MDCT for Differentiation of Category T1 and T2 Malignant Lesions from Benign Gastric Ulcers

OBJECTIVE. The purpose of this study was to evaluate MDCT parameters for differentiating malignant (category T1 and T2) from benign gastric ulcers and to evaluate the performance characteristics of these predictors with optimal cutoff points determined in receiver operator characteristic analysis.

SUBJECTS AND METHODS. The subjects were 26 patients with gastric cancer (11 with T1 lesions, 15 with T2 lesions) and 26 patients with benign gastric ulcer. MDCT and virtual gastroscopic findings were analyzed according to four qualitative criteria: ulcer shape, base, and margin and changes in adjacent folds. The quantitative criteria ulcer size, thickness of the gastric wall around an ulcer, thickness of the enhanced ulcer base, and enhancement around an ulcer were measured on multiplanar reconstruction images. We calculated the sensitivity and specificity of each quantitative criterion. Receiver operator characteristic analysis was used to identify cutoff points yielding optimal sensitivity and specificity for the diagnosis of gastric cancer.

RESULTS. On virtual gastroscopy, ulcer shape and margin and gastric fold changes had sensitivities of 80.8%, 84.6%, and 90.9% and specificities of 76.9%, 73.1%, and 77.8%, respectively, in the diagnosis of gastric cancer. On multiplanar reconstruction images, thickness of the enhanced ulcer base and enhancement around the ulcer had sensitivities of 80.8% and 73.1% and specificities of 100% and 100%.

CONCLUSION. MDCT combined with virtual gastroscopy and multiplanar reconstruction enhances the morphologic details of gastric ulcers and is a useful way to differentiate malignant (T1 and T2) and benign gastric ulcers.

Patients with benign gastric ulcer are at risk that the ulcer will undergo malignant transformation [1], and the symptoms of benign gastric ulcer are similar to those of gastric cancer [2]. Because the therapeutic outcome of gastric cancer is related to the stage of the disease at diagnosis [2–4], early diagnosis of malignant ulcer therefore is crucial. Unfortunately, the differential diagnosis of malignant and benign gastric ulcers on the basis of macroscopic endoscopic findings can be difficult [5, 6]. Graham et al. [7] reported that as many as 5% of malignant gastric ulcers may grossly appear to be benign. Therefore, it is imperative that all such lesions be evaluated histologically [7]. Acquisition of numerous biopsy specimens from the ulcer margin and base can increase the sensitivity of biopsy in the diagnosis of gastric cancer [7]. Bytzer [8] found that surgically curable cases of early gastric cancer were likely to be missed owing to reliance on appearance and histologic features alone and that follow-up endoscopy with repeated biopsy of unhealed ulcers is essential. However, repeated endoscopy with multiple biopsies is relatively invasive and expensive.

Endoscopic sonography, with its cross-sectional imaging of the gastric wall, is useful for determining the depth of invasion of gastric cancer. The findings, however, are not useful for differentiating malignant from benign gastric tumors [9]. For example, at endoscopic sonography symmetric hypoechoic areas of peptic ulcers resemble hypoechoic areas of cancerous invasion [10].

In a study of the utility of double-contrast upper gastrointestinal radiography for differentiating malignant from benign gastric ulcers, Shindoh et al. [11] found several pitfalls of the technique that allowed gastric cancer to be overlooked. Treichel [12] found that flat cancerous lesions with a diameter less than 1 cm were particularly difficult to detect. In
addition, the radiographic appearance of early gastric cancer sometimes resembles that of benign gastric ulcer [13]. False-negative findings on upper gastrointestinal radiographs have been reported to occur in as many as 50% of cases [14], and the sensitivity in the diagnosis of early gastric cancer can be as low as 14% [15]. Furthermore, lack of cooperation by patients causes a major technical problem with this technique.

