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<https://hdl.handle.net/2324/4110405>

出版情報：九州大学，2020，博士（医学），課程博士
バージョン：

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Efficacy of Novel Multispectral Imaging Device to Determine Anastomosis for Esophagogastrostomy

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ARTICLE INFO

Article history:

Received 3 January 2019

Received in revised form

29 March 2019

Accepted 9 April 2019

Available online 3 May 2019

Keywords:

Anastomosis

Esophagogastrostomy

Hemoglobin

Oxygen saturation

Quantitative imaging

ABSTRACT

Background: Biomedical imaging devices that utilize the optical characteristics of hemoglobin (Hb) have become widespread. In the field of gastroenterology, there is a strong demand for devices that can apply this technique to surgical navigation. We aimed to introduce our novel multispectral device capable of intraoperatively performing quantitative imaging of the oxygen (O₂) saturation and Hb amount of tissues noninvasively and in real time, and to examine its application for deciding the appropriate anastomosis point after subtotal or total esophagectomy.

Materials and methods: A total of 39 patients with esophageal cancer were studied. Tissue O₂ saturation and Hb amount of the gastric tube just before esophagogastric anastomosis were evaluated using a multispectral tissue quantitative imaging device. The anastomosis point was decided depending on the quantitative values and patterns of both the tissue O₂ saturation and Hb amount.

Results: The device can instantaneously and noninvasively quantify and visualize the tissue O₂ saturation and Hb amount using reflected light. The tissue Hb status could be classified into the following four types: good circulation type, congestion type, ischemia type, and mixed type of congestion and ischemia. Postoperative anastomotic failure occurred in 2 cases, and both were mixed cases.

Conclusions: The method of quantitatively imaging the tissue O₂ saturation and Hb level in real time and noninvasively using a multispectral device allows instantaneous determination of the anastomosis and related organ conditions, thereby contributing to determining the appropriate treatment direction.

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<https://doi.org/10.1016/j.jss.2019.04.033>

Introduction

Subtotal esophagectomy for esophageal cancer is a highly invasive treatment, and life-threatening complications, such as anastomotic failure, can occur.^{1–5} In a study by Lucas et al., the mortality rate of patients with esophageal cancer who underwent esophagectomy was reported to be 3.8%.² The evaluation of the gastric tube before anastomosis is important for the prevention of leakage.^{6–8} Currently, indocyanine green (ICG) fluorescence imaging devices are commonly used to image tissue blood flow. These devices can clearly image the

flow of ICG bound to proteins but do not image the flow of Hb itself.^{9–15} The reflected light of Hb has the characteristic of changing with the oxygen saturation and the amount of Hb.¹⁶ We hypothesized that the blood flow status at the tissue could be accurately determined by quantitative imaging the degree of oxygen saturation and the amount of Hb in the tissue. Therefore, the multispectral device developed for this purpose could allow clinicians to distinguish whether the decreased oxygen saturation of the tissue is due to an Hb inflow disorder (ischemia) or an outflow disorder (congestion) or both. Moreover, this device is useful for reducing anastomosis

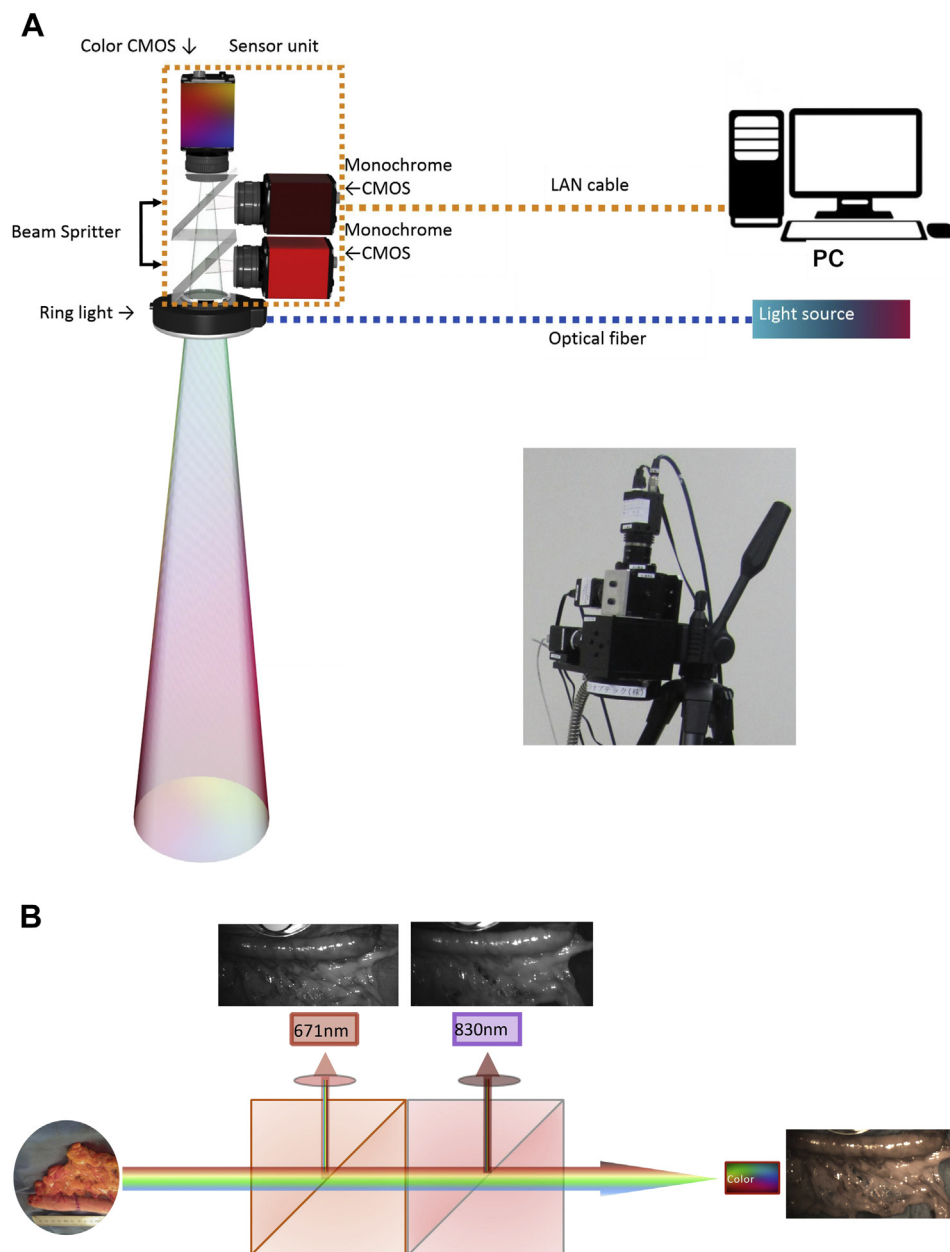


Fig. 1 – (A) Configuration of multispectral camera: sensor unit, lighting unit, and control and analysis PC unit. (B) Optical path in the sensor unit: reflected light from the subject was split in three directions using two beam splitters and simultaneously sensed by one RGB color CMOS sensor (SenTech, STC-SC 83 POE) and two monochrome CMOS sensors (SenTech, STC-CMB 2 MPOE-IR). (Color version of figure is available online.)

complications. The purpose of our study was to introduce our novel multispectral device that is capable of intraoperatively performing noninvasive and real time quantitative imaging of the oxygen saturation and Hb amount of tissues, and to examine its application in determining the appropriate anastomosis point after subtotal or total esophagectomy.

