Clinical Study

Blue Laser Imaging-Bright Improves Endoscopic Recognition of Superficial Esophageal Squamous Cell Carcinoma

Akira Tomie, Osamu Dohi, Nobuaki Yagi, Hiroaki Kitae, Atsushi Majima, Yusuke Horii, Tomoko Kitaichi, Yuriko Onozawa, Kentaro Suzuki, Reiko Kimura-Tsuchiya, Tetsuya Okayama, Naohisa Yoshida, Kazuhiro Kamada, Kazuhiro Katada, Kazuhiko Uchiyama, Takeshi Ishikawa, Tomohisa Takagi, Osamu Handa, Hideyuki Konishi, Yuji Naito, and Yoshito Itoh

1Department of Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan
2Department of Gastroenterology, Murakami Memorial Hospital, Asahi University, Gifu, Japan
3Department of Medical Oncology, Fukushima Medical University, Fukushima, Japan

Correspondence should be addressed to Osamu Dohi; osamu-d@koto.kpu-m.ac.jp

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Background/Aims. The aim of this study was to evaluate the endoscopic recognition of esophageal squamous cell carcinoma (ESCC) using four different methods (Olympus white light imaging (O-WLI), Fujifilm white light imaging (F-WLI), narrow band imaging (NBI), and blue laser imaging (BLI-bright)). Methods. We retrospectively analyzed 25 superficial ESCCs that had been examined using the four different methods. Subjective evaluation was provided by three endoscopists as a ranking score (RS) of each image based on the ease of detection of the cancerous area. For the objective evaluation we calculated the color difference scores (CDS) between the cancerous and noncancerous areas with each of the four methods. Results. There was no difference between the mean RS of O-WLI and F-WLI. The mean RS of NBI was significantly higher than that of O-WLI and that of BLI-bright was significantly higher than that of F-WLI. Moreover, the mean RS of BLI-bright was significantly higher than that of NBI. Furthermore, in the objective evaluation, the mean CDS of BLI-bright was significantly higher than that of O-WLI, F-WLI, and NBI. Conclusion. The recognition of superficial ESCC using BLI-bright was more efficacious than the other methods tested both subjectively and objectively.

1. Introduction

Esophageal squamous cell carcinoma (ESCC) is one of the most common causes of cancer death worldwide [1]; more than 10,000 people die from ESCC every year in Japan [2]. The early detection of ESCC leads to an improved prognosis, but when detected at a late stage, ESCC has a poor prognosis [3]. Conventional esophagogastroduodenoscopy with white light imaging (WLI) is frequently used, but it is often difficult to detect superficial ESCCs with this method. Iodine staining is the gold standard for detecting superficial ESCC [4–7] and is based on a chemical reaction between iodine and the glycogen that is contained in the normal epithelial cell microgranules in the stratum spinosum [8]. Dysplastic and cancerous cells are not stained by iodine because they do not contain glycogen due to their lack of cellular maturity. However, iodine staining often induces unpleasant side effects such as severe chest pain and discomfort owing to mucosal irritation [9–11], and its use is not practical in routine endoscopy.

In recent years, image-enhanced endoscopy (IEE) has been reported to improve the detection and diagnosis of superficial ESCC. Narrow band imaging (NBI) has been particularly useful for the detection and diagnosis of superficial ESCC when compared with WLI [12–14]. Blue laser imaging (BLI) is a novel IEE with two different lasers that enable
narrow band light observation. BLI is useful to establish the
diagnosis of esophageal lesions with or without magnification
based on the light-absorption characteristics of hemoglobin
(Hb). BLI produces a higher color contrast between the
brown esophageal cancer and the surrounding area without
magnification [15]. Moreover, BLI-bright is a brighter BLI
mode and is useful for endoscopic observation in a distant
view. The usefulness of BLI-bright observation in a distant
view for colorectal polyps and gastric cancer has already been
reported [16, 17]. However, few studies have compared the
ability of these different IIEEs to detect superficial ESCC. The
aim of this study was to evaluate the detection ability of WLI,
NBI, and BLI-bright by comparing lesion recognition in still
image distant views of ESCC.

2. Patients and Methods

2.1. Trial Design and Patients. We retrospectively enrolled
patients with superficial ESCC who underwent endoscopic
submucosal dissection (ESD) at Kyoto Prefectural University
of Medicine from March 2012 to December 2014. We selected
ESCCs that had endoscopic images obtained at the same
angle and distance with NBI and BLI-bright before ESD.
Finally, 25 ESCCs with both NBI and BLI-bright recorded
images were selected and analyzed in this study. A typical
ESCC was observed as a reddish area with the use of Olympus
white light imaging (O-WLI) and Fujifilm white light imaging
(F-WLI) or as a brownish area with the use of NBI and BLI-
bright in a distant view. In all cases, squamous cell carcinoma
was histopathologically diagnosed from a biopsy specimen
obtained prior to ESD. All patients provided written informed
consent for the endoscopic examinations, including the use
of NBI and BLI-bright. This study was approved by the
ethics committee of Kyoto Prefectural University of Medicine
and was registered in the University Hospital Medical Informa-
tion Network Clinical Trials Registry (UMIN-CTR) as number
UMIN000017869.

