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ORIGINAL ARTICLE

CT gastrography "wall-carving technique" of gastric cancer: impact of contrast enhancement based on layer depth

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Abstract

Purpose Wall-carving technique (WC) is a special volume rendering technique of three-dimensional CT gastrography that can illustrate the enhancement of gastric wall at an arbitrary depth. We conducted the present study to evaluate the impact of contrast enhancement based on layer depth on WC of gastric cancer and to correlate them with pathological findings.

Methods The subjects of this retrospective study consisted of 36 patients with advanced gastric cancer (22 men, 14 women; age range, 39–90 years; median, 67 years) who underwent contrast-enhanced CT before surgery. WC images of arterial phase were divided into first and second layer. Two radiologists in consensus evaluated the contrast enhancement of WC images for each layer and correlated with pathologic factors.

Results Twenty-six (72%) of the gastric cancers showed a well-enhanced lesion in the first layer at the arterial phase on WC images, and 18 (50%) showed a well-enhanced lesion in the second layer. The study of second layers showed that the well-enhanced group had significantly more cases of differentiated type histology and intermediate stroma than the normally to poorly enhanced group ($p = 0.008$ and 0.0026).

Conclusion The contrast enhancement on WC of gastric cancer showed a significant relationship with pathological factors based on layer depth.

Keywords Gastric cancer · Contrast enhancement · Wall carving

Introduction

Computed tomography (CT) has been used for preoperative gastric cancer staging. Multidetector row CT (MDCT) techniques have improved the ability to determine the tumor depth of gastric cancers as well as the nodal involvement and distant metastasis [1–3]. It is generally considered that most gastric cancers show moderate to marked enhancement in the early phase on contrast-enhanced CT [4–6]. However, gastric cancers show diverse CT enhancement patterns based on various pathological factors, including the histological type, differentiation, stroma, and infiltration patterns [7–10]. Komori et al. examined the CT enhancement of gastric cancer, focusing on the superficial layer. They reported that the extent of arterial tumor enhancement at the inner tumor margin appears to vary depending on the extent of tumor angiogenesis and the presence of lymphatic vessel invasion [11]. Tsurumaru et al. investigated the CT enhancement of diffuse-type gastric cancers, and they observed that these cancers tend to demonstrate double layers with a moderately enhanced inner layer and a mildly enhanced outer layer in the arterial phase. The above-cited findings suggested that gastric cancer may show different enhancement patterns by the layer depth on contrast-enhanced CT.

We have developed a special volume rendering CT technique that we named the 'wall-carving (WC) ' technique [12]. Wall carving can illustrate the enhancement of gastric wall at an arbitrary depth at the same viewpoint as that used for optical endoscopy or fluoroscopy. Theoretically,

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the CT enhancement of gastric cancer could be evaluated by layer depth using WC. We conducted the present study to evaluate the contrast enhancement of gastric cancer depending on the layer depth and to correlate these patterns with pathological findings.

Materials and methods

Patients

This retrospective study was approved by our institutional review board, and informed consent was waived. From January 2013 to March 2017, 51 consecutive patients with advanced gastric cancer (≥ T2) treated at our institution were evaluated by gastroscopy and contrast-enhanced CT before surgery. The diagnoses, staging, and treatment were determined according to the Japanese Classification of Gastric Carcinoma (3rd edition) as a reference standard [13]. Patients with esophagogastric junction cancer ($n=9$) were excluded, because WC was technically not available for them. Patients with gastric cancers that were poorly visualized on CT ($n=6$) because of small-sized lesions or poor gastric distension were also excluded. The cases of a final total of 36 patients were analyzed in this study. The patients' clinicopathological characteristics are presented in Table 1.

