JPRAS Open 41 (2024) 61–74

Contents lists available at ScienceDirect

JPRAS Open

journal homepage: www.elsevier.com/locate/jpra

Original Article

Tissue perfusion in DIEP flaps using Indocyanine Green Fluorescence Angiography, Hyperspectral imaging, and Thermal imaging ☆

Simone F. Kleiss [1,*], Marlies Michi [2,*], Simone N. Schuurman [1], Jean-Paul P.M. de Vries [1], Paul M.N. Werker [2], Steven J. de Jongh [2,#]

[1] *Department of Surgery, Division of Vascular Surgery, University Medical Center Groningen, Groningen, The Netherlands*
[2] *Department of Plastic Surgery, University Medical Center Groningen, Groningen, The Netherlands*

ARTICLE INFO

Article history:
Received 23 April 2024
Accepted 25 April 2024
Available online 1 May 2024

Keywords:
Breast reconstruction
Indocyanine Green Angiography
Perfusion imaging
Hyperspectral imaging
Thermal imaging
DIEP-flap reconstruction

ABSTRACT

Flap necrosis continues to occur in skin free flap autologous breast reconstruction. Therefore, we investigated the benefits of indocyanine green angiography (ICGA) using quantitative parameters for the objective, perioperative evaluation of flap perfusion. In addition, we investigated the feasibility of hyperspectral (HSI) and thermal imaging (TI) for postoperative flap monitoring.

A single-center, prospective observational study was performed on 15 patients who underwent deep inferior epigastric perforator (DIEP) flap breast reconstruction (n=21). DIEP-flap perfusion was evaluated using ICGA, HSI, and TI using a standardized imaging protocol. The ICGA perfusion curves and derived parameters, HSI extracted oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) values, and flap temperatures from TI were analyzed and correlated to the clinical outcomes.

☆ This article is not based on any previous communication to a society or meeting.

Corresponding author: S.J. de Jongh, MD, PhD, Department of Plastic Surgery, University Medical Center Groningen, Hanzeplein 1, 9713 GZ, Groningen, The Netherlands.
E-mail address: s.j.de.jongh@umcg.nl (S.J. de Jongh).
* Authors contributed equally and share first authorship.

https://doi.org/10.1016/j.jpra.2024.04.007

Post-hoc quantitative analysis of intraoperatively collected data of ICGA application accurately distinguished between adequately and insufficiently perfused DIEP flaps. ICG perfusion curves identified the lack of arterial inflow (n=2) and occlusion of the venous outflow (n=1). In addition, a postoperatively detected partial flap epidermolysis could have been predicted based on intraoperative quantitative ICGA data. During postoperative monitoring, HSI was used to identify impaired perfusion areas within the DIEP flap based on deoxyHb levels. The results of this study showed a limited added value of TI.

Quantitative, post-hoc analysis of ICGA data produced objective and reproducible parameters that enabled the intraoperative detection of arterial and venous congested DIEP flaps. HSI appeared to be a promising technique for postoperative flap perfusion assessment. A diagnostic accuracy study is needed to investigate ICGA and HSI parameters in real-time and demonstrate their clinical benefit.

Introduction

The deep inferior epigastric perforator (DIEP) flap is the most commonly applied flap for autologous breast reconstruction following mastectomy for breast cancer.[1,2] Inadequate flap perfusion may lead to necrosis and (partial) flap loss, which has a significant impact on aesthetic and patient-reported outcomes and may delay subsequent oncological treatment in primary reconstructions.[3,4] Early reintervention of anastomotic problems has been shown to improve survival rates of DIEP flaps.[5,6]

The current gold standard for DIEP-flap perfusion monitoring is clinical assessment using parameters such as flap color, temperature, and capillary refill, combined with handheld Doppler ultrasonography of arterial perforator flow.[7,8] However, clinical assessment is subjective and apparently incapable of preventing (partial) flap loss in 10% to 71% of the cases.[9-11] This emphasizes the need for a real-time and accurate evaluation of flap perfusion during surgery and follow-up.

Indocyanine green angiography (ICGA) is a promising near-infrared fluorescence imaging technique that is considered safe and easily applicable, with the potential to decrease flap perfusion problems.[11,12] Previous studies on ICGA, evaluating perioperative flap perfusion reported a wide variety of ICGA parameters that were not always associated with clinical outcomes and acquired using different fluorescence camera systems.[13] Moreover, the real-time interpretation of quantitative data is not yet possible. Consequently, the sensitivity and specificity of ICGA is insufficient at present for use as a gold standard for the detection of flap perfusion problems.

Furthermore, hyperspectral imaging (HSI) and infrared thermal imaging (TI) have shown promising results for postoperative flap evaluation.[14,15] HSI and TI are non-invasive techniques that can be applied in the patient ward and therefore seem better suited for routine and repeated postoperative imaging when compared to ICGA.

In this proof-of-concept study, we aimed to investigate the clinical benefit of ICGA for perioperative evaluation of DIEP-flap perfusion, by describing the qualitative and quantitative ICGA parameters that can be interpreted irrespective of the fluorescence imaging camera used and enable translation to a subsequent diagnostic accuracy study. In addition, we aimed to determine the feasibility of HSI and TI for postoperative evaluation of DIEP-flap perfusion.

