Review Article

Indocyanine green angiography in breast reconstruction: a narrative review

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Abstract: Sufficient tissue perfusion is important in achieving a successful breast reconstruction to provide the patient with an acceptable result in terms of shape, size, symmetry and possible sensation. Indocyanine green angiography (ICG-A) is a well-known imaging modality which can be applied to visualize the per-operative tissue perfusion assisting the surgeon in intraoperative decision making, flap design and trimming. The consequence of using per-operative ICG-A is reported to correlate with a decreased rate of complications and loss of reconstruction; thus, this technique may be a valuable intraoperative assessment tool for the breast reconstructive surgeon. This paper aims to provide a review of the recent knowledge on the use of ICG-A in breast reconstructive procedures. In addition, an evaluation of the favorable application in implant-based reconstruction, oncoplastic techniques and autologous breast reconstruction. The technique is presented with clinical examples illustrated by per-operative videos, photos and assessment of perfusion to provide the reader with a broader perspective on the application and use of ICG-A. There is a need for further standardization of the per-operative application and perfusion assessment using ICG-A in the field of breast reconstruction, also exploring the use of ICG-A in assessment of postoperative monitoring, microvascular anastomoses and venous insufficiency.

Keywords: Indocyanine green angiography (ICG-A); breast reconstruction; implant-based; autologous breast reconstruction; imaging technique

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Introduction

An increasing number of women seek a breast reconstruction, due to increased survival rate after breast cancer (1). A breast reconstruction aims to increase the quality of life and obtain a new breast with an acceptable size, shape and symmetry (2-5). Sufficient perfusion is important in achieving a successful implant-based, oncoplastic- or autologous breast reconstruction. Indocyanine green angiography (ICG-A) is an intraoperative imaging modality visualizing blood flow to the tissue of interest (6-8). The real-time assessment of perfusion supports the surgeon in intraoperative decision making, which consequently leads to a decreased risk of postoperative complications and loss of reconstruction (9-16). We present the following article in accordance with the Narrative Review reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-21-25/rc).

ICG-A—background

ICG-A has been used to assess skin perfusion for the last two decades (17-19) and is a widely used and well described imaging technique for evaluating tissue perfusion (6,8,20).

The modality is not only used to asses arterial perfusion, but has also been described for evaluation of microvascular anastomoses (21,22), venous congestion (23,24), augmentation mastopexy (25), breast reduction surgery (26) and investigation of perfusion zones (27-31).

Scoring and cut-off values in terms of sensitivity, specificity, positive predictive- and negative predictive values have been investigated by several authors (10,11,32-37). In mastectomy flaps, ICG-A has been reported with a sensitivity of 90% and specificity of 100% in reducing skin flap necrosis and overall complication rate (10,38-40). Moyer *et al.* suggested a cut-off perfusion score of 33% in preventing mastectomy flap necrosis (33). In autologous breast reconstruction establishment of a specific cut-off value and perfusion assessment have yet to be determined (15,41-45).

The majority of published studies on ICG-A in breast reconstruction are of lower level of evidence and consists of comparative, case and cohort studies. Only one randomized controlled trial (RCT)-study investigating ICG-A is published (15). The study investigated the use of ICG-A in deep inferior epigastric artery perforator (DIEP)-flaps and found a significant decreased incidence of fat necrosis (15).

A systematic review from 2020 on the use of ICG-A in autologous breast reconstruction, concluded that per-operative perfusion assessment by ICG-A was an effective tool in reducing fat necrosis compared with flaps assessed clinically (46). Mastectomy skin flap necrosis and the risk of repeated surgeries were reported significantly decreased in 2 reviews and 1 meta-analysis (36,37,47). A Cochrane review on ICG-A on mastectomy skin flap perfusion in immediate breast reconstructions was inconclusive due to lack of high-quality evidence (48). Johnson *et al.* investigated the overall use of ICG-A in breast reconstructions, and reported a reduced postoperative tissue loss when applying ICG-A, but emphasized the need for standardization (35).

In the following we present a narrative review and a description on how ICG-A may be used in implant-based, oncoplastic- and autologous breast reconstruction demonstrated by clinical examples.

ICG-A—methodology

ICG-A offers an objective, repeatable and real-time imaging of the vascularity and perfusion of tissue (7,49). Indocyanine green (ICG) is a water-soluble molecule excreted via the liver to the bile. The technique is repeatable due to a short half-life of 3–5 minutes. Upon intravenous injection of ICG during surgery a fluorescent near-infrared camera detects the molecule and visualizes perfusion within approximately 20 seconds (6). There is up until now no consensus on the intraoperative dose of ICG which is reported from 2 up to 250 mg (13,50,51).

Several imaging-systems exists among others the Fluobeam Clinical System® (Fluoptics, Grenoble, France, www.fluoptics.com), HyperEye Medical Systems® (Mizuho, Tokyo, Japan, www. mizuhomedical.co.jp) and IC-View® Pulsion Medical Systems. One of the most commonly used systems is the Spy-Elite Fluorescence Imaging System® which is able to quantify perfusion and apply relative values of blood flow in the tissue (33,52). Wearable technology in the form of smart glasses have also been described (53).

Preoperative information

Patients undergoing breast reconstruction should be informed of the rationale and use of per-operative ICG-A. Potential side-effects such as nausea, dizziness, discomfort, rash and sweating occur in up to 0.2–0.34%, and is thoroughly discussed with the patient (32,54-56). Patients allergic to iodine should be excluded due to risk of anaphylaxis (51).

