Live Pre03: Current Treatment of Nerve Injuries, Gaps and Neuromas

Co-Chairs: Shelley Noland, MD and Amber Leis, MD

Program Syllabus

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 – OCTOBER 2, 2021

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LEARNING OBJECTIVES
At the conclusion of this program, the attendee will:

- Understand the pathophysiology of nerve injury, have an approach to preoperative investigation as well as indications and timing for nerve reconstruction
- Understand the role of various nerve graft options in managing nerve gaps
- Understand the role of common nerve transfers to restore motor function after peripheral nerve injury
- Understand the techniques available for management of the painful nerve

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

Co-Chairs: Shelley S. Noland, MD and Amber Rachel Leis, MD

Description

In this pre-course, we will deliver a foundational approach to the preoperative investigation, timing, and treatment options for the nerve-injured patient. Indications, technical pearls, postoperative protocols, and outcomes for the management of nerve gaps, proximal nerve injuries, and the painful nerve will be explored. Through case-based debates, we will discuss controversies in the management of nerve gaps, the use of nerve transfers, and treatment of neuromas.

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- Understand the role of common nerve transfers to restore motor function after peripheral nerve injury.
- Understand the techniques available for management of the painful nerve.

Program

Session Chair(s)
Shelley S. Noland, MD | Amber R. Leis, MD

07:00 AM - 07:01 AM
Introduction & Overview
Shelley S. Noland, MD | Amber R. Leis, MD

07:01 AM - 07:40 AM
Part 1: Preoperative Considerations
Shelley S. Noland, MD

07:01 AM - 07:10 AM
Pathophysiology, Exam and Investigation of the Nerve Injured Patient
Kate Elzinga, MD, FRCSC

07:10 AM - 07:20 AM
A Surgeon's Guide to Interpreting Electrodiagnostic Studies
Christopher J. Dy, MD, MPH, FACS

07:20 AM - 07:30 AM
Timing and Indications for Nerve Reconstruction
Sara Atkins

07:30 AM - 07:30 AM
Principles of Nerve Repair: Tips and Pearls to Optimize Outcomes
Jonathan E. Isaacs, MD

07:40 AM - 08:20 AM
Part 2: Nerve Gaps
Amber R. Leis, MD

07:40 AM - 07:50 AM
Emerging Therapies to Enhance Regeneration: Drugs and Devices
Michael J. Morhart, MD

07:50 AM - 08:00 AM
Nerve Grafting: Autologous Nerve
Amber Rachel Leis, MD

08:00 AM - 08:10 AM
Nerve Grafting: Allograft Nerve
Bauback Safa, MD, MBA

08:10 AM - 08:20 AM
Long Nerve Gaps and Vascularized Nerve Grafts
Johnny Chuieng-Yi Lu

08:20 AM - 08:30 AM
Case Discussion
All Faculty

08:20 AM - 08:22 AM
Case Presentation
Amber R. Leis, MD

08:22 AM - 08:30 AM
Case-based Debate
Bauback Safa, MD, MBA | Amber Rachel Leis, MD

08:30 AM - 08:45 AM
Break
All Faculty

08:45 AM - 10:10 AM
Part 3: Nerve Transfers
Shelley S. Noland, MD

08:45 AM - 08:55 AM
Principles of Nerve Transfer: Tips and Pearls to Optimize Outcomes
Tom James Quick, MB, MA(Cantab), FRCS

08:55 AM - 09:05 AM
To Supercharge or Not Supercharge?
Susan E. Mackinnon, MD

09:05 AM - 09:15 AM
Nerve Transfers to Restore Shoulder Function
Jayme A. Bertelli, MD, PhD

09:15 AM - 09:25 AM
Nerve Transfers to Restore Elbow Function
Alexander Y. Shin, MD

09:25 AM - 09:35 AM
Nerve Transfers to Restore Extrinsic Finger Function
Fraser J. Leversedge, MD

09:30 AM - 09:45 AM
Nerve Transfers to Restore Intrinsic Function
Jennifer L. Giuffre, MD, FRCSC

09:45 AM - 09:55 AM
Therapy After Nerve Repair
Cecelia M. Skotak, OT/L, CHT

09:55 AM - 10:10 AM
Case Discussion
All Faculty

09:55 AM - 09:58 AM
Case Presentation(s)
Shelley S. Noland, MD

09:58 AM - 10:10 AM
Case-based Debate
Alexander Y. Shin, MD | Fraser J. Leversedge, MD

10:10 AM - 11:00 AM
Part 4: The painful Nerve
Amber R. Leis, MD

10:10 AM - 10:20 AM
Non-Surgical Management of Neuropathic Pain
Catherine Curtin, MD

10:20 AM - 10:30 AM
Conventional Techniques for Neuroma Management
Ryan W. Schmucker, MD

10:30 AM - 10:40 AM
Targeted Muscle Reinnervation
Jason H. Ko, MD, MBA

10:40 AM - 10:50 AM
Regenerative Peripheral Nerve Interfaces
Kyle R. Eberlin, MD

10:50 AM - 11:00 AM
Case Discussion
All Faculty

10:50 AM - 10:52 AM
Case Presentation
Amber R. Leis, MD

10:52 AM - 11:00 AM
Case-based Debate
Jason H. Ko, MD, MBA | Kyle R. Eberlin, MD

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:00 AM - 07:01 AM

Introduction & Overview

Shelley S. Noland, MD

No relevant conflicts of interest to disclose

Amber R. Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

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Shelley S. Noland, MD
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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:01 AM - 07:10 AM

Pathophysiology, Exam and Investigation of the Nerve Injured Patient

Kate Elzinga, MD, FRCSC

No relevant conflicts of interest to disclose

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Evaluation of Nerve Injury and Nerve Compression in the Upper Quadrant

Christine B. Novak, PT, MS
Division of Plastic and Reconstructive Surgery
Program in Occupational Therapy and Program in Physical Therapy
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St. Louis, Missouri

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Division of Plastic and Reconstructive Surgery
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St. Louis, Missouri

ABSTRACT: Evaluation of the patient with nerve compression and/or nerve injury should include a complete motor and sensory evaluation to establish the level and degree of injury and/or compression. No one test has been accepted as the standard procedure for the evaluation of sensibility. The various sensory tests available for patient assessment will yield different information regarding the integrity of the quickly and slowly adapting sensory receptors. Tests such as provocative maneuvers and sensory thresholds (cutaneous and vibration) will be more sensitive in the evaluation of patients with nerve compression, and other discriminatory measures will yield better functional information in patients with nerve injury.
J HAND THER. 2005;18:230–240.

Nerve injury and nerve compression may result in decreased sensory and/or motor function. Evaluation of the patient with nerve compression or nerve injury will provide information to identify the level of the lesion (injury or compression) and to document alterations in motor and/or sensory function.

CHRONIC NERVE COMPRESSION

Patients with chronic nerve compression have wide variability in the presenting subjective symptoms and physical signs. In the motor system, these changes may progress from muscle ache and weakness to muscle atrophy. Sensory complaints will vary from intermittent paraesthesia to constant numbness. This spectrum of patient presentation likely relates to the range of neural histopathologic changes that occur with chronic nerve compression (Figure 1). Documentation of chronic histopathologic changes in humans is uncommon and therefore the animal model has assisted in the understanding of the changes that occur with chronic nerve compression.[1–4] The histopathology of chronic nerve compression is a continuum of neural changes that occur dependent upon the amount and duration of compression. The initial neural changes involve a breakdown of the perineurial blood–nerve barrier with subperineurial edema, followed by connective tissue thickening, segmental demyelination, diffuse demyelination, and finally axonal degeneration.[5] Initially, these neural changes do not occur equally across the nerve but may vary depending on the distribution of compression across the nerve. In general, the fascicles that are most superficial are affected sooner, and when this occurs varying patient symptoms within a single nerve distribution may result.[6]

MULTIPLE AND DOUBLE CRUSH SYNDROMES

Upton and McComas[7] presented the concept of the double crush mechanism where a proximal level of nerve compression will cause the distal entrapment sites to be less tolerant to compressive forces. The authors presented a clinical patient review with a high prevalence of distal nerve compression with cervical root lesions.[7] Therefore, they concluded that the summation of neural compression may alter axoplasmic flow thus contributing to patient symptoms. Lundborg[6] introduced the concept of the reverse double crush where a distal compressive site will alter neural transmission, thus affecting the more proximal entrapment sites. The concept of the double or multiple crush should be considered in cases of nerve compression. Multiple sites of compression may cumulatively cause alteration in the neural transmission and produce patient symptoms, although each site in isolation may not be sufficient to cause patient symptoms (Figure 2).

This article has been modified from Novak CB. Evaluation of the nerve injured patient. Clin Plast Surg. 2003;30:127–38, with permission.

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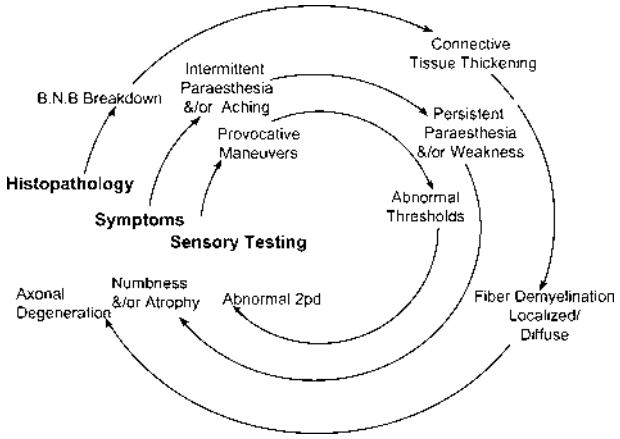

FIGURE 1. *The histopathology of chronic nerve compression spans a broad spectrum. Patient presentation and clinical findings will likely parallel the histopathologic changes occurring in the nerve. In the earliest stages of nerve compression, the patient may present with only intermittent symptoms and provocative maneuvers (positional and pressure) may be the only positive findings. In the later stages of nerve compression with Wallerian degeneration, patient complaints will include numbness and muscle atrophy. Sensory testing at this stage may reveal abnormal two-point discrimination. (Reproduced from Novak CB. Patient evaluation of nerve compression in the upper limb. In: Allieu Y, Mackinnon SE (ed). Nerve Compression Syndromes of the Upper Limb. London: Martin Dunitz; 2002, with permission.)*

The postures and positions that contribute to multiple levels of nerve compression may also contribute to muscle imbalance, which may further compress nerves (Figure 3).[8]

NERVE INJURY

Disruption of nerve continuity and neural transmission will result in a number of alterations, not only at the site of the injury, but also at the proximal and distal nerve segment, the distal sensory/motor end organ, the cell body, and the central cortex.

In 1943, Seddon[9] introduced a classification system for nerve injury that included three levels: neurapraxia, axonotmesis, and neurotmesis. Sunderland[10] expanded the classification of nerve injury to five degrees of nerve injury (I–V). A first degree injury is comparable to a neurapraxia. It is a demyelination of the nerve resulting in a temporary conduction block. There will not be any axonal degeneration/regeneration. With remyelination of the nerve, the presenting motor and sensory dysfunction will be resolved. Complete recovery usually occurs by 12 weeks after injury. A second-degree injury is more severe and it is comparable to an axonotmesis as described by Seddon. Wallerian degeneration and proximal axonal degeneration will occur; however, the endoneurial tubes remain intact. Electrodiagnostic studies will be positive and muscle changes will be evident with electromyography. Neural regeneration will occur at the rate of 1 mm per day or 1 inch per month and may be assessed with an advancing Tinel's sign. Recovery will be complete, provided that reinnervation occurs in a timely fashion before muscle degeneration. A third-degree injury is more severe. The nerve will undergo Wallerian and proximal axonal degeneration, similar to a second-degree injury except that the endoneurial tubes are not intact. Therefore, when axonal regeneration occurs, the regenerating axons may not return to reinnervate their original end organs. Patients with third-degree injuries and mismatching of the regenerating axons will benefit most from motor and sensory reeducation to maximize functional outcome. A fourth-degree injury is a neuroma-in-continuity. There will be a proximal Tinel's sign, but it will not advance beyond the neuroma. These patients require surgical intervention to excise the neuroma and subsequent nerve coaptation. The injury will then regenerate as described with a third degree injury. A fifth-degree injury is complete nerve

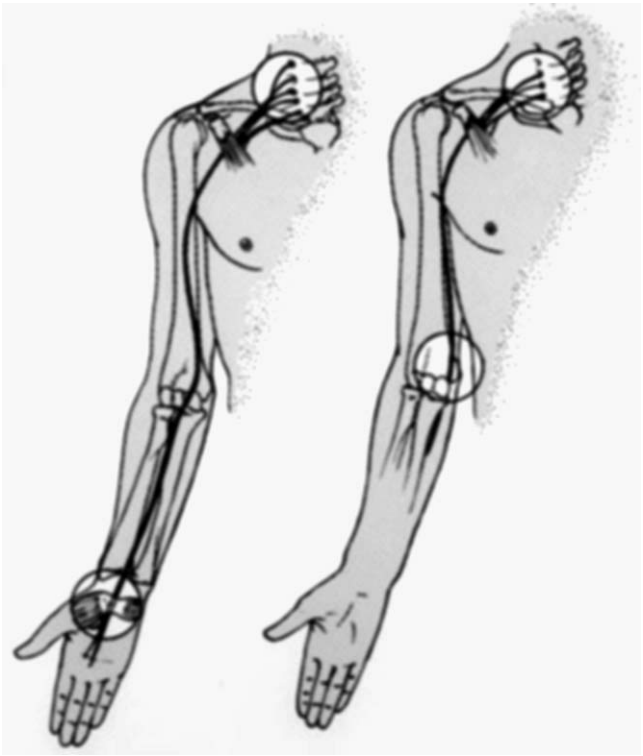

FIGURE 2. *Several sites of nerve compression in the same extremity can cumulatively produce symptoms, such as illustrated here with compression at the cervical spine and distally at the cubital tunnel and carpal tunnel producing sensory disturbances in both the median and ulnar nerve sensory distributions. In the case of double crush, compression of several sites can cumulatively produce alteration of sensation, but each isolated site may be insufficient to produce patient symptoms. (Reproduced from Mackinnon SE. Double and multiple crush and entrapment syndromes and compression nerve syndromes of the upper extremity. Hand Clin North Am. 1992;8: 369–90, with permission.)*

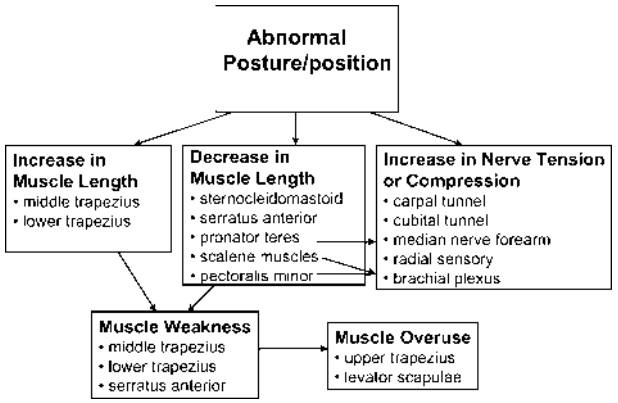

FIGURE 3. *Certain postures and positions may cause increased pressure or tension on nerves contributing to nerve compression (wrist flexion/extension, elbow flexion, arm elevation). These positions will also place muscles in elongated or shortened positions, which will contribute to muscle imbalance, particularly in the cervicoscapular region. If the shortened muscles cross over a nerve, then more compression may be placed on that nerve; i.e., the pronator teres muscle compressing the median nerve in the forearm, the pectoralis minor or scalene muscles compressing the brachial plexus. (Reproduced from Novak CB, Mackinnon SE. Thoracic outlet syndrome. Orthop Clin North Am. 1996;27:747–62, with permission.)*

transection and will require surgery to establish nerve continuity. After surgery, nerve regeneration will occur at the rate of 1 mm per day and can be monitored with an advancing Tinel's sign. A sixth-degree nerve injury is a term used for a mixed nerve injury where varying degrees of nerve injury occur within the same nerve.[11]

In Sunderland degree II, III, IV, and V injuries, axonal degeneration will occur proximal and distal to the site of nerve injury.[11] The distance of proximal degeneration will vary dependent on the nature of the injury, but will extend to the proximal node of Ranvier. In very traumatic nerve injuries, the proximal degeneration may extend more proximally than the next node of Ranvier and may result in cell body death. At the site of nerve injury, axonal sprouting may occur within 24 hours after injury. Each single axon will produce multiple regenerating units, and with correct contact with a distal sensory and motor end organ, the unit will remain viable.

Good motor and sensory function after nerve injury depends on the reinnervation of the motor end plates and sensory receptors.[11–14] Recovery of motor function requires a critical number of motor axons to reinnervate the muscle fibers.[13] Because prolonged denervation of the neuromuscular junction may preclude reinnervation of the muscle, the motor axons must reach the target muscle within a critical period. The exact period for motor fiber reinnervation is unknown, but the critical period is shorter for transection nerve injuries (Sunderland degree V injury) compared with axonotmetic nerve injuries (Sunderland degree II and III injuries).[11] Sensory recovery, however, is possible for many years after nerve injury, but the quality of the recovery decreases with long delays in reinnervation.[11]

EVALUATION

Motor Evaluation

Muscle strength can be assessed qualitatively or quantitatively. Initial changes with chronic nerve compression will include muscle aching followed by weakness and finally muscle atrophy. However, alteration in muscle function may not be detected in patients with mild nerve compression. Muscle atrophy, if present, can be graded by visual assessment as mild, moderate, or severe. This will only occur in cases of traumatic injury to a motor nerve or with severe nerve compression.

There are several grading systems that have been described to classify muscle strength. First published in 1943, the British Medical Research Council (MRC) grading system[15] was presented to assess muscle strength on a scale from 0 to 5, where 0 = no muscle contraction, 1 = a flicker of contraction, 2 = movement with gravity eliminated, 3 = full range of motion against gravity, 4 = full range of motion with resistance, and 5 = normal muscle strength. Birch et al.[12] describe another MRC grading system proposed by Highet that includes grades from M0 to M5, where M0 = no contraction, M1 = visible contraction in proximal muscles, M2 = visible contraction in proximal and distal muscles, M3 = all important muscles both proximally and distally contract against resistance, M4 = return of function that all synergistic and independent movements are possible, and M5 = complete recovery. Kline and Hudson[16] called this system Grading of the Entire Nerve. Another grading system of the entire nerve (American System) that includes grade M0 to M6 was then described.[16] The use of multiple grading systems can result in confusion in the reporting of postoperative results. If the MRC grading system or another motor function grading system is used, it is important to identify the muscle grading system used and to follow the described system to ensure consistency in patient comparison.

After a complete nerve injury, the patient will have immediate loss of function of those muscles innervated by the nerve. However, it may take several weeks for muscle atrophy to be visible, and this will vary with the type of muscle involved, with faster atrophy in type I muscles than in type II muscles. This may complicate patient examination immediately after a nerve injury when other uninjured muscles may provide a specific muscle action for the denervated muscle (i.e., shoulder abduction with supraspinatus for deltoid, elbow flexion with

brachioradialis for biceps). Resources such as the Medical Research Council handbook[15] can serve as an excellent reference for physical examination of individual muscle function.

A number of dynamometers have been described to quantify muscle strength.[17–21] Pinch and grip strength is commonly measured with closed hydraulic systems such as the B & L pinch gauge (B & L Engineering, Santa Fe, CA), Preston pinch gauge (Sammons Preston, Bolingbrook, IL) and Jamar pinch and grip dynamometer (Asimow Engineering Company, Los Angeles, CA). Reliability of measurement with these instruments has been demonstrated by taking the mean value of three measurements.[20] With five grip-handle positions on the Jamar, it is necessary to ensure that the same handle position is used for subsequent patient measures. Although grip strength is a common measure used in the evaluation of hand function, it will not yield information on a specific muscle or muscles. For example, grip strength weakness may result from weakness of the finger flexor or wrist extensor muscles. Also strength evaluation will not be very sensitive to the small changes that occur in the early stages of nerve compression. Weakness may not be evident until the nerve has undergone considerable degeneration from chronic nerve compression.

The Rapid Exchange Grip was described to identify patients giving submaximal effort with grip strength measurement.[22] However, with rapid alternating grip of the Jamar dynamometer, it has been reported that this test is not effective in detecting patients that are giving submaximal effort.[23,24] The simultaneous grip test uses one Jamar dynamometer in each hand and the patient grips both dynamometers simultaneously.[25] The authors reported good sensitivity and specificity with the simultaneous grip test, and noted that patients who did not give maximal effort also did not follow the test protocol.[25] To test simultaneous grip strength, the patient is instructed to hold one grip dynamometer in each hand and squeeze the dynamometers simultaneously, maximally, and quickly under the direction of the examiner for ten to 15 repetitions. Comparisons are made to the maximum static grip strength measured in both hands. In the patient who is giving submaximal effort, there will be increased grip strength measured in the affected hand or decreased grip strength noted in the unaffected hand. We have found measurement of simultaneous grip strength to be very useful in assessing maximal grip strength and degree of effort.

Provocative Testing for Chronic Nerve Compression

In the early stages of nerve compression, provocation testing may be the only positive finding (Figure 1). Clinical evaluation for carpal tunnel syndrome using Tinel's sign, Phalen's test and other provocation tests have been well described and this concept of increasing nerve tension and compression to provoke symptoms may be extrapolated to other sites of nerve compression.[11,26–37] The importance of the double crush mechanism cannot be under estimated in evaluating patients with suspected nerve compression. Because compression at the proximal sites may affect the more distal sites and vice versa, all entrapment sites in the upper extremity should be evaluated for nerve compression. If all sites of nerve compression are not identified, treatment at only a single site in patients with multiple levels of nerve compression will be unsuccessful in eliminating all symptoms.

Tests of provocation using movement, pressure, and the Tinel's sign can be used to identify the sites of nerve compression in the upper extremity.[31–34,37–40] Evaluation of the more proximal entrapment sites may produce patient discomfort, and therefore testing should begin at the most distal entrapment sites and progress proximally. A Tinel's sign is performed at each entrapment site by applying four to six digital taps, and is considered positive with reproduction of patient symptoms in the appropriate neural distribution. At the carpal tunnel, the examiner applies digital taps just proximal to the carpal canal on the median nerve. To assess the median nerve in the forearm, the nerve is tapped in the region of the pronator teres. At the cubital tunnel, a Tinel's sign is assessed along the course of the ulnar nerve beginning proximal to the cubital tunnel and progressing distal through the cubital tunnel. At the brachial plexus, the Tinel's sign is applied supraclavicularly between the scalene muscles and is positive with radiation of symptoms into the upper extremity. Many patients may have local tenderness to the scalenes and this should be noted but not recorded as a positive Tinel's sign.

