Original Investigation

Use of Laser-Assisted Indocyanine Green Angiography for Early Division of the Forehead Flap Pedicle

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IMPORTANCE The paramedian forehead flap is used to reconstruct medium to large nasal defects. The staged nature, with its vascular pedicle bridging the medial eyebrow to the nose, results in significant facial deformity. Earlier division lessens this morbidity.

OBJECTIVES To quantify flap neovascularization 2 weeks after the initial flap transfer and to describe an algorithm for earlier division of the flap pedicle in select patient populations.

DESIGN, SETTING, AND PARTICIPANTS We performed a prospective and retrospective study at the Ambulatory Surgery Center, Stanford University, Palo Alto, California, from October 14, 2014, through January 21, 2015. Patients with defects appropriate for paramedian forehead flap reconstruction had partial-thickness defects, vascularized tissue in more than 50% of the recipient bed, and no nicotine use. The patients underwent reconstructive surgery by a single surgeon from August 24, 2012, through September 12, 2014. Laser-assisted indocyanine green angiography was used for imaging before and immediately after the initial flap transfer, before pedicle division with the pedicle atraumatically clamped, and immediately after pedicle division and flap inset. Analysis of data and calculation of relative perfusion were performed using a postprocessing analysis toolkit.

MAIN OUTCOMES AND MEASURES Perfusion was calculated using the analysis toolkit as the percentage of the area of interest relative to a predetermined reference point in normal peripheral tissue.

RESULTS We enrolled a total of 10 patients. The mean (SD) relative perfusion of the forehead donor site before flap transfer was 61.2% (3.4%); at initial flap transfer, 81.4% (50.2% [range, 31%-214%]) (P = .70 compared with measurement before flap transfer). The mean (SD) relative perfusion of the forehead donor site was 57.5% (21.2% [range, 32%-89%]) at the time of atraumatic pedicle clamping and 58.6% (32.4% [range, 16%-127%]) after pedicle division and flap inset (P = .85 compared with measurement before flap transfer). No flap failures or other complications were observed.

CONCLUSIONS AND RELEVANCE In select patients (those meeting the inclusion criteria), division of the pedicle at 2 weeks after the initial flap transfer is safe. Earlier pedicle division and flap transfer reduces the duration of facial deformity for the patient.

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Nasal reconstruction after excision of a cutaneous malignant neoplasm or after trauma is one of the most common and challenging endeavors for facial plastic surgeons, plastic surgeons, and dermatologic surgeons. Nonmelanoma skin cancer (NMSC) accounts for most of these defects, which require nasal reconstruction. From 1992 to 2006, the total number of procedures for NMSC increased by 77% among patients with Medicare insurance coverage, with an approximately 14% increase in the number of patients with at least 1 procedure for NMSC.[1] The prevalence of NMSC was estimated to be 5 times higher than that of breast or prostate cancer.[2] Basal cell carcinoma is the most common, accounting for 76% to 85% of all NMSCs.[3] Most basal cell carcinomas affect the head and neck, with the nose a very common subsite. Mohs micrographic surgery remains the criterion standard for tumor extirpation, which allows for maximal tissue preservation, enables examination of all margins for tumor involvement, and offers excellent cure rates for NMSC.

The paramedian forehead flap remains a workhorse in the reconstruction of medium to large nasal defects.[4,5] Nasal reconstruction using a pedicled cheek flap is thought to have been described first by Sushruta in the *Sushruta Samhita*[6] sometime from 1000 to 800 BCE. The principles of Sushruta's pedicled cheek flap likely were used by later Indian and Nepalese surgeons who applied them to use of an interpolated forehead flap for nasal reconstruction, passing the technique on from father to son.[6,7] The procedure, termed *Indian rhinoplasty*, consisted of an interpolated median forehead flap pedicled on the bilateral supratrochlear vessels.[8] The median forehead flap was first described in western literature by Joseph Constantine Carpue in 1814, with publication of 2 such reconstructions in 1816.[9-12] Labat[13] described the median forehead flap pedicled on a single supratrochlear artery in his dissertation written in 1834. Millard[14-17] subsequently described the paramedian forehead flap and moved the entire axis of the flap over the supratrochlear artery. Use of the paramedian forehead flap was further refined and popularized by Burget and Menick[18-20] and by Menick.[8,21] The paramedian forehead flap is an axial interpolated flap based on the supratrochlear artery, with contributions from the supraorbital, superficial temporal, postauricular, occipital, and dorsal nasal arteries.[8,22,23] The robust axial blood supply accounts for the high rate of success using the paramedian forehead flap. The procedure may be performed as a single-staged procedure, a 2-staged procedure, or, as described by Menick,[21] a 3-staged procedure.