The incidence of anaphylactic shock is rare, and occurs in approximately 1 in 42,000 patients (56). Also, though extravasation is rare, extravasation of ICG may cause reversible discoloration of the skin (*Figure 1*).

ICG-A—intraoperative application

Implant-based breast reconstruction

Immediate reconstruction

Mastectomy, being it nipple-sparing or skin-sparing, is performed in the plane of the subcutaneous fascia to preserve the dermal blood supply. Hemostasis is secured using bipolar diathermia. After removal of the breast tissue, the surgeon evaluates the skin flaps estimating areas in risk of potential hypoperfusion. The breast surgeon should refrain from using vasoconstrictive agents such as Klein's fluid (Ringer lactate, lidocaine and adrenaline) to avoid distortion of the assessment of the ICG-A (*Figure 2*).

A sizer of appropriate size is inserted, and dermis is sutured temporarily. Twenty-five milligrams of ICG are diluted in 10 mL sterile water, an intravenous bolus administration of ICG (Verdye® 5 mg/mL) of 2.5 mg/mL

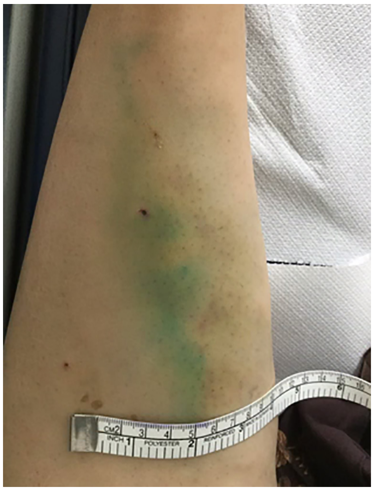
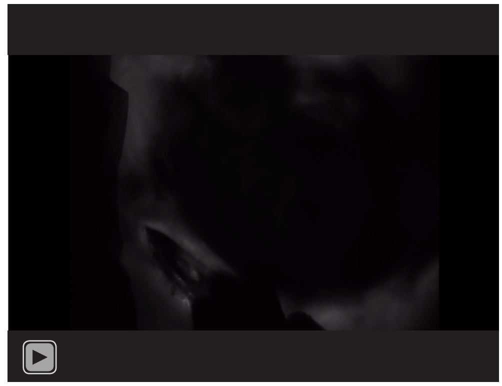


Figure 1 Patient with discoloration of the leg after extravasation of indocyanine green used per-operatively. The color diminished gradually within 3 months leaving no sequelae.



Video 1 The angiography shows general hypoperfusion of the mastectomy skin flaps due to the use of Klein's fluid for hydrodissection resulting in vasoconstriction.

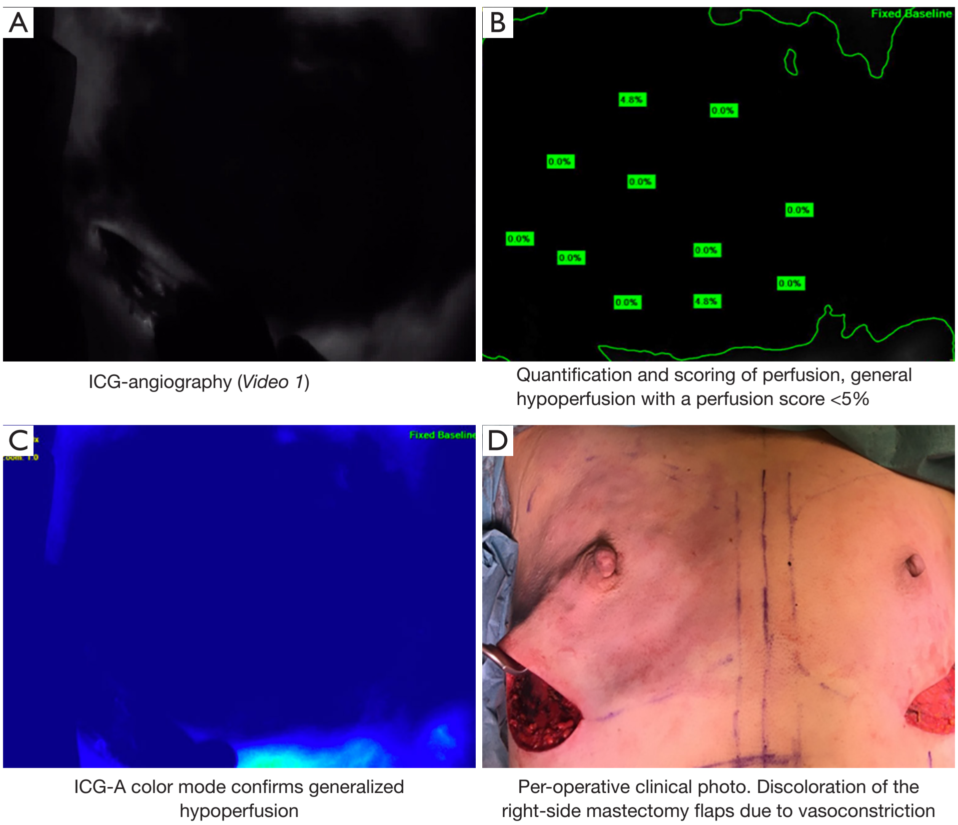


Figure 2 ICG-A performed on mastectomy flaps after a skin-sparing subcutaneous mastectomy using vasoconstrictive agents. (A) The angiography shows general hypoperfusion of the mastectomy skin flaps due to the use of Klein's fluid for hydrodissection resulting in vasoconstriction (*Video 1*). (B) Scoring perfusion by the Spy-Elite Fluorescence Imaging System®, perfusion is <5%. (C) ICG-A color mode showed hypoperfusion indicated by the dark blue color. (D) Per-operative clinical photo of the mastectomy flaps. The patients right side mastectomy flaps are thin and discolored due to the use of vasoconstrictive agents for the hydrodissection during mastectomy. ICG-A, indocyanine green angiography.