Patients and methods

Study design and patients

For this single-center prospective observational study, patients who underwent DIEP-flap reconstructive surgery from October 2020 to October 2021 were enrolled after obtaining their written informed consent. The study was performed according to the STROBE guidelines.

The inclusion of 15 patients was considered sufficient for this proof-of-concept study as the results will be translated in a subsequent diagnostic accuracy study.

Patients who were ≥18 years and scheduled for unilateral or bilateral DIEP-flap breast reconstruction according to standard clinical care were included. Exclusion criteria were pregnancy or lactation, severe hepatic or renal insufficiency, hyperthyroidism, thyroid adenoma, allergy to iodine or ICG, or participation in another fluorescence imaging study. Patient demographics including sex, age, body mass index (BMI), skin type,[16] time-point of reconstruction, clinical outcomes, and complications such as impaired wound healing, infections, (partial) flap loss, necrosis, and flap-related re-interventions with a follow-up of 1 year were collected from the medical records.

Indocyanine green fluorescence angiography

ICGA uses indocyanine green to visualize cutaneous blood flow patterns (ICG; $t_{1/2}$=150–180 s). ICG is a near-infrared fluorescence dye with a peak absorption and emission of 805 and 835 nm, respectively,[17-19] which is registered with the U.S. Food and Drug Administration and European Medicines Agency for visualization of (micro)circulation. The Novadaq Spy Elite® (Stryker Corp., Kalamazoo, MI, USA) is a CE-marked fluorescence camera system for intraoperative real-time ICG detection.

ICGA was performed 1) preoperatively, to evaluate baseline perfusion; 2) intraoperatively after flap harvest (pre-transfer), to evaluate flap perfusion solely by the perforator artery; 3) intraoperatively after the creation of the vascular anastomoses (post-transfer), to evaluate flap perfusion in the recipient area; and 4) on the first postoperative day, to evaluate flap perfusion.

Patients received an intravenous bolus injection of 10 mg ICG based on the Novadaq Spy® operating manual (Rev. C, 2016).[20] Only at time-point 2, an intravenous bolus of 5 mg ICG was administered, as this is deemed sufficient for perforator imaging and a lower ICG dose allows repetitive ICGA with limited influence on background fluorescence (Figure S1).[20] The maximum dose ICG used was 2 mg/kg.[20] The fluorescence camera was positioned perpendicular to the skin at a distance of 20 cm, set at a frame rate of 3.75/s with dimmed ambient lights. In case of a bilateral DIEP-flap reconstruction, one side was randomly included for ICGA, as the field-of-view of the camera precludes bilateral imaging and repetitive ICG injections required would exceed ICG dosages and cause significant background fluorescence.

Hyperspectral and Thermal imaging

HSI and TI were performed preoperatively to evaluate baseline perfusion of the abdominal skin, which was later used as a reference for the patient.[21] Postoperatively, HSI and TI were performed twice daily starting on the first postoperative day until discharge. In case of bilateral DIEP-flap reconstructions, both sides were included (Figure S1).

HSI uses visible light spectroscopy to determine the concentration of oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) in the superficial 1–2 mm of the skin. HSI is performed using the CE-marked, handheld HyperView™ camera system (HyperMed Inc, Memphis, TN, USA) perpendicular to the skin at a standard distance of 38 cm.

TI is performed using the CE-marked-, infrared FLIR camera T1030sc (FLIR systems® Inc, Wilsonville, OR, USA), which measures surface temperatures based on the emissive radiation from an object. Standard camera settings are used according to the user manual with emissivity at 0.98 corresponding to the qualities of skin surface.

Outcomes

The primary objective for carrying out ICGA was to quantitatively evaluate fluorescence intensities at pre-defined time points, in relation to the abovementioned gold standard for clinical assessment of flap perfusion, to provide objective values that facilitate the differentiation between areas with adequate and impaired perfusion. DIEP flaps with adequate tissue perfusion according to the gold standard were classified as "uncomplicated." DIEP flaps with delayed wound healing, epidermolysis, (partial) flap necrosis, suspected insufficient arterial inflow, impaired outflow, or infection were classified as "complicated." The secondary objective was to provide quantitative in- and outflow ICGA time-intensity curves. Analyses of ICGA curves was performed after surgery (post-hoc), as the current software precludes real-time quantitative analysis.

The following parameters were determined after selection of the available skin of the complete DIEP flap as a region of interest (ROI) (Figure S2): maximum fluorescence intensity (Fmax, arbitrary units (a.u.)); inflow time (s), defined as the time between the start of ICG inflow to Fmax; inflow time [10%–90%], the time from 10% to 90% intensity (s); maximum slope of the fluorescence intensity curve (a.u./s); slope [10%–90%], defined as the slope of the ICGA curve from 10% to 90% fluorescence intensity (a.u./s); outflow time, defined as the time from the maximum fluorescence intensity until a decrease of 20% was observed (s); outflow slope from maximum to 20% decrease in intensity (a.u./s). In "complicated" cases, complicated areas were selected as individual ROIs and analyzed similarly to differentiate between the areas with adequate and impaired perfusion within a DIEP flap.

The primary objective for performing HSI and TI was to determine the safety and feasibility for differentiation of complicated and uncomplicated DIEP flaps. The secondary objective was to quantify pre- and postoperative oxygenation values and local skin temperatures. ROIs were selected on the available skin of the complete monitoring island of the DIEP flap to determine oxyHb (a.u.) and deoxyHb (a.u.) values using HSI and flap temperature (°C) using TI. Parameters were compared between complicated and uncomplicated flaps both pre- and postoperatively.