Materials and methods

Technological background

The structure of the imaging device

Figure 1A shows the configuration of the multispectral camera. The camera consists of a sensor unit, lighting unit, and a control and analysis PC unit. Figure 1B shows the optical path of the sensor unit. Reflected light from the subject is split into three directions by two beam splitters, and sensing is simultaneously performed by one red, green, and blue complementary metal oxide–semiconductor field-effect transistor (CMOS) sensor located on the top of the device (Fig. 1A, STC-SC83POE, SenTech) (OMRON SenTech Co, Ltd, Kanagawa, Japan; <https://sentech.co.jp/>) and two monochrome CMOS sensors located on the side of the device (Fig. 1A, STC-CMB2MPOE-IR, SenTech). Narrow band filters (Fig. 1A, Edmund Optics, 671-nm center wavelength, 25-mm diameter, 10-nm bandpass filter; Edmund Optics, 830-nm center wavelength, 25-mm diameter, 10-nm bandpass filter) were each attached to the two monochrome CMOS sensors. The lighting unit was a halogen lamp installed outside the sensor (MHF-D 100 LR, MORITEX) with a homogeneous spectral distribution in the wavelength range of 200 to 900 nm and connected to a ring-shaped light installed coaxially via a converging optical fiber.

The principle of quantifying tissue oxygen saturation

Chang et al.¹⁶ measured the reflectance spectra with a specially designed fiber optic–based probe (Ocean Optics R400-7-UV-VIS, Dunedin, FL) (Fig. 2A). They adjusted porcine whole blood samples to oxygen saturations of 99%, 70%, and 0% and measured the reflectance. As a result, it was revealed that each blood

sample with different oxygen saturations has specific reflection characteristics. At 671 nm, the reflectance is high if the oxygen saturation is high, whereas the reflectance is low when the oxygen saturation is low. In addition, at 810 nm, the properties of the reflectance are reversed. Therefore, the ratio of reflected light at 671 nm and 810 nm increases as the oxygen saturation level increases and decreases as the oxygen saturation level increases (Fig. 3A). Utilizing this reflection rate characteristic, we calculated the tissue oxygen saturation of tissues as follows:

$$O_2\text{Saturation} = \frac{O_2Hb}{O_2Hb + dHb} = \frac{P_1R671}{P_1R671 + P_1R830}$$

where, O_2Hb : amount of oxyhemoglobin; dHb : amount of deoxyhemoglobin; P_1R671 : tissue reflection light of 671 nm of the measuring point; P_1R830 : tissue reflection light of 830 nm of the measuring point.

The principle of quantification of Hb amount

Chang et al.¹⁶ also measured whole blood reflectance spectra at various hematocrit (HCT) levels in porcine arterial blood samples (Fig. 2B). Figure 2B shows that reflection light increases with the increase in the Hb amount. Therefore, the Hb amount correlates to the sum of reflected light (Fig. 3B). Utilizing this characteristic, the Hb amount was calculated as follows:

$$Hb\text{amount} = O_2Hb + dHb = \frac{(R671 + iR830)}{(B + G)}$$

where i = coefficient for adjustment (because the light emission amount between the projector at 671 nm and at 830 nm was different); $B + G$: a value obtained by gray-scaling an image obtained by removing a red component (to remove the influence of Hb) from a color photograph. This value is required to correct the error by shape and shadow.

Clinical experiment

Subjects

Thirty-nine patients with esophageal cancer and two patients with comorbid pharyngeal and esophageal cancer were

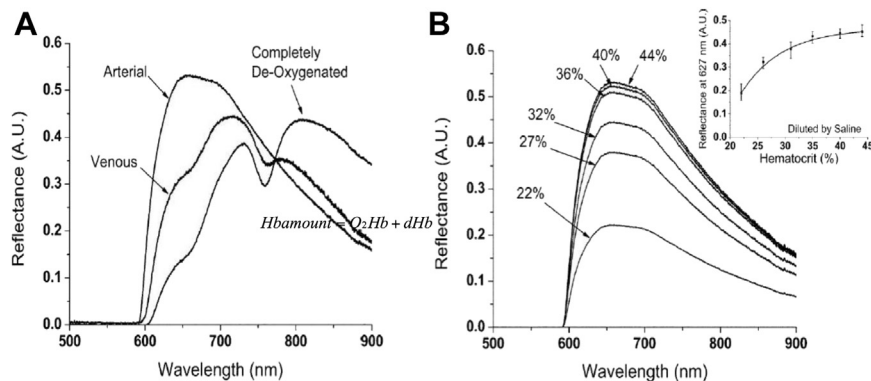


Fig. 2 – (A) Whole blood reflectance spectra: porcine whole blood samples of HCT ¼ 44% (arterial blood, oxygen saturation 99%; venous blood, oxygen saturation 70%; deoxygenated blood, oxygen saturation 0%). Each blood sample at different oxygen saturations has its own distinctive reflectance spectral shape.¹⁶ (B) Whole blood reflectance spectra at various HCT levels of porcine arterial blood samples: the reflectance spectra are shifted up as the HCT level increases, and the spectral signals are saturated as the HCT level reaches the normal HCT level of 44%. Inset, changes in the reflectance intensity at 627 nm.¹⁶

