

Sensory Nerve Transfers and Direct Neurotization: The New Frontier in Peripheral Nerve Surgery

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ABSTRACT

The field of peripheral nerve surgery has experienced significant growth over the past few years as a result of the development of more effective treatment strategies such as direct nerve coaptation or complex nerve transfers. The majority of reconstructive procedures place a high priority on restoring motor function, however sensory restoration is commonly neglected during these operations. The loss of protective sensation increases the risk of developing injuries to the body, such as corneal ulcers, pressure sores, and hand injuries on the ulnar edge. In addition, the increased risk of developing neuropathic pain or depression adversely impacts the quality of life of patients. Researchers and clinical centers have shown interest in sensory nerve reconstruction in a variety of anatomical locations. The purpose of the study is to provide a comprehensive review of the various options available for nerve transfers and direct neurotization in various parts of the body.

INTRODUCTION

The clinical manifestations and consequences of peripheral nerve injuries have been well documented since ancient times. Nevertheless, the concepts of axonal repair and nerve reconstruction were not developed until the 20th century. The primary purpose of peripheral nerve surgery is to restore motor function, with sensory function being a secondary goal [1].

The loss of protective sensation increases the likelihood of injuries to the body, such as corneal ulcers, pressure wounds, or damage to the ulnar border of the hand. There is also a possibility that sensory loss may lead to autonomic dysfunctions, such as dry skin, a lack of sweating, and even impaired wound healing [2]. There is evidence that neuropathic pain and depression associated with sensory loss may have a negative effect on a patient's quality of life [3,4]. Due to the importance of regaining sensory function, the study aims to provide a comprehensive literature review of techniques developed for restoring sensory function in various parts of the body.

RECONSTRUCTIVE STRATEGIES

Over the past decade, advances in surgical techniques have enabled a wide range of strategies to be employed to restore peripheral sensory function. Among the various methods of nerve reconstruction, primary nerve repair is considered the gold standard. When there is a long gap between nerves, surgical interventions such as nerve grafting, nerve transfers, or direct neurotization may be employed [5].

Through nerve grafting and nerve transfers, sensory function is restored by stimulating the growth of axons into a native recipient nerve. End-to-end nerve repairs are the most common type of nerve repair, but end-to-side repairs allow minimal sensation loss at the donor site, which leads to collateral sprouting in sensory nerves without an epineurial window [5,6].

If nerve endings cannot be repaired, direct neurotization may be the last option. The technique involves the connection of nerve fascicles to a target organ such as the cornea or skin. While the exact mechanism of action is unknown, it may also restore sensation and trophism [7].

In contrast to motor reconstruction, sensory reconstruction appears not to be time-sensitive, and there is no consensus regarding a maximum timeframe [6]. The following sections provide an overview of reconstructive procedures performed on the face, the breast, the upper extremities, and the lower body. Table 1 summarizes various nerve options that can be utilized in reconstructive surgery, depending on the area of the body being treated.

FACIAL REGION

Trigeminal Sensory Neuropathy

The trigeminal nerve transmits sensory information from the head and neck through its ophthalmic (V1), maxillary (V2), and mandibular (V3) divisions. There are several etiologies that may result in changes in facial sensation, such as fractures, intracranial tumors, and iatrogenic injuries [8]. With trigeminal anesthesia, there is a risk of injury to the soft tissues of the face [9]. Injuries commonly observed during trigeminal anesthesia are biting of the lip, cheek, and tongue on the affected side, which may occur without nociceptive feedback. Occasionally, trigeminal anesthesia can result in corneal ulceration, which can eventually lead to blindness in some cases. Trigeminal trophic syndrome can also develop in a subset of patients following trigeminal anesthesia [9].