Table 1 Patients' profile

	($n=36$)
Age (years, median, range)	67 (39–90)
Sex	
Male	22
Female	14
Tumor location	
U (upper third)	10
M (middle third)	20
L (lower third)	6
Size (mm, median, range)	55 (19–87)
Invasion depth	
MP	13
SS	17
SE	6
Pathological stage	
I	7
II	17
III	12

MP muscularis propria, *SS* subserosa, *SE* extra-serosa

CT protocol

CT was performed using an MDCT scanner: the 320-detector-row Aquilion ONE (Canon Medical Systems, Tokyo). After an overnight fast, each patient ingested 5.25 g of an effervescent agent (Baros Effervescent Granules-S; Horii Pharmaceutical Industries, Saitama, Japan) with a small amount of water just before the scanning to achieve gastric pouch distension; this corresponds to the three-dimensional (3D) CT technique of the stomach called 'CT gastrography' [14]. The patient was then given an intramuscular injection of 20 mg of scopolamine (Buscopan; Boehringer Ingelheim, Ingelheim am Rhein, Germany) to suppress peristalsis. The scanning covered the entire stomach during a single breath hold.

The CT scans were performed with a bolus triggered technique; 2 mL/kg of nonionic contrast material (Iopamiron 370; Bayer Health Care, Osaka, Japan) was injected by an automated power injector. The monitoring frequency from 10 s after the contrast injection was 1/s. The trigger threshold was an increase of 100 HU in the descending aorta. The delay from the trigger to the initiation of the scan was 15 s. The portal venous and delayed phases were acquired at 60 s and 240 s, respectively. The scan parameters were as follows: rotation time 0.5 s; section thickness and intervals 0.5 mm; 120 kVp, 200 mAs, and matrix 512 × 512. All CT datasets were transferred to a commercially available workstation equipped with image reconstruction software (Synapse Vincent, Fujifilm, Tokyo).

Volume rendering technique

After the datasets at the arterial phase were transferred to the workstation, they were converted into MPR and VE format using on-board software. In addition to these images, we also reconstructed the WC images to visualize localized tumor enhancement in the gastric wall. The main process of the volume rendering technique for WC is the extraction of volumetric data in the gastric wall at an arbitrary depth in the layer parallel to the air–mucosal interface. Since the gastric lumen was filled with gas, an air-filled gastric lumen was easily removed from the original source data at a threshold of − 150 HU (which is less than the attenuation of fat) in a negative gradient display.

Next, the non-distended pure gastric lumen (0 voxels) and the digitally distended gastric lumen at an arbitrary number of voxels (e.g., two, four, or six voxels) were each selected on the workstation and removed from the respective original 3D datasets to prepare the different range-expanded masks. The volumetric data of the gastric wall at an arbitrary depth were reconstructed using the image

subtraction technique from two different range-expanded masks. The maximal digital expansion was defined as six voxels (3.75 mm) from the air–mucosal tissue interface of the stomach on the basis of an estimated thickness of the normal gastric wall of approx. 3–4 mm [12].

We selected objects at a depth of 0–2 voxels (0–1.25 mm) and a depth of 2–4 voxels (1.25–2.50 mm) as the first and second layer for the purpose of this study. Object at a depth of more than four voxels were thought to be inappropriate according to our experience for the purpose of this study. These volumetric datasets were adjusted to a conventional abdominal window (level 40–60 HU; width 300–400 HU) in a positive gradient to visualize localized tumor enhancement in the gastric wall (Figs. 1, 2).

CT image analysis

The CT images were interpreted by consensus by two gastrointestinal abdominal radiologists with 11 and 20 years of experience in gastrointestinal imaging using optical endoscopic and/or fluoroscopic findings as a reference. Both readers were blinded to all clinical and pathological data except for the endoscopic and/or fluoroscopic findings. The radiologists reviewed the virtual endoscopy and transparency rendering images, and they determined the localization of the gastric lesion. They then switched the images to WC mode and subjectively evaluated the contrast enhancement of the first and second layers of the tumors. The contrast enhancement was defined as well or normally to poorly enhanced when the enhancement was higher or equal to or lower than that of the adjacent normal mucosa.