The timing of flap pedicle division varies by surgeon. Menick[21] proposed division of the pedicle at 3 to 4 weeks after the initial flap transfer for 2-stage reconstructions. Some surgeons will divide the pedicle at 2 weeks, others at 4 weeks, and still others at 6 weeks. The decision of how long to delay the second stage tends to be based on patient comorbidities, defect size, anatomic involvement of the defect, smoking status, and surgeon preference, among other factors.

Based on prior work,[24] we hypothesized that sufficient neovascularization of the flap occurs 14 days after the first stage. To that end, one of us (S.P.M.) currently divides the pedicle in patients meeting appropriate criteria at 2 weeks after the initial flap transfer based on real-time data from laser-assisted indocyanine green (ICG) angiography. Specifically, this procedure is performed in patients with an adequate vascular supply from the peripheral edges of the recipient site and the wound bed (partial-thickness defects with >50% of the wound bed consisting of vascularized tissue). In the present study, we quantify flap neovascularization and relative flap perfusion 2 weeks after the initial flap transfer using an intraoperative perfusion assessment system (SPY Elite; Novadaq Technologies Inc) and a postprocessing analysis toolkit (SPY-Q; Novadaq Technologies Inc) to describe an algorithm for flap pedicle division at 2 weeks in these select patients.

Methods

This prospective and retrospective study was performed at Stanford University, after approval by the university institutional review board. Prospective enrolled patients provided written informed consent. Prospective patients were screened during their initial visit to our clinic. Those patients with defects that are appropriate for paramedian forehead flap reconstruction were enrolled if the inclusion criteria were met. Retrospective patients were identified as those patients previously treated who met inclusion criteria. Because this protocol constitutes our standard treatment, the same algorithm was applied for both groups, and the data were analyzed together. All patients were treated by a single surgeon (S.P.M.) from August 24, 2012, through September 12, 2014. Data were analyzed from October 14, 2014, through January 21, 2015.

Inclusion criteria consisted of being 18 years or older with a nasal defect requiring forehead flap reconstruction, the presence of at least 50% of the wound bed with vascularized tissue (eg, any cartilage grafting occupied no more than 50% of the wound bed), partial-thickness defects, and the absence of nicotine use. Exclusion criteria consisted of being younger than 18 years or pregnant with defects inappropriate for paramedian forehead flap reconstruction, enrollment in any other investigational study, allergy to iodides, full-thickness nasal defects, the need for structural cartilage grafting of greater than 50% of the wound bed, and active nicotine use.

Perfusion was calculated using the SPY-Q software as the percentage of the area of interest relative to a predetermined reference point in normal peripheral tissue set as the relative 100%. In the present study, we used the point of maximum signal intensity in the cheek as the reference point. The measurement point of the forehead before flap transfer was immediately adjacent to the hairline because this point most reliably correlated with the location of the distal aspect of the flap. For subsequent measurements, the point of maximum signal intensity within the flap was used, and flow was calculated as a percentage relative to the point of maximum intensity within the cheek. The maximum overlay filter was used when possible during image analysis with the SPY-Q software. This filter gives the maximum signal intensity for all arterial ingress into the imaged tissues for the duration of imaging, thereby removing any mismatch in the rate of perfusion of various tissues. Use of the maximum overlay filter requires that the patient and camera are completely still during imaging. In 2 pa-

tients, use of the maximum overlay filter at the time of atraumatic pedicle clamping before pedicle division and flap inset was not feasible owing to motion artifact. In these 2 instances, relative perfusion was calculated manually by obtaining the absolute intensity of luminescence for the reference point and flap at the times of their respective maximum intensities.