Tactile sensation can be restored in the maxillary (V2) and mandibular (V3) territories by transferring axons from the contralateral infraorbital and mental nerves either directly or by means of cross-face grafts. Several studies have demonstrated that facial sensation can be restored within a few months following surgery. Kaban and Upton report the case of a female patient who gradually regained sensation of the left mental nerve

Table 1. Various Nerve Options for Reconstructive Surgery Depending on the Region of the Body

Anatomical region	Donor nerve	Recipient nerve
Face	Contralateral infraorbital nerve	Infraorbital nerve
	Contralateral mental nerve	Mental nerve
	Contralateral supraorbital or supratrochlear nerve	Sclerocorneal limbus
Breast	4 th to 7 th intercostal nerves	10 th to 12 th intercostal nerves (DIEP flap / TRAM flap); thoracodorsal nerve (LDM flap); cutaneous femoral nerve (ALT flap)
	4 th intercostal nerve	Nipple-areolar complex
Trunk	Lower intercostal nerves	Sciatic nerve
	Medial antebrachial cutaneous nerve	Lateral femoral cutaneous nerve
Upper extremities	Common digital nerve to the 4 th webspace or dorsal cutaneous branch (ulnar nerve)	First webspace nerve
	3 rd webspace nerve or palmar cutaneous branch (median nerve)	Ulnar sensory fascicle
	Lateral antebrachial cutaneous nerve (musculocutaneous nerve)	Radial sensory nerve
Lower extremities	Deep or superficial peroneal nerves	Tibial nerve
	Saphenous nerve	Tibial nerve / sural nerve
Penis	Femoral nerve / ilioinguinal nerve	Dorsal nerve of the penis / corpus cavernosum

ALT, anterolateral thigh; DIEP, deep inferior epigastric perforator; LDM, latissimus dorsi myocutaneous; TRAM, transverse rectus abdominus myocutaneous.

distribution as well as light touch and protective sensations one year after surgery [10]. Koshima et al. reported two cases of trigeminal nerve II palsy that were repaired by contralateral trigeminal nerve transfer without the use of any nerve graft [11]. The affected upper labial sensory recovery was 1.65 to 2.44 (Semmes-Weinstein values) and 15 to 30 mm (moving 2-point discriminations) in the 12 to 18 months following surgery. Catapano et al. published a case series in which the return of protective sensation was obtained after 5 months of surgery [12]. Moreover, tactile sensation in the lower lips was restored after 12 months of treatment. A case reported by Mucci and Dellon described a successful transfer of the supraclavicular nerve to the mental nerve, which resulted in the return of protective sensation and tactile sensation to the lower lip [13].

Neurotrophic Keratopathy

It is well known that neurotrophic keratopathy greatly increases the risk of corneal ulcers, scarring, and loss of vision. A potentially curative surgical procedure, corneal neurotization, has recently been introduced as a means of preventing complications associated with neurotrophic keratopathy for patients. It has been shown that this procedure can effectively restore corneal sensitivity and reverse corneal changes [14].

As early as 2009, Terzis et al. reported direct corneal neurotization through the transfer of contralateral supraorbital and supratrochlear nerves to the sclerocorneal limbus (direct corneal neurotization, Figure 1) [14]. The technique was later simplified by interposing nerve grafts between the contralateral supratrochlear nerve and the cornea (indirect corneal neurotization) [15]. Both direct and indirect approaches to corneal neurotization result in comparable improvements in corneal sensitivity, trophism, and sub-basal nerve restoration after surgery [16].

Lingual Nerve Neuropathy

The lingual nerve is particularly susceptible to iatrogenic damage during the extraction of the third molar due to the proximity of the nerves in the

area, resulting in pain, altered sensations, and even numbness in the anterior third of the tongue [17]. It has been demonstrated that indirect graft nerve repair, whether using an autograft or an allograft, is associated with improved subjective and objective nerve outcomes when compared to direct nerve repair [17]. However, in special circumstances such as large oncological resections where the ipsilateral trunk is not available, bridging from the contralateral lingual nerve may be necessary [2].

BREAST

The technique of oncological breast surgery has evolved towards less invasive techniques with improved aesthetics. Nevertheless, diminished breast sensation after a mastectomy remains one of the most common complaints. There is a possibility that spontaneous sensory recovery may occur, but the timing of recovery is unpredictable. According to the literature, the rate of recovery may vary between 0% and 47% [18-20].

