

Blue laser imaging endoscopy system for the early detection and characterization of colorectal lesions: a guide for the endoscopist

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Abstract: Blue laser imaging is a new system for image-enhanced endoscopy using laser light. Blue laser imaging utilizes two monochromatic lasers (410 and 450 nm) instead of xenon light. A 410 nm laser visualizes vascular microarchitecture, similar to narrow band imaging, and a 450 nm laser provides white light by excitation. According to three recently published reports, the diagnostic ability of polyp characterization using blue laser imaging compares favorably with narrow band imaging. No published data are available to date regarding polyp detection with blue laser imaging. However, blue laser imaging has the possibility to increase the detection of colorectal polyps by depicting brighter and clearer endoscopic images, even at a distant view, compared with first-generation image-enhanced endoscopy. A clinical trial to compare the detection between blue laser imaging and xenon light is warranted.

Keywords: image enhanced endoscopy, blue laser imaging, magnification colonoscopy, colorectal neoplasm, colon polyp, colorectal cancer

Introduction

Gastrointestinal cancers are a leading cause of death around the world. The introduction of gastrointestinal endoscopy has revolutionized the way we detect and treat gastrointestinal cancers, particularly in patients with early stage disease. Since the early 1960s, white light endoscopy has been widely used for the detection and characterization of colorectal polyps [Wolff and Shinya, 1971, 1973]. In the 1990s, magnification endoscopy using the dye spray technique attracted colonoscopists' attention [Kudo, 1993; Axelrad *et al.* 1996; Togashi *et al.* 1999]. In the 2000s, however, it was replaced by hardware-based image-enhanced endoscopy (IEE) [Machida *et al.* 2004] because the dye-based technique is complicated and inconvenient, whereas hardware-based techniques enable the colonoscopist to easily obtain an enhanced image by simply pushing a button. The original concept of IEE also includes dye-based techniques [Kaltenbach *et al.* 2008b], but hardware-based techniques are most commonly used. IEE can be used throughout the gastrointestinal tract to improve the discrimination of the

type of lesions and their malignant potential. Recently, hardware-based IEE has played an important role in not only the detection, but also in the characterization of colorectal polyps.

First-generation hardware-based IEE systems include narrow band imaging (NBI) [Machida *et al.* 2004], flexible spectral-imaging color enhancement (FICE) [Togashi *et al.* 2009] and i-SCAN [Hoffman *et al.* 2010a], all of which were initially released in the early 2000s. These systems do not involve injection of any dye and rely solely on hardware-based technology. However, first-generation IEEs have critical drawbacks, e.g. dark images at a distant view and low-resolution images. Thus, first-generation NBI does not demonstrate a higher adenoma detection rate than white light endoscopy in large clinical trials [Rex and Helbig, 2007; Kaltenbach *et al.* 2008a; Uraoka *et al.* 2008; Adler *et al.* 2009]. As for other hardware-based IEE techniques, one large clinical trial failed to demonstrate any objective advantage of the FICE technique over conventional high-resolution endoscopy in terms of

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improved adenoma detection rates [Aminalai *et al.* 2010], although a relatively small clinical trial (one arm: 100) in a single center showed a significantly higher adenoma detection rate in high-definition colonoscopy with i-SCAN, compared with standard resolution endoscopy [Hoffman *et al.* 2010b].

In 2013, blue laser imaging (BLI) was released by the Fujifilm Corporation. BLI has successfully achieved a bright and clear image even at a distant view [Osawa and Yamamoto, 2014]. These capabilities may lead to improved detection of polyps and more accurate diagnoses. The vast majority of gastroenterologists are not familiar with BLI due to general lack of availability of this equipment. The Japanese government approved reimbursement for BLI through the national health insurance system. Since introducing BLI to our medical center in 2013, we have used BLI for routine colonoscopy. In this review article, we describe the principles of BLI, tips for the use of BLI, polyp detection and polyp characterization using BLI.