Data and statistical analyses

Descriptive statistics were performed on patient characteristics and parameters obtained with ICGA, HSI, and TI. None of the parameters were normally distributed and consequently, data are presented as median values with interquartile range. The Friedman test was used to compare perfusion parameters at different time points using the Bonferroni post-hoc test to correct for multiple testing. Statistical analyses were performed using IBM SPSS Statistics (v28, IBM Corp, USA). A p-value of <0.05 was considered statistically significant. All clinical data were collected using REDCap (Vanderbilt University, USA). ICGA parameters were determined using Fiji (v2.3.0, ImageJ, USA). HSI data were analyzed using the standard software provided by HyperMed Inc, USA. Graphs were drawn using Graphpad Prism (v9.1.0, GraphPad Software Inc, USA).

Results

We included 15 patients who underwent a DIEP-flap breast reconstruction, among whom 9 underwent unilateral and 6 underwent bilateral breast reconstruction (n=21 DIEP flaps). Patient characteristics are displayed in Table 1. The mean age of the patients was 49.0±8.2 years and mean BMI was 26.9±2.3 kg/m^2. There were no (serious) adverse events related to any of the study procedures.

Among the 21 DIEP flaps, 16 were judged to be uncomplicated with adequate flap perfusion both peri- and postoperatively, according to standard clinical monitoring. Impaired flap perfusion was observed in 5 DIEP flaps (Figure 1, i.e., "complicated" cases). Three of these "complicated" DIEP flaps were caused by an arterial spasm pre-transfer, occlusion of the arterial anastomosis, and occlusion of the venous anastomosis post-transfer, all of which were detected intraoperatively and immediately resolved using lidocaine as local antispasmodic medication, re-anastomosis of the artery and vein, respectively. All three events were correctly identified using ICGA. The two remaining complications were detected postoperatively. One complicated case had venous congestion caused by a thrombus

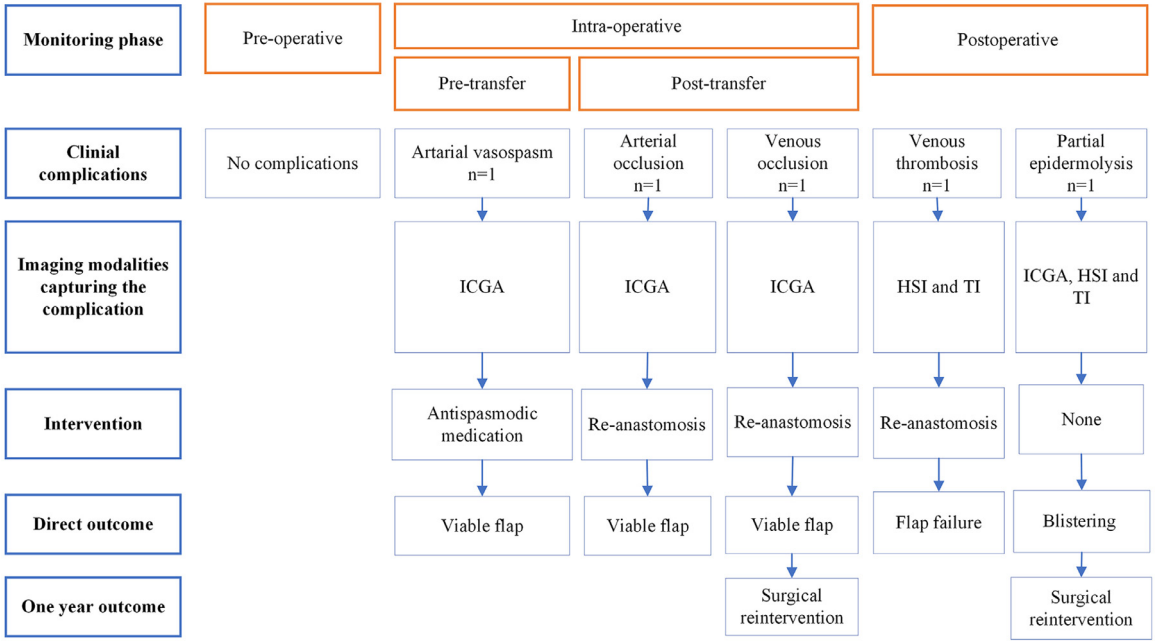

Figure 1. Schematic representation of the study complications. There were three intraoperative complications and two postoperative complications, none of which were related to any of the study procedures.

Table 1
Patient characteristics (n=15).

Ethnicity	White	12
	Hispanic	1
	Black	1
	Asian	1
Skin type	Type I	1
	Type II	11
	Type IV	2
	Type V	1
Smoking	No	6
	Yes	1
	Stopped	8
ASA	Asa I	2
	Asa II	13
Side reconstructed	Right	3
	Left	6
	Bilateral	6
Surgical characteristics (n=21 DIEP flaps)		
Indication for mastectomy	Oncological	14
	Preventive	7
Reconstruction	Primary	6
	Secondary	15

in the venous anastomosis, which was resolved by revising the venous anastomosis <6 h postoperatively. Unfortunately, only the contralateral flap of this patient was part of the ICGA cohort. Ultimately, persistent venous congestion resulted in flap failure; the flap was resected after 4 days. The other complicated case had partial epidermolysis that was observed on the second postoperative day. This was initially treated conservatively, although later a surgical debridement and skin grafting was performed.