Pathological findings

All pathological specimens were evaluated by experienced pathologists according to the Japanese Classification of Gastric Carcinoma (3rd edition) as follows. The histological types were classified as the differentiated type (well or moderately differentiated or papillary adenocarcinomas) or the undifferentiated type (poorly differentiated adenocarcinoma or signet-ring cell carcinomas). The cancer stromal volumes were classified into three categories: (1) the medullary type (med), with scanty stroma; (2) the scirrhous type (sci), with abundant stroma; and (3) the intermediate type (int), in which the quantity of stroma is intermediate between the medullary and scirrhous types.

The patterns of tumor infiltration (INF) into the surrounding tissues were also classified into three categories, as follows. (1) INFa: the tumor displays expanding growth with a distinct border from the surrounding tissue; (2) INFb: the tumor shows an intermediate pattern between INFa and INFc; and (3) INFc: the tumor displays infiltrative growth with no distinct border with the surrounding tissue. Capillary invasion was subdivided into lymphatic invasion (ly) and venous invasion (v). Lymphatic invasion was classified as ly0: no lymphatic invasion; ly1: minimal lymphatic invasion; ly2: moderate lymphatic invasion; and ly3: marked lymphatic invasion. The venous invasion was classified as v0: no venous invasion; v1: minimal venous invasion; v2: moderate venous invasion; and v3: marked venous invasion [13].

Statistical analysis

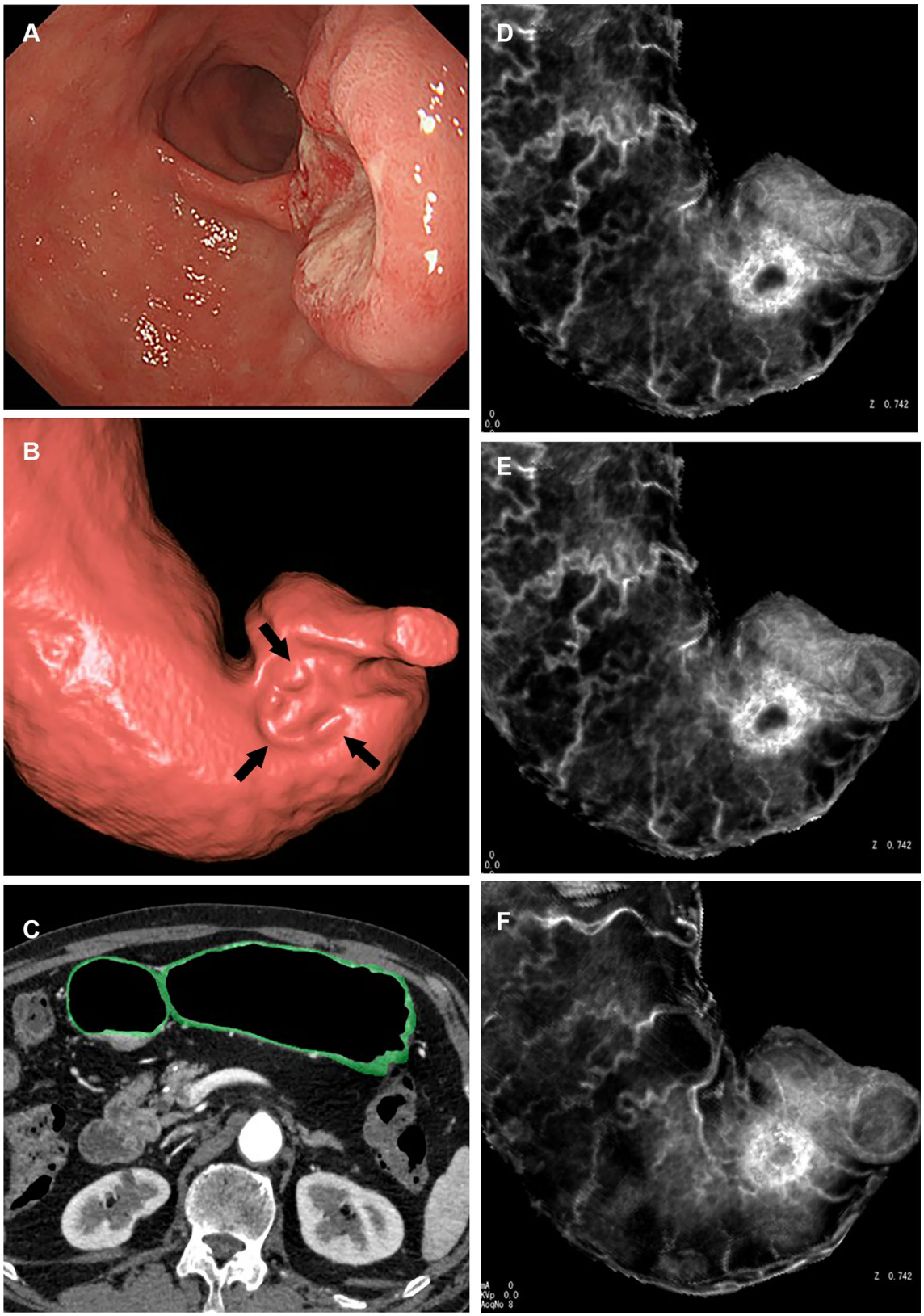
We compared the pathological factors of the well-enhanced group and the normally to poorly enhanced group for the first layer and second layer, respectively. The continuous and categoric variables were examined by Wilcoxon rank sum test and X^2 test or Fisher's exact test. These variables included tumor size (maximum length), gross type (1, 2, 3), invasion depth (muscularis propria, subserosa, extraserosa), histological type (differentiated, undifferentiated), stroma (med, int, sci), INF (a, b, c), lymphatic invasion (present, absent), venous vessel invasion (present, absent), and lymph node metastasis (present, absent). Differences with p values < 0.05 were accepted as significant. Statistical analyses were performed using SPSS 21.0 for Windows software (SPSS, Chicago, IL).

