## Development of a New Generation Endoscope System with Lasers "LASEREO"

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#### Abstract

We have developed a new generation endoscope system "LASEREO". A new laser illumination technology is applied to LASEREO. Having two kinds of lasers and phosphor, the new illumination is useful in detecting the structure of the mucous membrane. We realized the narrow band light observation BLI (Blue LASER Imaging) that can emphasize a minute change of the mucous membrane structure by using the new illumination technology together with our original image processing technology.

#### 1. Introduction

Conventionally, our endoscope systems employed Flexible spectral Imaging Color Enhancement (FICE) that allows easy observation of tissue characteristics and blood vessels by using signal processing to extract the spectral images of specific wavelengths from the white light generally used in such systems. However, it was regarded as difficult to produce high contrast images of microvessels on the surface of mucous membranes with white light illumination.

To address that issue, the new-generation endoscope system "LASEREO" (Fig. 1) released in September 2012 features a new laser illumination technology that combines two kinds of laser light with a phosphor and our original image processing technology. The system achieved the



Fig. 1 LASEREO system.

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\* Medical System Research & Development Center Research & Development Management Headquarters FUJIFILM Corporation Miyanodai, Kaisei-machi, Ashigarakami-gun, Kanagawa 258-8538, Japan narrowband light observation function, Blue LASER Imaging (BLI), which enables image-enhanced endoscopy to detect the minute changes on the mucosal surface as key information for cancer diagnosis.

This paper explains the outline, features, principles and capabilities of this new system and foresees the future possibilities of laser endoscopes.

### 2. Characteristics of the market

Gastroenterological endoscopy is available at the following three types of hospitals: a) core hospitals; b) general hospitals; and c) clinics. Core hospitals are further classified into two groups: Special Functioning Hospitals that provide highly advanced medical care; and Regional Medical Care Support Hospitals that back up general hospitals and clinics in local communities. In those hospitals, there is a strong need for magnifying endoscopy and image-enhanced endoscopy for definitive diagnosis before starting endoscopic therapies such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). In cancer diagnosis, in particular, treatment plans are often determined by closely observing the patterns of microstructures and microvessels on the mucosal surface and examining the condition of lesions with endoscopy. The diagnosis is made according to the classification of those patterns, which exist in several forms for each region such as a pharynx, esophagus, stomach and large intestine, because tissue structures and cancer onset morphology vary depending on the region. In the meantime, in clinics, screening is the main diagnostic method and magnifying endoscopy is hardly ever conducted. However, there is a need for image-enhanced endoscopy for screening.

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Image-enhanced endoscopy is classified into a) the optical method; b) the digital method; c) the optical digital method; and d) the dye spraying method. For the observation of the above-described superficial structures and microvessels, and also for the screening, the following methods are used: FICE (a digital method); NarrowBand Imaging (NBI) (an optical digital method); and indigo carmine dye spraying or Lugol's iodine solution spraying (a dye spraying method). In FICE, displayed images are enhanced with the organisms' reflection spectral information collected by processing signals obtained during the irradiation of white light. In NBI, the illumination used to collect spectral information is narrowband light obtained by passing white light through optical filters. Compared with the dye spraying methods that require preparation and take not only labor but also running costs before and after the use, there are high expectations for FICE and NBI because they need only button pressing to give a result.

#### 3. Outline and features of the system

LASEREO is the first gastroenterological endoscope system to employ lasers for its illumination. It incorporates not only a function for white light observation but also a function for narrowband light observation that utilizes the characteristics of laser light as standards. In addition, compared with conventional light sources using xenon lamps, its power consumption and heat emission are particularly low. The system configuration is as follows: the "PROCESSOR VP-4450HD"; the laser "LIGHT SOURCE LL-4450" and the special L590 series endoscopes (EG-L590ZW for upper GI magnification endoscope, EG-L590WR for general upper GI endoscope and EC-L590ZW for lower GI magnification endoscope and EC-L590WM for general lower GI endoscope).

#### 3.1 Features of the laser light source LL-4450

The laser light source LL-4450 uses two lasers with different wavelengths. It creates illumination suitable for either normal (white light) observation or narrowband light observation by changing the intensity ratio of those two lasers.

One is the white light mode laser (peak wavelength:  $450 \text{ nm} \pm 10 \text{ nm}$ ), which excites phosphors to create white

light illumination with broader spectral distribution suitable for normal observation. The other is the short-wavelength narrowband light laser (i.e., BLI laser, peak wavelength: 410 nm  $\pm$ 10 nm), which is used to obtain information about the microvessels and slight uneveness on the mucosal surface as well as the deep blood vessels as high-contrast signals by utilizing its characteristics: short-wavelength and narrow spectral width (Fig. 2).

