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New Diagnostic Imaging of Gastointestinal Tumors: A Preliminary Study of Three-dimensional Tumor Structure and Volumetry

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Abstract. *Background: The aim of the present report was to present preliminary results of the pre-operative evaluation of three-dimensional tumor structure and volumetry using three-dimensional computed tomography (3-D CT) and three-dimensional endoscopic ultrasonography (3-D EUS). Materials and Methods: Diagnostic imaging was performed for 2 patients (one with gastric cancer, one with a rectal tumor) using virtual endoscopy, 3-D CT for the patient with gastric cancer and 3-D EUS for the patient with the rectal tumor, for the pre-operative evaluation of tumor structure and volumetry. Computer-generated image analysis of resected tumors was also performed. Results: The gastric tumor was successfully visualized using 3-D CT and the rectal tumor was successfully visualized using 3-D EUS. The values obtained for volume of the stomach tumor, calculated using 3-D CT and resected materials, were 15.1 cm^3 and 11.4 cm^3, respectively. The values obtained for volume of the rectal tumor, calculated using 3-D EUS and resected materials, were 2.3 cm^3 and 3.9 cm^3, respectively. Conclusion: The present findings demonstrate that clinically useful results can be obtained by using 3-D CT and 3-D EUS for the pre-operative evaluation of 3-D tumor structure and volumetry of gastrointestinal tumors. We expect that further studies of these methods will lead to the establishment of new diagnostic criteria for gastrointestinal tumors based on tumor volume in the near future.*

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Recent advances in diagnostic imaging technology, such as three-dimensional computed tomography (3-D CT), virtual endoscopic images constructed from CT data and three-dimensional endoscopic ultrasonography (3-D EUS), enable clinicians to visualize and recreate normal anatomy and pathological conditions of the gastrointestinal tract in three dimensions (1-6). However, conventional radiography and endoscopy are still the primary methods used for diagnosis of gastrointestinal tumors, and there is a need for further assessment of the clinical utility and data interpretation of the newer diagnostic methods. Also, little is known about the significance of tumor volume in the management of gastrointestinal tumors, and clarification of this issue is necessary for accurate evaluation of the methods used to obtain 3-D tumor structure and volume.

Recently, we developed a new technique for evaluating the 3-D structure and volume of gastrointestinal tumors, in which computer-generated surface rendering is performed on pathological tissue sections of resected specimens (7, 8). Using this technique, we demonstrated that tumor volume is a probable indicator of biological malignancy and prognosis of gastric carcinoma (9, 10). However, this procedure was performed post-operatively. Before this technique can be applied to clinical practice, it is necessary to assess its performance in pre-operative evaluation of tumor structure and volumetry. In this report, preliminary results of the pre-operative evaluation of 3-D tumor structure and volumetry using 3-D CT and 3-D EUS are presented. Also, the possible roles and future prospects of 3-D imaging in the diagnosis of gastrointestinal tumors are discussed.

Materials and Methods

Patients. The subjects were 2 patients (a 61-year-old male patient with gastric cancer, and a 63-year-old female patient with rectal

