

# Intraoperative SPY Reduces Post-mastectomy Skin Flap Complications: A Systematic Review and Meta-Analysis

Edward H. Liu, MD\*

Sarah L. Zhu, BSc†

Jiayi Hu, MD\*

Nathan Wong, MD‡

Forough Farrokhyar, PhD§

Achilles Thoma, MD, MSc\*§

**Background:** Indocyanine-green and laser-assisted fluorescence angiography, known as the SPY system, is a recently developed tool that has shown promise in assessing tissue perfusion. Its intraoperative use is becoming more common particularly in breast surgery. This systematic review aims to determine whether SPY technology can reduce postoperative complications related to tissue ischemia, specifically skin necrosis of the mastectomy native breast skin flaps.

**Methods:** A systematic review of the literature was performed based on the PRISMA guideline. All studies that involved use of the SPY system to assess perfusion of postmastectomy skin flaps from January 1, 1960, to March 1, 2018 were included. Postoperative complications, including mastectomy skin flap necrosis were extracted from the selected studies. The perfusion-related complication rates and unexpected reoperation rates across multiple studies were then reviewed.

**Results:** Five relevant articles were identified including 902 patients undergoing mastectomy and native breast flap reconstructive procedures. Groups that used indocyanine-green angiography had statistically less incidence of native breast skin flap necrosis and unexpected reoperations due to perfusion-related complications compared with groups that monitored flaps with only clinical observation (odds ratio 0.54 for skin necrosis, and 0.36 for reoperation).

**Conclusions:** In this systematic review, the incidence of native breast skin flap necrosis and unexpected reoperations were found to be statistically lower in cases where SPY was used. However, more prospective studies are required to establish SPY angiography as an accurate and cost-effective tool for assessment of tissue perfusion. (*Plast Reconstr Surg Glob Open* 2019;7:e2060; doi: 10.1097/GOX.0000000000002060; Published online 25 April 2019.)

From the \*Department of Surgery, Division of Plastic Surgery, McMaster University, Hamilton, Ontario, Canada; †DeGroot School of Medicine, McMaster University, Hamilton, Ontario, Canada; ‡Department of Surgery, Division of Urology, McMaster University, Hamilton, Ontario, Canada; and §Health Research Methods, Evidence and Impact (HEI), McMaster University, Hamilton, Ontario, Canada.

Received for publication September 11, 2018; accepted October 17, 2018.

This systematic review and meta-analysis conforms to the standard of McMaster's Department of Health Research Methods, and did not require Institutional Review Board Approval as no confidential patient information, outside of the information within included studies, was utilized.

Copyright © 2019 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/GOX.0000000000002060

## BACKGROUND

Breast cancer is currently the second most common type of cancer worldwide and the most common cancer in women.<sup>1</sup> Currently, numerous options exist for breast reconstruction after mastectomy.<sup>2</sup> However, postoperative complication rate after reconstruction range from 5.8% to 63.9%.<sup>2</sup> These early postoperative complications are often associated with inadequate tissue perfusion of the mastectomy skin flap. This results in complications such as skin necrosis, wound healing delays, wound dehiscence, infection, and implant extrusion. These complications not only lead to prolonged hospitalization and delays in oncologic treatment but also increased morbidity for the patient and a financial burden on the healthcare system.

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

Supplemental digital content is available for this article. Clickable URL citations appear in the text.

Currently, the most common intraoperative method of assessing tissue perfusion and viability is based on clinical judgment that includes temperature, color, capillary refill, turgor, and bleeding. Unfortunately, this method of assessment lacks sensitivity and specificity, with up to 41% of cases developing mastectomy skin flap necrosis despite intraoperative clinical evaluation.<sup>3</sup>

A more accurate method of intraoperative assessment of tissue perfusion may facilitate timely excision of hypoperfused tissue, which would potentially decrease ischemia-related complications postoperatively.

Indocyanine-green (ICG) and laser-assisted fluorescence angiography (SPY Elite system, Novadaq Technologies, Kalamazoo, Mich.) is a new technology that has shown promise to provide accurate, real-time assessments of skin perfusion, helping the surgeon make intraoperative decisions regarding removal of nonviable tissue.<sup>3,4</sup> The ICG dye is a safe fluorescent agent that strongly binds to plasma proteins. When excited by an 805-nm laser, it emits fluorescence, which is captured by a video camera. This allows real-time visualization of the vascularity in a tissue. Although the SPY angiography has been shown to be useful in general surgery, lymph node biopsy, and cardiac surgery, it has not yet been widely adopted in breast surgery. Assessing the viability of native breast flaps, postmastectomy is increasingly relevant as there is a trend toward one-stage reconstructions with skin and nipple-sparing mastectomies. There is also a paucity of data on the technology's ability to reduce postoperative complications and improve overall outcomes.