Harvesting a sensory cutaneous nerve from the transferred flap is an option for providing sensation following autologous breast reconstruction. A variety of different nerves are commonly used as donor nerves. The 10th and 12th intercostal nerves are commonly used as donor nerves for abdominal flaps, the thoracodorsal nerve for the latissimus dorsi flap, and the lateral femoral cutaneous nerve for the anterolateral thigh flap. These nerves are usually coapted to the 4th to 7th intercostal nerves at the recipient site [21,22].

There is evidence from two systematic reviews that the sensory function of neurotized flaps may recover more quickly than that of non-neurotized flaps, which may result in improved quality of life for patients [18,23]. Research has shown that abdominal-based flaps and latissimus dorsi flaps provide the most favorable results. While neurotization has produced positive results, its effectiveness is still subject to debate due to its added operating time, donor site morbidity, and cost [23].

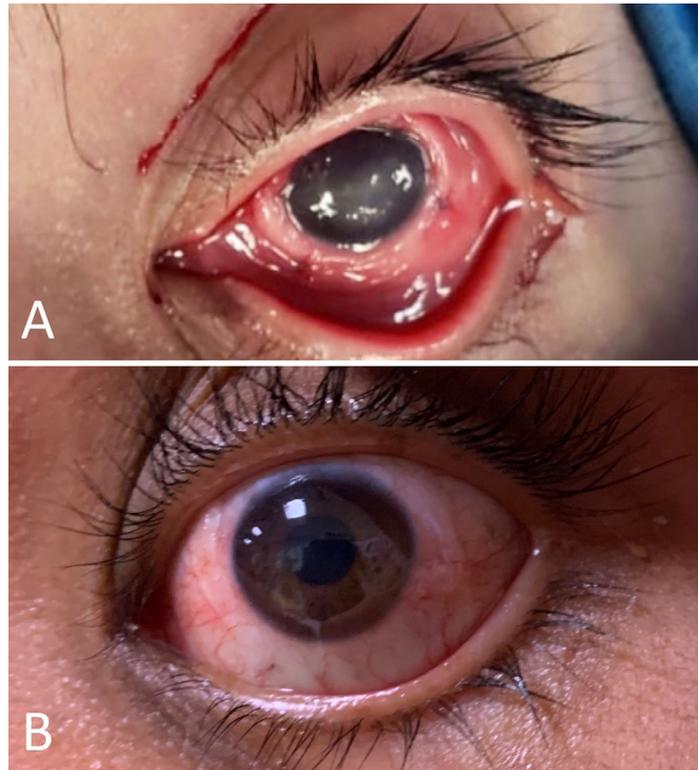


Figure 1. The case illustrates a 16-year-old male with neurotrophic keratopathy following the removal of an intracranial tumor. (A) A photograph taken during surgery demonstrates the opacity of the cornea and the nerve graft ends at the sclerocorneal limbus. (B) The postoperative photograph shows that the opacity has resolved one year following the procedure.

Recent studies have suggested that it may be possible to direct neurotize the nipple-areola complex by using the 4th intercostal nerve after nipple-preserving mastectomy. There have been several promising early reports on the recovery of sensation 10 to 15 months after the procedure [24-26].

UPPER EXTREMITIES

Hand and digital nerve reconstruction are commonly performed procedures to restore fingertip sensation, which is essential for fine motor tasks [27]. In most cases, direct nerve repair or nerve graft interposition results in successful results; however, distal nerve transfers are required in patients with large nerve gaps or proximal injuries [28-30].

Median Nerve Deficit

The median nerve deficit results in loss of sensation along the volar aspects of the thumb, index, long, and radial borders of the ring fingers. In order to restore sensory function to the first web space, terminal branches of the ulnar nerve (such as the common digital nerve) can be transferred to the fourth web space or the dorsal cutaneous branch to the first web space nerves in a direct end-to-end manner. It has been reported that the common digital nerves of the second and third web spaces can be transferred end-to-side to the ulnar digital nerve of the small finger to restore protective sensation in less critical distributions [30].