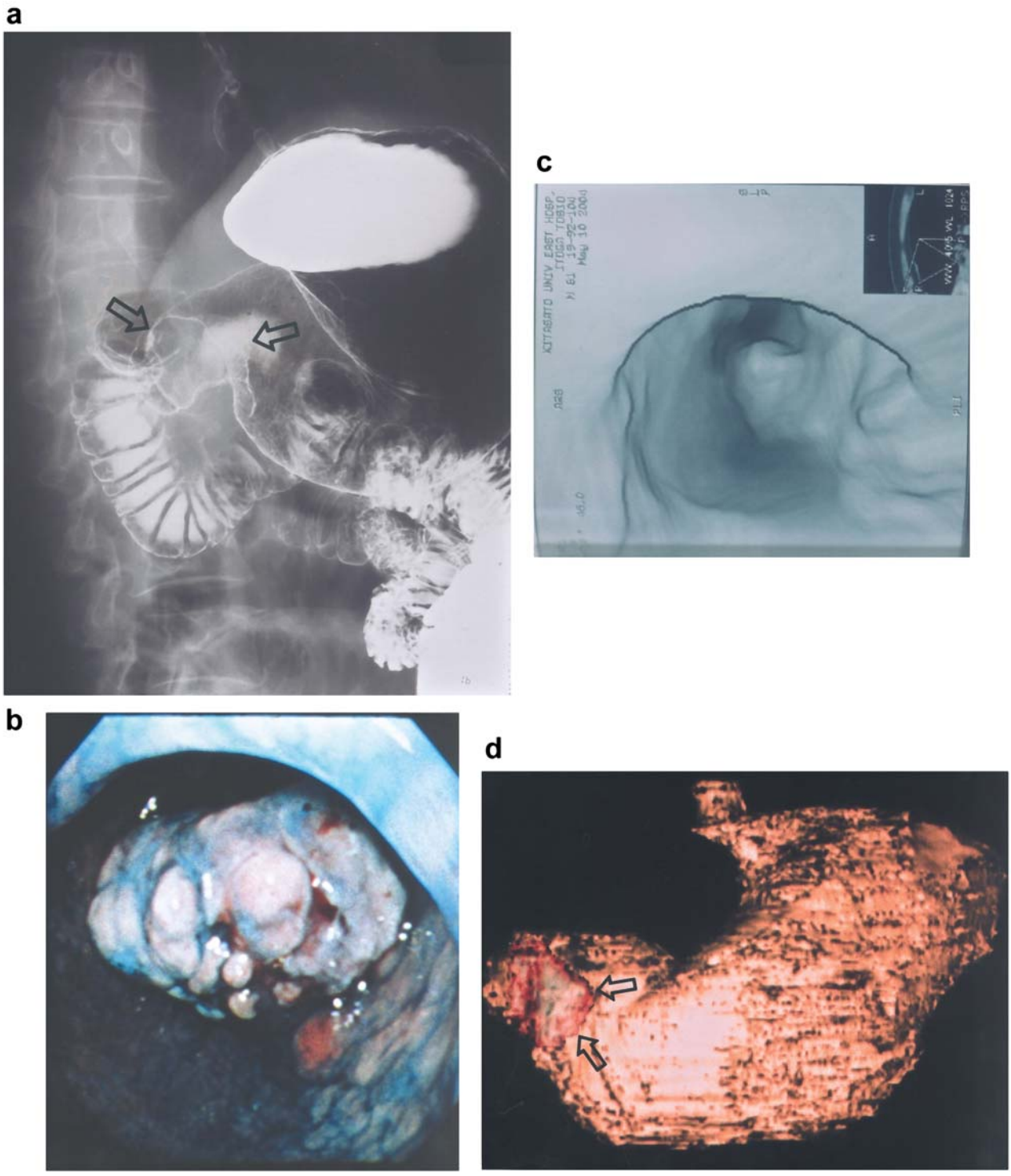

Figure 1. *Pre-operative diagnosis of the 61-year-old male patient with gastric carcinoma.*
a: Gastrointestinal radiography. Radiological examination showed an elevated lesion in the antrum of the stomach (arrow).
b: Gastrointestinal endoscopy. Endoscopic findings of the stomach after indigo carmine dye-dispersed test showed an elevated tumor in the antrum of the stomach.
c: Findings of virtual gastroscopy derived from CT scans.
d: Findings of 3-D CT examination. Orange-colored region is the tumor (arrow; tumor volume, 15.1 cm^3).

