



# Ability of blue laser imaging with magnifying endoscopy for the diagnosis of gastric intestinal metaplasia

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## Abstract

We aimed to determine the utility of blue laser imaging (BLI) with magnifying endoscopy (BLI-ME) for the prediction and diagnosis of gastric intestinal metaplasia (GIM). Participants, aged between 40 and 75 years, undergoing gastroscopy from January to April 2017 were included in this study. The ability of BLI-ME and white light endoscopy (WLE) to detect GIM was assessed by comparing the endoscopic findings with the histological findings. The correlation between the grades of light blue crest (LBC) appearance and histology grade of GIM was calculated. We included 100 participants in this study. GIM was diagnosed in 27 participants; 20 participants were detected by both BLI and WLE, four by BLI only, and three exclusively by random biopsies. The values of sensitivity, specificity, positive predictive values, and negative predictive values for detecting GIM were 34.9, 38.9, 25.4, and 57.1%, respectively, for WLE and 88.9, 96.7, 94.1, and 93.3%, respectively, for BLI-ME. The diagnostic accuracy for GIM was 43% for WLE and 94.0% for BLI-ME. A good correlation between the grades of LBC and the grades of GIM on histology was observed ( $P < 0.01$ ). BLI-ME achieved a good diagnostic efficiency for detection of GIM. LBC seen on BLI-ME is a typical indicator of GIM.

**Keywords** Blue laser imaging · White light endoscopy · Magnifying endoscopy · Intestinal metaplasia · Detection

## Introduction

Gastric intestinal metaplasia (GIM) is considered a high-risk factor for intestinal type gastric cancer [1]. Participants diagnosed with GIM have a six times higher risk for gastric cancer [2]. Shichijo et al. discovered that participants with histologic GIM and severe endoscopic atrophic gastritis have an elevated risk of developing gastric cancer even after eradication of *Helicobacter pylori* [3]. Hence, the surveillance of populations with GIM might expedite the detection of early precancerous lesions and gastric cancer [4]. The commonest

approach to confirm GIM is biopsy-based pathological diagnosis [5]. Five standardized biopsy samples should be obtained to assess the extent of GIM, according to the guideline of the updated Sydney System [6]. Due to this cumbersome process, several minimally invasive or real-time methods have been used to increase the diagnostic accuracy of GIM.

Since the 2000s, several image-enhanced endoscopy (IEE) systems, such as narrow-band imaging (NBI), flexible spectral imaging color enhancement (FICE), autofluorescence imaging, or confocal laser endomicroscopy, have shown a GIM diagnostic efficacy ranging from 65.70 to 86% [7–10]. In the NBI model, GIM appears as a bluish-whitish lesion with a regular mucosal pattern [11]. A recent meta-analysis proved that GIM detection using NBI is useful due to the instrument's low sensitivity and high specificity [12]. More specifically, some studies have found that the light blue crest (LBC) seen in the 400–430-nm reflection images using NBI with magnification endoscopy (NBI-ME) in the mucosa is a distinctive endoscopic finding for GIM in the stomach [13]. Uedo et al. found that GIM detection using NBI-ME had a high sensitivity and specificity [10]. These authors demonstrated that there was a positive correlation between the appearance of LBCs and histological GIM, with a sensitivity of 80% (95%CI: 67–

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Honglei Chen and Yanan Liu are the co-first author in this study.

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92), a specificity of 96% (95%CI: 93–99), positive predictive values of 84% (95%CI: 73–96), negative predictive values of 95% (95%CI: 92–98), and an accuracy of 93% (95%CI: 90–97) [14]. However, the light source of the conventional endoscope, as well as the current IEE endoscope systems, is a xenon lamp.