Ulnar Nerve Deficit

The ulnar nerve injury results in diminished sensation in the fourth web space and on the ulnar side of the small finger, which are essential for

grasping and protective sensation. Reconstruction can be accomplished by performing an end-to-end transfer from the median nerve fascicle to the third web space and to the ulnar sensory fascicle. In this area, alternative donors may include the palmar cutaneous nerve branch or even the median nerve proper [31]. When both the median and ulnar nerves are injured, it may be beneficial to transfer the superficial branch of the radial nerve to both targets to restore protective sensation to their respective territories [32,33].

Radial Nerve Deficit

The dorsum of the hand is not considered to be a critical surface, however, some strategies have been developed to restore sensory function in patients with radial nerve injuries, such as a direct end-to-side transfer of the radial nerve to the median nerve, or a lateral antebrachial cutaneous nerve transfer to the radial nerve [28].

LOWER BODY

Sensate reconstruction of the lower body is of significant benefit to patients who have suffered spinal cord injuries or peripheral nerve damage in their lower limbs. The loss of protective sensation can result in repeated trauma, chronic non-healing ulcers, infections, malnutrition, and even amputation of the limbs if it is not treated in time [34].

Transfer of Sensory Branches from the Peroneal Nerve

Several nerve transfers have been described for the legs, although these are far less common than those described for the upper extremities. It was initially reported by Gordon and Buncke [35] that nerve transfers from the

