



A technique for safe deep facial tissue dissection: Indocyanine green–assisted intraoperative real-time visualization of the vasa nervorum of facial nerve with a near-infrared camera

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ABSTRACT

During deep tissue dissection in the face, it is sometimes difficult to distinguish the facial nerve from surrounding tissue, leading to a risk of facial nerve injury. To identify the facial nerve during such procedures, we used a fluorescence-assisted near-infrared camera. Indocyanine green (ICG)-assisted direct visualization was used intraoperatively in 13 cases. The procedures included excision of neurofibromas ($n = 10$) and lymphatic malformations ($n = 3$). Intravenously injected ICG was distributed systemically and filled the lumen of epineural vessels around the nerves (vasa nervorum) within 1 min. The nerve trajectories were directly visualized using a fluorescence-detecting near-infrared camera. The facial nerve was distinguishable from surrounding tissues such as retaining ligaments and, in all cases, was safely secured, preserving postoperative facial nerve function. Postoperative mean differences of left/right facial volume were significantly reduced compared with preoperative values. Patient satisfaction ranged from satisfied to very satisfied. Injuries to the facial nerve could be effectively avoided via direct intraoperative visualization of the vasa nervorum of nerve through intravenous ICG injection. A portable near-infrared camera enabled direct and real-time visualization of the vasa nervorum, facilitating injury prevention. This technique might help to reduce the risk of disastrous complication of facial palsy through a simple and efficient method.

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1. Introduction

Facial nerve injury during deep facial tissue dissection is relatively rare but has disastrous complications when it occurs (Hohman et al., 2014). The reported incidence of iatrogenic facial nerve injury has ranged from 0.6% to 20% depending on the type and location of surgery (Azzadeh and Mashkevich, 2009; Niamtu, 2009; Nilssen and Wormald, 1997; Harner and Leonetti, 1996). In plastic surgery, many procedures require dissection of deep facial tissue where the facial nerve lies, such as tumor excision, reconstruction for facial paralysis, and cosmetic facelifts. Retaining

ligaments grossly resemble the features of the facial nerve, often making it difficult to distinguish which tissue to cut (Matarasso et al., 2000). In cases of facial deformities such as neurofibroma and lymphatic malformation, the normal facial tissue anatomy can be compromised, making it difficult to distinguish the facial nerve from other structures. In other cases, concerns about iatrogenic facial nerve injury results in insufficient tumor resection and an unsatisfactory surgical outcome.

Identifying and distinguishing the facial nerve from adjacent tissue during deep facial tissue dissection is crucial, not only for preserving facial motor functions but also for obtaining sufficient lifting effect in facelift procedures or sufficient tumor resection. Recent studies have reported a decreased occurrence of nerve complications after surgery; however, avoiding such complications is crucial, as nerve branch injuries with no intercommunication can result in permanent functional loss (Matarasso et al., 2000; Mendelson, 2013).

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There are many reports on preservation strategies using anatomical consideration to prevent facial nerve injury (Mendelson and Wong, 2013; Narasimhan et al., 2013; Roostaeian et al., 2015). Most such strategies have explained the trajectory of the facial nerve based on facial surface landmarks, or on the relative level and position to the surrounding structures. Although anatomical considerations provide invaluable information, it is often difficult to apply these concepts during the operation. Facial surface landmarks may differ due to skin-flap traction or difficulty in distinguishing the surrounding structures because of distortion. Owing to the limitations of current facial nerve visualization techniques, we utilized indocyanine green (ICG)-assisted direct visualization of the vasa nervorum of facial nerve during surgeries involving deep facial tissue dissection, to investigate the effectiveness of real-time direct visualization with a near-infrared camera.

2. Materials and methods

2.1. Patient population

The study was conducted prospectively from November 2014 to October 2016, and consecutive patients requiring deep facial dissection at our hospital during this period were prepared for ICG and near-infrared camera visualization in the operating room, except for one patient with a history of allergy to ICG. The inclusion criteria were (i) consent to study participation, (ii) availability of preoperative and postoperative three-dimensional (3D) facial scans, and (iii) facial asymmetry due to a tumor mass. The exclusion criteria were (i) a history of allergy to ICG, (ii) a patient who does not require ICG injection for evaluation of facial nerve. Informed consent for both study participation and publication of identifying images in an online open-access publication were obtained from all patients and the study design was reviewed and approved by Institutional review board of Asan Medical Center (Date of registration: 09/08/2018, Registration number: 2018-0949).

2.2. Medication and device

In our study, a customized near-infrared camera was made for facial nerve detection (Fig. 1). This device consists of a digital single-lens reflex (DSLR) camera equipped with a near-infrared light-emitting diode that produces light that can penetrate tissue more deeply than visible light. Fluorescence images from the ICG injection and near-infrared camera were digitalized for real-time imaging by using a personal computer.