Minami et al. [16] considered CT differentiation between benign ulcer and early gastric cancer with ulceration difficult because both entities manifest as lesions with defects of the normal inner layer of the gastric wall. Insko et al. [17] suggested that CT may be useful for differentiating benign gastric lesions from potentially malignant ones. The sensitivity for detection of malignant or potentially malignant gastric lesions was 100%, but the specificity was only 50% in that study. Stabile Janora et al. [18] found that they could not differentiate early gastric cancer from potentially malignant ones. The inclusion criteria were endoscopic finding suggestive of malignant gastric ulcer (n = 68), intractable gastric ulcer not healing after 8 weeks of treatment with proton pump inhibitors (n = 6), and endoscopic finding suggestive of benign gastric ulcer but insufficient to exclude the possibility of malignant gastric ulcer. Twenty-one (91%) of 23 patients who met the third criterion agreed to join the study for further image evaluation.

All patients enrolled underwent an MDCT protocol designed specifically for patients with gastric ulcer. All gastric ulcer patients underwent endoscopic biopsy 2–4 days before CT. The histopathologic results were used as the reference standard. The diagnosis of benign ulcer was confirmed with pathologic results and follow-up findings for more than 6 months. Malignant ulcers were confirmed with pathologic or surgical results or both. In the patients who met the first criterion, 43 T3 or T4 gastric lesions, six T1 lesions, 12 T2 lesions, and seven benign gastric ulcers were confirmed. In the patients who met the second criterion, two T1 and two T2 lesions and two benign gastric ulcers were diagnosed. In the patients who met the third criterion, there were three T1 and one T2 gastric lesions and 17 benign gastric ulcers. To test the performance of MDCT in the diagnosis of relatively early gastric cancer, the 43 patients with T3 or T4 gastric cancer were excluded.

**MDCT Techniques**

CT examinations were performed with a 16-MDCT scanner (Lightspeed H16, GE Healthcare) on patients who had fasted for at least 8 hours. For gastric distention, patients ingested 6 g of gas-producing crystals with 10 mL of water a short time before unenhanced CT and virtual gastroscopy. Patients with insufficient air distention of the stomach were given an additional 3 g of gas-producing crystals. Unenhanced upper abdominal CT scans from the diaphragmatic domes to 2 cm below the lower margin of the air-distended gastric body were obtained at 16 × 1.25 mm collimation, 27.5 mm/s table speed, 250–300 mAs, and 120 kVp. In three cases in which a great deal of residual fluid covered the stomach, the patient shifted to the other side, and additional scanning was performed. All procedures were performed under the guidance of an experienced radiologist.

Image Analysis

Virtual gastroscopic images—Virtual gastroscopic imaging was performed by an experienced abdominal radiologist blinded to endoscopic results, lesion size, and macroscopic features. This observer independently evaluated CT images on the workstation with a navigator tool for virtual gastroscopic images. One en face view, two profile views, and four oblique views around 30–45° of each ulcer were obtained in all cases. Virtual gastroscopic images were independently interpreted by two independent abdominal radiologists. Because endoscopic criteria for benign and malignant gastric ulcers had been well established [12, 13], we followed the criteria used by most endoscopists for virtual gastroscopic images. The following findings were taken to suggest malignant gastric ulcer (Figs. 1 and 2): virtual gastroscopic features of gastric ulcer with an irregular, angulated, or geographic...
shape; uneven base; irregular or asymmetric edges surrounding the ulcer; disruption of the gastric folds reaching the crater edge, clubbing of folds, or fold fusion; or a combination of these findings. In contrast, benign gastric ulcers (Figs. 3 and 4) had a smooth, regular shape; an even base; sharply demarcated or regular rounded edges; converging gastric folds with smooth tapering and radiation; or a combination of these findings. Differences in assessment were resolved by consensus.

**MPR images**—MPR images (3-mm slice thickness) of the ulcers were obtained by the same radiologist who obtained the virtual gastroscopic images. To choose the optimal plane of the ulcers and to avoid partial volume effects on MPR images, two vertical planes around the ulcer were used for unenhanced and contrast-enhanced imaging (Fig. 5).

