

# Role of linked color imaging for upper gastrointestinal disease: present and future

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Techniques for upper gastrointestinal endoscopy are advancing to facilitate lesion detection and improve prognosis. However, most early tumors in the upper gastrointestinal tract exhibit subtle color changes or morphological features that are difficult to detect using white light imaging. Linked color imaging (LCI) has been developed to overcome these shortcomings; it expands or reduces color information to clarify color differences, thereby facilitating the detection and observation of lesions. This article summarizes the characteristics of LCI and advances in LCI-related research in the upper gastrointestinal tract field.

**Keywords:** Barrett esophagus; Image enhancement; Linked color imaging; Neoplasms

## INTRODUCTION

With the ongoing development of endoscopic equipment, various efforts have been made to overcome the limitations of conventional white light imaging (WLI). Linked color imaging (LCI) and blue light imaging (BLI), developed by Fujifilm in 2013 as new image-enhanced endoscopy (IEE) technologies, are part of these efforts and are currently used worldwide. Although the use of this new IEE is relatively limited because Fujifilm endoscopes are not widely used in large hospitals in Korea, LCI is an imaging technique widely used in various countries, including Japan, China, and European countries.

In this review, the PubMed database was searched using the

keywords “LCI, linked color imaging” to identify relevant studies published until December 2022. Based on the results of previous studies, we reviewed the principles and use of LCI and its applications in clinical practice, focusing on the upper gastrointestinal (GI) tract. We evaluated the principles, usage, and clinical applications of LCI (e.g., Barrett’s epithelium, esophageal neoplasia, reflux esophagitis, gastric neoplasia, and prediction of *Helicobacter pylori* infection status).

## PRINCIPLES OF FUJIFILM IEE

A VP-7000 (Fujifilm Co.) four light-emitting diodes (four LED; blue-violet, blue, green, and red) can independently control the intensity of each color with high accuracy. It can project several images such as WLI, BLI, LCI, and BLI-bright (BLI-brt).<sup>1,2</sup> In WLI, blue, green, and red lights are combined to create a clear image. High contrast is maintained using blue-violet light (short wavelength, 410 nm). BLI can enhance the blue-violet wavelengths and reduce the remaining white light components. In this mode, a high-contrast image is created to visualize blood vessels and surface patterns more clearly.<sup>1</sup> Therefore, BLI plays a role similar to that of the narrow band imaging (NBI) of Olympus Co. NBI is excellent for observing the microvascular system

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of the mucosal surface;<sup>3-5</sup> however, its use is limited in terms of effectiveness for observing long distances from the stomach with a large lumen, owing to its inherent darkness. Therefore, BLI and NBI are useful for observing suspected lesions at close range only. To overcome these shortcomings, Fujifilm Co. developed the BLI-brt mode, which is useful for observing or detecting lesions from a distance by increasing the white light component to overcome the darkness of BLI.

LCI is the most important technology that distinguishes Fujifilm's IEE from those of other companies. LCI produces an image with the same wavelength spectrum as BLI-brt but has additional post-processing.<sup>1</sup> Signal processing in LCI was designed to increase color contrast by amplifying the intensity of reds and whites, while maintaining the natural color of the real object. As a result, the increased color contrast helps detect lesions and inflammation, allowing for a more accurate delineation of lesions.

### USE OF THE FUJIFILM 700 SERIES ENDOSCOPE

LCI and BLI modes are applicable only to the Fujifilm 700 series endoscope. The ELUXEO (Fujifilm 7000 System) comprises a light source and an endoscope video image processor. However, some models can apply LCI and BLI to the 6000 system (ELUXEO Lite; Fujifilm 6000 System).

Scope Button 1 allows screen capture. Observation modes (BLI, BLI-brt, and LCI) can be switched using Scope Button 2. In the continuous or step zoom mode, images can be magnified in stages by pressing a button to zoom in or out. The EG-760Z/EC-760ZP-V endoscope model are equipped with multi-zoom functions. The usefulness of the magnifying endoscope is maximized when BLI mode is used. The locations of the buttons are shown in Figure 1.

