Early Experience with Fluorescent Angiography in Free-Tissue Transfer Reconstruction

Ivo A. Pestana, M.D.
Brian Coan, M.D.
Detlev Erdmann, M.D., Ph.D.
Jeffrey Marcus, M.D.
L. Scott Levin, M.D.
Michael R. Zenn, M.D.

Durham, N.C.

Background: Soft-tissue and bony reconstruction with free-tissue transfer is one of the most versatile tools available to the reconstructive surgeon. Determination of flap perfusion and early detection of vascular compromise with prompt correction remain critical in free-tissue transfer success. The aim of this report is to describe the utility of laser-assisted indocyanine green fluorescent dye angiography in free-tissue transfer reconstruction.

Methods: From October of 2007 to March of 2008, 27 nonrandomized, nonconsecutive patients underwent surgical free flaps in conjunction with intraoperative Novadaq SPY fluorescent angiography.

Results: Twenty-seven patients underwent 29 free-tissue transfers. There was one partial flap loss in this group requiring operative revision. No complications attributable to indocyanine green fluorescent dye administration were noted. Imaging procedures (including dye administration) added minimal additional time to the operative time and anesthesia, and assisted in intraoperative decision-making.

Conclusions: Novadaq's SPY fluorescent angiography system provides simple and efficient intraoperative real-time surface angiographic imaging. This technology places control of vascular anastomosis evaluation and flap perfusion in the hands of the surgeon intraoperatively in a visual manner that is easy to use and is helpful in surgical decision-making. (*Plast. Reconstr. Surg.* 123: 1239, 2009.)

Soft-tissue and bony reconstruction with free-tissue transfer is one of the most versatile tools available to the reconstructive surgeon. These methods are routinely used in the reconstruction of soft-tissue deficits of the head and neck, breast, trunk, and lower extremities. Early detection of vascular compromise and its prompt correction remain critical in the success of free-tissue transfer.[1] Many intraoperative and postoperative monitoring devices and techniques have been developed, with varying success and clinical relevance. In conjunction with clinical evaluation (e.g., color, turgor, bleeding), monitoring includes both invasive and noninvasive techniques. Noninvasive studies include hand-held Doppler ultrasound, infrared thermography,[2] polarized spectral imaging,[3] and laser Doppler perfusion imaging.[4] Invasive evaluations include implantable Doppler probes,[5] microdialysis,[6] and venous pressure measurements with indwelling venous catheters.[7] Despite the various options, only few have gained universal acceptance.[8]

From Duke University Medical Center.
Received for publication September 1, 2008; accepted November 7, 2008.

DOI: 10.1097/PRS.0b013e31819e67c1

The SPY system (Novadaq Technologies, Inc., Concord, Ontario, Canada) is an intraoperative fluorescent angiographic imaging system that produces a real-time image of large- and small-caliber blood vessels. It is based on lyophilized indocya-

Disclosure: *Novadaq supplied the SPY fluorescent angiography system at no charge to Duke University Medical Center for the study. No other financial support was obtained. Since the acceptance of this article, Dr. Zenn has become a paid consultant for Novadaq Corporation. This change of disclosure does not affect this publication and has been so noted in the* Plastic and Reconstructive Surgery *and American Society of Plastic Surgeons disclosures submitted since.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text; simply type the URL address into any web browser to access this content. Clickable links to the material are provided in the HTML text of this article on the *Journal*'s Web site (www.PRSJournal.com).

nine green, a water-soluble tricarbocyanine dye that is excreted exclusively by the liver into the bile. The dye is administered by means of peripheral or central intravenous access, and its administration is painless. This dye has been studied extensively in humans and does not display toxicity at doses of 5 mg/kg and, in this application, is used in the range of 0.1 to 1 mg/kg.[9] The SPY imaging device houses a laser that causes excitation of the dye and subsequent emission of infrared energy, resulting in a fluorescent image of the vascular system being examined. The role of laser-assisted fluorescent angiography in reconstructive plastic surgery remains unknown. The aim of this report is to describe the utility of laser-assisted intraoperative indocyanine green fluorescent dye angiography (SPY system) in free-tissue transfer reconstruction. Initial experience, imaging findings, and recommendations for its use are described.