Other characteristics of this light source is the wide dynamic range of light control required from illumination. When applying narrowband light observation BLI, it is necessary to control the outputs so that the intensity ratio of the white light mode laser and the BLI laser is always constant over a wide range of light control. With the LL-4450, high-accuracy light control over the range is possible by combining multiple laser modulation drive methods.

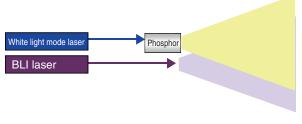


Fig. 2 Laser illumination.

# 3.2 Three kinds of illumination and four observational modes

LASEREO has four observational modes and employs three kinds of illumination with different spectral distributions (Fig. 3, Table 1).

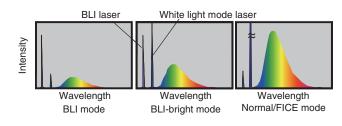


Fig. 3 Spectral distribution of illumination.

| Table 1 | Types of illumination and observation modes. |
|---------|--|
|---------|--|

|            | Purpose   | Laser intensity                   |         |   |
|------------|---|-----------------------------------|---------|---|
| Mode       |   | For white<br>light<br>observation | For BLI | Description   |
| Normal     | White light observation   | Strong                            | Weak    | Same color tone as conventional systems (xenon light source)  |
| FICE       | Color enhancement   | Same as Normal mode               |         | With spectral imaging, finer color changes are enhanced. By increasing the contrast of the colors of mucous membranes and blood vessels, the visibility of the blood vessels is enhanced. The brightness level is the same as normal images.  |
| BLI        | Observation of blood<br>vessels and superficial<br>mucosal structures | Weak                              | Strong  | Images suitable for the enhancement of the superficial microvessels are generated<br>by increasing the short-wavelength light components from lasers and improving the<br>contrast originating from the presence of hemoglobin.   |
| BLI-bright | Observation of blood<br>vessels and superficial<br>mucosal structures | Medium                            | Strong  | Bright images are generated even when viewing relatively distant targets by slightly increasing white light components compared with BLI mode. The contrast between blood vessels and superficial structures is higher than in Normal or FICE modes but a little weaker than in BLI mode. |

The conventional FICE function can be used for white light observation. The newly developed narrowband light observation BLI's illumination is the well-balanced mixture of short-wavelength narrowband light and white light. Figure 4 is the images which improved the contrast of a mucous membrane and the blood vessel by performing image processing for the signal of white light which has a wide wavelength range and the signal of short-wavelength narrowband light which has a narrow wavelength range.

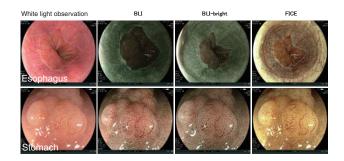


Fig. 4 Clinical images captured by LASEREO. (supplied by Kyoto Prefectural University of Medicine Hospital)

BLI produces higher-contrast images of superficial mucosal structures and microvessels by increasing the intensity ratio of the BLI laser and white light mode laser. On the other hand, BLI-bright can create brighter images than BLI, even when viewing relatively distant targets, by slightly decreasing its ratio.

#### 3.3 Difference between BLI and FICE

FICE generates several narrowband images by signal processing from a white light image, and reproduces RGB images from those narrowband images, then enhances them. In that way, it improves the contrast of mucous membranes and blood vessels (Fig. 5). On the other hand, BLI makes the same contrast improvement to irradiate strong shortwavelength narrowband light and enhance a image (Fig. 6).

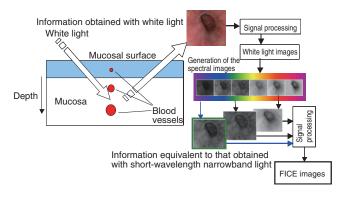


Fig. 5 Processing flow of FICE.

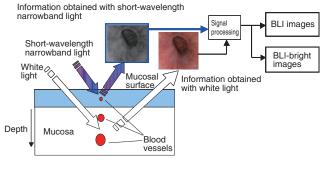


Fig. 6 Processing flow of BLI.

FICE, BLI and BLI-bright allow narrowband light observation. However, their image brightness and contrast intensity between mucous membranes and blood vessels are different as follows.

Brightness: Darker ←→→ Brighter BLI < BLI-bright < FICE ≅ White light observation Contrast: Higher ←→→ Lower BLI > BLI-bright > FICE > White light observation

## 4. Development of BLI

### 4.1 Principle of BLI

BLI is an image-enhanced technology that distinguishes microvessels on the mucosal surface and deep blood vessels based on the light-absorption characteristics of hemoglobin (Fig. 7) and the scattering characteristics of mucous membranes.

