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IDEAS AND INNOVATIONS

Peripheral Nerve

Technique and Expected Benefit of Intraoperative Perfusion Imaging of Peripheral Nerves

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Summary: Peripheral nerve surgery, particularly in cases of nerve compression syndrome (NCS), necessitates a comprehensive evaluation of intraneural blood flow, as localized reductions in nerve perfusion are integral to the etiopathogenesis of such conditions. Although nerve perfusion is currently guided by morphologic characteristics, this assessment is subjective and prone to bias. Intraoperative fluorescence-assisted perfusion imaging with indocyanine green (ICG) is an established tool in flap and lymphatic surgery to objectively assess perfusion intraoperatively. However, only a few unspecific applications of ICG in peripheral nerve surgery have been published so far. In this study, we performed intraoperative perfusion imaging using ICG in 16 consecutive operations within the peripheral nervous system, including microsurgical reconstructions after obstetric brachial plexus injury, decompression for NCS, and vascularized ulnar nerve interposition transfers. Our findings show the utility of ICG in delineating healthy perfusion borders at proximal and distal stump levels after neuroma resection, and we demonstrate a correlation between histological findings and these clinically observed perfusion patterns. In NCS cases, we demonstrate that ICG imaging is effective in highlighting reduced perfusion predecompression and improved perfusion postdecompression. Additionally, ICG proved valuable for assessing perfusion of free vascularized nerve grafts. Intraoperative ICG perfusion imaging is a valuable tool during surgery of the peripheral nervous system, providing insights into the etiopathogenesis of NCS and aiding in the visualization of perfusion. This study underscores the potential of ICG in nerve surgery and its applicability for improving surgical outcomes and advancing our understanding of peripheral nerve pathologies. *(Plast Reconstr Surg Glob Open 2024; 12:e6281; doi: 10.1097/GOX.0000000000006281; Published online 5 November 2024.)*

INTRODUCTION

Indocyanine green (ICG) is a fluorescent dye that, when administered intravenously, facilitates visualization of organ or flap perfusion.[1] Dermal/subdermal administration allows visualization of lymphatic flow.[2] There are few data regarding application of ICG to peripheral nerve surgery.[3] In this article, we detail valuable intraoperative insights from ICG use in peripheral nerve surgery, particularly regarding pathophysiology of nerve compression syndrome (NCS). These syndromes involve increased pressure on a nerve, leading to impaired nerve microcirculation. Ensuing ischemia induces edema, inflammation, scarring, demyelination, and axonal degeneration.[4] Animal models have demonstrated that applying external pressure of as little as 30 mm Hg to a nerve disrupts microcirculation, which can result in thickened epineurium and endothelium[5,6] as well as edema and fibrosis.[7] In a mouse model of NCS, ICG has been used to demonstrate reduced neural blood flow.[8] However, to date, no study detailing intraoperative evaluation of nerves' blood perfusion in human patients has been published.

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Currently, intraoperative frozen section diagnostics serve as a crucial tool for assessing quality of neuroma resection borders. Extent of endo-, peri-, and epineurial fibrosis; the presence of neuroma; and the degree of Schwann cell loss and nerve fiber regeneration are assessed.[9] Although this can be useful in guiding decisions regarding further stump resection, the process takes considerable time and resources. This study explores ICG-based perfusion evaluation of nerve stumps as a potential add-on.

METHODS

Depending on the nerve size, a Pentero800S surgical microscope (Zeiss, Oberkochen, Germany) or Fluobeam LM infrared camera (Fluoptics, Grenoble, France) was used for visualization of intraoperative perfusion. ICG solution (PULSION Medical Systems, Feldkirchen, Germany) was dissolved at a concentration of 2.5 mg/mL in aqua. Adults received an IV injection of 5 mL. In children, a weight-adjusted injection of 0.3 mg/kg of body weight was administered. Sixteen consecutive peripheral nerve procedures were evaluated: 4 microsurgical reconstructions after obstetric brachial plexus injury (OBPI), 9 decompressions for NCS, and 3 contralateral C7-transfers with vascularized ulnar nerve interposition. The cost of one application is approximately $170 and requires an additional operation time of less than 5 minutes.