Principles of BLI

First, we review the principles of NBI in generating endoscopic images similar to BLI. NBI uses optical filters to change the wavelength of the transmitted light, which in turn targets the microvessels of the mucosa. NBI utilizes two kinds of light: blue light (wavelength of 415 ± 30 nm) and green light (wavelength 540 ± 30 nm). The blue light penetrates the superficial epithelium and visualizes microstructures in the mucosa as well as the submucosa. This selective narrowing of the blue and green light, and the omission of red light, increases the fidelity of the images and improves visualization of microvessels as well as surface patterns resembling pit patterns.

The word ‘laser’ is an acronym for ‘light amplification by stimulated emission of radiation’. Laser light is characterized by spatial and temporal coherence, resulting in clearer images for vessel/surface microstructure of the mucosal surface through ‘further narrowing’. BLI uses two monochromatic lasers (410 ± 10 nm and 450 ± 10 nm) instead of xenon light to obtain image enhanced endoscopy, as shown in Figure 1. The 410 ± 10 nm laser is vital to visualize the vascular microarchitecture on the mucosal surface. The 450 ± 10 nm laser provides white light by

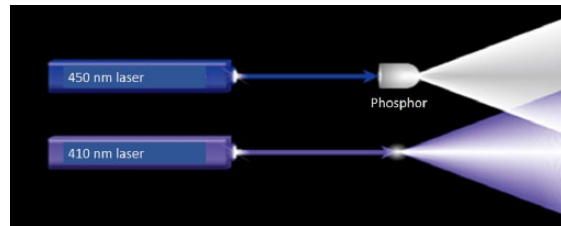


Figure 1. Laser illumination using two lasers and white light phosphor. A 410 nm laser looks blue light. A 450 nm laser stimulates the white light phosphor in the tip of the scope to produce the broadband white light.

excitation. This laser stimulates the white light phosphor in the tip of the endoscope to produce broadband white light, providing the standard view obtained with conventional xenon light sources. The brightness of the white light is controlled by the laser output power. In addition, longer wavelength light such as a 450 ± 10 nm laser is less absorbed by small vessels and reaches the deeper layers in the tissue, thus depicting larger blood vessels in the deeper layers.

Tips for the use of BLI

The BLI system utilizes three modes: BLI mode, BLI-bright mode and white light mode. To alter the mode, the colonoscopist simply selects the desired mode on the operating portion of the colonoscope with a button. Figure 2 shows the light spectrum in each mode. The intensity balance of the monochromatic lasers differs in each mode, enabling high contrast images of blood vessels over a wide range from distant images to close-up images, even with magnification.

1. BLI mode

The BLI laser power ratio is raised to maximize the contrast of the microvascular pattern seen. In this mode, the vascular pattern as well as the surface pattern can be most clearly visualized on the display. The BLI mode is dedicated to close-up views or magnified views.

2. BLI-bright mode

A brighter view is accomplished using the BLI high-contrast image by controlling the power ratio of the BLI laser and the white light laser. In contrast to conventional IEE, both the vascular

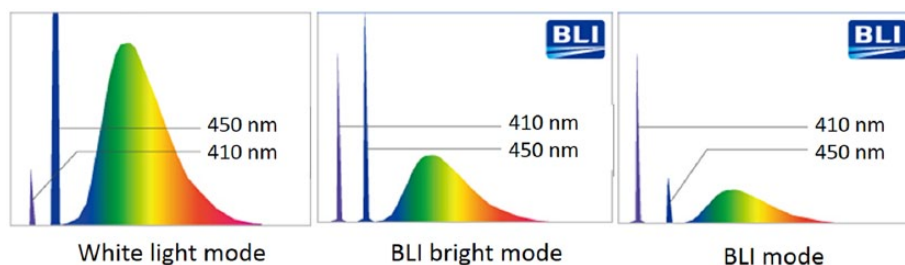


Figure 2. Light spectrum in each mode.
Note: white light mode contains 410 nm laser light.

pattern and the surface pattern are enhanced while maintaining the brightness, even at a distant view. The BLI-bright mode may be suitable for detection, whereas the BLI mode is suitable for more detailed magnified observations.