2.2. Endoscopy Systems and IEE Settings. Two different upper
GI endoscopic systems manufactured by Olympus Medical
Systems Co. and Fujifilm Co. were used in this study. A
high-resolution endoscope (GIF-H260Z; Olympus Medical
Systems Co., Tokyo, Japan) and a video processor with NBI
function (EVIS LUCERA; Olympus Medical Systems Co.,
Tokyo, Japan) were used for white light imaging (O-WLI)
observation and narrow band imaging (NBI) observation.
The structure enhancement of the endoscopic video proces-
sor was set to B-mode level 3 for O-WLI and B-mode level 8
for NBI. The color mode was fixed at level 1 for NBI.

A high-resolution endoscope (EG-L590ZW; Fujifilm Co.,
Tokyo, Japan) and a video processor with BLI-bright function
(LASEREO; Fujifilm Co., Tokyo, Japan) were used for white
light imaging (F-WLI) observation and blue laser imaging-
bright (BLI-bright) observation. The structure enhancement
of the endoscopic video processor was set to A-mode level
6 for BLI-bright. The color mode was fixed at level CI.
The depth of field for the GIF-H260Z and EG-L590ZW
endoscope was 7 to 100 mm and 6 to 100 mm, respectively.
The field of view for both endoscopes was 140 degrees.

2.3. Endoscopic Procedures. The endoscope was fixed at one
angle for observing the lesions, and each lesion was recorded
at that fixed angle using O-WLI, F-WLI, NBI, and BLI-bright
imaging.

2.4. Histopathological Diagnosis. After ESD resection, the
lesions were extended and fixed on boards with pins in
20% formalin, and a clinical pathologist histopathologically
confirmed the diagnosis of ESCC according to the Japanese
Classification of Esophageal Carcinomas.

2.5. Subjective Evaluation. For the subjective evaluation, the
endoscopists provided a ranking score (RS) of the endoscopic
images using the following 3-point ranking method based
on ease of recognition of the cancerous area. Images with
the easiest recognition were given 3 points; those with a
comparatively lower degree of clarity were given 2 points,
and obscure images scored only 1 point. Images obtained
with each modality (O-WLI, F-WLI, NBI, and BLI-bright)
were prepared for evaluation by placing them on a computer
monitor and displaying them independently of the images
obtained with the other endoscopic modality. A representa-
tive set of still images for the ESCC case is shown in Figure 1.
The endoscopists viewed the images individually, without
side-by-side comparison with other images of the same lesion
obtained by the other methods. Each image was scored using
the above scale with 1–3 points. The images were evaluated by
three endoscopists (NY, OD, and RK). Images were displayed
and observed with a personal computer in the standard and
widely supported red/green/blue (RGB) mode.

2.6. Objective Evaluation. The following methods were used
to ensure that the endoscopic images were objectively evalu-
ated. Each lesion and the surrounding mucosa were captured
for image processing, and the region of interest (ROI) was
highlighted. Representative still images illustrating the spots
captured for the color difference score (CDS) calculation of
the lesion and background mucosa are shown in Figure 2.
In order to ensure the accuracy of this method, the ROIs
were selected under the following conditions: (1) each ROI
in the set of four images was selected if located in the
same area of the lesion, (2) domains with excess brightness,
darkness, or particular halation were excluded, and (3) each
ROI figure was square shaped with a side length of more than
20 pixels. The color difference score (CDS; \( \Delta E = [\Delta L^*]^2 + 
(\Delta a^*)^2 + (\Delta b^*)^2]^{1/2} \)) of the pixel values based on L’a’b’
(Lab) color spaces within the ROI was used to evaluate the
recognition ability of each color image [18]. A Lab color
space is a color-opponent space with three dimensions. The
dimensions are lightness (L), redness/greenness (a),
and yellowness/blueness (b). Lab color space is based on how
the human eye interprets color not how RGB or CMYK color
models represent color. It is intended to provide perceptual
uniformity, and its L component closely matches the human
perception of lightness. It can thus be used to make accurate
color balance corrections by modifying output curves in the a
and b components or to adjust the lightness contrast by using
the L component. Therefore, \( \Delta E \), indicating the distance
2.7 Statistical Analysis. A post hoc power analysis was conducted to determine the power for the sample size \( n = 25 \). A post hoc power analysis was performed by using G*Power ver 3.1 [20]. Analysis of subjective evaluation compared to the total RS average for the four different methods by three endoscopists. The Wilcoxon signed-rank test was used to analyze the diagnostic capability of the four different methods both subjectively and objectively. A \( P \) value of <0.05 was considered statistically significant.