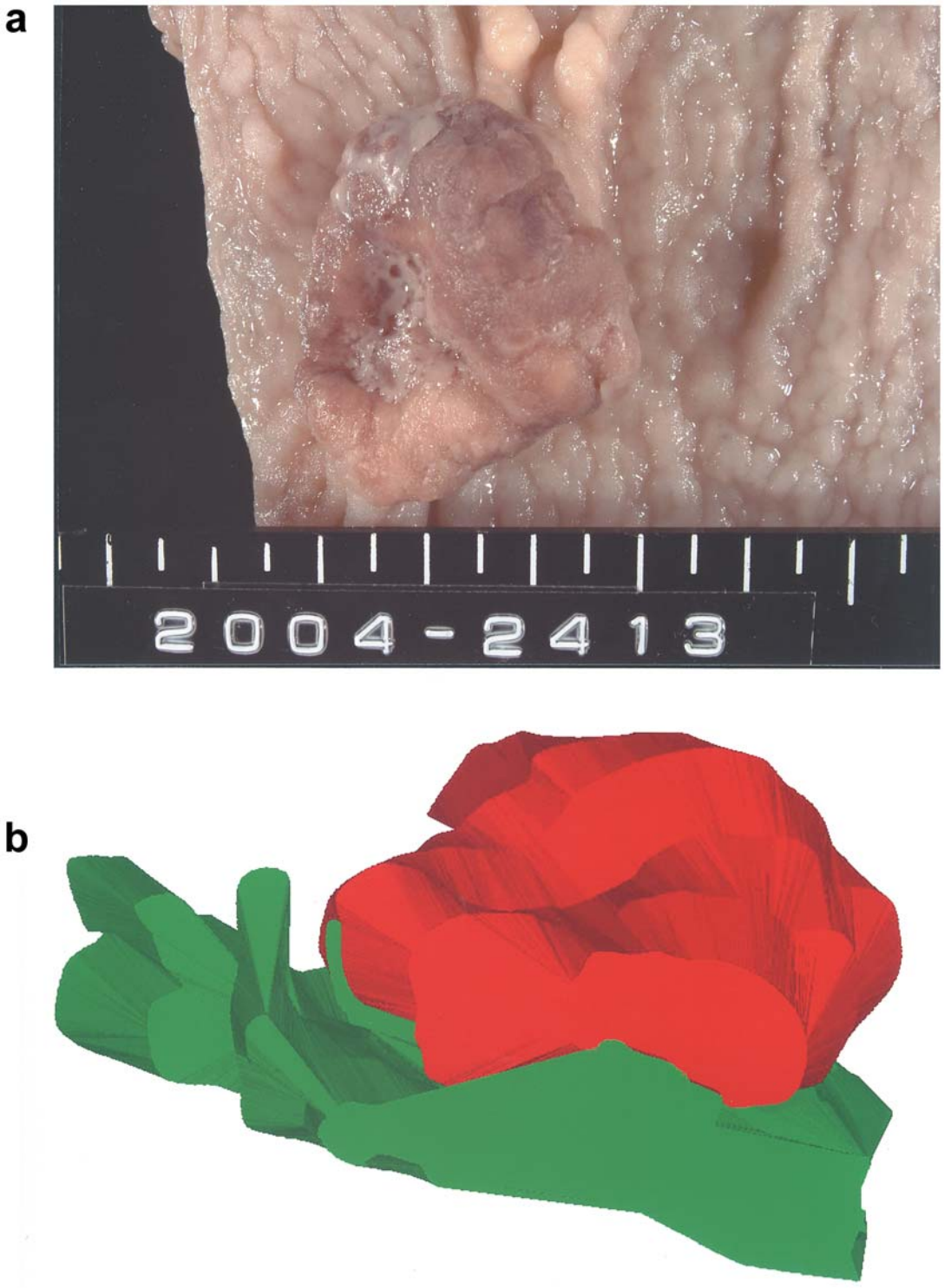

Figure 2. *Macroscopic appearance and 3-D reconstruction of tumor resected from the patient in Figure 1.*
a: Fixed specimen of resected tumor. Left margin of the resected specimen corresponds to distal cut end. The elevated tumor was histologically diagnosed as early gastric cancer (papillary adenocarcinoma, submucosal invasion).
b: Computer-generated 3-D image of tumor reconstructed from serial tissue sections (red region, tumor; green region, normal stomach wall).

