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OLGA- and OLGIM-based staging of gastritis using narrow-band imaging magnifying endoscopy

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Abstract

Background

As atrophic gastritis and intestinal metaplasia due to *Helicobacter pylori* have been considered risk factors for gastric cancer, it is important to assess their severity. In the West, the operative link for gastritis assessment (OLGA) and operative link for gastric intestinal metaplasia assessment (OLGIM) staging systems based on biopsy have been widely adopted. In Japan, however, narrow-band imaging (NBI)-magnifying endoscopic diagnosis of gastric mucosal inflammation, atrophy, and intestinal metaplasia has been reported to be fairly accurate. Therefore, we investigated the practicality of NBI-magnifying endoscopy (NBI-ME) for gastritis staging.

Methods

We enrolled 55 patients, in whom NBI-ME was used to score the lesser curvature of the antrum (antrum) and the lesser curvature of the lower body (corpus). The NBI-ME score classification was established from images obtained beforehand, and then biopsy specimens taken from the observed areas were scored according to histological findings. The NBI-ME and histology scores were then compared. Furthermore, we assessed the NBI-ME and histology stages using a combination of scores for the antrum and corpus, and divided the stages into two risk groups: low and high. The degree to which the stage assessed by NBI-ME approximated that assessed by histology was then ascertained.

Results

The degree of correspondence between the NBI-ME and histology scores was 69.1% for the antrum and 72.7% for the corpus, and that between the high- and low-risk groups was 89.1%.

Conclusion

Staging of gastritis using NBI-ME approximates that based on histology, and would be a practical alternative to the latter.

Keywords: Gastritis, Magnifying endoscopy, Narrow-band imaging, OLGA, OLGIM

Introduction

Atrophic gastritis and intestinal metaplasia associated with *Helicobacter pylori* are well known risk factors for gastric cancer[1)2)]. In the West, the OLGA (Operative Link for Gastritis Assessment) [3)4)] and OLGIM (Operative Link for Gastric Intestinal Metaplasia assessment) staging systems[5)] have become widely used. Both systems assess the risk for gastric cancer on the basis of several biopsy samples taken from the antrum and corpus. The OLGA staging system is based on the severity and topography of atrophy, whereas the OLGIM staging system is based on the severity and topography of intestinal metaplasia[3)4)5)]. In Japan, on the other hand, narrow-band imaging (NBI)-magnifying endoscopic diagnosis of inflammation, atrophy, and intestinal metaplasia of the gastric mucosa has been reported to be fairly accurate[6-10)]. If the staging of gastritis based on NBI-magnifying endoscopy were to approximate that based on histology of biopsy specimens, it would be as practical as optical biopsy and reduce the work burden of endoscopists, as well as medical costs and procedure time.

The present investigation was designed to determine whether gastritis staging by NBI-magnifying endoscopy is able to approximate that based on biopsy specimens. The main aim of this study was to investigate the degree of correspondence between the scores obtained by NBI-magnifying endoscopy and those obtained by biopsy.

Methods

Study design and setting

This was a cross-sectional study performed at Niigata Prefectural Yoshida Hospital between February and June 2014. This study protocol was approved by the institutional ethics committee.

Participants

We enrolled 55 patients from whom two endoscopists (AS and KY) were able to obtain informed consent in the outpatient department and were not using antithrombotic agents. Other patients who underwent gastric endoscopic examination were not enrolled. The patients had undergone endoscopic examinations for surveillance of gastric cancer with atrophic gastritis (n=16), follow-up for early gastric cancer after endoscopic submucosal dissection (ESD) (n=22), close examination of early gastric cancer before ESD (n=2), or health screening (n=15). The patients' primary diseases were gastric cancer (n=24), peptic ulcer (n=13), or other diseases (n=18). Patients with autoimmune gastritis, previous gastrectomy, or severe hepatorenal dysfunction were excluded.

