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PRS GLOBAL OPEN

ORIGINAL ARTICLE
Breast

Is It Reasonable to Use Indocyanine Green Fluorescence Imaging to Determine the Border of Pedicled TRAM Flap Zone IV?

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Background: The contralateral lateral section (zone IV) of a pedicled transverse rectus abdominis musculocutaneous (TRAM) flap is generally removed intraoperatively. The border of zone IV is usually identified anatomically using the Hartrampf classification. In this study, we used the indocyanine green (ICG) fluorescence method to determine the border of zone IV and find the correlation with clinical flap outcome.

Methods: The study recruited breast cancer patients who underwent a pedicled TRAM flap reconstruction. The border of zone IV was identified using the intraoperative ICG fluorescence imaging. The medial border of the removed specimen was sent for a pathological examination of vascular density.

Results: A total of 29 patients underwent a pedicled TRAM reconstruction. In 16 patients, the border of zone IV identified by ICG fluorescent imaging was identical to the anatomical border. The ICG imaging showed distinct perfusion patterns, which we divided into 4 categories: sequential, simultaneous, low midline scar, and delayed pattern. Overall, there were no patient with total flap loss, 1 patient had a partial flap loss and 4 patients had a fat necrosis. Neither the ICG perfusion time nor the pathological vascular density correlates with the clinical flap outcome. The delayed ICG perfusion pattern (category IV) has the highest fat necrosis rate, although it is not statistically significant.

Conclusions: In this study, more than half of the patients have ICG perfusion corresponding with the Hartrampf zone, which reflected the conventional practice of zone IV pedicled TRAM flap removal. Some ICG perfusion patterns could be helpful, especially in low midline and delayed pattern. *(Plast Reconstr Surg Glob Open 2020;8:e3093; doi: 10.1097/GOX.0000000000003093; Published online 24 September 2020.)*

INTRODUCTION

Pedicled transverse rectus abdominis musculocutaneous (TRAM) flap reconstruction is a well-known procedure for breast cancer surgery. Moon and Taylor's[1] study of vascular anatomy shows that a pedicled TRAM flap receives indirect blood supply from a deep superior epigastric artery. As a result, TRAM flaps are prone to flap congestion and necrosis. A poor assessment of tissue perfusion during reconstructive surgery may lead to flap complications. The common complications of this procedure are fat necrosis and flap necrosis, which occur at a rate of 14%–21% and 5%, respectively.[1] Cases with a large chest wall defect after a mastectomy require a higher amount of flap tissue for defect coverage, which can lead to an increased chance of flap complications.

The contralateral lateral segment (zone IV) of the TRAM flap is normally removed intraoperatively owing to insufficient perfusion.[2–4] The border of zone IV is usually identified anatomically using the Hartrampf classification.[5] However, breast cancer cases with a large chest wall defect may warrant cutting the flap more laterally to preserve a higher volume of tissue. The current practice for patients with a low midline surgical scar is that all tissue beyond the scar is removed, which may hinder the tissue volume even more.

There are a variety of intraoperative methods to assess flap perfusion, such as Doppler ultrasound, laser Doppler, fluorescence imaging, and oxygen saturation measurement. A meta-analysis found that fluorescence imaging

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Received for publication May 21, 2020; accepted July 7, 2020.

DOI: 10.1097/GOX.0000000000003093

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

and laser Doppler are the most suitable methods to assess tissue perfusion in free flaps.[6] As for the pedicle TRAM flap, the use of indocyanine green (ICG) fluorescence imaging has been reported by Yamaguchi et al. as a safe, quick, and accurate technique of flap perfusion analysis and may reduce fat necrosis.[7] However, there is currently no study that describes the vascular distribution in the subcutaneous fat layer of the zone 4 border identified by the ICG technique.

The purpose of this study was to find the correlation among ICG imaging, pathological vascular density, and clinical flap outcome in patients who received pedicled TRAM flap reconstruction with ICG fluorescence imaging.

PATIENTS AND METHODS

We performed a prospective single arm study on 29 breast cancer patients who underwent breast reconstruction with a pedicled TRAM flap between August 2017 and February 2020. The study included female patients with breast tumors that required a mastectomy and reconstruction, both immediate and delayed. We excluded patients who are current smokers or have upper transverse abdominal surgical scars.