We developed modified criteria [14, 15] for differentiating malignant ulcers (Fig. 5) from benign ulcers (Fig. 6) on contrast-enhanced MPR images. Our criteria were focused on enhancement patterns and thickness of the gastric wall around the ulcer. To determine the best predictors of an accurate differential diagnosis between benign and malignant ulcers, we quantified ulcer size (maximum diameter of the ulcer in the MPR image), thickness of the gastric wall around the ulcer (maximum length of the ulcer margin vertical to the gastric serosal margin), enhancement of the ulcer base (attenuation of gastric wall, which is vertical to the ulcer base, at the ulcer base), and enhancement around the ulcer on MPR images (maximal difference in periulcer attenuation between enhanced and unenhanced images) in each case (Figs. 7–9). To obtain these measurements, a fifth observer, an abdominal radiologist, selected the optimal MPR image of the ulcer from the images (3-mm slice thickness) of the ulcers obtained by the second radiologist. The measurements were made three times, and the mean of the three measurements was used.

**Statistical Analysis**

In all cases, 95% CIs for sensitivity and specificity were calculated to show variability. Sensitivity and specificity were calculated with qualitative criteria for the diagnosis of malignant gastric ulcer on virtual gastroscopic images. Statistical differences between malignant and benign ulcers on virtual gastroscopic images were analyzed with chi-square and Fisher’s exact tests. The final classification of ulcers as benign or malignant was proved with pathologic evidence.
Receiver operating characteristic curve methods were used to identify cutoff points for each quantitative criterion. This procedure maximized the likelihood of correct identification of malignant gastric ulcers. The cutoff value corresponding to the optimal diagnostic accuracy (defined as the highest sum of the values for sensitivity and specificity) and the area under the curve of the receiver operating characteristic plot were determined for each quantitative criterion obtained with imaging. Significant differences were inferred for a two-tailed \( p < 0.05 \). Statistical analysis was conducted with the program Stata/SE 9.1 (Stata) for Windows (Microsoft).

**Results**

The study population consisted of 26 men and 26 women (mean age, 59 years; range, 31–84 years). Eleven patients had T1 and 15 had T2 gastric lesions, and 26 patients had benign gastric ulcers. In all cases of benign ulcers the histologic findings were eroded or defective layers of the gastric mucosa with variable degrees of inflammation or granulomatous tissue infiltration in the lamina propria. According to standard gastric cancer classification [22], there were 11 differentiated gastric tumors (one papillary, 10 tubular adenocarcinomas) and 15 undifferentiated gastric tumors (nine poorly differentiated adenocarcinomas, six signet ring cell carcinomas) (Fig. 10). All ulcer lesions (52/52) were correctly detected on virtual gastroscopic images.

**Qualitative Criteria for Differentiating Malignant and Benign Gastric Ulcers on Virtual Gastroscopic Images**

Table 1 shows the sensitivity and specificity of each virtual gastroscopic imaging criterion in the detection of malignant gastric ulcers in all patients. In the detection of malignant ulcers, the sensitivity and specificity values were ulcer shape, 80.8% and 76.9%; ulcer margin, 84.6% and 73.1%; associated changes in gastric folds, 90.9% and 77.8%; and ulcer base, 53.9% and 76.9%. In the 32 patients without periulcer gastric folds, the ulcers were located in the antrum \( (n = 26) \) or the gastric angle \( (n = 6) \). There were significant differences between malignant and benign ulcers for each of these variables \( (p < 0.05) \).