ICGA

Among the 21 DIEP flaps, 15 were randomly selected for ICGA, as the field-of-view of the camera precludes bilateral imaging and repetitive ICG injections required would exceed ICG dosages and cause significant background fluorescence. ICGA parameters for uncomplicated DIEP flaps are presented in Figure 2A. The preoperative time-intensity curve showed a median inflow time of 29.9 s (22.5–38.4 s), max slope of 15.0 a.u/s (9.5–21.3 a.u/s), slope [10%–90%] of 6.7 a.u/s (3.8–9.4 a.u/s) and outflow time of 36.5 s (18.1–75.5 s) (Table 2).

Negligible fluorescence was observed using intraoperative ICGA in the patient with the arterial spasm prior to flap transfer due to a lack of ICG inflow (Figure 2B). ICGA demonstrated a significantly prolonged ICG inflow time and decrease of the slope [10%–90%] compared to uncomplicated cases (200.53 s vs. 96.8 s; 0.18 vs. 0.9 a.u./s, respectively). After using the spasmolytic, the blood flow was restored as visualized by ICGA, with parameters resembling those of the uncomplicated flaps (Figure 2B). Similarly, in the patient with the arterial occlusion post-transfer a limited increase in fluorescence was recorded (Figure 2C). Fluorescence intensities persistently increased in the patient with an occlusion of the venous anastomosis (Figure 2C), with a prolonged ICG inflow time and decreased slope [10%–90%] compared to uncomplicated cases (264.67 s vs. 96.8 s; 0.48 vs. 0.9 a.u./s, respectively).

Postoperative ICGA measurements were comparable to the corresponding preoperative data, indicating a restored blood supply (Table 2). Interestingly, intraoperative ICGA that was performed post-transfer accurately identified the area of epidermolysis, which was clinically observed on the second postoperative day (Figure 3). A prolonged inflow time and decreased slope were observed for the impaired perfused area compared to the surrounding flap (247.47 s vs. 112.80 s; 0.12 vs 0.87 a.u./s, respectively).

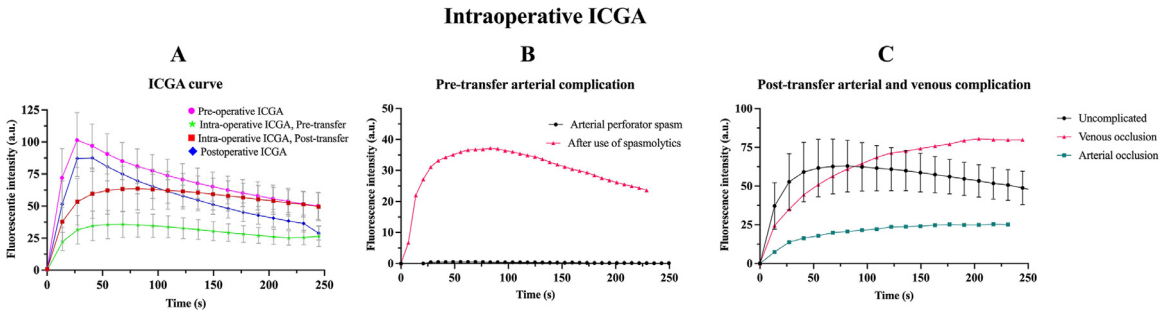

Figure 2. A) Indocyanine green angiography (ICGA) fluorescence intensities of uncomplicated flaps. Fluorescence intensities are presented as median±95% confidence intervals. B) Indocyanine green angiography (ICGA) fluorescence intensities of a complicated flap: ICGA measurements pre-transfer of the DIEP flap with an arterial perforator spasm that was resolved after application of local spasmolytic medication (lidocaine). C) Indocyanine green angiography (ICGA) fluorescence intensities of uncomplicated and complicated flaps: ICGA measurements post-transfer of uncomplicated flaps (n=13), one case of an occlusion of the arterial anastomosis and one occlusion of the venous anastomosis. Values are presented as median and 95%±confidence interval. ICG: indocyanine green.

Table 2
Preoperative ICGA perfusion parameters.

	Preoperative (n=14)		Intraoperative						Postoperative (n=15)		
			Pre-transfer (n=14)		*p*	Post-transfer (n=13)		*p*			*p*
Maximum intensity, Fmax (a.u.)	108.1	[92.1–134.4]	37.8	[25.0–44.7]	0.000	55.7	[45.0–98.7]	0.049	96.8	[85.0–118.2]	1.000
Inflow time (s)	29.9	[22.5–38.4]	67.1	[53.9–89.1]	0.003	92.0	[52.8–134.8]	0.000	34.1	[24.0–45.9]	1.000
Inflow slope [10%–90%] (a.u./s)	6.7	[3.8–9.4]	0.9	[0.6–1.7]	0.000	0.9	[0.6–3.3]	0.003	4.3	[3.0–7.1]	1.000
Inflow time [10%–90%] (s)	12.8	[10.9–21.5]	32.0	[22.3–43.0]	0.004	37.9	[19.6–58.4]	0.023	18.7	[13.9–22.4]	1.000
Max slope (a.u./s)	15.0	[9.5–21.3]	4.6	[2.5–5.3]	0.003	5.2	[3.6–7.6]	0.125	11.1	[6.8–17.2]	1.000
Outflow slope [max- 80%] (a.u./s)	−0.6	[−1.3–−0.3]	−0.1	[−0.1–0.0]*	0.042	−0.2	[−0.2–−0.1]#	0.300	−0.5	[−1.5–−0.4]	1.000
Outflow time [peak −80%] (s)	36.5	[18.1–75.5]	81.1	[71.3–15.1]*	0.300	103.2	[85.3–111.2]#	0.165	38.7	[16.0–49.6]	1.000