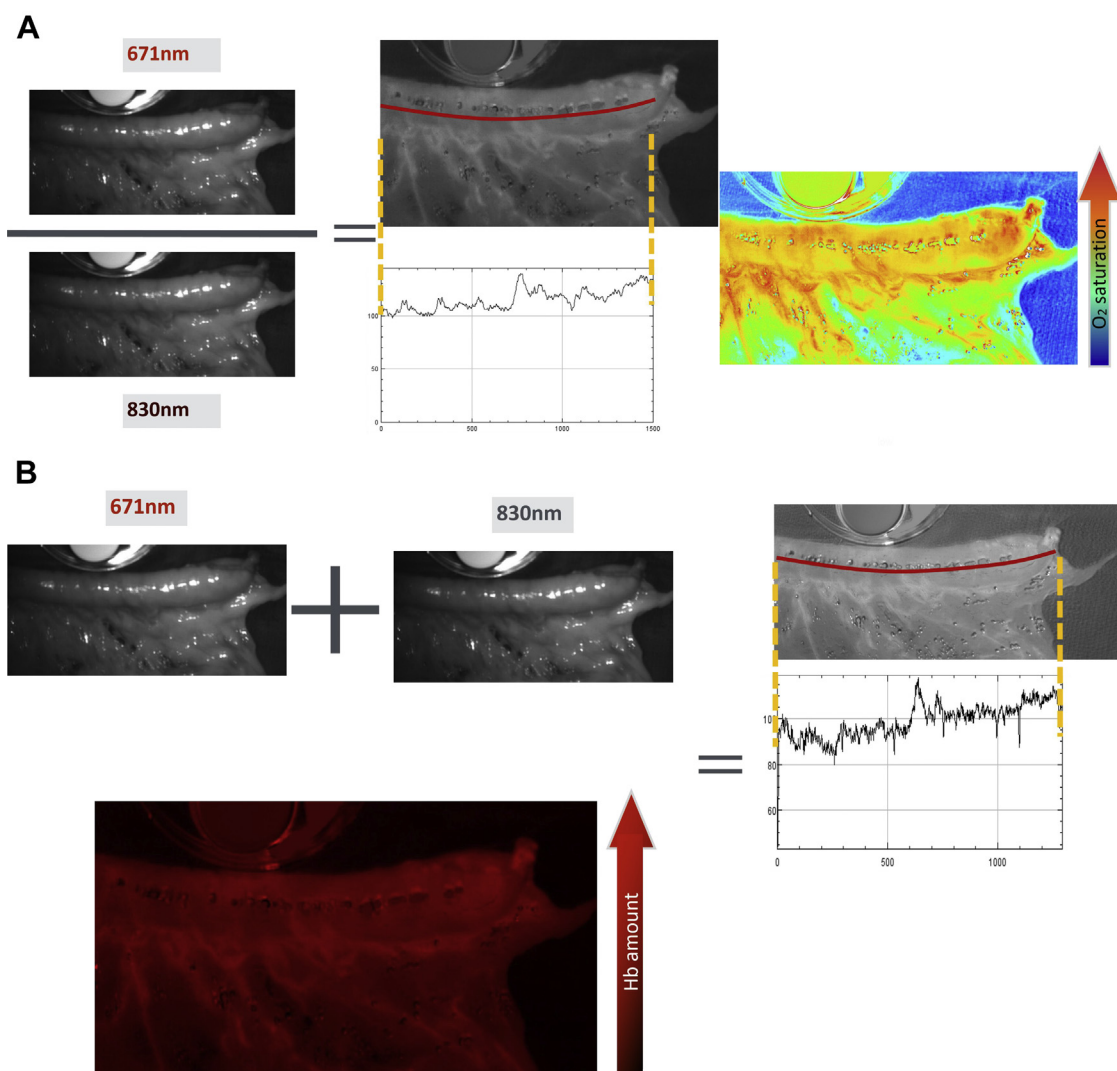


Fig. 3 – Gastric tube during esophagectomy with gastric reconstruction. (A) Oxygen saturation calculation image of gastric tube. The ratio of the 671 nm image (upper left) and 830 nm image (lower left) was taken and the image (center) of 671 nm/830 nm was pseudocolored (right). (B) Hemoglobin amount of the gastric tube. The sum of the reflected light amounts at a wavelength of 671 nm and 830 nm (upper left) was taken and the images (right) obtained were pseudocolored (lower left).

admitted in Kyushu University Hospital from April 2016 to November 2017. Consent to participate in the present study was obtained from all 39 patients. The present study was approved by the institutional review board of Kyushu University Hospital (Table 1). The overall mean values of HCT and Hb during imaging were $37.2\% \pm 5.4\%$ and 12.3 ± 1.9 g/dL, respectively (Table 1). Staging, surgical procedure, Hb status, types of gastric tube, postoperative leakage, and other complication are shown in Table 2. Subtotal esophagectomy and reconstruction using a gastric tube were performed in 31 of the 39 patients. Laryngoesophagopharyngectomy followed by gastric tube reconstruction was performed in 8 patients, including two with comorbid pharyngeal and esophageal cancers.

Operative procedure and image capturing

After subtotal esophagectomy, including removal of esophageal cancer lesions, a 3.5-cm-diameter gastric tube

preserving the right gastric artery/vein and the bilateral gastroepiploic arteries/veins was created. The gastric tube was placed on the body surface anterior to the sternum to simulate esophageal gastric tube anastomosis and was filmed at a position of 70 cm directly above (Fig. 4). Quantitative imaging of oxygen saturation and Hb amount was performed (Fig. 5A-D). HCT and Hb at the time of imaging were measured (Table 2). After the capture was completed, the gastric tube was lifted via the retrosternal route ($n = 27$) or mediastinal route ($n = 12$). Esophageal and gastric tubes were used in 29 patients of the 39 patients who underwent end-to-end anastomosis with an automatic device in the cervical region (other patients underwent hand-sewn anastomosis because of the short gastric tube). In the 2 patients who underwent laryngoesophagopharyngectomy, an additional free jejunal graft reconstruction was performed owing to the insufficient length of the reconstructed gastric tube. A

Table 1 – Patient characteristics.

Characteristics	Date
Age, y	
Mean (range)	65.9 (52-82)
Sex, n	
Male/Female	31/8
Diseases, n(%)	
Esophageal cancer only	37 (94.9)
Esophageal and pharynx cancer	2 (5.1)
Clinical stage*0/I/II/III/IV	
Esophageal cancer	10/7/7/12/3
Pharynx cancer	0/0/1/1
Surgical procedure, n(%)	
Subtotal esophagectomy	31 (79)
Laryngoesophagopharyngectomy	8 (21)
Reconstruction route, n(%)	
Retrosternal route	27 (82.2)
Mediastinal route	12 (17.8)
HCT, %	37.2 ± 5.4
Hb, g/dL	12.3 ± 2.9

stapling device was used in the gastric tube and anal side of the free jejunal graft, and an end-to-end hand-sewn anastomosis was created in the oral side of the free jejunal graft and pharyngeal remnant.

Evaluation of the gastric tube

The right gastroepiploic artery just before flowing into the gastric tube was set as the reference point C1. In the gastric tube, the site of inflow from the right gastroepiploic artery was defined as point C2, the part 2 cm from the gastric tube end was defined as point E, and the anastomosis was defined as point A. Points C2, E, and A were on the 1-cm line of the greater curvature margin of the gastric tube (Fig. 4). The oxygen saturation and Hb levels at point C1 was set to 100% each. The final measurement result at C2 and A was expressed as a ratio to C1. Based on the measured oxygen saturation and Hb amount, the placement of the anastomotic site and free jejunal reconstruction addition were determined (Fig. 6).

Postoperative course

Details regarding the treatment course for each patient, including postoperative anastomotic complications, were obtained from the medical records retrospectively.

Statistical analyses

JMP Pro software, version 12 (SAS Institute Inc, Cary, NC), was used to evaluate the dispersion of data in each group. The results presented are the mean values from the total number of each sample type analyzed. Mann–Whitney U-test was performed to assess the statistical significance of the results.

Results

Gastric tube blood flow status classification

We defined oxygen saturation less than 85% as ischemia and an Hb amount more than 120% as congestion and classified the blood flow state of the gastric tube into 4 types. Quantitative imaging characteristics are shown in Figure 5A–D. Figure 5A shows sufficient oxygen saturation (good circulation type) in the case with quantitative oxygen saturation values at the tip of the gastric tube at 93.6%. No significant change in the amount of Hb at the tip was observed. In these cases, it was judged that anastomosis was possible even at the tip of the gastric tube.