**Quantitative Criteria for Differentiating Benign from Malignant Gastric Ulcers on MPR Images**

We calculated sensitivity and specificity values for the utility of each quantitative criterion in accurate differentiation of malignant and benign ulcers. Cutoff values were determined with the maximum sum of sensitivity and specificity (Table 2). The sensitivity and specificity for thickness of the enhanced ulcer base (cutoff value, 0.27 cm) were 80.8% and 100%. The sensitivity and specificity for enhancement around the ulcer...
Our findings suggest that MDCT with 2D MPR and 3D virtual gastroscopic imaging can yield comprehensive information about gastric ulcers. Patients with gastric ulcer conventionally undergo three examinations—gastroscopy, endoscopic sonography, and CT—for the same purpose [23]. In our study, MDCT had results comparable with those of conventional gastroscopy in differentiation of malignant and benign gastric ulcers. The sensitivity was 80.8–90.9% and the specificity 73.1–77.8% on virtual gastroscopic images and the sensitivity 73.1–80.8% and the specificity 100% on MPR images. Our results are comparable with those of optical gastroscopy, which has a sensitivity of 76–84% and a specificity of 90–95% in the diagnosis of malignant gastric ulcer [24–26].

More important is that the high specificity on MPR images may help avoid delay in the treatment of patients with gastric cancer and thus improve their survival rate. In addition, all cases of gastric cancer in our study were in a relatively early stage (T1 or T2 lesions), which is usually more challenging for accurate diagnosis with any imaging technique currently available.

Like conventional gastroscopy, virtual gastroscopy is useful in the detection and evaluation of gastric ulcer. Compared with conventional gastroscopy, virtual gastroscopy can depict most abnormal endoluminal lesions without a limited field of view or blind areas [19]. The results in our study show that ulcer shape and margin on virtual gastroscopic images are accurate differentiating features of most malignant and benign gastric ulcers. In some cases, however, acute benign ulcers with severe per ulcer edema mimic malignant ulcers in terms of ulcer shape and ulcer margin. Conversely, some malignant ulcers mimic benign ulcers in shape and margin owing to a small size and

### Table 1: Sensitivity and Specificity of Qualitative Imaging Criteria for Differentiating Malignant and Benign Gastric Ulcers on Virtual Gastroscopic and Multiplanar Reformatted Images of All Patients (n = 52)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>No. of Patients</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer shape</td>
<td>52</td>
<td>80.8</td>
<td>64.9–96.6</td>
<td>76.9</td>
</tr>
<tr>
<td>Ulcer margin</td>
<td>52</td>
<td>84.6</td>
<td>7.01–99.1</td>
<td>73.1</td>
</tr>
<tr>
<td>Fold changes</td>
<td>20&lt;sup&gt;b&lt;/sup&gt;</td>
<td>90.9</td>
<td>71.9–100.0</td>
<td>77.8</td>
</tr>
<tr>
<td>Ulcer base</td>
<td>52</td>
<td>53.9</td>
<td>33.8–73.9</td>
<td>76.9</td>
</tr>
</tbody>
</table>

<sup>a</sup>Chi-square test.
<sup>b</sup>There were 32 patients without peri ulcer gastric folds.
<sup>c</sup>Fisher’s exact test.

### Table 2: Sensitivity and Specificity of Quantitative Imaging Criteria for Detection of Malignancy of Gastric Ulcers on Multiplanar Reformatted Images of All Patients (n = 52)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>No. of Patients</th>
<th>Cutoff Value</th>
<th>AUC Value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer size (cm)</td>
<td>52</td>
<td>2.28</td>
<td>0.405</td>
<td>7.7</td>
<td>0.0–18.4</td>
</tr>
<tr>
<td>Thickness of gastric wall around ulcer (cm)</td>
<td>52</td>
<td>1.32</td>
<td>0.374</td>
<td>30.8</td>
<td>12.2–49.3</td>
</tr>
<tr>
<td>Thickness of enhanced ulcer base (cm)</td>
<td>52</td>
<td>0.27</td>
<td>0.919</td>
<td>80.8</td>
<td>64.9–96.6</td>
</tr>
<tr>
<td>Enhancement around the ulcer (H)</td>
<td>52</td>
<td>66.0</td>
<td>0.893</td>
<td>73.1</td>
<td>55.3–90.6</td>
</tr>
</tbody>
</table>

Note—AUC = area under the receiver operating characteristic curve.