All patients received standard preoperative evaluations, including clinical examination, digital mammography, and breast ultrasonography. MRI is not used routinely in our institute. Informed consent was obtained from all patients. Patient data (including age, weight, height, Body Mass Index (BMI), comorbidities, previous surgeries, and neoadjuvant treatment) were recorded.

Fluorescence imaging with ICG was used intraoperatively to evaluate the perfusion of the pedicled TRAM flap, and we divided the flap according to ICG enhancement. The transected portion of the flap was sent to a pathologist to evaluate the vascular density. Postoperative complications were recorded. Fat necrosis was evaluated through physical and ultrasonographic examinations by the physician at 4–6 months after the operation.

The primary outcome is flap loss and fat necrosis after using the ICG guidance. The secondary outcome is the perfusion time and vascular density of zone IV.

Operative Technique

Pedicled TRAM flap was harvested using a standard elliptical incision in the lower abdomen. The abdominal flap was dissected in the direction of lateral to medial, identifying the arterial perforators along the way. The inferior epigastric vessels were identified and cut after dividing the rectus muscle at the arcuate line.

After fully harvesting the pedicled TRAM flap, we marked the flap zones based on the anatomy using Hartrampf concept ("anatomical borders"). Zone I is located at the pedicle side, zone II is the contralateral medial section, zone III is the ipsilateral lateral section, and zone IV is the contralateral lateral section of the TRAM flap. ICG was injected through a peripheral intravenous access at a dose of 0.25 mg/kg. The perfusion of the flap was visualized under a fluorescence camera (FLUOPTICS) and recorded for 5 minutes. We then cut the flap along the border between zones II and IV according to the ICG enhancement ("ICG borders") (Fig. 1). The removed zone IV tissue was sent to a pathologist for a vascular density examination (Fig. 2).

Pathological Evaluation of Vascular Density in Zone IV Tissue

The vascular density of the most medial part of zone IV tissue was histologically examined. After the zone IV tissue was adequately fixed in 10% buffered formalin, the most medial surface was selected and processed to be formalin-fixed and paraffin-embedded via a standard protocol for histopathology. In cases where the ICG border was medial to the Hartrampf anatomical border of zone IV, both the ICG border (the most medial surface) and the Hartrampf anatomical border of zone IV were selected. The tissue sections were cut into 3- to 5-μm-thick slices and stained using the hematoxylin and eosin technique. All tissue slides were examined under a light microscope. The number of arteries and arterioles in the area above and below the Scarpa fascia per mm^2 of subcutaneous fat was counted by a pathologist to evaluate the vascular density.

Statistical Analysis

All demographic data, clinicopathological reports, necrosis complications, and other postoperative complications

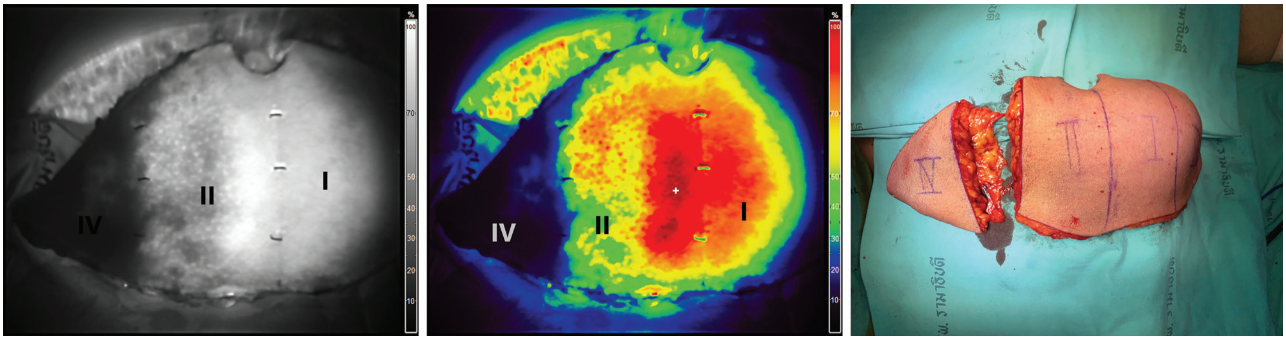

Fig. 1. View of the harvested medical TRAM flap. A and B, ICG fluorescent enhancement of the pedicled TRAM flap, with no perfusion in the contralateral lateral segment (zone IV). C, Zone IV was removed according to the border identified by the ICG imaging. (The ICG border and the anatomical border are identical in this case.)