Forty-eight patients had been examined for *H. pylori*, and 7 had not. The presence of *H. pylori* infection was determined by at least one of the following methods: the ^{13}C-urea breath test (UBIT, Otsuka, Tokushima, Japan), the *H. pylori* stool antigen test (Premier Platinum HpSA; Meridian, Cincinnati, OH, USA), the serum

immunoglobulin (Ig) G antibody test (E-plate, Eiken, Tokyo, Japan), and biopsy culture. Fourteen patients were *H. pylori*-positive and 34 were negative. Among the patients who were *H. pylori*-negative, 28 had undergone *H. pylori* eradication. All of the remaining 6 *H. pylori*-negative patients had atrophic gastritis. Therefore we considered that *H. pylori* infection had resolved naturally in some of the latter patients (Table 1).

Endoscopic procedures

The instruments used in the present study were a magnifying videoendoscope and an electronic endoscopic system (GIF-H260Z and EVIS LUCERA Spectum; Olympus Medical Systems, Tokyo, Japan). All of the endoscopic examinations were performed by two expert endoscopists (AS and KY), who observed the lesser curvature of the antrum (2 cm from the pyloric ring measured using a visual scale) and the lesser curvature of the lower body (4 cm from the angle measured using a visual scale) by NBI-magnifying endoscopy. The dominant mucosal patterns in each of the two areas were chosen, and photographs of them were taken after thorough observation for detection of any lesions. Using biopsy forceps, one biopsy sample was then taken from each of these two areas that had been photographed. The NBI-magnifying endoscopy score classification was based on established magnifying endoscopy criteria for gastritis[6-10] NBI-magnifying endoscopic scoring was performed by one endoscopist, and then later another endoscopist performed scoring on the basis of the pictures

obtained. The concordance of the scores was then confirmed. If the opinions of the endoscopists differed, a final judgment was arrived at by consensus following discussion of each individual case.

NBI-magnifying endoscopy score

Antrum

NBI-magnifying endoscopy scores for the lesser curvature of the antrum were classified into four grades, as detailed below, according to the severity of intestinal metaplasia based on the OLGIM staging system. We diagnosed mucosa showing at least one of either a light blue crest (LBC) [11] or a white opaque substance (WOS) [12)13)] (Figure 1) by NBI-magnifying endoscopy as intestinal metaplasia. LBC indicates a fine, blue-white line on the crests of the epithelial surface and gyri[11], whereas WOS indicates a white opaque substance appearing on part of the surface [12)13)]. Both have been reported to be strongly related to intestinal metaplasia[11)12)13)].

Score 0: Neither LBC nor WOS evident in the picture; score 1: LBC and/or WOS visible in less than one third of the picture; score 2: LBC and/or WOS visible in one third or more and less than half of the picture; score 3: LBC and/or WOS visible in half or more of the picture (Figure 2A).

Corpus

NBI-magnifying endoscopy scores for the lesser curvature of the lower body were

classified into the following four grades according to the severity of atrophy and intestinal metaplasia based on a combination of the OLGA and OLGIM staging systems.

Score 0: A mucosal pattern consisting of round pits, indicating normal oxyntic glands without atrophy[6-10]; score 1: A mucosal pattern consisting of oval or slit-like pits, indicating non-metaplastic atrophy of oxyntic glands[6-10]; score 2: A tubular or granular mucosal pattern without LBC and WOS, indicating pseudopyloric gland metaplasia[6-10]; score 3: A tubular or granular mucosal pattern with LBC or WOS, indicating intestinal metaplasia with/without pseudopyloric gland metaplasia[6-13] (Figure 2B).

Histological score

The biopsy samples were fixed in formalin and labeled according to their topographic site (antrum or corpus). They were adequately separated and distinguished during the paraffin-embedding procedure so that the identity of each was retained. Histologic sections were then obtained from each paraffin block and stained with hematoxylin and eosin. Histological scoring was performed by an expert pathologist (SN), blinded to any clinical information. In order to investigate the degree of correspondence between the scores obtained by NBI-magnifying endoscopy and those obtained by biopsy, histological scoring was performed using a histology-based system that incorporated the combined OLGA and OLGIM staging systems, which differed

slightly from the original ones.