Thus, the purpose of this systematic review and meta-analysis is to assess if the intraoperative use of SPY technology during mastectomies with reconstruction effectively identifies native breast skin flap ischemia to prevent subsequent skin flap necrosis, in comparison to clinical judgment alone. Secondary outcomes assessed are reoperation and overall complication rates.

## METHODS

### Search Strategy

A literature search was conducted with the assistance of a medical librarian in the MEDLINE, EMBASE, and PubMed databases from January 1, 1960, to March 1, 2018 (see appendix, Supplemental Digital Content 1, which displays the search strategy Medline, <http://links.lww.com/PRSGO/A941>).

Additional clinical trial databases including the Cochrane Central Register of Controlled Trials, International Clinical Trials Registry Platform (ICTRP) search portal (World Health Organization), and Clinicaltrials.gov were also searched. Reference lists of relevant articles were also reviewed.

Initial screening of titles and abstracts were independently carried out by 2 authors. Any paper with potential for inclusion, based on our predetermined criteria, were identified for full-text review. These papers were included or excluded based on our eligibility criteria. The senior author resolved any disagreements. The PRISMA guideline was used in the reporting of this systematic review

(see appendix, Supplemental Digital Content 2, which displays the PRISMA guideline checklist, <http://links.lww.com/PRSGO/A942>).

This systematic review was registered with PROSPERO with ID number 94302.

### Eligibility Criteria

The eligibility criteria as per Supplemental Digital Content 3 was created a priori and followed for the determination of study inclusion or exclusion (see table, Supplemental Digital Content 3, which displays the eligibility criteria, <http://links.lww.com/PRSGO/A943>).

### Assessment of Methodological Quality

The methodological quality of included studies were assessed independently by 2 reviewers using the Methodological Index for Non-Randomized Studies (MINORS)<sup>5</sup> criteria, a validated appraisal study tool based on a study's design features. Studies that received a score of at least 60% on MINORS were considered adequate for inclusion in our analysis.

### Data Extraction

A standardized data collection form was designed a priori to extract relevant data from each included article. Data collection was done in duplicates, then combined following discussion regarding any disagreements.

### Outcomes Assessed

Complications were assessed intraoperatively and during routine postoperative follow-up visits. Our primary outcome measure is the incidence of mastectomy skin flap complications stemming from poor perfusion, namely full-thickness skin necrosis. Secondary outcomes of this review includes reoperation, infection, prosthesis exposure, and prosthesis loss. The cumulative complication rates from all studies were pooled to derive the incidence rate of each complication.

### Statistical Analysis

Meta-analysis was performed with the Mantel-Haenszel method to calculate odds ratio (OR), random effect model,  $P < 0.05$  for significance, 0.5 zero-cell correction, and 95% confidence interval for complications as our primary outcome measure. Review Manager (RevMan) Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for our meta-analyses. An a priori decision was made to use the random effects model for meta-analysis to account for between study heterogeneity, as all studies were observational in design. Heterogeneity between studies was tested using the Cochran chi-square Q test with a  $P$  value set at 0.1 and quantified using the  $I^2$  statistic. A funnel plot was used to assess for publication bias.

## RESULTS

### Characteristics of Included Studies

The initial search identified 168 titles. After reviewing abstracts and removing duplicates, each reviewer inde-

pendently identified 7 articles for full-text review, which were included for analysis after applying our eligibility criteria<sup>5-9</sup> (Fig. 1). All included articles were comparative cohort studies published between 2013 and 2018. There were 1 prospective and 6 retrospective cohort studies.

### Study Methodological Appraisal

Each article was scored according to the MINORS questionnaire (Table 1). An average score of 17 out of 24 was achieved for the comparative studies. Data extracted from all studies were of adequate methodologic quality and were combined in a meta-analysis.

### Patient Characteristics

A total of 902 patients undergoing mastectomy and breast reconstruction were included in the analysis. Patient characteristics and follow-up lengths are summarized in Table 1. The predetermined standard follow-up time

was 3 or 6 months. Four studies reported their mean cohort age, which varied from 47 to 53. The remaining article by Diep et.al.<sup>6</sup> reported 60% of the patients in the ICG group as under 50 years of age, and 60% of the patients in the control group as over 50 years old.