Figure 5B-1 shows the patients who had congestion (congestion type) with slightly low oxygen saturation and high Hb level at the proximal part of the gastric tube. Figure 5B-1 shows that on the distal side, the oxygen saturation was high and the Hb amount tended to decrease (center congestion type). It could be suggested that there was arteriovenous communication except for in the central part of the gastric tube. In these cases, it was suggested that an anastomosis other than the congested part in the center of the gastric tube was possible.

Figure 5B-2 also shows a case of congestion type, although congestion was noted in the distal side. The proximal side of the gastric tube shows high oxygen saturation and a relatively lower Hb level. In these cases, it was suggested by the distal side congestion in the gastric tube (distal congestion type) that an anastomosis was possible at the proximal side.

Figure 5C shows a patient with an ischemic, that is, ischemic type with low oxygen saturation and low Hb level at the distal side of gastric tube. Such cases may be caused by blood inflow failure to the distal side of the gastric tube, and it was suggested that anastomosis should be performed on the proximal side of the ischemic area.

Figure 5D shows a patient of mixed type, who had low oxygen saturation and high Hb level in the distal side. In this case, the oxygen saturation was extremely decreased (75.2%) while the Hb levels were increasing (125.5%) along the blood vessels. In these cases, it was suggested that extreme congestion may also cause an inflow disorder or complication of venous thrombosis because of an inflow disorder. In such a case, a blood flow disorder may be mildly diagnosed macroscopically.

Determination of anastomotic site by gastric tube evaluation and postoperative course

The anastomotic site was determined as shown in Figure 6. Of the 39 cases, 10 cases were classified as good circulation type, 14 cases as congestion type, 10 cases as ischemic type, and 4 cases as mixed type.

All cases classified as good circulation type had good blood flow status through the anastomosis site. Fourteen cases were classified as congestion type. In the 5 cases with distal congestion, the congested part was removed in all cases, and anastomosis was performed in the proximal good blood flow status site. The other 9 cases classified as center congestion

Table 2 – Patients esophageal cancer stage, surgical procedure, comorbidity, neoadjuvant chemotherapy/chemo radiotherapy (NAC/NCRT), Hb status types of gastric tube, complication, and leakage.

No	Stage	Surgical procedure	Comorbidities	NAC or NCRT	Gastric tube type	Complication	Leak
1	0	Subtotal esophagectomy	DM	NAC	Mixed	SSI (neck)	(-)
2	II	Subtotal esophagectomy	None	NAC	Ischemic	Idiopathic hoarseness	(-)
3	0	Subtotal esophagectomy	Chronic leukemia	(-)	Ischemic	(-)	(-)
4	II	Subtotal esophagectomy	Alcoholic cirrhosis, HT	NAC	Ischemic	(-)	(-)
5	III	Subtotal esophagectomy	Hepatitis B	NAC	Good circulation	Urinary tract infection	(-)
6	I	Subtotal esophagectomy	Depression	NCRT	Good circulation	(-)	(-)
7	0	Subtotal esophagectomy	Colon polyp	(-)	Congestion	(-)	(-)
8	I	Laryngoesophagopharyngectomy	Depression	NCRT	Good circulation	(-)	(-)
9	III	Laryngoesophagopharyngectomy	None	NAC	Good circulation	(-)	(-)
10	II	Subtotal esophagectomy	Hypertension	NAC	Ischemic	Atrial fibrillation	(-)
11	II	Subtotal esophagectomy	Alcoholism	(-)	Good circulation	(-)	(-)
12	III	Subtotal esophagectomy	Hypertention	NAC	Congestion	(-)	(-)
13	I	Subtotal esophagectomy	IP, HT, HL	(-)	Ischemic	(-)	(-)
14	0	Laryngoesophagopharyngectomy	HT	NAC	Ischemic	Cervical lymphorrhea	(-)
15	II	Subtotal esophagectomy	Alcoholic liver disease	NAC	Congestion	Atrial fibrillation	(-)
16	III	Subtotal esophagectomy	DM	(-)	Mixed	(-)	(-)
17	I	Laryngoesophagopharyngectomy	Rheumatoid arthritis	NAC	Ischemic	Pneumonia	(-)
18	IV	Subtotal esophagectomy	None	NAC	Congestion	(-)	(-)
19	IV	Subtotal esophagectomy	None	NAC	Congestion	(-)	(-)
20	III	Laryngoesophagopharyngectomy	None	NAC	Good circulation	Pneumonia	(-)
21	III	Subtotal esophagectomy	COPD	(-)	Congestion	Pulmonary fistula	(-)
22	II	Laryngoesophagopharyngectomy	HT	NAC	Mixed	(-)	(+)
23	III	Subtotal esophagectomy	Basedow disease	(-)	Congestion	(-)	(-)
24	II	Laryngoesophagopharyngectomy	ASO	NAC	Congestion	(-)	(-)
25	0	Subtotal esophagectomy	Duodenal ulcer	NCRT	Congestion	(-)	(-)
26	IV	Subtotal esophagectomy	None	NAC	Congestion	(-)	(-)
27	III	Subtotal esophagectomy	HT	NCRT	Congestion	(-)	(-)
28	I	Subtotal esophagectomy	none	(-)	Mixed	(-)	(+)
29	0	Subtotal esophagectomy	ITP	(-)	Ischemic	Exacerbation of ITP	(-)
30	0	Subtotal esophagectomy	Lingual cancer	(-)	Ischemic	(-)	(-)
31	0	Subtotal esophagectomy	None	NAC	Congestion	SSI (neck)	(-)
32	0	Subtotal esophagectomy	None	(-)	Congestion	Vocal cord paralysis	(-)
33	III	Subtotal esophagectomy	Alcoholic cirrhosis	NAC	Ischemic	(-)	(-)
34	III	Subtotal esophagectomy	Lingual cancer	NAC	Good circulation	(-)	(-)
35	III	Subtotal esophagectomy	None	(-)	Good circulation	Pneumonia, chylothorax	(-)
36	I	Subtotal esophagectomy	DM	(-)	Good circulation	Vocal cord paralysis	(-)

(continued)

Table 2 – (continued)

No	Stage	Surgical procedure	Comorbidities	NAC or NCRT	Gastric tube type	Complication	Leak
37	I	Subtotal esophagectomy	HT, HL	(-)	Good circulation	(-)	(-)
38	0	Subtotal esophagectomy	HT	NAC	Congestion	(-)	(-)
39	III	Laryngoesophagopharyngectomy	DM, AOS	NCRT	Congestion	ARDS	(-)

AOS = arteriosclerosis obliterans; ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HT = hypertension; HL = hyperlipidemia; IP = interstitial pneumonia; ITP = idiopathic thrombocytopenic purpura; SSI = surgical site infection.

type included 7 cases that were able to be anastomosed in the good blood flow status site on the proximal or distal side of the congested area. However, in the remaining 2 cases, after removing the ischemic part, the stomach tube did not reach, and an anastomosis was performed with the addition of free jejunal reconstruction.