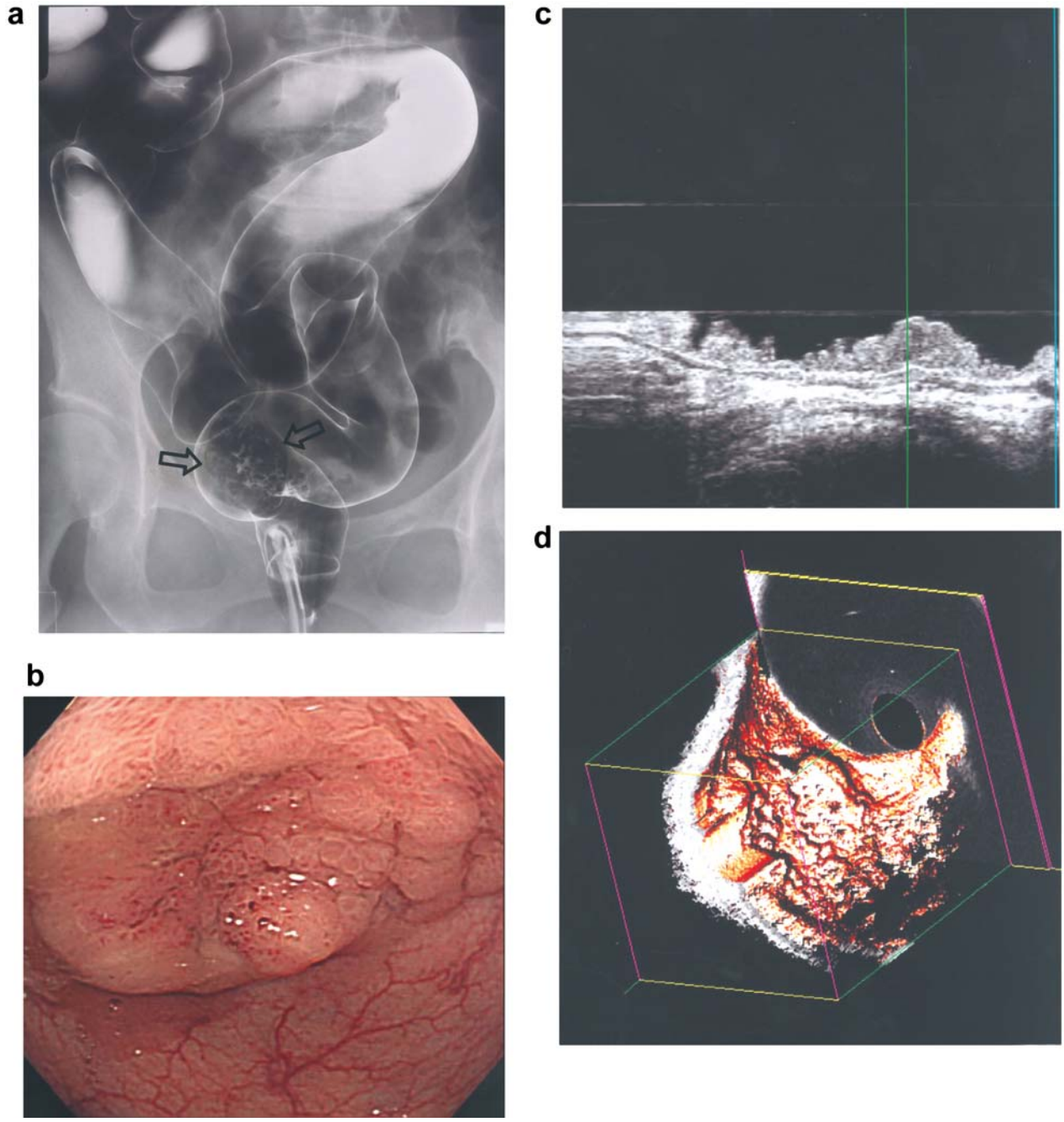

Figure 3. *Pre-operative diagnosis of the 63-year-old female patient with rectal tumor. A flat elevated tumor was found in the rectum (arrow).*
a: Colonography. Radiological examination showed a flat elevated lesion in the rectum.
b: Colonoscopy. Endoscopic findings showed a flat elevated tumor in the rectum.
c: Findings of 2-D endoscopic ultrasonography of the tumor (image of longitudinal section).
d: Findings of 3-D endoscopic ultrasonography. Tumor was visualized as a flat elevated lesion (tumor volume: 2.7 cm^3).

tumor), who underwent surgical resection at the Department of Surgery of Kitasato University East Hospital, Japan.