All studies collected data on demographic information, comorbidities, and identified risk factors for complications related to wound healing. Note was made regarding the baseline equivalence in comparative studies. No significant differences were found in body mass index, smoking status, history of irradiation, and lymph node dissection. In studies by Diep et.al.<sup>6</sup> and Sood and Glat,<sup>10</sup> mean or median expander fill volume was higher in the ICG group. Diep et.al.<sup>6</sup> reported a significantly younger ICG cohort. Hammer-Hansen et. al.<sup>10</sup> reported few differences in terms of patient population. The control group had significantly higher mastectomy weight ( $P = 0.002$ ), more hormone therapy ( $P = 0.013$ ), and

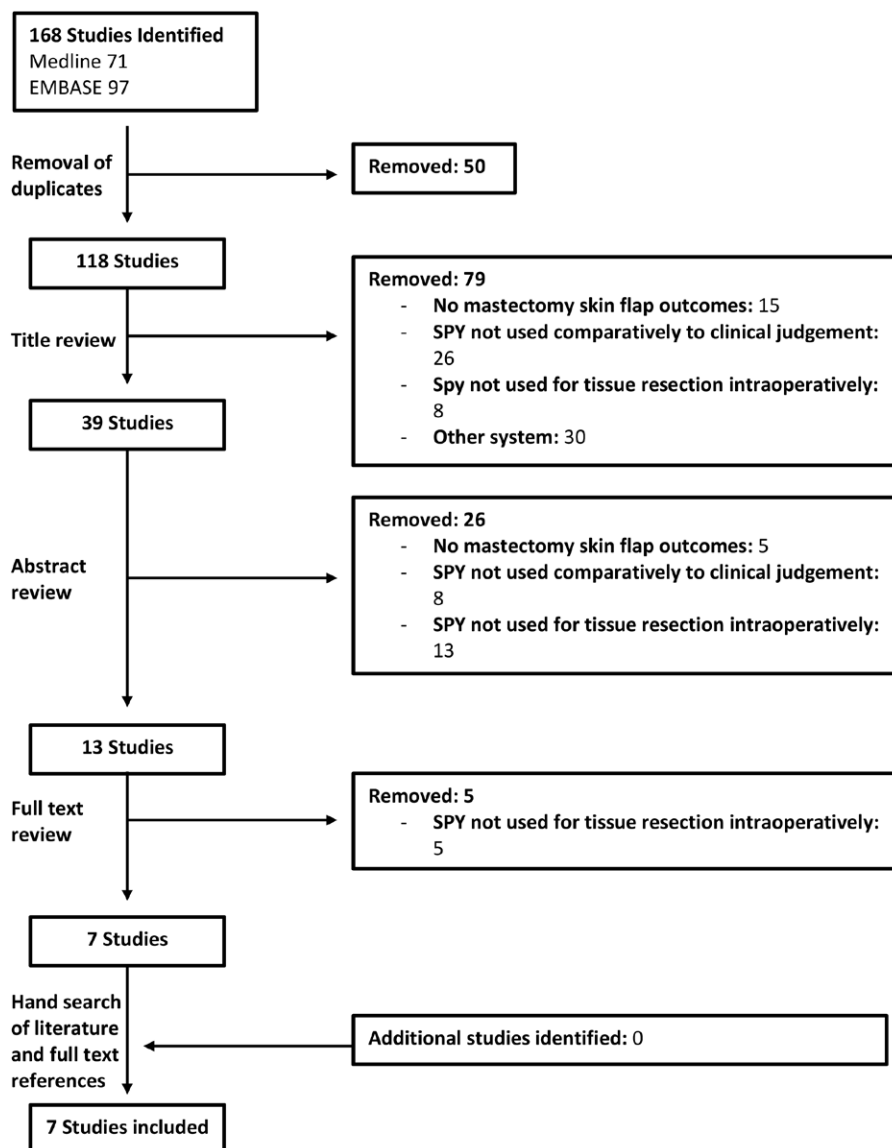


Fig. 1. Flow diagram of study selection.

**Table 1. Overview of Selected Studies**

Study Authors	Year of Publication	Study Design (Comparative or NonComparative)	Study Design (Prospective or Retrospective)	Years of Patient Records Included	No. Patients	No. Breasts	Mean Age (y)	Standard Follow-up Time (mo)	Mean Minors Score
Diep	2016	Comparative	Retrospective	2009–2013	114	NS	(ICG) 60% <50 (Control) 60% >50	3	19.5
Harless	2016	Comparative	Retrospective	2008–2013	269	467	(ICG) 50 (Control) 48	3	16
Rinker	2016	Comparative	Prospective	NS	60	99	(ICG) 47.2 (Control) 50.4	6	18.5
Duggal	2014	Comparative	Retrospective	2009–2011	368	NS	(ICG) 49.9 (Control) 50.0	3	14.5
Sood	2013	Comparative	Retrospective	2009–2011	91	142	(ICG) 51 (Control) 52	NS	13.5
Hammer-Hansen	2017	Comparative	Retrospective	2012–2015	92	128	(ICG) 44.6 (Control) 46.7	3	19.5
Gorai	2017	Comparative	Retrospective	2006–2014	181	184	NS	NS	17.5

NS, not specified.

more chemotherapy ( $P = 0.04$ ) before surgery while the ICG group had a significantly higher number of nipple-sparing procedures ( $P = 0.02$ ).