Values are presented as median and interquartile range. One preoperative measurement is missing due to a fluorescence camera malfunction. Pre-transfer, one case was excluded from the analysis due to an invalid measurement as a result of hemodynamic instability. Post-transfer, two measurements are missing due to complications during the procedure. *Indicates that in 13 out of 14 measurements, the parameters could be calculated as the intensity did not reach 80%. #Indicates that in 7 out 13 measurements the parameters could be calculated as the intensity did not reach 80%. *p*=*p*-value for difference compared to preoperative measurements.

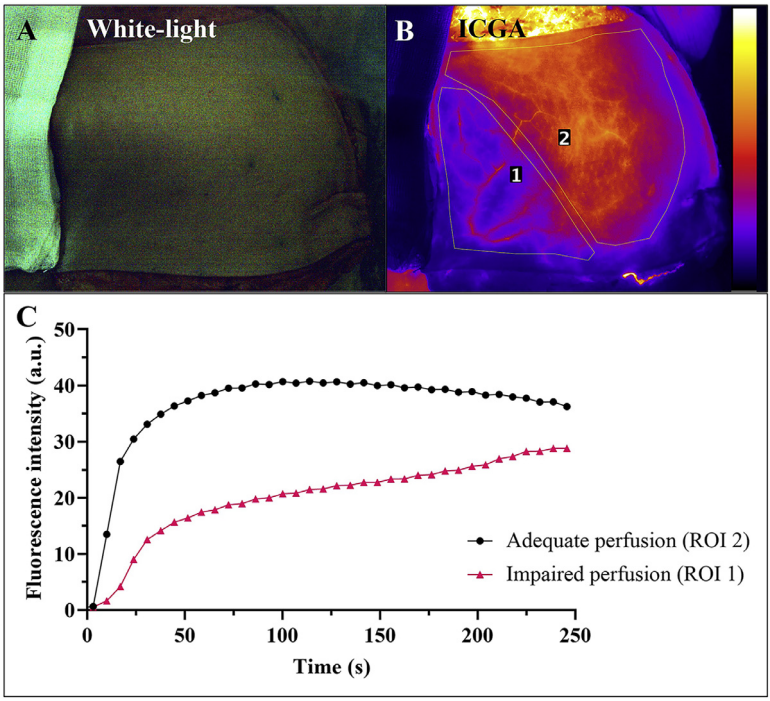

Figure 3. Representative intraoperative ICGA images post-transfer of the DIEP flap with partial epidermolysis. A) White-light image. B) Corresponding fluorescence image with a delineation of the impaired (1) and adequately (2) perfused area as defined by standard clinical care. C) Graph of fluorescence intensities for both ROIs, with a significantly higher fluorescence intensity in the adequately perfused area.

Table 3
Postoperative tissue perfusion values of uncomplicated DIEP flaps.

	OxyHb (a.u.)	DeoxyHb (a.u.)	*n*	Temperature (°C)	*n*
Baseline	8.0 [2.0–2.0]	46.0 [39.0–65.0]	15	32.7 [32.0–33.7]	19
T1	28.0 [15.0–30.5]	48.0 [41.0–64.0]	17	35.1 [34.2–35.8]	19
T2	32.0 [17.5–44.0]	49.0 [38.5–57.0]	17	35.8 [35.3–36.4]	19
T3	18.0 [9.0–32.0]	51.0 [45.5–57.5]	17	35.5 [34.6–35.9]	19
T4	18.0 [10.0–30.0]	50.0 [44.0–58.0]	17	35.9 [35.2–36.2]	18
T5	17.0 [7.5–31.0]	47.0 [33.5–61.0]	17	35.3 [33.6–35.9]	19
T6	27.0 [10.5–52.5]	44.0 [31.3–52.3]	12	35.8 [35.0–36.7]	15
T7	17.0 [7.5–41.25]	48.5 [37.8–60.5]	12	35.3 [33.8–35.5]	15
FU	20.0 [8.0–36.5]	53.0 [53.0–40.8]	18	33.3 [32.3–34.6]	17

Values are presented as median and 25th and 75th quartile. OxyHb: oxyhemoglobin. DeoxyHb: deoxyhemoglobin. O2sat: oxygen saturation. T1-7: Measurement every 12 h post-surgery. FU: follow-up measurement 1–2 weeks post-surgery.

Fluorescence intensities did not decrease to 80% of Fmax and consequently, ICG outflow parameters such as the time from Fmax to 80% or slope were not calculated for all intraoperative measurements (n=13 pre-transfer; n=7 post-transfer).