3. White light mode

Different from conventional white light generated by a xenon light source, white light mode using the BLI system uses a 410 ± 10 nm laser to enhance vascular images. Thus, the vascular microstructure is more clearly depicted using the white light mode compared with that obtained using xenon light.

Recommended approach

It is important to match the mode and application properly. At the beginning, perform an overall observation of the lesion using the white light mode with normal magnification. As mentioned above, white light mode may provide a clearer image than that using xenon light. Next, the BLI-bright mode without magnification is applied. The extent of the lesion should be evaluated using this mode. Then, use the BLI-bright mode to identify the region with advanced histological atypia based on changes in color tone and superficial structure. Finally, apply the BLI mode to obtain magnified images of the surface pattern and vascular pattern by focusing on the region identified. An example of such a region is shown in Figure 3 (adenoma) and Figure 4 (nonadenoma).

Polyp detection using BLI

Similar to previous clinical trials investigating the detectability of NBI, a recent clinical trial using the latest generation NBI colonoscopes (designated the 190 series or Exera III) has failed to demonstrate an increased detection rate of colon

polyps [Rex *et al.* 2015]. No data on the detection of polyps using BLI is available to date. It has been reported recently that BLI-bright mode improves the visibility of colorectal polyps [Yoshida *et al.* 2015], suggesting the possibility of a high yield using BLI-bright mode. Also, in the latest report making a direct comparison between BLI and NBI, only BLI-bright maintained adequate brightness and contrast up to 40 mm with significantly longer observable distances compared with NBI and BLI modes, although the new NBI system was not used [Kaneko *et al.* 2014]. In our experience, BLI-bright mode, as well as white light mode, allows a bright and clear image to be obtained, even at a distant view. Therefore, BLI may increase the detection rate of colorectal polyps in a future clinical trial. At present, a multicenter randomized clinical trial to compare the detection rate of BLI-bright mode and xenon white light is ongoing in Japan. Final results should be available in the spring of 2016.

Polyp characterization using BLI

So far, only two reports of polyp characterization using BLI have been published by the same group [Yoshida *et al.* 2014a, 2014b]. Sufficient evidence is still lacking in this field. According to these reports, the diagnostic accuracy of BLI with no magnification for differentiating between neoplastic and non-neoplastic polyps <10 mm in diameter is 95.2%, which is greater than that using white light (83.2%). In addition, the diagnostic accuracy of BLI magnification in the NBI classification was 74.0% (77/104), similar to that of NBI magnification (77.8%). The authors concluded that the diagnostic effectiveness of this method is similar to that of NBI magnification.

Indeed, our reading test on an image library of 80 small (≤ 5 mm) colorectal polyps demonstrated similar results regarding the diagnostic ability of