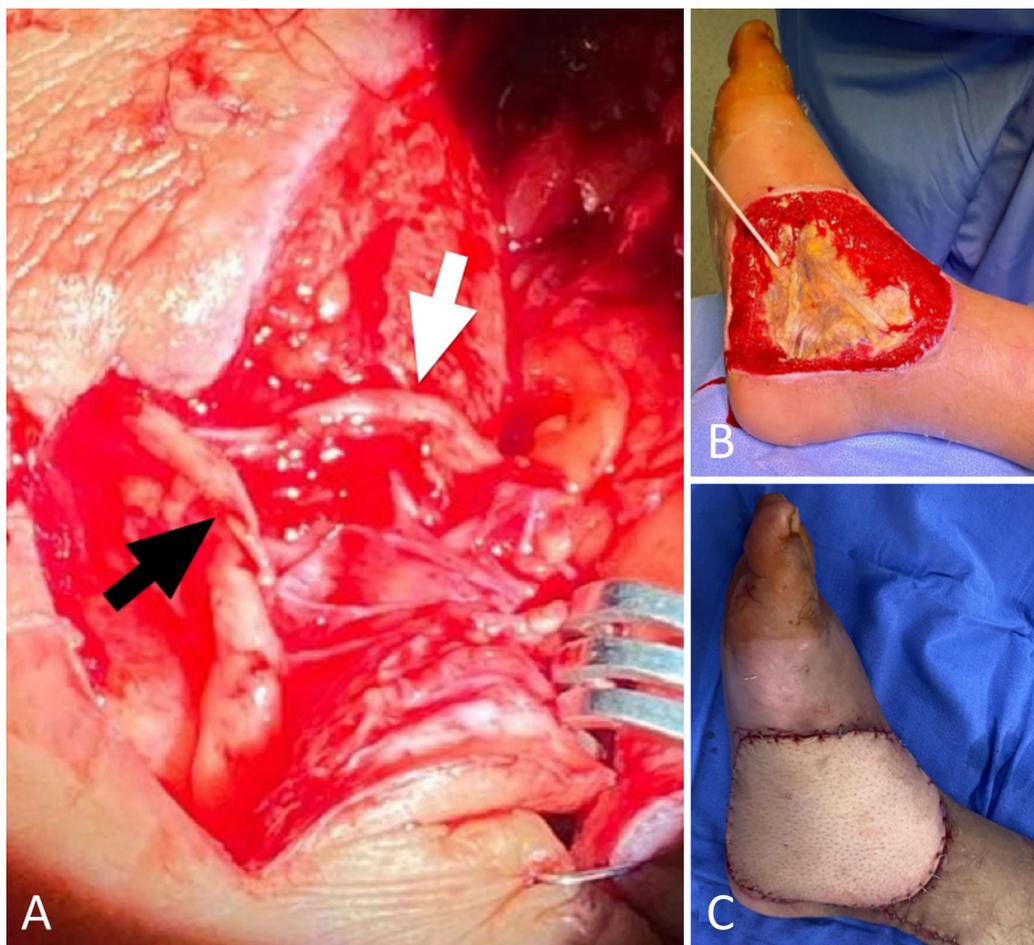


Figure 2. This case illustrates the neurotized anterolateral thigh flap performed on a 50-year-old male with third degree burns on his lower leg and foot. (A) This intraoperative photograph illustrates the end-to-side neurorrhaphy from the femoral cutaneous nerve (white arrow) to the superficial peroneal nerve (black arrow). (B) A photograph taken prior to surgery. (C) The postoperative outcome.

sensory branches of the peroneal nerve to either the tibial nerve or the sural nerve can restore protective sensation to the plantar region [35-37].

Transfer of the Saphenous Branch of the Femoral Nerve

In cases where there is no access to the peroneal nerves, such as when proximal sciatic nerve injuries have occurred, it may be possible to transfer the saphenous branch of the femoral nerve to the distal tibial nerve or sural nerve. The method has been shown to be capable of recovering sensitivity up to useful discriminatory sensitivity in accordance with the British Medical Research Council classification in two case studies [38,39].

Pressure Ulcers

The incidence of pressure ulcers among patients with spinal cord injuries ranges from 10 to 20% [34]. Typical management strategies include continuous mobilization of the patient as well as regional flap rotation to eliminate dead spaces. Unfortunately, insensate flaps may also result in ulceration over time.

Although several motor nerve transfers have been described for tetraplegic patients, only two types of sensory nerve transfers have been reported to prevent paraplegic pressure ulcers in patients by improving sacral sensation or providing sensory feedback to pressure-bearing areas. According to Mackinnon et al. [40], the medial antebrachial cutaneous nerve can be transferred to the lateral femoral cutaneous nerve. In one study,

Viterbo and Ripari performed nerve transfers from the intercostal nerve to the sciatic nerve [41].

In the 1970's, Dibbell [42] and Daniel et al. [43] described a technique for mobilizing sensate tissue over an anesthetic area using long flaps innervated by the intercostal nerves. It should be noted that in subsequent studies several regional sensate flaps were described, with the ideal flap often depending on the level of injury. As one example, the tensor fascial lata flap can be performed if the lesion is below the level of the L3/4 [44], and the sensate pedicled anterolateral thigh flap can be performed if the lesion is below the level of the L2 [45].

Anterolateral Thigh Flaps

With the advancement of microsurgery, it is now possible to create sensate free flaps using sensory nerves that are available in the lower limbs or above the level of spinal cord damage [46]. Anterolateral thigh flaps that are neurotized by the lateral femoral cutaneous nerve have been the most extensively studied flaps, with reported superior aesthetic results and the possibility of early rehabilitation and function. In the study, 100% of the subjects had regained touch and nociception, and 85% had regained thermal sensitivity (Figure 2) [47]. Comparison between neurotized and non-neurotized flaps found that 76% of patients had sensory recovery after 3 months in the neurotized group, compared to 20% in the non-neurotized group [48].

GENITALIA

Erectile dysfunction is a common complication after a radical prostatectomy. Currently, the majority of management strategies are based on pharmacological interventions. In some cases, surgeons have attempted direct repair or grafting of the pudendal nerve, but the results have been unsatisfactory [49,50]. Souza et al. reported in 2017 that the femoral nerve may be used to neurotize the dorsal nerve of the penis and the corpus cavernosum [50]. Thirteen months after reinnervation surgery, 60% of patients were able to achieve full penetration. According to their findings, penile reinnervation surgery proved to be a viable and effective method for treating erectile dysfunction following radical prostatectomy.

In patients with low spinal injuries and normal inguinal sensations, it is possible to improve sensation, sexuality, and quality of life through the TOMAX (TO MAXimize sensation, sexuality, and quality of life) procedure, which consists of neurotizing the dorsal nerve of the penis with the ilioinguinal nerve. According to its proponents, 24 of 30 patients (80%) reported a return to glans sensation after receiving the TOMAX procedure [51].