PATIENTS AND METHODS

From October of 2007 to March of 2008, patients who presented to the Duke University Medical Center Plastic Surgery Unit requiring free-tissue transfer for management of soft-tissue and bony defects were considered for intraoperative evaluation using SPY fluorescent angiography. Operative procedures were performed by multiple surgeons on the faculty at Duke University Medical Center (J.M., M.Z., L.S.L.), and the decision to use this technology was made by the surgeon on a case-by-case basis. Because the sterile dye used contained sodium iodide, patients with a known allergy to iodides were excluded from evaluation with this technology. Although the occurrence of adverse reactions is low, the incidence of reaction to the dye is increased in patients with poor kidney function on hemodialysis. For this reason, patients with renal insufficiency were also excluded. All doses administered were less than the toxic dose of 5 mg/kg. Data were collected prospectively, with retrospective chart review for follow-up where required.

Imaging Technique

After written informed consent was obtained, patients were marked according to the planned tissue transfer. Patients were taken to the operating room, general anesthesia was induced, and appropriate preoperative antibiotics were administered. Patients were then positioned for dissection of the planned flap. According to the protocol approved by the Duke University Medical Center Institutional Review Board, intraoperative image evaluation of the flap with fluorescent angiography was performed using two different intravenous bolus doses of indocyanine green. Ten milligrams of indocyanine green was administered to evaluate flap perfusion and skin graft–covered flaps once inset. Five milligrams of indocyanine green was administered for flap pedicle and microsurgical anastomosis imaging. Repeat dosing was performed as needed, usually a minimum of 15 minutes after the previous injection. Even with multiple injections, the dye load never exceeded 1 mg/kg.

Indocyanine green was administered by means of bolus predominantly through peripheral intravenous catheters and, occasionally, though not required, through central venous catheters when placed by anesthesia for other reasons. Approximately 60 to 90 seconds after bolus administration, the flap pedicle (before transection), completed microsurgical anastomosis, and flap perfusion were imaged and real-time video fluorescent angiography recorded. Postoperative free flap monitoring for patients consisted of Cook Doppler probe placement intraoperatively and monitoring of either arterial, venous, or both signals postoperatively, along with serial clinical examination of flap perfusion. SPY imaging was only used intraoperatively in this study.

RESULTS

Twenty-seven patients were included in the study (Table 1). The average patient age at the time of surgery was 43 years (range, 10 to 76 years). There were 11 male patients and 16 female patients. Twenty-nine free-tissue transfers for head and neck, breast, and lower extremity reconstruction were performed with multiple different donor sites (Fig. 1). The cause of the tissue deficits was wide ranging (Table 1) and included traumatic injuries, oncologic postablative defects of the head and neck and breast, and facial reanimation procedures. Flap choice was made by the surgeon based on the needs of the case and the available donor sites. There was one partial flap loss in this group. No complications attributable to indocyanine green fluorescent dye administration were noted. Review of the operative logs revealed that the imaging procedures, including dye administration, added minimal additional time to operative time and anesthesia.

In addition to the basic function of providing real-time intraoperative angiography, there are several notable cases in this series that indicate the potential benefits of SPY technology. In planned perforator-based free-tissue transfers, preopera-

Table 1. Summary of 27 Patients with Free-Tissue Transfers Completed with the Use of SPY Fluorescent Angiography