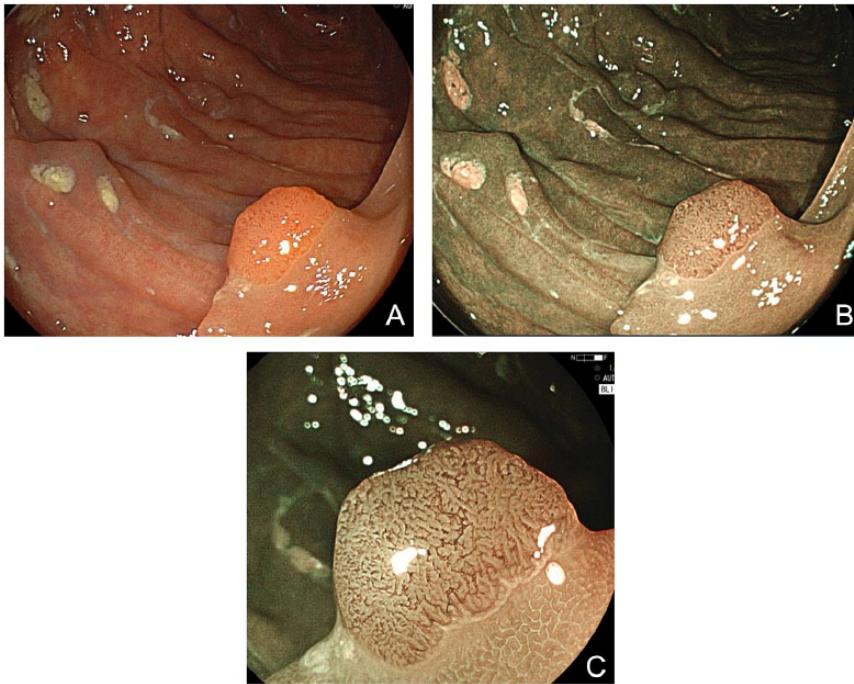


Figure 3. (A) White-light mode. A sessile adenoma measuring 6 mm in size is clearly identified, but its superficial structure is not depicted clearly. (B) BLI-bright mode. Surrounding normal mucosa is depicted clearly and brightly even in a distant view. The vessel pattern of the polyp as well as the surface pattern is clearly depicted without magnification. (C) BLI mode. Magnified view shows a regular structure, suggesting a low-grade adenoma.

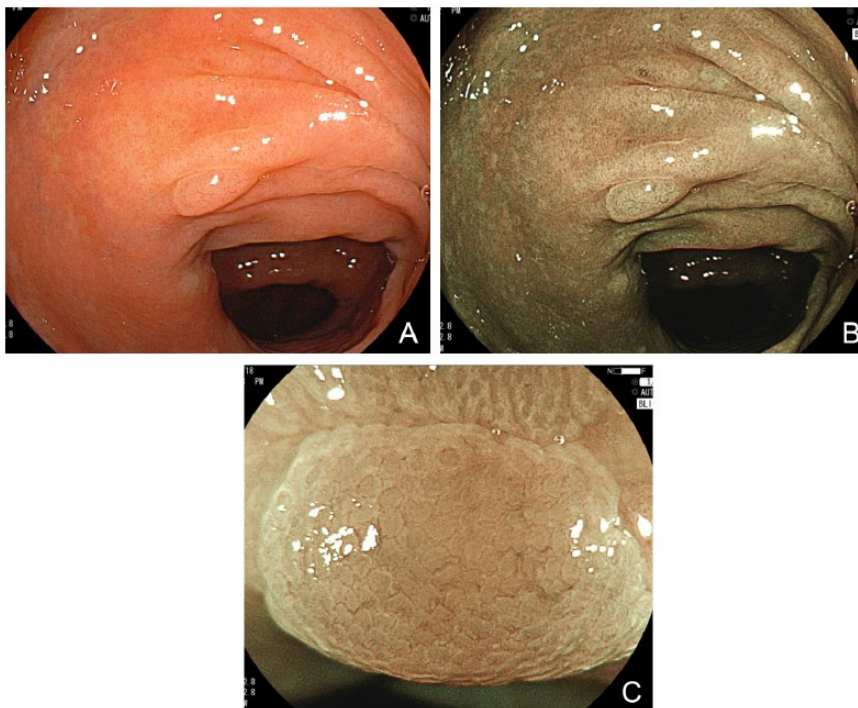


Figure 4. (A) White-light mode. A hyperplastic polyp measuring 6 mm shows a pale appearance. (B) BLI-bright mode. Demarcation line of the polyp is clearly seen in a distant view. (C) BLI mode. Magnified view does not show any distinct structure, but only small vessels are observed on the polyp surface, suggesting a non-neoplastic polyp.