Recently, a new IEE endoscope system named LASEREO was developed by FUJIFILM Corporation (Tokyo, Japan) [15]. This novel system contains a narrow-band light model, named blue laser imaging (BLI), as well as a white light model [16]. The BLI endoscope system is equipped with two types of lasers: the 450-nm wavelength laser and the 410-nm wavelength laser [17, 18]. BLI produces excellent images and increases the detection of upper gastrointestinal lesions [19]. The 410-nm wavelength laser allows BLI endoscopy for a narrow-band observation [20]. Thus, LBC, which was only seen in the 400–430-nm reflection images, might also be detected by BLI-ME.

No published data are available about GIM detection with BLI. In this study, we aimed to investigate the utility of BLI-ME for detecting GIM through the visualization of LBCs in the stomach. A secondary aim was to identify any correlation with the histological assessment of GIM grade.

## Methods

### Participants

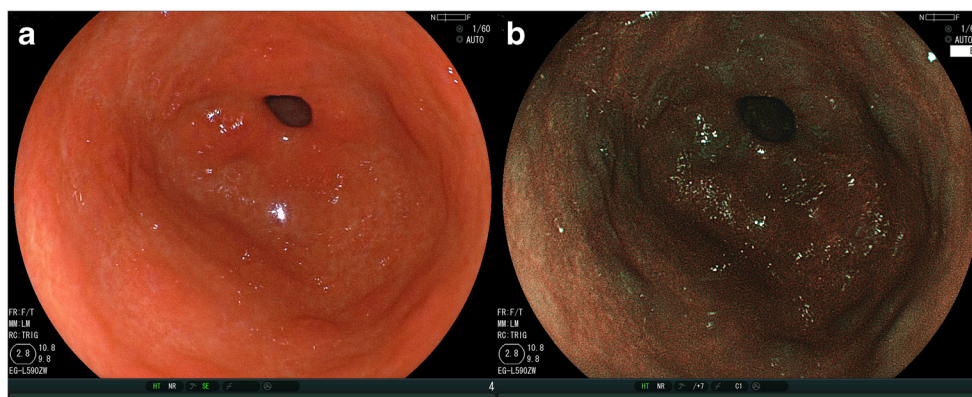
In all, 100 consecutive participants aged between 40 and 75 years who underwent endoscopic examination were included in the present study at the Sixth Affiliated Hospital, Sun Yat-sen University, from January 2017 to May 2017. The exclusion criteria were participants with advanced gastric cancer, previous stomach surgeries, receiving anticoagulant, non-steroidal anti-inflammatory, or antiplatelet medication, and the presence of gastrorrhagia or hemorrhagic diseases.

### Study protocol

Demographic data such as age and gender and clinicopathological characteristics such as the chief symptoms and treatment were retrieved from the endoscopic computerized database. Gastroscopy with the BLI-ME system was used to determine the presence or absence of GIM. Five standardized biopsy specimens were obtained (two from the antrum, one from the angulus, and two from the corpus) to evaluate the extent of GIM according to the guidelines of the updated Sydney System. All participants were asked to sign a written informed consent before the examination. The Ethics Committee of the Sixth Affiliated Hospital, Sun Yat-sen University approved this study. We registered this study on the website of Chinese Clinical Trial Registry (ChiCTR-17011381). This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

### Endoscopic procedure

All the endoscopic examinations were performed by experienced endoscopists (Honglei Chen, Xutao Lin, and Yi Lu) who were blinded to the medical histories of the participants. The endoscopists received training from experts, for detection of GIM using BLI-ME, before starting the study. In this study, EG-L590ZW endoscopes with magnification capability and the LASEREO system developed by FUJIFILM Company were used. All participants ingested simethicone solution (Zigong Honghe Pharmaceutical Co., Ltd. Sichuan, China) before the procedure. The gastric mucosal surface was rinsed with an additional simethicone solution in case of poor visualization. All participants were under conscious sedation. The stomachs were carefully examined by white light endoscopy (WLE), BLI, and BLI-ME in all participants by the same endoscopist during a single procedure. Since there are no standard criteria for detecting GIM using WLE, any abnormal