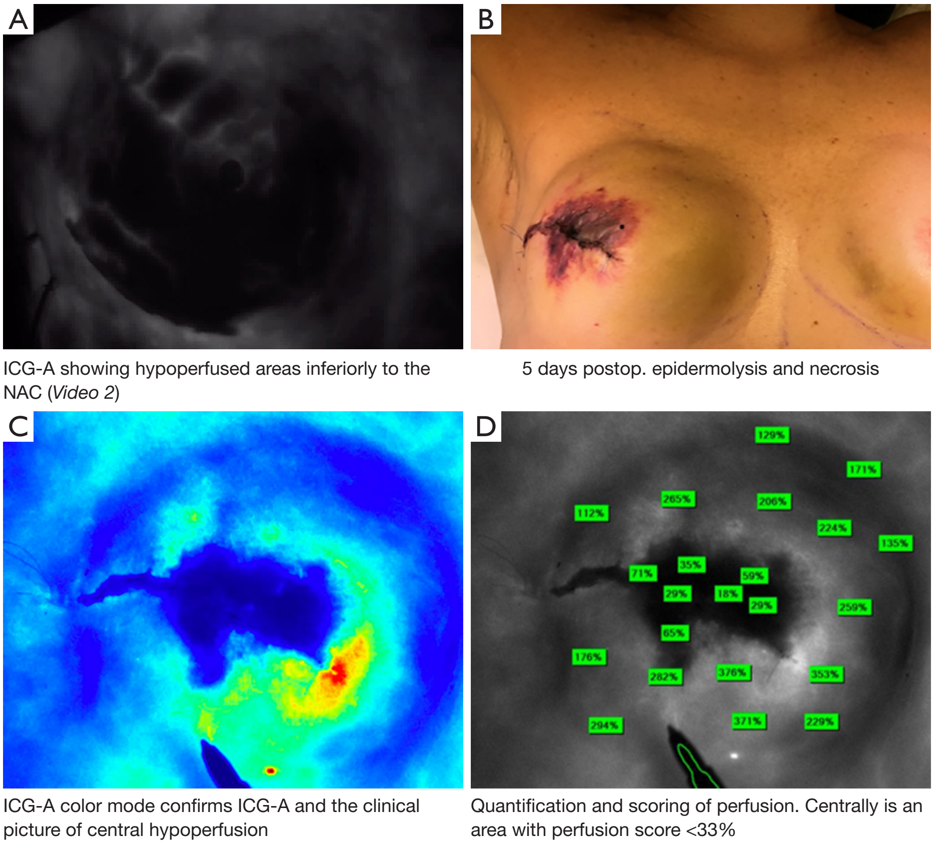
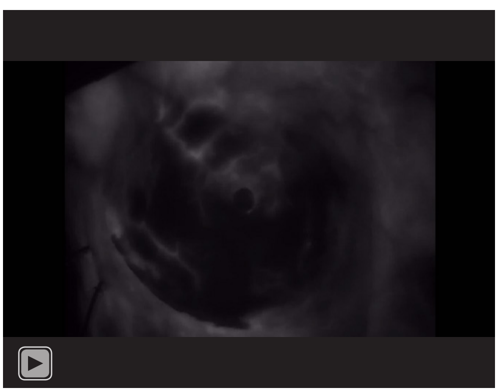


Figure 3 A case where the surgeon chose not to excise the hypoperfused areas indicated by the ICG-A. (A) ICG-A showing hypoperfused areas (<33%) of the mastectomy flap after insertion of sizer before prepectoral breast reconstruction with implant and ADM (*Video 2*). (B) Clinical photo. The patient developed epidermolysis and necrosis 5 days postoperatively corresponding to the ICG-A. The necrotic areas were excised, the implant extracted and the patient underwent 2-stage reconstruction with TE. (C) ICG-A color mode shows central hypoperfusion as seen on the ICG-A. (D) Scoring perfusion by the Spy-Elite Fluorescence Imaging System® 5 days postoperatively, perfusion is centrally <33% corresponding to the clinic. NAC, nipple areola complex; ADM, acellular dermal matrix; ICG-A, indocyanine green angiography.



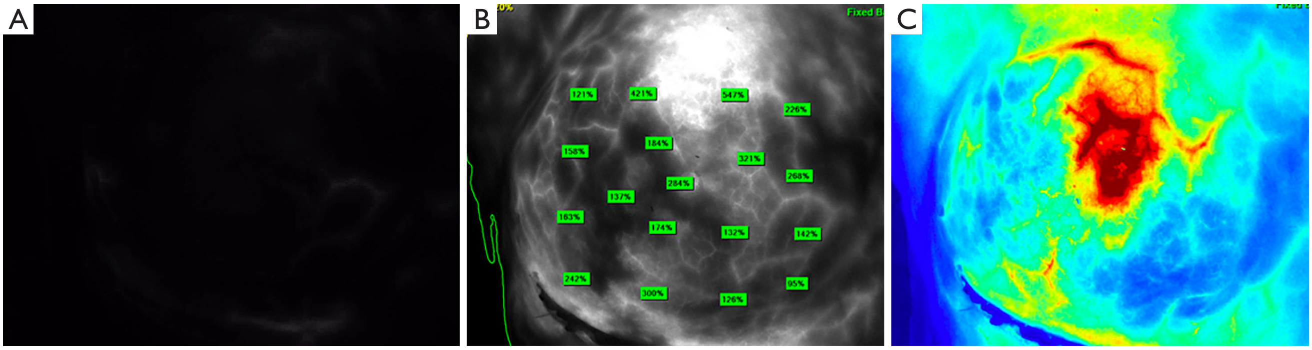
Video 2 Indocyanine green angiography (ICG-A) showing hypoperfused areas (<33%) of the mastectomy flap after insertion of sizer before prepectoral breast reconstruction with implant and acellular dermal matrix (ADM).

is followed by a 10 mL flush with normal saline (2.5 mL of ICG solution for each administration).