Antrum

Histological scores for the lesser curvature of the antrum were classified into the following four grades according to the severity of intestinal metaplasia based on the OLGIM staging system. Score 0: No intestinal metaplasia in the biopsy specimen; score 1: Intestinal metaplasia in less than one third of the biopsy specimen; score 2: Intestinal metaplasia in one third or more and less than half of the biopsy specimen; score 3: Intestinal metaplasia in half or more of the biopsy specimen (Figure 3A).

Corpus

Histological scores for the lesser curvature of the lower body were classified into the following four grades according to the severity of atrophy and intestinal metaplasia based on the combined OLGA and OLGIM staging systems.

Score 0: Normal oxyntic glands without atrophy; score 1: Non-metaplastic atrophy in oxyntic glands; score 2: Pseudopyloric gland metaplasia; score 3: Intestinal metaplasia with/without pseudopyloric gland metaplasia (Figure 3B).

Evaluation of the degree of correspondence between the scores obtained by NBI-magnifying endoscopy and those obtained from biopsy specimens

We investigated the distribution of the scores obtained by NBI-magnifying endoscopy and those obtained from biopsy specimens in the antrum and corpus, and also assessed the degree of correspondence between them.

Evaluation of the degree of correspondence between low- and high-risk groups determined by NBI-magnifying endoscopy and from biopsy specimens

We tabulated the scores obtained by NBI-magnifying endoscopy and from biopsy specimens based on both the OLGA and OLGIM staging systems (Figure 4) and obtained the gastritis stages determined using both approaches. We then divided the stages into two groups – low risk (Stages 0, I, and II) and high risk (Stages III and IV) – and assessed the degree of correspondence between NBI-magnifying endoscopy and biopsy in each group.

Distribution of gastritis stages in patients with gastric cancer determined by NBI-magnifying endoscopy and biopsy

We assessed the distribution of gastritis stages in patients with gastric cancer, peptic ulcer and other diseases, and then evaluated whether the cluster of gastric cancer patients in the high risk group (stage III and IV) determined by NBI-magnifying endoscopy was similar to that determined on the basis of histology.

Results

Table 2 shows the distribution of the scores for the antrum determined by NBI-magnifying endoscopy and by histological examination of biopsy specimens. The overall rate of correspondence between the scores obtained by NBI-magnifying endoscopy and by histology was 69.1% (Table 2). Table 3 shows the distribution of the

corresponding scores for the corpus. The overall rate of correspondence between these scores was 72.7% (Table 3). Table 4 shows the distribution of the stages determined according to the scores obtained by NBI-magnifying endoscopy and histology. The stages were divided into two groups - low risk (Stages 0, I, and II) and high risk (Stages III and IV) - and the degree of correspondence between the groups determined on the basis of NBI-magnifying endoscopy and histology was 89.1% (49/55) (Table 5). The distribution of gastritis stages among 55 patients with gastric cancer, peptic ulcer and other diseases is shown in Table 6. Among the patients with gastric cancer, 75.0% (18/24) were clustered in the high-risk group (stages III and IV) on the basis of NBI-magnifying endoscopy whereas 79.2% (19/24) were so clustered on the basis of histology (Table 6).

