### ORIGINAL ARTICLE

# Indocyanine green fluorescence/thermography evaluation of intercostal muscle flap vascularization

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#### Keywords

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### Abstract

**Background:** During anatomical lung resection in high-risk patients, the bronchial stump is covered with tissue flaps (e.g. pericardial fat tissue and intercostal muscle) to prevent bronchopleural fistula development. This is vital for reliable reinforcement of the bronchial stump. We evaluated the blood supply of the flap using indocyanine green fluorescence (ICG-FL) and thermography intraoperatively in 27 patients at high risk for developing a bronchopleural fistula.

**Methods:** Before reinforcing the stump with a flap, the fluorescence agent was intravenously injected and the blood supply was evaluated. The surface temperature of the flap was measured with thermography. The two modalities were then compared.

**Results:** ICG-FL intensity and surface temperature on the distal compared to the proximal side of the flap decreased by  $32.6 \pm 29.4\%$  (P < 0.0001) and  $3.5 \pm 2.0^{\circ}$ C (P < 0.0001), respectively. In patients with a higher ICG-FL intensity value at the tip than the median, the surface temperature at the tip decreased by  $2.7 \pm 1.7^{\circ}$ C compared to the proximal side. In patients with a lower ICG-FL value at the tip, the surface temperature decreased by  $4.6 \pm 1.7^{\circ}$ C (P = 0.0574). The bronchial stump reinforced the part of the flap with adequate blood supply; none of the patients developed a bronchopleural fistula.

**Conclusions:** ICG-FL confirmed variation in the blood supply of the intercostal muscle flap, even if prepared using the same surgical procedure. Thermography analysis tends to correlate with the fluorescence method, but may be influenced by the state of flap preservation during surgery.

### Introduction

A bronchopleural fistula (BPF) is a serious complication of anatomical lung resection. The probability of developing a BPF after lobectomy is 0.3%,<sup>1</sup> and the reported mortality rate is very high (18–50%).<sup>2</sup> Therefore, the bronchial stump is reinforced intraoperatively with various dressings to prevent BPF development. Methods used to cover the bronchial stump include patching with a polyglycolic acid sheet,<sup>3</sup> spraying fibrin glue,<sup>4,5</sup> patching the fibrin gluecoated collagen fleece,<sup>6</sup> and suturing pericardial fat tissue.<sup>7,8</sup> A pedicled intercostal muscle flap (IMF) is used as the covering material for high-risk cases of BPF.<sup>9–11</sup> A high risk of BPF has been reported in surgical procedures such as pneumonectomy or right lower lobectomy, and when induction chemoradiotherapy or chemotherapy is performed.<sup>12</sup>

When reinforcing the bronchial stump using an IMF, it is best to ensure adequate blood supply to the tip of the IMF. However, the adequacy of the blood supply to the IMF covering the bronchial stump is unclear during surgery. If the blood supply of the flap is poor, the IMF may atrophy or lead to necrosis in the thoracic cavity.<sup>12,13</sup>

The indocyanine green fluorescence (ICG-FL) method has been attempted to evaluate the blood supply of various organs in the surgical field. When ICG is intravenously injected, the blood supply to the organs can be confirmed by near infrared fluorescence. This method is used to evaluate the blood supply of muscle flaps for plastic surgery,<sup>14</sup> in the intestinal tract,<sup>15</sup> for coronary artery bypass,<sup>16</sup> and to identify sentinel lymph nodes in breast cancer surgery.<sup>17</sup>

Ultrasound is a non-invasive and repeatable method of blood flow evaluation and has therefore been used to evaluate the intercostal arterial blood flow.<sup>18,19</sup> However, no reports on the use of ultrasound to evaluate the blood supply of the IMF have been published.

Surface temperature measurement using a thermal imaging camera is another new modality that could be used to evaluate the local circulation of muscle flaps. It is a noninvasive, non-contact method; therefore, it can indicate the overall and localized temperatures at a glance. The infrared radiation thermometer of a thermal camera passively detects the emitted infrared radiation and measures its temperature distribution.<sup>20</sup> Therefore, thermography has been used clinically for the evaluation of limb ischemia, such as in Burger's disease and arteriosclerosis obliterans.<sup>21,22</sup> However, there have also been no reports of the use of thermography to evaluate the blood supply of an IMF.

Previously, the blood supply of an IMF has only been evaluated by ICG-FL.<sup>23</sup> In this study, the blood supply of the IMF was evaluated intraoperatively using two different modalities, ICG-FL and thermography, to determine the adequacy of the blood supply of IMFs harvested during the same surgical procedure. We also determined whether a blood supply evaluation could be performed using thermography, which is a less invasive modality.

