SPY Elite’s Ability to Predict Nipple Necrosis in Nipple-Sparing Mastectomy and Immediate Tissue Expander Reconstruction

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Background: Nipple-sparing techniques have improved the aesthetics of reconstruction following mastectomy, but nipple necrosis complicates up to 37% of procedures, distressing patients, delaying adjuvant therapy, and compromising outcomes. No method reliably detects nipple necrosis better than clinical assessment of tissue perfusion. We prospectively assessed the accuracy of intraoperative indocyanine green laser angiography to predict nipple necrosis.

Methods: Twenty consecutive women undergoing immediate tissue expander breast reconstruction following 32 nipple-sparing mastectomies underwent indocyanine green fluorescence imaging to assess nipple perfusion immediately before and after intraoperative tissue expansion. Imaging findings were correlated with postoperative nipple viability.

Results: Among the 32 nipple-sparing mastectomies (8 unilateral, 12 bilateral) in 20 women (mean age, 48 years), partial or full-thickness necrotic changes developed in 3 breasts of 2 patients (10%). Imaging identified impaired perfusion and predicted necrosis in these cases.

Conclusions: In this initial series, intraoperative indocyanine green laser angiography correctly identified patients who developed nipple necrosis during mastectomy and tissue expander breast reconstruction. (Plast Reconstr Surg Glob Open 2017;5:e1334; doi: 10.1097/GOX.0000000000001334; Published online 23 May 2017.)

BACKGROUND

Breast cancer is among the most common malignancies and, increasingly, patients undergo mastectomy with or without immediate reconstruction.1–2 Nipple necrosis complicates 3–37% of nipple-sparing mastectomy (NSM) operations,3,5 creating emotional stress, delaying postoperative therapy, and increasing costs. Nipple ischemia is usually clinically detected based on subjective criteria, but indocyanine green (ICG) angiography is a promising method to assess viability3,6–8 with nearly 95% correlation to clinical outcomes.4

Intravenously injected ICG binds plasma proteins, fluoresces under near-infrared light, and distinguishes areas of relative hypoperfusion. In most studies, intraoperative management was guided by clinical observations and imaging results, limiting assessment of its predictive value.3,4,6,9 We correlated intraoperative perfusion measurements with clinical outcomes without allowing intraoperative ICG data to influence surgical management.

PATIENTS AND METHODS

The institutional review board governing human subject research approved the study, and each patient gave written informed consent preoperatively. Twenty consecutive patients underwent NSM by 6 breast surgeons, all with pre- and postoperative antibiotics, and 3 plastic surgeons (M.V., A.M., and V.S.) performed tissue expander (TE) reconstruction using acellular dermal matrices. ICG imaging was combined with laser-generated light (SPY Elite, Novadaq Corporation, Mississauga, Ontario, Canada). Nipple areolar viability was assessed immediately after mastectomy and again after expansion. Relative perfusion was calculated using proprietary SPY-Q software at 90 seconds, with ischemia defined at a threshold ≤ 5% of surrounding normal tissue perfusion to reduce bias toward the technol-
ogy. Intraoperative management was not changed based on imaging results. Postoperatively, patients were assessed weekly for a month and at 3, 6, and 12 months for nipple and mastectomy flap viability. Results were analyzed using Fisher’s exact test, and significance accepted at \( P \leq 0.05 \).

**RESULTS**

Among 20 women undergoing 32 NSM (8 unilateral and 12 bilateral) with TE reconstruction, 3 breasts in 2 patients developed partial or full-thickness necrosis (10%). One patient, aged 48 years, developed partial bilateral nipple necrosis and hypopigmentation after bilateral mastectomies (Figs. 1–4). She did not require debridement and underwent successful implant exchange 3 months later. Another, aged 57 years, who had previously undergone oncoplastic breast reconstruction and external beam irradiation, developed flap and total nipple necrosis after unilateral mastectomy requiring excision and TE removal. When mammography identified additional calcifications and ductal carcinoma in situ, she underwent completion mastectomy.

In each patient developing at least partially compromised nipple viability, ICG imaging identified impaired perfusion intraoperatively, whereas perfusion patterns were normal in successfully operated on breasts (sensitivity and specificity, 100%; positive predictive value [PPV], 100%; and negative predictive value [NPV], 100% [\( P < 0.0002 \), Table 1]). Full-thickness necrosis was identified with 100% sensitivity and 94% specificity (PPV, 33% and NPV, 100%; \( P < 0.094 \), Table 2). False-positive readings occurred bilaterally in 1 patient with partial nipple necrosis.