The ICG is injected and the perfusion scored by the SPY-Elite® system. A perfusion below 33% may lead to reevaluation of the reconstructive procedure by reducing volume of the sizer to eliminate the skin tension (33).

In cases with perfusion below 33% on the first ICG-A, the technique is repeated and re-evaluated using the same dose of ICG, after 20 minutes (6). Consequently, a perfusion <33% on the 2. angiography will result in excision of the hypoperfused area (if located near incision area), a smaller implant or result in reconstruction with subpectoral placement of a tissue expander (TE) (*Figure 3*).

In cases with sufficient perfusion, the reconstruction proceeds with either a pre-pectoral implant wrapped in

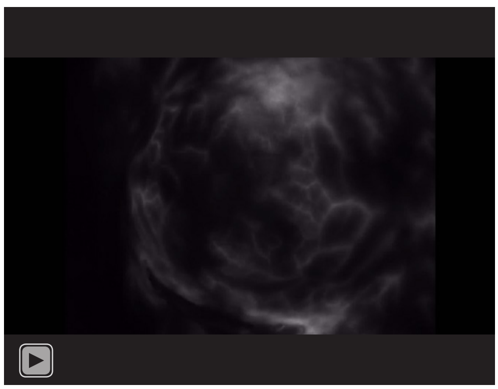


ICG-A shows sufficient perfusion. The surgeon proceeds with prepectoral implant wrapped in ADM (*Video 3*)

Quantification and scoring of perfusion. Perfusion is generally >33%

ICG-A color mode confirms sufficient perfusion

Figure 4 Pre-pectoral breast reconstruction with implant and ADM. (A) ICG-A showing sufficient perfusion after pre-pectoral breast reconstruction with implant and ADM (*Video 3*). (B) Scoring perfusion by the Spy-Elite Fluorescence Imaging System®, perfusion is generally >33% and indicates sufficient perfusion to proceed with the planned reconstruction. (C) ICG-A color mode indicating sufficient perfusion. ADM, acellular dermal matrix; ICG-A, indocyanine green angiography.



Video 3 Indocyanine green angiography (ICG-A) showing sufficient perfusion after pre-pectoral breast reconstruction with implant and acellular dermal matrix (ADM).

acellular dermal matrix (ADM) or a subpectoral implant or TE.

After completing the breast reconstruction, ICG-A is then performed again to confirm and ensure sufficient perfusion (*Figure 4*).

Oncoplastic techniques

Oncoplastic techniques have been used for several decades and can be applied to achieve an acceptable aesthetic result after breast conserving therapy (57-59). Corrective techniques span from Z-plasties and local flaps to larger transposition, advancement and perforator flaps (57). The oncoplastic surgery aims to balance and restore the shape of the breast subsequent to oncologic resection (59). Reshaping and relocation of tissue can compromise perfusion and makes ICG-A a valuable tool in oncoplastic breast surgery (58).

After removing the cancer and intraoperative confirmation of adequate resection, the lateral intercostal artery perforator (LICAP) flap is raised to replace volume and reshape the breast (60). ICG-A can be used per-operatively to assess and score perfusion before after raising the flap, after advancement and before wound closure (*Figure 5*). In oncoplastic displacement (e.g., breast reduction oncoplasty), the ICG-A technique is used as