Positional and pressure provocative tests are held for a total of one minute and recorded as positive if there is alteration of sensation in the correct neural distribution. Pressure provocative maneuvers should be performed by placing digital pressure at each entrapment site including the carpal tunnel (median nerve proximal to the wrist crease), median nerve in the forearm (level of the pronator teres), cubital tunnel (ulnar nerve proximal to the cubital tunnel), and brachial plexus (supraclavicular between the scalene muscles).[31–34,37,38,40] Positional maneuvers should include carpal tunnel (wrist flexion or extension), cubital tunnel (elbow flexion), and brachial plexus (arm elevation).[31–34,37–40] Maximal provocation to the nerve can be performed by combining tension and digital pressure on the nerve (Table 1).

Cervical nerve root impingement can be clinically assessed with a Spurling's test.[41] The foraminal nerve encroachment test is performed by placing the

TABLE 1. **Provocative Tests for Nerve Compression in the Upper Extremity**

Nerve	*Site of Entrapment*	*Provocative Test*
Brachial plexus	Supra/infraclavicular	Arm elevation Pressure on the brachial plexus between the scalene muscles
Radial nerve	Distal forearm	Forearm pronation with wrist ulnar deviation Pressure over tendinous junction of extensor carpi radialis and brachioradialis
Ulnar nerve	Cubital tunnel	Elbow flexion and pressure on ulnar nerve at cubital tunnel region
	Guyon's canal	Pressure at Guyon's canal
Median nerve	Proximal forearm	Forearm supination with pressure in region of the pronator teres
	Carpal tunnel	Wrist flexion and/or extension with pressure proximal to carpal tunnel

patient's head in slight cervical extension and side flexion. Axial compression is then applied to the patient's head, and a positive response is noted when there is a ''spray'' of symptoms into the arm. The test should be repeated with cervical side flexion to the opposite side.

With a positive response to any provocation, the patient should be permitted time for the symptoms to cease before testing the next entrapment site. These provocation tests will allow identification of all entrapment sites, which are compressing the nerve(s) and potentially contributing to the patient's symptomatology. These tests, however, will not provide quantification of the neural changes or intensity of patient symptoms.

Sensory Testing

Many instruments and assessment tools have been described for the evaluation of sensibility with little consensus on the standard procedure.[42–60] There is no one test that will be optimal in terms of sensitivity, specificity, and predictive values in all stages of nerve compression and nerve injury. Different sensory tests evaluate various parameters of nerve function. Therefore some assessment tools will be more useful in the varying stages of nerve compression or with nerve injury.

Sensory testing evaluates the different responses of the quickly and slowly adapting sensory receptors. Four sensory receptors have been described in the glabrous skin of the hand, and these receptors have been classified by receptive field and response qualities. Both quickly and slowly adapting receptors have been identified in human glabrous skin. The slowly adapting receptors (Merkel cell neurite complex and Ruffini end organ) respond to static touch. The Merkel cell neurite complexes are found in the basal layer of the epidermis. The Ruffini end organs have been identified electrophysiologically but not histologically in the glabrous skin. The quickly adapting receptors (Meissner and Pacinian corpuscles) respond to moving touch and the discharge impulses vary dependent on the stimulus frequency. The Meissner corpuscles are most sensitive to frequencies up to 30 Hertz and the Pacinian corpuscles respond to the higher frequencies.

Threshold refers to the minimum stimulus necessary to elicit a response. It can be assessed with vibration thresholds (quickly adapting receptors) and cutaneous pressure thresholds (slowly adapting receptors). Innervation density represents the number of innervated sensory receptors and can be assessed with two-point discrimination (2pd). Threshold testing of the sensory receptors will permit the earliest quantification of changes occurring with chronic nerve compression.[32,44,49,52,53,61–65] Alterations in the innervation density will not occur until the later stages of chronic nerve compression and measures of two-point discrimination will remain normal until the patient has more severe nerve compression.[11,32,66,67]

Light Moving Touch

Evaluation of light moving touch can provide a quick screening of the large A-Beta fibers. This can be performed using the Ten Test.[60] The light moving touch test allows the patient to compare their sensation on the affected limb on a scale (from 0–10) to normal sensation on the contralateral limb. Strauch et al.[60] compared the Ten Test to Semmes-Weinstein monofilament testing and reported good validity and reliability. Patel and Bassini[68] compared the Ten Test to the Weinstein Enhanced Sensory Test and 2pd and reported the Ten Test to be the most sensitive test in patients with carpal tunnel syndrome. To perform the Ten Test, a moving light touch stimulus is applied with the examiner's finger to a normal area of sensation on the unaffected contralateral digit. This is to be ranked as normal sensation at 10/10. Then a similar stimulus is applied simultaneously to the digit to be tested and the patient is asked to assess the sensation on a scale from 0 to 10, with 0 = no sensation and 10 = perfect sensation.

Vibration Thresholds

Vibration thresholds can be used to assess the quickly adapting receptor threshold and may be evaluated either qualitatively or quantitatively. Qualitatively, vibration thresholds may be evaluated with a tuning fork. A low-frequency tuning fork (30 cps) will be most useful in documenting return

of sensation in patients with nerve injuries. It is one of the first indications of reinnervation of the sensory receptors.[45] The tuning fork is applied to the area to be assessed and the patient indicates if the stimulus is felt. A positive response indicates reinnervation of the low-frequency quickly adapting receptors.

However, with chronic nerve compression, it is hypothesized that the high frequency quickly adapting receptors are first affected.[53] Therefore, assessment with a low frequency tuning fork will not be useful to detect nerve compression and assessment with a high-frequency tuning fork (i.e., 256 cps) will be more sensitive to neural function changes in the earlier stages of nerve compression. The tuning fork is applied to the digit pulp and a comparison is made to the contralateral area. The patient reports if the stimulus is more intense, less intense or the same. This test, however, requires subjective assessment by the patient regarding the intensity of the stimulus, and because the stimuli are not applied simultaneously, the patient must recall the previously applied vibration for comparison. Application of the tuning fork stimulus may vary with alteration of examiner technique. Therefore, accurate patient comparison requires that the examiner apply the same stimulus force each time and variations of application force have been reported.[69] This test may not be used in patients with bilateral hand symptoms.

Quantification of the vibration threshold may be assessed with a vibrometer and a number of vibrometers have been described.[45,46,48,49,52,53,63] The Vibratron II (Physitemp, Clifton, NJ) is a fixed-frequency (120 Hz) variable-amplitude device used to evaluate the minimal vibration stimulus necessary to elicit a response.[48,57] This fixed-frequency vibrometer has a non–force-sensitive transducer on which the patient places his or her digit and indicates when the vibration is felt. Through a method of limits and force choice methodology, good reliability has been reported with this vibrometer.[57] The greatest limitation with the Vibratron II is that the vibration threshold is assessed only at a single frequency. If the higher frequencies are abnormal, then a single-frequency vibration threshold at a lower frequency will not detect the abnormality. In the early stages of nerve compression, the patient may be asymptomatic at rest and measurement at a single frequency without any provocation may not detect abnormalities in vibration thresholds. When using a single-frequency vibrometer and baseline measures are within normal limits, patient testing of vibration thresholds should be combined with provocation of symptoms. In a group of thoracic outlet syndrome patients, vibration thresholds in the small finger were significantly elevated after provocation (arms elevated), whereas baseline measures remained normal.[32] However, in another study evaluating vibration thresholds in TOS patients, baseline thresholds were not significantly different than normal control subjects.[70]

The Bruel and Kjaer vibrometer (Type 9627, Naerum, Denmark) allows the measurement of vibration thresholds at seven frequencies ranging from 8 to 500 Hz.[52,53] The patient places the digit on a 5-mm^2 probe and the intensity of the vibration is controlled by a switch in the nontest hand. The vibration threshold is determined by a method of limits. It is hypothesized that the higher vibration frequencies are usually first affected in the early stages of chronic nerve compression and with increasing age.[53] Therefore, evaluation of these higher frequencies may permit earlier identification of these discrepancies.[53]

Cutaneous Pressure Thresholds

Cutaneous pressure thresholds evaluate the threshold of the slowly adapting sensory receptors (Merkel cell neurite complexes). Initially, Von Frey described using hair of varying diameters to evaluate pressure thresholds and Semmes-Weinstein monofilaments (Sammons Preston, Bolingbrook, IL) are now commonly used to measure pressure thresholds.[42,71] These nylon monofilaments vary in diameter thereby requiring different application forces thus producing different pressure thresholds (Figure 4). Between each monofilament within the set there is an incremental increase on a logarithmic scale (log 10 force of 0.1 mg). The monofilaments are applied to the test area in a consistent fashion and the smallest filament that is perceived by the patient is recorded as the threshold. Alteration in the monofilament diameter or in the application technique will alter the stimulus and thus the recorded pressure threshold.[51,72] In a recent evaluation of normal subjects, variability in Semmes-Weinstein monofilament measures was found with repeated testing.[73] Criticism of the Semmes-Weinstein monofilaments includes the logarithmic scale between the monofilaments and the variability in the size and shape of the nylon filament.[74]

More recently, a computerized one-point discrimination system has been described. This system permits measurement of cutaneous pressure thresholds on a continuous scale.[75] This system has a two rounded, blunt, 0.9 mm probes that allow the assessment of one-point or two-point discrimination.[75] For one-point discrimination, the probe is applied to the patient's digit and the patient indicates when the stimulus is felt by pressing a button in the contralateral hand. After five trials, the highest and lowest values are discarded and the mean value of the remaining three values is recorded as the cutaneous pressure threshold.[74]

Two-point Discrimination

Tactile discrimination measured with 2pd more accurately reflects the quantity of innervated sensory

FIGURE 4. *Semmes-Weinstein monofilaments are applied to the digit pulp and the smallest filament that the patient can detect is the pressure threshold.*

FIGURE 5. *The Disk-Criminator can be used to measure moving and static two-point discrimination (2pd) by applying the probes to the digit pulp. The smallest distance by which the patient can differentiate two probes from one probe is recorded as the 2pd.*

receptors.[45] Initially, Moberg[55,56,76] described using a paper clip to measure 2pd. However, because of inconsistency in the distance between the ends and unreliable blunt ends, instruments such as the Disk-Criminator (Neuroregen, Baltimore, Maryland) and the Two-point Aesthesiometer (Smith + Nephew, Germantown, WI) were introduced.

To evaluate static 2pd, either one or two probes are applied to the digit pulp with only enough force to produce minimal skin deformation and the probes are held in one place for 5 seconds. The patient is asked to identify if one or two probes were applied. The smallest distance that the patient can correctly differentiate one from two probes is recorded as the static 2pd. To evaluate moving 2pd, testing is performed by placing the probes perpendicular to the digit and moving them longitudinally along the digit pulp (proximal to distal). The smallest distance that the patient can correctly identify two probes from one is documented as the moving 2pd. The Disk-Criminator with dull rounded probes permits 2pd measures between 2 mm to 15 mm in 1-mm increments with good interrater reliability (Figure 5).[57,77]

The description of static 2pd measurement does not differentiate whether the probes are to be placed perpendicular or parallel to the digit pulp, and many reports indicate that the probes were placed parallel to the digit.[56,76,78] In Onne's[79] review of patients with nerve injury, some of the reported 2pd were very large and could only have been obtained by placing the probes parallel to the digit pulp. However, the measurement of moving 2pd was described by placing the probes perpendicular to the digit pulp, and therefore assessment with the probes placed parallel to the digit pulp is using incorrect measurement technique.[43] In some cases, patients with nerve injury or with severe nerve compression may not be able to identify two probes before the distance between the probes exceeds the diameter of the patient's finger when placed perpendicular to the digit. In our experience, a 2pd that exceeds 10 or 11 mm is the ''functional'' equivalent of no 2pd. Therefore, in our measures, we have standardized the measurement of moving and static 2pd to apply the probes perpendicular to the digit pulp. If the distance between the probes exceeds the digit diameter, then this is recorded as no 2pd. Standardization of measurement technique is necessary to ensure reliable measurement of both moving and static 2pd. Some authors have advocated five out of seven trials; however, patient fatigue can influence the assessment, and we use two out of three trials for the correct response. Criticism of 2pd assessment includes variability in the application force and not knowing the application force.[43,69,80] However, testing with the Disk-Criminator has been shown to have good intertester reliability when used in a consistent fashion.[57,77]

Sensory Recovery Grading System

The sensory grading system is less defined than the numerous motor grading systems. Highet's[12] scheme included grades from S0 (no sensation) to S4 (complete recovery). This scheme was modified by Zachary and Holmes[45] to gradations of recovery within the grading scale and then the system was modified to include 2pd. The modification of the sensory classification system includes the following: S0 = no sensation, S1 = recovery of deep pain sensibility, S1+ = recovery of superficial pain sensibility, S2 = recovery of pain and some touch sensibility, S2+ = recovery of pain and some touch sensibility with some over-response, S3 = recovery of pain and some touch sensibility with no over-response with 2pd greater than 15 mm, S3+ = sensory localization and 2pd recovery between 7 and 15 mm, and S4 = complete recovery with 2pd between 2 and 6 mm.[45]

Not all sensory evaluation tools will be equally effective in the assessment of nerve injury and nerve compression. Tests that are most useful in detecting abnormalities in nerve injury may not be the most sensitive measures in the different stages of nerve compression. In the early stages of nerve compression, all sensory tests may be normal because symptoms are intermittent and the histopathologic changes in the nerve are minimal. Therefore initially tests of provocation to identify the site of compression may be the only positive test. However, with increased compression and progression to more chronic nerve compression, the threshold measures will become abnormal and finally with severe nerve compression, 2pd will become abnormal. Because 2pd becomes abnormal in the severe stages of nerve compression, it will not be a very sensitive measurement in many patients with chronic nerve compression.[31,32]

Patients with brachial plexus nerve compression often have pain associated with the positions that compress the brachial plexus, and therefore patients will alter their positions to minimize discomfort. Because the progression of nerve compression is dependent upon the duration of compression, brachial plexus nerve compression is less likely to progress to the more severe stages. Therefore, clinical findings and testing will reflect these changes with positive provocative maneuvers and abnormal sensory thresholds, whereas 2pd will remain normal.[31,32]

After nerve injury, 2pd may be a better indicator of functional recovery than threshold measures because threshold measures may not return to normal values. Object identification is often used as a functional outcome to evaluate patient recovery after nerve reconstruction or decompression. A strong correlational relationship has been reported between object identification and 2pd[57,81,82]; therefore, with respect to object identification, 2pd is a good predictor of function.

Pain Evaluation

Pain can be a significant component of patient complaints with nerve injury and/or nerve compression. Particularly in patients with multiple level nerve compression and soft-tissue disorders, the patient's response to pain can impact on successful management. Therefore, assessment of pain and the impact of this pain on the patient's life is an important component of the total evaluation. Our pain evaluation,[83] which has been modified from the McGill pain questionnaire,[84] Hendler's back pain questionnaire,[85] and a previous modification of the pain questionnaire,[11,33] consists of a series of questions (e.g., regarding work, home, medications), pain descriptors, a body diagram, and visual analogue scales for pain, stress, and coping. Each component is scored and considered positive with use of more than three descriptors, a body diagram that does not follow a known anatomical pattern, or a questionnaire score exceeding 20. If more than two of these components are positive, the patient should be sent for further psychological evaluation to determine the impact of pain on their life. Successful management will only be achieved if the psychological component of this problem is also addressed. The first page of this pain evaluation questionnaire, which includes the body diagram, pain adjectives and the 1- cm visual analogue scales for pain can be used at subsequent patient visits to monitor progress.

Evaluation of the Cervicoscapular Region

Patients with brachial plexus nerve compression will often present with pain and discomfort resulting from muscle imbalance in the cervicoscapular region. A thorough evaluation of the shoulder, scapular and cervical movements should be included in patients who report proximal symptoms. Relaxed standing posture is evaluated with comparison to the ideal posture[86]; patients typically have a head-forward posture with loss of cervical lordosis, increased thoracic flexion, scapulae abduction, and shoulder internal rotation. Prolonged positioning in altered postures will result in adaptation of the muscle length and resultant muscle imbalance.[87] Cervical range of motion should be evaluated for the degree of movement in addition to associated pain and movement abnormalities. Individual muscles in the cervicoscapular region should also be evaluated for evidence of tightness, weakness and tenderness. Shoulder range of motion should be evaluated in addition to the associated scapular motion. With active shoulder flexion and abduction, weakness in the serratus anterior or trapezius muscles, if present,

can be seen with abnormal scapular winging and/or motion.

Neural tension and length must also be considered in the evaluation of patients with upper quadrant symptoms, particularly in those with complaints of paraesthesia and numbness.[88–90] Because the nerve is composed of connective tissue, prolonged duration in shortened positions may produce relative neural shortening. There will also be increased fibrosis at the entrapment sites and perhaps adhesions, which may tether the nerve at these sites. Neural tissue is relatively intolerant of being stretched without causing symptoms, and thus excessive stretching will cause increased symptoms both proximally and distally extending to the nerve's sensory distribution. Therefore, overstretching of the neural line will potentially increase symptoms throughout the upper quadrant. The irritability of the patient's condition must guide the aggressiveness of the evaluation and the time at which neural tension testing will provide the most useful information. Butler's proposed neural stress tests of the upper extremity are important in determining decreased mobility of the neural tissues.[89] However, these tests can also produce pain patterns in asymptomatic individuals, and the therapist can best attain the most useful information by becoming familiar with the response in asymptomatic individuals before applying these tests to the patient with nerve-related symptoms. These tests are best used in the later stages of management, when the irritability of the condition has decreased and segmental mobility of the cervical spine and scapula has been achieved.

CONCLUSION

The evaluation of patients with nerve injury and/or nerve compression requires an accurate history and subjective report to determine the tests that will be most useful in providing the essential information. Motor and sensory evaluation are necessary in global mixed nerve injuries, but in cases of nerve compression, tests of provocation will give more accurate information in detecting the site of nerve compression. Multiple levels of nerve compression can increase sensory sensitivity and can confuse the interpretation of findings. However, because there is no standard test in the evaluation of patients with nerve injury and/or compression, a battery of valid and reliable sensory and motor tests will provide the most complete information to formulate a treatment plan.

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A Surgeon's Guide to Interpreting Electrodiagnostic Studies

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Review Article

Interpretation of Electrodiagnostic Studies: How to Apply It to the Practice of Orthopaedic Surgery

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ABSTRACT

Electrodiagnostic studies may help orthopaedic surgeons to identify and confirm nerve pathology, determine severity of disease, localize the lesion, identify concomitant or alternative pathology, and prognosticate potential outcomes with nonoperative or operative treatment. Surgeons should recognize the indications for electrodiagnostic studies, principles of their performance, and how to assess the primary data generated by the examination and how it can inform their treatment plans.

Electrodiagnostic studies (EDX) can be used to assess the function of the peripheral nervous system. Outpatient EDX typically comprise both nerve conduction studies (NCSs) and needle electromyography (EMG). NCSs examine the integrity of the nerve fiber itself and its constitutive components (axon and myelin), whereas EMG interrogates the resting membrane electrical activity of muscle. Although EDX are frequently used to diagnose and guide treatment for patients with compressive neuropathy and nerve injury, they can be costly, uncomfortable, and anxiety provoking for patients.

As with all diagnostic tests, the sensitivity and specificity of EDX for specific conditions are related to the cutoff values used[11] and no consensus reference standard is observed for the diagnosis of compression neuropathies at the carpal or cubital tunnel. In the absence of a consensus reference standard, the difficulty lies in quoting a sensitivity or specificity for objective pathology based on subjective symptoms and interpretation of the physical examination. The clinical usefulness of EDX also heavily depends on the pretest probability of disease.[1] When disease is likely, EDX can be used to measure severity for prognosis, or location, when it is in question. When disease is unlikely, and especially for nonspecific symptoms, the low pretest odds of disease increase the probability that EDX may be inconclusive or even misleading. In low prevalence testing circumstances, a normal test makes disease very unlikely and indicates normal or near normal nerve physiology.

Surgeons familiar with the diagnosis and treatment of peripheral nerve issues may use the test as confirmatory, whereas others who are less familiar may use it as a screening tool. Nevertheless, when compared with other diagnostic tests, such as patient questionnaires, the sensitivity of EDX in the diagnosis of carpal tunnel syndrome (CTS) ranges from 82% to 85%, with some studies showing false-negative rates as high as 10% to 20%, and a

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reported specificity between 95% and 99%.[2,3] The diagnostic performance of EDX in cubital tunnel syndrome (CuTS) is reported as lower, with sensitivity between 37% and 86% and specificity estimated at >95%.[4-6] NCSs are more sensitive than EMG in detecting both CTS and CuTS.[2,7]

Most common conditions affecting peripheral nerves, such as CTS, CuTS, cervical radiculopathy, and traumatic nerve injury, are diagnosed and treated based on history and clinical examination. Normal EDX may indicate very mild neuropathy, which typically would be treated nonoperatively. EDX are most useful to orthopaedic surgeons to determine severity of disease, localize a neurologic lesion, exclude concomitant pathology, and prognosticate potential outcomes with nonoperative or operative treatment. EDX should not be perceived as the *sine qua non* of assessing peripheral nerve pathology. Rather, EDX should be seen as an extension of the clinical assessment and, while limited, may be particularly helpful in certain situations, such as monitoring changes in nerve pathology over time or clarifying examination findings. EDX may also be helpful in settings where symptoms are not clearly described by the patient, or the physical examination is equivocal or difficult to obtain.

Basics of Electrodiagnostic Studies

In this review, we provide an overview and direct readers to the excellent description by Lee et al[8] in a previous *JAAOS* article for additional details on the anatomic and physiologic basis of EDX.