Results

According to the radiologists' subjective analyses, the study sample was classified into well-enhanced tumors in 26 (72%) patients and normally to poorly enhanced tumors in 10 (28%) patients based on the contrast enhancement of the first layer, and the sample was classified as well enhanced in 18 (50%) patients and normally to poorly enhanced in 18 (50%) patients based on the contrast enhancement of the second layer. The examinations of the first layers revealed no significant differences between the two groups. The examinations of the second layers showed that the well-enhanced group had significantly more cases of differentiated type histology and intermediate stroma than the normally to poorly enhanced group ($p = 0.008$ and 0.0026). The other variables had no significant correlation with the degree of contrast enhancement (Tables 2 and 3). Examples of the CT images are shown in Figs. 1 and 2.

Discussion

The results of our present retrospective analyses demonstrated that 72% of the gastric cancers (26 of the 36 cases) showed a well-enhanced lesion compared to the adjacent normal mucosa in the first layer at the arterial phase on WC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◂**Fig. 1** Advanced gastric cancer in a 70-year-old man. Pathological result after surgery confirmed it as histologically well-differentiated adenocarcinoma, MP, int, INFb, ly0, v0. Lymph node metastasis was positive. **a**, **b** Endoscopy and CT gastrography (transparency rendering) showed type 2 cancer in the posterior wall of the gastric antrum (arrows). **c**, **d** The first layer on WC image (selected mask is highlighted in green on axial image **c** shows good enhancement compared to the adjacent normal mucosa except for central necrosis. **e**, **f** The second layer on the WC image also shows good enhancement

images. In general, the greatest angiogenesis is found at the tumor surface. As a tumor grows, its central portion becomes relatively hypovascular and eventually dies by apoptosis and necrosis [15]. In advanced gastric cancer, dynamic contrast-enhanced imaging with multiplanar reconstruction (MPR) shows that most well-enhanced advanced gastric cancers have a thickened gastric wall and undergo gradational inner-to-outer marked transmural enhancement from the arterial phase to the delayed phase [1].