There is evidence that phalloplasty may be complemented by flap neurotization. This can either be done on the dorsal nerve of the penis in males, or on the inguinal nerve in transgender individuals. A complete return to sensation was observed in both groups [52,53].

In recent studies, it has been suggested that females who have suffered genital mutilation may benefit from the reconstruction of the sensate clitoris through the use of neurotized flaps attached to the pudendal nerve [54] and sensate labial flaps [55], although the results from such procedures are currently limited.

CHALLENGES

Although many advances have been made in the field of sensory nerve transfers and direct neurotization, it appears that specialized rehabilitation protocols capable of facilitating the reconstruction of sensory functions will be the direction of this field in the future. A second concern is the difficulty of objectively evaluating postoperative outcomes due to the wide range of parameters that can be measured, including tactile sensation, temperature, vibration, and erogenous sensation.

CONCLUSIONS

Sensory nerve reconstruction is one of the most fascinating, innovative, and pioneering chapters in peripheral nerve reconstruction. Numerous surgical techniques have been described in the literature; however, evidence-based results are lacking, as most of the reports are retrospective case studies, which are likely to be biased. A surgeon should be aware, however, that sensory restoration is an achievable goal during peripheral nerve reconstruction and should be explored as a potential means of improving the patient's quality of life.

CONVERSATIONS WITH EXPERT MENTORS

The corresponding author, Dr. José E. Telich-Tarriba, met with the editors and expert mentors of SciTeMed to maximize the impact and dissemination of the article. We were delighted to have five distinguished guests participate in this webinar, including Dr. Ronald M. Zuker, Dr. Sami Tuffaha, Dr. Peter Neligan, Dr. Hari Venkatramani, and Dr. Tommy Nai-Jen Chang. Dr. Tommy Nai-Jen Chang is the Editor-in-Chief of the International Microsurgery Journal. Dr. Ronald M. Zuker and Dr. Peter Neligan both serve as Honorary Editors-in-Chief of the International Microsurgery Journal. The webinar was moderated by Dr. Urška Čebtron, a medical doctor and researcher

at the HELIOS Klinikum Emil von Behring in Berlin, Germany. The recording of this webinar can be accessed by clicking on the following link: <https://doi.org/10.24983/scitemed.imj.2022.00167>

Ronald M. Zuker, MD, FRCS, FACS, FAAP, FRCSEd (Hon)

Dr. Ronald M. Zuker is one of the most prominent pioneers in the field of microsurgery. His publications include more than 100 peer-reviewed scientific papers and book chapters. A notable achievement of his career has been the publication of *Principles and Practice of Pediatric Plastic Surgery* (co-edited with Bruce Bauer and Mike Bentz), which is the standard text for pediatric plastic and reconstructive surgery. Dr. Zuker is best known for his work as the "Smile Doctor" since he has dedicated himself to restoring function to patients suffering from facial paralysis and Moebius syndrome. He has revolutionized the approach to the treatment of established facial paralysis through the use of free functioning muscle transfers, in which the gracilis muscle plays a critical role. The experience of Dr. Zuker in separating conjoined twins (seven) is one of the largest in the world. Through the implementation of microsurgery into the liver transplant team, Dr. Zuker has set the bar high and created unprecedented success rates following living donor liver transplants. In addition, he performed the first lower limb allotransplant in the world. There is an anatomic point named after him. In June 2014, Dr. Zuker was awarded the Canadian Society Lifetime Achievement Award for his contributions to the field of Plastic & Reconstructive Surgery.

Sami Tuffaha, MD

Dr. Sami Tuffaha is a hand surgeon with fellowship training at The Curtis National Hand Center. He is also an Assistant Professor in the Departments of Plastic Surgery, Orthopedic Surgery, and Neurosurgery at Johns Hopkins University. Dr. Tuffaha completed his residency at the Johns Hopkins/University of Maryland Plastic and Reconstructive Training Program. Following this, he completed a fellowship in Hand and Upper Extremity Surgery at the Mayo Clinic, where he focused on microsurgery and peripheral nerve surgery. Dr. Tuffaha has a special interest and expertise in treating peripheral nerve disorders. His research program integrates basic, translational, and clinical research in order to develop strategies to enhance nerve regeneration and functional recovery following peripheral nerve injury. Among these efforts is an ongoing clinical trial examining the efficacy of a therapeutic agent he developed in the lab.