In 4 OBPI cases (patients 5–12 months of age), ICG imaging was performed during supraclavicular exploration of each affected brachial plexus to differentiate nerve segments affected by in-continuity neuroma from adjacent intact nerve, and excision was performed at this transition point (Fig. 1). Perfusion of the resected border was then assessed. (**See figure, Supplemental Digital Content 1**, which illustrates the resection border, **http://links.lww.com/PRSGO/D593**.) The resected material was sent for histological analysis. Histological examination consistently showed good quality of the cut edge, as evidenced by intact fascicular structures with little or no neuroma tissue or fibrosis. In healthy nerves, there were larger blood vessels in surrounding tissue. The neuroma contained a high number of disorganized small blood vessels which were diffusely distributed (Fig. 2).

Nerve decompression [Guyon canal, superficial branch of the radial nerve, cubital tunnel, the thoracic outlet, posterior interosseous nerve (PIN), and peroneal nerve] was performed in nine patients (aged from 26 to 74 years). Before decompression, a weakened ICG signal was noted along each of these nerves, including the segment proximal to the compression sites, indicating reduced perfusion (Fig. 3). After decompression, the blood flow of the ulnar nerve normalized (Fig. 4). In cases of PIN syndrome, although a weak signal was noted in the PIN, increased signal intensity was noted in the adjacent, unaffected superficial branch of the radial nerve and in the motor branches to the wrist extensors. After PIN decompression at the level of the arcade of Frohse, perfusion of the PIN normalized after a few minutes, and the ICG signal was similar to that from the adjacent unaffected nerves. [**See Video (online)**, which displays the weak signal of ICG in the PIN before decompression can be seen first. After decompression, 7 minutes after first visualization, without any additional injection, the perfusion of the PIN normalized.]

Takeaways

Question: Is there an advantage of intraoperative perfusion imaging in peripheral nerve surgery by using indocyanine green in neuroma resection, nerve decompression, and vascularized ulnar nerve transfer?

Findings: In this study, we demonstrate the possibility of assessing quality of cutting edges after neuroma resection, an improvement of peripheral nerve perfusion after decompression and the blood perfusion of free vascularized nerve grafts.

Meaning: The use of indocyanine green to assess blood flow to peripheral nerves provides new intraoperative information and benefits intraoperative decision-making.

In severe brachial plexus lesions with limited intraplexic axon donors, often associated with multiple root avulsions, use of extraplexic nerve donors such as contralateral C7 (cC7) may become necessary.[10] Direct coaptation of C7 root with a recipient nerve is rarely an option, and interposition grafts must be used. In three patients (16–21 years of age), the ulnar nerve of the injured upper limb was transplanted as free vascularized nerve graft to the contralateral C7 root. Perfusion was visualized using ICG before coaptation of the ulnar nerve to the C7 roots and contralateral recipient nerve. Blood supply was provided through an anastomosis of vasa nervorum to the