### Methods

### **Patient enrolment**

Patients who underwent anatomical lung resection at the Department of Thoracic Surgery of Kochi Medical School at Kochi University between December 2014 and March 2018 were enrolled. In total, 27 patients who were at high risk of the development of a BPF were enrolled. Patient characteristics are listed in Table 1. Preoperative lung conditions included eight (29.6%) cases of emphysema, four (14.8%) of interstitial pneumonia, and seven (25.9%) of combined pulmonary fibrosis and emphysema. Induction chemoradiotherapy was administered to three (11.1%) patients and induction chemotherapy to two (7.4%). There were five (18.5%) cases of respiratory infection, such as obstructive pneumonia and Aspergillus infection. Three (11.1%) patients were administered steroids or immunosuppressive drugs orally for interstitial pneumonia or collagen diseases before surgery. Lobar resection with bronchoplasty was performed in eight (29.6%) patients to completely resect the tumor.

Table 1 Patient of	characteristics
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		No. of cases	(%)
No. of patients		27	
Gender	(Male/Female)	25/2	
Age		$72.0\pm9.4$	
Pack year		$47.0\pm45.7$	
c-Stage	IA	2	(7.4)
	IB	6	(22.2)
	IIA	2	(7.4)
	IIB	5	(18.5)
	IIIA	7	(25.9)
	IIIB	5	(18.5)
Preoperative			
treatments	N/A	19	(70.4)
	Chemoradiotherapy	3	(11.1)
	Chemotherapy	2	(7.4)
	Steroid or	3	(11.1)
	immunosuppressive		
	drug use		
Preoperative			
complications	Interstitial pneumonia	4	(14.8)
	Emphysema	8	(29.6)
	CPFE	7	(25.9)
	Respiratory infection	5	(18.5)
	Cardiovascular disease	9	(33.3)
	Cerebrovascular disease	2	(7.4)
	Diabetes mellitus	11	(40.7)
	Hypertension	15	(55.6)
Surgical			
procedure	Right upper lobectomy	8	(29.6)
	Right lower lobectomy	6	(22.2)
	Right middle and	1	(3.7)
	lower lobectomy		
	Left upper lobectomy	2	(7.4)
	Left lower lobectomy	4	(14.8)
	Pneumonectomy	1	(3.7)
	Segmentectomy	4	(14.8)
	Unresectable	1	(3.7)
Bronchoplasty		8	(29.6)

CPFE, combined pulmonary fibrosis and emphysema.

### Ethics, consent, and permissions

Patients provided written informed consent to participate in the study and for individual patient data to be published. The institutional review board of Kochi Medical School, Kochi University approved the study (IRB-103154).

### Intercostal muscle flap (IMF) harvesting

The surgical procedure used to harvest and evaluate the IMF is shown in Figure 1. When opening the chest, a pedicle of IMF was harvested. First, using the periosteum peeler, the intercostal muscle and periosteum were separated from the ribs. The rib from which the IMF was harvested was then cut and the chest was opened at the site of



Figure 1 Surgical procedures used to harvest the intercostal muscle flap (IMF) and reinforce the bronchial stump. (a) Harvesting the IMF; (b) evaluation of the blood supply of the IMF in the operative field; and (c) after anatomical lung resection, the bronchial stump was covered by the IMF (yellow arrow: bronchial stump).

the cut rib bed. The intercostal muscle was cut at the ventral end. The dorsal side of the IMF, including the intercostal artery running from the descending aorta to the IMF, was preserved. During lung resection, the IMF was placed in the thoracic cavity. After lung resection, the blood supply of the IMF was evaluated, and the bronchial stump was covered by a section of the IMF with good blood supply.

# Evaluation of IMF blood supply using the indocyanine green fluorescence (ICG-FL) method

The IMF was placed on the surgical drape in the surgical field. To evaluate ICG-FL, ICG 7.5 mg/body was

intravenously injected and the operation room was darkened. IMF recordings were obtained using the Hyper Eye Medical System (Mizuho Medical Co., Ltd., Tokyo, Japan) in the operative field for three minutes, and ICG-FL was visualized (Fig 2). The distance from the camera head to the muscle flap surface was set at approximately 30 cm.

## Measurement of IMF surface temperature using thermography

The surgical field, including the IMF, was photographed using a Thermo Shot F30W (Nippon Avionics Co. Ltd., Tokyo, Japan). As with the ICG-FL method, the distance from the camera to muscle flap surface was set at



Figure 2 Intraoperative assessment of the blood supply using indocyanine green fluorescence (ICG-FL). (**a**–**c**) Color photographic images of three representative intercostal muscle flaps (IMFs). (**d**) Excellent blood supply in the tip of the muscle flap; (**e**) the blood supply was disrupted in the middle of the flap; and (**f**) poor blood supply. WL, white light mode.

approximately 30 cm. Surface temperature data were saved in a dedicated image data format that included the geographical distribution of temperature.