Pre-operative diagnosis. Conventional gastrointestinal radiography and endoscopic examination were performed for both patients. Upper abdominal 3-D CT was performed for the patient with the gastric tumor. Stomach insufflation was achieved by oral administration of a gas-forming agent (Baros, Horii Co., Japan) immediately before CT scanning, which was performed in the supine position. A single slice CT scanner (HSASG, GE, USA) was

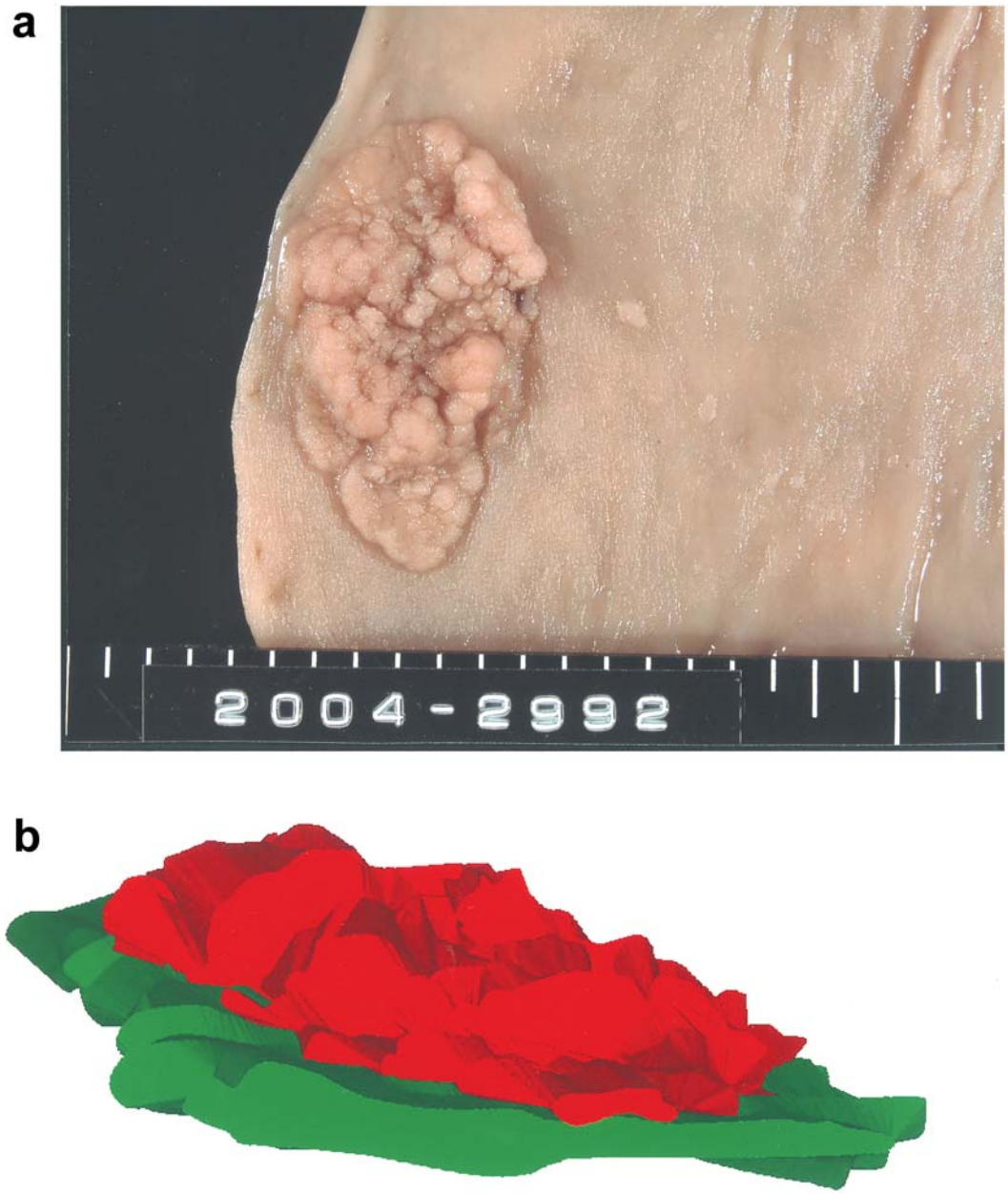

Figure 4. *Macroscopic appearance and 3-D reconstruction of tumor resected from patient in Figure 3.*
a: Fixed specimen of resected tumor. Right margin of the resected specimen is proximal cut end. The flat elevated tumor was histologically diagnosed as tubulo-villous adenoma of the rectum.
b: Computer-generated 3-D image of tumor reconstructed from serial tissue sections (red region, tumor; green region, normal rectal wall).

used with a table speed of 3.75 mm per second, a reconstruction interval of 2.0 mm and scanner settings of 240 mAs and 120 kVp. Image processing (3-D CT and virtual gastroscopy) and calculation of tumor volume were performed using a series of 2-D images, according to the protocol of the software on the work station (Advanced Volume, GE, USA).

3-D EUS was performed for the patient with the rectal tumor. A conventional endoscopic examination was performed using 2-channel flexible colonoscopy (2TQ240, Olympus, Japan). The EUS probe (DP 20-25R, Olympus) was then inserted through a channel of the colonoscope. After the rectum had been filled with de-aereated water, the tumor lesion was scanned continually with a 20-MHz transducer. The data was input into the data files. The 3-D tumor structure was reconstructed with an interval of 0.5 mm. The tumor volume was calculated from a series of 2-D images with an interval of 2.5 mm, according to the protocol of the software on the work station (Endoecho system, Olympus).