Of the 4 cases classified as mixed type, 2 cases as having a poor blood flow status area were resected and anastomosed on the proximal side. However, in the other two cases, it was expected that the gastric tube would not be reached if an area with poor blood flow status was resected. In addition, blood circulation was visually judged to be milder than ischemic type and congestion type. As a result, in one suspected vein thrombosis, vein reconstruction using the internal jugular vein was performed after anastomosis (super drainage¹⁷), and the other one was anastomosed at the site where the decrease in oxygen saturation was combined with the increase in Hb amount. The former had an oxygen saturation of 75.2% and an Hb amount of 125.5%, and the latter had an oxygen saturation of 79.6% and an Hb amount of 140.3%.

Postoperative complications of anastomosis

Patients' esophageal cancer stage, surgical procedure, comorbidity, neoadjuvant chemotherapy/chemo radiotherapy, Hb status types of gastric tube, complication, and leakage are shown in Table 2. Anastomotic leakage did not occur in 37 of the 39 patients who had anastomosis performed at the good Hb status site of the gastric tube. The 2 patients that developed anastomotic leakage were both mixed type cases who had anastomosis at a site where the oxygen saturation was low and the Hb amount was increased (Fig. 6). The 2 patients with anastomotic failure improved conservatively, and no surgery-related death was observed.

Comparison of tissue oxygen saturation and hemoglobin amount at each measurement point

The relative mean value and the standard deviation of the oxygen saturation values at each measurement point when point C1 was set to 100 were examined. The mean oxygen

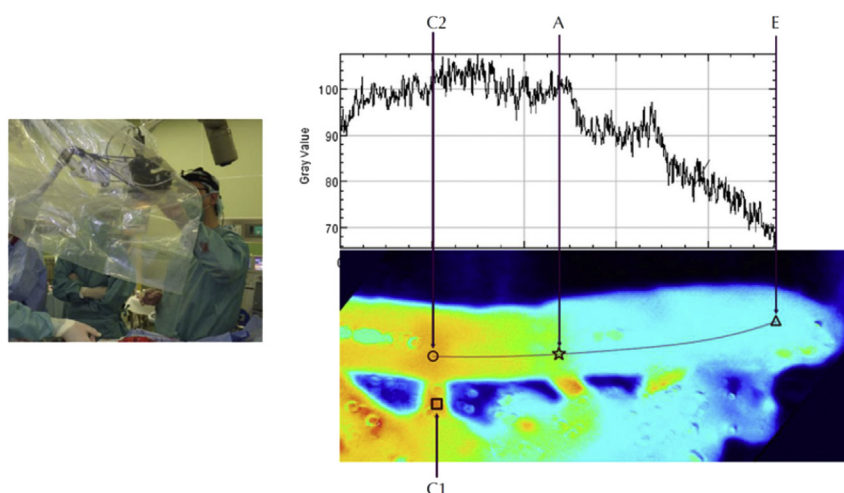


Fig. 4 – Intraoperative imaging of the gastric tube; the gastric tube was placed on the body surface anterior to the sternum and filming of the gastric tube was performed from 70 cm directly above (left). The right gastroepiploic artery just before flowing into the gastric tube was set as point C1, the site of inflow of the right gastroepiploic artery into the gastric tube as C2, the part 2 cm from the gastric tube tip as point A, and the anastomosis as point A. The points C2 and A were on the 1 cm line of the greater curvature of the gastric tube and the measured values were graphed (upper right). The images (671/830) obtained by taking the ratio of 671 nm and 830 nm were pseudocolored (lower right). C1: Control point of artery (last branch of rt. GEA); C2: Control of gastric tube (entering point of rt. GEA); A: Planned point of anastomosis. E: 2 cm from the edge of the gastric tube.