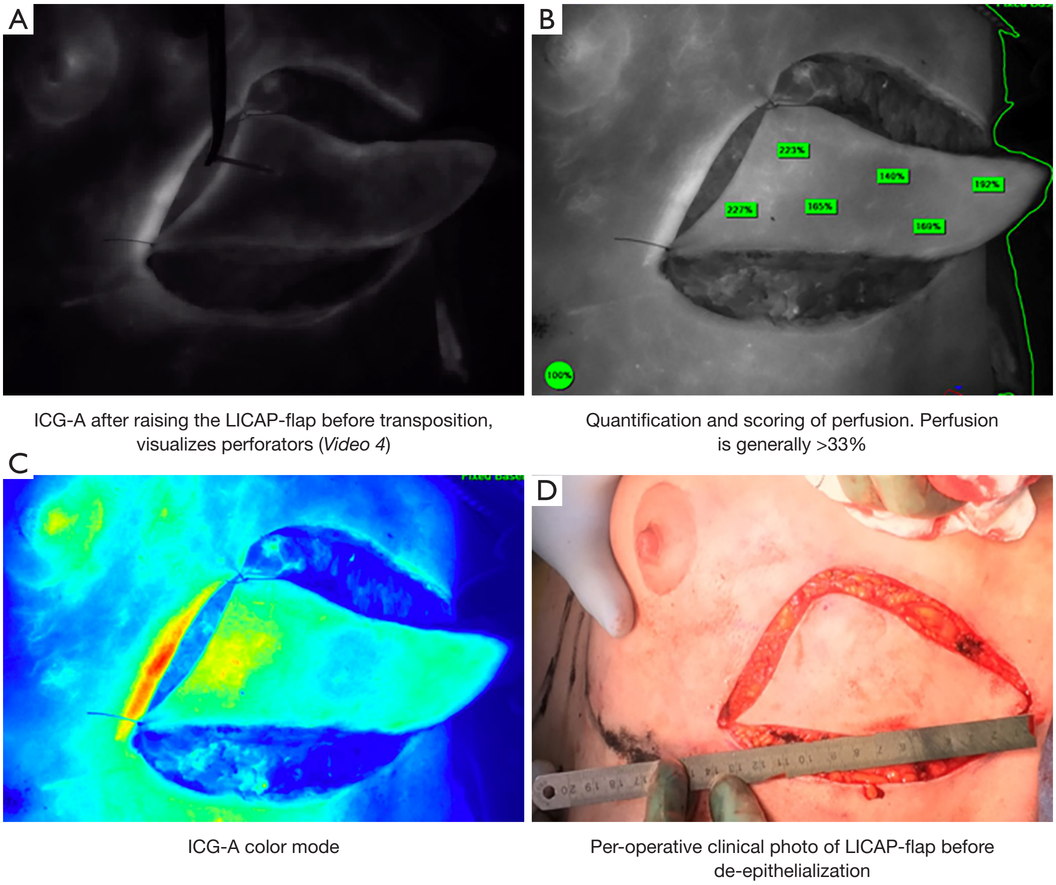
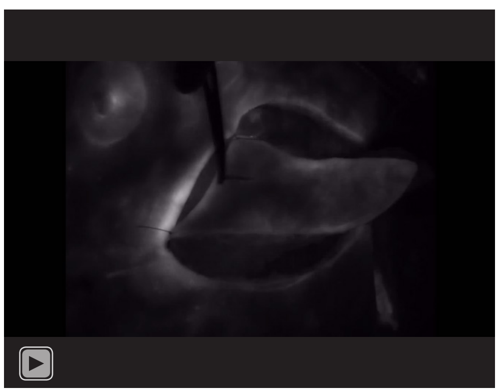


Figure 5 Assessment and scoring of perfusion of LICAP-flap before the flap was deepithelialized and advanced in to the breast. (A) ICG-A after raising the LICAP. Angiography visualizes perforators entering the flap (*Video 4*). (B) Quantification and scoring of perfusion shows sufficient perfusion of the entire flap. (C) ICG-A color mode with sufficient perfusion. (D) Clinical photo of the LICAP-flap before the flap was deepithelialized and advanced in to the breast. ICG-A, indocyanine green angiography; LICAP, lateral intercostal artery perforator.



Video 4 Indocyanine green angiography (ICG-A) after raising the lateral intercostal artery perforator (LICAP). Angiography visualizes perforators entering the flap.

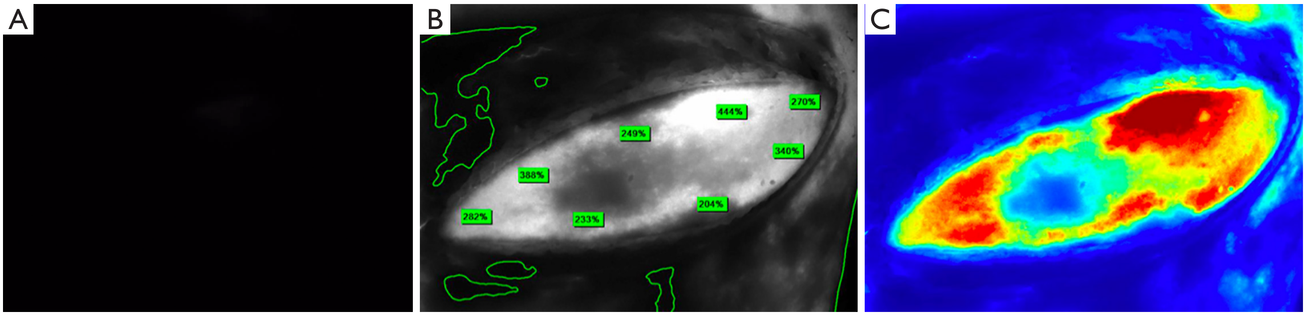
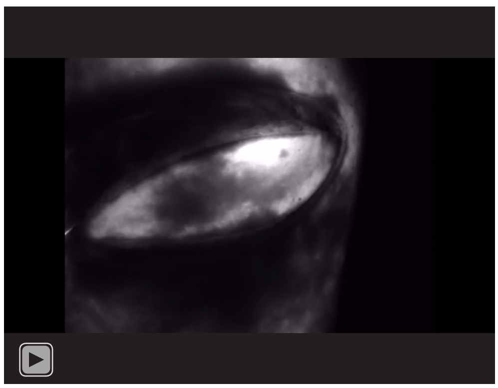


Figure 6 Per-operative ICG-A of a LD-flap after incision around the flap, before flap is elevated on the pedicle. The angiography visualizes the perforators entering the flap. Scoring of perfusion by the Spy-Elite Fluorescence Imaging System®. (A) Intraoperative angiography confirms perforators entering the flap (*Video 5*). (B) Quantification and scoring of perfusion shows sufficient perfusion of the entire flap. (C) ICG-A color mode visualizes perforators and perfusion. ICG-A, indocyanine green angiography; LD, latissimus dorsi.