Nerve Conduction Studies

In an NCS, a stimulus is applied along the course of the nerve and recorded over a muscle. An example of a setup for median nerve sensory and motor NCS, often used in CTS,[9] is shown in Figure 1. The performance of NCS is reliant on technical factors, including a thorough knowledge of surface anatomy and appropriate measurement of distances between the recording electrode and the location of stimulus. Physiologic variables, such as room temperature, skin temperature, patient age, and patient height, can also affect the reliability of NCS measurements.[9] Accordingly, normal values for each NCS laboratory should be noted.

An understanding of neural anatomy is paramount when interpreting NCS because each component of the NCS reflects the health or function of a particular part of the nerve. Peripheral nerves have both sensory and motor fibers, and therefore, NCSs comprise sensory nerve action potentials (SNAPs) and compound motor action potentials (CMAPs). The three main measures assessed on NCSs are as follows: (1) latency (peak latency for SNAPs and onset latency for CMAPs; measured in milliseconds), (2) nerve conduction velocity (NCV; measured in meters per second), and (3) amplitude (measured in microvolts for SNAPs and millivolts for CMAPs). Both latency and NCV reflect the speed of conduction along a nerve, which directly reflects the integrity of the myelin around the axon. Healthy myelin is essential to rapid conduction of nerve signals through the process of saltatory conduction.

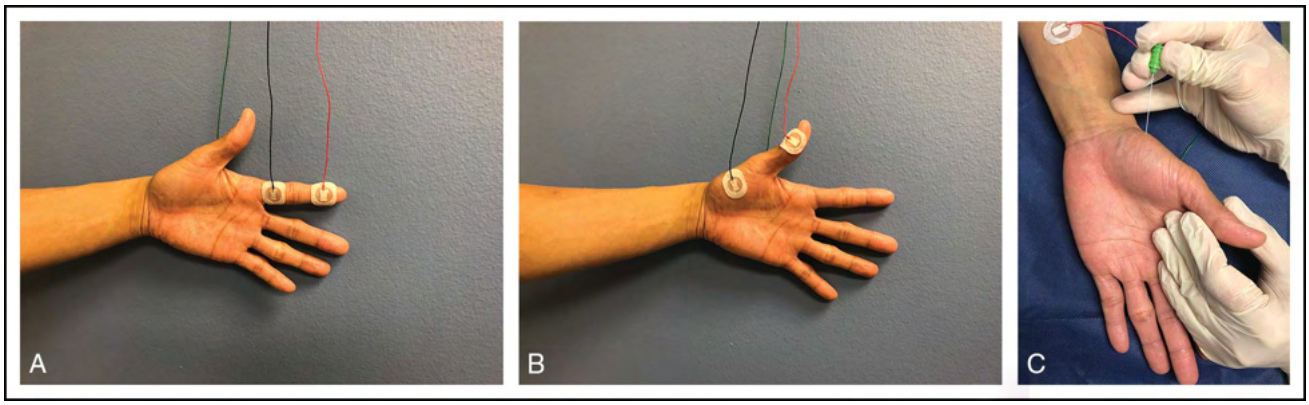
Latency is a measurement of how long it takes for nerve transmission from the two points of stimulus to recording: This increases if the myelin is injured. The NCV is calculated by dividing the conduction time by the distance between the points of stimulus to recording, and conversely, this decreases with myelin injury. It should be noted that proximal nerve segments generally conduct faster than distal segments,[10] a property intrinsic to the architecture of the nerve, as explained below.

The fastest conducting portions of the nerve are the large myelinated fibers responsible for motor, light touch, and vibration.[9] Smaller diameter and unmyelinated fibers within a nerve detect pain and temperature.[10] During assessment with latency and NCV, the smaller and slower fibers may be "overshadowed" by the faster and larger fibers driving the first recorded impulse.[10] This distinction marks a potential limitation of using latency and NCV in the assessment of peripheral nerve function—a relatively small number of large myelinated fibers can make latency and NCV values appear "normal," even if other portions of the nerve are affected.

Amplitude is the other main parameter assessed on NCS. It reflects the number of functioning fibers within the nerve and is not reliant on the speed of nerve conduction. Abnormalities in the amplitude are best seen in the waveform of the NCS (Figure 2). In general, more axons firing in concert give a tall, narrow peak as their voltages are summed together over a relatively short period. Fewer axons' firing, or the same axons' firing over a longer period, gives a lower amplitude.

Chronic compressive neuropathy can lead to axonal loss because of intraneural fibrosis and subsequent loss of amplitudes on NCS.[9] However, a more proximal site of neuropathology that leads to axonal loss, such as concomitant cervical radiculopathy, may also manifest as a loss of amplitude on NCS. Power et al[11] demonstrated the association between CMAP amplitude and motor function (grip and pinch strength) in patients with

Figure 1



Photograph showing (**A**) median nerve sensory nerve conduction study (NCS) setup (Copyright corresponding authors), (**B**) median nerve motor NCS setup (Copyright corresponding authors), and (**C**) electromyography needle insertion into abductor pollicis brevis (Copyright corresponding authors).

CuTS. Their findings suggest that loss of CMAP amplitude is a sensitive indicator of advanced ulnar neuropathy and a possible predictor of outcomes after surgical treatment. CMAP amplitudes are generally considered more reliable than SNAP amplitudes because the former are more easily detected because of motor neurons activating multiple muscle fibers.

Abnormalities in the components of the NCS will reflect the pathophysiologic processes of individual diseases and their various stages of severity. For example, early CTS is a focal demyelinating process and is reflected by abnormalities in NCS latencies. Later-stage CTS has axonal loss from chronic ischemia, which is demonstrated by the decreases in NCS motor amplitudes. Purely neurapraxic peripheral nerve injuries will demonstrate slowing of latency and NCV but normal motor NCS amplitudes, whereas axonotmetic injuries will show decreased motor amplitudes.

Electromyography

In a needle EMG study, a needle is inserted into a muscle, which is then interrogated both at rest and with voluntary muscle contraction. Thorough knowledge of surface anatomy is necessary to ensure accurate needle placement, and ultrasound-guided needle placement can improve the accuracy of insertion into deep muscles. Importantly, an individual needle EMG assessment only reflects a single-neuromuscular unit. Repeating the study in different portions of the same muscle can decrease variability and increase diagnostic sensitivity of the assessment[12] because it is possible that the injured fascicles within one nerve may be associated with partially denervated portions of the muscle.

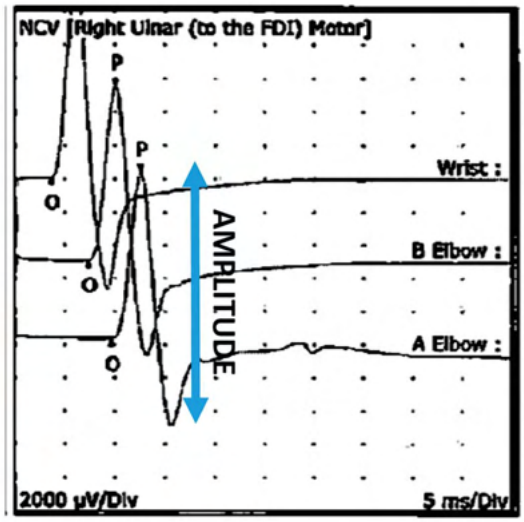
An EMG study has three phases: insertional activity (when the needle is inserted), resting phase (when the muscle is not contracting), and activation phase (when the muscle is contracting)[9] (Figure 3). *Insertional activity* is noted as being increased or decreased. In the setting of a hyperexcitable muscle membrane, which can occur with Wallerian degeneration after peripheral nerve injury, the insertional activity will be increased. In chronic muscle atrophy with fibrosis and/or fatty infiltration, the insertional activity will be decreased. The *resting phase* activity on EMG may include spontaneous potentials occurring within the muscle even when it is not contracting. When individual muscle fibers are deprived of their innervation, there is spontaneous depolarization because of muscle fiber hypersensitivity. This hypersensitivity is reflected in the generation of fibrillation potentials and positive sharp waves, ranging from persistent, single runs in two areas (1+) to continuous discharges in all areas (4+). These changes are present with both partial and complete nerve injuries, may occur as early as 10 days postinjury, and be present for months. In the *activation phase*, the characteristics of the motor unit action potential (MUAP) are analyzed (referred to as the M wave in Figure 3). MUAP analysis helps determine the presence of a disorder whether it is neuropathic or myopathic, the time course of the disorder, and its severity. MUAPs will be absent after neurotmetic (complete) injuries and decreased or absent after high-grade axonotmetic injuries. The rate and pattern of MUAP recruitment provide qualitative assessments of activity within a muscle. After nerve injury, there is a decrease in the number of muscle fibers contracting. This leads to a reduced recruitment pattern, which can be visualized in the waveform and audibly discerned during waveform capture. Electromyographers will typically provide a characterization of

Figure 2

A

CMAP amplitude for first dorsal interosseous				
	Onset (ms)	Normal Onset (ms)	Onset-Peak Amplitude (mV)	Normal Onset-Peak Amplitude (mV)
Wrist	3.6	<4.6	11.0	>5.1
Below elbow	7.3		10.4	
Above elbow	9.7		10.0	

Site 1	Site 2	Delta-Onset (ms)	Distance (cm)	Velocity (m/s)	Normal velocity (m/s)
Below elbow	Wrist	3.7	22.0	59	>52
Above elbow	Below Elbow	2.4	10.0	***42***	>43



B

CMAP amplitude for abductor digiti minimi				
	Onset (ms)	Normal Onset (ms)	Onset-Peak Amplitude (mV)	Normal Onset-Peak Amplitude (mV)
Wrist	3.5	<3.7	***0.5***	>7.9
Below elbow	8.8		***0.5***	
Above elbow	13.5		***0.3***	

Site 1	Site 2	Delta-Onset (ms)	Distance (cm)	Velocity (m/s)	Normal velocity (m/s)
Below elbow	Wrist	5.3	25.5	***48***	>52
Above elbow	Below Elbow	4.7	10.0	***21***	>43

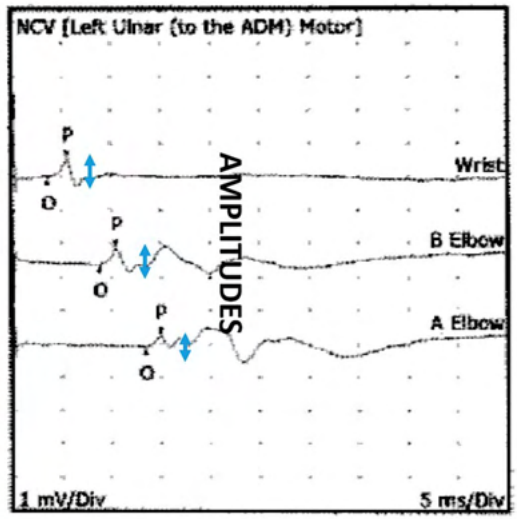


Diagram showing (**A**) motor nerve conduction study from the first dorsal interosseous muscle in a patient with mild cubital tunnel syndrome. Note that the normal CMAP amplitude levels are normal, but there is some slight slowing in the nerve conduction velocity across the elbow (Copyright corresponding authors). (**B**) Motor nerve conduction study from the abductor digiti minimi muscle in a patient with severe cubital tunnel syndrome. There is muscle wasting and loss of two-point discrimination on this patient's clinical examination. Note the drastically decreased CMAP amplitude levels in addition to marked slowing in the nerve conduction velocity across the elbow (Copyright corresponding authors). CMAP = compound motor action potential

muscle recruitment by describing the interference pattern, grading them as full or normal, reduced, discrete, a single MUAP, or absent MUAP. In a full or normal pattern, individual MUAPs cannot be detected because of the density of contracting motor units. In a reduced pattern, some individual MUAPs are detected, but many MUAPs overlap. In a discrete pattern, each individual MUAP is detectable, reflecting a very low density of contracting motor units and a more severe level of denervation. Single MUAPs and absent MUAPs portend an even poorer prognosis.[13]

The amplitude of the MUAP reflects the number of motor fibers recorded nearest to the needle, whereas the duration of the MUAP indicates the number of muscle fibers within a motor unit. The amplitude and duration of the MUAP may be altered in subacute and chronic denervation and reinnervation settings. After partial nerve injury, any surviving motor neurons expand the number and density of muscle fibers they innervate (collateral sprouting of injured neurons into denervated muscle).[14] This is reflected with high-amplitude and long-duration MUAPs. Increased amplitude is typically associated with chronic denervation/reinnervation changes, whereas increased duration is typically seen in the subacute setting. With true nerve regeneration (nerve regrowth down and endoneural tube into denervated muscle), the MUAP will be low in amplitude with variable (low, normal, or possibly long) duration.[13] Although detecting nascent MUAPs can be helpful in establishing axonal continuity and successful regeneration, it is subject to inter- and intrarater variability because of the technical difficulty of picking up low-amplitude signals.

How to Counsel Your Patients About Electrodiagnostic Studies

Electrodiagnostic testing can take anywhere from 30 minutes to over 90 minutes depending on the condition(s) being tested and the findings of each portion. Although generally well tolerated, patients may experience discomfort with electrical stimulations during NCS and with insertion of the needle electrode during the EMG. The most common adverse effect of EDX is pain, which can be attributed to several patient, physician, and study-related factors. Pain has been shown to negatively affect EDX results by preventing completion of the tests; therefore, judicious selection of muscles to be tested may improve accuracy and patient compliance.[15,16] We advise our surgical trainees to observe the performance of EDX whenever possible and to better understand the perspectives of both the patient and the electromyographer.

It is also important to consider the additional cost associated with obtaining EDX. In their analysis of commercially insured patients undergoing treatment for CTS, Sears et al[17] demonstrated that preoperative EDX added nearly $1,000 in additional cost (and $112 of additional out-of-pocket cost) compared with clinical diagnosis alone.

Collaboration With the Physician Conducting the Electrodiagnostic Studies

To guide the EDX, the physiatrist or neurologist conducting the testing should understand the differential diagnoses and treatment options being considered by the referring team. This referral should convey the symptoms being evaluated and the disorder(s) being ruled in or out. This enables the electromyographer to do the appropriate examination to address the clinical question(s). It is also important for the electromyographer to understand the potential surgical interventions being considered. Surgeries, such as nerve transfers, may prompt the electromyographer to do additional testing to evaluate the function of potential donor nerves.

What Will Electrodiagnostic Studies Tell You? What Will They Not?

EDX can be used to confirm the diagnosis of nerve pathology, determine concomitant pathology such as a more proximal lesion or demyelinating disease, and help in localizing the level(s) of neurologic lesions. EDX can aid in staging severity of chronic compressive neuropathy. Associations between EDX-graded severity of nerve compression and response to surgical release are less well defined and beyond the scope of this article.

In the setting of peripheral nerve injury, EMG studies can help determine the likelihood of spontaneous nerve recovery. Although this assertion is based on expert opinion rather than higher levels of evidence, the absence of MUAPs by 3 months after nerve injury is commonly used as a predictor of a nerve that is unlikely to recover on its own, particularly for suspected stretch injuries.[18,19] Based on our clinical experience, it is our opinion that prognosis after ballistic injuries to nerves is harder to predict as recovery can occur as early as 3 months and as late as 9 months.[20] This variable course may make early EMG less useful after ballistic injuries.

EMG studies are also helpful to determine whether denervated muscle is still receptive to reinnervation because irreversible fibrosis may occur within 9 to 12 months of nerve injury. Typically, muscles with remaining fibrillations and/or sharp waves in the resting phase are still "salvageable." However, the absence of these findings likely reflects muscles with fibrosis related to denervation and lack of capacity for reinnervation.[21] Similarly, muscles severely damaged from trauma may be unable to fire motor units in a coordinated fashion and demonstrate poor CMAP response even in the setting of normal nerve conduction.

Figure 3

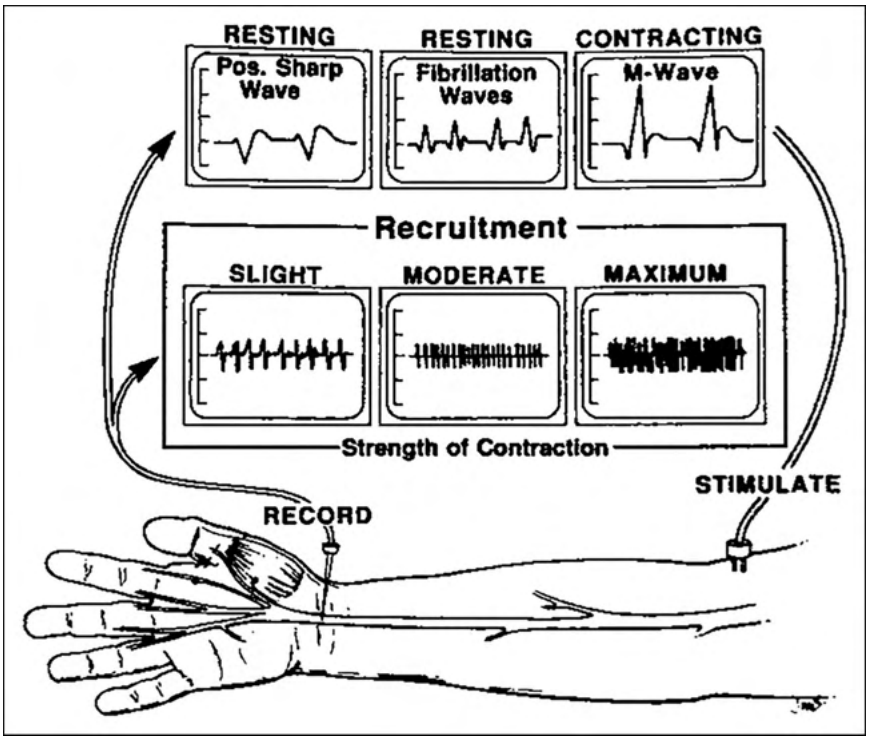


Illustration showing waveforms seen during insertion, resting, and activation phases of electromyography. (Reproduced with permission from Gelberman RH: Operative Nerve Repair and Reconstruction [Fig 10-2]; Ed: Gelberman RH, 1991. Lippincott.)

EMG can be used as a supplement to the physical examination to determine the health of donor neuromuscular units for potential nerve transfer. Ideally, completely healthy and uninjured nerves are used as donors for nerve transfer. In some settings, partially injured nerves can recover adequately and can be used as donors for nerve transfer.[22,23] Tzou et al and Chang et al demonstrated in animal models that motor recovery is possible after using partially injured donor nerves, but that greater recovery is seen with healthier donors.[22,23] Schreiber et al[24] demonstrated that donor nerve units that were normal or had reduced recruitment patterns were associated with superior outcomes compared with donor units with discrete recruitment patterns.

Common Conditions

Carpal Tunnel Syndrome

Compressive neuropathy of the median nerve at the wrist can manifest as CTS. Classic clinical findings are paresthesias and decreased sensation in the median nerve distribution. Although clinical assessment remains the foundation for diagnosis, EDX can help correlate this with physiologic changes in median nerve function at the wrist, but the ultimate diagnosis relies on the clinician's summation of all findings.[25]

CTS results from compression of the median nerve within the carpal tunnel beneath the transverse carpal ligament. Because myelin is the first component of the nerve to be affected, early changes found on NCS are attributable to deficits in myelin, leading to increased latency. Progressive axonal loss indicates more severe disease and increased damage to the nerve, manifesting as decreasing SNAP and CMAP amplitudes and EMG abnormalities in the median-innervated thenar muscles.[26] Although a previous version of the American Academy of Orthopaedic Surgeons clinical practice guidelines for the diagnosis of CTS recommended EDX before surgery,[27] the most recent version does not mandate them and instead suggests that EDX be ordered based on clinical judgment.[28]

The natural history of resolution of these pathologic electrophysiologic changes after carpal tunnel release is not completely documented nor understood. Electrophysiologic recovery does not seem to correlate well with patient-reported outcomes, with symptomatic and functional improvement occurring much earlier in the postoperative period, within the first few weeks to months.[29,30] Long-term follow-up studies of

electrophysiologic tests after surgery have shown that the most notable changes occur in the first 3 months before reaching a plateau, although there is some degree of continued improvement of all NCS parameters for up to 2 years because the nerve continues to heal and regenerate.[31,32] In particular, distal motor latency and NCV may continue to advance toward physiologic values, although the results seldom reach normal limits even years after clinical resolution of symptoms.[31,32] Merolli et al demonstrated that, among other parameters, there was persistence of a double-peak shift, which presents as two distinct SNAPs on NCS representing the latency difference between radial and median nerves, in 84% of patients who were 2 to 20 years postsurgical treatment.[24,32]

Cubital Tunnel Syndrome

Compressive neuropathy of the ulnar nerve at the elbow may manifest as CuTS. Paresthesias, numbness, and tingling in the ring and small fingers are classically associated symptoms. The pathophysiology of CuTS differs from that of CTS. Although compression of the median nerve occurs because of increased pressure within the carpal tunnel, compression of the ulnar nerve at the cubital tunnel is theorized to be due to a combination of both compression and traction. Flexion of the elbow causes narrowing of the space beneath the arcuate ligament, leading to the compression of the ulnar nerve from increased extraneural pressure.[33,34] Flexion of the elbow also lengthens the ulnar nerve because it stretches across the medial epicondyle, adding a traction neuropathy.[35]

In early stages of CuTS, EDX may be normal despite persistent and bothersome clinical symptoms (sensitivity ranging from 37% to 86%),[4-6] although changes in nerve morphology, such as increased cross-sectional area, may be evident.[36,37] The patient's clinical symptoms may correspond to demyelination of smaller diameter fibers and compression of unmyelinated fibers, and the presence of functioning large myelinated fibers may produce false-negative results in electrophysiologic testing,[38] reflecting relatively mild compression. The benefit of surgery in these EDX-normal patients who fail nonoperative management is unclear.[39] Additional diagnostic testing, such as peripheral nerve blocks, may be helpful in these settings. The wide range of sensitivity of EDX has led to an interest in using ultrasonography for diagnosis of CuTS.[3,40]

Cervical Radiculopathy

Cervical radiculopathy is attributable to symptomatic compression of one or more cervical nerve roots at or near the neural foramen because they exit the spinal cord. Proximal compression of the nerve root can manifest as pain in a defined dermatomal pattern that is not well explained by peripheral nerve innervation patterns. Severe compression can result in weakness and EMG changes within multiple muscles innervated by different peripheral nerves. Atypical presentations of weakness or sensory disturbances that do not match those described above for common peripheral nerve compression should alert the clinician to the potential for cervical radiculopathy. Changes in NCS when interrogating individual nerves are not distinct in cervical radiculopathy compared with peripheral neuropathy, but the pattern of neuromuscular involvement should increase clinician suspicion for cervical radiculopathy being an alternative or concurrent diagnosis.