We used the paired 2-tailed *t* test to compare the mean relative perfusion during atraumatic clamping of the pedicle with that after division of the pedicle and inset of the flap. Statistical analysis was performed using commercially available software (Microsoft Excel; Microsoft Corp). Unless otherwise indicated, data are expressed as mean (SD).

Laser-Assisted ICG Angiography

Laser-assisted ICG angiography (using the SPY Elite system) consists of near-infrared imaging in conjunction with ICG intravenous contrast. This technology allows noninvasive angiography without the use of radioactive contrast. The system itself consists of a computer, an 806-nm near-infrared laser, and a high-resolution camera. This system has been approved by the US Food and Drug Administration since 2005 for cardiovascular surgery and since 2007 for plastic and reconstructive surgery. The ICG is injected intravenously and binds completely to intravascular plasma proteins, with a plasma half-life of 3 to 4 minutes.[25,26] Illumination of an area of interest by the 806-nm laser integral to the SPY system causes ICG dye within the intravascular space to fluoresce. This process is captured by a near-infrared video camera, which is also integral to the SPY system. Using the SPY-Q software, a quantitative value of perfusion based on the intensity of fluorescence may be determined. Perfusion within an area of interest can be calculated as an absolute value (based on the intensity of fluorescence) or as a percentage relative to a predetermined reference point in normal peripheral tissue. Multiple injections of ICG may be performed without concern for toxic effects and with a low risk for adverse reactions, including allergy and anaphylaxis.[27-29]

Surgical Technique

All surgical procedures were performed at the Ambulatory Surgery Center, Stanford University, under general oral endotracheal anesthesia. During the first stage, before sterile preparation and draping, the forehead donor site underwent laser-assisted ICG angiography, which provided real-time data about the quality of blood flow to the prospective flap. Laser-assisted ICG angiography of the forehead before flap elevation can be seen in the **Figure**, A. At this time, a flap may be raised from the right or the left side. The ICG angiogram clearly demonstrates the arterial and venous supply of the forehead, which allows the most robust vascular pedicle to be selected and the flap to be raised from that side. The vascular pedicle is marked with a sterile skin-marking pen, and the patient undergoes sterile preparation and draping. The nasal subunits are marked, a template is created, and the defect is prepared for flap inset in the standard fashion. The flap is then designed using the template, and the flap is elevated, transposed, and inset to the nose. The SPY-Q system is then covered with the supplied sterile drape per the guidelines of the operating room. The ICG dye is again administered at the surgeon's direction, and laser-assisted ICG angiography is performed, as can be seen in the Figure, B (stage 1). The patient is then awakened, extubated, transferred to a postanesthesia recovery unit, and spends the evening in the hospital for wound care, postoperative teaching, and pain control. The patient is discharged home on the morning of postoperative day 1.

Patients are then seen at postoperative day 6 or 7 for suture removal and flap check, to review instructions for care, and to sign consent for the second stage of surgery. For the second stage of surgery, patients are again taken to the operating room. The flap pedicle is atraumatically clamped using a red rubber catheter placed circumferentially around the pedicle to prevent flap perfusion from the vascular pedicle. The flap is then imaged using laser-assisted ICG angiography, as demonstrated in the Figure, C (stage 2A). If the flap has appropriate neovascularization detected by the angiogram, the second stage of surgery proceeds with division of the pedicle, inset of the flap to the nose, and adjacent tissue transfer of the brow. The flap is again imaged using laser-assisted ICG angiography after pedicle division and flap inset, as demonstrated in the Figure, D (stage 2B). If the angiogram suggests a reason for concern about flap health, the patient is awakened and the case is rescheduled for 2 weeks later (in total, 4 weeks after the initial flap transfer). Patients are discharged home from the postanesthesia recovery unit after the second stage of surgery.