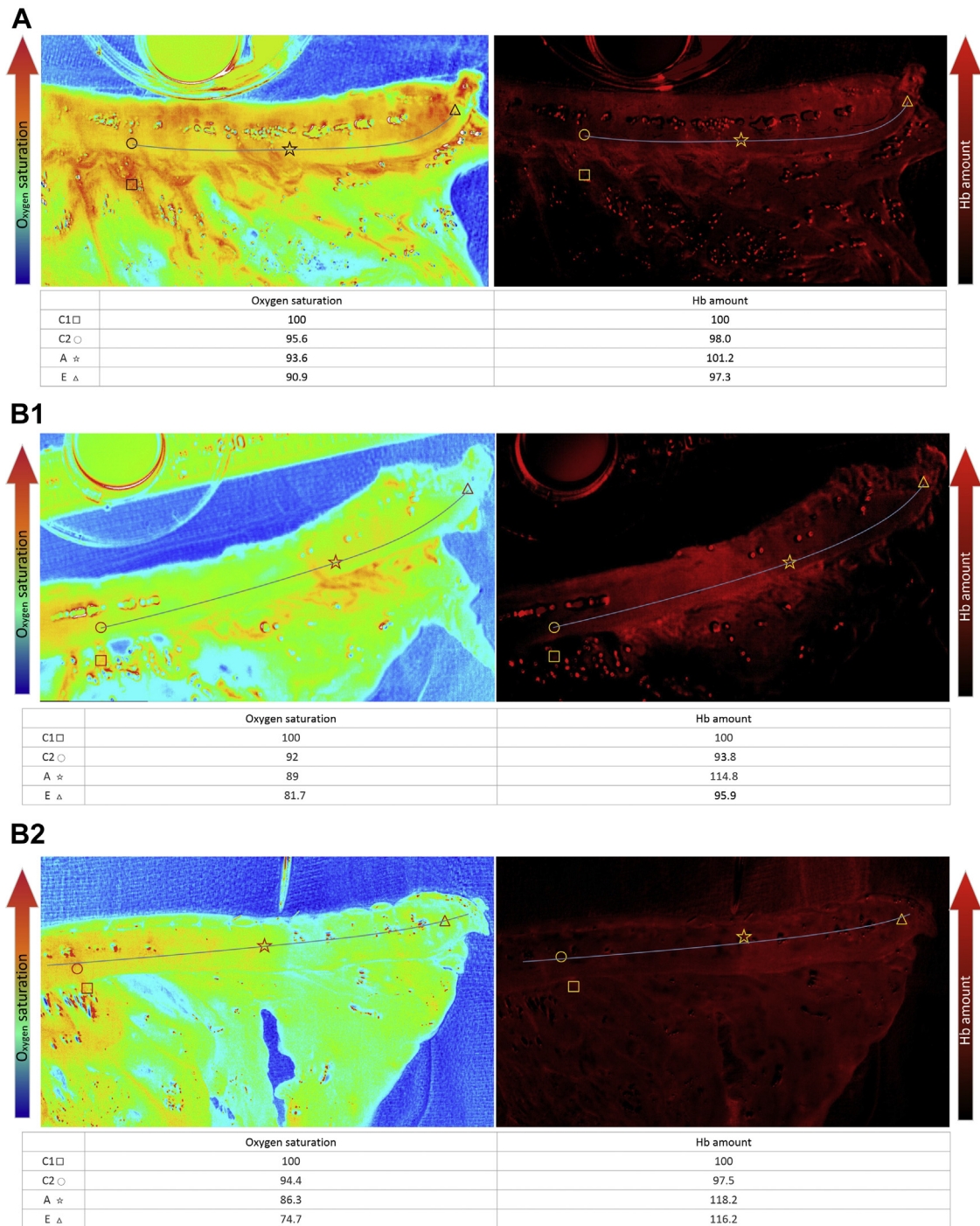


Fig. 5 – Characteristic gastric tube oxygen saturation and quantitative imaging findings of the hemoglobin (Hb) amount. The quantitative value of oxygen saturation up to the tip of the gastric tube was 85% or higher. There were no noticeable changes in Hb amount until the tip (A, good circulation type). A patient with slightly low oxygen saturation and high Hb amount in the center of the gastric tube (B-1, center congestion type) and the distal side of the gastric tube (B-2, distal congestion type). A patient with low oxygen saturation and relatively low Hb amount at distal side of the gastric tube (C, ischemic type). An anastomosis was created at the point of sufficient oxygen saturation (89.5%). A case with continuous low oxygen saturation and increased Hb amount from point C2 to the tip (D, mixed type). Linear oxygen saturation was extremely low in the periphery of the anastomosis (75.2%), a site with a high Hb amount (125.5%) was noted, and venous thrombosis was suspected (arrows). After anastomosis, a venous anastomosis between the internal jugular vein and the gastroepiploic vein was created, but the patient developed postoperative anastomotic failure.

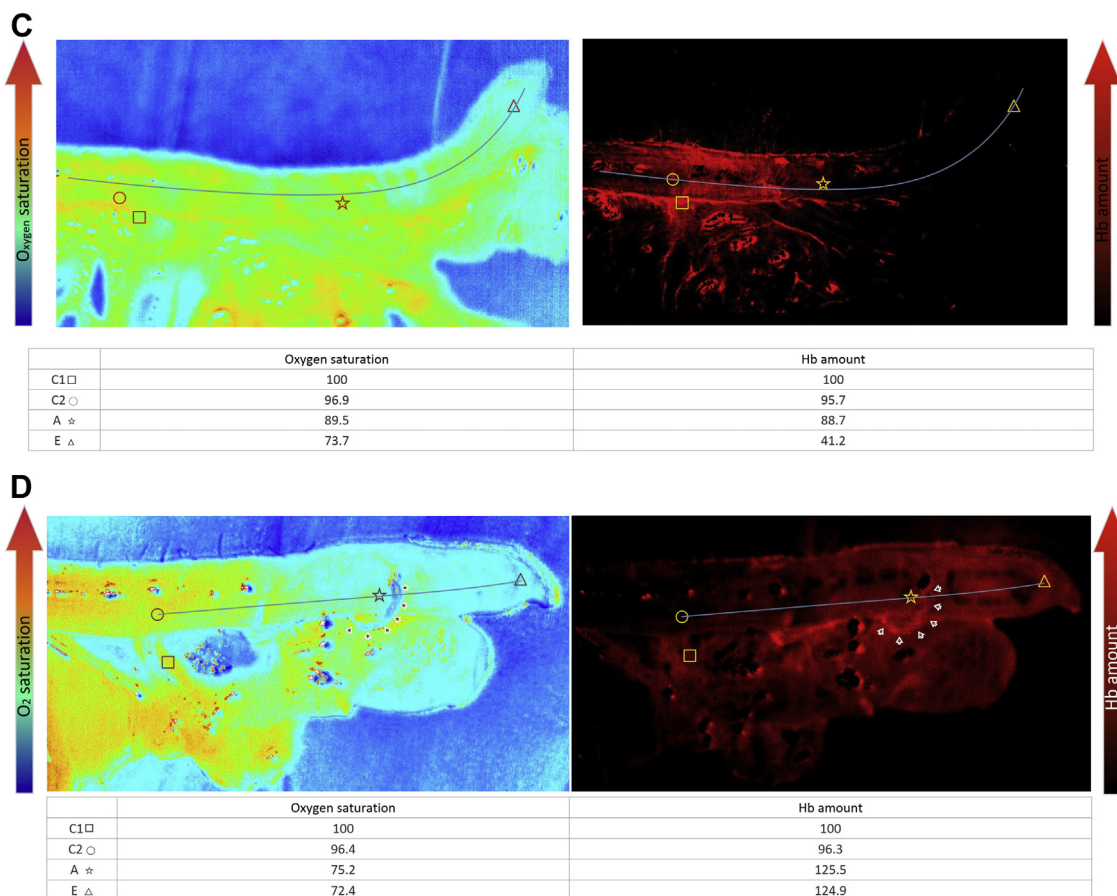


Fig. 5 – (continued).

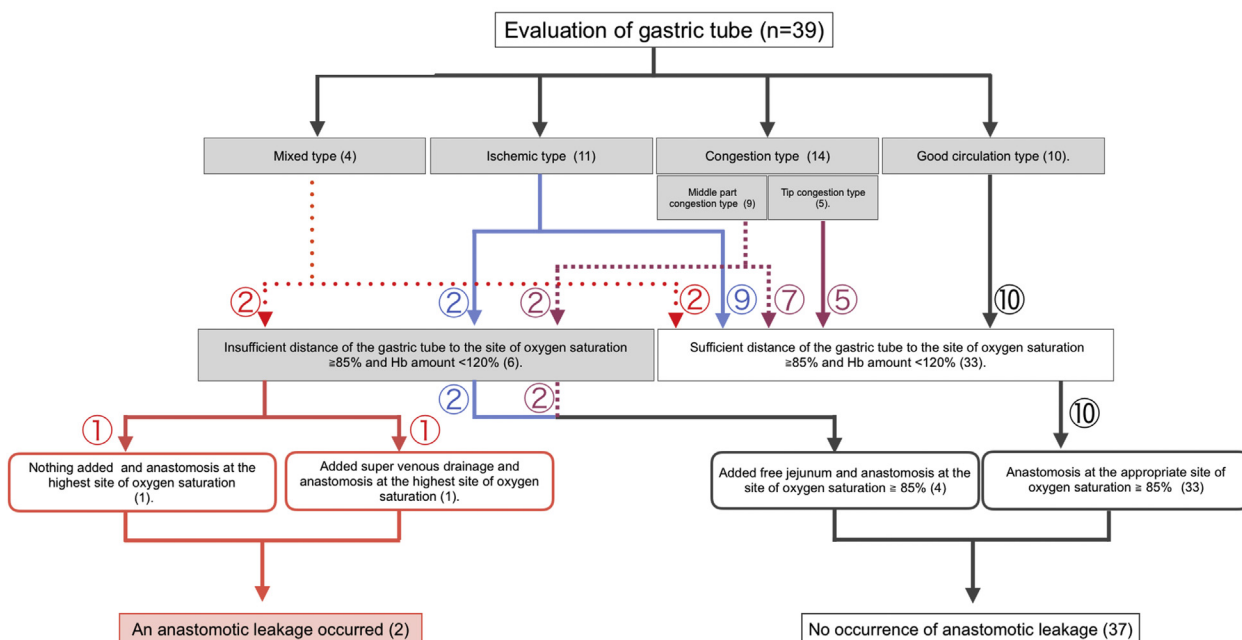


Fig. 6 – Flow chart for gastric tube evaluation and anastomotic determination. We aimed to perform anastomosing at a point where the oxygen saturation is 85% or more. Leakage occurred in 2 patients with oxygen saturation less than 85%. Both patients were mixed type. (Color version of figure is available online.)