HSI and TI

HSI and TI parameters of the 16 uncomplicated DIEP flaps are presented in Table 3. Overall, oxyHb showed a greater variation over time compared to deoxyHb levels (median of 17.0–32.0 a.u. vs. 44.0–53.0 a.u.). In uncomplicated DIEP flaps, oxyHb levels were increased from the first postoperative day

compared to baseline (Figure 4A), whereas deoxyHb levels changed negligibly (Figure 4B). TI showed slightly higher skin temperatures from the first postoperative day compared to baseline (Figure S3F). At follow-up, TI values were lower than those during admission (33.3°C vs. 35.1°C–35.9°C).

In the DIEP flap with a venous thrombosis causing venous congestion, a slight increase in oxyHb was observed, whereas deoxyHb more than doubled (Figure 4A, B). No changes in skin temperature were observed (Figure 4C). In the DIEP flap with a partial epidermolysis (representative HSI image in Figure 5), oxyHb and deoxyHb levels evidently increased, whereas the skin temperature decreased compared to the uncomplicated flaps (Figure 4A-C).

Follow-up

No additional complications were recorded during the one-year follow-up. As mentioned earlier, the DIEP flap with epidermolysis and venous thrombosis required surgical reintervention.

Discussion

This feasibility study showed that post-hoc analysis of quantitative ICGA perfusion parameters, in particular inflow time and slope, enable an objective and reproducible interpretation of ICGA data that correlated to clinical outcomes in DIEP-flap reconstructive surgery. The relevance of ICGA was supported by the intraoperative detection of arterial and venous DIEP-flap perfusion impairment and by the potential to intraoperatively highlight areas that may be at risk for impaired perfusion post-operatively. Moreover, HSI and TI are feasible and safe techniques. HSI showed the potential to distinguish between areas of adequate and impaired perfusion within the DIEP flap based on deoxyHb levels. Both ICGA and HSI could provide information about the microcirculation in the flap, whereas TI could not. These monitoring modalities appear to have a potential clinical benefit in addition to clinical assessment to prevent (partial) flap failure.

Currently, ICGA results are interpreted by visual appearance, which is subjective and lacks reproducibility. This is the first study to provide ICGA perfusion parameters at different phases during DIEP-flap reconstruction, including cases of venous and arterial perfusion impairment. Although previously a potential reduction in DIEP-flap fat necrosis has been demonstrated,[11,22] there is a wide variation in methodology and proposed qualitative and quantitative ICGA parameters.[13] In parallel to the results of van den Hoven et al, we demonstrated that ICG inflow parameters provide a reliable assessment of flap perfusion.[23] ICG outflow-related parameters appeared to be less relevant, as fluorescence values only slowly decreased. This suggests that resection of all collateral veins apart from the anastomosed concomitant vein of the DIEP flap substantially impacts venous drainage and therefore ICG outflow. Although ICG outflow was previously suggested as a suitable parameter,[24] a recording-time of 5 min appeared to be insufficient, which hampers clinical implementation.

Subtle changes in flap perfusion are challenging to detect by clinical evaluation alone, which still results in fat necrosis or (partial) flap loss.[3,9-11,25] HSI showed increased deoxyHb levels immediately postoperatively for both flaps with venous congestion. This makes the technique worthwhile, considering flaps monitoring is most valuable during the first 48 h.[26] The higher sensitivity of HSI compared to clinical examination alone for the detection of venous congestion within the first 24 h was demonstrated by Shen et al, although sensitivity and specificity were comparable afterward.[27] In general, oxyHb levels varied more, both in our and previous studies.[21,28] Interestingly, both venously congested flaps also demonstrated increased oxyHb levels. When hypothesizing, this might be explained by an initial compensatory venous dilatation to supply more oxygenated blood to prevent tissue hypoxia. Although no arterial occlusion was observed postoperatively, previous studies suggest HSI has the potential to identify arterial insufficiency.[15,29]

Based on the current data, the added value for TI appeared to be limited for postoperative flap monitoring. Although literature in vascular surgery suggests that TI can be used for complication detection,[30] limited data are available for reconstructive surgery. Hummelink et al. reported a 5.5°C decrease in temperature for failed rectus abdominis flaps in pigs[31] and De Weerd et al. demonstrated that intraoperative dynamic infrared thermography could detect complications in patients undergoing a DIEP-flap reconstruction.[32] This suggests that TI has the potential to be further explored.

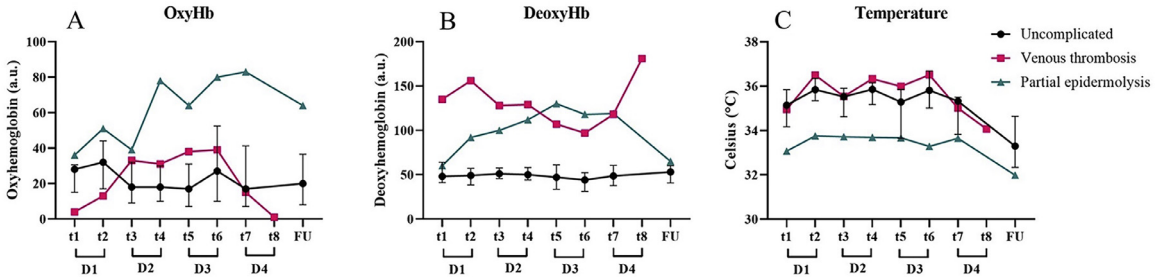

Figure 4. HSI and TI measurements. Postoperative oxyhemoglobin (A, oxyHb) and deoxyhemoglobin (B, deoxyHb) of HSI and skin temperatures of TI for the uncomplicated DIEP flaps (n=19) plotted against two complicated postoperative cases (venous thrombosis and partial epidermolysis). t1 and t2 are on the first day (D1), t3 and t4 are on the second day (D2), and so on. Follow-up (FU) was 1 to 2 weeks postoperatively.