2.3. Surgical procedure and ICG nervography

For patients with neurofibromas and lymphatic malformations, surgery was performed for tumor resection. In some cases, a facelift was simultaneously performed when facial drooping was anticipated. During dissection for complete tumor excision, further deep facial tissue dissection complicated the distinction between the nerve and surrounding structures. In the aforementioned situations, the prepared ICG solution was injected intravenously. ICG (25 mg) was mixed in 5 mL normal saline solution, and one to three injections were done in each case. ICG has a half-life of 150–180 s and it stays for up to 30 min in the vessels. Within 1 min, intravenously injected ICG was distributed systemically, filling the lumen of vasa nervorum (Video 1). After the systemic distribution of ICG, the enhanced facial nerve could be distinguished from non-enhanced surrounding structures through direct visualization with the custom-made infrared camera. Once the enhanced facial nerve was distinguished, dissection and tumor excision were performed.



Fig. 1. Customized near-infrared camera for detecting the facial nerve.

In cases where a simultaneous sub-superficial muscular aponeurotic system (sub-SMAS) facelift procedure was performed, ICG injection was performed, if needed.

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.jcms.2019.07.011>

2.4. Characteristics of vasa nervorum

When ICG is injected not only vasa nervorum but also surrounding capillaries were enhanced, therefore, careful observation is necessary to distinguish peripheral blood vessels from nerves. Fortunately, there are typical characteristics of vasa nervorum. The nerve itself is not enhanced by injected ICG and appears dark. So vasa nervorum appear to be running around the dark tube structure which is nerve. And also, correlation with general visual findings under visible light is necessary. Because there are many sizable vessels among the structures that are enhanced in ICG, most of vessels are distinguished easily under visible light (Fig. 2). Because of this point, even though injected ICG is better seen under visible light off, ICG test was performed under visible light on in order to compare with visual findings in some cases. And above all, to evaluate these structures in detail, thorough hemostasis is required before ICG injection to prevent ICG from leaking.

2.5. Evaluation of facial nerve function

Preoperative and immediate postoperative facial nerve function was assessed with the House-Brackmann facial palsy grade system 14: grade I, normal; grade II, mild paralysis; grade III, moderate

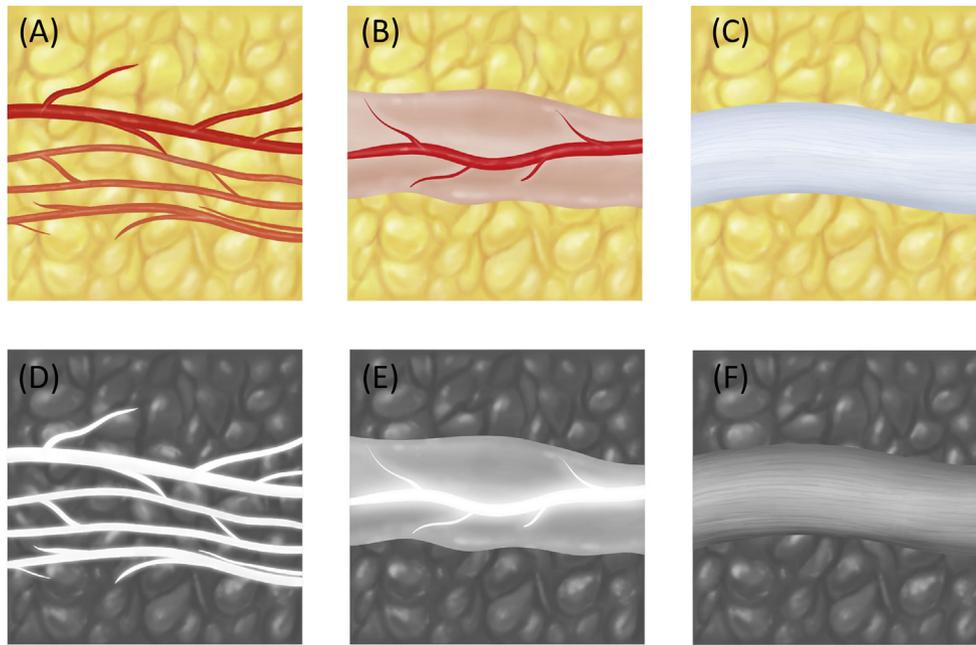


Fig. 2. Character of vessel, nerve, and ligament under visible light and indocyanine green (ICG). (A) Vessel under visible light (B) Nerve under visible light (C) Ligament under visible light (D) Vessel under ICG injection (E) Nerve under ICG injection (F) Ligament under ICG injection.

paralysis; grade IV, moderately severe; grade V, severe; and grade VI, total paralysis (House and Brackmann, 1985).