Video 5 Intraoperative angiography confirms perforators entering the flap.

described for the displacement techniques.

Autologous breast reconstruction

Pedicled flap

Preoperatively a doppler ultrasonography can be used to mark the perforators or artery(ies) if the chosen pedicled flap is a muscle sparing latissimus dorsi (msLD) or a thoracodorsal artery perforator flap (TAP). Perfusion of the flap can then be scored by ICG-A [as described (33)] performed after incision around the flap to the fascia. The angiography indicates the number of perforators within the flap (*Figure 6*).

We recommend repeating ICG-A after the flap is completely raised on its pedicle—before transposition/advancement—which allows assessment of the chosen perforator or artery in order to evaluate possible changes in perfusion—assessing the angiosome if the flap is designed as a perforator flap. The final angiography is performed after the flap is transposed to the recipient site. Areas with hypoperfusion (<33%) should be excised.

The angiographies can aid the surgeon in the intraoperative surgical decision making, and the perfusion measurement may identify areas in risk of postoperative necrosis due to hypoperfusion (*Figure 7*).

Free flap

For breast reconstruction using a free abdominal flap, e.g., deep inferior epigastric artery perforator flap (DIEP), superficial inferior epigastric artery (SIEA) or muscle sparing transverse rectus abdominis (msTRAM) flap, ICG-A can be used to evaluate perfusion of the flap, aiding

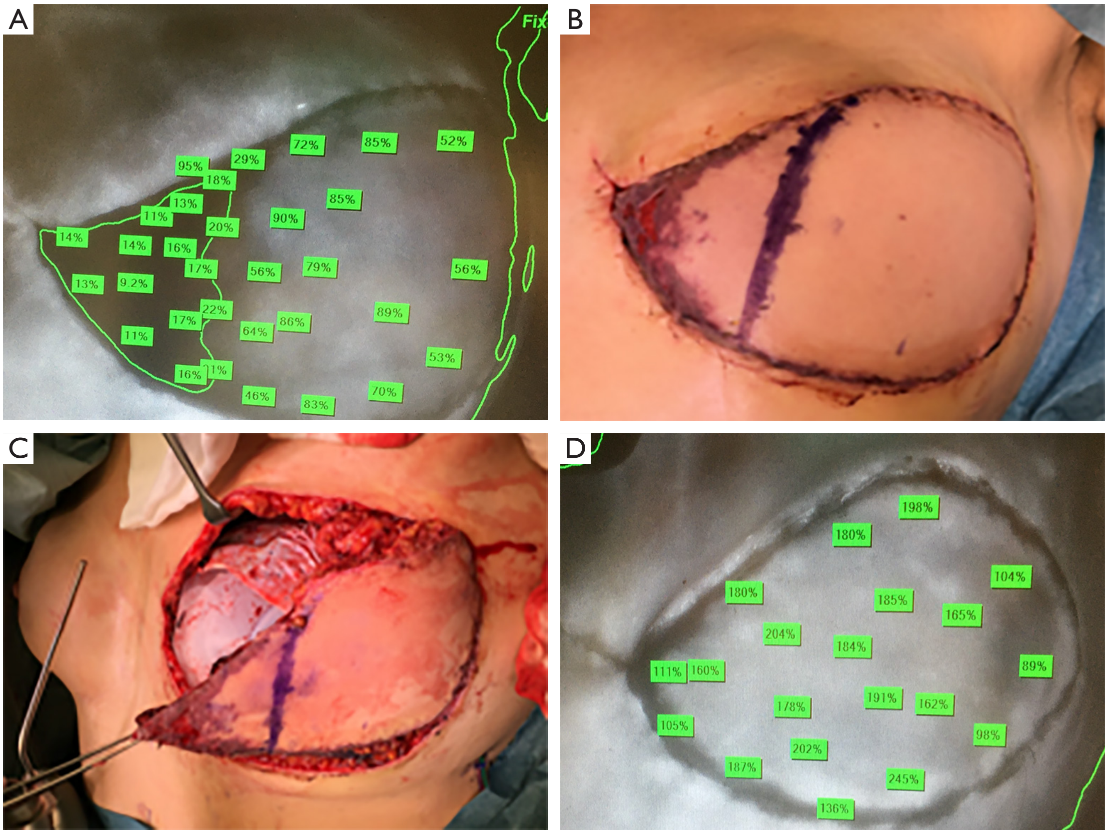


Figure 7 Delayed breast reconstruction using a msLD flap combined with a tissue expander. (A) Intraoperative ICG-A showed hypoperfusion (<33%) of the medial part of the flap, but the area was not excised. (B) Demarcation, epidermolysis and necrosis developed 2 days postoperatively at the medial part of the flap, corresponding to the per-operative ICG-A. (C) Take-back surgery with removal of TE and excision of necrotic tissue. (D) ICG-A confirmed sufficient perfusion and the patient healed uneventfully. Green numbers indicate the relative perfusion score. msLD, muscle sparing latissimus dorsi flap; ICG-A, indocyanine green angiography; TE, tissue expander.

flap design, identification of perforators and assessing perfusion zones, microvascular anastomoses, venous insufficiency etc.