**Operative Technique**

Operative details regarding the mastectomy and reconstruction were reported in all studies (Table 2). After the completion of the mastectomy, skin flap viability was assessed intraoperatively either with clinical judgment or ICG. There were 424 patients in ICG group and 458 patients in clinical judgment/direct visualization group. In the study by Rinker,<sup>8</sup> a third assessment method was included - fluorescein dye and Wood’s lamp.

Standard procedure was followed in all papers with regard to intraoperative utilization of the ICG/SPY technology. Briefly, ICG was administered by IV push, followed by normal saline flush. The digital camera on the SPY system was then used to capture real-time fluorescent images. When areas of low fluorescence—indicating limited perfusion—were noted on ICG, the skin was marked and sharply excised. Similarly, in the control group, any area deemed to be hypo-perfused from clinical judgment was marked for resection. When tissue expanders were involved<sup>6,9</sup> they were deflated partially or completely to improve skin perfusion before resection was carried out.

**Outcomes Assessed**

A summary of primary and secondary outcomes from the included studies is presented in Table 3. Patients were followed postoperatively over a range of 3–16.9 months. The overall rates of complication, skin necrosis, and reoperation was significantly lower in the group that utilized ICG angiography. ICG cases had an overall complication rate of 26.9%, compared with 30.7% of the clinical assessment group ( $P = 0.03$ ). The overall rate of skin necrosis for the ICG group was 9.8%, whereas clinical assessment group had 15.2% ( $P = 0.001$ ). The rate of reoperation in the ICG was 6.8%, while this rate was 15.2% in the clinical assessment group ( $P \leq 0.01$ ). The indications for reoperations included debridement of skin necrosis and removal of infected prosthesis.

Our meta-analysis also shows that ICG use in assessment of mastectomy skin flap perfusion is associated with a significantly reduced rate of postoperative skin necrosis, reoperation, and overall complications. Comparing the rate of skin necrosis between 2 groups, weighted OR was 0.56 [95% confidence interval (CI), 0.35–0.89;  $P = 0.02$ ;  $I^2 = 40\%$ ] favoring the ICG group (see figure, Supplemental Digital Content 4, which displays (a) OR and forest plot of OR of skin necrosis in ICG and Control groups. (b) OR and forest plot of OR of reoperation in ICG and Control groups. (c) OR and forest plot of OR of overall complications in ICG and Control

**Table 2. Overview of Operative Information**

Study Authors	Type of Mastectomy	Timing of Reconstruction	Type of Reconstruction	Use of SPY Angiography (Patients)	Use of Clinical Assessment (Patients)	Use of Other Monitoring Methods*
Diep	Skin/nipple sparing	Immediate	TE	61	53	
Harless	Skin/nipple sparing	Immediate	TE/I	120 (213 cases)	149 (254 cases)	
Rinker	Skin sparing	Immediate	TE/TRAM	20 (35 cases)	20 (30 cases)	20 (34 cases) - Fluorescein
Duggal	Skin sparing	Immediate and delayed	TE, autologous	184	184	
Sood	Skin/nipple sparing	Immediate	TE/I	39	52	
Hammer-Hansen	Skin sparing	Immediate	I	46	46	
Gorai	Skin sparing	Immediate	TE	81	100	

\*Wood’s lamp, other dye.

TE, tissue expander; TE/I, tissue expander or implant; TRAM, transverse rectus abdominis musculocutaneous flap.