In addition, there is a button for adjusting the image tone enhancement level on the endoscopic video image processor (VP-7000). Generally, when using BLI, the color enhancement level is adjusted to C1 in the esophagus and C2 in the stomach and duodenum. C2 or C3 color enhancement is also recommended for the LCI mode.<sup>1</sup> According to a recent study, when observing the gastric mucosa, visibilities for BLI and LCI with C2 color enhancement are significantly better than those with C1 enhancement.<sup>6</sup> Recently, EG-840T and EG-840TP (Fujifilm), which are next-generation endoscopes, have been developed, but have not yet been introduced in Korea.

### CLINICAL APPLICATION IN THE UPPER GI TRACT

#### Barrett's esophagus and esophageal neoplasia

Various studies have been conducted on the clinical application



Fig. 1. Fujifilm 700 series endoscope. LCI, linked color imaging; BLI, blue light imaging.

of LCI in upper GI endoscopy. Several studies have investigated the role of LCI in the diagnosis of Barrett's esophagus (BE) and esophageal cancer. BE is a condition marked by an abnormality in the lining of the lower esophagus.<sup>7</sup> In some BE patients, precancerous changes in the tissue, known as dysplasia, can develop and are likely to develop into esophageal cancer.

A Japanese study revealed that LCI could improve the visibility of short-segment BE by 44.4% compared with WLI under both subjective and objective evaluations.<sup>8</sup> This improvement was also greater in trainees (55.6%) than in experts. A recent Dutch study reported similar results. The use of BLI and LCI improves visualization and provides important additional information to non-expert endoscopists when diagnosing and evaluating Barrett's neoplasms.<sup>9</sup> Furthermore, Japanese studies performed in the same year later showed that LCI could increase the visibility of BE and early adenocarcinoma and improve the detection of these lesions.<sup>10,11</sup> The visibility score for BE using LCI was significantly higher than those for WLI and BLI-brt, while visibility scores for esophageal adenocarcinoma using LCI and BLI-brt were significantly higher than that of WLI.<sup>11</sup> In a recent Japanese study, improved visibility of esophageal squamous cell carcinoma, when compared to WLI, was found in 37.0% (17/46) of patients using LCI and 39.1% (18/46) of patients using BLI-brt.<sup>12</sup> This suggests that LCI is of similar use as BLI-brt for observing esophageal squamous cell carcinoma.<sup>12</sup>

### Reflux esophagitis

Reflux esophagitis can be diagnosed by the endoscopic detection of visible breaks in the distal esophageal mucosa. However, previous studies have shown that interobserver agreement in the endoscopic diagnosis of reflux esophagitis is not satisfactory.<sup>13-15</sup> To overcome this limitation, various hardware-based IEE technologies have been developed and applied to the diagnosis of esophagitis.

A study by Takeda et al.<sup>16</sup> revealed that LCI might improve the visibility of reflux esophagitis. When LCI mode was used, visibility was improved in 28.2% (40/142) of all cases, 19.2% (10/52) of LA-M (minimal change) esophagitis, 34.6% (18/52) of LA-A, 37.5% (9/24) of LA-B, 27.3% (3/11) of LA-C, and 0% (0/3) of LA-D, compared to when WLI mode was used. Since the BLI mode showed no improvement in visibility in this study, LCI might be more useful than WLI or BLI for the endoscopic observation of reflux esophagitis.

However, a recent Korean study showed that the interobserver agreement for the diagnosis of reflux esophagitis was

very low for both experts and trainees, even after using BLI-brt or LCI.<sup>17</sup> This interobserver discrepancy was particularly prominent in grade LA-M reflux esophagitis. Therefore, further research is required to determine whether LCI is useful for the diagnosis of gastroesophageal reflux disease.