Three-dimensional reconstruction of tumors from serial tissue sections by computer graphics. All procedures were performed according to a previously reported protocol (7, 8). Briefly, the material was prepared using conventional histological techniques. Six serial sections containing lesion tissue were cut from the stomach tumor (interval, 5-7 mm; average, 6.6 mm), and 12 sections were cut from the rectal tumor (interval, 3-8 mm; average, 4.1 mm). Computer-generated 3-D reconstruction of the tumors from serial tissue sections and calculation of tumor volume were performed using image editing software (Paint Shop Pro, version 3.2J, Mets Co., Tokyo, Japan) and a computer graphics analysis program (OZ95: Rise Co., Miyagi, Japan).

Results

Pre-operative diagnosis of the gastric tumor is shown in Figure 1. Gastrointestinal radiography and endoscopy identified an elevated tumor in the antrum of the stomach (Figures 1a, 1b). Findings of virtual gastroscopy derived from CT scans and 3-D CT are shown in Figures 1c and 1d, respectively. The 3-D tumor structure was visualized and a tumor volume of 15.1 cm^3 was obtained. Distal gastrectomy combined with lymph node dissection was performed for this patient. The macroscopic appearance of the fixed specimen and the computer-generated 3-D image of the tumor reconstructed from serial tissue sections are shown in Figures 2a and 2b, respectively. The elevated tumor was histologically diagnosed as early gastric carcinoma (papillary adenocarcinoma, submucosal invasion, no metastasis to lymph nodes), with a tumor volume of 11.4 cm^3.

Pre-operative diagnosis of the rectal tumor is shown in Figure 3. Gastrointestinal radiography and endoscopy identified a flat elevated tumor in the rectum (Figures 3a, 3b). Findings of 2-D (longitudinal section) and 3-D EUS are shown in Figures 3c and 3d, respectively. The 3-D tumor structure was visualized and a tumor volume of 2.3 cm^3 was obtained. Low anterior rectal resection was performed for this patient. The macroscopic appearance of the fixed specimen and the computer-generated 3-D image of the tumor reconstructed from serial tissue sections are shown in Figures 4a and 4b, respectively. The flat elevated tumor was histologically diagnosed as tubulovillous adenoma, with a tumor volume of 3.9 cm^3.