Discussion

The updated Sydney System was drawn up mainly for diagnosis of *H. pylori*-associated gastritis, and is a quantitative scoring system based on five parameters evident in five biopsy samples: atrophy, intestinal metaplasia, neutrophils, mononuclear cells and *H. pylori* [14]. Recently in the West, the OLGA[3)4)] and OLGIM[5)] staging systems based on the updated Sydney System have become widely used. The OLGA staging system is a histological measure of the severity and topography of atrophy, whereas the OLGIM staging system is based on the severity and topography

of intestinal metaplasia. Using these systems, determination of cases with a high risk of gastric cancer based on biopsy samples has been attempted[5)15)16)]. Rugge et al.[15)] reported that in stages 0, I and II, no neoplastic lesions were detected, as they were all clustered in stages III and IV. In Japan, however, due to the aging of the population, there has been an increase in the number of patients taking antithrombotic agents, and therefore many elderly patients have a risk of bleeding if stomach biopsy is attempted. On the other hand, withdrawal of antithrombotic agents to avoid biopsy-related bleeding may lead to thrombosis, which can be a reason for medical malpractice litigation. Under these circumstances, taking several biopsy specimens for gastritis staging tends to be avoided in Japan. Furthermore, this approach for gastritis staging imposes a considerable burden on endoscopists, and substantially increases medical costs and procedure time.

By contrast, we have reported an imaging diagnostic system for *H. pylori*-negative normal stomach and *H. pylori*-associated gastritis using NBI-magnifying endoscopy [6-10)]. This system was established by comparing NBI-magnifying endoscopy findings with histological findings. We have diagnosed atrophy and intestinal metaplasia of the gastric mucosa using this NBI-magnifying endoscopy system and have recognized that the findings approximate those of histology[6-12)]. It would be very useful if this imaging diagnostic system could be used for gastritis staging instead of biopsy histology, as it would eliminate bleeding risk, reduce the burden on endoscopists, and

help to reduce medical costs and procedure time. In the present study, therefore, we attempted to evaluate whether gastritis staging based on the OLGA and OLGIM staging systems using NBI-magnifying endoscopy is equivalent to that determined by histology.

First, we determined the scores based on histological findings in the antrum and corpus, and then decided the scores obtained by NBI-magnifying endoscopy corresponding to each histological score. We carried out NBI-magnifying endoscopic observation and took biopsy specimens from the lesser curvature of the antrum and corpus of 55 patients. We then obtained the scores based on NBI-magnifying endoscopy and biopsy histology and investigated the degree of correspondence between them. This revealed a score correspondence rate of 72.7% for the corpus and 69.1% for the antrum. The rates of correspondence between the scores based on NBI-magnifying endoscopy and those based on biopsy histology were higher for scores of 0 and 3 than for scores of 1 and 2. This suggested that normal oxyntic glands without atrophy, mucosa without intestinal metaplasia, and mucosa with extensive intestinal metaplasia would be easy to diagnose by NBI-magnifying endoscopy. The stages of the 55 patients were then decided according to the scores obtained by NBI-magnifying endoscopy and histology, and divided into two groups: low risk (stages 0, I, II) and high risk (stages III, IV). The degree of correspondence between NBI-magnifying endoscopy and histology for the two groups was 89.1%.

In the antrum, we investigated the severity of intestinal metaplasia according to the OLGIM staging system because no methods for diagnosis of pyloric gland atrophy by NBI-magnifying endoscopy have been reported previously. On the other hand, the presence of oxyntic gland atrophy in the corpus revealed by NBI-magnifying endoscopy has already been reported[6-10]. Therefore, for the corpus, we decided to determine the severity of atrophy and intestinal metaplasia with reference to the OLGA and OLGIM staging systems. Only patients from whom two endoscopists (AS and KY) could obtain informed consent in the outpatient department were enrolled in this study. Other patients who underwent gastric endoscopic examination were not enrolled. Therefore, the number of patients examined in this study was small. Accordingly, it will be necessary to investigate more patients in the future, and to validate this new combination of criteria.

We investigated only two parts of the stomach, the antrum and lower corpus, because gastritis staging using biopsy specimens has not spread and tends to be avoided in Japan, and for this reason assessment of gastritis by taking several biopsy specimens was not approved by our institutional ethics committee.

