multilocular lesions, cystic with fluid-fluid levels (12-15).

The incidence of metastases (liver and peritoneum) at presentation in the largest clinical series of malignant GISTs approached 50% (6.14). In our patients, liver metastases were multiple and large, with central cystic areas.

The liver is the most common metastatic site at both presentation and disease relapse (18,19). Metastases to bone and the lung have been previously described, but they are distinctly uncommon. The incidence of lymph node metastases is very rare (11,14,16). Unlike lymphoma or leiomyosarcoma, lymphadenopathy was not a feature of any of the GISTs in our study, and this was confirmed during surgery. The peritoneal metastases found in our patients were multiple and not calcified. These features help in differentiation from the carcinoid tumors.

In all cases included in our study, we correctly imaged the location, extension, size, contours, structure of the tumors and the presence of hepatic or peritoneal metastases. We did not establish a histological diagnosis of GIST on the basis of imaging findings, at the moment of the CT evaluation.

The imaging diagnosis of malignant GIST can be suggested in the presence of a large, complex, gastric or intestinal mass with liver lesions but without significant lymphadenopathy (8-11,16-18), but the gold standard remains the histological diagnosis. However, transabdominal biopsy is not recommended in potentially resectable cases because of the risk of tumor seeding.

Differential diagnosis is made with leiomyomiomas, which are benign mesenchymal tumors, most commonly located in the esophagus, sharply defined spherical masses with homogeneous or discreet heterogeneous enhancement. Focal calcifications may be present (8).

The differentiation from other primary GI malignancies can be made on the basis of specific findings. Lymphoma diagnosis can be suggested in the presence of a circumferential mural thickening with homogeneous enhancement and/or lymph node enlargement (8). Carcinoids are found in the terminal ileum and excite a desmoplastic reaction (15). Carcinomas produce local infiltration and visceral obstruction, especially in large tumors. Metastases are multifocal masses, in a context of primary known malignancy.

Our study does have some limitations. It was a retrospective study, including a small radiological series of immunohistologically proven GISTs. We confirmed the previously reported CT findings such as presence of heterogeneously enhancing primary and metastatic disease, as well paucity of ascites, absence of adenopathy and bowel obstruction. We did not follow-up the patients regarding outcome, except for two cases of malignant GISTs, who were evaluated by CT 6 months and 1 year after surgery, with development of hepatic metastases (1 case) and peritoneal metastases (1 case).

Conclusions

Imaging studies, especially CT, play an important role not only in the detection and the localization but also in the evaluation of the extension and follow-up of theses tumors. Small GISTs are intraluminal, localized, and well-defined, whereas extensive GISTs are large and hypervascular and may contain cystic and necrotic tumor components combined with an intra-/extraluminal tumor growth. CT diagnosis of malignant GISTs can be suggested in the presence of a large, complex, gastro-intestinal mass, without significant lymphadenopathy. It is difficult to differentiate, using only CT imaging, the GIST from other soft-tissue tumors. In all cases, histological diagnosis is essential and compulsory.

Conflict of interest

None to declare.

References

1.Miettinen M, Lasota J. Gastrointestinal stromal tumors: definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Virchows Archiv 2001; 438: 1–12.

2. Ray-Coquard I, Cesne AL, Blay JY. STI571 and gastro intestinal stromal tumors. Bull Cancer 2001;88:661-662.

3. Pidhorecky I, Cheney RT, Kraybill WG, Gibbs JF. Gastrointestinal stromal tumors: current diagnosis, biologic behavior, and management. Ann Surg Oncol 2000;7:705-712.

4. Strickland L, Letson GD, Muro-Cacho CA. Gastrointestinal stromal tumors. Cancer Control 2001;8:252-261.

5. Demetri GD, Benjamin R, Blanke CD, et al. NCCN task force report: optimal management of patients with gastrointestinal stromal tumors (GIST)-expansion and update of NCCN clinical practice guidelines. J Natl Compr Cancer Netw 2004;2:S1–S26.

6. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg 2000; 231: 51–58.

7. Levine MS. Benign tumors of the stomach and duodenum. In: Gore RM, Levine MS, eds. *Textbook of gastrointestinal imaging.* 2nd ed. Philadelphia, Saunders 2000; 584–587.

8. Koehler RE, Memel DS, Stanley RJ. Gastrointestinal tract. In: Lee JKT, Heiken JP, Sagel SS, Stanley RJ, eds. *Computed body tomography with MRI correlation.* 3rd ed. Philadelphia, Lippincott- Raven, 1998; 649–653.

9. Levine MS, Megibow AJ. Other malignant tumors of the stomach and duodenum. In: Gore RM, Levine MS, eds. *Textbook of gastrointestinal imaging.* 2nd ed. Philadelphia, Saunders, 2000; 645– 648.

10. Sharp RM, Ansel HJ, Keel SB. Best cases from the AFIP: gastrointestinal stromal tumor. Armed Forces Institute of Pathology. Radiographics 2001; 21:1557–1560.

11. 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 2006; 26:481–495.

12. Choi H, Charnsangavej C, de Castro Faria S, et al. CT evaluation of the response of gastrointestinal stromal tumors after imatinib mesylate treatment: a quantitative analysis correlated with FDG PET findings. AJR Am J Roentgenol 2004; 183: 1619–1628.

13. Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Gastrointestinal stromal tumors: radiologic features with pathologic correlation. Radiographics 2003;23:283–304.

14. Burkill GJ, Badran M, Al-Muderis O, et al. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. Radiology 2003;226:527–532.

15.Buckley JA, Fishman EK. CT evaluation of small bowel neoplasms: spectrum of disease. Radiographics 1998; 18:379-392.

16. Shojaku H, Futatsuya R, Seto H, Tajika S, Matsunou H. Malignant gastrointestinal stromal tumor of the small intestine: radiologic-pathologic correlation. Radiat Med 1997; 15:189-192.

17.Hama Y, Okizuka H, Odajima K, Hayakawa M, Kusano S. Gastrointestinal stromal tumor of the rectum. Eur Radiol 2001; 11:216-219.

18. Ghanem N, Altehoefer C, Furtwangler A, et al. Computed tomography in gastrointestinal stromal tumors. Eur Radiol 2003;13: 1669-1678.

19. Sandrasegaran K, Rajesh A, Rushing DA, Rydberg J, Akisik FM, Henley JD. Gastrointestinal stromal tumors: CT and MRI findings. Eur Radiol 2005; 15: 1407-1414.