Laser-assisted indocyanine green (ICG) fluorescence angiography (SPY Imaging; LifeCell Corp, Branchburg, New Jersey) is a form of intraoperative imaging that provides assessment of tissue perfusion. The ICG dye binds to plasma proteins and emits fluorescence when excited by an 805-nm laser. This fluorescence is recorded by the device camera, allowing for real-time visualization of vascular supply in a tissue or organ. SPY angiography is becoming widely used in a variety of settings, including plastic surgery, cardiac surgery, general surgery, and neurosurgery.1,6

This technology has been applied in breast reconstruction to assess the viability of both mastectomy skin flaps and tissue flaps since 2007. ICG imaging has been found to have up to 90% sensitivity for predicting mastectomy flap necrosis and can be a useful adjunct to clinical judgment for predicting the survival of mastectomy skin.7,9 ICG

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A retrospective review was performed on a database of 184 patients who underwent breast reconstruction in which ICG angiography was used intraoperatively. The senior author (AL) performed these procedures from April 2009 (when ICG angiography was introduced at Emory University Hospital) to December 2011. All patients who presented for breast reconstruction were included regardless of the methodology of reconstruction.

To create a historical control cohort for comparison, data were collected on the 184 consecutive patients who underwent breast reconstruction between October 2007 and April 2009, immediately prior to the introduction of ICG angiography. These procedures were also performed by the senior author. No inclusion or exclusion criteria were applied; all consecutive patients undergoing breast reconstruction were included.

The mastectomies were all skin sparing, performed by 3 different breast surgical oncologists using Bovie electrocautery (Bovie Medical, Clearwater, Florida). None were nipple-sparing mastectomies. None included the use of tumescence. Methylene blue was injected for cases involving sentinel lymph node biopsies but did not interfere with ICG angiography analysis, since all nipple-areolar complexes were resected during the mastectomy.

Data collected included patient age, body mass index (BMI), smoking status, and history of radiation therapy as well as the timing and type of reconstruction. Postoperative complications noted included mastectomy skin necrosis, flap necrosis, fat necrosis, flap loss, seroma, hematoma, infection, and implant exposure. Mastectomy skin necrosis was defined clinically at postoperative visits and further broken into 3 categories: mild (skin necrosis healing in less than 1 month and requiring no intervention), moderate (healing in 1-3 months and requiring in-office debridement), and severe (requiring operative debridement and local flap or skin graft coverage). Complications assumed to be related to ischemia were mastectomy skin necrosis, flap necrosis, fat necrosis, infection, dehiscence, and implant extrusion. Fat necrosis was clinically diagnosed on physical examination at follow-up appointments. Unexpected reoperations due to perfusion-related complications were recorded for both groups and compared.

In the control cohort, debridement of mastectomy skin flaps and tissue flaps was completed based on clinical assessment of color, capillary refill, and dermal edge bleeding. In the ICG cohort, debridement of mastectomy skin flaps and tissue flaps was completed based on a combination of the same clinical assessment criteria as well as SPY perfusion analysis. After resection, the skin flaps were not reimaged a second time before closure.

Statistical analysis was performed using SAS software, version 9.2 (SAS Institute, Cary, North Carolina), and P values less than .05 were considered significant. Demographics were compared between the ICG cohort and the control cohort using χ² tests for comparison of proportions (smoking status/radiation proportion) and 2-sample t tests for continuous measures (age and BMI). Incidence of complications and incidence of unexpected reoperation were compared using χ² tests.

The cost of unexpected reoperations was calculated by adding the operative costs (including operating room costs, anesthesia charges, and physician code charges) and the inpatient hospital costs. The ICG cost was calculated based on a per-case rate of $795, which included use of the machine, sterile drapes, and ICG dye.