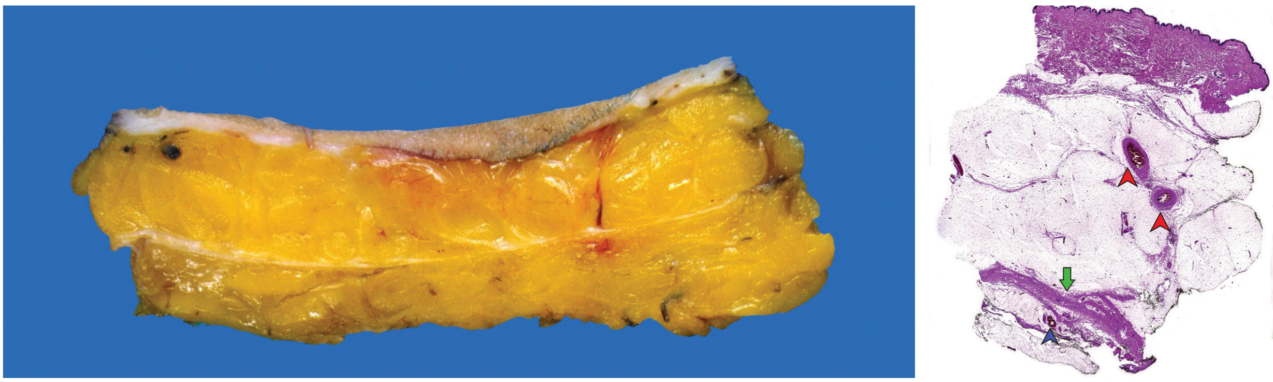

Fig. 2. A, Gross pathological picture demonstrating the cut surface of a TRAM flap at the Hartrampf zone IV. B, Microscopic view of arteries and arterioles within the TRAM flap showing the location of the Scarpa fascia (green arrow), artery above the Scarpa fascia (red arrow heads), and arteriole below the Scarpa fascia (blue arrow head).

were presented with descriptive statistics. Patient characteristics were compared using a Student *t*-test or Mann-Whitney test for continuous variables, and a Chi-square or Fisher exact test for categorical variables. All statistical analyses were performed with Stata, v.14 (StataCorp LP, College Station, Tex.). Statistical values were considered significant at $P < 0.05$.

RESULTS

Twenty-nine patients underwent breast reconstructions using pedicled TRAM flaps during the study period. The baseline characteristics of patients are shown in Table 1. The mean age was 50.1 years (range, 38–68 years), and the mean BMI was 25.99 kg/m^2 (range, 17.02–38.85 kg/m^2). Four patients had undergone a neoadjuvant chemotherapy and 4 patients had a low midline surgical scar. In 16 patients (55.2%), the border of zone IV identified by ICG fluorescent imaging was identical to the anatomical border.

The ICG perfusion time and pattern were documented by reviewing the recorded video and captured images. The mean ICG perfusion times to zone I, II, and III were 49.82 seconds (range, 23–90 seconds), 113.86 seconds (range, 38–312 seconds), and 104.27 seconds (range, 48–275 seconds), respectively. There were 15 patients (55.6%) with a completely absent perfusion to zone IV. The ICG perfusion time to each zone was not different between patients who had fat necrosis and those who had not (Table 2).

The ICG fluorescence imaging showed distinct perfusion patterns, which we divided into 4 categories: sequential, simultaneous, low midline scar, and delayed pattern (Table 3, Fig. 3). We termed this as "YaYa's classification." The majority of cases fall into the sequential (category 1) or simultaneous (category 2) perfusion pattern, with 11 patients in category 1 and 12 patients in category 2. In patients with a low midline surgical scar (category 3), 3 of 4 patients (75%) had a clear ICG perfusion beyond the scar (category 3a). We cut the flap according to ICG fluorescence guidance and we found no flap necrosis or fat necrosis in these patients.

The pathological report is complete in 27 patients. The number of arteries per area was very small (average, 0.0026/mm^2); therefore, we used only the number of arterioles per area to represent the vascular density. The mean number of arterioles per area of superficial fat in the medial part of zone 4 above the Scarpa fascia is 0.08 / mm^2 and 0.14 /mm^2 below the Scarpa fascia.