(cutoff value, 66 H) were 73.1% and 100%. Ulcer size (cutoff value, 2.28 cm) and thickness of the gastric wall around the ulcer (cutoff value, 1.32 cm) did not allow statistically significant differentiation between malignant and benign gastric ulcers (chi-square value, < 3.84; p > 0.05).

### Discussion

Our findings suggest that MDCT with 2D MPR and 3D virtual gastroscopic imaging can yield comprehensive information about gastric ulcers. Patients with gastric ulcer conventionally undergo three examinations—gastroscopy, endoscopic sonography, and...
the presence of minimal peri ulcer edema. Associated change in peri ulcer gastric folds was a useful criterion. Nevertheless, in a distended stomach, ulcers in the antrum and angle are always free of folds. The disadvantage of virtual gastroscopy is its lack of color change at the ulcer base, which can be clearly visualized at conventional gastroscopy. This factor may explain why an uneven ulcer base on virtual gastroscopic images was insufficiently sensitive for differentiating malignant from benign gastric ulcers in our study.

As does endoscopic sonography, MPR imaging provides useful information about the gastric wall, including stratification [16], horizontal extension, and depth of tumor invasion [16, 20]. In our study, the peri ulcer enhancement pattern was a good indicator for differentiating malignant from benign gastric ulcers. To maximize the sensitivity of detecting gastric cancer by depiction of its neovascularity, we selected maximum CT attenuation from three peri ulcers regions during the portal venous phase. This technique may minimize the volume-averaging effects caused by heterogeneous tumor components. In accordance with previous reports [20, 27, 28], our study showed that most malignant gastric ulcers have significantly enhanced tumor parts in the portal venous phase. Benign gastric ulcers, in contrast, exhibited no significant enhancement on contrast-enhanced MPR images [18, 27].

Signet ring cell carcinoma (Fig. 10) is a subtype of undifferentiated gastric cancer. The hypovascularity of this tumor has been reported [29, 30]. In our study, four of six malignant gastric ulcers of signet ring cell carcinoma had no strong enhancement in the tumor areas on contrast-enhanced images. The incidence of neovascularity of gastric signet ring cell carcinomas may be low because this tumor is characteristically of the scirrhous subtype [31] and because a predominant component (> 50%) of isolated carcinoma cells contains mucin [32]. These factors may explain why the criteria enhanced ulcer base and enhancement around the ulcer on MPR images are inadequate for differentiating the malignant gastric ulcer of signet ring cell carcinoma from benign gastric ulcer. On the other hand, ulcer shape and margin on virtual gastroscopic images are proper indicators for differentiating most malignant gastric ulcers of signet ring cell carcinomas from benign gastric ulcers. Therefore, in lesions with malignant-appearing virtual gastroscopic morphologic features but no obvious peri ulcer enhancement, signet ring cell carcinoma should be considered.

In our study, ulcer size and peri ulcer wall thickening showed no significant differences between malignant and benign gastric ulcers, probably because peri ulcer wall thickening can be identified in all benign and malignant ulcers. An unexpected finding was that malignant ulcers did not produce more gastric wall thickening than did benign ulcers. An explanation may be that only subjects with T1 and T2 gastric lesions rather than more advanced adenocarcinomas were enrolled in the study. This limitation can be overcome by use of two additional quantitative criteria on MPR images. For example, in benign ulcers, thickened walls are due to edema, which always has a normal mural enhancement pattern and preservation of wall stratification. On the other hand, peri ulcer wall thickening together with strong enhancement of tumor parts and loss of normal wall stratification is observed in malignant ulcers [18].