**Table 3. Overview of Outcome Measures**

Study Authors	With ICG Use			Control (without ICG Use)		
	Overall Complication, n (%)	Skin Necrosis, n (%)	Reoperation, n (%)	Overall Complication, n (%)	Skin Necrosis, n (%)	Reoperation, n (%)
Diep	31 (50.8)	17 (27.9)	7 (11.5)	23 (43.4)	10 (18.9)	11 (20.8)
Harless	14 (6.6)	2 (0.9)	2 (0.9)	35 (13.8)	17 (6.7)	12 (4.7)
Rinker	12 (34)	5 (14)	5 (15)	13 (42)	8 (27)	6 (20)
Duggal	79 (42.7)	24 (13)	11 (5.9)	86 (46.7)	43 (23.4)	26 (14.1)
Sood	7 (17.9)	4 (10)	11 (28.2)	19 (36.5)	9 (17)	32 (61.5)
Hammer-Hansen	35 (53)	3 (4.5)	26 (39.3)	42 (67.7)	5 (8.1)	28 (45.2)
Gorai	27 (32.5)	17 (20.5)	6 (7.2)	56 (55.4)	32 (31.7)	14 (18.8)

groups, <http://links.lww.com/PRSGO/A944>). The odds of undergoing a reoperation in the ICG group were shown to be 68% (95% CI, 0.21–0.49;  $P \leq 0.00001$ ;  $I^2 = 19\%$ ) less than in the clinical assessment group (**Supplemental Digital Content 4**). Finally, our meta-analysis showed patients who had intraoperative ICG were less likely to experience postoperative complications by 38% (weighted OR, 0.62; 95% CI, 0.41–0.94;  $P = 0.06$ ;  $I^2 = 54\%$ ) compared with the control group (**Supplemental Digital Content 4**).

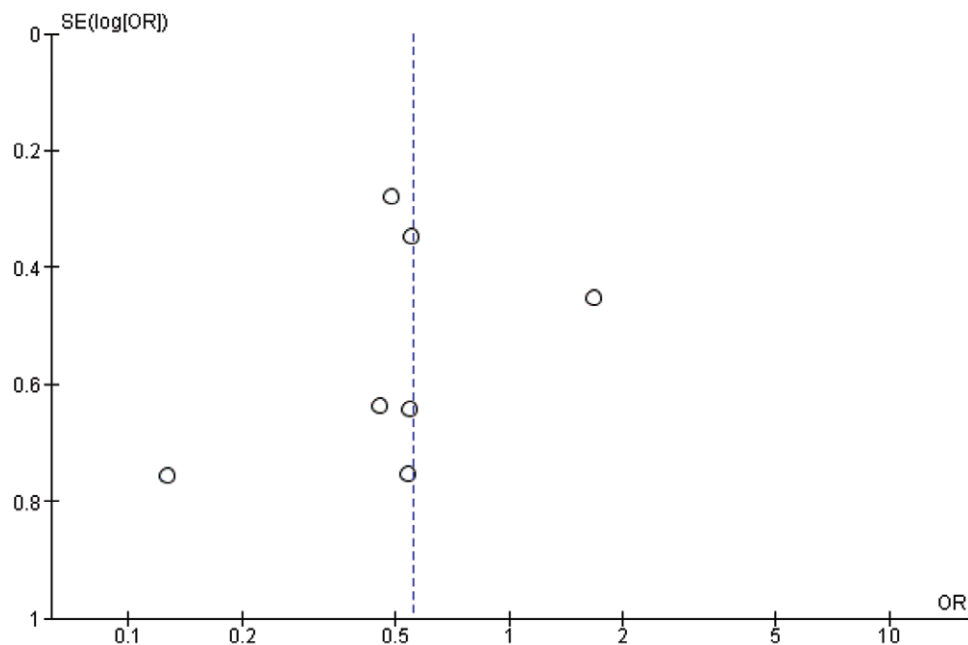
A funnel plot of the included studies revealed a symmetric distribution, suggesting no apparent publication bias. Studies largely revealed no difference (Fig. 2).

#### Conflict of Interest Disclosures

Disclosed conflict of interest by authors included speaker role, consultant, and/or financial support from company (Table 4). Rinker<sup>8</sup> was the only study with no declared associations. There were no consistent differences in conclusions from studies which reported conflicts and Rinker,<sup>8</sup> who did not.

## DISCUSSION

Skin-sparing mastectomy with immediate reconstruction has led to major aesthetic and functional advancement in breast cancer care, without compromising local breast cancer recurrence rates.<sup>10–12</sup> An important complication that undermines these benefits is the high rate of mastectomy skin flap necrosis, which increases morbidity and worsens reconstructive outcomes. As mastectomy skin flap necrosis has been shown to complicate more than 20% of skin-sparing and nipple-sparing mastectomy procedures with the traditional intraoperative clinical assessment of tissue ischemia,<sup>13–19</sup> multiple studies have looked at the effect of using an alternative method of detecting mastectomy skin flap ischemia in decreasing postoperative complications. One such method that has been receiving attention is the SPY system due to its multiple benefits such as a short half-life, quantifiable images and ability to visualize perfusion in the subdermal plexus and superficial tissues. In our article, we aimed to assess the quality of current evidence concerning the use of SPY technology in



**Fig. 2.** Funnel plot for the meta-analysis of the ratio of adverse events following a mastectomy with intraoperative ICG use in comparison to clinical judgment.