Partial flap necrosis was found in 1 patient (3.3%). There was no patient with total flap loss in our study. The only other non-TRAM-flap–related complication was a partial nipple–areolar complex/skin necrosis, which occurred in 7 patients (23.3%). The patient who had the partial flap necrosis need reoperation. This patient was obese (BMI 38.85 kg/m^2), underwent post neoadjuvant

Table 1. Baseline Characteristics of 29 Patients Who Underwent Pedicled TRAM Flap Reconstruction from August 2017 to February 2020

Patient Characteristics	Summary
Age (year): mean (SD)	49.86 (6.44)
Height (cm): mean (SD)	154.36 (5.75)
Weight (kg): mean (SD)	61.88 (11.37)
BMI (kg/m^2): mean (SD)	26.04 (5.01)
Post NACT (n)	4
Breast reconstruction:	
• Delayed (n)	2
• Immediate (n)	27
Operation:	
• Skin sparing mastectomy (n)	15
• Nipple sparing mastectomy (n)	14
• Previous abdominal surgery (n)	4
• Cutting line by ICG corresponded with Hartrampf (n)	16

NACT, neoadjuvant chemotherapy.

Table 2. Perfusion Time of ICG Fluorescence to Each Hartrampf Zone in 29 Patients Receiving Pedicled TRAM Flap Reconstruction

	Time to Each Zone by ICG Fluorescence (s), mean (SD)			
Zone	All patients	No fat necrosis	Fat necrosis	*P*
I	49.82 (16.86)	49.20 (16.29)	53.75 (22.51)	0.625
II	113.86 (53.05)	111.88 (54.95)	126.25 (43.26)	0.623
III	104.27 (55.07)	105.04 (55.56)	99.50 (59.76)	0.855
IV	113.93 (130.96)	102.16 (129.81)	187.50 (129.96)	0.232

s, seconds.

Table 3. ICG Fluorescence Enhancement Pattern Classified by YaYa's Classification in 29 Patients Who Underwent a Pedicled TRAM Flap Reconstruction

Category	Pattern	n (%)
Category 1: sequential	1a: Zone I and then zone III	6 (20.7)
	1b: Zone I and then zone II	5 (17.2)
Category 2: simultaneous	2a: Zone I and zone III	7 (24.1)
	2b: Zone I and zone II	5 (17.2)
Category 3: low midline scar	3a: Presence of ICG across midline	3 (10.3)
	3b: Faint (or loss of) ICG across midline	1 (3.5)
Category 4: delayed pattern	4: Delayed perfusion of ICG at zone II (>120s)	2 (6.9)