2.6. Evaluation of facial asymmetry with a 3D scanner

A Morpheus 3D® light-emitting diode-based white structured light scanner (Morpheus Co., Ltd., Seongnam, Gyunggi-do, Korea) was used to take 3D photographs of the participants while they were sitting with a neutral head position, with approximately 600 mm from the participants' face to the lens of the 3D scanner. Patients were photographed without makeup. Each scan was performed with the same brightness, and done three times preoperatively and postoperatively in the frontal, left, and right oblique views. A 3D facial image was reconstructed by merging all the images, and then the entire scanned image was automatically reoriented. The horizontal plane was set to contain the right and left pupils and the nasion, the sagittal plane was set as a perpendicular plane containing the nasion and subnasale, and the coronal plane was set to be perpendicular to the other planes. Various facial landmarks of the patients were defined to evaluate the right and left side facial volume: (i) trichion (Tr), lowest point of hairline in the center of the face; (ii) soft tissue glabella (G'), midpoint between the center of the eyebrows, the transecting point of the vertical line; (iii) subnasale (Sn), central junction of the columella and upper cutaneous lip; (iv) soft tissue menton (Me'), inferior midpoint on the soft tissue chin; (v) tragion (Tr), point located at the upper margin of each tragus, left and right; (vi) cervical point (C), neck–throat junction: the junction of the inferoposterior extension of the soft tissue chin and the neck; (vii) tragion (T), point located at the upper margin of each tragus, left and right; (viii) soft tissue gonion (Go'), lateral point on the soft tissue contour of each mandibular angle; (ix) soft tissue C point (C'), meeting point of the straight line from Tr and T and the horizontal plane passing through G', left and right; (x) soft tissue D point (D'), meeting point of the straight line from each T and C and the horizontal plane passing through the Sn, left and right; and (xi) soft tissue E point (E'), meeting point of the straight line from T and C and the horizontal

plane passing through the menton (Table 1). Preoperative and postoperative left and right facial volume was calculated with 3D Morpheus software (Morpheus Co., Ltd.), using the facial volume anterior to the bilateral line connecting Tr, C', T, D' Go, E', C, and Me'. Then, the left and right volume was split and recorded using the plane consisting of Tr, G', Sn, and Me' (Fig. 3).

2.7. Evaluation of patients' satisfaction

Patients' postoperative subjective satisfaction score for facial symmetry was evaluated using the visual analogue scale (VAS) (1, very unsatisfied; 2, unsatisfied; 3, neutral; 4, satisfied; 5, very satisfied).

Table 1
Landmarks for facial volume analysis.

Landmarks	Abbreviation	Definition
Trichion	Tr	Lowest point of hairline in the center of the face
Soft tissue glabella	G'	Midpoint between the center of the eyebrows, the transecting point of the vertical line
Subnasale	Sn	Central junction of the columella and upper cutaneous lip
Soft tissue menton	Me'	Inferior midpoint on the soft tissue chin
Cervical point	C	Neck–throat junction: the junction of the inferoposterior extension of the soft tissue chin and the neck
Tragion	T	Point located at the upper margin of each tragus, left and right
Soft tissue gonion	Go'	Lateral point on the soft tissue contour of each mandibular angle
Soft tissue C point	C'	Meeting point of the straight line from Tr and T and the horizontal plane passing through G', left and right
Soft tissue D point	D'	Meeting point of the straight line from each T and C and the horizontal plane passing through the Sn, left and right
Soft tissue E point	E'	Meeting point of the straight line from T and C and the horizontal plane passing through the menton, left and right

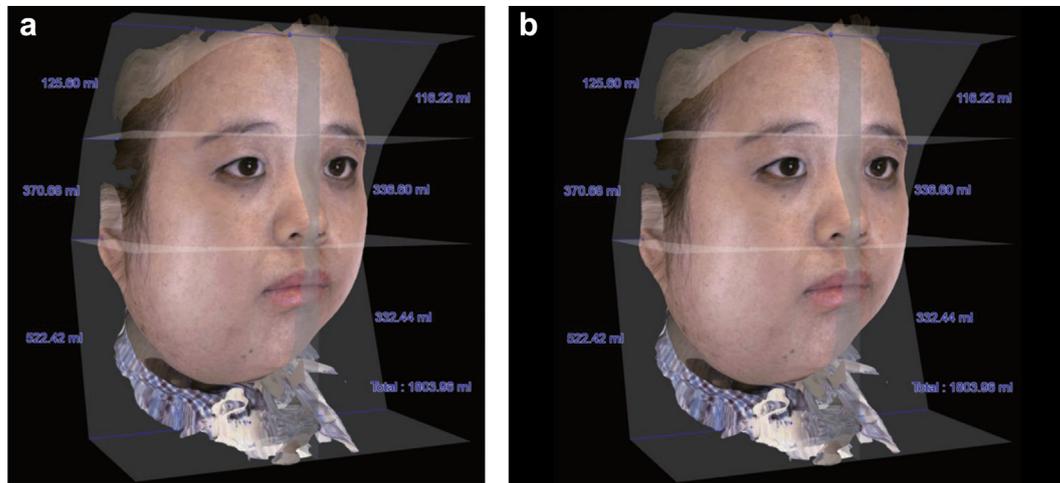


Fig. 3. Morpheus software tool was used for three-dimensional photogrammetric analysis (Morpheus Inc., Seoul, South Korea): volumetric analyses.

