Detection of Skin Perforators by Indocyanine Green Fluorescence Nearly Infrared Angiography

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Perforator-based island flaps are widely used to reconstruct skin defects. For this procedure to succeed, a perforator with adequate blood flow must be selected, and precise preoperative prediction of the location of the perforators is required. To identify perforators, a variety of methods have been used clinically.[1–10] Imaging with a near-infrared camera and indocyanine green as a fluorescent marker, which is called indocyanine green fluorescence near-infrared angiography[11] (indocyanine green angiography), has already been applied to visualize arteries such as the retinal arteries. Indocyanine green angiography has also been reported to be effective for detecting the distribution of flap blood flow both intraoperatively and postoperatively.[12–21] In the present study, we evaluated the utility of preoperative indocyanine green angiography for identifying skin perforators.

PATIENTS AND METHODS

The subjects were 14 patients who were scheduled to undergo perforator-based island flap surgery for reconstruction of skin defects (Table 1). This study was approved by the institutional review board. Indocyanine green angiography was performed with Diagnogreen (25 mg/5 ml) (Daiichi Sankyo Company, Tokyo, Japan), and a near-infrared video camera system (PDE; Hamamatsu

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Table 1. Sites Involved and Diagnoses

Patient	Age (yr)	Sex	Site	Diagnosis
1	55	M	Right hand	Degloving injury
2	21	M	Left hand	Degloving injury
3	72	M	Right leg/pretibial region	Squamous call carcinoma
4	31	M	Left anterolateral thigh	Dermatofibrosarcoma protuberans
5	52	F	Right anterior thoracic region	Local recurrence of breast cancer
6	75	F	Left leg/pretibial region	Squamous call carcinoma
7	55	M	Left dorsolumbar region	Squamous call carcinoma
8	43	M	Left gluteal region	Malignant melanoma
9	89	F	Right cheek	Basal cell carcinoma
10	67	M	Left scapular region	Malignant melanoma
11	65	M	Right sole	Malignant melanoma
12	65	M	Left posterior thigh	Epithelioid hemangioendothelioma
13	70	F	Left leg/sural region	Dog bite
14	33	F	Left greater trochanter region	Decubitus ulcer

M, male; F, female.

Photonics, Hamamatsu, Japan). Before performing indocyanine green angiography, the location and size of the skin defect were determined and marked on the skin with a felt-tipped pen. At the candidate donor site adjacent to the defect, dots were drawn on the skin as landmarks in a reticular pattern at intervals of 2 to 4 cm. The patient was positioned with the affected site up, and the hand probe of the PDE system was fixed at 20 to 40 cm above the skin using a clamp. When the target region was in the territory of the femoral artery or the brachial artery, 1 to 2 ml of an indocyanine green solution (5 mg/ml) was administered intra-arterially. If the target region was on the face or trunk, a dose of 2.5 to 5 ml was administered through the femoral vein. Recording with the PDE system was commenced at the time of starting intravascular administration. Based on the images thus recorded, the location of each perforator, the direction of blood flow, and the branches of the perforators were marked on the skin with ink. Then, a pedicled island flap was planned using the perforator(s) thus detected. During surgery, the perforators were explored and it was confirmed whether the locations of the actual vessels corresponded with those predicted by indocyanine green angiography.

RESULTS

Preoperative indocyanine green angiography detected two to six perforators in all 14 patients, and all of these vessels were found at the deep fascial level during surgery (Table 2). The skin flaps raised in all 14 patients were island flaps for which the feeding vessels were limited to the per-