### Semi-quantitative analysis of ICG-FL

The IMFs were divided into six areas (areas A–F) from the proximal to the distal parts of the IMF. The ICG-FL intensities in areas B–F were semi-quantified, with the ICG-FL intensity in area A used as the reference (Fig 3). ICG-FL intensity was quantified using densitometry (ImageJ version 6; NIH, Bethesda, MD, USA).

## Measurement of surface temperature by thermography

The IMFs were divided into six areas (areas A–F) from the proximal to the distal parts. The surface temperature distribution image was read using Thermography Studio software (Nippon Avionics Co. Ltd.), and the average temperature of areas A–F was calculated (Fig 3).



Figure 3 Indocyanine green fluorescence (ICG-FL) and surface temperature within one intercostal muscle flap (IMF). The muscle flap area was evenly divided into six areas (from proximal to distal) to evaluate the segmental levels of each area (**A**–**F**). The level of ICG-FL and temperature of each area were measured. Both the ICG-FL and local temperature were remarkably lower in areas **E** and **F** than in areas **A**–**D**. WL, white light mode.

### **Statistical method**

A Wilcoxon rank test was used to compare ICG-FL intensity and surface temperature in areas A–F in two related groups. A difference of P < 0.05 was considered significant. In each area, the median values of ICG-FL intensity and surface temperature were calculated, and approximate curves were created. The R<sup>2</sup> value of the approximate curve – the square of the correlation coefficient – was then calculated. JMP version 13 (SAS Institute Japan Co. Ltd., Tokyo, Japan) was used for statistical analyses.

### Results

Among the 27 patients, the length of the IMF in the major axis direction was  $10.0 \pm 1.8$  cm. The IMF was harvested when opening the chest, and blood supply evaluation of the IMF was performed after lung resection. The ICG-FL of the IMF was evaluated in 27 patients, and the surface temperature of the IMF was measured in 18 patients. The time interval between procurement of the IMF and the measurement was  $160.0 \pm 58.3$  minutes (range: 70-320). The time taken for the intravenous injection of ICG-FL to appear in the IMF was then observed for three minutes. ICG-FL intensity was quantified when it reached a steady state after  $20.0 \pm 17.1$  seconds (range: 3.0-64.0) from the time the ICG-FL first appeared.

Using the ICG-FL method, the blood supply level of the IMF varies from case to case (Fig 2). For all 27 patients, the ICG-FL intensities in area A of the IMF were set as the reference (100%), and a scatter plot was created using the ICG-FL intensities in areas B–F (Fig 4a). The relative ICG-FL intensity gradually decreased from area A to F. Compared to area A, the ICG-FL intensity significantly decreased in areas D (P = 0.0411), E (P < 0.0001), and F (P < 0.0001).

A scatter plot of the 18 patients who underwent thermography was created using the surface temperature in each area of the IMF (Fig 4b). Compared to area A, the surface temperature decreased significantly in areas B–F (P < 0.0001).

To investigate the relationship between the ICG-FL method and surface temperature measurement using thermography, patients were divided into two groups according to the level of ICG-FL intensity in area F: group H, which had a higher ICG-FL intensity than the median; and group L, which had a lower ICG-FL intensity than the median. Differences in surface temperature between areas A and F were compared between these two groups (Fig 5). The surface temperature in area F compared to area A decreased by  $2.7 \pm 1.7^{\circ}$ C in group H and by  $4.6 \pm 1.7^{\circ}$ C



**Figure 4** Scatter plots of indocyanine green fluorescence (ICG-FL) intensity and surface temperature in each area of the intercostal muscle flap (IMF). (a) Relative ICG-FL levels of blood distribution in each of the six areas evaluated for 27 patients. When area A was defined as 100%, ICG-FL intensity decreased gradually toward the tip. In area F, the ICG-FL was only 32.6  $\pm$  29.4% of area A. In the approximate curve of each area, ICG-FL decreased in a curvilinear fashion (R<sup>2</sup> = 0.9854). (b) The surface temperature of IMF measured by thermography in each of the six areas for 18 patients. Compared to area A, the temperature was  $3.5 \pm 2.0^{\circ}$ C lower in area F. In the approximate curve of each area, the surface temperature decreased in a curvilinear fashion (R<sup>2</sup> = 0.9940). ICG-FL shows a sharp drop in value as it advances to the tip of the muscle valve compared to the result shown by thermography. ICG-FL reflects a decrease in blood flow itself, and thermography may be affected by a secondary temperature decrease.

in group L. The surface temperature was lower in group L than in group H (P = 0.0574).