2.8. Statistical analysis

All statistical analyses were performed using SPSS 24.0 (SPSS Inc., Chicago, IL). Data from each group were analyzed to determine the mean p-value, as well as the standard deviation of each measurement. The between-group mean differences were calculated using the Mann–Whitney U-test with the significance level set to $p < 0.05$.

3. Results

Of the 64 cases, a fluorescence assisted visualization test was performed intraoperatively in 13 patients who required it to

distinguish the facial nerve. 51 cases who did not require a fluorescence-assisted visualization test were excluded. 51 cases were all face lift surgery for cosmetic benefit, and these patients had no specific disease. So surrounding anatomy was well maintained and facial nerve dissection was easily performed. There were eight female and five male patients, with ages ranging from 5 to 60 years (median: 35 years). Their preoperative conditions included neurofibromas ($n = 10$) and lymphatic malformations ($n = 3$). The patients' demographics are listed in Table 2.

In all cases, the facial nerve was visualized through real-time imaging and recorded using an infrared camera. Black-and-white images were obtained, with the facial nerve appearing as a white structure when perfused with ICG. There were no complications

Table 2
Demographic information and operative results of patients who underwent ICG nervography for facial nerve localization during operations requiring deep facial tissue dissection.

Patient no.	Sex	Age (years)	Primary diagnosis	Surgical procedure(s)	Fluorescein image emergence after ICG injection (s)	Number of ICG injections during operation	Facial nerve function (preop.)	Facial nerve function (immediate postop.)	Patient satisfaction (VAS)
1	M	46	Plexiform neurofibroma, Lt. face	Excision	33, 39, 53	3	Grade 1	Grade 1	5
2	F	22	Plexiform neurofibroma, Rt. face, neck	Excision, sub-SMAS facelift	59, 38	2	Grade 2	Grade 2	4
3	F	34	Lymphatic malformation, Rt. cheek	Excision, sub-SMAS facelift	46, 58	2	Grade 1	Grade 1	5
4	M	5	Plexiform neurofibroma, Rt. face, neck	Excision, sub-SMAS facelift	41	1	Grade 3	Grade 3	4
5	F	35	Lymphatic malformation, Rt. cheek	Excision	47	1	Grade 1	Grade 1	3
6	F	32	Neurofibroma, Lt. cheek	Excision, sub-SMAS facelift	38, 42, 42	3	Grade 1	Grade 1	4
7	M	5	Plexiform neurofibroma, Rt. face, neck	Excision	43, 37	2	Grade 2	Grade 2	4
8	M	49	Neurofibroma, Lt. face	Excision	42, 55, 35	3	Grade 1	Grade 1	5
9	F	9	Plexiform neurofibroma, Lt. face	Excision	53	1	Grade 1	Grade 1	5
10	F	60	Plexiform neurofibroma, Lt. neck	Extended SMAS facelift	30	1	Grade 1	Grade 1	4
11	F	56	Lymphatic malformation, Rt. cheek	Excision	36, 42, 56	3	Grade 1	Grade 1	4
12	F	19	Neurofibroma, Rt. face	Excision	43, 49	2	Grade 1	Grade 1	5
13	M	59	Neurofibroma, Rt. cheek	Excision	38	1	Grade 1	Grade 1	3

ICG, indocyanine green; preop., preoperatively; postop., postoperatively; VAS, visual analogue scale Lt., left; Rt. right; SMAS, superficial muscular aponeurotic system.

due to ICG injection. Facial nerve injury was prevented during the resection of retaining ligaments, as the adjacent soft tissue was clearly distinguishable (Figs. 4–6). Facial nerve function was preserved in the immediate postoperative phase. The average follow-up period was 12.6 months (range, 6–27 months), and no facial nerve dysfunction was observed during the follow-up period. The preoperative mean difference for right and left facial volume was 114.32 ± 45 mL, and the postoperative mean difference was 27.84 ± 27 mL. The difference between preoperative and postoperative facial volume values was statistically significant ($p = 0.013$) (Fig. 7). The mean VAS score for postoperative patient satisfaction was 4.23 (range, 3–5), corresponding to a level of “satisfied” to “very satisfied.” The results of the study are summarized in Table 2 (Figs. 8 and 9).