This was primarily a pilot study to investigate whether or not gastritis staging by NBI-magnifying endoscopy would be feasible and approximate the results of histology. We considered that the results were assessed fairly. In order to improve the accuracy of gastritis staging using NBI-magnifying endoscopy and make it universal, we think

that it should be investigated at multiple institutions and its weak points clarified. However, we consider that it is feasible to clarify the overall distribution of mucosal atrophy and intestinal metaplasia and make our approach more reproducible by observation of more areas by NBI-magnifying endoscopy.

In conclusion, staging of gastritis using NBI-magnifying endoscopy is able to approximate that determined by histology, and is expected to be a practical approach that can replace staging based on the histology of biopsy specimens.

Acknowledgements and disclosures

Competing interests: the authors have no competing interests.

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Figure legends

Figure 1

Left: NBI-magnifying endoscopic features of the light blue crest (LBC). The LBC appears as a fine, blue-white line on the crests of the epithelial surface and gyri.

Right: NBI-magnifying endoscopic features of the white opaque substance (WOS). The WOS appears as a white opaque substance on the surface.

Figure 2A

Images of NBI-magnifying endoscopy in the antrum.

LBC: light blue crest, WOS: white opaque substance

Figure 2B

Images of NBI-magnifying endoscopy in the corpus.

LBC: light blue crest, WOS: white opaque substance

Figure 3A

Histological appearance of biopsy specimens from the antrum.

IM: intestinal metaplasia

Figure 3B

Histological appearance of biopsy specimens from the corpus.

Figure 4

Table of gastric staging for NBI-magnifying endoscopy and histology used in this study, based on a combination of the OLGA and OLGIM staging systems.

IM: intestinal metaplasia

Table 1. *H. pylori* status of the 55 patients.

H. pylori positive	14/55
H. pylori negative	34/55
After *H. pylori* eradication therapy	28/34
Resolved naturally	6/34
Unknown	7/55

Table 2. Distribution of scores obtained by NBI-magnifying endoscopy and by histology of biopsy specimens for the antrum.

		NBI-ME score			
		0 (25 cases)	1 (9 cases)	2 (5 cases)	3 (16 cases)
Histological score	0	**18**	2	0	0
	1	5	**3**	0	2
	2	1	0	**3**	0
	3	1	4	2	**14**

Correspondence of NBI-ME score to histological score, 69.1% (38/55)

NBI-ME: NBI-magnifying endoscopy

Table 3. Distribution of scores obtained by NBI-magnifying endoscopy and by histology of biopsy specimens for the corpus.

		NBI-ME score			
		0 (10 cases)	1 (17 cases)	2 (4 cases)	3 (24 cases)
Histological score	0	**10**	4	0	0
	1	0	**7**	1	0
	2	0	2	**0**	1
	3	0	4	3	**23**

Correspondence of NBI-ME score to histological score, 72.7% (40/55).

NBI-ME: NBI-magnifying endoscopy

Table 4. Distribution of stages determined by NBI-magnifying endoscopy and histology of biopsy specimens.

		Stage by NBI-ME				
		Stage 0 (9 cases)	Stage I (17 cases)	Stage II (4 cases)	Stage III (6 cases)	Stage IV (19 cases)
Stage by histology	Stage 0	7	3	0	0	0
	Stage I	2	7	0	0	0
	Stage II	0	3	3	1	0
	Stage III	0	3	0	1	3
	Stage IV	0	1	1	4	16

NBI-ME: NBI-magnifying endoscopy

Table 5. Distribution of groups determined according to the scores of NBI-magnifying endoscopy and histological score.

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		Group by NBI-ME	
		Low risk (30 cases)	High risk (25 cases)
Group by Histological score	Low risk	**25**	1
	High risk	5	**24**

Correspondence of group determined by NBI-ME to that determined by histology, 89.1% (49/55).