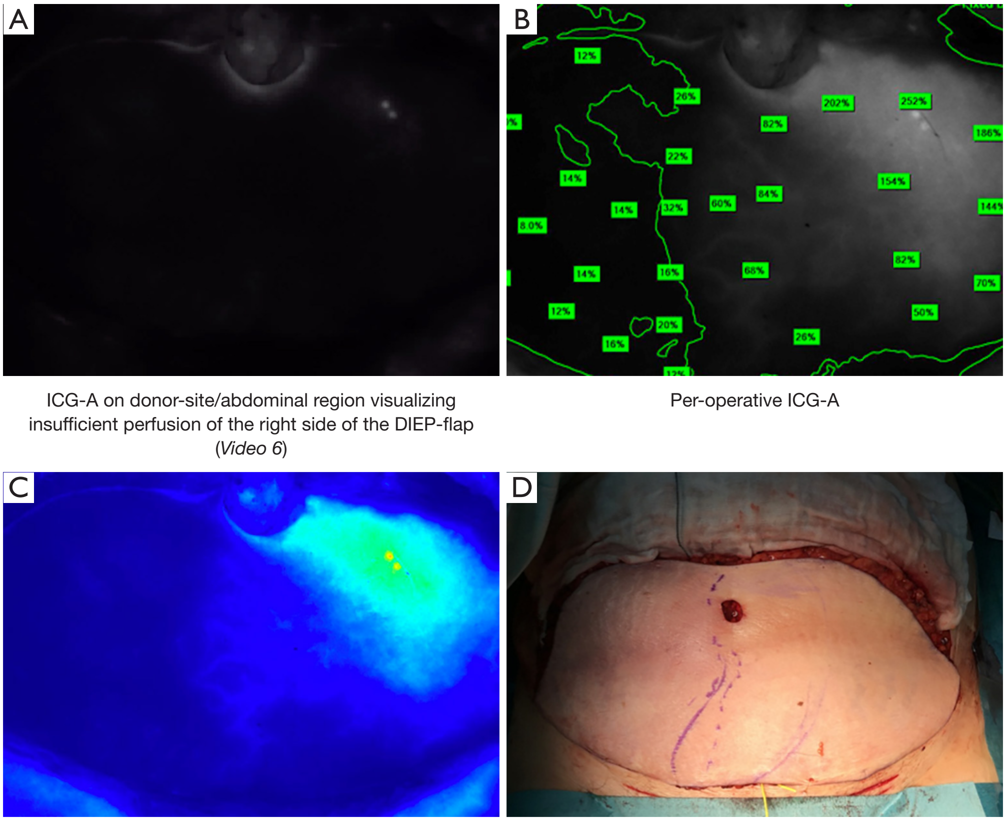
A preoperative computed tomography angiography (CT-A) is done to identify the perforators and the intramuscular course of the vessels in the flap. By performing ICG-A (as described above) upon incision around the flap to the fascial level—before entering the subfascial plane—the complete number of perforators entering the flap can be identified and compared with the preoperative CT-A.

Based on this assessment, the best/most reliable perforators may be dissected, and the angiography repeated, allowing real-time assessment of the perfusion while aiding the intraoperative flap design. If the angiography indicates areas of insufficient perfusion, the surgeon is able to reevaluate and adjust the reconstructive procedure (*Figure 8*).

After the flap is raised with complete pedicle dissection, ICG-A is repeated allowing a final assessment of flap perfusion before transposition to the breast.

Upon completing the microvascular anastomoses, a repeated angiography may display possible hypoperfused areas of the flap, venous insufficiency or insufficient intra-flap perfusion (*Figure 9*).

Using ICG-A intraoperatively informs the surgeon of possible insufficiently perfused areas of the flap and aids in reevaluating the breast reconstruction strategy to prevent



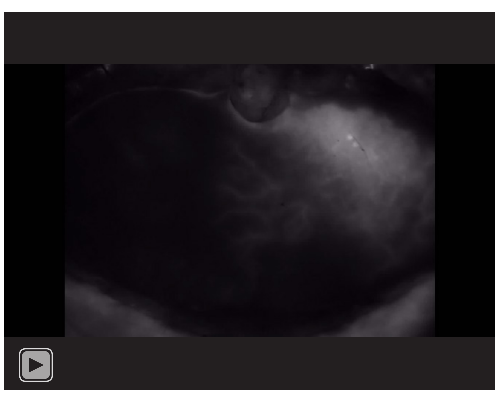
A: ICG-A on donor-site/abdominal region visualizing insufficient perfusion of the right side of the DIEP-flap (*Video 6*)