Discussion

Tumor volume appears to be an important indicator of the biological malignancy of solid tumors. Although gastrointestinal radiography and endoscopic examination are now commonly available for the diagnosis of gastrointestinal tumors, these methods are not well suited to visualization of the 3-D shape of tumors or for calculating the volume of tumors. In addition, the significance of tumor volume is not well understood, and exact diagnosis of metastasis to lymph nodes is generally difficult for such tumors. Consequently, the depth of invasion, which is an important factor in the staging systems in current use (11, 12), has generally been used as the key factor in pre-operative gastrointestinal tumor staging. However, tumor depth is not always accurately diagnosed, even when EUS is used, and diagnostic accuracy sometimes depends on the skill of the examiner (13, 14). Thus, diagnosis of gastrointestinal tumors on the basis of surface morphology and 2-D expansion of the lesion is currently performed using subjective judgements. It may be possible to make diagnosis more objective if the tumor volume can be calculated routinely before surgery, and if that correlates well with tumor progression and true tumor size.

There have been many studies of volume measurement of normal organs or tumors using CT or US (15-20). There have been few studies of calculation of the volume of gastrointestinal tumors, due to the poor understanding of its clinical significance. However, in a recent study in which the volume of gastrointestinal tumors was evaluated using 3-D EUS, this procedure was shown to provide accurate values of tumor volume (21). In the present study, we found that 3-D CT and 3-D EUS can provide accurate 3-D reconstruction and volumetry of gastric and rectal tumors, suggesting that these methods have potential for clinical use in the pre-operative evaluation of 3-D tumor structure and volume. However, the present findings also show that tumor volume differed between pre-operative and final (using resected material) calculations. Further studies with a large numbers of cases are needed to assess the clinical significance of pre-operative tumor volumetry and to determine the diagnostic accuracy of these methods in practical applications.

In a previous study of tumor volumetry of resected materials, we found that tumor staging based on volume may have advantages over conventional staging systems for gastric cancer (22). Current staging systems for gastrointestinal tumors, which are based on tumor depth, lymph node metastasis and distant metastasis (11, 12), are very complicated and are easily affected by the extent of surgical resection (23). Thus, a new staging system based on tumor volume may lead to changes in treatment strategy. We speculate that further research into the use of 3-D CT and 3-D EUS for measurement of the volume of gastrointestinal tumors will lead to the establishment of new diagnostic criteria for gastrointestinal tumors based on tumor volume in the near future.

References

1 Ogata I, Komohara Y, Yamashita Y, Mitsuzaki K, Takahashi M and Ogawa M: CT evaluation of gastric lesions with three-dimensional display and interactive virtual endoscopy: comparison with conventional barium study and endoscopy. Am J Roentgenol *172(5)*: 1263-1270, 1999.