Low risk: stage 0, stage I and stage II
High risk: stage III and stage IV

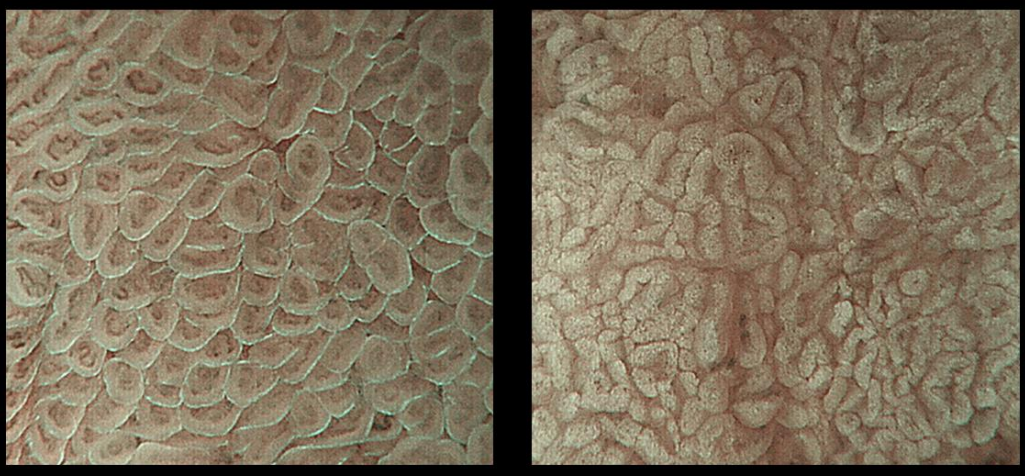
NBI-ME: NBI-magnifying endoscopy

Table 6. Case distribution of gastritis staging in 55 patients with gastric cancer, peptic ulcer and other diseases by NBI-magnifying endoscopy and histology.

	Stage by NBI-ME				
	Stage 0	Stage I	Stage II	Stage III	Stage IV
Gastric cancer	1	3	2	4	14
(n=24)	(4.2%)	(12.5%)	(8.3%)	(16.7%)	(58.3%)
Peptic ulcer	5	5	0	0	3
(n=13)	(38.5%)	(38.5%)	(0%)	(0%)	(23.1%)
Others	3	9	2	2	2
(n=18)	(16.7%)	(50.0%)	(11.1%)	(11.1%)	(11.1%)

	Stage by histology				
	Stage 0	Stage I	Stage II	Stage III	Stage IV
Gastric cancer	0	3	2	2	17
(n=24)	(0%)	(12.5%)	(8.3%)	(8.3%)	(70.8%)
Peptic ulcer	4	2	1	2	4
(n=13)	(30.8%)	(15.4%)	(7.7%)	(15.4%)	(30.8%)
Others	6	4	4	3	1
(n=18)	(33.3%)	(22.2%)	(22.2%)	(16.7%)	(5.6%)

NBI-ME: NBI-magnifying endoscopy



Light blue crest (LBC)

White opaque substance (WOS)

Figure 1

Score	0	1	2	3
LBC or WOS	Absent	< 1/3	≥ 1/3 and < 1/2	≥ 1/2

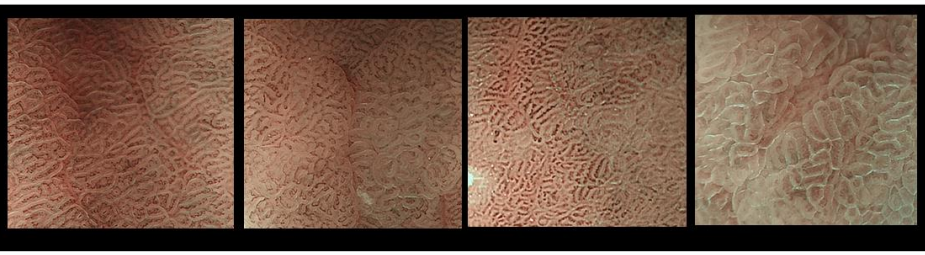


Figure 2A

Score	0	1	2	3
Mucosal pattern	Round pit	Oval or slit-like pit	Tubular or granular	Tubular or granular
LBC or WOS			(-)	(+)