Figure 5. Representative images of HSI and TI of the DIEP flap with partial epidermolysis. A) white-light image; B) hyperspectral image of deoxyhemoglobin levels; and C) thermal image on the third day postoperative (t6).

In the present study, we minimized circumferential influences on our imaging results using standardized imaging protocol.[33] The set of parameters suggested for ICGA data analysis should be usable irrespective of the fluorescence imaging system, which enables an objective and reproducible evaluation of ICGA data. These requirements are in line with a recently published standardized methodology for clinical ICGA implementation[24] and a recent study on ICGA in DIEP-flap reconstruction.[23]

This study contributes to finding a non-invasive, safe, and efficient diagnostic technique for perioperative monitoring of tissue perfusion. Preventing flap failure by detecting early complications is essential to increase treatment success.

A limitation to our study is the relatively small sample size and consequently, the small number of complications. To determine ICGA and HSI cut-off values, a larger study population is required to show that our findings on the complicated DIEP flaps remain clinically significant. In general, the use of our techniques may be limited when relatively small skin paddles are available for postoperative flap monitoring. Moreover, ICGA and HSI perfusion parameters are yet to be available in real-time. This would require adaptation of the current imaging software or application of an algorithm, as we believe real-time quantitative data are prerequisites for clinical implementation. Finally, the optimal dose of ICG remains to be further explored, as different doses were used previously. For this reason, we used the recommended dose based on the Novadaq operating manual.

In conclusion, we demonstrated that quantitative, post-hoc analysis of ICGA data produces objective and reproducible parameters that enable the intraoperative detection of arterial and venous congested DIEP flaps. HSI appeared to be a safe and promising technique for postoperative flap perfusion assessment. A diagnostic accuracy study is needed to investigate ICGA and HSI parameters in real-time and to demonstrate a clinical benefit for DIEP-flap reconstructive surgery in a larger cohort. Ultimately, this might lead to a faster and more accurate diagnosis of inadequate flap perfusion, thereby decreasing complications after free flap reconstructive surgery.

Disclosure statement

Paul M.N. Werker is DMC member for Fidia ltd, Milan, Italy and renumerations are used for research purposes, however this was not related to the content of this article. The other authors have no financial interest to declare in relation to the content of this article.

No funding was received for this study.

Acknowledgments

We would like to acknowledge the reconstructive plastic surgeons at the University Medical Center Groningen who facilitated the intraoperative imaging and the patients who participated in this study.

Ethical statement

The study protocol was approved by the institutional review board of the University Medical Center (NL71808.042.19, METc/201900520) Groningen, performed according to the principles of the Declaration of Helsinki and the Medical Research Involving Human Subjects Act. The trial was registered in the Netherlands Trial Registry (NL8380).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.jpra.2024.04.007.

References

1. Patel NG, Ramakrishnan V. Microsurgical tissue transfer in breast reconstruction. *Clin Plast Surg*. 2020;47(4):595–609.
2. Healy C, Allen Sr RJ. The evolution of perforator flap breast reconstruction: Twenty years after the first DIEP flap. *J Reconstr Microsurg*. 2014;30(2):121–125.