Komori et al. [11] investigated the relationship between the arterial enhancement of the superficial layer and pathological and prognostic factors of gastric cancer, and they reported that the arterial tumor enhancement was correlated with both the microvessel density and lymphatic vessel invasion. Lymphatic vessel or lymphovascular invasion (defined as tumor cells' spread through the lymphatic vessels) has shown a significant relationship with the lymph node metastasis of gastric cancer [16–18]. In the present study, we observed that the arterial enhancement of the first layer was not significantly correlated with lymph node metastasis or with lymphatic vessel invasion. This discrepancy is probably due to differences in evaluation methods between the studies. Komori et al. calculated the tumor-to-normal enhancement ratio (TNR) by measuring CT attenuation values, and they divided their study sample into high- and low-TNR groups based on the mean TNR. We subjectively evaluated the contrast enhancement by comparing it with that of the adjacent normal mucosa.

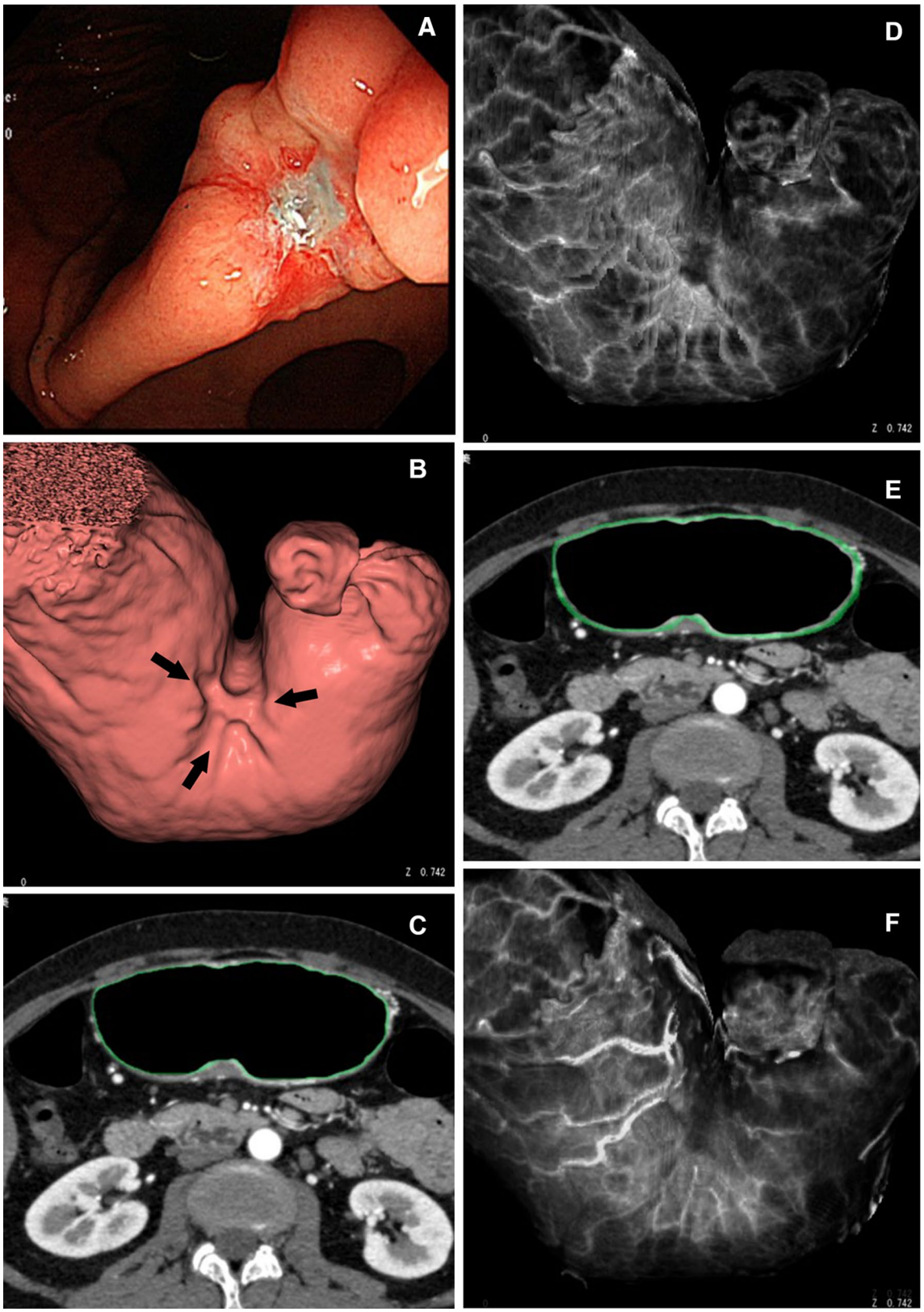
The results of our analyses revealed that 18 (50%) cases showed a well-enhanced lesion and 18 (50%) cases showed a normally to poorly enhanced lesion in the comparison with adjacent normal mucosa in the second layer at the arterial phase on WC images. Our findings also showed that the well-enhanced lesions had a significant relationship with the histologically differentiated type and intermediate tumor stroma, indicating that the gastric cancers with a well-enhanced second layer had smaller amounts of stroma compared to the gastric cancers with a normally to poorly enhanced second layer. Other parameters including the histological type had no correlation with the contrast enhancement in the second layer.