4. Discussion

Many patients with facial deformities such as neurofibromatosis, lymphatic malformation, and incomplete facial palsy develop facial asymmetry. Dissection of deep facial tissue is helpful for correcting facial asymmetry; however, there is a risk of injuring the facial nerve. During deep facial tissue dissection, facial nerve injury is a relatively rare but serious complication. The reported incidence of facial nerve injury ranges from <1% to

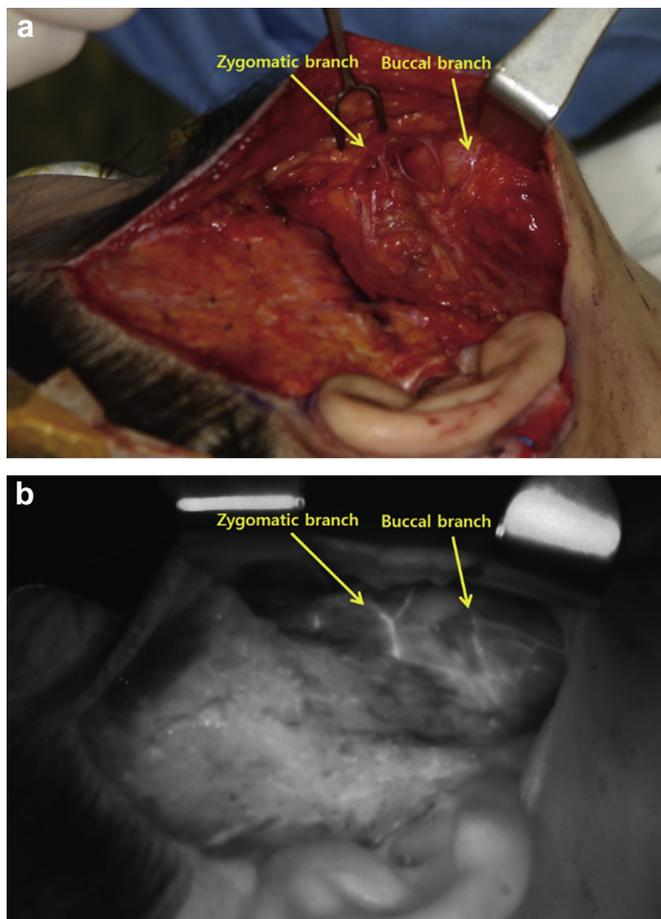


Fig. 4. Intraoperative real-time indocyanine green (ICG) nervography. (a) It was not possible to distinguish the zygomatic branch of the facial nerve from the zygomatic-cutaneous ligament grossly; (b) however, it was successfully distinguished using ICG nervography with visualization of the vasa nervorum.

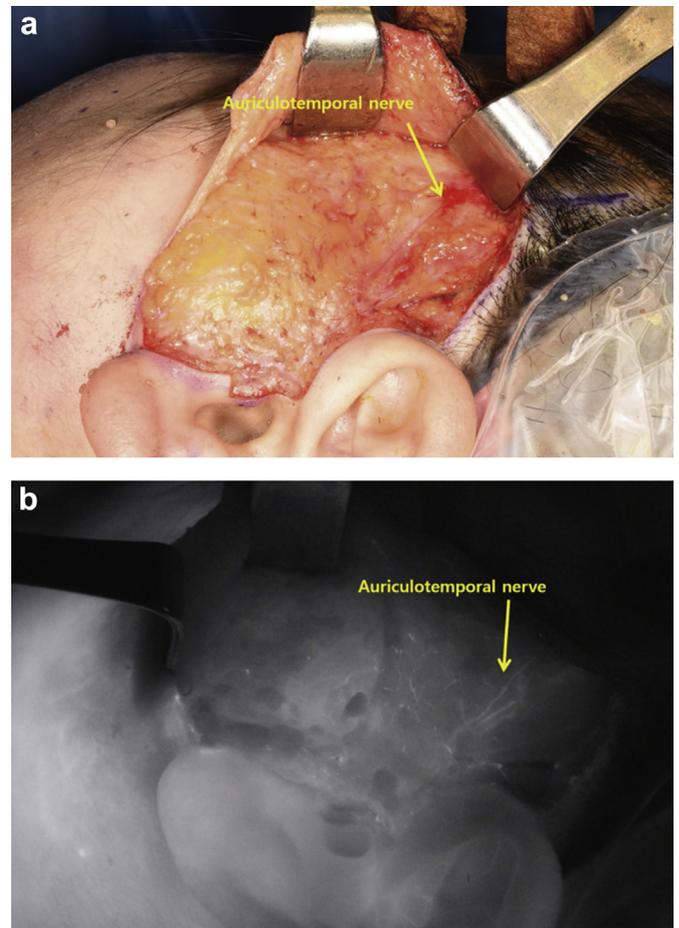


Fig. 5. Intraoperative real-time indocyanine green (ICG) nervography. (a) There were superficially lying nerve expected to be the auriculotemporal nerve; (b) it was successfully distinguished using ICG nervography with visualization of the vasa nervorum.

as high as 20%, with most studies reporting an incidence well below 1%. Jason et al. reported that it is important for surgeons to be aware of the regions where the risk of nerve injury is greatest. The facial nerve is at the greatest risk of injury in the region where the nerve branches sit most superficially and lie adjacent to retaining ligaments. To prevent facial nerve injury, plastic surgeons place great interest on identifying the specific location of the facial nerve during facelift procedures.