Inter- and intraobserver concordance was evaluated by calculating the \( \kappa \)-value. Interobserver variation was calculated from the results of the second reading. Intraobserver variation was determined by comparing the first and second assessments for each endoscopist. A \( \kappa \)-value of >0.8 indicated excellent agreement, 0.6–0.79 indicated substantial agreement, 0.4–0.59 indicated moderate agreement, 0.2–0.39 indicated fair agreement, and <0.2 indicated slight or very poor agreement. All statistical analyses were performed using SPSS software, Version 22.0 for Windows (IBM Japan, Ltd, Tokyo, Japan).

in Lab space, is suitable for estimating the difference between colors (Figure 3). The average color value in the ROI was calculated by using Photoshop CS4 image-editing software (Adobe Systems Inc.) as follows: (1) the image was opened, (2) the ROI was placed manually by using the Rectangular Marquee mode to locate the same area in the corresponding images, (3) the color mode was transformed from RGB to Lab, (4) the average of the color values \( (L, a, b) \) in the ROI was determined from the Histogram panel, and (5) these color values were converted into the units of CIE LAB. The conversion utilized the following formula:

\[
L^* = \frac{L}{255} \times 100, \quad a^* = a - 128, \quad b^* = b - 128, \tag{1}
\]

where \( (L, a, b) \) are the color values determined with Photoshop and \( (L^*, a^*, b^*) \) are the color values in the CIE LAB unit [19].
Figure 2: Representative still images illustrating the spots captured for the color difference score (CDS) calculation of the lesion and background mucosa (Figure 1). (a) O-WLI image, (b) F-WLI image, (c) NBI image, and (d) BLI-bright image. The lesion was captured for image processing, and the region of interest (ROI) was highlighted to calculate the CDS using each of the four methods.

Figure 3: In the $L^*a^*b^*$ color space system the color differences are visualized as distances in a diagram. $L^*$: color brightness ($L^* = 0$ is black and $L^* = 100$ is white). $a^*$: position between red and green (negative values are progreen; positive values are prored). $b^*$: position between yellow and blue (negative values are problue; positive values are proyellow).
Table 1: Clinicopathological features of patients.

| Patients/lesions | 25/25 |
|------------------|-------|
| Median age, years (range) | 70 (55–87) |
| Sex | |
| Male | 20 |
| Female | 5 |
| Mean tumor size, mm (range) | 20.5 (4–42) |
| Depth | |
| Intramucosal | 24 |
| Submucosal | 1 |
| Macroscopic type | |
| 0-IIa type | 3 |
| 0-IIb type | 14 |
| 0-IIc type | 8 |

Table 2: Inter- and intraobserver agreement (κ-value) for ranking score.

| | NY to OD | NY to RK | OD to RK |
|------------------|---------|---------|---------|
| Interobserver agreement | 0.613 | 0.382 | 0.317 |
| NY OD RK | |
| Intraobserver agreement | 0.673 | 0.873 | 0.599 |

The results of the current study suggest that BLI-bright has a higher detection ability for superficial ESCCs than WLI. Therefore, BLI-bright might improve the detection rate of superficial ESCCs during screening endoscopy in a manner similar to NBI.
BLI-bright facilitates the detection of ESCCs that show a well-demarcated brownish area. An important element for the detection of a brownish area in a distant view is the background coloration of the epithelium between each of the intraepithelial papillary capillary loops (IPCL). Recently, it has been reported that the presence of hemoglobin in the epithelium of ESCC is an important factor affecting background coloration [21]. BLI-bright light is composed of two specific wavelengths that are strongly absorbed by hemoglobin. Therefore, it is possible that BLI-bright detects ESCC as a well-demarcated brownish area as well as in detection with NBI.

We compared the endoscopic recognition of superficial ESCCs using four different methods (OWL, F-WLI, NBI, and BLI-bright). Our study showed the utility of IEE compared with WLI by both RS and CDS. Furthermore, we also showed the utility of BLI-bright compared with NBI by both RS and CDS. In this way, lesions detected with BLI-bright were significantly more visible than those detected with the other methods, both subjectively and objectively. Additionally, the differences between the Olympus and Fujifilm system specifications, such as field of view and depth of field, were negligible and did not influence the results of our study.

The $\kappa$-value of interobserver agreement for subjective evaluations was fair to substantial (0.317–0.613). One endoscopist (RK) had a high evaluation standard with WLI, decreasing the $\kappa$-value. The $\kappa$-value for intraobserver agreement was moderate to excellent (0.599–0.873). Post hoc
power analysis indicated that our research had sufficient to moderate power to detect significant group differences for BLI, FWL, and NBI [20].

Our study has three major limitations. First, we evaluated NBI images with a first-generation NBI system in this study. Since BLI-bright provides a brighter image than the first generation of NBI, it is possible that this contributed to the higher detection ability in the distant view. Second, the number of cases was small, and the data were gathered from a single center. Third, we evaluated only still images. Therefore, further multi-institutional studies with a larger number of cases are required to compare real-time images for ESCC detection with WLI, BLI-bright, and NBI.

5. Conclusion

In conclusion, BLI-bright visualized superficial ESCC better than the other methods tested (O-WLI, F-WLI, and NBI), both subjectively and objectively. BLI-bright may be a useful tool for detecting superficial ESCCs during screening endoscopy.

Competing Interests

Yoshito Itoh has an affiliation with a domination-funded department from Fujifilm Medical Co., Ltd. The other authors have no financial conflict of interests.

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