Paraspinal muscles are innervated solely by cervical nerve roots, and not peripheral nerves; thus, they provide an objective measure to assess the proximal extent of the nerve pathology. If a paraspinal muscle to an isolated cervical nerve root is affected (on EMG or motor NCS), it is suggestive of cervical radiculopathy. A thorough radiculopathy screen involving five or more muscles should be done to best identify the presence of a radiculopathy.[41] EDX in the cervical spine also suffer from the same diagnostic testing limitations noted in the limbs. A recent study evaluating inter- and intrarater reliability in diagnosing cervical radiculopathy found 77% sensitivity, 71% specificity, and relatively poor interrater reliability, but good intrarater reliability,[42] suggesting that diagnostic uncertainty may persist even with the use of EDX and that their clinical usefulness depends on the pretest probability of disease. EDX of the cervical nerves are sometimes ordered to evaluate for double crush syndrome, where a peripheral nerve is compressed at two or more locations along its course. Double crush syndrome is a controversial diagnosis because some feel it is used to create an objective explanation for persistent subjective symptoms and/or dissatisfaction.[43] However, peripheral and compressive neuropathy can coexist, which may contribute to suboptimal outcomes after nerve decompression.

Peripheral Nerve Injury

Early diagnosis of peripheral nerve injuries can aid in establishing prognosis and guide treatment, with early intervention potentially leading to improved recovery in both sensory and motor outcomes.[44] Because abnormalities in EDX are unlikely to appear until Wallerian degeneration has occurred, initial postinjury EDX are not typically obtained until 3 to 4 weeks postinjury, if

clinical recovery is not already apparent. In these cases, EDX can help guide treatment depending on the nerve injured and distance to the target end organs.

When the degree of nerve injury (neurapraxic, axonotmetic, or neurotmetic) is not clear, NCS and EMG can help make the distinction. Neurapraxia is caused by a focal injury to myelin, resulting in a conduction block across the injury site. Stimulation proximal to the nerve site will demonstrate an increased latency and decreased velocity compared with stimulation distal to the injury site on both motor and sensory NCSs. Stimulation and measurement of segments distal to the injury will show a normal waveform because of the absence of Wallerian degeneration.[45] EMG stimulation distal to the conduction block will show normal waveforms without any evidence of spontaneous activity, but stimulation proximal to the conduction block may show reduced or absent recruitment. Therefore, if at the 4 week post-injury EMG there is nerve conduction distal to the lesion, the neurons are intact (neurapraxia) and recovery prognosis is good.

Axonotmetic injuries represent a distinctly different pathology because of the presence of Wallerian degeneration. Wallerian degeneration occurs after axonal loss and results in reduction of the amplitude of the sensory or motor action potential. In a partial axonotmetic injury, preserved fibers may demonstrate near normal NCV and latency, but the overall lower number of intact axons signaling to motor fibers will result in lower conduction waveform amplitude and lower amplitude EMG signals. The presence of spontaneous activity (such as fibrillations and positive sharp waves) during the rest phase of an EMG differentiates axonotmetic injuries from neurapraxic injuries beacuse these findings will not be present in the latter because of the lack of Wallerian degeneration.

In complete neurotmetic lesions, there will be no response during NCS. In the months after an acute injury, there will be spontaneous activity during the rest phase on EMG. There will be no motor unit recruitment on EMG. Distinguishing a high-grade axonotmetic injury from a neurotmetic injury can be challenging on EDX because objective findings can be identical. Serial EDX may provide the best clue as to the extent of injury—axonotmetic injuries have potential for recovery if the endoneural tubes are intact, whereas complete neurotmetic injuries do not recover without surgical intervention, but the decision to obtain EDX and the frequency of studies while awaiting nerve recovery should be a shared decision between surgeon and patient.

Summary

EDX are an important extension of the clinical assessment of patients with peripheral nerve pathology. Surgeons should be aware of how EDX are done, how to assess the primary data generated by the examination, and how to use EDX to guide their management. Detailed understanding of EDX can aid surgeons in localizing neurologic lesions, determining the presence of concurrent or alternative diagnoses, and guiding the selection of nonsurgical and surgical treatments.

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:20 AM - 07:30 AM

Timing and Indications for Nerve Reconstruction

Sara Atkins

No relevant conflicts of interest to disclose

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:30 AM - 07:30 AM

Principles of Nerve Repair: Tips and Pearls to Optimize Outcomes

Jonathan E. Isaacs, MD

- Integra - Advisor
- Axogen - Researcher
- Neuraptive - Researcher
- Polyganics - Researcher

ASSH
American Society for Surgery of the Hand

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Principles of Nerve Repair Tips & Pearls to Optimize Outcomes
ASSH Annual Meeting 2021
San Francisco, CA

Jonathan Isaacs, M.D.
Professor and Chief, Division of Hand Surgery
Department of Orthopaedic Surgery
Virginia Commonwealth University Medical Center
Richmond, Virginia

Introduction: Nerve repairs don't do well- Across the board 50% change of a good result(Ruijs, Jaquet et al. 2005)

- **Why do repairs do so poorly?**
    - Multifaceted problem
        - Neuron death
        - Axon regeneration
        - Misdirection/lost/fail
        - Atrophy
        - Cortical plasticity
- **Principles (we can all agree on!)**
    - Time is your enemy!
    - Suturing scarred or injured nerve to scarred or injured nerve just gives you more scar
    - (Excessive) tension is bad!
    - Must direct axons into endoneurial tubes
- **Once axons are cut→Wallerian degeneration…the clock starts ticking**
- **Goal: axonal regeneration to target**
    - **Before…Denervation Atrophy (Muscle)**
        - loss of muscle mass, muscle fiber size, and contractile composition of chronically denervated muscle(Sunderland and Ray 1950)
        - Alteration in protein degradation/synthesis
            - Scar blocks reinnervation of muscle(Gutmann and Young 1944, Fu and Gordon 1995)
    - **Nerve**
        - Loss of guidance cues, deactivation of Schwann cells, accumulation of chondroitin proteoglycans(Fu and Gordon 1995, Hoke 2006)
- How to increase changes of success: Timing
    - Clean/sharp lacerations: Early
        - Easier mobilization
        - Biological advantages
        - Improved neuron survival
        - May not be fully demarcated
    - Clean/sharp lacerations: Late
        - Retraction

        - Fibrosis
        - Loss of land-marks
    - Some injuries need to demarcate
    - Closed injuries need further work up and timing is variable
- **Must cut back to healthy nerve**
    - Suture scar to scar= scar
    - Must be able to see fascicular pattern–
        - Fascicles should "pooch" out
        - Tissue should be soft
- **Getting the ends together**
    - Tension is bad!
        - Severe reduction in blood flow(Clark, Trumble et al. 1992)
            - At little as 8% stretch (transient)
            - 15%-- no recovery (but sutures pull out with this much tension) (mean mechanical failure rate of median or ulnar nerves around 20%)(Millesi, Zoch et al. 1995)
        - Tension inhibits axon growth(Miyamoto 1979) and Schwann cell activation(Yi and Dahlin 2010)
        - 10% generally considered OK
    - But—much better results if direct repair can be achieved (so don't knee-jerk graft everything)
        - Direct repair
            - 16/18 primary radial nerve repairs→M4&5(Gurbuz, Kayalar et al. 2011)
            - 90% out of 75 ulnar nerve repairs with "good recovery"(Emamhadi, Alijani et al. 2015)
            - 51/65 median/ulnar nerve repairs→ good or exc(Mohseni, Pour et al. 2010)
        - Vs…
            - Autograft median and ulnar nerve repairs: 39, 33, 31% good results(Herrera-Tenorio, Chavez-Galvan et al. 2010, Mohseni, Pour et al. 2010, Emamhadi, Alijani et al. 2015)
    - Alleviate tension
        - Mobilization (increase amount "10%" spread over)
            - Median nerve
                - Can gain 4-6 cm
            - Ulnar nerve
                - Anterior transposition helpful at elbow (and prox)
                - Transposition at Guyon's can gain 1-2cm
    - Temporary tension relief
        - Sciatic nerves with 6cm defect acute repair directly with knee flexion x 6 weeks(Oberlin and Rantissi 2011)
            - M4 in 5 and M3 in 1

        - Rabbit median and peroneal nerves(Ruch, Deal et al. 2004, Kurklu, Demiralp et al. 2005)
            - Grafting vs direct repair (with or without ex-fix)
                - Better with direct repair
            - 4 patients treated this with ex fix and gradual lengthening(Ruch and Smith 2003)
- **Proper alignment must be obtained**
    - Proper orientation
        - Organ specificity
            - "preferential motor reinnervation"
                - (misdirected axons pruned back)
            - Motor axons will go to which ever pathway is most trophic
        - Strategies: Visual (topography and blood vessels)
    - Fascicles aligned
        - In cadaver studies approximately 40% of sutured repairs not well aligned(Bernstein, Hamilton et al. 2013, Isaacs, Safa et al. 2016)
- **Repair (co-aptation)**
    - Epineurial stitches
        - Less traumatic
        - Less control over alignment of deep fascicles
        - Ends "kissing"
    - Fascicular repair
        - Strip outer epineurium
        - Ultimate control of alignment (good and bad)
        - Traumatic
    - Grouped fascicular repair
        - Combo
        - Especially in areas of defined topography (median and ulnar nerves)
    - Use the fewest sutures necessary
            - Time consuming
            - Resource expensive
        - Sutures generate scar tissue(Cham, Peimer et al. 1984)
    - Alternative techniques
        - Fibrin glue
            - Mixing concentrated components of clotting cascade
            - Thrombin activates fibrinogen→gel like clot
                - Applied as adhesive cylinder
        - Connector assisted (Stick ends in, suture to epineurium)
            - Blocks scar tissue/escaping axons
                - Less pain at repair site(Leuzzi, Armenio et al. 2014)
                - Fewer neuromas(Neubrech, Sauerbier et al. 2018)
            - Alleviates tension
            - Less sutures at nerve end

        - Allows end organ specificity?(Evans, Bain et al. 1991)
        - Improves alignment (cadaver studies)(Isaacs, Safa et al. 2016)
- **Post-op**
    - If possible, protect for 3-4 weeks
        - Data from dogs and rabbits showing that about 50% of tensile strength of intact nerve at just one week but at 3 to 4 weeks approached normal(Mukherjee 1953)

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:40 AM - 08:20 AM

Part 2: Nerve Gaps

Amber R. Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:40 AM - 07:50 AM

Emerging Therapies to Enhance Regeneration: Drugs and Devices

Michael J. Morhart, MD

No relevant conflicts of interest to disclose

76TH ANNUAL MEETING OF THE ASSH
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Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

07:50 AM - 08:00 AM

Nerve Grafting: Autologous Nerve

Amber Rachel Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:00 AM - 08:10 AM

Nerve Grafting: Allograft Nerve

Bauback Safa, MD, MBA

- Axogen – Researcher/Consultant; Speaker

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:10 AM - 08:20 AM

Long Nerve Gaps and Vascularized Nerve Grafts

Johnny Chuieng-Yi Lu

No relevant conflicts of interest to disclose

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Use of Vascularized Nerve Graft in Long Nerve Gaps

Johnny Chuieng – Yi Lu, MD, MSCI

Division of Reconstructive Microsurgery, Peripheral Nerve Surgery Team

Department of Plastic and Reconstructive Surgery, Chang Gung Memorial Hospital, Linkou, Taiwan

1

Long Nerve Gaps (>10cm)

- ☐ Peripheral Nerve Injuries
  - ! Radial / Ulnar nerve / Median nerve
  - ! Lower extremity
- ☐ Brachial Plexus Injuries, especially avulsion of C8-T1 roots

2

Nerve Autografts

✓ Golden standard in bridging gaps

✖ Unpredictable outcomes:

- ! Long nerve gaps
- ! Prolonged denervation of target muscles

Hoben GM, Plast Reconstr Surg. 2018;142(4):952
Saheb-Al-Zamani M. Exp Neurol. 2013;247:165-77

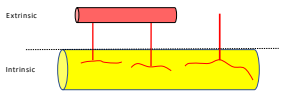
3

Every Tissue Needs Vascularization

4

Vascularization of Nerve Grafts

1. Accompanying nutrient vessel: directly nourishes the nerve
2. Longitudinal inosculation: nerve stumps
3. Centripetal revascularization: surrounding tissue



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5

Nonvascularized Nerve grafts

1. No direct nourishment by pedicle
2. Longitudinal: 42%
3. Centripetal: wound environment

- ➢ *fascicle revascularization: 3rd day*
- ➢ *cable* > trunk grafting: prevent central necrosis

Lind R. *J Reconstr Microsurg.* 1986;2(4):229-234.
Wongtrakul S. *J Hand Surg Am.* 2002;27(2):277-285.

6

Vascularized Nerve Grafts (VNG)

1. Accompanying pedicle
   - *Fascicle revascularization: Day 1*
   - *Trunk grafting:* acceptable
2. Longitudinal neovascularization: not main criteria
3. Centripetal revascularization: more tolerable to poor environment

Chuang DC. J Hand Surg Am. 2012;37(2):270-6
Terzis JK, Plast Reconstr Surg. 2009;123(4):1276-91
Gu Y. JHS. 1992;17(5):518-21

7

Vascularized Sural Nerve Graft

Doi K. Microsurgery. 1984;5(4):175-84
Doi K. J Hand Surg Am. 1987;12(5 Pt 1):677-84

8

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Shin A. Green's textbook 6th edition, Chapter 38
El-Barrany WG. Surg Radiol Anat. 1999;21(2):95-102.

9

Possible Causes: Vascular Insufficiency, Excessive axon sprouting within trunk nerve graft, Chronic denervation of nerve graft before surgery

Bertelli JA, J Hand Surg Am. 2010;35(5):769-75.

10

11

VUNG Blood Supply

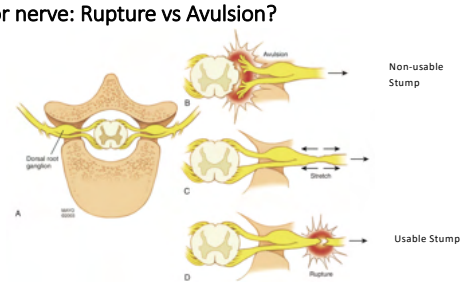
Ulnar artery	vs	Superior Ulnar Collateral Artery
Ulnar vein	vs	Concomitant vein
Free VUNG (one stage)	vs	Pedicled VUNG (two staged)

12

Proximal Nerve Stump

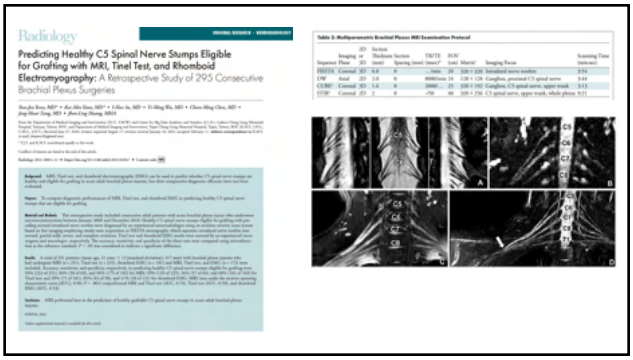
13

Donor nerve: Rupture vs Avulsion?



Shin A. Green's textbook 6th edition

14



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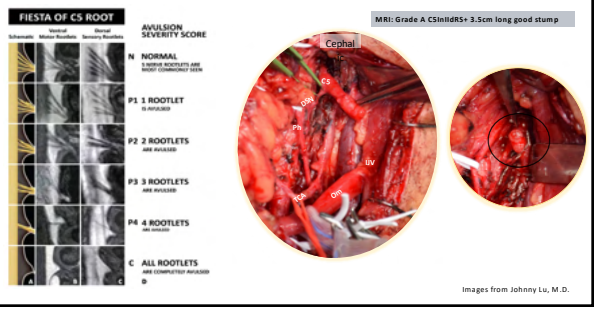
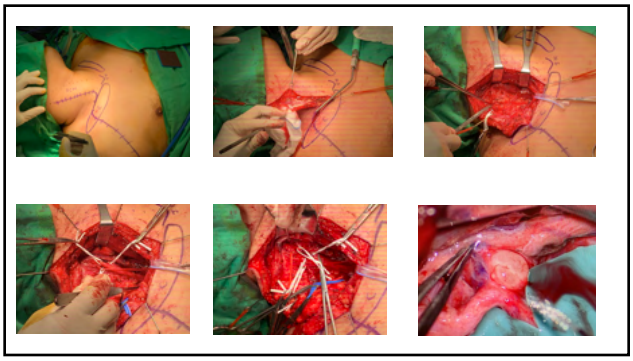
Level I Root Evaluation: Severity Grading



Images from Johnny Lu, M.D.

16



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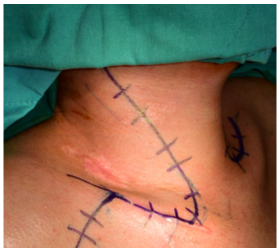
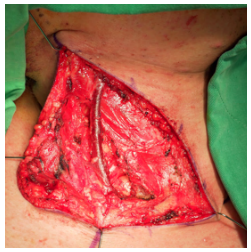
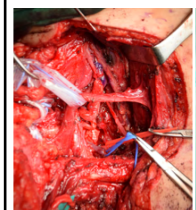
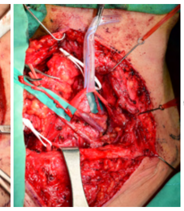
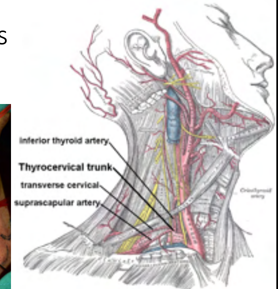
Donor Vessels

18

19

Transverse Cervical Vessels

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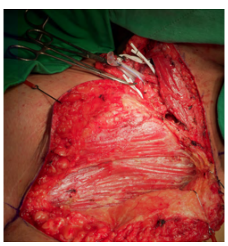
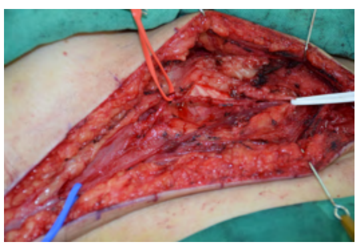
Thoracoacromial Vessels

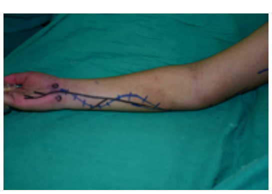
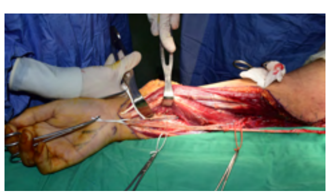



21

Graft Harvest

22

Vascularized Ulnar Nerve "Graft"

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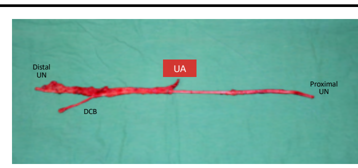

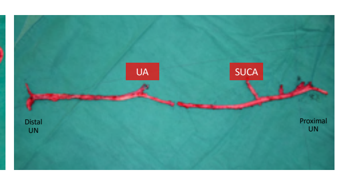

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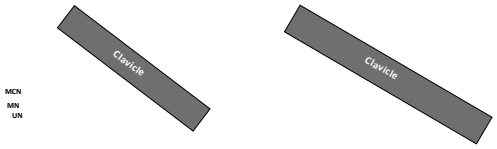
Vascularized Sural Nerve "Graft"

Pictures Courtesy of Dr. Tommy Chang

25

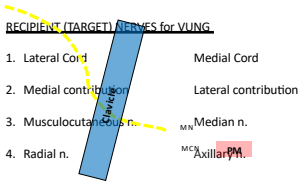
Recipient Nerves

26



Shin A. Green's textbook 6th edition

27



28

All patients had the C5 root stump grafted to the musculocutaneous nerve through one or 2 cables of a sural graft, averaging 17.4 cm in length (range, 10 –23 cm).

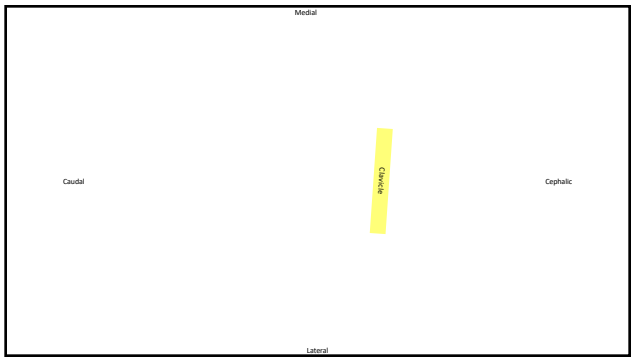
The C6 root was available for grafting in 11 patients. In 10 of these patients, it was connected to the radial nerve through 2 or 3 cable grafts, averaging 22 cm in length (range, 17–30 cm).

- Strength of elbow flexion was similar to that obtained when short grafts were used to connect the C5 root to the anterior division of the upper trunk.
- Length of the graft not detrimental to elbow flexion recovery.
- Targeting the repair seems to counteract the increased rate of fiber misdirection observed in long grafts.

29

From a practical point of view, the results of this study lead us to believe that very proximal targets, like the anterior division of the upper trunk, should be avoided, especially since graft length does not appear to be particularly influential for nerve transfers like the PN and SAN. In this way, we could reduce the risk of axonal misrouting.