**RESULTS**

### Patient Demographics

There were no significant differences between the patients in the SPY cohort and the patients in the historical control cohort with respect to age, BMI, smoking status, or incidence of preoperative radiation. Specific demographic information for each group is shown in Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICG Angiography Cohort (SPY Imaginga)</th>
<th>Historical Control Cohort</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>49.91 ± 10.08</td>
<td>50.02 ± 10.15</td>
<td>.918</td>
</tr>
<tr>
<td>Body mass index, mean ± SD</td>
<td>30.36 ± 16.1</td>
<td>28.15 ± 15.1</td>
<td>.187</td>
</tr>
<tr>
<td>Smoking status</td>
<td>21 (11.4)</td>
<td>25 (13.6)</td>
<td>.533</td>
</tr>
<tr>
<td>Immediate reconstruction</td>
<td>160 (86.5)</td>
<td>169 (91.8)</td>
<td>.131</td>
</tr>
<tr>
<td>Bilateral reconstruction</td>
<td>47 (25.4)</td>
<td>62 (33.7)</td>
<td>.088</td>
</tr>
<tr>
<td>Preoperative radiation</td>
<td>28 (15.1)</td>
<td>24 (13.0)</td>
<td>.654</td>
</tr>
<tr>
<td>Follow-up, mean ± SD, mo</td>
<td>8.27 ± 6.2</td>
<td>24.7 ± 11.8</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Values are presented as number (%) unless otherwise indicated.

*aLifeCell Corp (Branchburg, New Jersey)*.
(24.7%), 19 latissimus dorsi–only reconstructions (5.1%), 84 pedicled TRAM reconstructions (22.8%), and 46 free-TRAM or deep inferior epigastric perforator (DIEP) reconstructions (12.5%) were performed. There were no significant differences ($P = .202$) between the ICG cohort and the historical control cohort with respect to the distribution of reconstruction types. The control cohort exhibited a significantly longer follow-up (24.7 vs 8.27 months; $P = .000$) than the ICG cohort, which was expected.

**Mastectomy Skin Necrosis**

The overall incidence of mastectomy skin necrosis (of any degree) was significantly lower in the ICG cohort (13%, $n = 24$) than in the control cohort (23.4%, $n = 43$; $P = .010$), as shown in Table 2.

In the ICG group, 10 of the 24 cases of skin necrosis (41.7%) were mild and 6 (25.0%) were severe. In the control group, 9 of the 43 cases of skin necrosis (20.9%) were mild, and 19 (44.1%) were severe ($P = .175$). Figure 1 shows the severity of mastectomy skin necrosis for each group. The mean severity of skin necrosis in the ICG group was 1.83 compared with 2.22 in the control group ($P = .065$). Among patients who had undergone preoperative radiation ($n = 51$), the incidence of mastectomy skin necrosis remained lower in the ICG cohort (10.7%, $n = 3$ of 28 patients; $P = .281$) than in the historical control cohort (21.7%, $n = 5$ of 23 patients), although the trend did not reach significance in this population.

**Flap Necrosis in TRAM Patients**

Among TRAM reconstruction patients ($n = 130$), the incidence of total flap loss was 2.3% ($n = 3$). This was similar for the ICG group and the control group (1.4% vs 3.4%; $P = 1.00$). Table 3 shows the TRAM outcomes for each group. There was a trend toward lower partial flap necrosis and fat necrosis rates in the ICG group compared with the control group (14% vs 22%; $P = .237$).

**Table 2. Outcome Comparison**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICG Angiography Cohort</th>
<th>Historical Control Cohort</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reoperation</td>
<td>11 (5.9)</td>
<td>26 (14.1)</td>
<td>.009</td>
</tr>
<tr>
<td>Mastectomy flap necrosis*</td>
<td>24 (13.0)</td>
<td>43 (23.4)</td>
<td>.010</td>
</tr>
<tr>
<td>Dehiscence</td>
<td>4 (2.2)</td>
<td>1 (0.5)</td>
<td>.372</td>
</tr>
<tr>
<td>Infection</td>
<td>18 (9.7)</td>
<td>20 (10.9)</td>
<td>.785</td>
</tr>
<tr>
<td>Implant exposure</td>
<td>3 (1.6)</td>
<td>3 (1.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Seroma</td>
<td>18 (9.7)</td>
<td>17 (9.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hematoma</td>
<td>5 (2.7)</td>
<td>7 (3.8)</td>
<td>.574</td>
</tr>
<tr>
<td>Overall complications</td>
<td>79 (42.7)</td>
<td>86 (46.7)</td>
<td>.484</td>
</tr>
</tbody>
</table>

*LifeCell Corp (Branchburg, New Jersey).

*Necrosis refers to grades 1, 2, and 3.