On the basis of our findings, we concluded that MDCT combined with virtual gastroscopy and MPR is a promising strategy that combines the features of endoscopic viewing and multiplanar cross-sectional imaging [22]. The technique can be a powerful tool for noninvasive evaluation of both endoluminal morphologic changes and intraluminal and extraluminal information on gastric ulcers. Optical gastroscopy can be difficult to perform on patients who have difficulty swallowing. Virtual gastroscopy is a good alternative diagnostic tool under these circumstances. Furthermore, MDCT with virtual gastroscopy and MPR can assist endoscopists in planning repeated gastroscopic biopsy and should increase the probability of finding malignancy within a gastric ulcer. Findings with this protocol may raise suspicion of malignancy in gastric ulcers with negative biopsy results and suggest repetition of endoscopy sooner than would occur with the conventional approach. In our study, one patient had initial negative histologic results for malignancy, but gastric cancer was suspected at gastroscopy and MDCT. Biopsy repeated 3 days after MDCT showed early gastric cancer. On the other hand, two patients had gastroscopic findings suggesting malignant ulcers, but findings at histologic examination of a biopsy specimen and MDCT were normal. Biopsies repeated 14 days after MDCT and at 6- and 11-month follow-up evaluations confirmed the finding of benign gastric ulcer.

Our study had limitations. First, all CT scans were obtained 2–4 days after endoscopic biopsy, which may raise concern about local inflammation and confounding CT findings. Results of animal studies [33–35], however, have shown that epithelial restitution of injured gastric mucosa can happen within minutes to hours. Therefore, effects on CT images should be limited. Nevertheless, this limitation would not change our results significantly because patients with both malignant and benign gastric ulcers underwent the same protocol. Prospective randomized studies comparing MDCT and gastroscopy are needed to validate the use of our protocol. Second, there was a potential bias due to patient population. Although blinded to the results of endoscopic examinations and histopathologic analyses, the readers were aware of the presence of an ulcer. Thus the ability of MDCT to depict gastric ulcers might have been overestimated. However, the aim of this study was to investigate the utility of MDCT in differentiating malignant from benign gastric ulcers rather than to investigate the detectability of gastric ulcers with MDCT. Third, the virtual gastroscopic reconstruction used in our study was relatively time-consuming. It demanded that well-trained radiologists process a relatively large number of CT images, which may limit wider clinical use.

Although unlike optical endoscopy, MDCT does not show color change or provide the opportunity to perform biopsy, virtual gastroscopy does provide an excellent overview of mucosal change with less restriction than with conventional gastroscopy and allows the operator to measure gastric ulcers with accuracy. MPR images provide useful information about the gastric wall around an ulcer. Furthermore, MPR images provide information not only about intraluminal and extraluminal gastric lesions but also about conditions outside the stomach. These ancillary findings are useful in cancer staging and in differential diagnosis, although they were beyond the scope of this study. In addition, MDCT is less invasive than optical endoscopy. Although CT has not been a routine examination for the detection of gastric ulcer, with continued advances in CT scanners and computer technology, MDCT may play an increasingly important role in the detection of malignant gastric ulcers in patients at high risk and in preoperative cancer staging. Whether use of the technique will translate into improved overall survival among patients with gastric cancer or even cost saving.
MDCT of Gastric Ulcers

is not clear. Randomized double-blind studies with larger patient groups are needed to validate the role of MDCT in the diagnosis of gastric cancer.

Our study showed that MDCT with virtual gastroscopy and MPR shows useful morphologic details and mural enhancement patterns of gastric ulcers, which are valuable for differentiating malignant from benign gastric ulcers. Furthermore, thickening of an enhanced ulcer base is the most important feature in differentiating a malignant ulcer from a benign ulcer. In lesions with a malignant appearance on virtual gastroscopy but without obvious per ulcer enhancement or thickening of an enhanced ulcer base, signet ring cell carcinoma should be considered.

References

23. Kim JH, Eun HW, Goo DE, Shim CS, Auh YH. Imaging of various gastric lesions with 2D MPR and CT gastrography performed with multidetector CT. Radiographics 2006; 26:1101–1116