30



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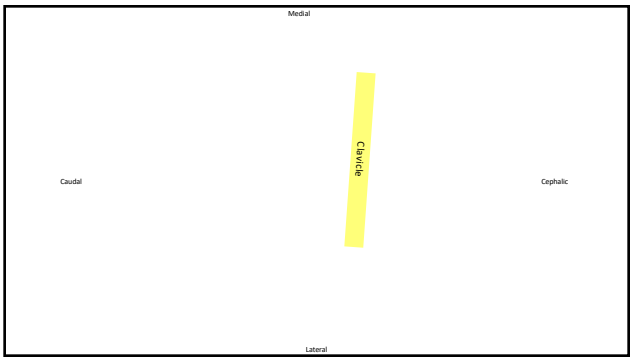

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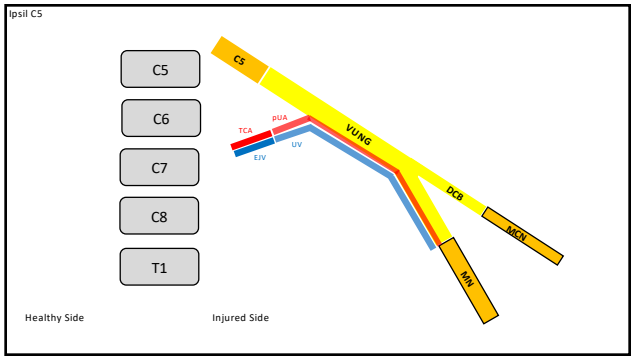

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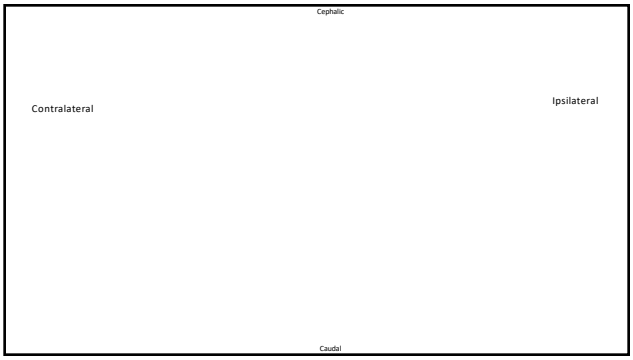

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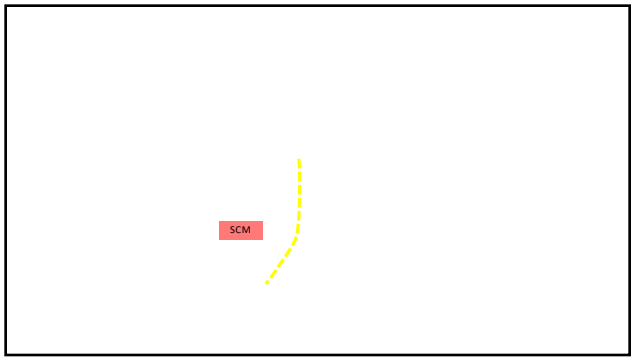

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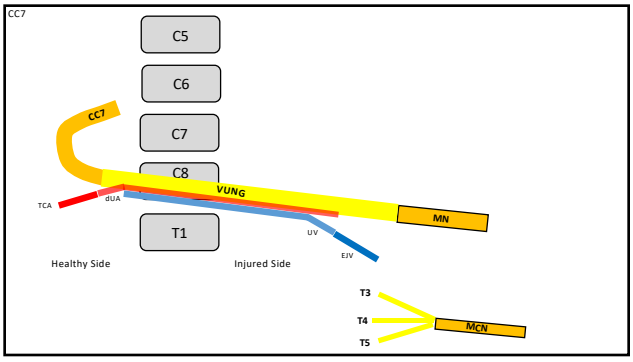

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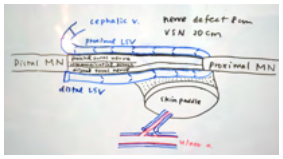
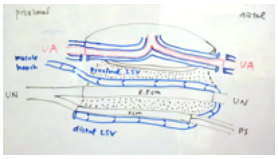
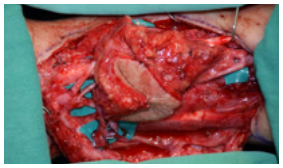
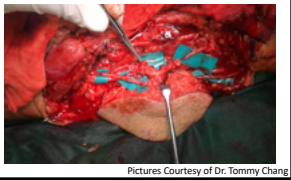








Pictures Courtesy of Dr. Tommy Chang

37

Treat VNG as a Free Flap

38

Flap: Vascular pedicle & Nerve

Vascular

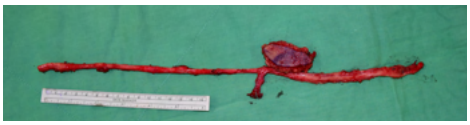
- Liable to compression / traction
- Size discrepancy of artery AND vein
- Possibility of vessel thrombosis

Nerve

- Graft length
- Trunk graft vs Multiple cables (need more fascia)

Skin paddle

- Monitor nerve graft perfusion



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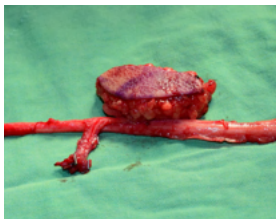

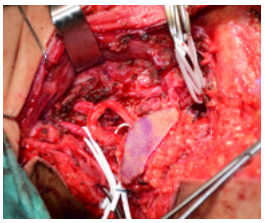

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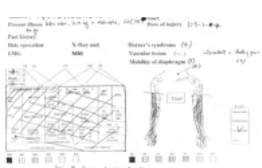
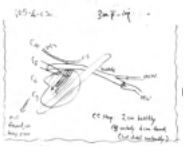
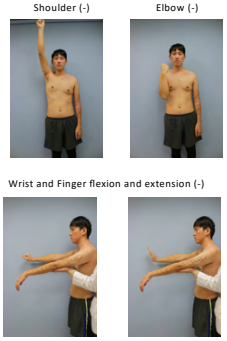
Case Demonstration

41







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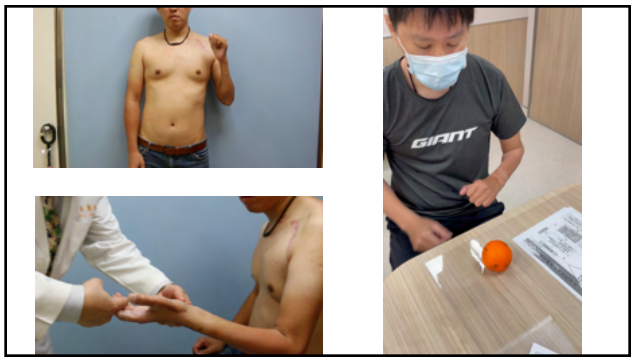

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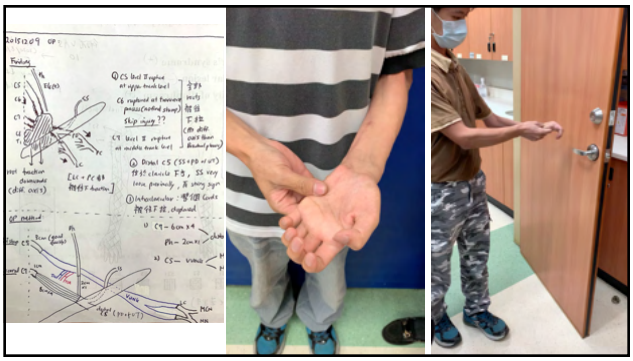

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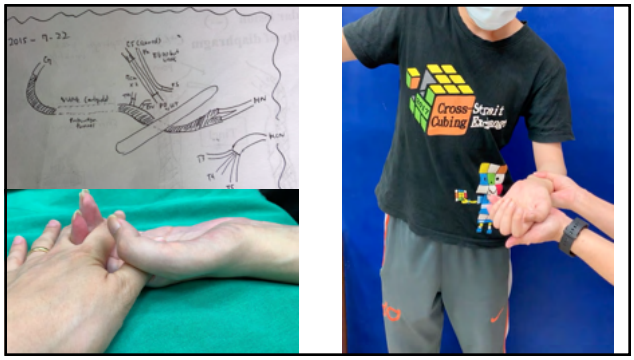

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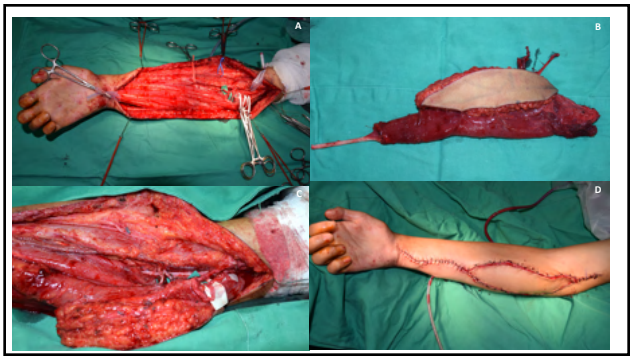

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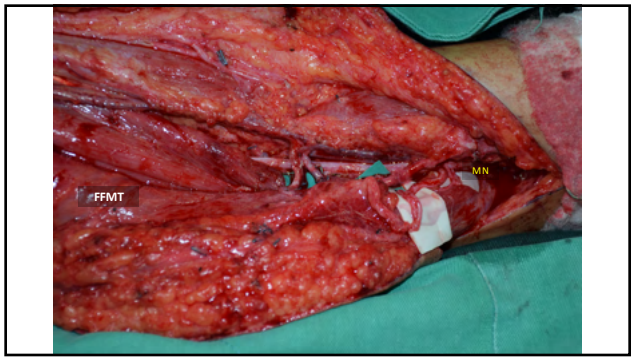


47

Conclusion

- Vascularized Nerve Graft:
  - *not difficult*
  - *ability to reinnervate multiple target muscles* even in long nerve gaps
- VUNG: Donor site morbidity justified in Total BPI
  - Free > Pedicled
  - Ulnar artery > SUCA

48

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:20 AM - 08:30 AM

Case Discussion

All Faculty

No relevant conflicts of interest to disclose

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:20 AM - 08:22 AM

Case Presentation

Amber R. Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:22 AM - 08:30 AM

Case based Debate

Bauback Safa, MD, MBA

- Axogen – Researcher/Consultant; Speaker

Amber Rachel Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:30 AM - 08:45 AM

rea

All Faculty

No relevant conflicts of interest to disclose

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:45 AM - 10:10 AM

Part 3: Nerve Transfers

Shelley S. Noland, MD

No relevant conflicts of interest to disclose

ASSH
American Society for Surgery of the Hand

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:45 AM - 08:55 AM

Principles of Nerve Transfer: Tips and Pearls to Optimize Outcomes

Tom James Quick, MB, MA(Cantab), FRCS

No relevant conflicts of interest to disclose

ASSH
American Society for Surgery of the Hand

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

76TH ANNUAL MEETING OF THE ASSH

knowledge commitment compassion

PRINCIPLES OF NERVE TRANSFER

Tips & Tricks

Precourse 03: Current Treatment of Nerve Injuries, Gaps and Neuromas

Date: Wednesday, September 2 Session Time: 7:00 AM – 11:00 AM Pacific

Co-Chairs: Shelley Noland and Amber Leis

Tom J Quick
Consultant Surgeon, Royal National Orthopaedic Hospital, UK
Honorary Associate Professor UCL

ASSH
American Society for Surgery of the Hand

San Francisco, CA SEPTEMBER 30 – OCTOBER 2, 2021

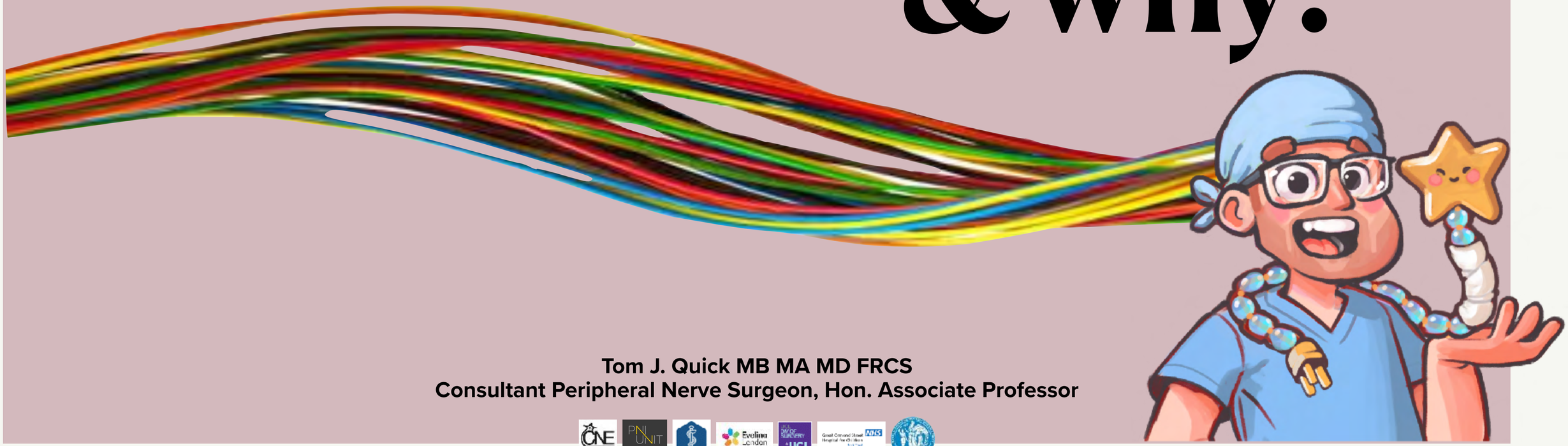
I have no financial disclosures

TOM J QUICK MB MA MD FRCS FHEA

Nerve Transfers

What, why, when & how

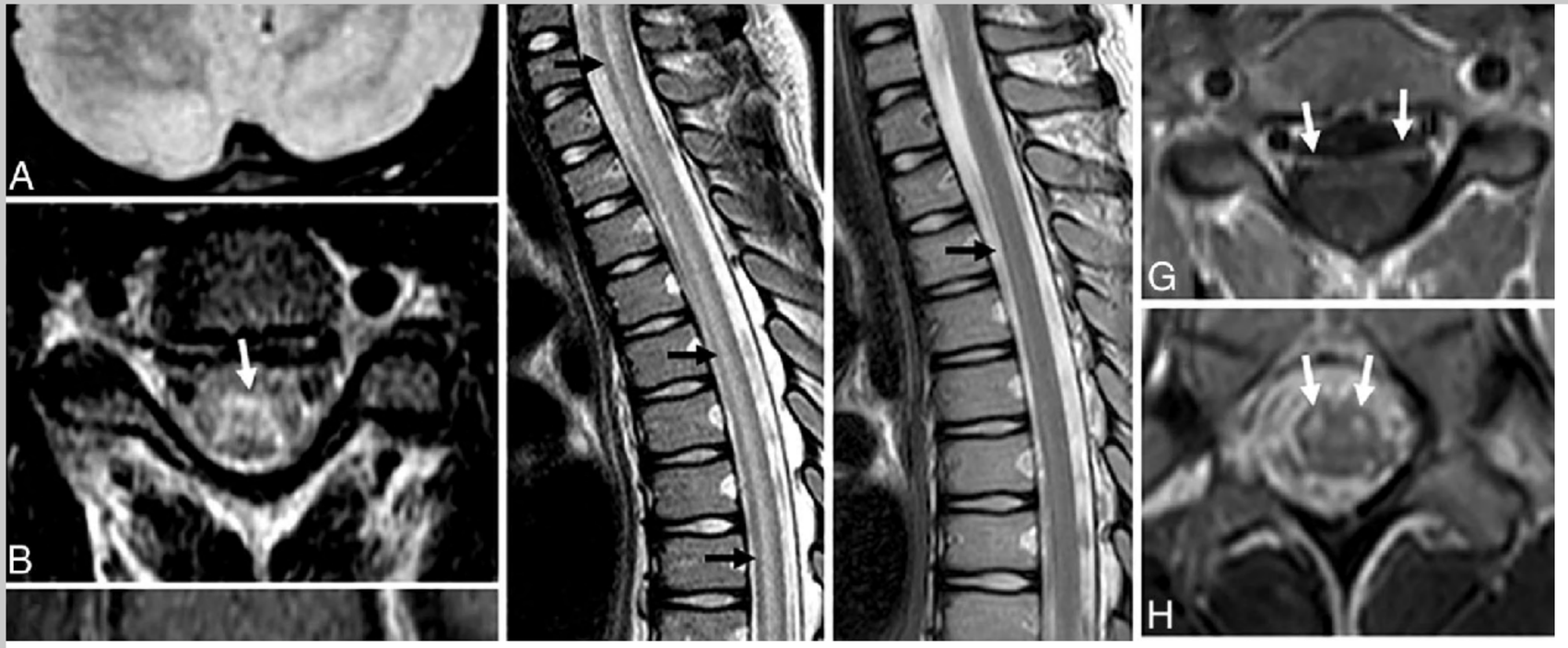
Which wire, where? & why?

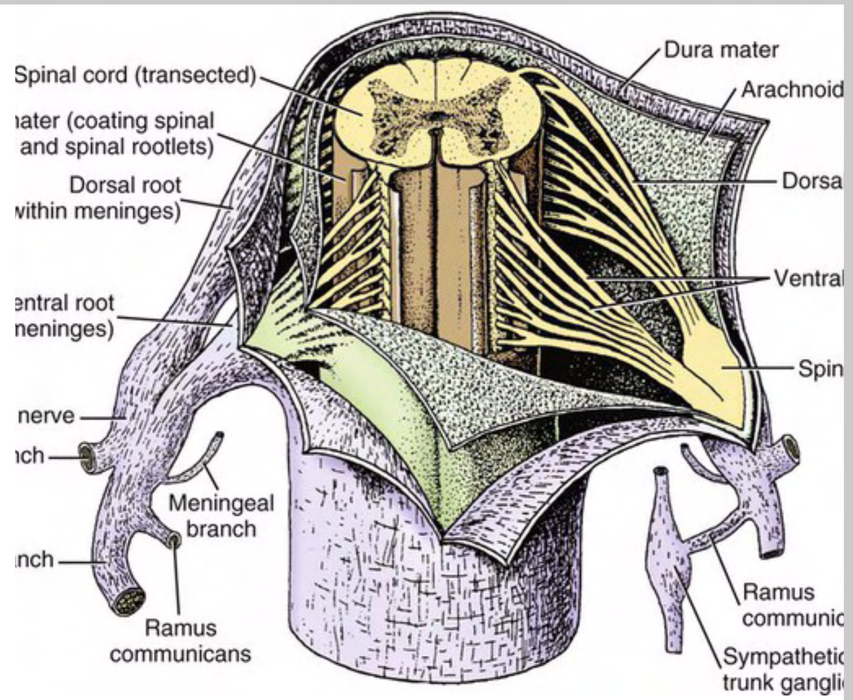


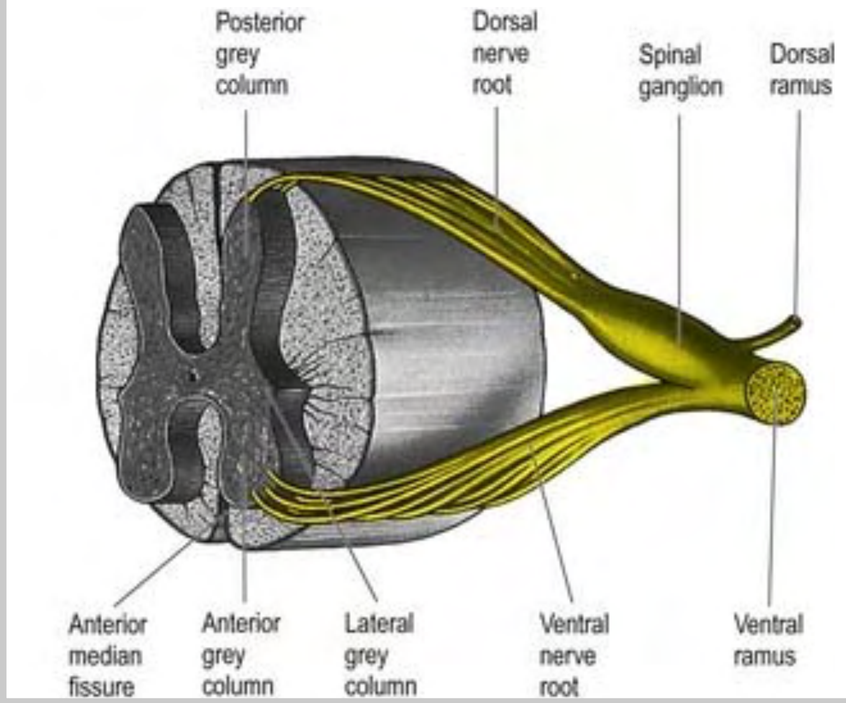
Tom J. Quick MB MA MD FRCS
Consultant Peripheral Nerve Surgeon, Hon. Associate Professor

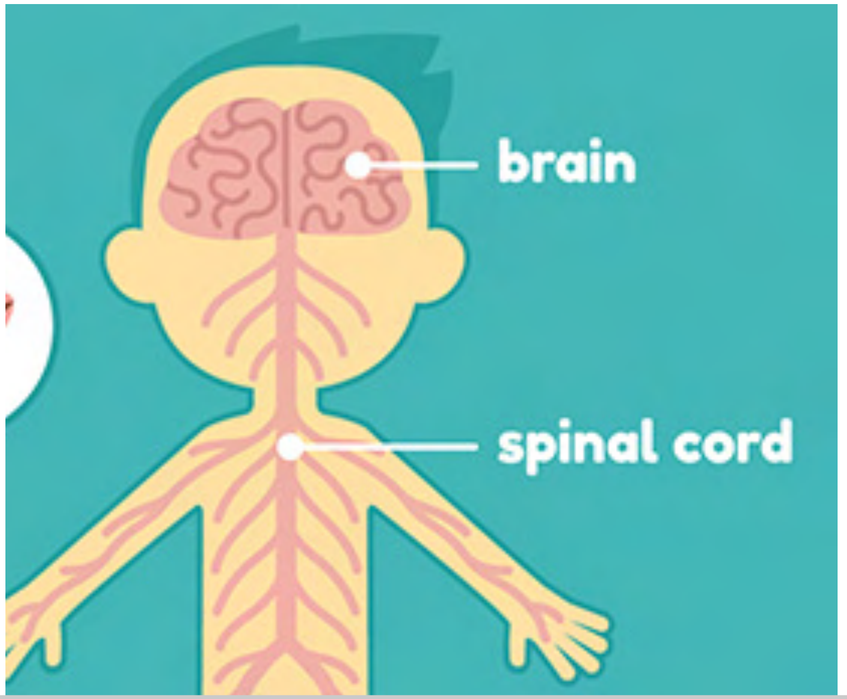
Reinnervating function

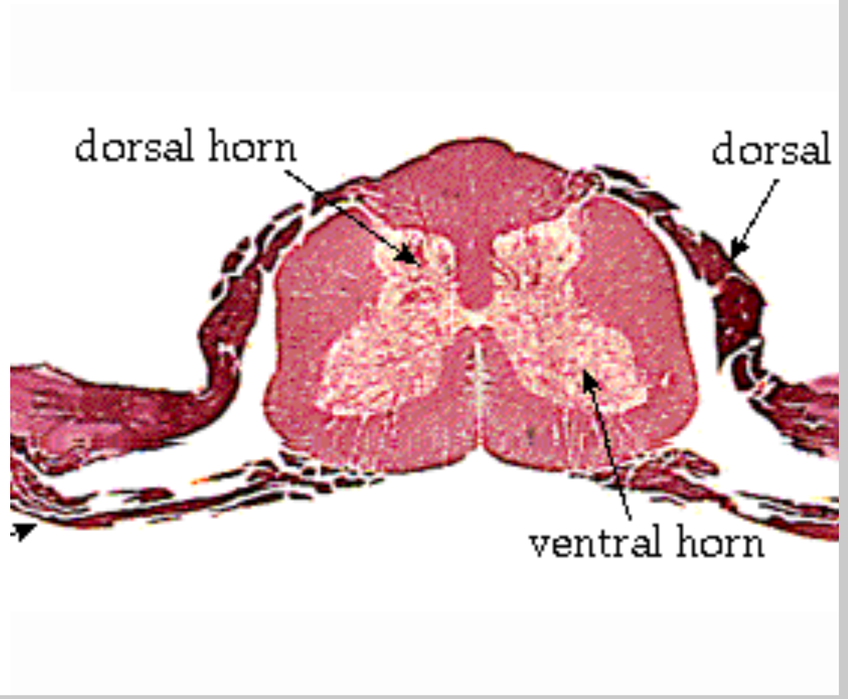
- What?
  - Motor (Sensory)
- Why?
  - Peripheral nerve injury
  - Spinal cord injury (trauma, inflammation)
  - FFMT
  - TMR
- When?
  - 9-12 months?
- How?
  - Set plays
  - Combined with tendon transfers?