Patient	Age (yr)	Free-Tissue Transfer/Procedure	Indication	Complications
1	49	Gracilis, STSG	Fall, LE fracture	Partial STSG loss
2	58	TRAM	Breast cancer	None
3	33	Gracilis, STSG	GSW	Pedicle compression after orthopedic tendon repair; donor-site infection
4	68	Gracilis, STSG	LE fracture	None
5	18	Anterolateral thigh, STSG	GSW	None
6	56	SGAP	Breast cancer	Venous compromise caused by hematoma
7	53	SIEA and DIEP	Bilateral breast cancer	Abdominal seroma
8	10	Innervated gracilis	Congenital facial paralysis	None
9	69	Radial forearm	Exposed hardware after hammertoe repair	Donor-site hematoma
10	48	SGAP	Breast cancer	Donor-site seroma
11	26	Gracilis, STSG	GSW	None
12	24	Latissimus dorsi, STSG	MVC, tibia/fibula malunion	None
13	50	SGAP	Breast cancer	Partial flap necrosis; donor-site seroma
14	54	Latissimus dorsi, STSG	Sarcoma resection defect	Loss of STSG
15	55	TRAM	Breast cancer	None
16	34	Bilateral gracilis myocutaneous	Bilateral breast cancer	Donor-site seroma/cellulitis
17	34	Lateral arm	Previous LE fracture with osteomyelitis	Distal flap necrosis
18	37	Latissimus dorsi, STSG	MCC	Venous compromise caused by hematoma
19	32	Latissimus dorsi, STSG	Heterotopic ossification	None
20	30	Anterolateral thigh	Osteogenesis imperfecta with adenocarcinoma	Choledocholithiasis requiring cholecystectomy
21	63	Fibula vascularized bone graft	Failed knee replacement, osteomyelitis	None
22	47	TRAM	Breast cancer	None
23	76	Scapular osteocutaneous	Mandible SCC	Intraoral fistula
24	37	TRAM	Breast cancer	None
25	33	Femoral corticoperiosteal vascularized bone graft	MVC, LE fracture nonunion	None
26	37	Gracilis, STSG	Previous LE fracture with osteomyelitis	None
27	35	TRAM	Breast cancer	None

STSG, split-thickness skin graft; TRAM, transverse rectus abdominis myocutaneous; DIEP, deep inferior epigastric artery perforator; LE, lower extremity; GSW, gunshot wound; MVC, motor vehicle collision; MCC, motorcycle collision; SCC, squamous cell carcinoma; SGAP, superior gluteal artery perforator.

tive images of donor sites were scanned externally after indocyanine green administration. A fluorescent "blush" of different sizes and intensities was noted on the skin correlating with cutaneous arterial perforator vessels. SPY fluorescent angiography proved useful for imaging perfusion of the distalmost aspects of muscle and myocutaneous flaps (Fig. 2). In a case of autologous breast reconstruction using a superior gluteal artery perforator flap, despite clinically well-perfused appearance of the entire flap, an area of poor perfusion on the lateral aspect of the flap was identified with intraoperative SPY imaging [**see Video, Supplemental Digital Content 1,** which demonstrates a clinical example of a superior gluteal artery perforator flap anastomosed to the internal mammary artery and internal mammary vein, ***http://links.lww.com/A833***. This SPY image demonstrates a patent microscopic anastomosis with filling of both the artery and the vein. Further panning to the distal flap reveals diminished flow by SPY but more robust dermal bleeding centrally. This area of diminished flow went on to ischemia and eschar formation (Fig. 3)]. Postoperatively, this patient's course was complicated with partial flap necrosis in the poorly perfused area identified with fluorescent angiography (Fig. 3). Another notable case where SPY imaging was quite useful was in the facial reanimation case included in this series. After completion of the microsurgical anastomosis, a venous Doppler signal could not be obtained. It was unclear whether this was attributable to a low-flow state or to no flow. SPY was implemented to evaluate venous drainage of the flap and venous flow was directly visualized [**see Video, Supplemental Digital Content 2,** which demonstrates a clinical example of an innervated split gracilis muscle free flap for facial reanimation, ***http://links.lww.com/A834***. Implantable Doppler used this SPY image to confirm venous outflow from the flap not