**Table 4. Overview of Disclosures**

Study Authors	Speaker Role	Consultant	External Financial Support	None Declared
Diep		Yes		
Harless		Yes	No	
Rinker				Yes
Duggal	Yes		No	
Sood	Yes		Yes (From LifeCell)	
Hammer-Hansen				Yes
Gorai				Yes

Disclosure involves at least 1 author (may not be first author) with LifeCell Corp or Mentor Corp, or Novadaq.

the skin-sparing mastectomies. Based on our assessment of current clinical data, the use of the SPY system is associated with a lower incidence of mastectomy skin flap necrosis, unanticipated reoperations and overall complications.

All included studies support the safety of ICG angiography use in mastectomy procedures. None of the included studies reported adverse outcomes or complications attributed to the use of ICG dye. This is congruent with the current integration of ICG angiography in other operative procedures such as coronary artery bypasses and microvascular free-tissue transfers.<sup>20</sup> It is possible that there may be long-term complications associated with intraoperative use of ICG angiography in mastectomy procedures, as the studies included in this review had relatively short-term follow-up periods that varied from 90 days to 22 months. However, this is unlikely as ICG has been well documented to have an excellent safety profile, with a shown adverse event rate of approximately 1 in 42,000.<sup>21,22</sup>

In addition to its clinical safety, the majority of the included studies agreed that intraoperative ICG angiography use is associated with significantly decreased incidence of postmastectomy skin necrosis. The one inconsistency to this statement is from Diep et al.,<sup>6</sup> where no significant difference was found in overall rates of flap necrosis between ICG angiography use and gross clinical examination. However, Diep et al.<sup>6</sup> did observe that the rates of severe flap necrosis were significantly decreased with the intraoperative use of ICG angiography. This finding is supported by a study from Duggal et al.,<sup>9</sup> as their finding of a statistically significant decrease in overall skin necrosis rate following ICG angiography was attributed exclusively to the reduction in incidence of severe necrosis.

With ICG angiography, a statistically significant reduction in the incidence of reoperation for ischemia-related complications was observed. The only study that reported an insignificant difference in reoperation rates was from the study by Diep et al.<sup>9</sup> However, although a majority of unexpected reoperations (83.3%) in patients receiving clinical assessment were for the purpose of necrotic tissue debridement, only 33.3% of patients receiving ICG angiography returned for the same reason. Instead, patients who had ICG angiography were being brought back to the operating room for tissue expander infections and reasons unrelated to tissue hypoperfusion such as hematoma evacuation.

This finding is complementary to the finding in the studies by Diep et al.<sup>6</sup> and Duggal et al.<sup>9</sup> regarding decreased incidence of necrosis with ICG use, as it is often severe necrosis that requires reoperation, rather than

mild necrosis, which generally can be managed at bedside. These conclusions lead to the postulation that the largest potential benefit from incorporation of ICG angiography may be in decreasing the incidence of severe necrosis and through that, rates of reoperation.

An alternative tool against which ICG angiography has been compared is fluorescein dye with Wood's lamp imaging. A prospective cohort study by Rinker<sup>8</sup> in 2015 reported that use of intravenous fluorescein angiography was associated with the lowest rate of mastectomy flap necrosis, followed by ICG angiography and finally by clinical assessment. However, this was contradicted by a prospective trial by Phillips et al.<sup>3</sup> in 2011, which reported that ICG angiography is a better predictor of mastectomy skin flap necrosis than fluorescein dye angiography and clinical judgment. Although the study by Rinker<sup>8</sup> is more recent, the results from Phillips et al.<sup>3</sup> are highly supported. In the study by Phillips et al.,<sup>3</sup> ICG was found to have higher specificity, positive and negative predictive values than fluorescein dye angiography. In support of Phillips et al.,<sup>3</sup> Duggal et al.<sup>9</sup> also reported that while both had similar sensitivities, ICG angiography was significantly more specific ( $P = 0.002$ ) than fluorescein dye angiography. This difference in specificity is a significant concern. Several studies have included the concern of the prediction of fluorescein dye angiography to overpredict potential areas of necrosis.<sup>23</sup> Over-excision of healthy tissue limits the amount of skin-flap available for reconstruction and increases the complication of reconstruction. The significant difference in specificities between the 2 tools can be attributed to their inherent properties. Fluorescein rapidly leaks from the capillaries into the interstitium, a process that is further exacerbated by local ischemia.<sup>24,25</sup> This accounts for the relatively high false-positive results. In comparison, ICG binds to plasma proteins and as such is distributed evenly through the capillaries without leakages. In addition, due to a half-life of 4 hours, fluorescein dye can likely only be used once during the operation and the angiography will not be able to detect temporary vasospasms that resolves with time.<sup>23-25</sup> In contrast, ICG can be readministered within 9 minutes or less due to its short half-life.<sup>10,11,25,26</sup> This means that ICG can be utilized repeatedly intraoperatively to assess perfusion in real-time. Therefore, the decreased rate of mastectomy flap necrosis observed in the study by Rinker<sup>8</sup> may largely be attributed to the overresection of tissue and not reflective of the predictive value of fluorescein dye. Studies have also shown the increased detail to which perfusion can be visualized with ICG angiography due to ICG absorbing light near