A
B
G
H


Spinal cord (transected)
ıater (coating spinal
and spinal rootlets)
Dorsal root
within meninges)
ıntral root
neninges)
nerve
ıch
ınch
Meningeal
branch
Ramus
communicans
Dura mater
Arachnoid
Dorsa
Ventral
Spin
Ramus
communic
Sympathetic
trunk ganglia


Posterior
grey
column
Dorsal
nerve
root
Spinal
ganglion
Dorsal
ramus
Anterior
median
fissure
Anterior
grey
column
Lateral
grey
column
Ventral
nerve
root
Ventral
ramus


brain
spinal cord


dorsal horn
dorsal
ventral horn

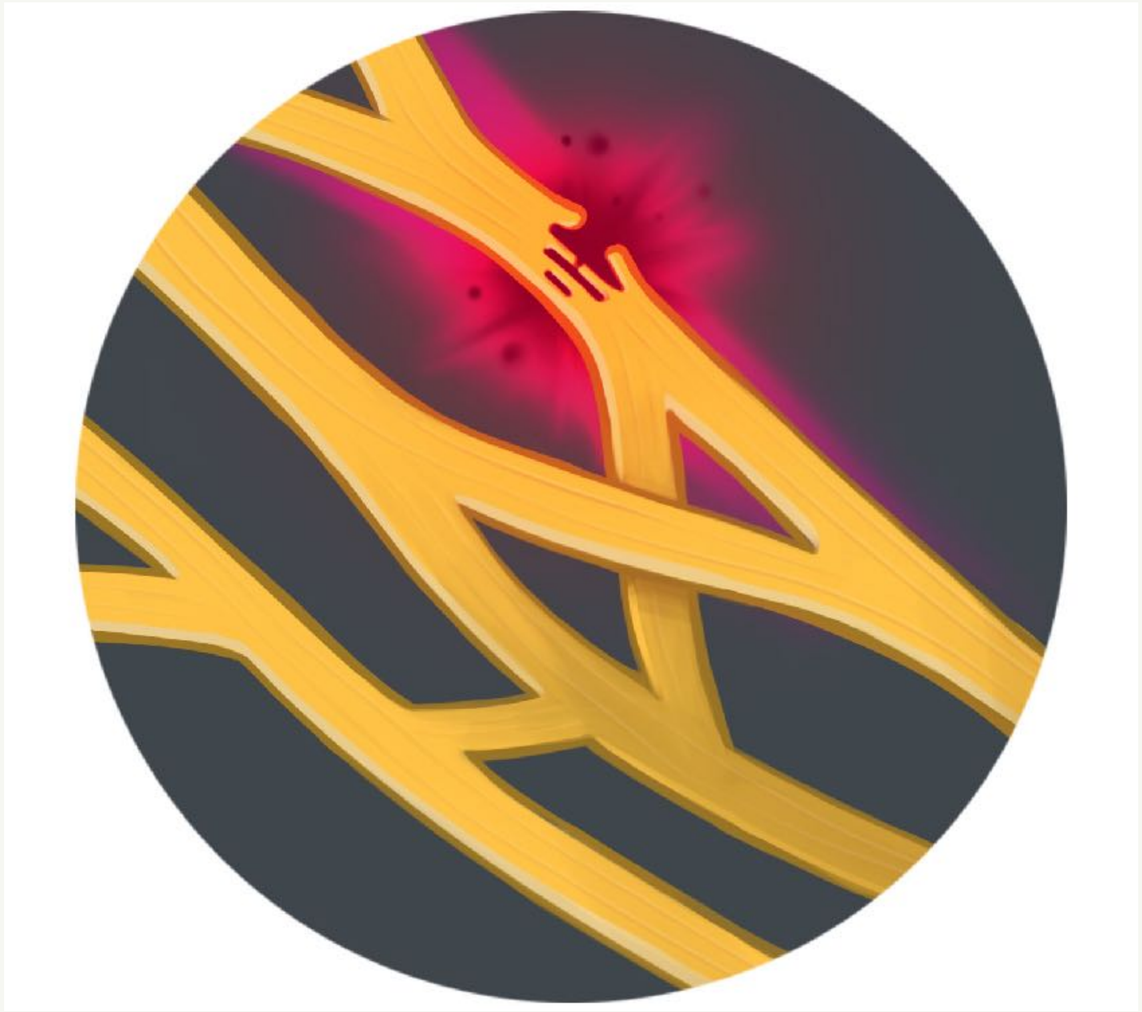
Thoughts

Nerve transfer is a technique not a treatment

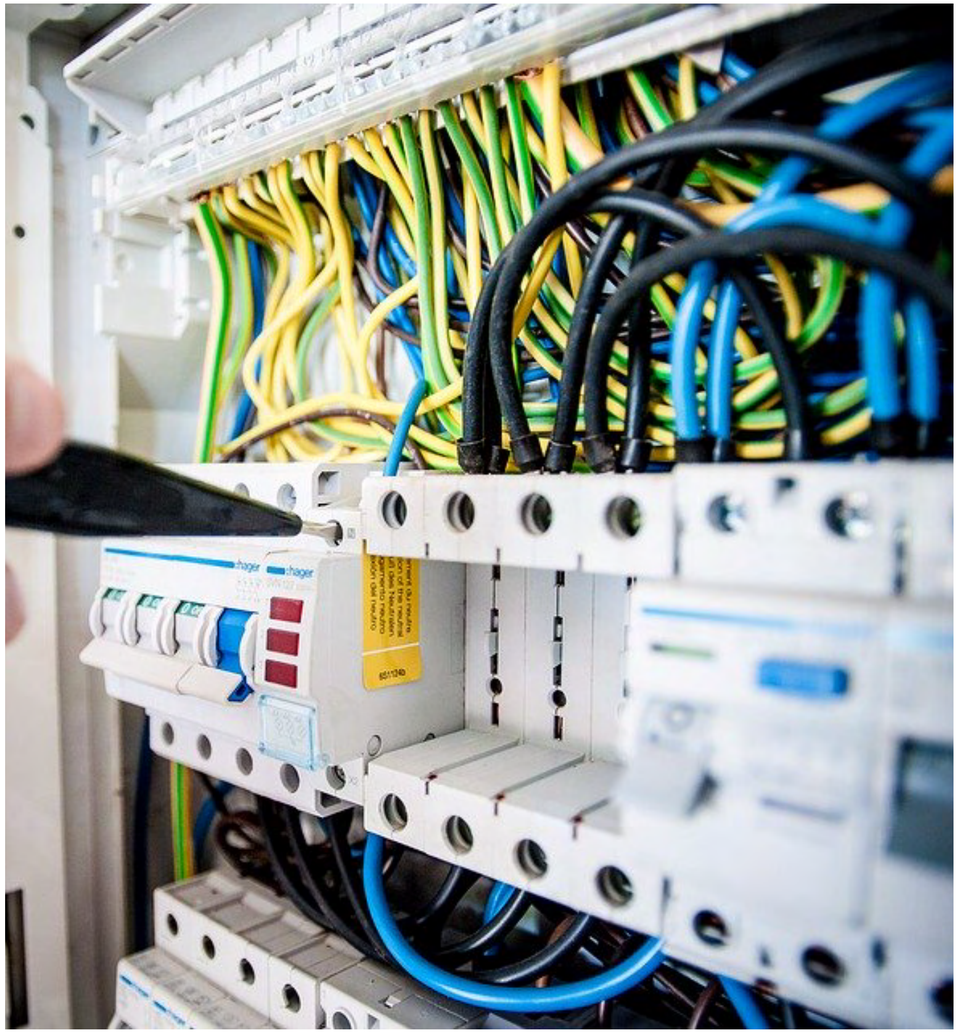
Learning post re-innervation function is key

Planning , Prehab and Rehab key

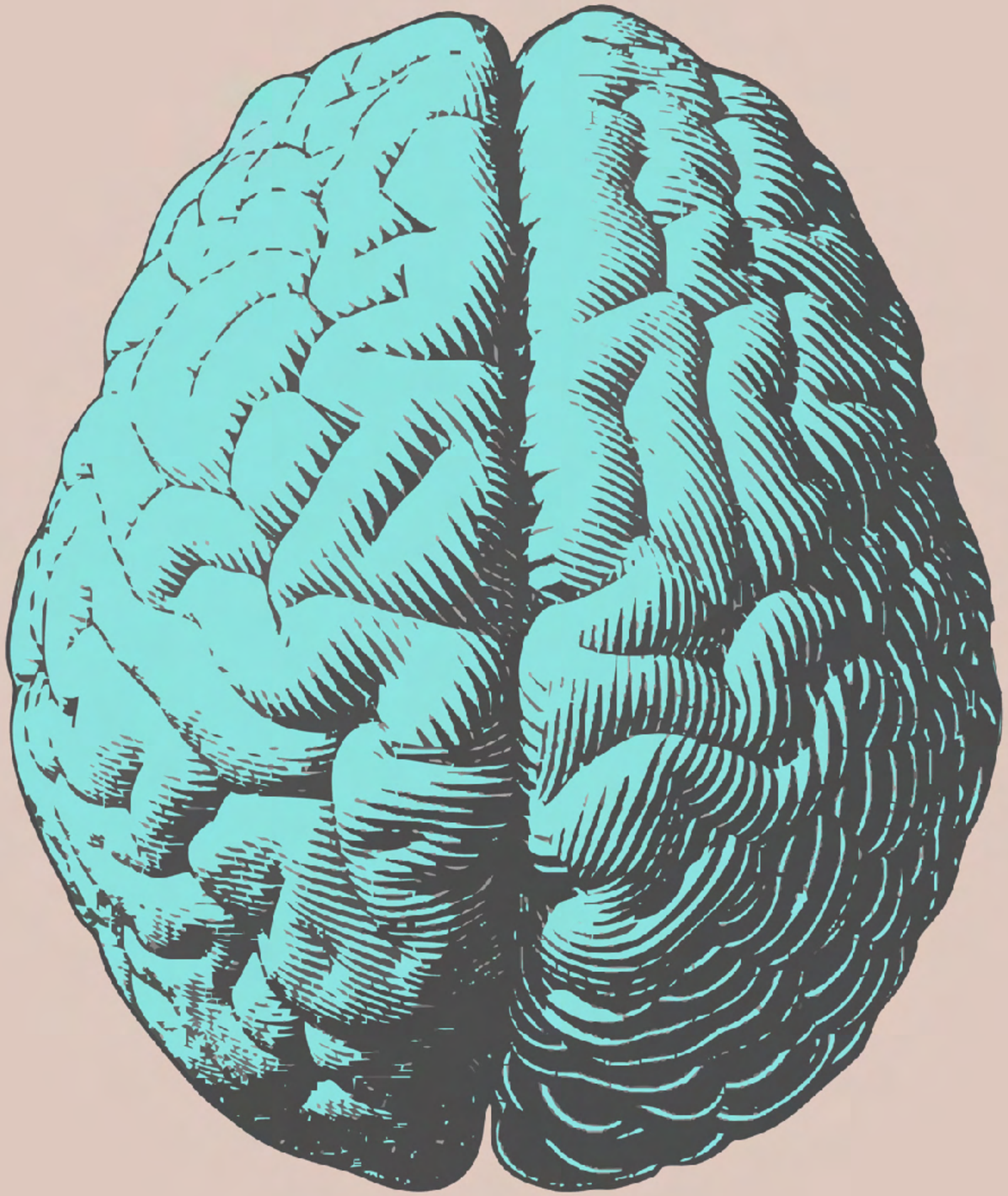
What when it fails or goes wrong?

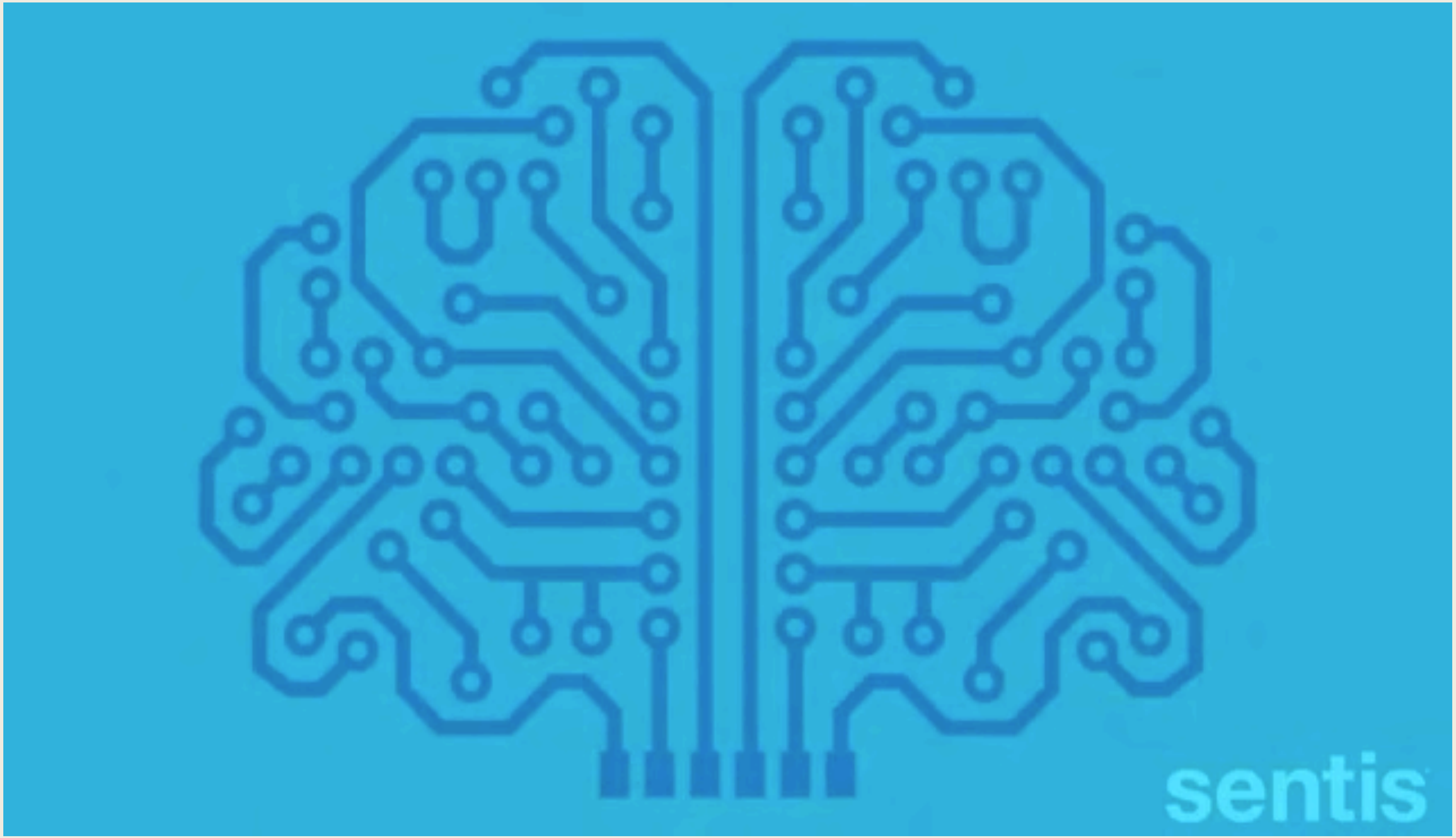


WHAT IS A NERVE TRANSFER?

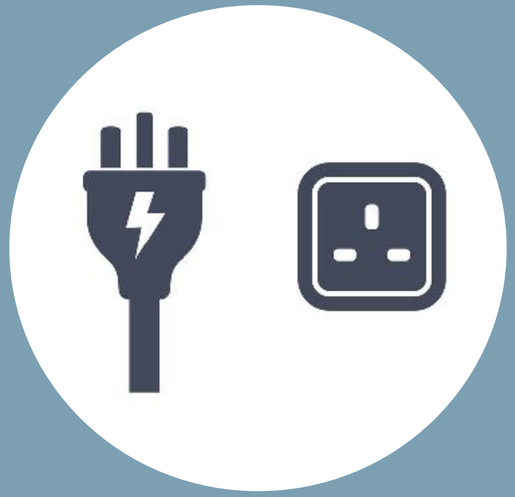


- USING WORKING NERVE CONNECTED TO THE BRAIN
- ROBBING PETER TO PAY PAUL
- REDIRECTING NERVES TO GROW TO A NEW MUSCLE
- BRAIN 'PLASTICITY' TO CONTROL THE NEW FUNCTION

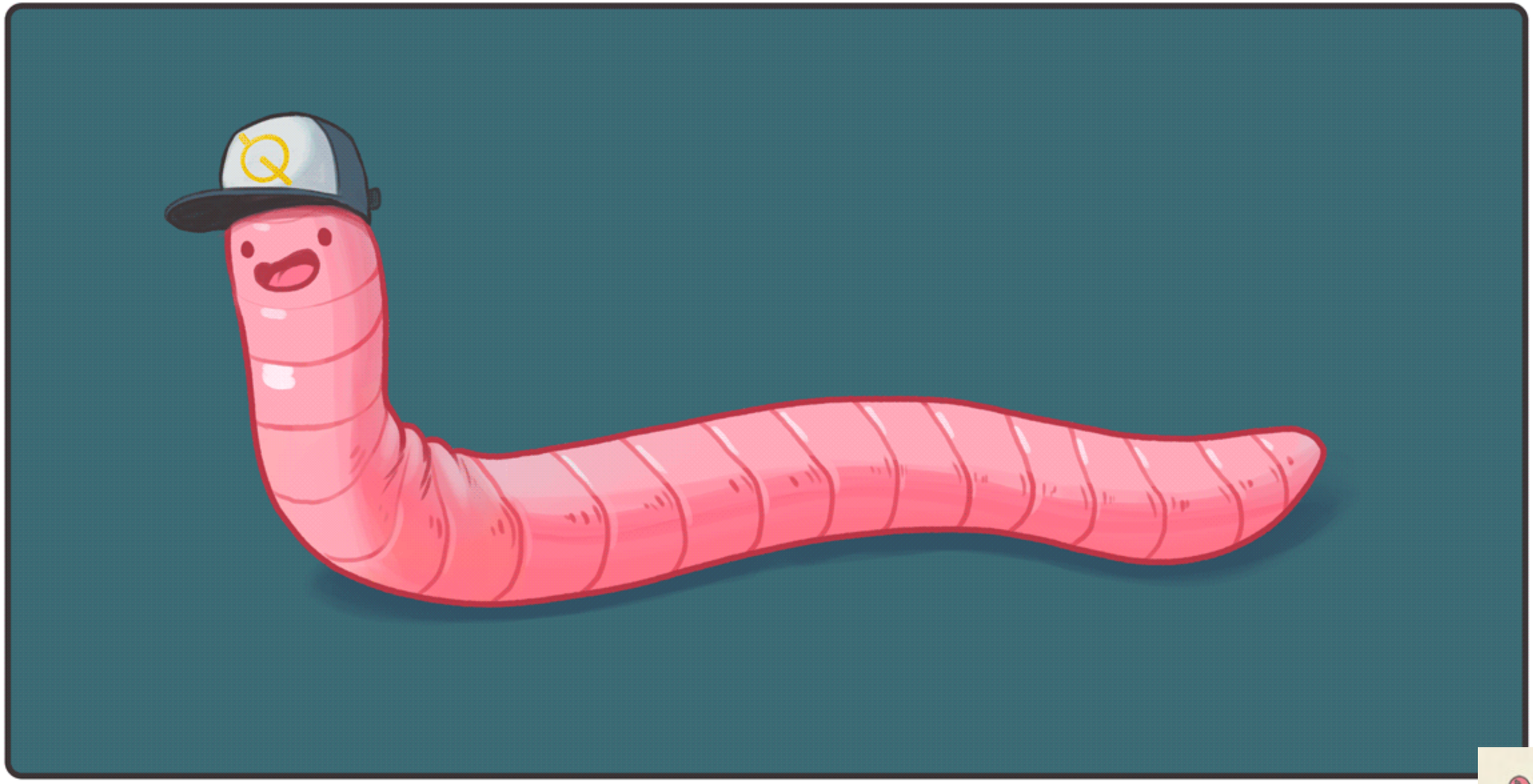



sentis

Simple answer is:
We have a denervated muscle ...
and a donor...