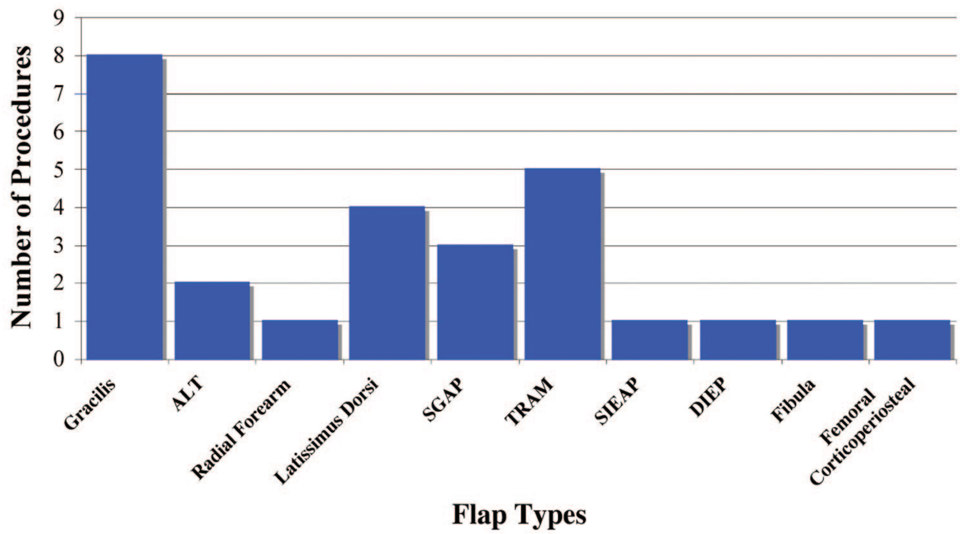

Fig. 1. Summary of soft-tissue and bony defects requiring free-tissue transfer reconstruction and flap donor sites used. *ALT*, anterolateral thigh; *SGAP*, superior gluteal artery perforator; *TRAM*, transverse rectus abdominis myocutaneous; *SIEAP*, superficial inferior epigastric artery perforator; *DIEP*, deep inferior epigastric artery perforator.

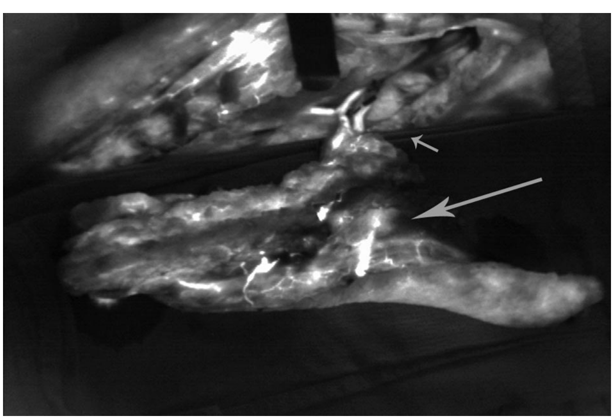

Fig. 2. Snapshot image of SPY angiography of osteocutaneous fibula flap before harvest. Note the excellent perfusion of the skin paddle and the demonstration of two dominant perforators to the skin paddle (*large arrow*). Note also the filling of the peroneal artery and vein (*small arrow*) demonstrating inflow and outflow to the flap before harvest.

Fig. 3. A clinical case of a superior gluteal artery perforator flap for breast reconstruction. An area of diminished flow was noted on SPY angiography (**see Video, Supplemental Digital Content 1, *http://links.lww.com/A833***) but not appreciated clinically, and the tissue was retained with the transferred flap. The flap had no problems postoperatively with the microscopic anastomoses or flow but did demonstrate ischemia in the zone seen by SPY, seen here on postoperative day 6.

detectable. Initial filling of the arterial anastomoses is noted and secondary perfusion of the muscle transplant (noted running across the upper third of the screen). Venous outflow is then documented (the vein has a coupler at its anastomosis site mid vessel). The patient had an uncomplicated postoperative course]. The flap did well postoperatively, without thrombosis or compromise, and the patient's recovery was uneventful. SPY technology also proved useful in cases of transverse rectus abdominis myocutaneous, deep inferior epigastric artery perforator, superficial inferior epigastric artery, and transverse upper gracilis reconstruction where areas of poorer perfusion by SPY were removed before inset and shaping (Fig. 4). This aspect will be especially important in the performance of SIEA and deep inferior epigastric artery perforator flaps, where perfusion across the midline can be variable.

