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EDITORIAL

In Living Color: Linked Color Imaging for the Detection of Early Gastric Cancer

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Gastric cancer is the fifth most common cancer and third major cause of cancer-related deaths in the world [1]. It is essential to detect and treat gastric cancer at an early stage in order to ensure a good prognosis. Endoscopic screening is used to detect gastric cancer at an early stage, and minimally invasive endoscopic treatments, such as endoscopic mucosal resection and endoscopic submucosal dissection, have been developed to treat early gastric cancers (EGC) that have negligible lymph node metastases. These treatments ensure high curability and preserve the patient's quality of life post-treatment. Endoscopic examination includes the detection of lesions, preliminary diagnosis of cancer, and assessment of its extent and depth. Finally, a definitive diagnosis is established via biopsy.

Reportedly, *Helicobacter pylori* infection is a major risk factor for gastric cancer; its incidence increases if advanced atrophic gastritis is present [2]. Thus, the endoscopic assessment of atrophic gastritis and the presence of *H. pylori* can assist in determining the risk of developing gastric cancer. The Kyoto classification of gastritis has clarified the findings for assessing *H. pylori* infection status. When performing endoscopic screening of the stomach, it is important to divide gastritis into three phases: never infected, currently infected, and previously infected, including an after-eradication phase, in order to evaluate the risk of gastric cancer development.

Occasionally, clinicians encounter cases where diagnosis of gastric cancer or *H. pylori* infection status with conventional white light imaging (WLI) is challenging. Image-enhanced endoscopy (IEE) was developed to improve the visibility of such findings. Although the use of indigo carmine dye to produce contrast was previously commonplace, new IEE methods such as narrow-band imaging (NBI) and blue-light imaging (BLI) are widely accepted in clinical practice. Both NBI and BLI are reportedly useful for the qualitative diagnosis of EGC when combined with magnifying endoscopy. The magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G) has been proposed as a unified diagnostic system [3] that identifies EGC by evaluating the demarcation between lesions and healthy tissue and detects irregularities in the microvascular and micro-surface patterns of the gastric mucosa. Magnifying endoscopy with NBI or BLI is useful for the qualitative diagnosis of EGC; as an optical biopsy, it is expected to reduce the need for conventional histological biopsy. Nevertheless, such IEEs did not improve gastric cancer detection as predicted due to insufficient light intensity for mid-to-long range observations used for gastric screening.

Linked color imaging (LCI) is a newly developed IEE modality based on the BLI technique with digital image processing (LESEREO endoscopic system; Fujifilm Co., Tokyo, Japan). LCI combines a laser light source with two wavelengths—a 450-nm white light laser and a 410-nm short-wavelength narrow-band laser. The effectiveness of LCI is explained with the L*a*b* color space: the a*–b* plane represents hue and saturation, whereas the L*-axis

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represents brightness (Fig. 1). Red (+a*) and yellow (+b*) directions are enhanced by signal processing, which emphasizes the color of the gastric mucosa; most EGCs are thus observed as light colors with high b* values in the reddish gastric mucosa. In contrast, intestinal metaplasia is observed as a purple-colored region with a low b* value. Brightness is ensured by maintaining the relevant component of the L* axis. Thus, LCI differentiates mucosal colors that are important for EGC diagnosis while maintaining sufficient brightness for the mid-to-long range observation in gastric screening.

Kanzaki et al. (2017) reported a more significant color difference between gastric cancer and the surrounding mucosa in the L*a*b* color space when using LCI than when using WLI [4]. The study by Yasuda et al. (2021) demonstrated the superiority of LCI over the indigo carmine contrast method and BLI in color differences between the differentiated-type gastric cancer and surrounding mucosa in the L*a*b* color space [5]. Therefore, LCI improves endoscopic detection of gastric cancer during screening and assists in the determination of *H. pylori* infection status. Dohi et al. (2016) reported that LCI improves endoscopic diagnosis of active *H. pylor*i infections [6]; the infection was identified using LCI by enhancing the red appearance of the fundic gland mucosa. Compared with WLI, 10%–15% improvements were noted in the accuracy, sensitivity, and specificity of LCI for *H. pylori* infection diagnosis. Ono et al. (2020) conducted a multicenter prospective study to compare the accuracies of WLI and LCI for endoscopic diagnosis of *H. pylori* gastritis [7]. LCI was significantly more accurate than WLI in patients with past infections. Ono et al. (2018) also demonstrated that the lavender color in LCI enables noninvasive detection of gastric intestinal metaplasia [8].