A few studies have investigated the relationship between CT enhancement patterns and some histological features of gastric cancer. One of those studies evaluated gastric cancers in cross-sectional images subjectively or objectively by placing regions of interest (ROIs) in several parts of the tumor or covering the entire tumor [7–9]. We speculate that the contrast enhancement of those ROIs corresponds to that of the second layer of the lesions examined in the present study, because the authors of the above study did not consider the concept of a superficial enhancement of gastric cancer on contrast-enhanced CT. According to their results, histologically undifferentiated-type gastric cancers (including signet-ring cell carcinoma) shows gradual enhancement peaking in a later phase [7]. Those authors also suggested that the CT enhancement pattern of gastric cancer would be based on the degree of intratumoral fibrosis, because most of the signet-ring cell carcinomas tended to show diffusely infiltrative growth of malignant cell groups intermingled with immature and mature fibrosis [19]. Tsurumaru et al. [20] reported that most of the early gastric cancers with ulceration composed of peritumoral fibrosis demonstrated weak enhancement in the portal phase, with gradual enhancement on the delayed phase on triphasic contrast-enhanced CT; they suggested that the underlying mechanisms are related to peritumoral fibrosis.

The use of our new WC technique can illustrate the enhancement of gastric wall at an arbitrary depth at the same viewpoint as optical endoscopy or fluoroscopy, which can be easily, at a glance, evaluated by interpreters. This is the main advantage of the WC technique. In contrast, conventional axial images, MPR, and other 3D CT modalities such as virtual endoscopy hardly illustrate the enhancement of an entire tumor. This new display method may potentially have another advantage of illustrating tumor component of gastric cancer. Especially, the imaging feature of the second layer on WC that reflects pathological feature of gastric cancer could provide clinically important information, which may cover the pathological diagnosis by endoscopic biopsy that the specimen consisted of only a small amount of gastric tumor tissue. Our study has several limitations. First, it was a single-institution study with a small sample size. Second, the analysis may be less objective because a quantitative analysis for the measurement of CT attenuation values on WC images was not available due to the limited ability of our workstation. Third, we analyzed two layers as a total depth of 0–4 voxels (0–2.50 mm from the air–mucosa interface) of gastric cancer because of limited depth of normal gastric wall. It is not yet known whether this layer was appropriate for the evaluation because the thickness of each of the tumor studied herein varied.