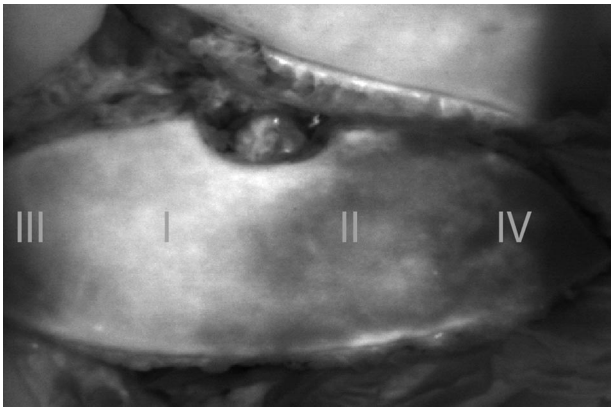

Fig. 4. Snapshot image of SPY angiography of a deep inferior epigastric artery perforator flap before flap harvest. Note the demonstration of zones I through IV visually. This information is helpful in the decision-making process to remove less-well-perfused tissue before transfer. The areas of demarcation were not as clinically apparent as pictured here by SPY angiography.

DISCUSSION

Microvascular free-tissue transfer is a dependable reconstructive method for complex tissue deficits. Technological advancements in magnification, surgical instrumentation, and suture material, and increased experience with microsurgical techniques, have contributed to its high success rates. Despite this fact and even in the most experienced hands, there is still a 1 to 2 percent risk of flap compromise that could result in flap loss. Such a loss is often catastrophic, as it may produce an even larger tissue deficit and the possibility of additional donor-site morbidity. In addition, partial flap loss continues to plague reconstructive surgeons, as the vascularity and perfusion of these free flaps is not always complete. As such, the search for the ideal method of intraoperative flap perfusion and microsurgical anastomosis evaluation continues.[10] Contrast angiography remains the standard method with which other techniques of vascular anatomy evaluation are compared. Accepted techniques of intraoperative angiography using intravenous contrast agents are cumbersome, add risk to the patient from the contrast, expose the patient and the operating room staff to radiation, and are largely inappropriate for free-tissue transfer cases.

In our study, we present a novel form of fluorescent angiography based on indocyanine green dye. This technology combines the visual properties of contrast angiography with the ease of use and safety of Doppler ultrasound. The utility of fluorescent angiography has been described extensively in the ophthalmologic literature where fluorescein is used for the visualization of retinal blood supply and diseases of the vascular system.[11] Application of fluorescein angiography to other arenas has been limited by the compound's extravasation and binding properties, with resultant slow dye washout. Unlike fluorescein, indocyanine green is strongly bound to plasma proteins and therefore remains in the intravascular space, resulting in rapid dye washout and allowing consecutive measurements and reduced extravascular fluorescence.[12] Because of these properties, its biliary excretion, and the dye's low risk of toxicity, laser-assisted indocyanine green fluorescent dye angiography has been used in the evaluation of coronary artery bypass grafts[13] and solid organ transplantation requiring vascular reconstruction.[14]

We applied this technology to the intraoperative evaluation of free-tissue transfers. Using minimal equipment and peripheral intravenous access, the SPY angiography system allowed visualization of microsurgical anastomoses and confirmed arterial inflow, venous outflow, and flap perfusion throughout the flap tissues. No complications attributable to the administration of indocyanine green dye were identified in the study group, and the time added to operative duration and anesthesia was negligible.

Although the administration of indocyanine green dye is safe and the procedures associated with vascular imaging are straightforward, the technology's image-capture hardware and software are currently in the early stages of development for reconstructive surgical purposes. The image-capture area available in current models of SPY systems is approximately 3 × 3 inches. Although this may be sufficient for the evaluation of microsurgical anastomoses, it is relatively small when a larger surface area must be imaged, such as in the case of scanning skin for fluorescent blushes correlating with cutaneous arterial perforators. An 8 × 8-inch prototype is already in use and should address this concern. Digital data storage is also an area that will require advancement to allow multiple image-capture sessions with a delay. This point is critical to prevent wasted dye administration resulting from the inability to reset and record quickly. Improvements by the manufacturer in this regard are already underway.