**Table 3. TRAM Outcome Comparison**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICG Angiography Cohort</th>
<th>Historical Control Cohort</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of TRAM flaps</td>
<td>71</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Total flap loss (TRAM flaps)</td>
<td>1 (1.4)</td>
<td>2 (3.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Partial flap necrosis or fat necrosis (TRAM flaps)</td>
<td>10 (14.0)</td>
<td>13 (22.0)</td>
<td>.237</td>
</tr>
</tbody>
</table>

TRAM, transverse rectus abdominis myocutaneous.

*LifeCell Corp (Branchburg, New Jersey).

**Figure 1.** Severity of mastectomy skin flap necrosis: a comparison of the indocyanine green angiography (SPY Imaging; LifeCell Corp, Branchburg, New Jersey) cohort and the historical control cohort ($P = .175$).

**Unexpected Reoperation**

There was a significantly lower incidence of unexpected reoperation for perfusion-related complications in the ICG group (5.9%; $n = 11$) compared with the control group (14.1%, $n = 22$; $P = .009$). Table 2 shows the reoperation rates for each group. Reasons for reoperation included debridement of necrotic skin, drainage of gross infection or abscess, and implant removal for cases of exposure.

**Other Outcomes**

There were no significant differences between the 2 groups in the rates of nipple necrosis, fat necrosis, dehiscence, infection, seroma, hematoma, or implant exposure. Table 2 shows the incidence of each outcome.

**Cost Analysis**

The total cost associated with unexpected reoperation, including inpatient hospitalization charges, was $158,282.62 for the 11 patients in the ICG group compared with $417,576.27 for the 25 patients in the control group. At Emory University, the ICG angiography costs $795 per case; for the 184 patients in the ICG cohort, the total cost to use ICG was $146,280.

For the ICG group, the total cost of reoperation plus the cost of using the ICG angiography technology was
Skin-sparing mastectomies provide improved morbidity as well as cost. Several studies have found ICG angiography to be highly accurate at predicting skin necrosis, but ICG was significantly more specific (P = .002).

Similarly, in a retrospective study of 20 skin-sparing mastectomy flaps, Newman et al. noted wound-healing complications in 9 (45%) breasts. Of these, 25% were severe enough to require reoperation. Retrospective analysis of ICG angiography done intraoperatively on these breasts demonstrated a 95% correlation between imaging and clinical course with 100% sensitivity and 91% specificity. Moyer and Losken used SPY-Q software to determine that 33% of maximal perfusion was an accurate cutoff between viable and nonviable tissue with a sensitivity of 87.5%.

Despite evidence of ICG angiography’s high sensitivity and specificity in predicting mastectomy skin necrosis, few studies have demonstrated the degree to which the technology improves outcomes overall.

Komorowska-Timek and Gurtner used ICG angiography intraoperatively in 24 breast reconstruction cases (16 tissue expander reconstructions and 8 autologous tissue flaps) and found an ischemic complication rate of 4%—a significant reduction from the complication rate of 15% found among a similar cohort of 148 patients on whom ICG was not used. Of the 24 breasts, 10 tissue expander reconstructions demonstrated ischemia angiographically but not clinically; all underwent tissue resection based on the intraoperative imaging. These results are similar to our findings that overall skin necrosis rates were reduced from 23% to 13% with the use of ICG, and complications requiring reoperation were reduced from 14% to 6%. Our reoperative complications included all events that could have been influenced by ischemia, including infection and implant exposure, along with skin necrosis.

There have been many suggestions over the past several decades as to the “safe” zones of the unipedicled TRAM flap that help to avoid postoperative fat necrosis and partial flap loss. Yamaguchi et al. visualized flap perfusion using ICG imaging in 10 patients and found variable perfusion of zones 2 and 3. In 3 of 10 cases, ICG imaging demonstrated that an area of poor perfusion was left in place to create an adequate breast mound, resulting in postoperative skin and fat necrosis. In our cohorts, there was less postoperative fat necrosis in the ICG cohort (14%) than in the control cohort (22%), but this was not statistically significant. This supports the hypothesis that clinical assessment is an accurate predictor of autologous tissue survival.