### Gastric neoplasm

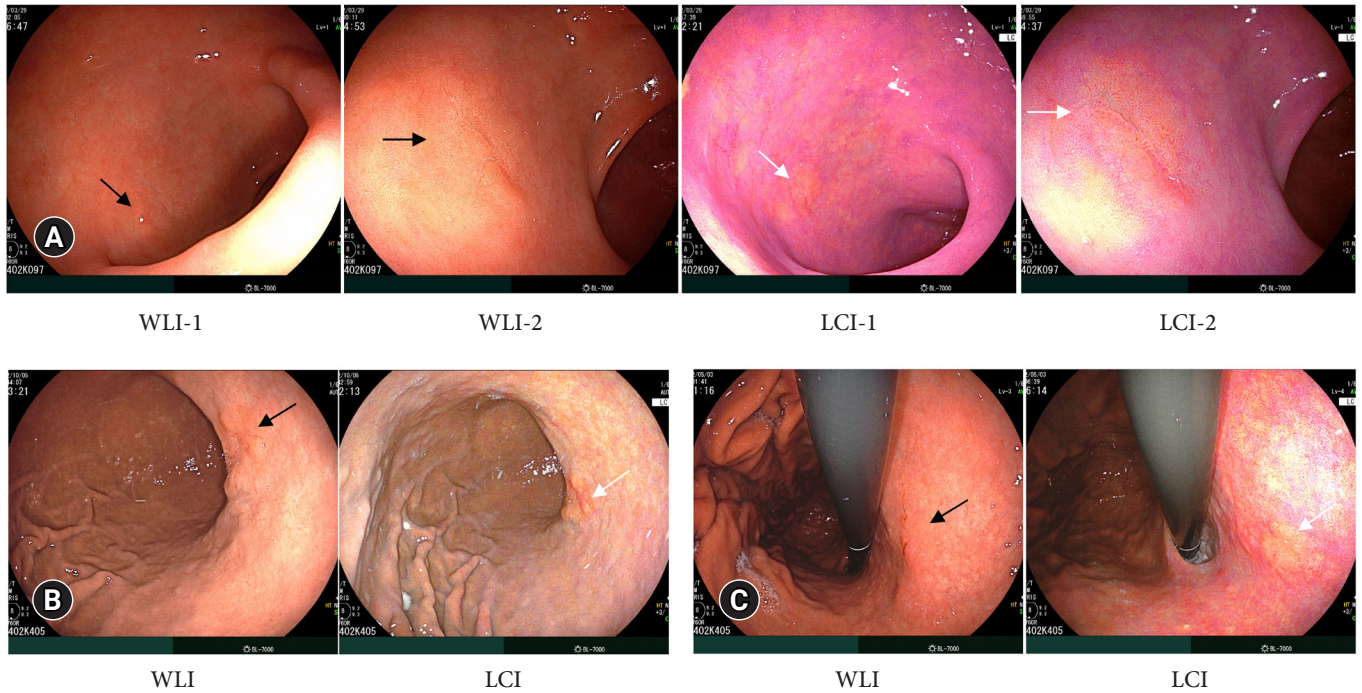
In LCI mode, intestinal metaplasia appears as deep purple or pale purple (lavender color),<sup>18,19</sup> whereas gastric cancer exhibits high color contrast with the surrounding purple mucosa. Most early gastric cancers (EGCs) appear orange-red, orange, or orange-white in LCI.<sup>1</sup> LCI can improve the visibility of EGC.<sup>20-22</sup> A Japanese study revealed that the use of LCI improves EGC visibility regardless of the endoscopist's experience level or *H. pylori* eradication treatment. This improvement was particularly prominent for EGCs with a reddish or whitish color and was significantly higher with LCI than with BLI.<sup>21</sup>

Recently, the results of a multicenter study conducted at 19 centers in Japan (the FIND study) were published.<sup>23</sup> During the study, endoscopy was performed in 1,502 patients who were under surveillance because of a previous or current history of GI cancer. LCI and WLI were used to detect new upper GI tumor lesions. The results showed that the detection rate of neoplastic lesions in the upper GI tract using LCI was 1.67 times higher than that with WLI. A Chinese study also found that the detection rate of gastric tumors was higher in the LCI+WLI group than in the WLI group alone.<sup>24</sup> These results indicate that LCI is more effective than WLI for not only improving the visibility of esophageal or gastric cancer but also detecting upper GI tumor lesions. **Figure 2** shows examples of gastric tumor detection in the LCI mode.