Peter Neligan, MB, FACS, FRCSI, FRCS

Dr. Peter Neligan is the Honorary Editor-in-Chief of the International Microsurgery Journal. He is a former president of the Plastic Surgery Foundation, of the American Society for Reconstructive Microsurgery, and of the North American Skull Base Society. He is also a former board member of the American Head & Neck Society. Previously, he served as a trustee of the American Society of Plastic Surgeons. Dr. Neligan has authored more than 12 books, 85 book chapters, and over 200 peer-reviewed publications. At present, he serves as Editor-in-Chief of Plastic Surgery, a six-volume textbook used throughout the world for plastic surgery training. He has been invited to over 300 universities and major societies as a visiting professor or honored guest. Besides serving on several editorial boards, he has previously served as Editor-in-Chief of the Journal of Reconstructive Microsurgery.

Hari Venkatramani, MD

With over 21 years of experience as a plastic and reconstructive surgeon, Dr. Hari Venkatramani is an expert in his field. He specializes in reconstructive surgery, including the reconstruction of major limbs and the reconstruction of the brachial plexus. He also performs microsurgery for the reconstruction of cancer and the treatment of lymphedema. Currently, he is a senior consultant at the Department of Plastic, Hand, and Reconstructive

tive Microsurgery at the prestigious Ganga Hospital in Coimbatore, which is one of the largest trauma, plastic surgery, and orthopedic hospitals in India. Dr. Venkatramani serves as secretary of the Indian Society for Reconstructive Microsurgery as well as the Brachial Plexus Surgery Group of India. During his career, he has published 75 peer-reviewed journal articles as well as 12 book chapters.

Tommy Nai-Jen Chang, MD

Dr. Tommy Nai-Jen Chang is a board-certified plastic surgeon in Taiwan. He is an Associate Professor in the Division of Reconstructive Microsurgery, Department of Plastic and Reconstructive Microsurgery, Chang-Gung Memorial Hospital, Linkou Medical Center, Taiwan. In his current position, Dr. Chang is collaborating with Professor David Chwei-Chin Chuang in the area of peripheral nerve reconstruction for brachial plexus injuries in adults and children, facial paralysis, upper and lower extremity reconstruction, as well as decompression neuropathy, including carpal tunnel syndrome, ulnar tunnel syndrome, thoracic outlet syndrome and neurogenic tumors. A total of 80 articles have been published in the literature until the year 2022, mainly in the field of reconstructive microsurgery. Among his research interests are peripheral nerve regeneration and reconstruction, as well as the use of social media in microsurgery education. Dr. Chang founded the International Microsurgery Club in 2016; until now, this group represents the largest online microsurgery platform. Dr. Chang was appointed editor-in-chief of the International Microsurgery Journal in 2017, and in 2018, he founded the International Microsurgery Website to provide educational resources for microsurgery surgeons worldwide.

ARTICLE INFORMATION

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Received: Mar. 29, 2022; **Accepted:** Sep. 13, 2022; **Published:** Nov. 30, 2022

DOI: 10.24983/scitemed.imj.2022.00167

Acknowledgements: The authors would like to thank Dr. Tommy Nai-Jen Chang for his valuable input and for taking the time to share his insights with them. Additionally, the authors wish to acknowledge the support provided by the International Microsurgery Journal and the International Microsurgery Club.

Disclosure: The manuscript has not been presented at any meetings on the topic.

Ethics Approval and Consent to Participate: The study is in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The authors obtained permission from the participants in the human research prior to publishing their images or photographs.

Funding: This research has received no specific grant from any funding agency either in the public, commercial, or not-for-profit sectors.

Conflict of Interest: There are no conflicts of interest declared by either the authors or the contributors of this article, which is their intellectual property.

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