**DISCUSSION**

Postmastectomy tissue ischemia is challenging, and poor outcomes associated with this complication point to the need for reliable methods to supplement clinical assessment. In previous studies, ICG angiography showed promise for detecting intraoperative nipple hypoperfusion in patients at risk of necrosis,\(^{10}\) and less necrosis developed when angiography was used to supplement clinical
is operator-dependent, subject to a learning curve, and factors could influence measurements. Because tissue and fluctuations in blood pressure or other physiological ph does not assess longitudinal changes in perfusion, studies from < 7% (sensitivity, 88%; specificity, 83%) up on clinical impression or imaging, it is difficult to corre-

because intraoperative management was adjusted based on clinical impression as marginal. Nevertheless, initial observations suggest tissue perfusion assessed by ICG before and after tissue expansion may supplement clinical assessment in women undergoing NSM. When this technique finds relative perfection satisfactory, the risk of tissue necrosis is low.

Table 1. Ability of Spy Elite to Predict At Least Partial Necrosis

| SPY Used | Partial Necrosis + | Partial Necrosis - | Total |
|----------|-------------------|-------------------|-------|
| SPY +    | 3                 | 0                 | 3     |
| SPY -    | 29                | 32                | 61    |
| Total    | 31                | 32                | 63    |

Identifying partial necrosis: sensitivity, 29/(29 + 32) = 94%; PPV, 29/(29 + 0) = 100%; NPV, 0/(0 + 32) = 0; Fisher’s exact test 2-sided P value = 0.0002.

Table 2. Ability of Spy Elite to Predict Full Necrosis

| SPY Used | Partial Necrosis + | Partial Necrosis - | Total |
|----------|-------------------|-------------------|-------|
| SPY +    | 1                 | 2                 | 3     |
| SPY -    | 29                | 29                | 58    |
| Total    | 30                | 58                | 88    |

Identifying partial necrosis: sensitivity, 1/(1 + 2) = 33%; specificity, 29/(29 + 0) = 100%; PPV, 1/(1 + 2) = 33%; NPV, 29/(29 + 0) = 100%; Fisher’s exact test 2-sided P value = 0.094.

As its favorable side effect profile and short half-life facilitates sequential imaging, ICG has largely replaced fluorescein for this application. Perfusion rates associated with necrosis vary across studies from < 7% (sensitivity, 88%; specificity, 83%) up to 33%. No single cutoff applies to all patients and, because intraoperative management was adjusted based on clinical impression or imaging, it is difficult to correlate intraoperative perfusion with clinical outcomes. Our study is unique, as no changes in intraoperative management were permitted based on imaging results, allowing assessment of independent predictive value. We found ICG angiography a useful adjunct to clinical assessment in identifying patients at risk of nipple necrosis, especially when perfusion was clinically estimated as marginal.

An instantaneous index of perfusion, ICG angiography does not assess longitudinal changes in perfusion, and fluctuations in blood pressure or other physiological factors could influence measurements. Because tissue perfusion is dynamic, no static measurement is entirely predictive of necrosis. This may account for occasional false positives, where relative perfusion < 5% predicted necrosis. Accordingly, SPY should supplement, rather than replace, clinical assessment. Of 3 breasts with nipple perfusion meeting this criterion, 1 developed total necrosis; 2 with partial necrosis healed without intervention. The technology predicted at least partial necrosis (sensitivity and specificity, 100%), but if cases of partial necrosis are considered false positives for the endpoint of complete necrosis, specificity drops to 94%. Adequate ICG perfusion predicts a low risk of necrosis, so SPY may be most useful when tissue viability is clinically indeterminate.

Patient age, comorbidities (e.g., diabetes and peripheral vascular disease), and pharmacology influence nipple viability, and the value of ICG diminishes in smokers. Previous studies suggest that ICG may lower cost in high-risk (e.g., obese or large-breasted) patients, though routine use may not be cost effective. ICG angiography is operator-dependent, subject to a learning curve, and confounded by tumescence. Clinicians should not rely solely on imaging but integrate this with other data and clinical observations to form a comprehensive assessment.

The main limitations of this study are small size and infrequency of necrotic complications, widening confidence bounds around predictive value. Valid calculation of net reclassification index would require a larger, diverse population, with more frequent suboptimal outcomes. Nevertheless, initial observations suggest tissue perfusion assessed by ICG before and after tissue expansion may supplement clinical assessment in women undergoing NSM. When this technique finds relative perfection satisfactory, the risk of tissue necrosis is low.

CONCLUSIONS

Intraoperative ICG angiography can identify patients at risk of nipple necrosis during NSM, though technological limitations may cause discrepancies. ICG is a useful adjunct when perfusion is difficult to assess based on clinical observations alone, but additional studies are needed to identify patients in whom the technique provides greatest value.

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