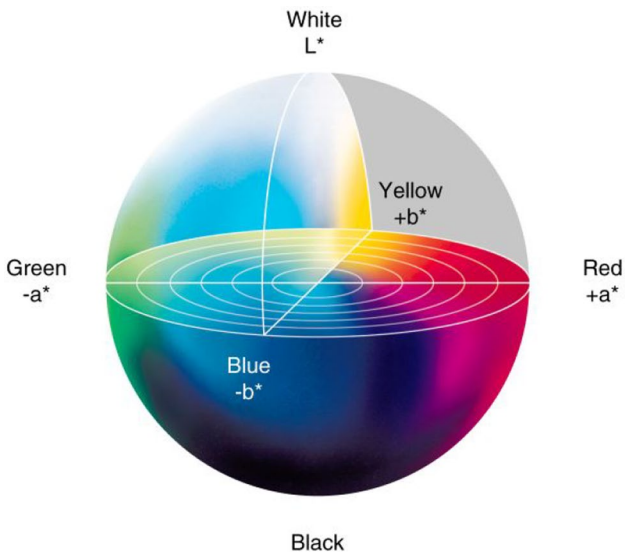

Fig. 1 The CIE 1976 L*a*b* color space

Subsequent to endoscopy with a laser light source, endoscopy with light-emitting diodes (LEDs) (ELUXEO endoscopic system; Fujifilm Co., Tokyo, Japan) was developed. This LED endoscopy system, which consists of four colors, including blue-violet (approximately 410 nm), blue (approximately 450 nm), green (500–600 nm), and red (approximately 630 nm), enables the use of BLI with an LED light source (LED-BLI) and LCI with an LED light source (LED-LCI) instead of a laser light source. By controlling each of the four LEDs independently, light is produced with an appropriate ratio for image-enhanced endoscopy. LED-LCI is expected to have the same diagnostic performance as conventional LCI (Laser-LCI).

In this issue of *Digestive Diseases and Sciences*, Ishida et al. (2021) reported a comparison between laser and LED endoscopies in order to evaluate the enhanced visibility of EGC and *H. pylori*-associated gastritis [9]. Videos were taken of both methods being performed on 88 patients, evaluating 99 EGC lesions and the associated background gastric mucosa at a single center. Videos obtained with laser endoscopy were first recorded using WLI (Laser-WLI) followed by the use of LCI (Laser-LCI). On different days, videos with LED endoscopy were recorded for the same lesion using WLI (LED-WLI) and LCI (LED-LCI). The videos were randomized, displayed on a monitor, and evaluated by five experienced endoscopists. The visibility of each lesion and other findings assessing *H. pylori* infection status according to the Kyoto classification of gastritis were scored (4-point score). The visibility scores for WLI and LCI were compared between LED and laser endoscopy.

The visibility scores of the EGC lesions evaluated by Laser-WLI, LED-WLI, Laser-LCI, and LED-LCI were 2.97 ± 0.05, 3.14 ± 0.05, 3.35 ± 0.05, and 3.39 ± 0.04, respectively. The differences between Laser- and LED-WLI and between Laser- and LED-LCI were 0.17 ($p = 0.01$; 95% CI 0.04–0.30) and 0.04 ($p = 0.47$; 95% CI − 0.07–0.16), respectively. Furthermore, the visibility scores of LED-LCI were significantly higher than those of LED-WLI for EGCs ($p < 0.001$), intestinal metaplasia ($p < 0.001$), and map-like redness ($p < 0.001$).

The authors concluded that LED endoscopy was equivalent to laser endoscopy in detecting EGC and assessing *H. pylori* infection status. Moreover, LCI with LED for detecting EGCs and evaluating *H. pylori*-associated gastritis was more effective than WLI. Nevertheless, this study involved a review of endoscopic videos and not real-time observation. Ono et al. (2021) conducted a multicenter, randomized controlled trial to compare the performance of LCI with WLI in detecting neoplastic lesions in the upper gastrointestinal tract, including gastric cancer, with real-time data of endoscopic observation, reporting a significantly higher detection ratio for LCI than for WLI [10]. Furthermore, the proportion of overlooked neoplasms was lower in LCI than in WLI.

LCI is more effective than WLI for detecting neoplastic lesions in the pharynx, esophagus, and stomach. Further clinical trials focusing on the stomach with a much larger sample size are desired in the future.

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