Conclusions

Wall carving (WC), a special technique of volume rendering of CT gastrography, can give a detailed description of the contrast enhancement of gastric wall and cancers at an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◂**Fig. 2** Advanced gastric cancer in a 53-year-old woman. Pathological result after surgery confirmed it as histologically poorly differentiated adenocarcinoma, MP, sci, INFc, ly0, v0. Lymph node metastasis was negative. **a**, **b** Endoscopy and CT gastrography (transparency rendering) showed type 3 cancer in the lesser curvature of the gastric angle (arrows). **c**, **d** The first layer on WC image (selected mask is highlighted in green on axial image **c** shows good enhancement compared to the adjacent normal mucosa except for central necrosis. **e**, **f** The second layer on the WC image also shows poor enhancement

Table 2 First layer

	Well enhanced ($n=26$)	Normally to poorly enhanced ($n=10$)	p values
Size (cm, median, range)	52.5 (19–140)	64 (34–73)	0.663
Gross type			
1	2	1	0.181
2	11	1	
3	13	8	
Invasion depth			
MP	11	2	0.236
SS	5	1	
SE	10	7	
Histological type			
Differentiated	13	5	1.000
Undifferentiated	13	5	
Stroma			
Int	20	7	0.667
Sci	6	3	
INF			
a	1	1	0.427
b	21	6	
c	4	3	
ly			
Positive	14	3	0.199
Negative	12	7	
v			
Positive	4	2	0.739
Negative	22	8	
Lymph node metastasis			
Positive	18	5	0.282
Negative	8	5	

MP muscularis propria, *SS* subserosa, *SE* extra-serosa

arbitrary depth in the layer parallel to the air–mucosal interface. The first "superficial" layer on WC demonstrated good enhancement in most of the gastric cancer cases. In addition, the good enhancement of second "deeper" layer was significantly correlated with a differentiated type histology and intermediate stromal volume.

Table 3 Second layer

	Well enhanced ($n=18$)	Normally to poorly enhanced ($n=18$)	p values
Size (cm, median, range)	55 (25–90)	45 (19–140)	0.571
Gross type			
1	2	1	0.239
2	8	4	
3	8	13	
Depth			
MP	7	6	0.669
SS	2	4	
SE	9	8	
Histology			
Differentiated	13	5	0.008
Undifferentiated	5	13	
Stroma			
Int	16	10	0.026
Sci	2	8	
INF			
a	1	1	0.105
b	16	11	
c	1	6	
Ly			
Positive	9	8	0.738
Negative	9	10	
v			
Positive	3	3	1.000
Negative	15	15	
Lymph node metastasis			
Positive	13	10	0.298
Negative	5	8	

MP muscularis propria, *SS* subserosa, *SE* extra-serosa

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest associated with this manuscript other than that grant.

Ethical approval This study was approved by the institutional review board of our institution.

References

1. Chen CY, Hsu JS, Wu DC, Kang WY, Hsieh JS, Jaw TS, et al. Gastric cancer: preoperative local staging with 3D multi-detector row CT—correlation with surgical and histopathologic results. Radiology. 2007;242(2):472–82.
2. Park HS, Lee JM, Kim SH, Lee JY, Yang HK, Han JK, et al. Three-dimensional MDCT for preoperative local staging of gastric