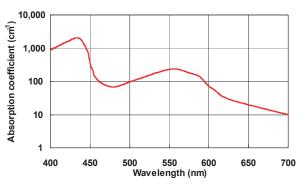


Fig. 7 Absorption spectrum of hemoglobin.

Figure 8 illustrates the basic principle of BLI. Shortwavelength light does not penetrate into deep layer of mucous membranes and can detect the superficial microvessels with high contrast (Fig. 8a). Conversely, long-wavelength light penetrates into deep layer of mucous membranes. Therefore, the light propagation process to deep layer makes the image of sperficial microvessels blurred and low-contrast by scattering, while the deep blood vessels are processed into a high-contrast image (Fig. 8b).

By using those two images, the superficial microvessels and deep blood vessels can be showed in different colors.

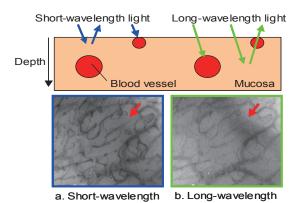


Fig. 8 Principle of BLI.

#### Conditions of the light source 4.2

In endoscopy the clear identification of superficial microvessels is required. It was known that illumination using short-wavelength narrowband light filters could improve the contrast of microvessels. However, this is limited to qualitative interpretation of the relationship between the contrast of microvessel and the wavelength.

In this paper, we firstly confirmed whether high-contrast superficial microvessel images can be obtained with shortwavelength narrowband laser light by conducting simulation. Then, we determined the specifications of the BLI light sources by experiments measuring oral mucosa.

#### 4.2.1 Assessment using simulation

With the spectral distribution of illumination and mucosal model, image signal values can be calculated from the following equation.

 $S(c, m) = \int L(\lambda) M(m, \lambda) C(c, \lambda) d\lambda \dots (1)$ S (c, m): Image signal value  $L(\lambda)$ : Spectral distribution of illumination  $M(m, \lambda)$ : Mucosal spectral reflectance  $C(c, \lambda)$ : CCD spectral sensitivity *c*: R, G, B *m*: Mucosa, superficial microvessels, deep blood vessels

The spectra used for  $L(\lambda)$ , the spectral distribution of

illumination, were those of several short-wavelength lasers and also the white light mode laser in conjunction with its phosphor material.

The unknown mucosal spectral reflectance,  $M(m, \lambda)$ , was calculated with the data of the gastric mucosa and blood by the simulation of light propagation. Figure 9 exemplifies the reflection spectra of the mucosa and superficial microvessels thus calculated by the simulation of light propagation.

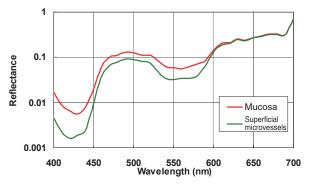


Fig. 9 Reflection spectra obtained by simulation.

The contrasts of the blood vessels by simulation with illumination of several intensity ratios of short-wavelength lasers and a white light mode laser, illumination of a xeon lamp and illumination of a xeon lamp with a narrowband light filter were compared (Fig. 10).

As a result, the following findings were obtained: the selection of lasers with appropriate wavelengths enables to realize high-contrast images; increasing the intensity of short-wavelength lasers against white light mode laser creates a high-contrast effect. In conclusion, a BLI laser with a wavelength of 410 nm was found to be suitable for observing superficial microvessels.

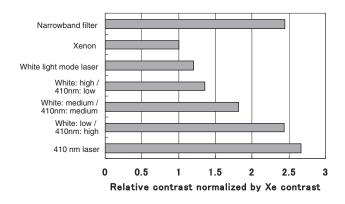


Fig. 10 Contrasts in microvessel images obtained by simulation.

#### 4.2.2 Experiment with the oral mucosa

Based on the results obtained by simulation, the conditions under which high-contrast blood vessel images can be created were verified with the oral mucosa while changing the intensity ratio of the BLI laser and white light mode laser.

The contrast between the oral mucosa and superficial microvessels (ratio of the signal values of the mucosa and the superficial microvessels) under each light source condition is shown in Fig. 11 and the respective images in Fig. 12.

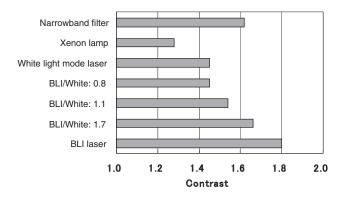


Fig. 11 Contrasts in microvessel images obtained in an experiment.

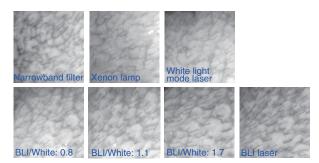


Fig. 12 Experimental results using oral mucosa.