infrared range while fluorescein dye absorbs light in the UV range.<sup>24,25</sup> This means that the images of ICG displays superior image quality and visualizes perfusion in the subdermal plexus and superficial subcutaneous tissues in mastectomy procedures.<sup>24,25</sup> In addition, the SPY technology can quantify the perfusion of images, while images on the wood's lamp are interpreted based on subjective user judgment.<sup>23</sup> Due to these molecular differences, it is biologically plausible that ICG leads to better outcomes than fluorescein dye.

This article does include limitations. First, there is a paucity of randomized controlled studies available with regard to the question of interest. Thus, possibility of selection bias should be considered alongside the inherent limitations within each included study. Limitations of individual studies include being single institution-based and small sample sizes. Second, with 7 relevant articles, we recognize there is a low number of studies included in our review. In addition, the included studies have high heterogeneity in both population and design. To address the heterogeneity, the random effects model was used in the meta-analysis. And although there are low number of studies included, the technology of the SPY system is rapidly changing. Changing with it are its features and the potential for its integration into mastectomy procedures. Since all articles included are within the last 7 years, our review contains contemporary evidence that is applicable to the current and relevant capabilities of the SPY system.

To strengthen our understanding of the potential role of ICG angiography in decreasing complications postmastectomy, there is need for future multiple-center prospective studies with larger sample sizes and longer follow-up times. As evidence supporting potential implementation of the SPY system continues to build, so too does practical concerns. Future investigation into differences in operative time and cost-utility analysis would significantly advance our understanding of its benefits and costs, as well as feasibility of incorporation into the surgical health care of mastectomy patients.

## CONCLUSIONS

In our meta-analysis of current literature, the use of intraoperative SPY/ICG angiography was associated with significantly lower incidence of skin flap necrosis, reoperation rate, and overall complication rate in postmastectomy patients. In comparison to clinical judgment alone, ICG was shown to offer more reliable and objective intraoperative visualization of tissue perfusion, allowing the surgeon to perform more accurate removal of any tissue at risk of necrosis. We hope this review article can lead to further evaluation of the benefit of ICG angiography through prospective, randomized trials, and cost-effectiveness analyses.

Achilles Thoma, MD, FRSC, FACS  
101–206 James Street South  
Hamilton, ON  
L8P 3A9  
E-mail: athoma@mcmaster.ca