AXONAL REGENERATION



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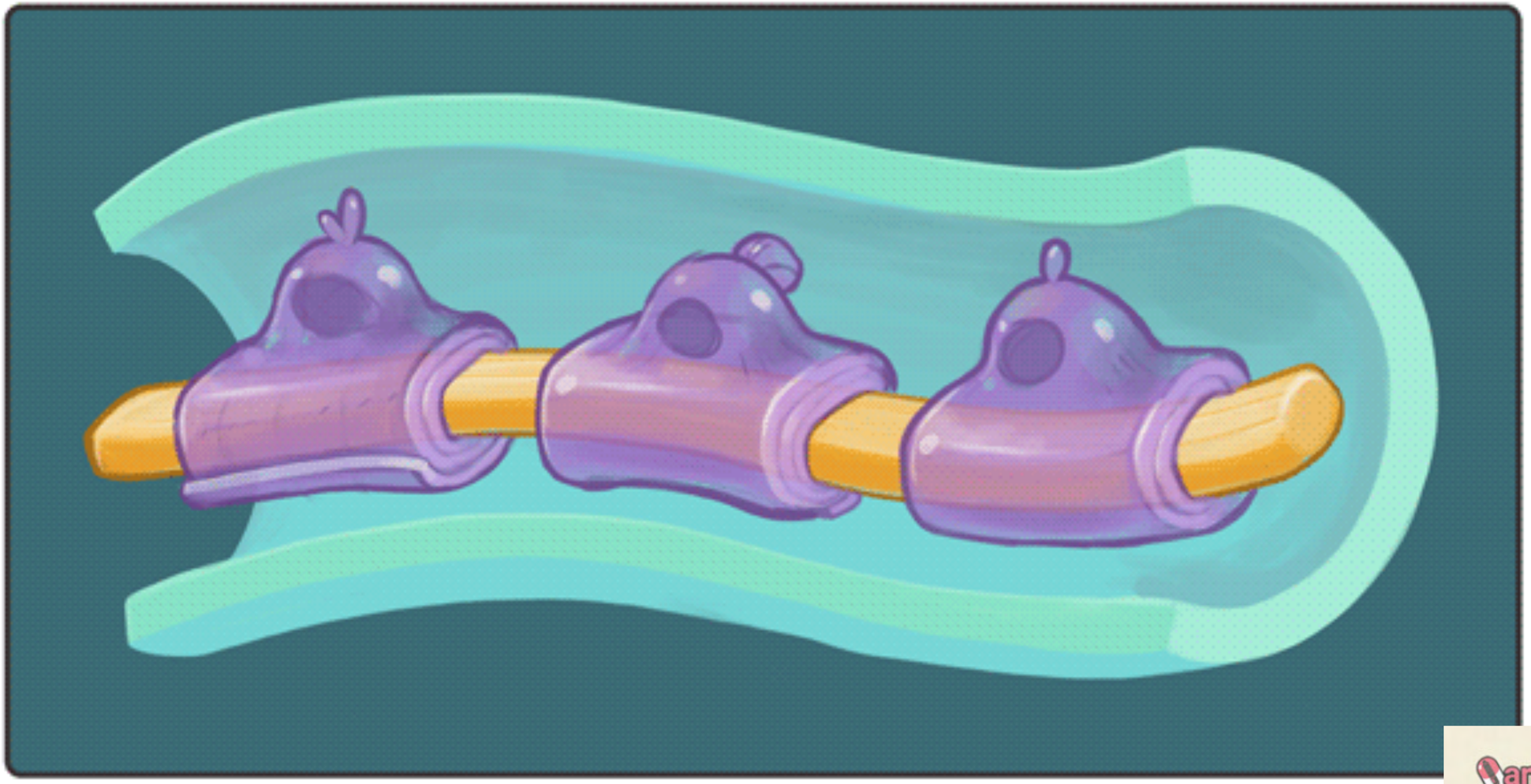
NERVE REGENERATION



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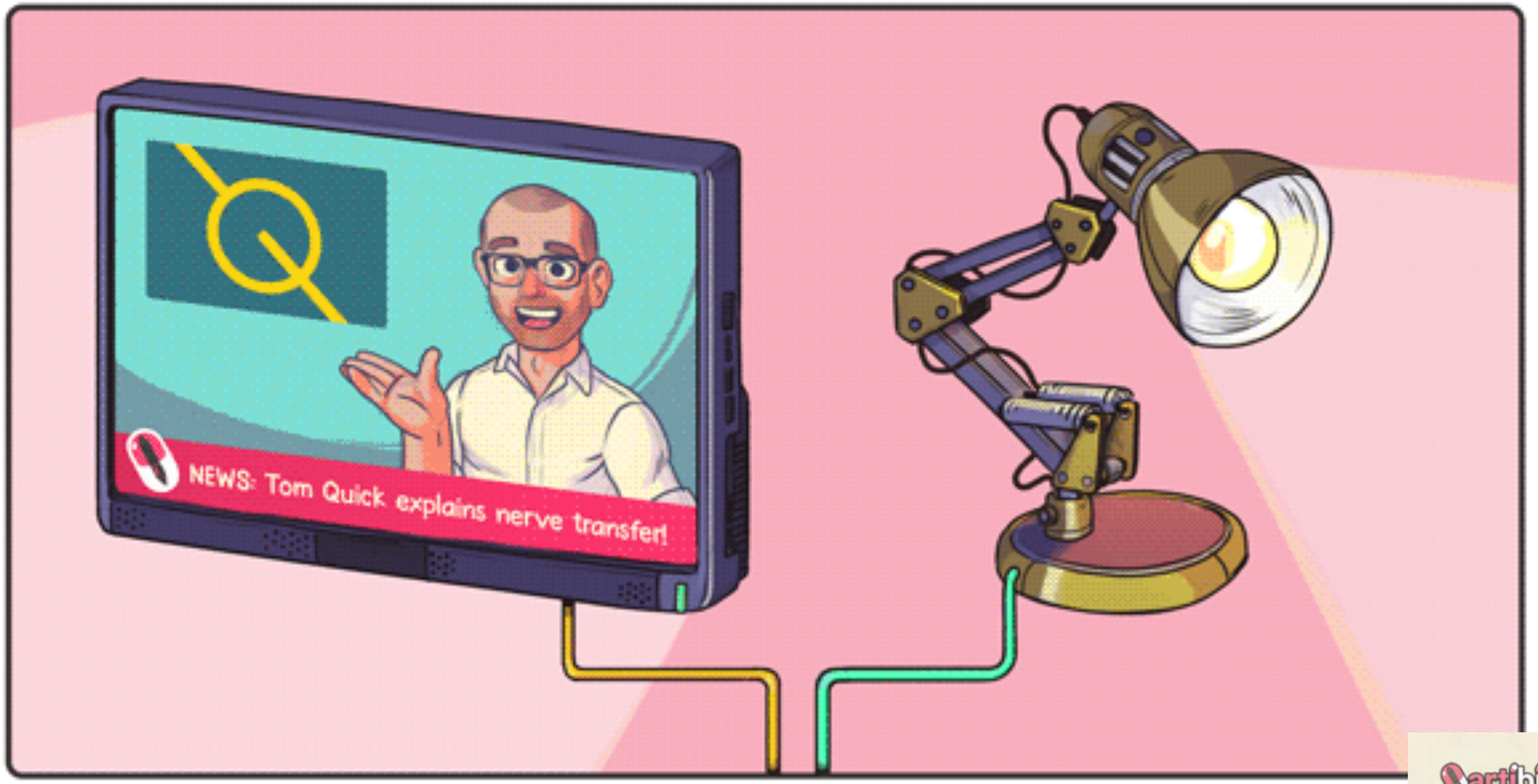
NERVE TRANSFER

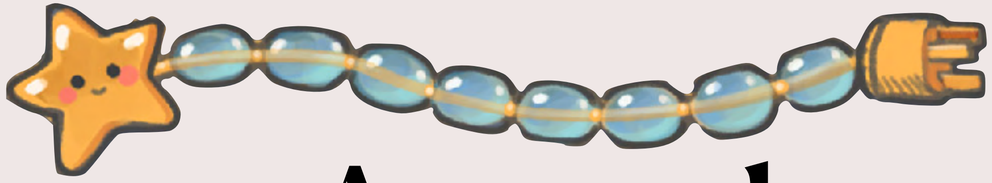


PROCESS OF REINNERVATION

REDIRECT WORKING NERVES

TIME TO GROW INTO NEW MUSCLE

RELEARN FUNCTION



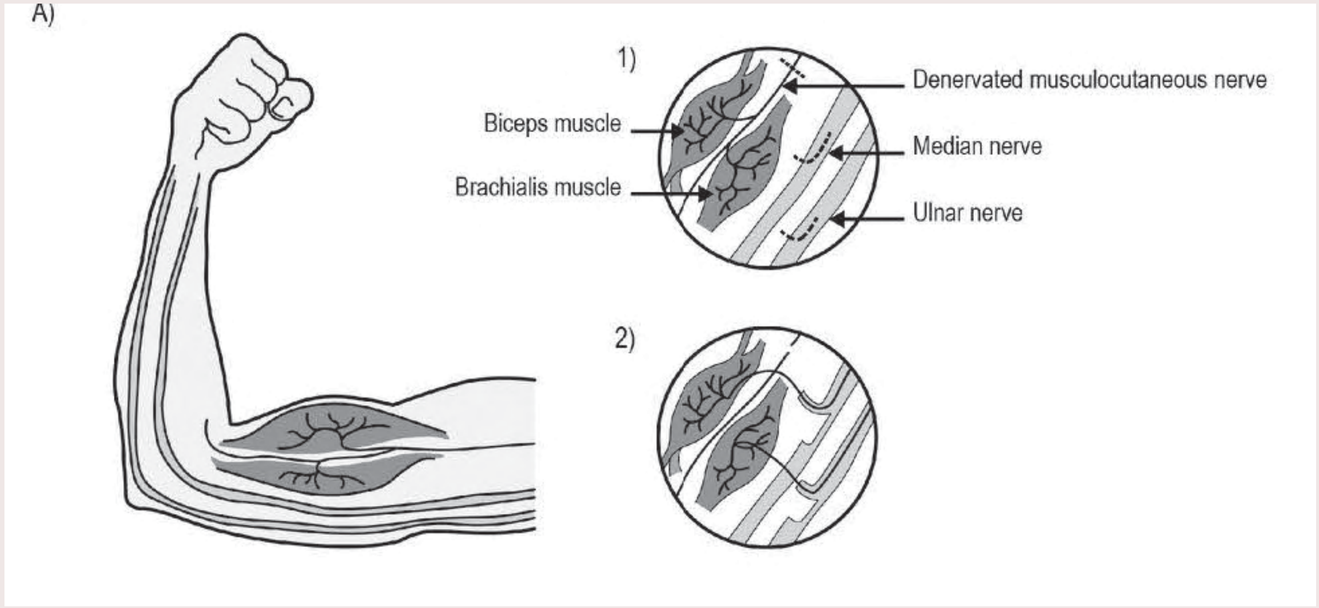
Approach

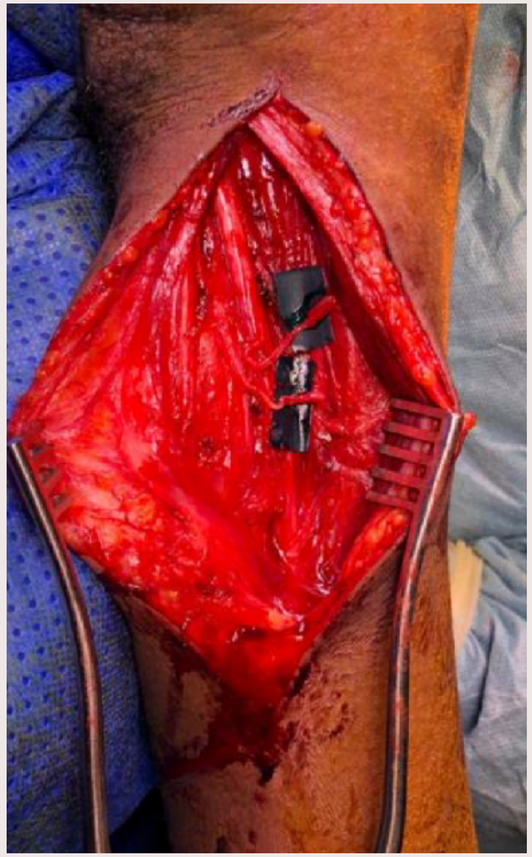
London

- Exploration of injury site is mandated - no CI evident, not clear diagnosis, more information required.
- Intra-operative decision making. Try to scope pre-op.
- Personalised care, get to know the aims of the patient.
- Team work - can’t do this alone.

Nerve Transfer Reconstruction

Double transfer for elbow flexion





Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

08:55 AM - 09:05 AM

To Supercharge or Not Supercharge

Susan E. Mackinnon, MD

No relevant conflicts of interest to disclose

ASSH
American Society for Surgery of the Hand

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:05 AM - 09:15 AM

Nerve Transfers to Restore Shoulder Function

Jayme A. Bertelli, MD, PhD

No relevant conflicts of interest to disclose

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

Live Pre03:
Current Treatment of Nerve Injuries, Gaps, and Neuromas (AM21)

Nerve Transfers to Restore Shoulder Function

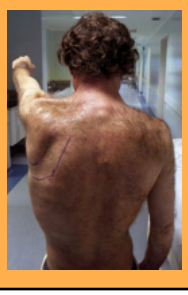
Dr Jayme A Bertelli

1

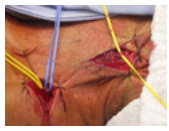
Nerves of the Shoulder Girdle

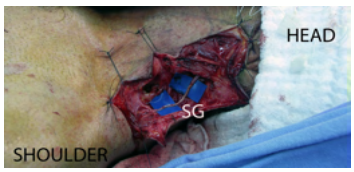
2

Accessory Nerve



Nerve Grafting





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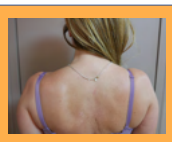
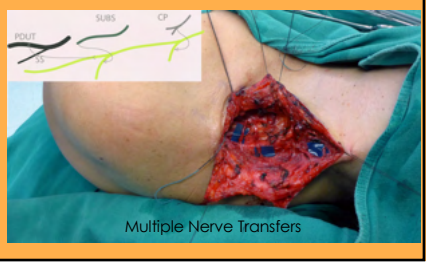
No Proximal Stump





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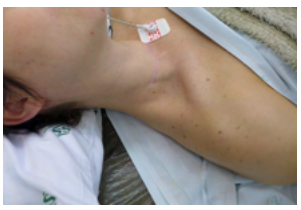
Multiple Nerve Transfers

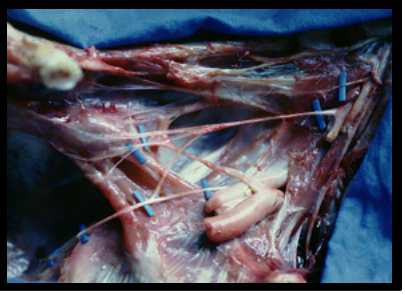
Robotic Thyroidectomy



5

Right Brachial Plexus

Long Thoracic Nerve



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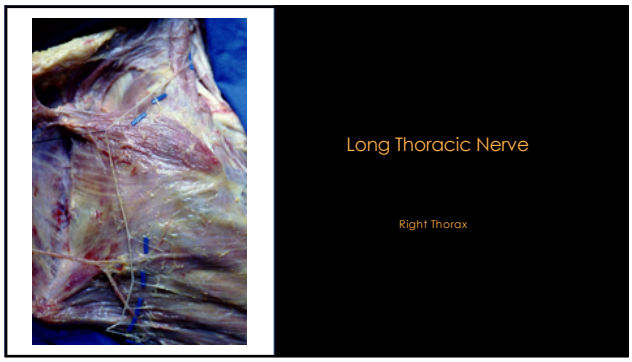
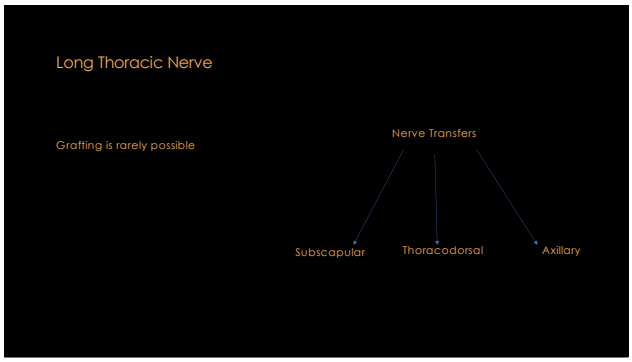
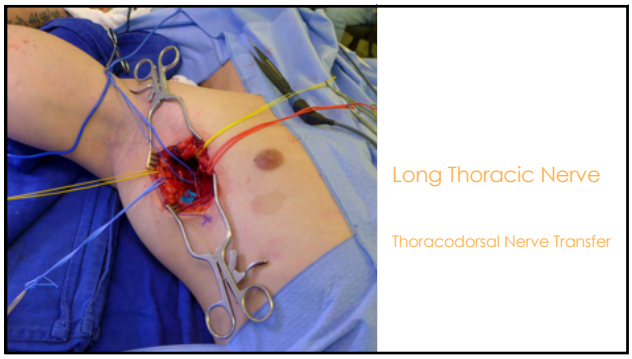

Long Thoracic Nerve
Right Thorax

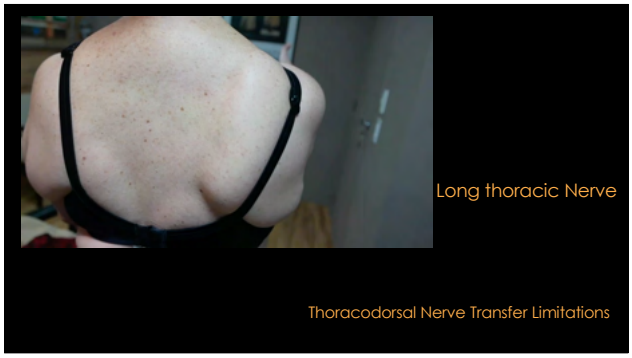
7


Long Thoracic Nerve
Grafting is rarely possible
Nerve Transfers
Subscapular
Thoracodorsal
Axillary

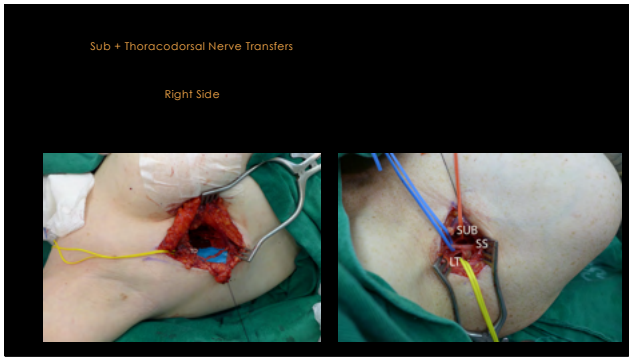
8


Long Thoracic Nerve
Thoracodorsal Nerve Transfer

9


Long thoracic Nerve
Thoracodorsal Nerve Transfer Limitations

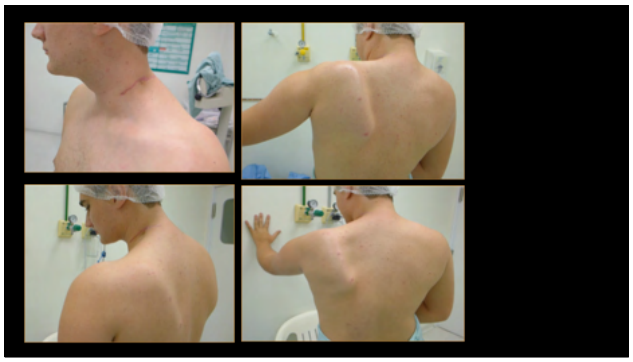
10


Sub + Thoracodorsal Nerve Transfers
Right Side
SUB
SS
LT

11


Branch to middle deltoid + Branch to Thoracodorsal
Long Thoracic Nerve
Dr Jayme A Bertelli

12



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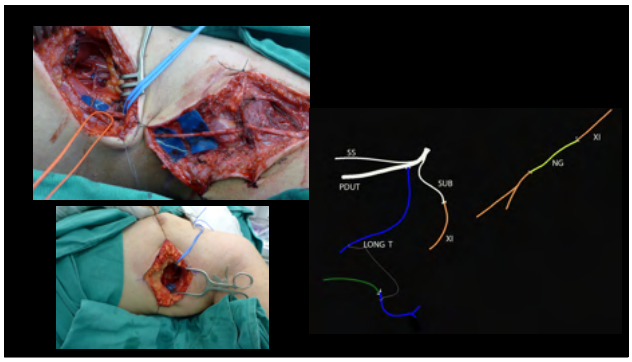

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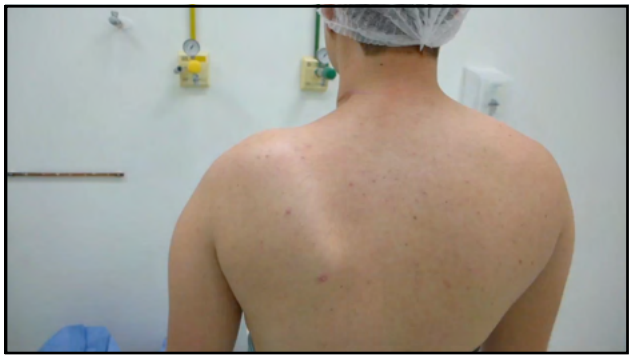
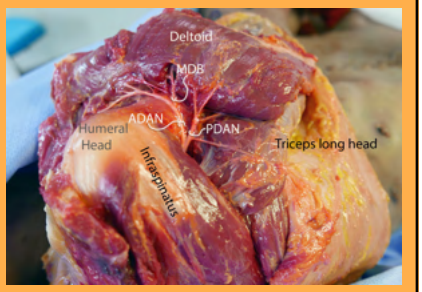


15

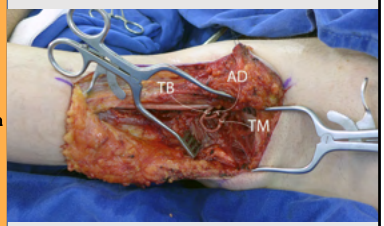
Axillary Nerve



16

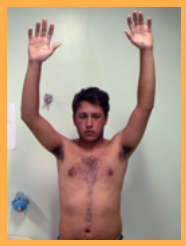
Axillary Nerve Repair in Brachial Plexus Paralysis