Figure 11 shows that the setting of a proper light intensity ratio of the BLI laser and white light mode laser can create high-contrast microvessel images and there are equivalent to microvessel images with narrowband light filter whose center wavelength is 420 nm.

Figure 12 confirms that various levels of microvessel contrasts can be obtained by changing the intensity ratio of those two lasers. It indicates the possibility for the realization of illumination suitable for each purpose and observation target.

The microvessel contrasts to the oral mucosa obtained by experiment correspond respectively to the light source conditions for blood vessel contrasts obtained by simulation. Thus, the validity of the selection of light source conditions by simulation was proved.

## 4.2.3 Setting of two narrowband light observational modes

Taking into consideration the individual strengths of the BLI laser and white light mode laser, we have set up the following two narrowband light observational modes in LASEREO.

•BLI mode:

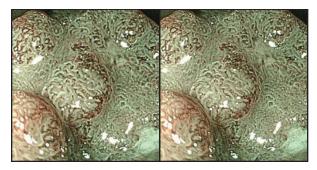
In this mode, the ratio of the BLI laser is increased to enhance the contrast of the microvessels on the mucosal surface. The main intended usage is the observation of targets at a short distance and magnifying endoscopy. •BLI-bright mode:

In this mode, the BLI laser and white light mode laser are included in illumination in due ratio to improve the contrast of blood vessels while brightness is maintained. The main intended usage is the observation of targets at a middle to short distance.

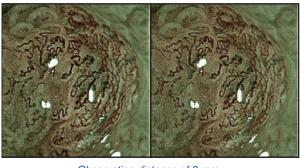
These two modes achieved bright, non-magnifying endoscopy as well as high-contrast blood vessel magnifying endoscopy in LASEREO's narrowband light observation.

#### 4.3 Structure enhancement

The targets of endoscopy are diverse, such as lesions with a diameter of a few centimeters from a relatively distant viewpoint and microvessels with a diameter of about 10  $\mu$ m in a magnified view as shown in Fig. 13 (Observation distance of 2 mm). Moreover, in magnifying endoscopy, not only 10- $\mu$ m microvessels but also a target like the marginal crypt epithelium bordered white in Fig. 13 (Observation distance of 5 mm) can be observed to determine future treatment plans. To cover an extensive range of observational conditions, two enhancement modes with different frequency bandwidths are incorporated in the BLI. A-mode, which is suitable for the enhancement of low-frequency regions, is suitable for the enhancement of areas and structures. B-mode is designed to enhance only thin lines. This is suitable for observing microvessels.



Observation distance of 5 mm



Observation distance of 2 mma. A-modeb. B-mode

Fig. 13 Two modes of structure enhancement.

#### 4.4 **Color enhancement**

The mucosal epithelium and the blood vessel density of the gastrointestinal tract vary depending on the region. Therefore, the reproduced color tones can be diverse. In BLI, color enhancement modes (i.e., C1, C2 and C3) are provided to make lesions stand out in each region of a pharynx, esophagus, stomach and large intestine. In BLI-bright, the "No color enhancement" tone, which is similar in color to the one in white light observation, is provided additionally (Fig. 14).



**C3** 

No color enhancement (for BLI-bright only)

Fig. 14 Color enhancement by BLI and BLI-bright.

#### 5. Conclusion

The gastroenterological endoscope system LASEREO employs a laser light source for its illumination. By utilizing the characteristics of the high brightness and narrow bandwidth particular to laser light sources, we have succeeded in the incorporation of the narrowband light observation BLI function into the system, which enables the display of the mucosa and blood vessels with high contrast. In addition, we have realized BLI-bright in which bright narrowband light observation at a relatively distant viewpoint is possible by changing the intensity of the BLI laser and white light mode laser.

To establish endoscopy systems useful for the detection of early cancerous lesions and the determination of treatment strategies, it is necessary to develop technologies that can visualize a great variety of biological and functional changes in cancer.

LASEREO has the potential for the development of new diagnostic technologies that enable the visualization of biological and functional changes in cancer by using laser light sources with different light wavelengths.

We have already engaged, in cooperation with National Cancer Center Hospital East, in the development of a technology with a laser light source that visualizes a type of biological and functional change in cancer: the hypoxia of cancerous lesions. In the future, we will keep striving to further develop LASEREO as an endoscopy system that promotes the early discovery of cancerous lesions and the determination of treatment strategies.

#### Acknowledgement 6.

We express our special thanks to Satoshi Ozawa who had been involved in the concept making of the system from the beginning of its development and Jun Matsunaga, Masayuki Takahira and Azuchi Endo who played central roles respectively in developing the scope, processor and light source of LASEREO.

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