### Prediction of *H. pylori* infection state

*H. pylori* gastritis can be diagnosed based on typical endoscopic findings such as mucosal nodularity, mucosal edema, rugal hyperplasia, turbid gastric juice, and hemorrhagic spots in the corpus mucosa.<sup>25</sup> However, the usefulness of endoscopic diagnosis of *H. pylori* gastritis is limited because the diagnostic yield of conventional WLI is relatively low.<sup>26-28</sup> The most frequently selected endoscopic findings are loss of the regular arrangement of collecting venules, atrophy, and red streaks.<sup>27</sup> In contrast, the most accurate endoscopic findings are nodularity and mucosal swelling. The reported accuracy of endoscopic diagnosis of *H. pylori* infection using WLI is 67% to 74%.<sup>27,29</sup>

Since LCI can improve the visibility of various types of en-

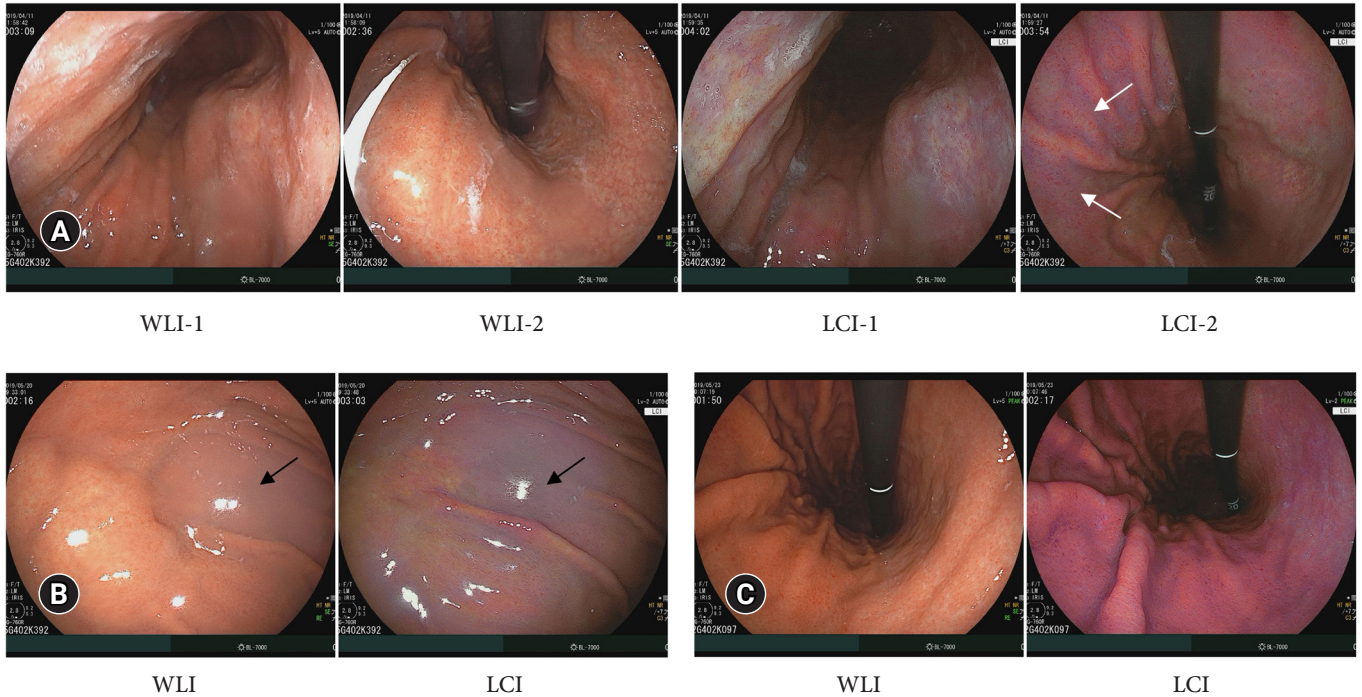


**Fig. 2.** Endoscopic findings of gastric tumors using white light imaging (WLI) and linked color imaging (LCI). (A) A I**ib**+I**ic** tumor is located at the anterior wall side of the antrum. WLI showed a slightly irregular surface mucosa with the same color as the surrounding mucosa (black arrows). LCI showed an orange-red lesion surrounded by purple mucosa (white arrows). The histologic results revealed a tubular adenoma with high-grade dysplasia. (B) A I**ia**+I**ic** tumor located at the postero-lesser curvature side of the lower body was noticed under WLI mode (black arrow). LCI showed an orange lesion, suggestive of cancer, surrounded by pale atrophic mucosa (white arrow). The final histopathological finding is a well-differentiated tubular adenocarcinoma invading the mucosa (lamina propria). (C) WLI shows a slightly irregular lesion on the lesser curvature of the body (black arrow). LCI showed an orange-red lesion partially surrounded by purple mucosa (white arrow). The final histologic result revealed a tubular adenoma with low-grade dysplasia. In all three cases, lesions were distinguished more easily by color contrast in LCI mode than in WLI mode. The mucosal colors in Cases A and C were diffuse redness in WLI and crimson in LCI and those in Case B were orange in WLI and apricot in LCI. Finally, Cases A and C were identified as *Helicobacter pylori*-positive patients, and Case B was identified as a patient with past infection.

Endoscopic findings, it can be helpful in the diagnosis of active *H. pylori* infection (Fig. 3).<sup>30</sup> Several studies on the role of LCI in diagnosing the presence or absence of *H. pylori* infection have been conducted. In *H. pylori*-positive patients, a marked or slight diffuse redness in WLI and crimson (deep red) coloring in LCI were observed.<sup>18,29,31</sup> In patients with past infection, orange mucosa in WLI and apricot coloring in LCI were observed. In patients with no infection, orange mucosa without diffuse redness in WLI and apricot color in LCI were observed. When LCI was used, patchy or spotty redness of the corpus mucosa became clear because of high color contrast.<sup>32,33</sup>