The buccal branch is considered the most commonly injured facial nerve branch; however, owing to its significant arborization, the injuries are typically short-lived and are often less clinically significant than injury to other facial nerve branches. Short-lived temporary paresis due to facial nerve injury can be significantly distressing for both patients and surgeons, making injury prevention essential (Mendelson and Wong, 2013; Roostaeian et al., 2015).

The key to preventing injury of the zygomatic and buccal branches is to be aware of the relative danger zones adjacent to retaining ligaments. As noted, some of the zygomatic and buccal branches can be < 1 mm deep in the region adjacent to the upper masseteric ligaments; therefore, this region must be approached with extreme caution. Techniques such as extended SMAS, high SMAS, and finger-assisted malar elevation are safely performed by taking advantage of the watershed area over the zygomatic

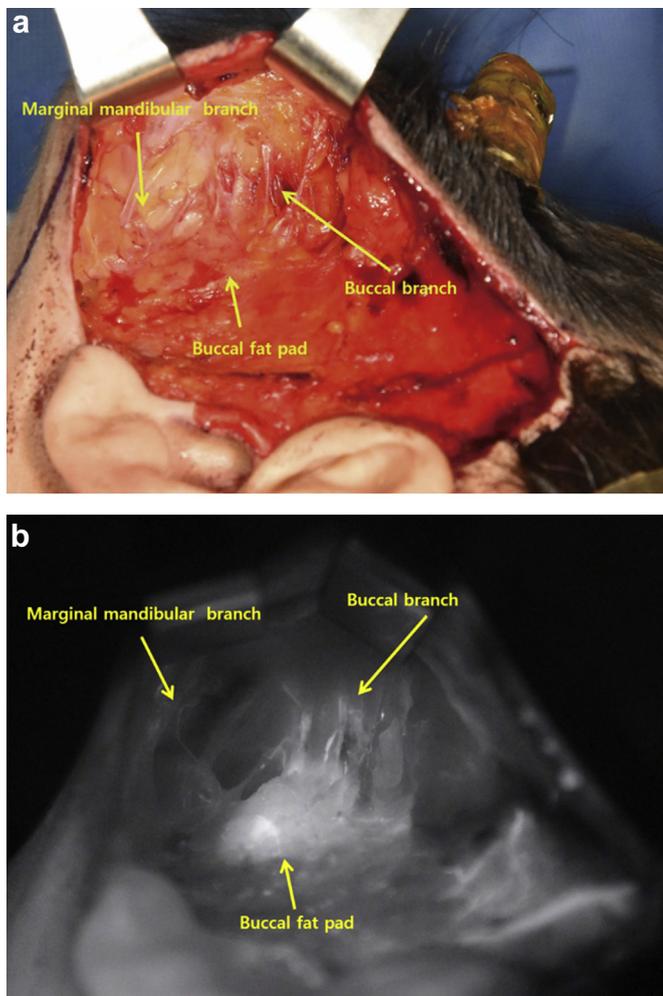


Fig. 6. Intraoperative real-time indocyanine green (ICG) nervography. (a) In deep tissue dissection of a neurofibroma, the anatomical structure is atypical and situations wherein structures cannot be distinguished mandibular retaining ligament from marginal mandibular nerve. (b) At this time, the structure can be evaluated by using ICG nervography.

eminence and staying deep in relation to the malar fat pad but superficial to the mimetic muscles.

Without direct visualization of the vasa nervorum of facial nerve trajectory, there is always a risk of nerve injury. Facial palsy is one of the most disastrous complications that can occur following a facelift surgery. There have been many efforts to identify the facial nerve during facelift surgeries. Conventional methods for visualizing the facial nerve, such as with a nerve stimulator, have been used in facial tissue dissection surgery;

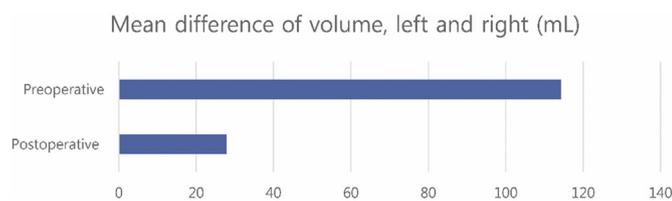


Fig. 7. Preoperative and postoperative mean difference of the right and left facial volume, with statistical significance ($p = 0.013$).

however, there are limitations, including low specificity and indirect identification of facial nerves. Furthermore, the application of the nerve stimulator on the face causes patient discomfort (Mendelson, 2013; Narasimhan et al., 2013; Roostaeian et al., 2015; Stuzin, 2007).