Patients are seen at postoperative day 6 or 7 for suture removal, flap check (based on results of the clinical examination), and review of instructions for care. Patients are seen at 1 month from the date of the second stage of surgery, and flap viability is again characterized clinically.

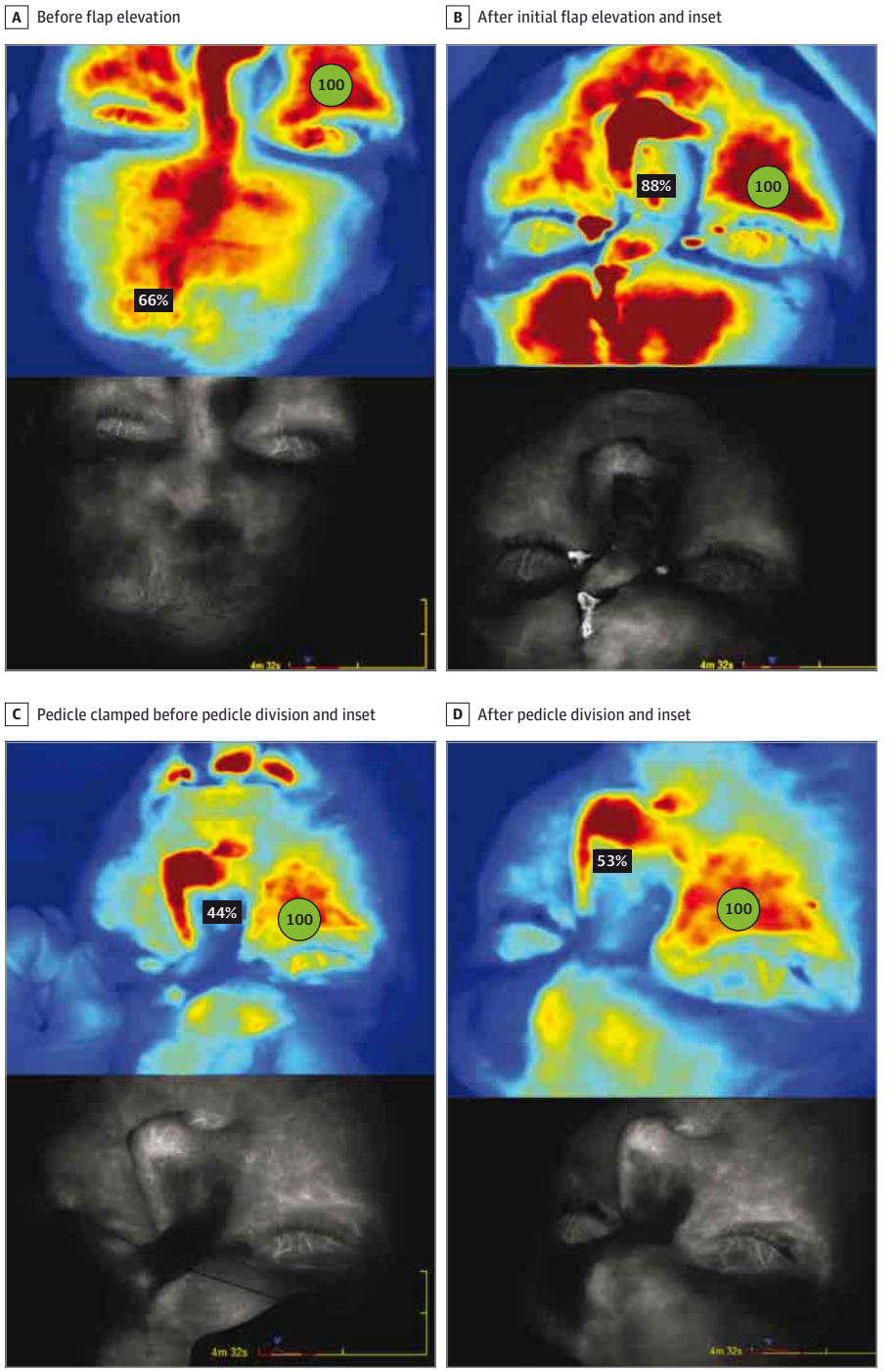
Results

A total of 10 patients met inclusion criteria, of whom 5 were men and 5 were women. Nine patients had basal cell carcinoma and 1 had squamous cell carcinoma. Nine patients had left-sided paramedian forehead flaps, whereas 1 had a right-sided flap. Patient age ranged from 55 to 78 years, with a mean of 68 years. We encountered no intraoperative or postoperative complications.

Six of 10 patients underwent measurement of the forehead donor site before any incision. In these patients, the mean relative perfusion of the forehead donor site before flap transfer was 61.2% (3.4% [range, 56%-66%]) (**Table**). All patients underwent all subsequent measurements. The mean relative perfusion at the initial flap transfer was 81.4% (50.2% [range, 31%-214%]) (P = .70 compared with measurement before flap transfer). The mean relative perfusion at the time of atraumatic pedicle clamping was 57.5% (21.2% [range, 32%-89%]). The mean relative perfusion after pedicle division and flap insetting was 58.6% (32.4% [range, 16%-127%]) (P = .85 compared with measurement before flap transfer).

We calculated the change in tissue perfusion at each stage in the 6 patients with measurement of perfusion in the donor site (Table). In these 6 patients, the mean change in relative

Figure. Laser-Assisted Angiography of the Surgical Technique



The top images depict postprocessing analysis using the SPY-Q toolkit (Novadaq Technologies Inc) with the maximum overlay filter. The bottom images are the raw laser-assisted indocyanine green angiograms. A, The forehead before flap elevation. B. The flap is shown after initial flap elevation and inset. C. The flap is seen with the pedicle clamped atraumatically before pedicle division and inset. D, The flap after pedicle division and inset.