Table 3 – Gastric tube evaluation and postoperative course.

Characteristics	Data
Gastric tube type, n	
Good circulation/congestion/ischemic/mixed	10/14/11/4
Oxygen saturation, mean $\pm$ SD%	
C2	95.7 $\pm$ 3.2
A	91.8 $\pm$ 5.0
E	84.3 $\pm$ 15.4
Hb amount, mean $\pm$ SD	
C2	94.9 $\pm$ 10.6
A	102.9 $\pm$ 16.4
E	99.3 $\pm$ 25.2
Anastomosis at oxygen saturation >85%, n(%)	37 (94.8)
Postoperative leakage, n(%)	2 (5.1)

saturation at each measurement point was as follows: C2: 95.7% $\pm$ 3.2%; A: 91.8% $\pm$ 5.0%; and E: 84.3% $\pm$ 15.4% (Table 3). The comparison of oxygen saturation and Hb amount at points C1, C2, and A in the 39 patients is presented in Table 4. The oxygen saturation values decreased when measured at the tip of the gastric tube. Point A was significantly lower than point C2 ($P < 0.0001$).

The mean values and standard deviations of the relative Hb amount at each point when the C1 point was set to 100% were examined. The mean Hb amount at each measurement point was as follows: C2: 94.9% $\pm$ 10.6%; A: 102.9 $\pm$ 16.4; and E: 99.3% $\pm$ 25.2% (Table 3). Point A was significantly higher than point C2 ($P < 0.04$, Table 4). Scatter plots of oxygen saturation and Hb amount at each measurement point are shown in Figure 7. In each of the two leakage cases, the oxygen saturation was less than 85% at point A. Regarding oxygen saturation, 82.2% was the boundary with the greatest margin separating leakage cases and other cases.

Discussion

In the present study, we evaluated the reconstructed gastric tube in esophageal cancer surgery. We have evaluated the

blood flow of the gastric tube in a previous study, which was considered important for preventing the onset of anastomotic failure, by ICG fluorescence imaging.^{11,12} Given that ICG binds to proteins with a mass of 50 to 200 μ g in plasma and fluoresces by excitation to near-infrared rays, it allows visualization of the existing blood vessels, showing blood flow. However, ICG does not bind to Hb itself, and it has several disadvantages in the quantification of blood flow; thus, only morphological observations can be performed. Furthermore, it is necessary to observe the conditions in which the administered ICG reaches the gastric tube, such as by the systemic circulation, leakage into the tissue from the capillary, or reflux inside the vein. It is difficult to accurately visualize and quantify blood flow because ICG migrates to the bile duct, urinary tract, and digestive tract and deposits in lymph nodes and cancer. In addition, it is necessary to administer ICG each time the test is conducted and to wait until the ICG is metabolized before reimaging.^{9,10}

Therefore, we focused on the reflected light characteristics of Hb and developed a tissue oxygen saturation and Hb amount imaging technique. This device allowed instantaneous calculation of the Hb amount and the oxygen saturation level of the tissue by measuring and imaging reflected light. Evaluation of the tissue status related to blood flow using the optical properties of Hb is widely used in saturation monitoring, near-infrared spectroscopy,^{18,19} etc., although some of these devices require patient contact. Our devices are contactless and can be used safely during surgery.

In this study, only 2 patients had anastomotic leakage, which was lower than the incidence rate reported in previous studies.^{4,14} This is probably because the anastomotic site can be determined by looking at the numerical value. It was considered useful for the reduction of anastomotic leak. This method is noninvasive, and it can be used repeatedly, especially after anastomosis or arteriovenous reconstruction. In the present study, detection of the artery for determining the correction value was macroscopically performed, and we intend to incorporate the ability to automatically detect arterial pulse and set correction values in original software.

In this study, 29 of the 39 cases (those other than good circulation type) had decreased oxygen saturation. Thus, the area and value of the tissue Hb status can be detected in real time by the imaging device, and it is considered to be useful for preventing leakage. One of the patients with leakage had hypertension, and the other had no comorbidity. Neoadjuvant chemotherapy was performed in one patient. However, these factors were difficult to consider as a risk factors for leakage.^{6,20–22} They showed low oxygen saturation and a high Hb amount (mixed type). These patients were considered to have severe congestion, which could be due to intravenous thrombosis, and the arterial inflow also finally decreased. Because of the short gastric tube, it was impossible to select a completely saturated area as the anastomotic site; thus, it resulted in leakage. Therefore, extra-free jejunal reconstruction is recommended, similar to the procedure for the case shown in Figure 5D. In the determination of the anastomotic site, because the optimal value of oxygen saturation was not clear, 85% was set as a temporary target. However, from the measurement results, it is expected that an oxygen saturation of about 82% increases the risk of leakage. As the number of

Table 4 – Comparison of oxygen saturation and Hb amount at each measurement point.

Measurement point	Oxygen saturation	p value	Hb amount	p value
C1	100 $\pm$ 0.0(%)	< 0.0001*	100 $\pm$ 0.0 (%)	<0.001*
C2	95.7 $\pm$ 3.2(%)		94.9 $\pm$ 10.6 (%)	
A	91.8 $\pm$ 5.0(%)		102.9 $\pm$ 16.4 (%)	

*Significant difference ($P < 0.05$).