Undoubtedly, vascular compromise of free-tissue transfer will occur despite best circumstances and surgeon experience. Implementation of simple, reliable, and efficient methods and technology that can aid in the rapid identification of vascular compromise or discrete areas of poor perfusion would allow intervention and increase the likelihood of flap salvage. The SPY imaging system combines safety and efficiency with real-time intraoperative visual data. The SPY system returns control to the operative surgeon to perform immediate evaluation, interpreted by the surgeon. For any given case, the SPY system can be used for perforator identification before committing to flap design, for evaluation of perfusion once the flap is raised, and for anastomotic evaluation if difficulties with the microscopic anastomoses arise. No other comparable technology gives the surgeon this range and versatility in the operating room. Further study of this technology will help to characterize it strengths and weaknesses and its possible uses in preoperative evaluation of vascular anatomy and postoperative flap monitoring.

CONCLUSIONS

The SPY fluorescent angiography system provides simple and efficient intraoperative real-time angiographic imaging. This technology places control of vascular anastomosis evaluation and flap perfusion evaluation in the hands of the surgeon intraoperatively in a real-time visual manner.

Michael Robert Zenn, M.D.
Baker House 139/Trent Drive
Duke University Medical Center
Durham, N.C. 27710
michael.zenn@duke.edu

REFERENCES

1. Kubo T, Yano K, Hosokawa K. Management of flaps with compromised venous outflow in head and neck microsurgical reconstruction. *Microsurgery* 2002;22:391–395.
2. de Weerd L, Mercer JB, Setså LB. Intraoperative dynamic infrared thermography and free-flap surgery. *Ann Plast Surg.* 2006;57:279–284.
3. Erdmann D, Sweis R, Wong MS, et al. Current perspectives of orthogonal polarization spectral imaging in plastic surgery. *Chirurg* 2002;73:827–832.
4. Hölzle F, Loeffelbein DJ, Nolte D, Wolff KD. Free flap monitoring using simultaneous non-invasive laser Doppler flowmetry and tissue spectrophotometry. *J Craniomaxillofac Surg.* 2006;34:25–33.
5. Pryor SG, Moore EJ, Kasperbauer JL. Implantable Doppler flow system: Experience with 24 microvascular free-flap operations. *Otolaryngol Head Neck Surg.* 2006;135:714–718.
6. Setälä L, Papp A, Romppanen EL, Mustonen P, Berg L, Härmä M. Microdialysis detects postoperative perfusion failure in microvascular flaps. *J Reconstr Microsurg.* 2006;22:87–96.
7. Sakurai H, Nozaki M, Takeuchi M, et al. Monitoring the changes in intraparenchymatous venous pressure to ascertain flap viability. *Plast Reconstr Surg.* 2007;119:2111–2117.
8. Swartz WM, Jones NF, Cherup L, Klein A. Direct monitoring of microvascular anastomoses with the 20-MHz ultrasonic Doppler probe: An experimental and clinical study. *Plast Reconstr Surg.* 1988;81:149–161.
9. Leevy CM, Smith F, Longueville J, Paumgartner G, Howard MM. Indocyanine green clearance as a test for hepatic function: Evaluation by dichromatic ear densitometry. *JAMA.* 1967;200:236–240.
10. Disa JJ, Cordeiro PG, Hidalgo DA. Efficacy of conventional monitoring techniques in free tissue transfer: An 11-year experience in 750 consecutive cases. *Plast Reconstr Surg.* 1999;104:97–101.
11. Dzurinko VL, Gurwood AS, Price JR. Intravenous and indocyanine green angiography. *Optometry* 2004;75:743–755.
12. Kuebler WM, Sckell A, Habler O, et al. Noninvasive measurement of regional cerebral blood flow by near-infrared spectroscopy and indocyanine green. *J Cereb Blood Flow Metab.* 1998;18:445–456.
13. Balacumaraswami L, Abu-Omar Y, Choudhary B, Pigott D, Taggart DP. A comparison of transit-time flowmetry and intraoperative fluorescence imaging for assessing coronary artery bypass graft patency. *J Thorac Cardiovasc Surg.* 2005;130:315–320.
14. Sekijima M, Tojimbara T, Sato S, et al. An intraoperative fluorescent imaging system in organ transplantation. *Transplant Proc.* 2004;36:2188–2190.