B: Per-operative ICG-A

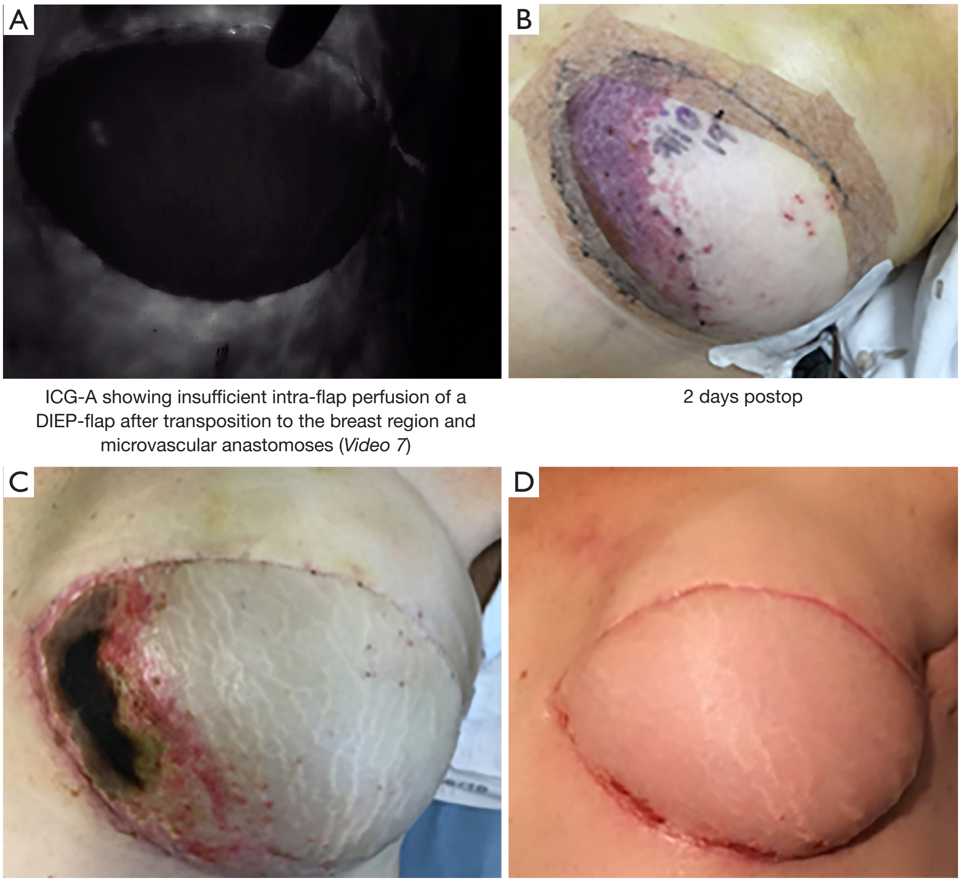
C: ICG-A color mode depicts insufficient perfusion of the right side of the DIEP-flap

D: Per-operative clinical photo. Inked skin marks the area of insufficient perfusion as indicated by the ICG-A

Figure 8 Planned breast reconstruction with bilateral DIEP-flap. ICG-A performed per-operatively at donor-site/abdominal region, after dissection of perforators before entering the abdominal subfascial plane, showed insufficient perfusion of the right half of the flap. The angiography aided the surgeon to reevaluate the reconstructive procedure. (A) Per-operative ICG-A on donor-site/abdominal region visualizing insufficient perfusion of the right side of the DIEP-flap (*Video 6*). (B) Per-operative ICG-A. Scoring of the perfusion shows perfusion <33% on the right side of the flap. (C) ICG-A color mode depicts insufficient perfusion of the right side of the DIEP-flap. (D) Per-operative clinical photo. Area with insufficient perfusion is marked on the skin. ICG-A, indocyanine green angiography; DIEP, deep inferior epigastric artery perforator flap.



Video 6 Per-operative indocyanine green angiography (ICG-A) on donor-site/abdominal region visualizing insufficient perfusion of the right side of the deep inferior epigastric artery perforator (DIEP)-flap.



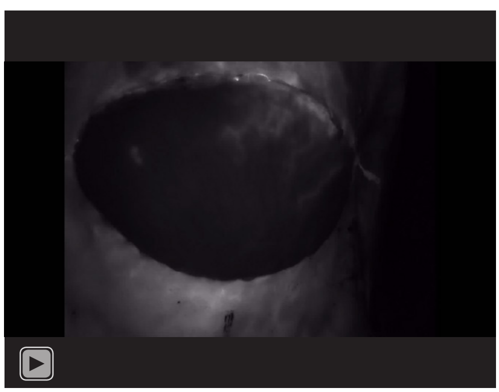
ICG-A showing insufficient intra-flap perfusion of a DIEP-flap after transposition to the breast region and microvascular anastomoses (*Video 7*)

2 days postop

18 days postop

60 days postop

Figure 9 Delayed breast reconstruction with a DIEP-flap (left breast). Pictures of the postoperative complications corresponding to intraoperative ICG-A. (A) ICG-A showing insufficient intra-flap perfusion of a DIEP-flap after transposition to the breast region and microvascular anastomoses. Patient experienced partial flap loss of the medial 20% of the flap corresponding to the intraoperative angiography (*Video 7*). (B) Two days postoperatively, clinical demarcation and epidermolysis of medial segment of the flap. (C) Eighteen days postoperatively, the necrosis of medial segment. (D) After secondary revision and excision of medial segment with necrosis, the patient healed with no further complications. ICG-A, indocyanine green angiography; DIEP, deep inferior epigastric artery perforator flap.



Video 7 Indocyanine green angiography (ICG-A) showing insufficient intra-flap perfusion of a deep inferior epigastric artery perforator (DIEP)-flap after transposition to the breast region and microvascular anastomoses. Patient experienced partial flap loss of the medial 20% of the flap corresponding to the intraoperative angiography.

postoperative complications.

Conclusions

A successful breast reconstruction requires sufficient blood perfusion preventing postoperative complications and loss of reconstruction.

ICG-A provides the surgeon with real-time accurate assessment of the tissue and intraoperative perfusion (7,49). Making information on real-time tissue perfusion available intraoperatively can assist the surgical decision making, providing the opportunity to reevaluate and adapt the reconstruction technique. Repeated intraoperative use of this imaging technique supplies valuable information on perfusion in every step of the reconstruction.

Surgical decision making often relies on clinical experience and judgement. ICG-A can assist the surgeon by providing real-time assessment, scoring and quantification of tissue perfusion.

The role of ICG-A in breast reconstructive procedures is not exhausted.

Determining cut-off values for perfusion, correlating these to postoperative fat necrosis rates or ultimately flap loss remains yet to be investigated. Moreover, further studies, exploring the role of ICG-A in postoperative monitoring, assessment of venous congestion and microvascular anastomoses may further expand the applications of ICG-A in breast reconstructive surgery.

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