2 Yoshino J, Nakazawa S, Inui K, Katoh Y, Wakabayashi T, Okushima T, Kobayashi T and Watanabe S: Surface-rendering imaging of gastrointestinal lesions by three-dimensional endoscopic ultrasonography. Endoscopy *31(7)*: 541-545, 1999.
3 Bhandari S, Shim CS, Kim LH, Jung IS, Cho JY, Lee JS, Lee MS and Kim BS: Usefulness of three-dimensional, multidetector row CT (virtual endoscopy and multiplanar reconstruction) in the evaluation of gastric cancer: a comparison with conventional endoscopy, EUS, and histopathology. Gastrointest Endosc *59(6)*: 619-626, 2004.
4 Christensen AF, Nielsen MB, Engelholm SA, Roed H, Svendsen LB and Christensen H: Three-dimensional anal endosonography may improve staging of anal cancer compared with two-dimensional endosonography. Dis Colon Rectum *47(3)*: 341-345, 2004.
5 Johnson DC, Harmsen WS, Wilson LA, MacCarty RL, Welch TJ, Ilstrup DM and Ahlquist DA: Prospective blinded evaluation of computer tomographic colonography for screen detection of colorectal polyps. Gastroenterology *125*: 311-319, 2003.
6 Pickhardt PJ, Choi R, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, Wong RK, Nugent PA, Mysliwiec PA and Schindler WR: Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. New Eng J Med *349*: 2191-2200, 2003.
7 Kikuchi S, Hiki Y, Sakakibara Y, Kakita A and Kuwao S: Measuring the tumor volume of gastric carcinoma by computer image analysis: clinical significance. World J Surg *24*: 603-607, 2000.
8 Kikuchi S, Matsuzaki H, Kondo K, Ohtani Y, Ihara A, Hiki Y, Kakita A and Kuwao S: Three-dimensional reconstruction of colorectal tumors from serial tissue sections by computer graphics: a preliminary study. Hepatogastroenterolory *47*: 669-671, 2000.
9 Kikuchi S, Sakuramoto S, Kobayashi N, Shimao H, Sakakibara Y, Sato K and Kakita A: Tumor volumetry: proposal of a new concept to predict lymph node metastasis in early gastric cancer. Anticancer Res *20*: 3669-3674, 2000.
10 Kikuchi S, Hiki Y, Shimao H, Sakakibara Y and Kakita A: Tumor volumetry: a novel prognostic factor in patients who undergo curative resection for gastric cancer. Langenbeck's Arch Surg *385*: 225-228, 2000.
11 Sobin LH, Wittekind C: TNM Classification of Malignant Tumors (6th ed.). New York, Wiley and Sons, pp. 57-80, 2002.
12 Japanese Research Society for Gastric Cancer: Japanese Classification of Gastric Carcinoma (1st English ed.). Tokyo, Kanehara, pp. 1-71, 1995.
13 Kida M, Tanabe M, Watanabe M, Kokutou I, Kondou I, Yamada Y, Sakaguchi T and Saigenji K: Staging of gastric cancer with endoscopic ultrasonography and endoscopic mucosal resection. Endoscopy *30*: A64-A68, 1998.
14 Meenan J, Anderson S, Tsang S, Reffitt D, Prasad P and Doig L: Training in radial EUS: what is the best approach and is there a role for the nurse endoscopist? Endoscopy *35(12)*: 1020-1023, 2003.
15 Wheatley JM, Rosenfield NS, Heller G, Feldstein D and LaQuaglia MP: Validation of a technique of computer-aided tumor volume determination. J Surg Res *59(6)*: 621-626, 1995.
16 De Odorico I, Spaulding KA, Pretorius DH, Lev-Toaff AS, Bailey TB and Nelson TR: Normal splenic volumes estimated using three-dimensional ultrasonography. J Ultrasound Med *18(3)*: 231-236, 1999.
17 Lin XZ, Chang TM, Tsai HM, Sun YN, Sheu BS and Jen CM: Liver, spleen and tumor volume measured by personal computer. Hepatogastroenterology *46(26)*: 838-842, 1999.
18 Sohaib SA, Turner B, Hanson JA, Farquharson M, Oliver RT and Reznek RH: CT assessment of tumour response to treatment: comparison of linear, cross-sectional and volumetric measures of tumour size. Br J Radiol *73(875)*: 1178-1184, 2000.
19 Kim HC, Han MH, Do KH, Kim KH, Choi HJ, Kim AY, Sung MW and Chang KH: Volume of cervical lymph nodes using 3D ultrasonography. Differentiation of metastatic from reactive lymphadenopathy in primary head and neck malignancy. Acta Radiol *43(6)*: 571-574, 2002.
20 Yetter EM, Acosta KB, Olson MC and Blundell K: Estimating splenic volume: sonographic measurements correlated with helical CT determination. Am J Roentgenol *181(6)*: 1615-1620, 2003.
21 Watanabe M, Kida M, Yamada Y and Saigenji K: Measuring tumor volume with three-dimensional endoscopic ultrasonography: an experimental and clinical study. Endoscopy *36(11)*: 976-981, 2004.
22 Kikuchi S, Sakuramoto S, Kobayashi N, Shimao H, Sakakibara Y, Sato K and Kakita A: A new staging system based on tumor volume in gastric cancer. Anticancer Res *21*: 2933-2936, 2001.
23 Bodner BE: Will Rogers and gastric carcinoma. Arch Surg *123*: 1023, 1988.

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