### **NEW METHODS: Clinical Endoscopy**

# Magnified endoscopic observation of early colorectal cancer by linked color imaging with crystal violet staining (with video)



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**Background and Aims:** Many reports have shown the usefulness of magnification endoscopy with crystal violet (CV) staining for delineating the pit pattern in the diagnosis of colorectal carcinoma. However, the diagnostic accuracy of this method is not adequate for assessing the depth of invasion of early stage cancers. The novel technology of linked color imaging (LCI) combined with CV staining is expected to improve the accuracy of determining the depth of invasion.

**Methods:** We studied 3 patients with early stage colorectal cancer who were referred to our hospital. After CV spraying, high-magnification endoscopy was conducted by using the LCI mode. Efficacy of this modality was evaluated by comparing the preoperative diagnostic endoscopic images with posttreatment histopathologic findings.

**Results:** In 2 cases of rectal cancer, although conventional endoscopic examination could not exclude the possibility of submucosal cancer, use of the LCI mode with CV staining confirmed mucosal cancer. Eventually, EMR was conducted and achieved curative resection. In 1 case of sigmoid colon cancer, both conventional and CV magnification endoscopy suggested submucosal cancer. However, mucosal cancer was diagnosed by the novel method, and EMR achieved curative resection.

**Conclusions:** LCI high-magnification endoscopy combined with CV staining provides images close to histopathologic findings and is expected to improve the accuracy of endoscopic diagnosis of the depth of invasion for early stage colorectal cancer.

Abbreviations: BII, blue laser imaging; CV, crystal violet; LCI, linked color imaging.

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Many reports have indicated the usefulness of magnification endoscopy enhanced by crystal violet (CV) staining for the diagnosis of colorectal cancer. 1-5 According to these reports, the method is effective in differentiating between non-tumor and tumor, differentiating between adenoma and carcinoma, and determining the depth of cancer invasion. The pit pattern classification proposed by Kudo and Tsuruta is currently the standard for magnifying endoscopic diagnosis of colorectal cancer in Japan.<sup>2</sup> Especially, a type V<sub>N</sub> pit pattern is regarded to be a useful indicator of submucosal cancer type 2 (SM2) cancer. On the other hand, a type V<sub>I</sub> pit pattern includes lesions from cancer in situ to deep submucosal invasive cancer. At the Hakone Consensus Meeting in 2004, subclassification of a type V<sub>I</sub> pit pattern into mildly irregular and highly irregular was proposed; the former indicating M-SM1 and the latter indicating SM2 or deeper. In this proposal, high irregularity of a type VI pit pattern is defined as a narrowed pit lumen, irregular margin, unclear contour, decrease in or loss of stainability in the stromal area, and the scratch sign.<sup>6-8</sup> However, evaluation of such detailed findings is by no means easy.

Recently, image-enhanced endoscopy by using a narrow-band light source, such as the narrow-band imaging and blue laser imaging (BLI) modalities, has been reported to be effective for the diagnosis of colorectal cancer. However, the performance of these methods is not superior to magnification endoscopy by using CV.<sup>9-12</sup>

Another new image-enhanced endoscopy modality, linked color imaging (LCI), provides color images, in contrast to the monochrome images of conventional image-enhanced endoscopy. On top of its high performance in depicting blood vessels, additional image processing that enhances color separation for red color allows clear visualization of the red blood vessel and the white pit. Use of LCI with CV staining can be expected to facilitate pit pattern identification and detailed assessment of pit morphology. This report describes the use of LCI magnification endoscopy with CV staining for the diagnosis of colorectal cancer in the clinical setting.

#### **PATIENTS AND METHODS**

#### **Patients**

We studied 3 patients referred to our hospital because of colorectal cancer, who underwent LCI highmagnification endoscopy with CV staining for preoperative diagnosis and also posttreatment pathology evaluation.

#### The novel image-enhancing mode LCI

An endoscopic system with a laser light source (LASEREO, Fujifilm) was used. This system has 2 lasers with different wavelengths. One is white-light laser (wavelength  $450 \pm 10$  nm), providing wide-spectrum white-light illumination suitable for general observation. The other is a BLI mode laser (wavelength 410  $\pm$ 10 nm) with characteristics of short wavelength and narrow band. The BLI mode is used as high contrast signals to obtain information regarding capillaries on the mucosal surface, slight mucosal irregularity, and deep blood vessels. The intermediate mode BLIbright, which has a higher white-light intensity ratio, provides a brighter image. The LCI used in the present study is a novel image-enhanced mode based on a BLI-bright image with additional image processing that enhances color separation of red color to depict red and white colors more vividly. When used with CV staining, the white region corresponding to the pit appears even whiter and is distinctly separated from the stained glandular ducts in the surrounding area. Furthermore, the red vascular region is enhanced and can be depicted simultaneously with the glandular ducts.

#### **Methods**

For endoscopic observation, initially the lesion was observed conventionally by using white light. Then the lesion was stained with 0.05% CV, and magnifying observation was conducted. Finally, the light source was switched to LCI mode, and magnifying observation was again performed. In conventional magnification endoscopy,

observation is conducted at  $\times 80$  magnification. With the present system, observation at up to  $\times 135$  magnification is possible. A further 2-fold magnification can be obtained by electronic zoom. With this high-magnification endoscopic system, a lesion can be diagnosed endoscopically at a level similar to a histopathologic diagnosis.

#### **RESULTS**

Case 1 involved a 49-year-old man referred to our hospital because of a rectal tumor. Conventional endoscopic examination showed a 10-mm type IIa+IIc lesion surrounding by white spots. The whole lesion was markedly irregular; together with the presence of depression in the center, the findings were suggestive of submucosal invasion. We performed high-magnification observation by using the novel LCI mode with CV staining. Although mildly irregular ductal structure and network-like irregular blood vessels were observed, there was no structureless or avascular region. A type V<sub>I</sub> pit pattern showed mild irregularity, and mucosal cancer was diagnosed. The treatment option of EMR was selected with a high level of confidence. Posttreatment histopathologic results confirmed complete resection of the mucosal cancer (Fig. 1), (Video 1, available online at www.giejournal.org).

Case 2 involved an 83-year-old man. As in case 1, this case was diagnosed as mucosal cancer with a high level of confidence. EMR was conducted, and histopathologic findings confirmed the diagnosis (Fig. 2).

Case 3 involved a 71-year-old man with sigmoid colon cancer. Conventional observation by using white light showed irregular elevations with tightness as well as depressions, suggesting SM2 cancer. Magnification endoscopy with CV staining showed poor staining in some regions, and a  $V_{\rm N}$  pit pattern was suspected. High-magnification endoscopy by using the LCI mode clearly depicted the pit structure in the poorly stained region. Network-like blood vessels were observed. Observation under high magnification showed only mild pit pattern irregularity and no disappearance or severe destruction of the pit pattern. Without evidence of deep invasion, the findings were interpreted as a type  $V_{\rm I}$  pit pattern with mild irregularity, and mucosal cancer was diagnosed. EMR was conducted, and histopathologic findings confirmed mucosal cancer (Fig. 3). Surgery was avoided in this case.

#### DISCUSSION

Many articles have reported magnifying observation with CV staining in the endoscopic diagnosis of colorectal cancer, and the effectiveness of this modality has been adequately confirmed. However, there is still room for improvement on the accuracy of diagnosing the depth of invasion of early colorectal cancer. The present findings suggest that the novel image-enhanced system LCI contributes to improving the diagnostic performance of magnification endoscopy. Conventionally, pit pattern evaluation by magnification endoscopy with CV staining and vascular evaluation by

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