Table 2. Results

Patient	Type of Flap	Injected Vessel	Dose of ICG (ml of 5 mg/ml)	Quality of Video Angiograms*	Complications
1	Distally based radial forearm	Femoral vein	4	Good	No
2	Distally based radial forearm	Brachial artery	1	Excellent	No
3	Anterior tibial artery perforator	Femoral artery	2	Good	No
4	Anterolateral thigh	Femoral artery	2	Excellent	No
5	Superior epigastric artery perforator	Femoral vein	2.5	Good	No
6	Anterior tibial artery perforator	Femoral artery	2	Fair	Superficial necrosis†
7	Lumbar artery perforator	Femoral vein	5	Fair	No
8	Superior gluteal artery perforator	Femoral vein	5	Good	No
9	Transverse facial artery perforator	Femoral vein	2.5	Good	No
10	Intercostal artery perforator	Femoral vein	4	Good	No
11	Medial plantar artery perforator	Femoral artery	2	Excellent	No
12	Profunda femoris artery perforator	Femoral artery	1.5	Excellent	No
13	Medial gastrocnemius perforator	Femoral artery	1.5	Excellent	No
14	Profunda femoris artery perforator	Femoral vein	3	Fair	No

ICG, indocyanine green.
*The quality of the images was classified into the following four categories: *excellent,* very-high-contrast web-like or linear visualization of subcutaneous arteries, with the location and direction of blood flow being precisely defined; *good,* high-contrast image that allows the location of the perforators to be precisely defined; *fair,* low-contrast image with background fluorescence, but the locations of the perforators can be presumed; and *poor,* very-low-contrast image and the locations of perforators are difficult to determine.
†Superficial necrosis caused by venous congestion occurred, but conservative treatment achieved healing by 4 weeks after surgery.

forator(s), and there was no arterial inflow from other sources. At the time of flap elevation, the presence of satisfactory blood supply was assessed from the color of the flap skin and from bleeding at the margins. The flap remained viable in all 14 patients. There were no adverse reactions to the infusion of indocyanine green.

CASE REPORTS

Patient 4

Patient 4 was a 31-year-old man who underwent extended excision of the residual tumor and reconstructive surgery after excisional biopsy of dermatofibrosarcoma protuberans on the left thigh (Tables 1 and 2 and Figs. 1 and 2). Preoperative indocyanine green angiography revealed five vessels