Although multiple studies have shown ICG imaging to be safe and effective at predicting skin and tissue perfusion, the cost-effectiveness of using the new technology in breast reconstruction remains in question. In 2007, a new International Classification of Diseases (ICD) code was assigned to coronary artery bypass grafting (CABG) with use of intraoperative fluorescence vascular angiography (IFVA). When compared with CABG without IFVA (which is used to test graft patency and distal perfusion), the cases utilizing IFVA had a shorter length of hospital stay and lower average costs.

We have shown that the use of ICG angiography technology in breast reconstruction decreased the incidence of

Figure 2. Cost analysis of the indocyanine green angiography (SPY Imaging; LifeCell Corp, Branchburg, New Jersey) cohort and historical control cohort.

$304,562.62. Subtracting this from the cost of complications in the control cohort, we found the use of ICG angiography in our cohort of 184 patients saved $113,013.65, or $614 per patient. This cost analysis is shown in Figure 2.

DISCUSSION

Ischemic complications in breast reconstruction include direct complications such as mastectomy skin necrosis, free tissue flap loss, partial flap loss or fat necrosis, and indirect sequelae such as infection, dehiscence, and implant exposure. These complications reportedly occur in more than 40% of breast reconstruction cases and can be influenced by age, smoking history, BMI, breast size, and history of radiation therapy. Besides appropriate patient selection and maintenance of sterile technique, ensuring skin and flap viability is critical to reducing postoperative morbidity as well as cost.

Clinical examination has long been the most common method of predicting skin viability, but recent technology has improved our ability to accurately predict tissue perfusion. Skin-sparing mastectomies provide improved aesthetic results, but the risk of skin necrosis is a concern. Phillips et al. published an all-inclusive skin necrosis rate of 41.2% and a reoperative necrosis rate of 9% when using clinical judgment. Prior to the introduction of ICG angiography, we found a comparable overall skin necrosis rate of 23.4% and a rate of necrosis requiring operative debridement of 9.7%.

Several studies have found ICG angiography to be highly accurate at predicting mastectomy skin flap viability in breast reconstruction. In a clinical trial that compared laser-assisted ICG angiography with fluorescein dye angiography and clinical judgment in the prediction of mastectomy skin necrosis, use of both ICG and fluorescein significantly improved prediction of viable skin. Of the 9 breasts (17.6%) that underwent debridement based on clinical assessment alone, 7 resulted in postoperative skin necrosis. Both ICG and fluorescein dye were 90% sensitive at predicting skin necrosis, but ICG was significantly more specific (P = .002).

Similarly, in a retrospective study of 20 skin-sparing mastectomy flaps, Newman et al. noted wound-healing complications in 9 (45%) breasts. Of these, 25% were severe enough to require reoperation. Retrospective analysis of ICG angiography done intraoperatively on these breasts demonstrated a 95% correlation between imaging and clinical course with 100% sensitivity and 91% specificity. Moyer and Losken used SPY-Q software to determine that 33% of maximal perfusion was an accurate cutoff between viable and nonviable tissue with a sensitivity of 87.5%.

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We have shown that the use of ICG angiography technology in breast reconstruction decreased the incidence of
reoperative complications from 14% to 6%. We have also found that for our group of 184 patients, the use of ICG reduced costs by $113,000 due to a decrease in reoperative costs and unexpected hospital admissions.

This study was not intended to be a technical or methodological description of the use of ICG angiography (or SPY imaging). We did not calculate the specificity or sensitivity of ICG angiography in our cohort. Our goal was to demonstrate whether a change in outcomes occurred after the technology’s introduction.

Limitations of our study include the retrospective nature and the use of an historical control group as a comparison. Given previous demonstrations of ICG angiography’s utility, we chose not to randomize patients to a control group. Variables not controlled for included the type of breast reconstruction and the timing of reconstruction; this was consistent for both the ICG group and the historical control group. We acknowledge that not all cases of infection or dehiscence are attributable to ischemia, but our goal was to achieve consistency by using the same inclusion criteria in both cohorts.

CONCLUSIONS

The routine use of intraoperative angiography during post-mastectomy breast reconstruction at our institution decreased the incidence of mastectomy skin necrosis and of unexpected reoperations for perfusion-related complications. Use of the technology was cost-effective when compared with the costs of reoperative complications.

Disclosures

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REFERENCES