## REFERENCES

- DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. *CA Cancer J Clin.* 2014;64(1):52–62.
- Lucas DJ, Sabino J, Shriver CD, Pawlik TM, Singh DP, Vertrees AE. Doing more: trends in breast cancer surgery, 2005 to 2011. *Am Surg.* 2015;81(1):74–80.
- Phillips BT, Lanier ST, Conkling N, et al. Intraoperative perfusion techniques can accurately predict mastectomy skin flap necrosis in breast reconstruction: results of a prospective trial. *Plast Reconstr Surg.* 2012;129(5). doi:10.1097/PRS.0b013e31824a2ae8
- Komorowska-timek E, Gurtner GC. Intraoperative perfusion mapping with laser-assisted indocyanine green imaging can predict and prevent complications in immediate breast reconstruction. *Plast Reconstr Surg.* 2010;125(4):1065–1073.
- Diep GK, Hui JYC, Marmor S, et al. Postmastectomy reconstruction outcomes after intraoperative evaluation with indocyanine green angiography versus clinical assessment. *Ann Surg Oncol.* 2016;23(12):4080–4085.
- Harless CA, Jacobson SR. Tailoring through technology: a retrospective review of a single surgeon's experience with implant-based breast reconstruction before and after implementation of laser-assisted indocyanine green angiography. *Breast J.* 2016;22(3):274–281.
- Rinker B. A comparison of methods to assess mastectomy flap viability in skin-sparing mastectomy and immediate reconstruction: a prospective cohort study. *Plast Reconstr Surg.* 2016;137(2):395–401.
- Duggal CS, Madni T, Losken A. An outcome analysis of intraoperative angiography for postmastectomy breast reconstruction. *Aesthet Surg J.* 2014;34(1):61–65.
- Sood M, Glat P. Potential of the SPY intraoperative perfusion assessment system to reduce ischemic complications in immediate postmastectomy breast reconstruction. *Ann Surg Innov Res.* 2013;7(1):9.
- Hammer-Hansen N, Juhl AA, Damsgaard TE. Laser-assisted indocyanine green angiography in implant-based immediate breast reconstruction: a retrospective study. *J Plast Surg Hand Surg.* August 2017:1–5.
- Carlson GW, Grossl N, Lewis MM, Temple JR, Styblo TM. Preservation of the inframammary fold: what are we leaving behind? *Plast Reconstr Surg.* 1996;98(3):447–450.
- Carlson GW, Styblo TM, Lyles RH, et al. Local recurrence after skin-sparing mastectomy: tumor biology or surgical conservatism? *Ann Surg Oncol.* 2003;10(2):108–112.
- Kroll SS, Khoo A, Singletary SE, et al. Local recurrence risk after skin-sparing and conventional mastectomy: a 6-year follow-up. *Plast Reconstr Surg.* 1999;104(2):421–425.
- Sullivan SR, Fletcher DRD, Isom CD, Isik FF. True incidence of all complications following immediate and delayed breast reconstruction. *Plast Reconstr Surg.* 2008;122(1):19–28.
- Hultman CS, Daiza S. Skin-sparing mastectomy flap complications after breast reconstruction: review of incidence, management, and outcome. *Ann Plast Surg.* 2003;50(3):249–255; discussion 255.
- Newman MI, Samson MC, Tamburrino JF, Swartz KA. Intraoperative laser-assisted indocyanine green angiography for the evaluation of mastectomy flaps in immediate breast reconstruction. *J Reconstr Microsurg.* 2010;26(7):487–492.
- Antony AK, Mehrara BM, McCarthy CM, et al. Salvage of tissue expander in the setting of mastectomy flap necrosis: a 13-year experience using timed excision with continued expansion. *Plast Reconstr Surg.* 2009;124(2):356–363.
- Woerdeman LAE, Hage JJ, Smeulders MJC, Rutgers EJT, van der Horst CMAM. Skin-sparing mastectomy and immediate breast reconstruction by use of implants: an assessment of risk factors for

- complications and cancer control in 120 patients. *Plast Reconstr Surg*. 2006;118(2):321–330; discussion 331–332.
19. Woerdeman LAE, Hage JJ, Hofland MMI, Rutgers EJT. A prospective assessment of surgical risk factors in 400 cases of skin-sparing mastectomy and immediate breast reconstruction with implants to establish selection criteria. *Plast Reconstr Surg*. 2007;119(2):455–463.
  20. Kobraei EM, Nimtz J, Wong L, et al. Risk factors for adverse outcome following skin-sparing mastectomy and immediate prosthetic reconstruction. *Plast Reconstr Surg*. 2012;129(2):234e–241e.
  21. Zenn MR. Fluorescent angiography. *Clin Plast Surg*. 2011;38(2):293–300.
  22. Benya R, Quintana J, Brundage B. Adverse reactions to indocyanine green: a case report and a review of the literature. *Cathet Cardiovasc Diagn*. 1989;17(4):231–233.
  23. Hope-Ross M, Yannuzzi LA, Gragoudas ES, et al. Adverse reactions due to indocyanine green. *Ophthalmology*. 1994;101(3):529–533.
  24. Losken A, Styblo TM, Schaefer TG, Carlson GW. The use of fluorescein dye as a predictor of mastectomy skin flap viability following autologous tissue reconstruction. *Ann Plast Surg*. 2008;61(1):24–29.
  25. Rübber A, Eren S, Krein R, Younossi H, Böhler U, Wienert V. Infrared videoangiography of the skin with indocyanine green–rat random cutaneous flap model and results in man. *Microvasc Res*. 1994;47(2):240–251.
  26. Holm C, Mayr M, Höfner E, Becker A, Pfeiffer UJ, Mühlbauer W. Intraoperative evaluation of skin-flap viability using laser-induced fluorescence of indocyanine green. *Br J Plast Surg*. 2002;55(8):635–644.