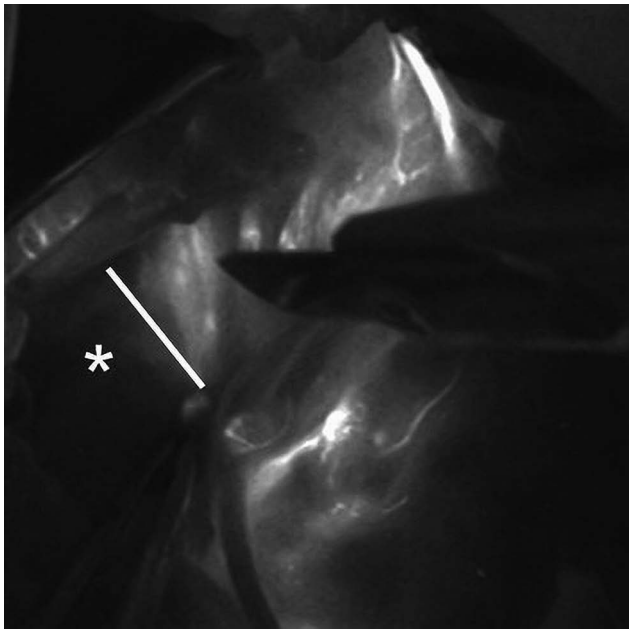

Fig. 1. Intraoperative images of a neuroma excision. ICG imaging of the border between a poorly perfused neuroma (*) of the brachial plexus after OBPI and the well-perfused nerve structure (white color indicates normal perfusion). The resection border is marked by the line.

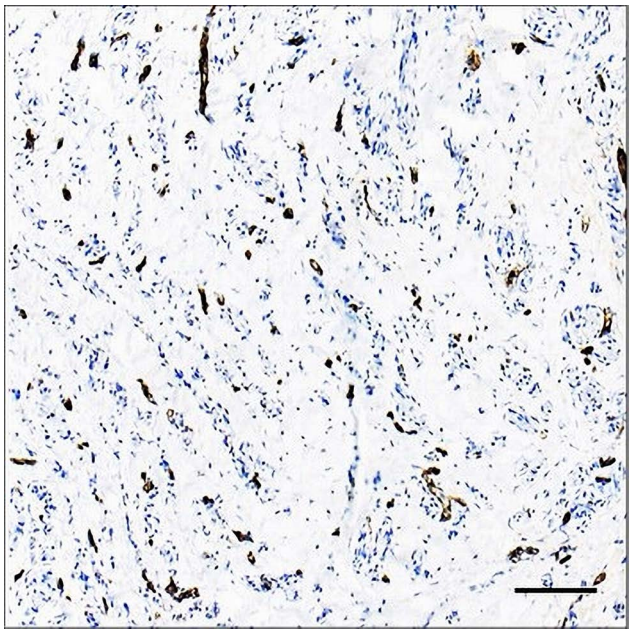

Fig. 2. Several irregular, randomly oriented, mostly capillary or collapsed small vascular structures in between numerous groups of sprouting nerve fibers (so-called minifascicles) in neuroma. No larger blood vessels are seen (endothelial cell specific immunostaining, detected antigen CD31/PECAM-1; scale bars = 65 µm).

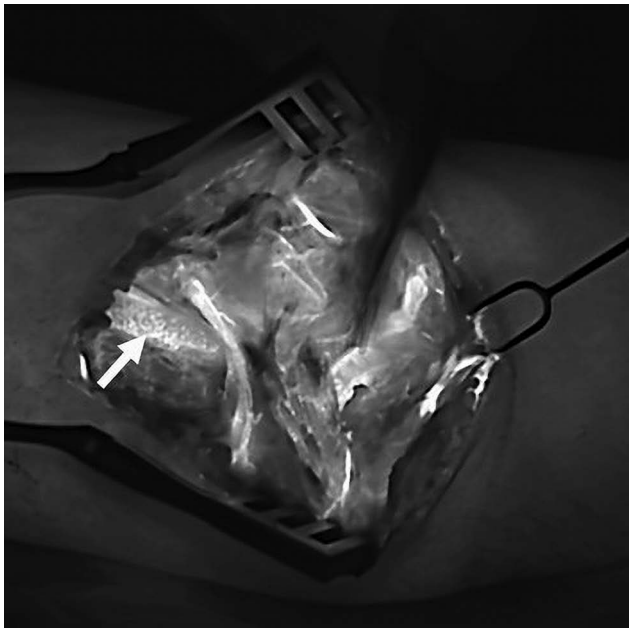

Fig. 3. Intraoperative images from a cubital tunnel decompression. The ulnar nerve shows reduced perfusion in its course in the cubital tunnel (→).

transverse cervical artery and vein and was confirmed using ICG angiography. (**See figure, Supplemental Digital Content 2**, in which blood flow after anastomosis is shown, **http://links.lww.com/PRSGO/D594**.)