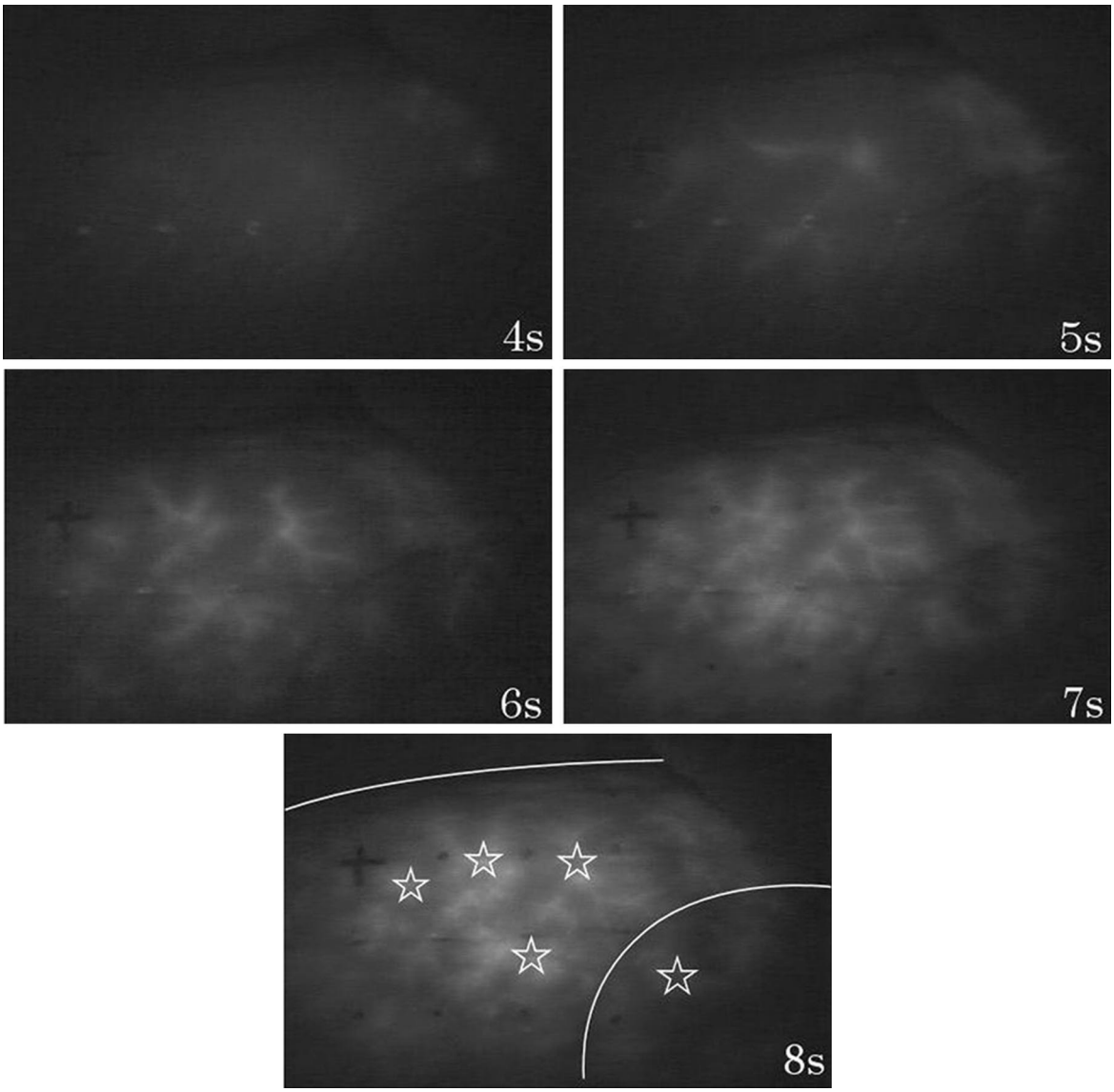

Fig. 1. Indocyanine green angiograms of patient 4. The patient was placed in the supine position and the skin at the candidate donor site for the flap was marked with dots. Then, 1 ml of indocyanine green (Diagnogreen, 25 mg/5 ml) was injected into the left femoral artery through a 22-gauge needle and recording was started immediately with the near-infrared video camera. Approximately 4 seconds after injection, pulsating vessels appeared that were considered to be perforators. Analysis of the video recording revealed five perforators (*stars*). The number in the lower right corner of each sequential image indicates the number of seconds after indocyanine green injection. On the final image, the *upper white line* and *lower right white line* show the contour of the thigh and the expected resection line, respectively, and *stars* indicate the locations of the perforators. (Reproduced, in part, from Azuma, R., Morimoto, Y., Yanagibayashi, S., et al. Indocyanine green near infrared angiography to detect the perforators of the anterolateral thigh flap. *Jpn. J. Plast. Surg.* 50: 679, 2007.)

Fig. 2. Preoperative planning and postoperative appearance of patient 4. (*Left*) A scar (7 cm in length) from the previous excisional biopsy procedure is present on the lateral aspect of the left thigh. The perforators detected by indocyanine green angiography were marked (*circles*) on the skin. Points where pulsation was detected with an ultrasonic Doppler stethoscope are also marked (*x's*). The island flap was designed so that one perforator (*asterisk*) formed the vascular pedicle. (*Right*) Perforators (1 to 1.5 mm in diameter) corresponding to all five vessels detected by indocyanine green angiography were demonstrated. A 1.5-mm-diameter muscular perforator (*asterisk*) was used and the other perforators were ligated. The skin flap was rotated 180 degrees to cover the defect. (Reproduced, in part, from Azuma, R., Morimoto, Y., Yanagibayashi, S., et al. Indocyanine green near infrared angiography to detect the perforators of the anterolateral thigh flap. *Jpn. J. Plast. Surg.* 50: 679, 2007.)

that were considered to be perforators, which were marked with ink and used as a reference when planning the operation.

All five of the perforators were found to be present intraoperatively, and their locations agreed exactly with those observed by angiography. In addition, no other cutaneous perforators were noted at sites where vessels had not been seen on indocyanine green angiography. Reconstruction was performed with an anterolateral thigh flap, using one perforator identified by indocyanine green angiography as the pedicle. The flap showed complete viability and there were no problems postoperatively (**see Video, Supplemental Digital Content 1,** which demonstrates indocyanine green angiography in patient 4, ***http://links.lww.com/A498***).