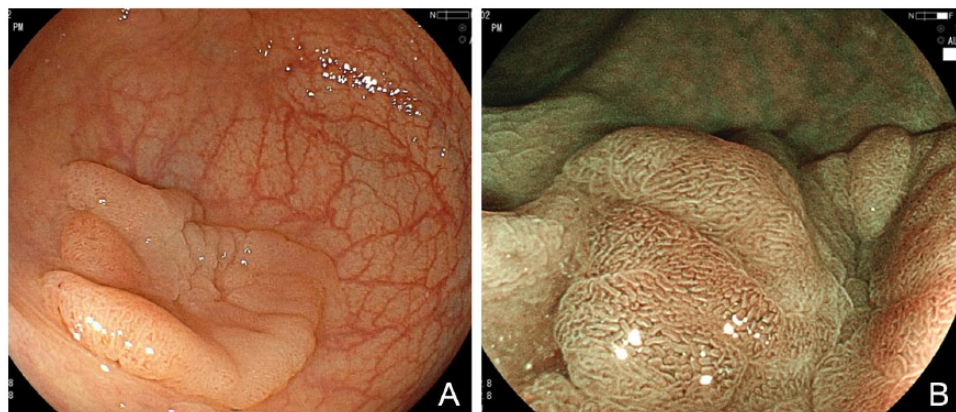


Figure 5. (A) White-light mode. Laterally spreading tumor measuring 28 mm in maximum size is clearly identified in a plain image. (B) BLI mode. Magnified view shows regularly arranged structure, suggesting a low-grade tubular adenoma.

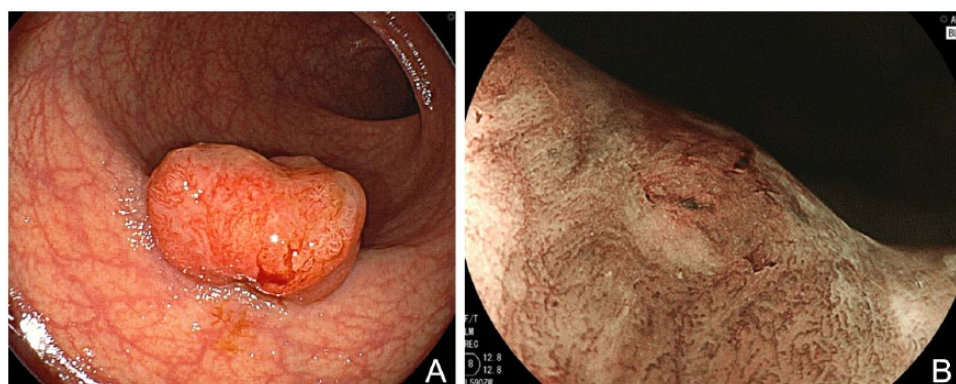


Figure 6. (A). White-light mode. Protruding tumor measuring 18 mm shows an irregular surface in a plain image. (B) BLI mode. Magnified view shows an irregular vascular pattern and an avascular area can be seen partially. Surface pattern also shows irregularity. These findings definitely indicate substantially invasive cancer.

BLI with magnification. High diagnostic sensitivity ($\leq 96\%$ by all three raters) was achieved using BLI mode [Togashi *et al.* 2014a]. Furthermore, the sensitivity of endoscopic diagnosis using white light images (84–94%) compared favorably with that of BLI, implying that white light mode also contains a 410 ± 10 nm laser to enhance vascular imaging. This finding is not consistent with previously published data. Further research is required to validate these observations.

BLI facilitates discrimination of adenoma from invasive cancer. BLI magnification by laser source could predict invasion depth of colorectal neoplasms [Yoshida *et al.* 2014a]. In our experience [Togashi *et al.* 2014b], clinical impact of this method was equivalent to that of NBI magnification. So far only one report is available in this

field. Figure 5 represents a typical mucosal lesion, whereas Figure 6 represents deeply invasive cancer.

Conclusion

A new hardware-based IEE system, the BLI system, provides endoscopic images similar to NBI, since BLI uses a 410 ± 10 nm monochromatic laser to enhance the vascular images. The diagnostic ability of BLI is almost equivalent to that of NBI, although conclusive evidence is still lacking. Based on our preliminary data, the white light generated using the BLI system may allow more accurate discrimination of adenomas from non-adenomatous lesions compared with conventional white light. Further studies are required to validate these observations.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

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