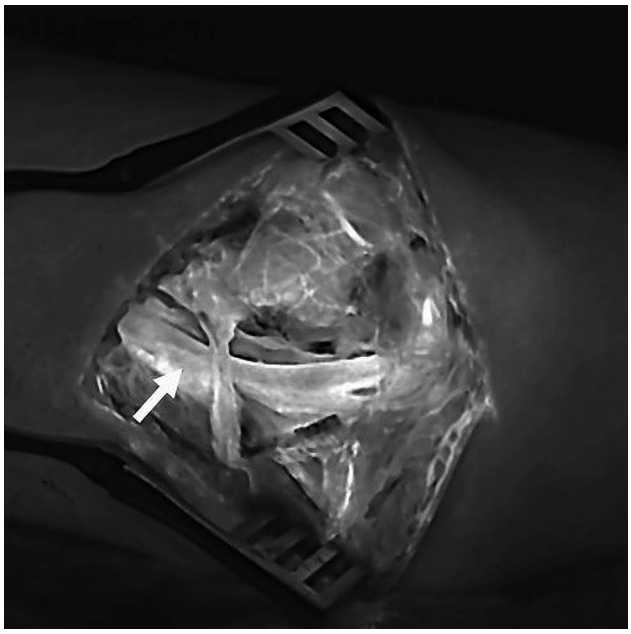

Fig. 4. After decompression, normal perfusion of the ulnar nerve quickly becomes apparent (→).

DISCUSSION

NCS is characterized by diminished blood flow to the peripheral nerve. In this article, we show that this phenomenon can be effectively visualized through ICG imaging techniques, which are safe, straightforward and require only a few minutes.[11] Our study demonstrates the potential of ICG in revealing enhanced blood flow after decompression, which may determine the surgical endpoint of adequate decompression while minimizing unnecessary exposure. This technique is limited by the need for a clear view of the nerve. In addition, the ICG signal of adjacent perfuse tissue my interfere, leading to the erroneous impression of a well-perfused nerve. The need for full visualization of a nerve without any interference may prove problematic in many NCS procedures, as target nerves may only be partially visualized.

It has been demonstrated that vascular patency in free nerve grafts may be observed by incorporating a monitor skin island into the graft design. We demonstrate that ICG can show perfusion across a vascularized nerve graft, ensuring that the nerve remains well-perfused in its new positioning; however, once a procedure is complete and the nerve can no longer be directly visualized, ICG has no further utility.

Our comparison of ICG-based perfusion characteristics of the cut edges of a nerve during neuroma resection with histological examination reveals a correlation between the edge of visualized perfusion and histologic characteristics. Surrounding vessels of healthy nerve are probably visualized, whereas perfusion of capillaries within the neuroma cannot be imaged. However, although blood flow serves as 1 criterion for assessing nerve quality, factors such as the formation of new (myelinated) nerve fibers, the presence

of minifascicles, the loss of Schwann cells, and the degree of scarring can only be assessed histologically. Thus, although ICG imaging provides valuable information, it cannot replace histological examination. In a recently published study, Yang et al[12] used ICG to visualize injuries. In this study, the impaired axonal transport was visualized in a mouse model. In our investigations, we showed the perfusion of the nerves as a marker.

Future studies will include more patients, covering a wider range of surgical interventions. In conjunction with intraoperative observations, we plan to develop structured processing of both intraoperative ICG imaging and histological analysis to optimize the value of these data. It would certainly be useful to perform animal studies that specifically examine the benefits of the technology in the context of NCS.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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