ICG is a near-infrared fluorescent tricarbo-cyanine dye with established diagnostic use in assessing cardiologic and hepatic functions. ICG was approved by the FDA in 1956 and has traditionally been used for detecting larger vessel diseases or investigating the small vessels of brain tumors during neurological surgeries.

ICG is also used for detecting lymph nodes during lymphedema surgery or the skin-flap blood supply in ischemic conditions. The reported adverse effects of ICG administration include urticarial and anaphylactic shock, which have only been reported to in a few cases (Kim et al., 2013; Tanaka et al., 2015). ICG has peak spectral absorption at about 800 nm and infrared frequency penetrating the retinal layers.

In our study, the facial nerve was traced with an injection of ICG and detected using a near-infrared camera. Before dissection of deep facial tissue, ICG mixed with normal saline was injected intravenously. Within 1 min after ICG injection, the dye was distributed systemically, filling the lumen of vasa nervorum. Thereafter, we could locate the facial nerve by using the near-infrared camera. The vessels reflect the facial nerve trajectory and distinguish the nerve from the retaining ligaments. Although the overall operative field is enhanced over time, the directly enhanced vessels are easily distinguishable from surrounding soft tissues.

Devices such as nerve stimulators have been utilized intraoperatively for identifying the facial nerve. A nerve stimulator can identify the facial nerve through intraoperative stimulation of facial expression muscles; however, it can be nonspecific and could not visualize the facial nerve itself. Moreover, lidocaine injection or use of muscle relaxants should be limited when using the nerve stimulator. Chen et al. reported the visualization of the vasa nervorum of facial nerve with fluorescence and a near-infrared camera during a mastoidectomy procedure. Using ICG can provide information about the regional blood flow during the surgery (Kim et al., 2013).

In some cases of facial deformity such as neurofibromatosis and lymphatic malformation, the facial anatomy is abnormal. During dissection of deep facial tissue, the facial nerve can be confused with surrounding ligamentous tissues, which compromises safety during tissue dissection. To confirm safe surgical conditions, direct visualization of the vasa nervorum of facial nerve by using ICG and a near-infrared camera can be helpful. ICG can also be applied to some cosmetic surgeries such as facelift procedures. Retaining ligaments resemble the appearance of the facial nerve, and the resection of retaining ligaments is critical for a successful facelift surgery. Distinguishing the facial nerve from ligaments through direct visualization could effectively assist the face-lifting procedure and avoid facial nerve injury. Moreover, direct facial nerve visualization can save surgical time by minimizing hesitation and reducing the anxiety of both patients and surgeons.

Besides facial tumors, visualization with a near-infrared camera after ICG injection can be useful in other patients who require dissection of deep facial tissue. Although not discussed in this paper, our technique can also be used in facial reanimation surgeries such as functional gracilis muscle transfer. Our center has applied ICG with near-infrared camera visualization for the detection of the vasa nervorum from the main pedicle to the obturator nerve in

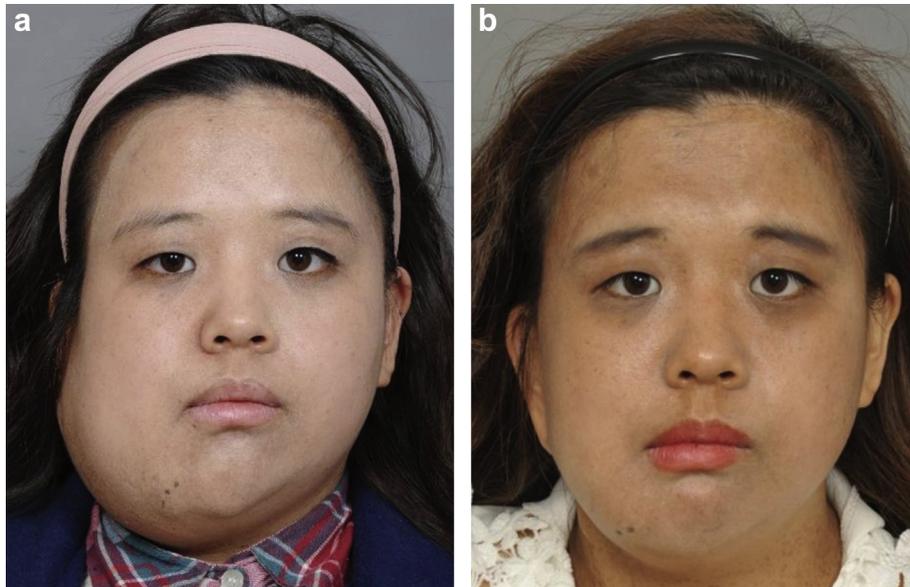


Fig. 8. A 22-year-old female with plexiform neurofibroma on her right face underwent tumor excision via preauricular incision. Through the debulking and sub-SMAS facelift combined with ICG and near-infrared camera, maximal excision of neurofibroma was performed. (a) Preoperative photograph (b) Photograph taken 6 months postoperatively.