**Fig. 1** Appearance of intestinal metaplasia in the antrum of the same patient under different endoscopic models. **a** The lesion shows reddish areas with a regular mucosal pattern in white light model. **b** The lesion shows bluish-whitish areas with a regular mucosal pattern in the BLI model

**Table 1** Demographic and clinical characteristics of participants

Characteristic	Participants
Age, mean (SD)	51 (7.5)
Sex	
Male	54
Female	46
<i>H. pylori</i> infection	
Positive	32
Negative	68
Alcohol	
Non-drinker	72
Current drinker	28
Smoking	
Non-smoker	69
Current smoker	20
Former smoker	11
PPI users	
Yes	25
No	75

SD standard deviation

mucosal change in the stomach, such as rough areas and localized discoloration, was considered a suspicious lesion of GIM. After WLE observation, the endoscopists switched to the BLI model and multiple flat or depressed blue whitish patchy areas, with a regular mucosal pattern, were detected, as LBCs were frequently observed in these areas (Fig. 1) [21]. Following this, the endoscopists switched to BLI-ME and observed the blue whitish patchy areas carefully at maximum magnification. The LBCs were defined as blue-white lines on the crests of the epithelial surface of the mucosa, as mentioned in previous studies [11]. LBC positive was defined if LBCs were observed in any of the image fields. The extent of appearance of the LBCs was used to quantify the degree of LBCs [10]. The degree of LBCs was scored as follows: less than 20% of the area with LBC appearance was scored as weak (+), 20–80% was scored as moderate (++), 80% or more was scored as strong (+++). The locations of the lesions detected by WLE or BLI-ME were recorded and precision biopsies were obtained. If no suspected lesions were identified by WLE or BLI, five standardized biopsy specimens were obtained (two from the antrum, one from the angulus, and

two from the corpus) according to the guideline of the updated Sydney System [6].

### Histological assessment

All biopsy specimens were fixed in 4% formalin and embedded in paraffin. The slides were routinely processed with hematoxylin and eosin stains. The histologic analyses were performed by an experienced gastrointestinal pathologist who was blinded to results of the endoscopy. The histological diagnosis was reported according to the updated Sydney Classification for chronic gastritis and the modified Vienna criteria for neoplasia [6, 22]. GIM was also expressed as a percentage of the metaplastic glands on the entire antral or oxyntic mucosal specimens. *Helicobacter pylori* were evaluated in each sample.

### Statistical analysis

For an individual patient analysis, the sensitivity, specificity, positive predictive values, negative predictive values, and diagnostic accuracy rate for predicting GIM were calculated. For participants with more than one lesion, the participant was considered as one unit and the most severe precancerous grade was recorded for analysis. For example, a participant having both chronic gastritis and GIM was classified as GIM only. For per-biopsy analysis, the detection accuracy of GIM by targeted biopsies using BLI-ME and WLE models were measured. The chi-squared test was used to access the differences between the two groups. The nonparametric Spearman correlation test was used to identify the correlation between the histological GIM and the grades of LBC appearance, respectively. A value of  $P < 0.05$  was defined as being statistically significant. Statistical calculations were performed using SPSS software for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

### Participants' characteristics

From January to May 2017, in all, 100 eligible participants at the Sixth Affiliated Hospital, Sun Yat-sen University, were

**Table 2** Diagnostic accuracy of endoscopy in participants with GIM by WLE and BLI-ME

GIM	Sensitivity	Specificity	PPV	NPV	Accuracy
WLE	34.9% (15/43)*	38.9% (28/72)*	25.4% (15/59)*	57.1% (28/49)*	43.0% (43/100)*
BLI-ME	88.9% (32/36)	96.9% (62/64)	94.1% (32/34)	93.9% (62/66)	94.0% (94/100)

PPV positive predictive value, NPV negative predictive value

\*WLE versus BLI-ME:  $P < 0.001$

**Table 3** Relationship between LBC grade and GIM grade detected by histological assessment

GIM	LBC (n)			Total (n)
	LBC (+)	LBC (++)	LBC (+++)	
No GIM	11	0	0	11
Mild GIM	38	7	0	45
Moderate GIM	8	25	3	36
Marked GIM	0	3	7	10

included. The baseline characteristics of the participants are listed in Table 1. Male participants represented 54% (54/100) of the cohort. In addition, 28% (28/100) of the participants were alcohol consumers and 20% (20/100) of the participants were current smokers. *Helicobacter pylori* was detected in 32 participants. Of the participants, 25% (25/100) were on proton pump inhibitors when they underwent the examination.