3. Casey 3rd WJ, Rebecca AM, Silverman A, et al. Etiology of breast masses after autologous breast reconstruction. *Ann Surg Oncol*. 2013;20(2):607–614.
4. Lee J, Park HY, Kim WW, et al. Natural course of fat necrosis after breast reconstruction: A 10-year follow-up study. *BMC Cancer*. 2021;21(1):166.
5. Siemionow M, Arslan E. Ischemia/reperfusion injury: A review in relation to free tissue transfers. *Microsurgery*. 2004;24(6):468–475.
6. Kamali A, Docherty Skogh AC, Edsander Nord Å, et al. Increased salvage rates with early reexploration: A retrospective analysis of 547 free flap cases. *J Plast Reconstr Aesthet Surg*. 2021;74(10):2479–2485.
7. Kohlert S, Quimby AE, Saman M, Ducic Y. Postoperative free-flap monitoring techniques. *Semin Plast Surg*. 2019;33(1):13–16.
8. Chao AH, Lamp S. Current approaches to free flap monitoring. *Plast Surg Nurs*. 2014;34(2):52–56 quiz 7-8.
9. Malagón-López P, Vilà J, Carrasco-López C, et al. Intraoperative indocyanine green angiography for fat necrosis reduction in the deep inferior epigastric perforator (DIEP) flap. *Aesthet Surg J*. 2019;39(4):Np45–Np54.
10. Casey 3rd WJ, Connolly KA, Nanda A, Rebecca AM, Perdikis G, Smith AA. Indocyanine green laser angiography improves deep inferior epigastric perforator flap outcomes following abdominal suction lipectomy. *Plast Reconstr Surg*. 2015;135(3):491e–497e.
11. Varela R, Casado-Sanchez C, Zarbakhsh S, Diez J, Hernandez-Godoy J, Landin L. Outcomes of DIEP flap and fluorescent angiography: A randomized controlled clinical trial. *Plast Reconstr Surg*. 2020;145(1):1–10.
12. Johnson AC, Colakoglu S, Chong TW, Mathes DW. Indocyanine green angiography in breast reconstruction: Utility, limitations, and search for standardization. *Plast Reconstr Surg Glob Open*. 2020;8(3):e2694.
13. Goncalves LN, van den Hoven P, van Schaik J, et al. Perfusion parameters in near-infrared fluorescence imaging with indocyanine green: A systematic review of the literature. *Life (Basel)*. 2021;11(5).
14. Thiessen FEF, Tondu T, Cloostermans B, et al. Dynamic InfraRed Thermography (DIRT) in DIEP-flap breast reconstruction: A review of the literature. *Eur J Obstet Gynecol Reprod Biol*. 2019;242:47–55.
15. Kohler LH, Köhler H, Kohler S, et al. Hyperspectral Imaging (HSI) as a new diagnostic tool in free flap monitoring for soft tissue reconstruction: A proof of concept study. *BMC Surg*. 2021;21(1):222.
16. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol*. 1988;124(6):869–871.
17. Ott P. Hepatic elimination of indocyanine green with special reference to distribution kinetics and the influence of plasma protein binding. *Pharmacol Toxicol*. 1998;83(Suppl 2):1–48.
18. Li K, Zhang Z, Nicoli F, et al. Application of indocyanine green in flap surgery: A systematic review. *J Reconstr Microsurg*. 2018;34(2):77–86.
19. Liu DZ, Mathes DW, Zenn MR, Neligan PC. The application of indocyanine green fluorescence angiography in plastic surgery. *J Reconstr Microsurg*. 2011;27(6):355–364.
20. SPY Elite Operators Manual. Revisie: A, 2017; Editie: Nederlands(VERDYE™, ICG 5mg/ml, Diagnostic Green GmbH, Munich, Germany.).
21. Kleiss SF, Ma KF, Schuurmann RC, et al. Hyperspectral imaging for noninvasive tissue perfusion measurements of the lower leg: Review of literature and introduction of a standardized measurement protocol with a portable system. *J Cardiovasc Surg (Torino)*. 2019;60(6):652–661.
22. Hembd AS, Yan J, Zhu H, Haddock NT, Teotia SS. Intraoperative assessment of DIEP flap breast reconstruction using indocyanine green angiography: Reduction of fat necrosis, resection volumes, and postoperative surveillance. *Plast Reconstr Surg*. 2020;146(1):1e–10e.
23. Van Den Hoven P, Verduijn PS, Van Capelle L, et al. Quantification of near-infrared fluorescence imaging with indocyanine green in free flap breast reconstruction. *J Plast Reconstr Aesthet Surg*. 2022;75(6):1820–1825.
24. Noltes ME, Metman MJH, Heeman W, et al. A novel and generic workflow of indocyanine green perfusion assessment integrating standardization and quantification toward clinical implementation. *Ann Surg*. 2021;274(6):e659–e663.
25. Kleban SR, Ogley SC, MacDavid JC, et al. Nursing monitoring of microsurgical free flaps: Identifying and addressing knowledge gaps. *J Reconstr Microsurg*. 2020;36(9):673–679.
26. Shen AY, Lonie S, Lim K, Farthing H, Hunter-Smith DJ, Rozen WM. Free flap monitoring, salvage, and failure timing: A systematic review. *J Reconstr Microsurg*. 2021;37(3):300–308.
27. Schulz T, Nuwayhid R, Houschyar KS, Langer S, Kohler L. Diagnostical accuracy of hyperspectral imaging after free flap surgery. *J Plast Surg Hand Surg*. 2023;58:48–55.
28. Kleiss SF, Ma KF, El Moumni M, et al. Reliability assessment of hyperspectral imaging with the HyperView™ system for lower extremity superficial tissue oxygenation in young healthy volunteers. *J Clin Monit Comput*. 2022;36(3):713–723.
29. Becker P, Blatt S, Pabst A, et al. Comparison of hyperspectral imaging and microvascular Doppler for perfusion monitoring of free flaps in an in vivo rodent model. *J Clin Med*. 2022;11(14).
30. Al Shakarchi J, Inston N, Dabare D, et al. Pilot study on the use of infrared thermal imaging to predict infrainguinal bypass outcome in the immediate post-operative period. *Vascular*. 2019;27(6):663–667.
31. Hummelink S, Kruit AS, van Vlaenderen ARW, Schreinemachers MJM, Steenbergen W, Ulrich DJO. Post-operative monitoring of free flaps using a low-cost thermal camera: A pilot study. *Eur J Plast Surg*. 2020;43(5):589–596.
32. de Weerd L, Mercer JB, Setså LB. Intraoperative dynamic infrared thermography and free-flap surgery. *Ann Plast Surg*. 2006;57(3):279–284.
33. Pruimboom T, van Kuijk SMJ, Qiu SS, et al. Optimizing indocyanine green fluorescence angiography in reconstructive flap surgery: A systematic review and ex vivo experiments. *Surg Innov*. 2020;27(1):103–119.