Patient 5

Patient 5 was a 52-year-old woman who had recurrent breast cancer in the right precordial region (Tables 1 and 2 and Fig. 3). A perforator arising from the superior epigastric artery was detected by indocyanine green angiography, and an island flap was elevated to cover the defect using this vessel as the pedicle. This flap remained completely viable without any problems (**see Video, Supplemental Digital Content 2,** which demonstrates indocyanine green angiography in patient 5, ***http://links.lww.com/A499***).

DISCUSSION

After indocyanine green is injected intravascularly, it binds to plasma proteins immediately. Although it remains protein-bound, indocyanine green is a fluorescent substance that absorbs light with a maximum at 805 nm and emits fluorescence with a maximum at 835 nm.[10] Light at a wavelength of approximately 800 nm (the near-infrared range) is little absorbed by either water or hemoglobin and is not scattered by the tissues. Thus, indocyanine green fluorescence occupies a "biological spectral window" that allows excellent visualization of deep structures in the living body.[22] Indocyanine green shows extremely rapid excretion into the bile, and its plasma half-life is only 3 to 4 minutes in healthy adults. We confirmed that indocyanine green fluorescence was hardly detectable by 30 minutes after indocyanine green injection in a pilot study. There have been very few reports of anaphylactic reactions to indocyanine green. However, its use is contraindicated in patients with iodine allergy because the product contains iodine.[23] In the present study, blood vessels could be outlined at a depth up to 2 cm from the body surface. This depth corresponds approximately to the fascial level, suggesting that indocyanine green angiography is suitable for preoperative identification of perforators before raising a flap. If the imaging method only achieves visualization of shallower structures, the course of perforators becomes difficult to observe. In contrast, if blood vessels at a greater depth are also delineated along with the skin perforators, it becomes difficult to distinguish the perforators from the deeper arteries and muscular branches that have no role in skin blood flow, so that false-positive results may be obtained, as frequently occurs with the Doppler stethoscope. Image contrast was generally better after intraarterial injection than after intravenous