The IMF blood supply was evaluated in 27 patients. The bronchial stump was reinforced at the section in which the blood supply of the IMF was maintained in 24 patients, with good blood supply according to ICG-FL. In two patients with poor IMF blood supply according to ICG-FL, the IMF was not used; instead, pericardial fat tissue was used to reinforce the bronchial stump. In one patient, the IMF was not used after evaluation of the blood supply because complete resection of the tumor was impossible because of pleural dissemination and multiple lung metastases; therefore, the procedure was changed to reduction surgery. Within three months after surgery, a steroid pulse was administered to two patients because of acute



**Figure 5** The relationship between indocyanine green fluorescence (ICG-FL) intensity and surface temperature in area F. When the 18 patients were divided into two groups according to the levels of ICG-FL intensity in area F, the differences in the surface temperature between areas A and F were compared. In group L with low ICG-FL intensity in area F, the surface temperature was lower than that in group H (P = 0.0574).

exacerbation of interstitial pneumonia or respiratory failure because of severe pneumonia. During the remote postoperative follow-up examination, IMFs consistently covered the bronchial stump, despite some atrophic changes observed on computed tomography imaging (Fig 6). During the follow-up period of  $14.0 \pm 11.0$  months, none of the patients developed a BPF (n = 24).

### Discussion

To the best of our knowledge, this is the first report to evaluate the blood supply of the IMF intraoperatively by both ICG-FL and thermography. A comparison of these methods revealed that the ICG-FL intensity and surface temperature decreased significantly in the tip of the IMF.

A BPF is a serious postoperative complication, thus a bronchial stump needs to be reliably reinforced. Various muscle flaps are used for plastic and reconstructive surgery.<sup>24–26</sup> In the field of thoracic surgery, it is impossible to observe a muscle flap reinforcing the bronchial stump from the body surface after the thoracotomy has been closed; this is in contrast to muscle flaps used for reconstruction of the skin surface in the field of plastic surgery. Therefore, it is necessary to evaluate the blood supply during the surgical procedure. The blood supply of the muscle flap itself is important for long-term viability. In general, new vascularization develops after creating the anastomosis from the recipient to the donor tissue. However, in the case



Figure 6 Postoperative computed tomography images of the intercostal muscle flap reinforcing the bronchial stump. (**a–d**) The thickness of the muscle flap gradually decreased from 11.4 mm to 8.3 mm over 13 months.

of IMF coverage of the bronchial stump, the development of new blood vessels and increased blood circulation from the bronchus to the IMF are not expected because the blood supply of the bronchial stump itself is poor as a result of lymph node dissection or bronchoplasty.<sup>27-29</sup> Therefore, the blood supply of the IMF used to reinforce the bronchial stump should be ensured intraoperatively.<sup>30</sup> In this study, the part of the muscle flap with the best blood supply was selectively used to reinforce the bronchial stump.

The surface temperature in group L tended to be lower than in group H, but there was no significant difference (P = 0.0574) (Fig 5). In two patients in group L, there were only small differences (0°C and 0.8°C) in the surface temperature between areas A and F. In these two patients, the muscle flaps were kept outside of the thoracic cavity during surgery, and the surface temperature of area A (26.5°C and 27.9°C) was lower than the median value for all area A surface temperatures. Before reinforcing the bronchial stump, the whole muscle flap was cooled outside of the thoracic cavity during surgery. Therefore, secondary changes, such as contraction of the capillaries, could occur as a result of exposure to low temperatures. We conclude that as all areas from A to F were cooled, the temperature difference between A and F was reduced.

The ICG-FL method and thermography have advantages and disadvantages. The ICG-FL method allows the blood supply of the muscle flap to be evaluated at a glance; however, it is necessary to evaluate ICG-FL using a dedicated near-infrared camera immediately after ICG intravenous injection. By contrast, thermography can be used iteratively and is non-invasive. However, surface temperature is a relative evaluation that may be affected by preservation conditions during surgery. For reliable reinforcement of the bronchial stump using IMF, evaluation of the blood supply of the IMF is indispensable. The ICG-FL method and thermography were compared to evaluate the blood supply of the IMF. The blood supply was significantly lower in the distal part of the IMF than in the proximal part. Compared to the ICG-FL method, evaluation of the surface temperature may be influenced by the intraoperative preservation state of the muscle flaps. By reinforcing the bronchial stump with a muscle flap with good blood supply, it is possible to maintain the muscle flap during the remote postoperative phase and reduce the risk of BPF development.

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### Disclosure

No authors report any conflict of interest.

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