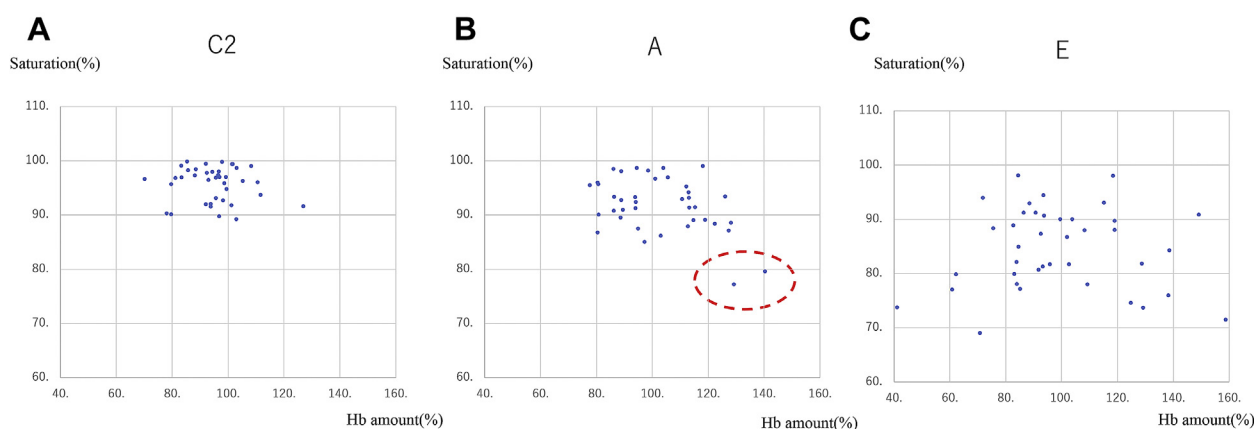


Fig. 7 – The oxygen saturation and hemoglobin amount values at the C2 point in 39 cases. All of them had oxygen saturation of 85% or higher (A). Quantitative values of oxygen saturation and hemoglobin amount at point A in 39 patients. Two of the 39 cases had oxygen saturation of less than 85%, and of these, four had a hemoglobin amount of 120% or higher (circle). Furthermore, these 2 patients developed anastomosis leakage (B). Oxygen saturation and Hb amount at point E; it varies widely among patients (C). (Color version of figure is available online.)

cases increases, the detailed relationship between the leakage, oxygen saturation, and Hb amount becomes apparent, and an accurate standard of Hb status necessary for anastomosis can be created. Our study had a few limitations. The number of cases was small, inhomogeneous, and only demonstrates the possibility of the occurrence of anastomotic failure. We plan to increase the number of cases and establish criteria in the near future. In the assessment of the gastric tube, it was possible to keep the positioning of camera light and tissue constant and minimize the influence of ambient light. However, further resourcefulness may be necessary to noninvasively determine the viability of other organs such as the rectum and liver in real time.

Conclusions

By simultaneously imaging the same site using a multispectral device, it is possible to quantitatively perform imaging of tissue oxygen saturation and Hb amount related to the gastric tube noninvasively and in real time. The device we developed for the purposes of the study may be useful for evaluating and preventing anastomotic complications.

Acknowledgment

The authors would like to thank Kyocera, Kyocera Optics, and Genial Light Co Ltd for their cooperation in creating multispectral cameras and developing programs. This research was supported by JSPS KAKENHI Grant Number 17H06102.

Authors' contributions: R.T. designed the study and wrote the initial draft of the article. T.I. contributed to analysis and interpretation of data and assisted in the preparation of the manuscript. All other authors have contributed to data collection and interpretation and critically reviewed the

manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

This study was partially supported by JSPS Grant-in-Aid for Scientific Research on Innovative Areas (26108010).

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

REFERENCES

1. Saeki H, Masuda T, Okada S, et al. Impact of perioperative peripheral blood values on postoperative complications after esophageal surgery. *Surg Today*. 2010;40:626–631.
2. Lucas DJ, Pawlik TM. Quality improvement in gastrointestinal surgical oncology with American college of surgeons national surgical quality improvement program. *Surgery*. 2014;155:593–601.
3. Alanezi K, Urschel JD. Mortality secondary to esophageal anastomotic leak. *Ann Thorac Cardiovasc Surg*. 2004;10:71–75.
4. Rutegård M, Lagergren P, Rouvelas I, et al. Intrathoracic anastomotic leakage and mortality after esophageal cancer resection: a population-based study. *Ann Surg Oncol*. 2012;19:99–103.
5. Aminian A, Panahi N, Mirsharifi R, et al. Predictors and outcome of cervical anastomotic leakage after esophageal cancer surgery. *J Cancer Res Ther*. 2011;7:448–453.
6. Briel JW, Tamhanker AP, Hagen JA, et al. Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: gastric pull-up versus colon interposition. *J Am Coll Surg*. 2004;198:536–541.
7. Koyanagi K, Ozawa S, Oguma J, et al. Blood flow speed of the gastric conduit assessed by indocyanine green fluorescence:

- new predictive evaluation of anastomotic leakage after esophagectomy. *Medicine (Baltimore)*. 2016;95:e4386.
8. Pacheco PE, Hill SM, Henriques SM, et al. The novel use of intraoperative laser-induced fluorescence of indocyanine green tissue angiography for evaluation of the gastric conduit in esophageal reconstructive surgery. *Am J Surg*. 2013;205:349–352.
 9. Cherrick GR, Stein SW, Leevy CM, et al. Indocyanine green: observations on its physical properties, plasma decay, and hepatic extraction. *J Clin Invest*. 1960;39:592–600.
 10. Ishige F, Nabeya Y, Hoshino I, et al. Quantitative assessment of the blood perfusion of the gastric conduit by indocyanine green imaging. *J Surg Res*. 2019;234:303–310.
 11. Raabe A, Beck J, Gerlach R, et al. Near-infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow. *Neurosurgery*. 2003;52:132–139.
 12. Kawaguchi Y, Ishizawa T, Masuda K, et al. Hepatobiliary surgery guided by a novel fluorescent imaging technique for visualizing hepatic arteries, bile ducts, and liver cancers. *J Am Coll Surg*. 2011;212:e33–e39.
 13. Kisu I, Banno K, Mihara M, et al. Indocyanine green fluorescence imaging for evaluation of uterine blood flow in cynomolgus macaque. *PLoS One*. 2012;7:e35124.
 14. Yukaya T, Saeki S, Kasagi Y, et al. Indocyanine green fluorescence angiography for quantitative evaluation of gastric tube perfusion in patients undergoing esophagectomy. *J Am Coll Surg*. 2015;221:e37–e42.
 15. Nakashima Y, Saeki H, Yukaya T, et al. Blood flow assessment with indocyanine green fluorescence angiography for pedicled omental flap on cervical esophagogastric anastomosis after esophagectomy. *J Am Coll Surg*. 2016;222:e67–e69.
 16. Chang H, Kim YL, Hassan A, et al. Whole blood reflectance for assessment of hematologic condition and detection of angiographic contrast media. *Appl Opt*. 2009;48:2435–2443.
 17. Morita M, Saeki H, Ikeda K, et al. Technical improvement of total pharyngo-laryngo-esophagectomy for esophageal cancer and head and neck cancer. *Ann Surg Oncol*. 2014;21:1671–1677.
 18. Jubran A. Pulse oximetry. *Crit Care*. 2015;19:272.
 19. Watanabe E, Yamashita Y, Maki A, et al. Non-invasive functional mapping with multi-channel near infrared spectroscopic topography in humans. *Neurosci Lett*. 1996;205:41–44.
 20. Shridhar R, Takahashi C, Huston J, et al. Anastomotic leak and neoadjuvant chemoradiotherapy in esophageal cancer. *J Gastrointest Oncol*. 2018;9:894–902.
 21. Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg*. 2014;260:259–266.
 22. Mota FC, Ceconello I, Takeda FR, et al. Neoadjuvant therapy or upfront surgery? A systematic review and meta-analysis of T2N0 esophageal cancer treatment options. *Int J Surg*. 2018;54:176–181.