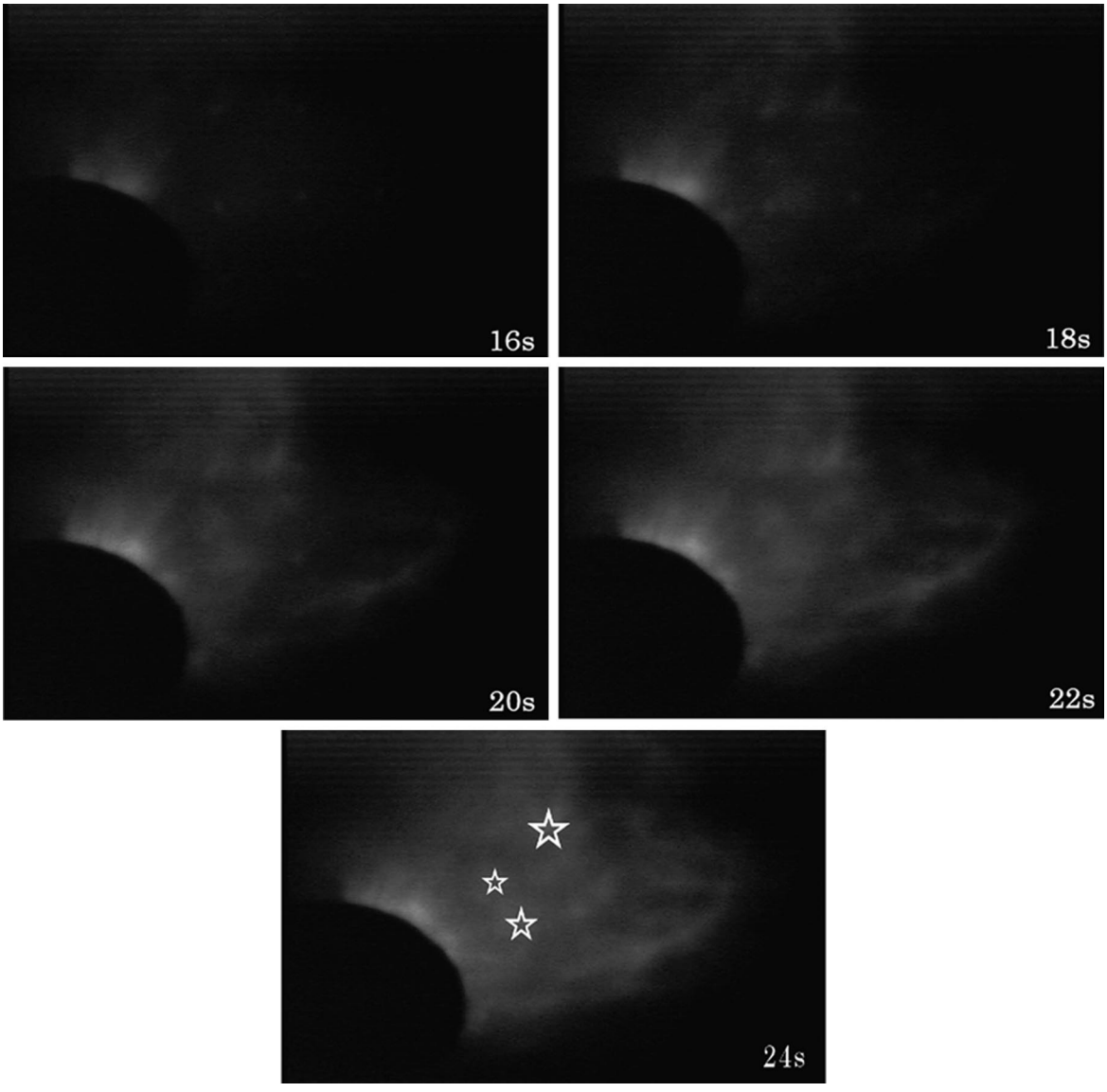

Fig. 3. Indocyanine green angiography of patient 5. The patient was placed in the supine position and the hand probe of the PDE system was fixed 30 cm above the skin using a clamp. The tumor had a high blood flow and was erythematous, suggesting that fluorescence would be generated by indocyanine green, so it was covered with a black rubber sheet. In the right epigastric region, which was the candidate site for the flap, dots were marked at 3-cm intervals. A dose of 2.5 ml of indocyanine green (5 mg/ml) was injected into the left femoral vein and recording was started immediately with the near-infrared video camera. Pulsating vessels appeared at three locations from 16 seconds after the intravenous injection of indocyanine green. The number in the lower right corner of each image indicates the number of seconds after injection of indocyanine green.

injection, probably because the concentration of indocyanine green in the perforators increases very rapidly after intraarterial injection.

Perforator-based flaps have been widely used over the past decade, and there is an increasing demand for better selection of donor sites, a shorter operating time, and smaller flaps. Therefore, the precise detection of perforators preoperatively has become more important than before. Conventional angiography,[1] magnetic resonance angiography,[2] computed tomographic angiography,[3] ultrasonic Doppler flowmetry,[4–7] laser Doppler imaging,[8] and recovery-enhanced thermography[9,10] have all been used clinically for this purpose. Compared with those imaging techniques, indocyanine green angiography has the advantage of more precisely identifying the perforators and the direction of blood flow, and the information provided can be applied

directly to the planning of skin flaps. Precise visualization of perforators with indocyanine green angiography is achieved by the high resolution (6 million pixels and 60 frames/second) of the new video camera system. In addition, this system has the advantage of low background noise because a light-emitting diode is used as the excitation light source. Although visualization in the arterial phase lasts for only a few seconds, computer-aided recording and analysis allow precise mapping of the perforators on the skin.

Sufficient information about the perforators for the performance of flap surgery was obtained in all of the patients in the present series. Therefore, identification of perforators by indocyanine green angiography is considered to be a useful preoperative examination that can improve the safety and reliability of flap surgery.

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