perfusion of the flap tissue after inset at stage 1 was 9.3% (20.3% [range, −16.4% to 37.3%]). The mean change in relative perfusion of the flap tissue at atraumatic clamping of the pedicle (stage 2A) was −5.1% (33.7% [range, −39.3% to 39.7%]) (P = .37 compared with measurement at stage 1). The mean change in relative perfusion of the flap tissue after pedicle division and inset (stage 2B) was −1.9% (61.1% [range, −71.4% to 101.6%]) (P = .84 compared with stage 2A measurement during clamping).

Discussion

Laser-assisted ICG angiography to evaluate tissue perfusion has been used by cardiologists, ophthalmologists, gastrointestinal tract surgeons, and facial plastic and plastic surgeons and is well-described in the literature. This technology has been applied to local adjacent, local pedicled, regional pedicled, and free tissue transfers. Duggal and colleagues[30] prospectively studied the

Table. Relative Perfusion of Tissue Measured With Intravascular ICG Angiography[a]

	Relative Donor Site Perfusion, %	Relative Perfusion at Flap Transfer, %			Change in Flap Tissue Perfusion Compared With Donor Site, %		
		Stage 1	Stage 2A	Stage 2B	Stage 1	Stage 2A	Stage 2B
1	NA	214	38	48	NA	NA	NA
2	NA	31	67	25	NA	NA	NA
3	NA	97	89	86	NA	NA	NA
4	NA	70	32	63	NA	NA	NA
5	61	51	76	51	−16.4	24.6	−16.4
6	62	61	43	36	−1.6	−30.6	−41.9
7	63	77	88	127	22.2	39.7	101.6
8	66	79	44	56	19.7	−33.3	−15.2
9	59	81	64	78	37.3	8.5	32.2
10	56	53	34	16	−5.4	−39.3	−71.4
Mean (SD)	61.2 (3.4)	81.4 (50.2)	57.5 (21.2)	58.6 (32.4)	9.3 (20.3)	−5.1 (33.7)	−1.9 (61.1)
No. of patients	6	10	10	10	6	6	6
P value[b]	NA	.34	.69	.85	NA	.37	.84

Abbreviations: ICG, indocyanine green; NA, not applicable.