Fig. 9. A 32-year-old female patient with neurofibromatosis on her left face underwent debulking procedure. With the help of ICG angiography, satisfactory debulking improved the patient's facial asymmetry and sensation in the temporal area, and the preauricular lesion was completely preserved without facial nerve dysfunction. (a) Preoperative photograph (b) Photograph taken 6 months postoperatively.

patients undergoing FGMC. During the dissection of the pedicle between the gracilis and adductor magnus, the tiny vasa nervorum, separated from the main pedicle along the obturator nerve, can be visualized after ICG injection (Fig. 10).

This study has some limitations. First, this was a pilot study that primarily assessed the safety and feasibility of our technique. We did not intend to conclude definitive outcomes concerning the impact of ICG fluorescence on the preservation of the facial

nerve during deep facial tissue dissection. Second, a relatively small cohort of patients was studied and their heterogeneous diagnoses limit some of our interpretations. Finally, the intra-operative visibility and confirmation of the facial nerve location with a near-infrared camera by the surgeon was subjective, and provided only qualitative results. Further studies comprising control groups should be conducted to obtain quantitative and objective data.

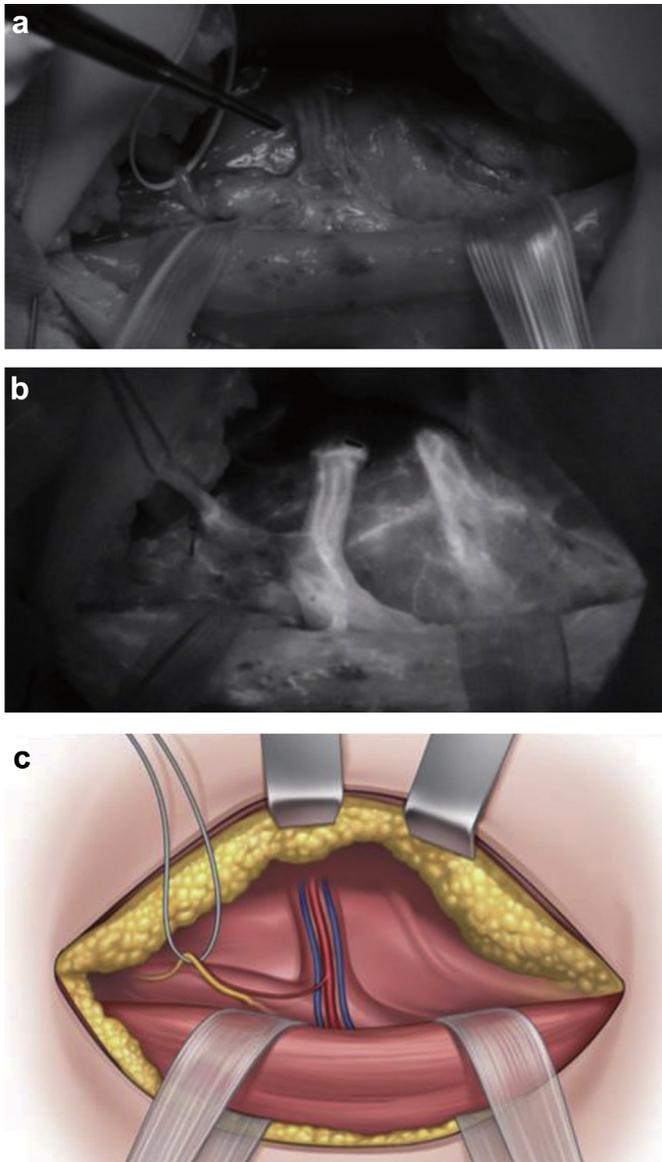


Fig. 10. Direct visualization of the obturator nerve during functional gracilis muscle transfer. (a) Complicated anatomy near the obturator nerve is ambiguous. (b) After indocyanine green injection, the vasa nervorum, which is separated from the main pedicle and runs along the obturator nerve, is clearly detected.

5. Conclusion

Injuries to the facial nerve can be effectively avoided through direct visualization of the vasa nervorum with intravenous ICG injection. A portable near-infrared camera allows direct and real-time visualization of the vasa nervorum of facial nerve, facilitating injury prevention. This technique might help to reduce the

risk of disastrous complication of facial palsy through a simple and efficient method.

Ethics statement

All procedures were conducted in accordance with the Institutional review board of Asan Medical Center.

Financial disclosure statement

This study was supported by a grant (2016-7022) from the Asan Institute for Life Sciences, South Korea.

Author contributions

Joon Pio Hong, Jong Woo Choi, Kyung Suk Koh, and Tae Suk Oh performed operations. Jin Geun Kwon, and Sung Chan Kim analysed the results. Young Jun Choi reviewed the paper from the point of view of the department of radiology. All authors reviewed the manuscripts.

Competing interests

The authors declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcms.2019.07.011>.

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