### Per-patient analysis

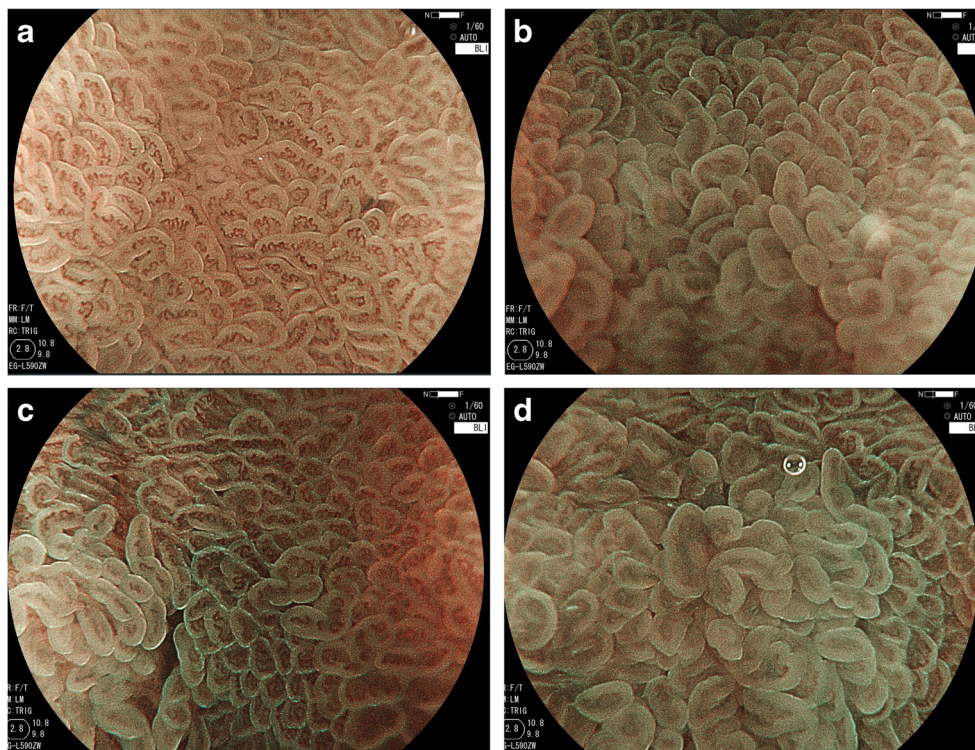
The overall prevalence of GIM on histological analysis was 36% (36/100). During the upper WLE procedure, GIM was suspected in 51 participants (51%), while only 15 cases were confirmed as GIM. During the BLI-ME examination, the LBC appearance was seen in 34 participants (34%), while 32 cases

were confirmed as GIM. Moreover, only 5 participants (6%) were identified as LBC positive in the gastric body, and 4 participants were also identified as LBC positive in the antrum. Random biopsy detected 4 (2%) participants as GIM positive. Table 2 shows the sensitivity, specificity, positive predictive values, negative predictive values, and the detection accuracy of WLE and BLI-ME.