[a] Stages are described in the Surgical Technique subsection of the Methods section.

[b] Represents comparison with donor site baseline measurements.

incidence of reoperative complications in breast reconstruction and found that the use of laser-assisted ICG angiography decreased the risk for reoperative complications from 14% to 6%.

The aim of the present study was to quantify flap neovascularization using the SPY-Q system and laser-assisted ICG angiography to describe an algorithm for flap pedicle division 2 weeks after initial flap transfer in select patient populations (those meeting inclusion criteria). Our hope is to present data illustrating that flap division in selected patients is safe, given the robust revascularization, with or without the use of ICG angiography.

As previously noted, the timing of pedicle division varies between surgeons, who base the decision of how long to delay the second stage on patient comorbidities, defect size, anatomic involvement of the defect, smoking status, and surgeon preference, among other factors. The presence of the flap pedicle results in significant patient morbidity because it is disfiguring, often can obscure the visual fields, and precludes the use of eyeglasses. Earlier pedicle division results in decreased patient morbidity and downtime.

Somoano et al[31] reported dividing the pedicle at as early as 1 postoperative week. The surgeon in the present study (S.P.M.) divides the pedicle in patients meeting appropriate criteria (per the inclusion criteria) at 2 weeks after the initial flap transfer based on real-time data from laser-assisted ICG angiography. Several studies[24,32,33] have examined the utility of laser-assisted ICG angiography in determining the safety of paramedian forehead flap pedicle division. Shah and Au[33] published a case report detailing the use of laser-assisted ICG angiography 28 days after initial flap transfer and before pedicle division in a patient who used nicotine products. Similarly, Christensen and colleagues[32] published a case report detailing the use of this technology in an active smoker with hepatitis C virus infection and polycythemia vera to assess flap perfusion before the pedicle division 21 days after the initial flap transfer. Lee and colleagues[34] recently studied the use of laser-assisted ICG angiography to measure the vascular delay technique in locoregional head and neck flaps.

Woodward and Most[24] published a prospective study evaluating flap perfusion at flap transfer, at postoperative days 7, 14, and 21, and at pedicle division (postoperative day 28) using laser-assisted ICG angiography. Significant neovascularization was found beginning at 1 week after the initial flap transfer.[24] The present study expands on the previous application of this technology to determine the optimal timing for pedicle division and flap inset in select patients meeting inclusion criteria. This study represents a novel algorithm for nasal reconstruction using the paramedian forehead flap and reducing the time of facial deformity for the patient before the final result is achieved.

A relative tissue perfusion of 25% to 27% has been shown in previous studies to be the threshold for tissue ischemia when using laser-assisted ICG angiography.[35-40] In a recent retrospective review of postmastectomy breast reconstruction, Giunta et al[36] recommend a relative perfusion of 30% as the clinical threshold, below which a surgeon should be concerned about skin necrosis. Moyer and Losken[39] found that a relative perfusion of 45% or greater correlated with a high probability of survival. We found mean relative perfusion at the time of atraumatic pedicle clamping to be 57.5% (range, 32%-89%), which is well above the established ischemic threshold of 25% to 30%. Repeated imaging after pedicle division and flap inset demonstrated mean relative perfusion to be 58.6% (range, 16%-127%).

Conclusions

The present study demonstrates that in select patients (those meeting our inclusion criteria), division of the pedicle at 2 weeks after the initial flap transfer is safe. Application of the

established ischemic threshold of 25% to 30% using intraoperative laser-assisted ICG angiography and the surgeon's clinical judgment allows earlier pedicle division and inset in appropriate patients. This finding is significant in that earlier pedicle division and flap inset reduce the duration of facial deformity and morbidity for the patient.

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