cancer using gas and water distention methods: a retrospective cohort study. Am J Roentgenol. 2010;195(6):1316–23.
3. Kumano S, Murakami T, Kim T, Hori M, Iannaccone R, Nakata S, et al. T staging of gastric cancer: role of multi-detector row CT. Radiology. 2005;237(3):961–6.
4. Minami M, Kawauchi N, Itai Y, Niki T, Sasaki Y. Gastric tumors: radiologic-pathologic correlation and accuracy of T staging with dynamic CT. Radiology. 1992;185(1):173–8.
5. Cho JS, Kim JK, Rho SM, Lee HY, Jeong HY, Lee CS. Preoperative assessment of gastric carcinoma: value of two-phase dynamic CT with mechanical iv. injection of contrast material. Am J Roentgenol. 1994;163(1):69–75.
6. Kim HS, Han HY, Choi JA, Park CM, Cha IH, Chung KB, et al. Preoperative evaluation of gastric cancer: value of spiral CT during gastric arteriography (CTGA). Abdom Imaging. 2001;26(2):123–30.
7. Lee JH, Park MS, Kim KW, Yu JS, Kim MJ, Yang SW, et al. Advanced gastric carcinoma with signet ring cell carcinoma versus non-signet ring cell carcinoma: differentiation with multidetector CT. J Comput Assist Tomogr. 2006;30(6):880–4.
8. Takao M, Fukuda T, Iwanaga S, Hayashi K, Kusano H, Okudaira S. Gastric cancer: evaluation of triphasic spiral CT and radiologic-pathologic correlation. J Comput Assist Tomogr. 1998;22(2):288–94.
9. Tsurumaru D, Miyasaka M, Muraki T, Nishie A, Asayama Y, Oki E, et al. Histopathologic diversity of gastric cancers: relationship between enhancement pattern on dynamic contrast-enhanced CT and histological type. Eur J Radiol. 2017;97:90–5.
10. Tsurumaru D, Miyasaka M, Muraki T, Asayama Y, Nishie A, Oki E, et al. Diffuse-type gastric cancer: specific enhancement pattern on multiphasic contrast-enhanced computed tomography. Jpn J Radiol. 2017;35(6):289–95.
11. Komori M, Asayama Y, Fujita N, Hiraka K, Tsurumaru D, Kakeji Y, et al. Extent of arterial tumor enhancement measured with preoperative MDCT gastrography is a prognostic factor in advanced gastric cancer after curative resection. Am J Roentgenol. 2013;201(2):W253–W261261.
12. Kawanami S, Komori M, Tsurumaru D, Matsuura S, Nishie A, Honda H. Description of early gastric cancer with wall-carving technique on multidetector computed tomography. Jpn J Radiol. 2011;29(1):76–82.
13. Japanese Gastric Cancer A. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer. 2011;14(2):101–12.
14. Kim HJ, Kim AY, Oh ST, Kim JS, Kim KW, Kim PN, et al. Gastric cancer staging at multi-detector row CT gastrography: comparison of transverse and volumetric CT scanning. Radiology. 2005;236(3):879–85.
15. Miles KA. Tumour angiogenesis and its relation to contrast enhancement on computed tomography: a review. Eur J Radiol. 1999;30(3):198–205.
16. Gao P, Zhou GY, Zhang QH, Xiang L, Zhang SL, Li C, et al. Clinicopathological significance of peritumoral lymphatic vessel density in gastric carcinoma. Cancer Lett. 2008;263(2):223–30.
17. Zhang CD, Ning FL, Zeng XT, Dai DQ. Lymphovascular invasion as a predictor for lymph node metastasis and a prognostic factor in gastric cancer patients under 70 years of age: a retrospective analysis. Int J Surg. 2018;53:214–20.
18. von Rahden BH, Stein HJ, Feith M, Becker K, Siewert JR. Lymphatic vessel invasion as a prognostic factor in patients with primary resected adenocarcinomas of the esophagogastric junction. J Clin Oncol. 2005;23(4):874–9.
19. Lee JK, Glazer HS. Controversy in the MR imaging appearance of fibrosis. Radiology. 1990;177(1):21–2.
20. Tsurumaru D, Miyasaka M, Nishimuta Y, Asayama Y, Nishie A, Kawanami S, et al. Differentiation of early gastric cancer with ulceration and resectable advanced gastric cancer using multiphasic dynamic multidetector CT. Eur Radiol. 2016;26(5):1330–7.