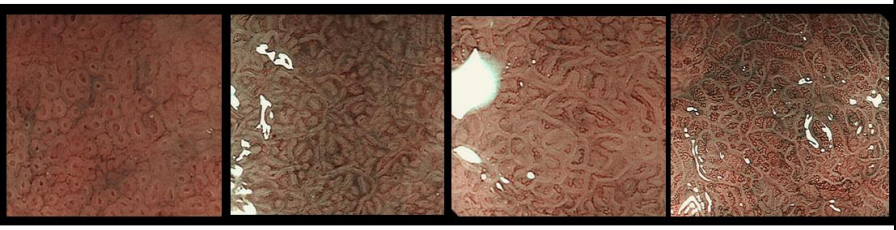


Figure 2B

Score	0	1	2	3
IM (Histology)	Absent	< 1/3	≥ 1/3 and < 1/2	≥ 1/2

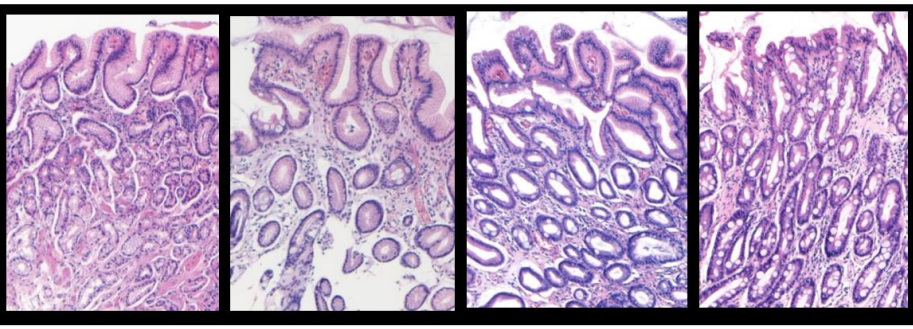


Figure 3A

Score	0	1	2	3
Histology	Fundic gland without atrophy	Fundic gland with atrophy	Pseudopyloric gland metaplasia	Intestinal metaplasia

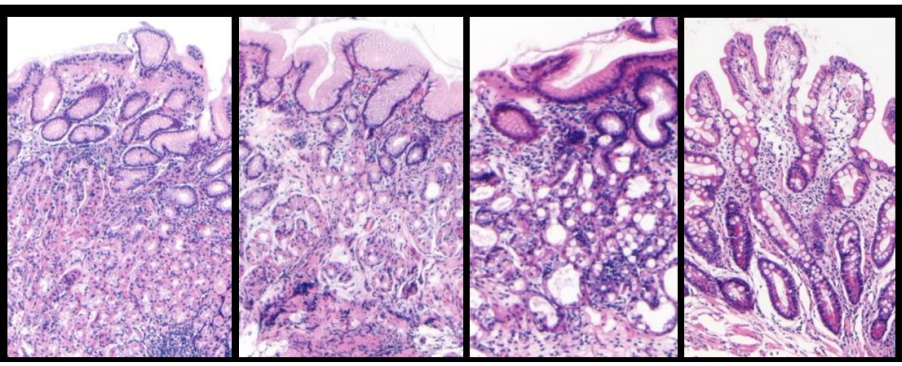


Figure 3B

IM score \ Atrophy score		Corpus			
		No atrophy (score 0)	Mild atrophy (score 1)	Moderate Atrophy (score 2)	Severe atrophy (score 3)
Antrum	No IM (score 0)	STAGE 0	STAGE I	STAGE II	STAGE II
	Mild IM (score 1)	STAGE I	STAGE I	STAGE II	STAGE III
	Moderate IM (score 2)	STAGE II	STAGE II	STAGE III	STAGE IV
	Severe IM (score 3)	STAGE III	STAGE III	STAGE IV	STAGE IV

Figure 4