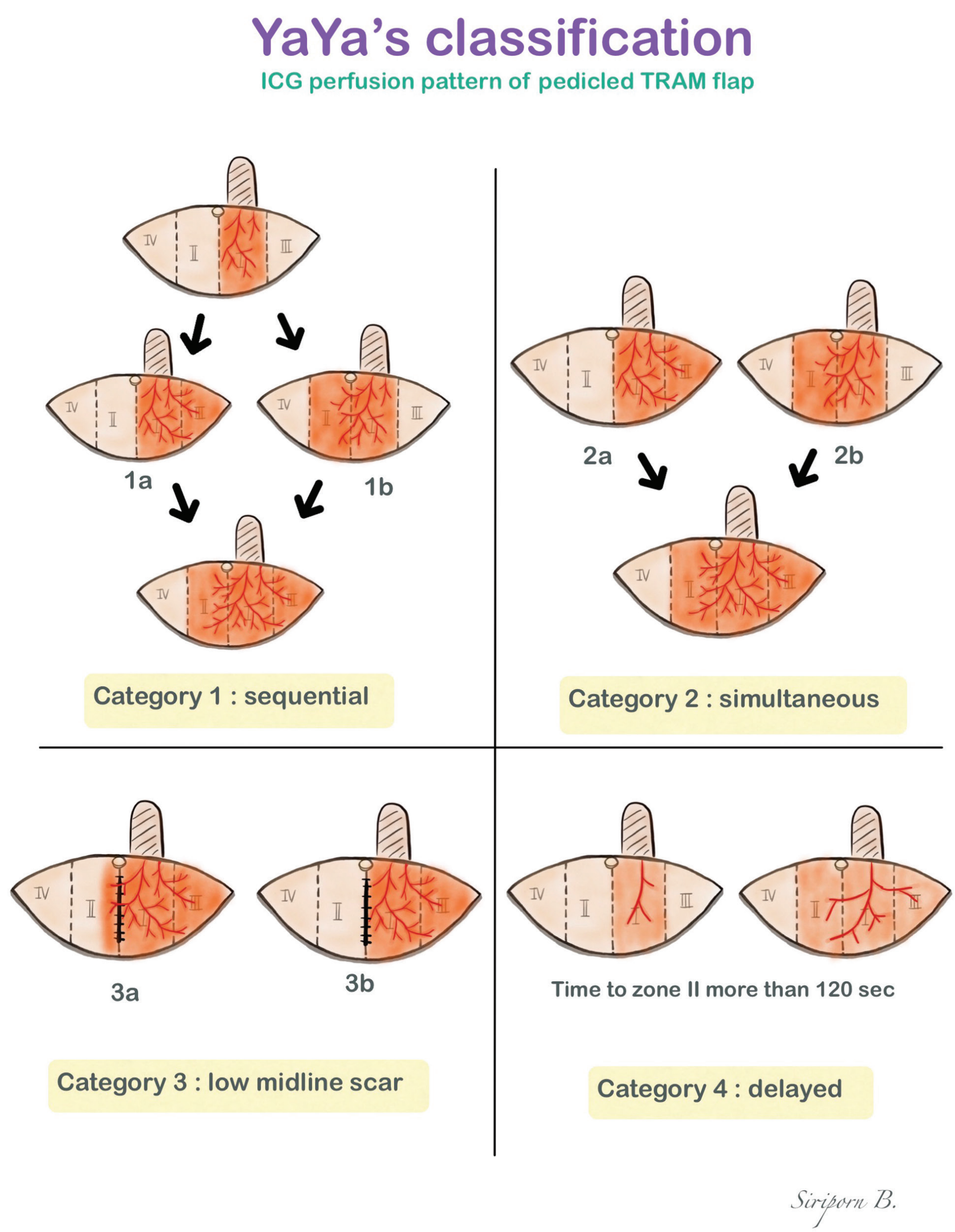

Fig. 3. Four categories of ICG perfusion pattern. Category 1 (sequential) consists of 1a (sequential perfusion in zone I, then III, and then II) and 1b (sequential perfusion in zone I, then II, and then III). Category 2 (simultaneous) consists of 2a (simultaneous perfusion of zone I and III, then perfusion of zone II) and 2b (simultaneous perfusion of zone I and II, then perfusion of zone III). Category 3 (patient with midline surgical scar) consists of 3a (clear perfusion beyond the scar) and 3b (faint or loss of perfusion beyond the scar). Category 4 is the delayed pattern, meaning the presence of ICG at zone II takes more than 120 seconds.

Table 4. Comparative Outcome between Each Factor Associated with Fat Necrosis

Parameters	Total (n = 29)	No Fat Necrosis (n = 25)	Fat Necrosis (n = 4)	*P*
Age (year): mean (SD)	49.86 (6.44)	49.88 (6.81)	49.75 (4.03)	0.970
BMI (kg/m^2): mean (SD)	26.04 (5.01)	25.15 (3.86)	31.59 (8.25)	0.217
Comorbidity (DM, HT): n (%)	5 (17.24)	4 (16)	1(25)	0.553
Vascular density above Scarpa: mean (SD) (n/mm^2)	0.07 (0.04)	0.08 (0.04)	0.06 (0.04)	0.458
Vascular density below Scarpa: mean (SD) (n/mm^2)	0.14 (0.07)	0.15 (0.07)	0.10 (0.05)	0.267
Perfusion pattern category:				0.215
• Category 1 (n)	11	11	0	
• Category 2 (n)	12	10	2	
• Category 3 (n)	4	3	1	
• Category 4 (n)	2	1	1	

DM, Diabetes mellitus; Hb, Hemoglobin; HT, Hypertension.

chemotherapy treatment, and had a delayed pattern (category IV) of ICG enhancement.

After a follow-up of 6 months, 4 cases (13.33%) of fat necrosis were reported via an ultrasonographic examination. BMI, age, vascular density, and the ICG perfusion pattern were not significantly different between the fat necrosis group and the no fat necrosis group (Table 4).

DISCUSSION

The DIEP (deep inferior epigastric perforator) free flap is the best procedure of TRAM flap, but it has a limitation of requiring microvascular surgery. Other techniques such as preoperative delay[8,9] as well as internal mammary artery and vein supercharge[10] have been proposed to increase the vascular flow to the pedicled TRAM flap. Such techniques also need more surgeon experience.