A study by Dohi et al.<sup>29</sup> showed that the accuracy, sensitivity, and specificity of *H. pylori* infection diagnosis using WLI were 74.2%, 81.7%, and 66.7%, respectively. When LCI was used, the

accuracy, sensitivity, and specificity of *H. pylori* infection diagnosis were 85.8%, 93.3%, and 78.3%, respectively. The accuracy and sensitivity of LCI were significantly higher than those of WLI.<sup>29</sup> In a Korean study, the accuracy, sensitivity, and specificity of *H. pylori* infection diagnosis using WLI were 70.8%, 32.4%, and 93.3%, respectively.<sup>34</sup> When LCI was used, the accuracy, sensitivity, and specificity of *H. pylori* infection diagnosis were 78.8%, 57.4%, and 91.3%, respectively. The accuracy and sensitivity of LCI were significantly higher than those of WLI.<sup>34</sup> Therefore, LCI is considered to have a better diagnostic accuracy for *H. pylori* infection status than WLI. Recently, computer-aided diagnostic systems for classifying the status of *H. pylori* infection using LCI have been developed and have shown good results.<sup>35-38</sup>



**Fig. 3.** Endoscopic findings of *Helicobacter*-associated gastritis using white light imaging (WLI) and linked color imaging (LCI). (A) Both modes showed mucosal edema, atrophic mucosa, and hemorrhagic spots in the mid to high body of the stomach. Under LCI mode, hemorrhagic spots on the body are more apparent (white arrows). (B) Turbid gastric juices on the gastric fundus were seen in both modes (black arrows). (C) Atrophic change and hemorrhagic spots on the gastric corpus were noticed in both modes. In all three cases, the mucosal color was crimson in LCI mode but slightly red in WLI mode. *H. pylori* infection was confirmed in all cases.

### Other recent findings

Even when using an ultraslim endoscope (EG-L580NW or EG-L580NW7), LCI can be useful for identifying neoplastic lesions in the upper GI tract.<sup>39-42</sup> Additionally, a recent study has suggested that LCI could improve the endoscopic diagnosis of eosinophilic esophagitis, although further research is required.<sup>43</sup>

## CONCLUSIONS

LCI can improve the visibility of BE, esophageal squamous cell carcinoma, esophageal adenocarcinoma, reflux esophagitis, and EGC. In addition, LCI is more effective than WLI for detecting tumor lesions in the pharynx, esophagus, and stomach. LCI significantly aids in diagnosing and detecting lesions on upper GI endoscopy. Various studies on LCI are expected to be published in the future.

### Conflicts of Interest

The author has no potential conflicts of interest.

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