### Per-lesion analysis

For WLE, specimens from 132 suspected lesions were taken. Of these, a histological diagnosis of GIM was confirmed in 39 specimens, and mild or moderate chronic inflammation was confirmed in the remaining 93 specimens. For BLI-ME, a total 102 of lesions were observed as LBC positive; 57 of the LBC lesions were classified as LBC+, 35 lesions were classified as LBC++, and 10 lesions as LBC+++ (Fig. 1). Of these, a histological diagnosis of GIM was confirmed in 91 specimens, and moderate chronic inflammation was confirmed in the remaining 11 specimens, which were observed as LBC+. Thus, for the per-biopsy analysis, a significantly greater ability to detect GIM was found in the BLI-ME model compared to WLE, with 89.2% (91/102) versus 29.5% (39/132) ( $P < 0.001$ ). The correlation between the histological grade of GIM and the grades of LBC is shown in Table 3. The correlation analysis indicated that there is a significant correlation between the grades of histological GIM and the grades of LBC appearance ( $P < 0.01$ ) (Fig. 2).

**Fig. 2** BLI-ME examination and the degree of light blue crest appearance. **a** Normal mucosal aspects. **b** Light blue crest (LBC)+, less than 20%. **c** LBC++, 20–80%. **d** LBC+++, 80% or more



## Discussion

BLI-ME could detect vascular and surface patterns clearly and provided excellent endoscopic images of the stomach, and the diagnostic efficacy of BLI-ME for early gastric cancer and colorectal neoplasms was similar to that of NBI-ME [16, 23–25]. To date, no prospective data are available on the diagnostic utility and accuracy of BLI-ME to detect GIM in an unselected population presenting at an endoscopy unit in routine clinical practice.

Our study showed that BLI-ME can detect GIM with a sensitivity of 88.9%, specificity of 96.9%, positive predictive values of 94.1%, negative predictive values of 93.9%, and diagnostic accuracy of 94%. These values are notably higher than those of WLE and were consistent with previous studies of NBI-ME [10, 14].

The prevalence of histologically observed GIM in our cohort (36%) was similar to the prevalence estimated in the general Chinese population (16.79–38.56%) [26]. These prospective data indicated that BLI-ME could detect the GIM similar to NBI magnification without a selection bias. BLI-ME is a useful technique for GIM detection in participants who underwent gastroscopy.

Previously, Uedo et al. reported that a significant correlation was observed between the grade of LBC and the grade of histological markers of GIM [10]. Moreover, Savarino et al. showed a good correlation between the percentage of histologic GIM and LBC appearance [14]. In our study, there was a statistically significant correlation between the grades of LBC appearance and the grades of histological GIM, which was consistent with the study of NBI-ME [12, 27].

However, LBCs were not observed in four cases which were histologically diagnosed as GIM. A marginally turbid band is another sign for the detection of GIM (accuracy, 81.7%) and is useful for predicting atrophy (accuracy, 79.6%) [28]. On retrospective review of the pictures, marginally turbid band was found in two GIM cases, which were LBC negative. These findings might explain the missed detection of GIM and a search for additional signs for GIM detection on BLI-ME are necessary.

Some limitations of this study should be mentioned. First, this research was performed at a single center; multicenter prospective studies are needed to confirm the findings from the present study. Second, WLE and BLI were performed by the same endoscopist during a single procedure; thus, there is a possibility of bias during BLI-ME due to the previous WLE observations. Finally, several studies reported that the incidence rate of GIM is age related. In our study, we only included participants older above 40 years of age. The detection rate in young participants needs investigation in the future.

In conclusion, LBC observed by BLI-ME in the gastric mucosa is a highly accurate sign for the presence of GIM. In

routine clinical practice, BLI-ME was shown to be a useful technology for detection of GIM.

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## Compliance with ethical standards

**Conflict of interest** Honglei Chen has received funding from Guangdong province medical science and technology research fund project (grant number: A2017273). For the remaining authors, none were declared.

**Ethical approval** The study was approved by the Ethics Committee of the Sixth Affiliated Hospital, Sun Yat-sen University, and has been performed in accordance with the Declaration of Helsinki. The study was registered with Chinese Clinical Trial Registry (ChiCTR-17011381).

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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