A pedicled TRAM flap receives blood supply indirectly from the superior epigastric vessels via the choke system. Zone IV of the TRAM flap has the lowest blood supply and is routinely discarded, but the blood supply to zone II and III are unpredictable. Fluorescent imaging has previously been used to evaluate flap perfusion but mostly for free flap reconstructions. A meta-analysis by Smit et al. concluded that fluorescent imaging and laser Dopplers are the most suitable modalities for intraoperative free flap tissue perfusion assessment and that utilizing them can improve flap survival.[6]

ICG is a water-soluble dye that emits infrared energy within 2 minutes of injection. Currently, it is approved for evaluating cardiac output, hepatic function, hepatic blood flow, and ophthalmic vasculature.[11] ICG is also used intraoperatively in many other surgical procedures, including breast reconstruction.[12]

In this study, we used ICG fluorescence angiography to evaluate the perfusion of the flap, particularly the border between zone II and IV. The perfusion patterns we found are described in Table 3. The most common pattern was the simultaneous pattern (category 2), which is an ICG enhancement seen in zone I simultaneously with either zone II or III. We hypothesized that this pattern signifies more blood flow to the TRAM flap, which should have resulted in less chance of fat necrosis but the data showed that the occurrence of fat necrosis is no different from the other patterns.

The perfusion times to zone I, II, and III in this study were 50, 115, and 106 seconds, respectively. These times are longer than those of ICG fluorescent imaging done in DIEP flaps.[14] The perfusion times in the DIEP flaps were 25, 41, and 32 seconds for zone I, II, and III, respectively. Only 33% of the DIEP flap study population has complete absence of blood flow to zone IV compared with 55.6% in this study. The longer perfusion times and higher proportion of cases with an absence of blood flow to zone IV encountered in this study may be due to the indirect blood supply nature of a pedicled TRAM flap.

In the majority of patients (3 of 4) with low midline surgical scars, the fluorescence imaging showed an ICG enhancement beyond the midline, which enabled us to preserve more tissue for the flap. There was neither flap necrosis nor fat necrosis in all 3 patients. This corresponds with the findings by Wu et al,[13] who used a preoperative color-flow duplex scan to evaluate flap perfusion in low midline scar patients before pedicled TRAM flap reconstruction. They found that there is enough blood supply to zone II and no significant difference in flap complications. These discoveries may change the current practice of transecting the flap at the midline scar to transecting more laterally in cases where ICG imaging or color-flow duplex scans show sufficient perfusion.

We found that there is a higher density of arterioles in the area both above and below the Scarpa fascia in patients with no fat necrosis when compared with the fat necrosis group; however, it is not statistically significant. We conclude that the number of arterioles does not correlate with the flap outcome.

We transected all TRAM flaps according to the ICG perfusion. Even though in the majority of cases, the ICG border was identical to the anatomical border, there were also instances where the ICG border is more lateral than the anatomical border and vice versa. Therefore, we cannot conclude that using the ICG will ensure a larger flap size. The overall fat necrosis rate in our study is 13.33%, which is quite similar to the fat necrosis rate in conventional pedicled TRAM flap operations in the literature (14%–21%).[1,3] The limitation of our study is that it is a prospective, non-randomized study, which however creates potential for further RCT trials. A study by Kim et al. found that if a higher amount of zone II tissue (more than 20% of the overall flap tissue) is included in the flap, there is an increased risk of fat necrosis.[3] Hence, another research potential would be to determine the complication rate in cases where the ICG border is more lateral to the anatomical border compared with the reversed situation.

CONCLUSIONS

This study found that the ICG fluorescence imaging technique is not significantly different from an anatomy-based surgical technique in pedicled TRAM flap reconstruction but it is still a helpful tool in identifying the flap transection border, especially in complex cases such as those with low midline scars or when a large area of flap coverage is required. This may lead to the optimum amount of tissue removal and minimizes fat necrosis in the remaining tissue.

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ACKNOWLEDGMENTS

We acknowledge Ms. Suraida Aeesoa for help with statistical analysis and Dr. Panya Thaweepworadej, Dr. Chayanoot Rattadilok, and Dr. Chuleekorn Lawonggerd for helping to acquisition the data.

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