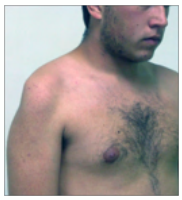
Abduction and External Rotation Reconstruction –
Teres Minor Reinnervation



17

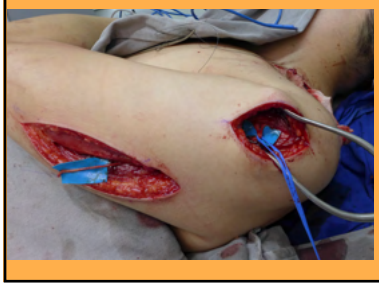
Axillary nerve paralysis





18

Trans-Deltoid Approach



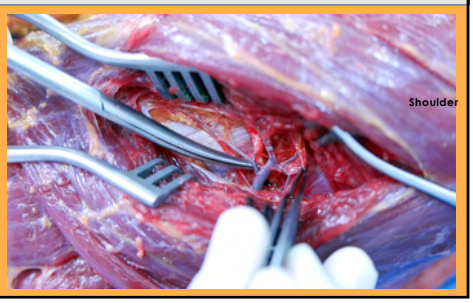
Isolated Injury of the Axillary Nerve

Gains in Endurance
Restoring Shoulder Contour
Targeting Anterior and Middle Deltoid

19

Trans deltoid Approach

Axillary Nerve

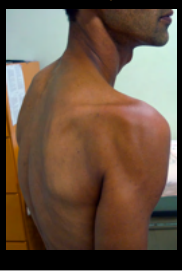


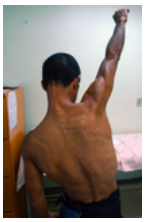
Dr Jayme A Bertelli

20

Suprascapular Nerve

Isolated Injury

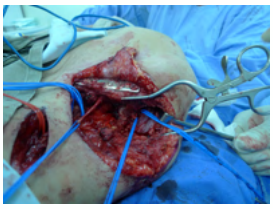


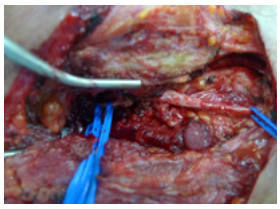


21

Suprascapular Nerve Injury

Dr Jayme A Bertelli





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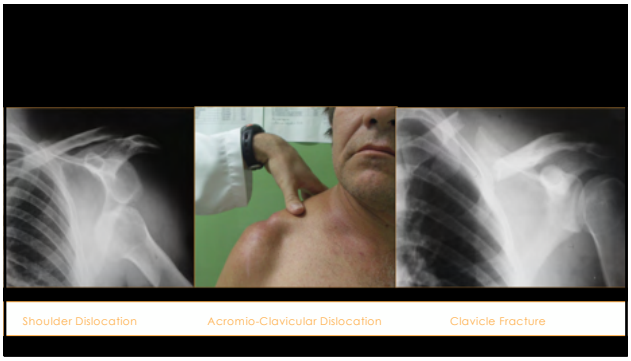
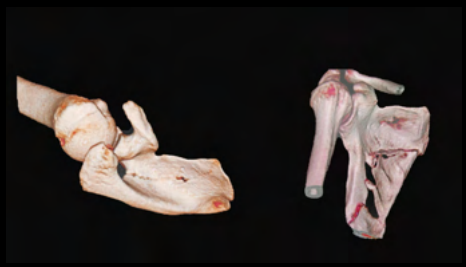


Shoulder Dislocation | Acromio-Clavicular Dislocation | Clavicle Fracture

23

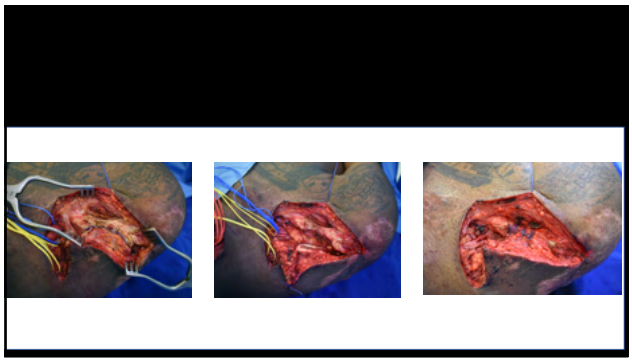
Scapular Fractures



24


SN
XI
Suprascapular Nerve Exposure
in Brachial Plexus Injuries

25



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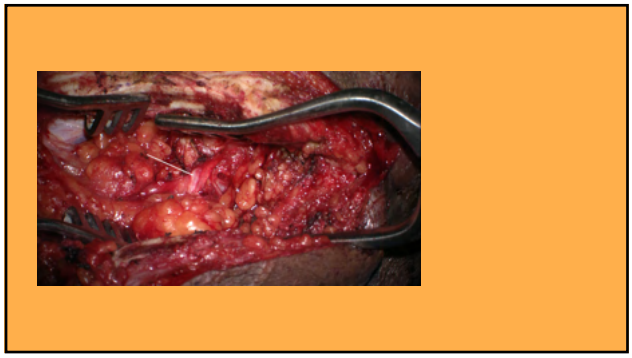

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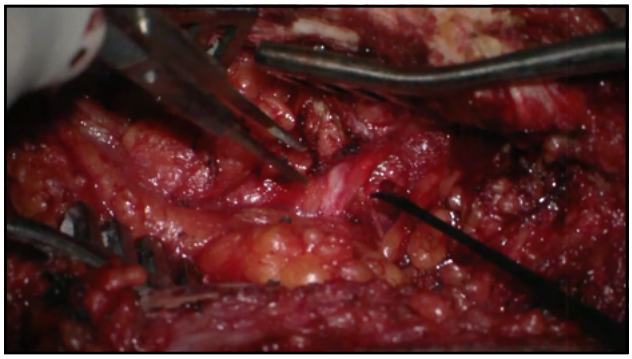

28

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:15 AM - 09:25 AM

Nerve Transfers to Restore Elbow Function

Alexander Y. Shin, MD

- TriMed Orthopaedics / Mayo Medical Ventures - Royalties or patent beneficiary
- Aptis Medical – Speaker Bureau

ASSH
American Society for Surgery of the Hand

76TH ANNUAL MEETING OF THE ASSH
SEPTEMBER 30 - OCTOBER 2, 2021

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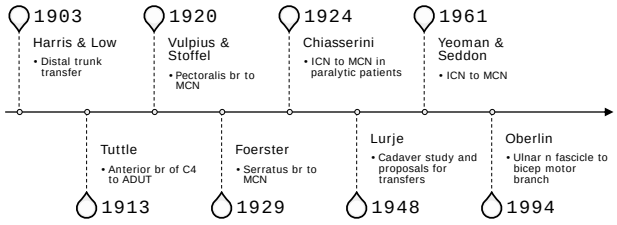
Nerve Transfers to Restore Elbow Flexion

Alexander Y. Shin, MD
Mayo Clinic
Rochester, Minnesota

3

Nerve Transfers for Elbow Flexion: History



4

Role of Elbow Flexion

- Most important function to restore in brachial plexus injury
- Anatomy
  - Biceps
  - Brachialis
  - Brachioradialis
  - Inadvertant flexors

5

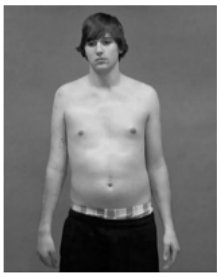
Clinical Findings of C5-6 (Classic)

- Loss elbow flexion
- Loss of shoulder function/stability
  - Abduction
  - External rotation
- Loss FCR/Pronator

6

Clinical Findings of C5-7 (Classic)

- C5-6 loss plus
  - Serratus
  - Triceps
  - ± Latissimus
  - ± Radial nerve



7

Clinical Findings C5-T1 (Classic)

- No biceps
- No shoulder
- No triceps
- No hand
- No Sensation

8

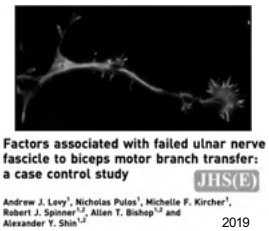
Indication for Nerve Transfer

- Available donor nerve(s)
- Presentation within an appropriate time frame from injury
- Orthopedic stability and mobility
- Age

9

Donor Nerve(s)

- Redundant function
- Free from injury
  - mBMRC >4
  - EMG
- Synergistic function
- Anatomically feasible
- Minimize morbidity



Factors associated with failed ulnar nerve fascicle to biceps motor branch transfer: a case control study

JHS(E)

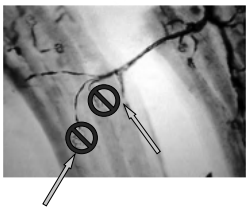
Andrew J. Levy[1], Nicholas Pulos[1], Michelle F. Kircher[1], Robert J. Spinner[1,2], Allen T. Bishop[1,2] and Alexander Y. Shin[1,2]

2019

10

Time from Injury

- 3-6 months
  - Ideal
- 6-9 months
  - Feasible
- > 12 months
  - Concerning for failure



Motor Endplates

11

Age

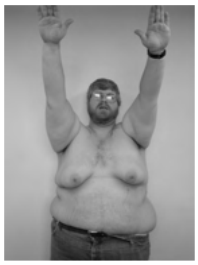
- Is it a factor?
- How old is too old?
- Chronological vs physiologic old?

Ayhan et al, Microsurgery 2020
Lee et al, JHS A, 2012

12

BMI

- Does it have an effect?
- Are decisions changed with excessive BMI?



Influence of body mass index on the outcome of brachial plexus surgery: are there any differences between elbow and shoulder results?

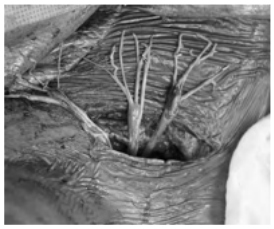
Mariano Socolovsky · Roberto S. Martins · Gilda Di Masi · Gonzalo Bonilla · Mario G. Siqueira

Acta Neurochir (2014) 156:2337–2344
DOI 10.1007/s00701-014-2256-9

13

Decision Making

- Dependent on type of injury
  - Nerve Injury

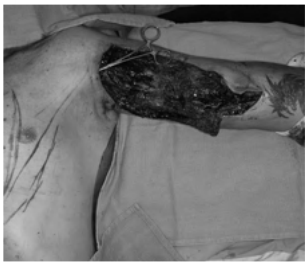


14

Decision Making

- Dependent on type of injury
  - Soft tissue

"hard to reinnervate a biceps that is missing"

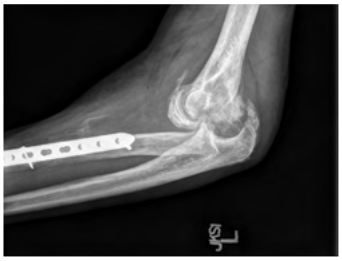


15

Decision Making

- Dependent on type of injury
  - Osseous

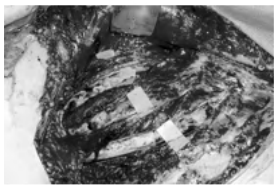
Need to optimize joint function and determine if nerve transfer will be effective or not

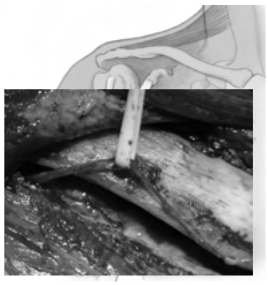


16

Nerve Transfers for Elbow in Pan Plexus

- Intercostal to MCN
  - Yeoman & Seddon 1961
  - Hara 1969



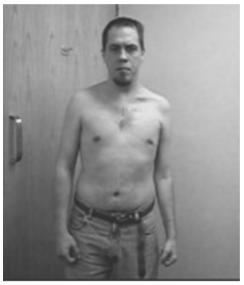


17

Nerve Transfers for Elbow in Pan Plexus

- ICN to MCN
  - Lifelong ROM limitations
  - Interposition grafting
    - ↓ results 47% vs 72%
  - Non-intuitive activation

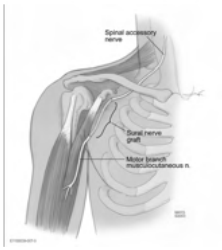
Merrel et al, JHS-A 2001



18

Nerve Transfers for Elbow in Pan Plexus

- SPA to MCN with an interposed nerve graft
  - Typically done when few options available
  - Outcome time dependent
  - 72% M3 or better

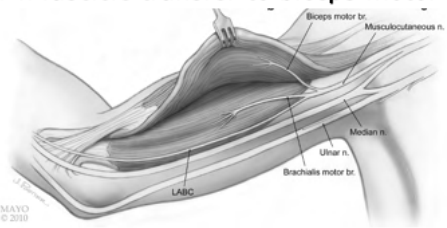


Samii et al, J Neurosurg, 2003

19

Nerve Transfers for Elbow C5-6 Injury

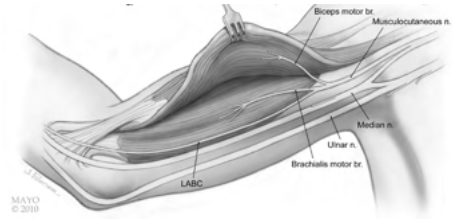
- Ulnar n fascicle transfer to biceps motor branch



20

Nerve Transfers for Elbow C5-6 Injury

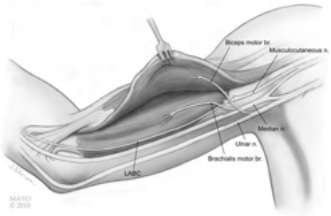
- Median n fascicle transfer to brachialis motor branch



21

Nerve Transfers for Elbow C5-6 Injury

- Combined - Double



22

Ulnar Nerve Fascicle Transfer

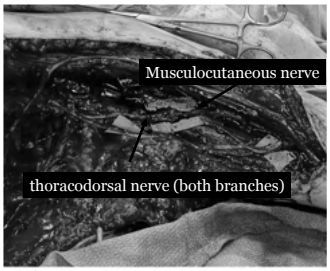
23

Double Fascicle Nerve Transfer

24

Nerve Transfers for Elbow C5-6 Injury

- Pectoral nerve to MCN
- Thoracodorsal nerve to MCN



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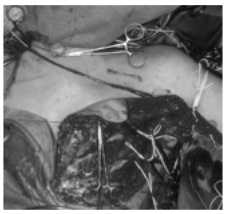
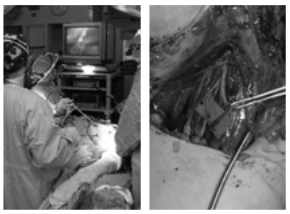
Nerve Transfer

- Others



Contralateral C7



Phrenic

26

Controversies

- Distal only surgery (no grafting of roots)
  - In Pan Plexus
    - Need all possible donors
  - In Upper trunk
    - Prefer nerve transfer (Ulnar n fascicle)
    - Will always explore and use roots if available for shoulder

27

Controversies

- Single versus Double fascicles -Controversial

Outcomes of Single versus Double Fascicular Nerve Transfers for Restoration of Elbow Flexion in Patients with Brachial Plexus Injuries: A Systematic Review and Meta-Analysis

Plastic and Reconstructive Surgery • July 2019

2020 WILEY

Is one nerve transfer enough? A systematic review and pooled analysis comparing ulnar fascicular nerve transfer and double ulnar and median fascicular nerve transfer for restoration of elbow flexion after traumatic brachial plexus injury

Comparison of Single versus Double Nerve Transfers for Elbow Flexion after Brachial Plexus Injury

Plastic and Reconstructive Surgery • January 2011

28

Controversies

- Use of recovered nerves for transfer

Factors associated with failed ulnar nerve fascicle to biceps motor branch transfer: a case control study

JHS(E)

Andrew J. Lovy[1], Nicholas Pulos[1], Michelle F. Robert J. Spinner[1,2], Allen T. Bishop[1,2] and Alexander Y. Shin[1,2]

2019

29

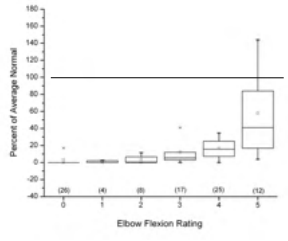
Controversies

- Measuring outcomes
  - Many modifications of BMRC
  - Grade IV
    - 96% of the entire scale
  - Surgeon's Measurement bias

Mc Avoy & Green, JHS A, 2007
Shahgholi, et al, AJ PMR, 2012

30

Biceps BMRC rating vs % Normal



31

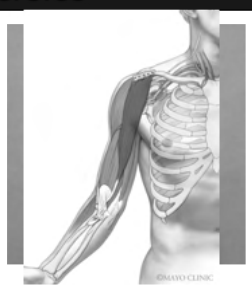
Table 3. Results of Case Series

Case No.	Age (yr)	Gender	Dominant Hand	Mechanism	Injury	Primary Intervention	Secondary Procedures	Interval to Surgery (mo)	Elbow Flexion	Shoulder Abduction	Follow-Up (mo)
1	21	M	No	MCA	AV (C6-T1), Com (UT)	Nrf XI-SS, NG of UT	Shoulder fusion	6	NA	0	86
2	67	M	No	MVA	AV (C6-T1), Com (UT)	Nrf XI-SS; IC (3, 4, 5)-MC; NG C5-AX and RD 15 cm		5	0	3*	72
3	23	M	Yes	ATV	AV (C6-T1), Com (UT)	Nrf IC (3-4)-AX, MP, RD, NG UT-MC, SS		4	NA	4*	78
4	39	M	No	MVA	AV (C6-T1), Inc (UT)	Nly UT, Nrf IC (3-7)-MN, AX, and MC		4	3	0	34
5	32	M	No	Industrial	AV (C5, 6)	Nrf XI-SS, IC (3-5)-MC, Swindler		5	85	4	37
6	32	M	Yes	MCA	AV (C6-8), Inc (UT)	Nrf XI-AX, IC (4-6)-MC; Nly SS		5	5	0	32
7	7	M	Yes	MVA	AV (C5-7)	Nrf XI-SS, IC (4-6)-MC		5	4	4	28
8	23	M	Yes	Moped	AV (C6, 7), Com (UT)	Nrf XI-SS, IC (4-6)-AX, MP-MC	Swindler	5	31	4*	48
9	48	M	Yes	MCA	AV (C5-T1)	Nrf XI-SS, IC (4-6)-MC	Shoulder fusion	5	4	0	28
10	28	M	Yes	MCA	AV (C6-8), Com (UT), Inc (MT)	Nrf XI-SS, IC (5-7)-MC		4	3	3	19
11	19	M	No	ATV	AV (C6-T1), Com (UT)	Nrf XI-SS, IC (4-6)-MC; NG UT-AX		8	4	3*	12
12	9	M	No	MVA	AV (C5-T1)	Nrf XI-SS, IC (3, 4)-MC, IC (5, 6)-AX		5	4	2*	19
13	26	M	No	MCA	AV (C5, 6), Com (MT)	Nrf XI-SS, IC (4-7)-MC, MP-AX		5	5	4*	18
14	31	M	Yes	MCA	AV (C5, 6), Inc (MT)	Nrf XI-SS, IC (4-6)-MC, MP-AX		7	4	3*	17
15	40	M	Yes	Explosion	AV (C5-T1)	Nrf XI-SS, IC (3-5)-Oswilio		6	NA	0	17

32

Controversies

- Addressing failures
  - Tendon transfer
    - Triceps
    - Latissimus
    - Bipolar Pectoralis
  - FFMT



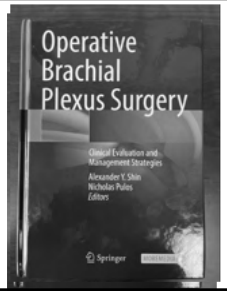
33

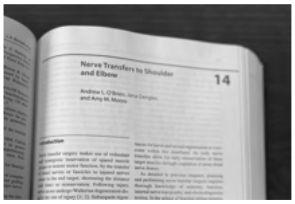
Nerve Transfers for Elbow Flexion

- Summary
  - Critical decision making
  - Careful comparison of results
  - Options for failures

34

References





35

Thank You

36

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:25 AM - 09:35 AM

Nerve Transfers to Restore Extrinsic Finger Function

Fraser J. Leversedge, MD

- Axogen – Researcher/Consultant
- Stryker - Consultant
- Bioventus - Consultant
- CoNextions - Consultant
- Wolters Kluwer - Royalties or patent beneficiary

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SEPTEMBER 30 - OCTOBER 2, 2021

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:30 AM - 09:45 AM

Nerve Transfers to Restore Intrinsic Function

Jennifer L. Giuffre, MD, FRCSC

No relevant conflicts of interest to disclose

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Anterior Interosseous-to-Ulnar Motor Nerve Transfers: A Single Center's Experience in Restoring Intrinsic Hand Function

Graham J McLeod[1], Blair R Peters[1], Tanis Quaife[1], Tod A Clark[1], Jennifer L Giuffre[1]

- PMID: 32696669
  DOI: 10.1177/1558944720928482

Abstract

Background: Transfer of the anterior interosseous nerve (AIN) into the ulnar motor branch improves intrinsic hand function in patients with high ulnar nerve injuries. We report our outcomes of this nerve transfer and hypothesize that any improvement in intrinsic hand function is beneficial to patients.

Methods: A retrospective review of all AIN-to-ulnar motor nerve transfers, including both supercharged end-to-side (SETS) and end-to-end (ETE) transfers, from 2011 to 2018 performed by 2 surgeons was conducted. All adult patients who underwent this nerve transfer for any reason with greater than 6 months' follow-up and completed charts were included. Primary outcome measures were motor function using the British Medical Research Council (BMRC) grading system and subjective satisfaction with surgery using a visual analog scale. Secondary outcome measures included complications and donor site deficits.

Results: Of the 57 patients who underwent nerve transfer, 32 patients met the inclusion criteria. The average follow-up and average time to surgery were 12 and 15.6 months, respectively. The overall average BMRC score was 2.9/5, with a trend toward better recovery in patients who received earlier surgery (<12 months = BMRC 3.7, ≥12 months = BMRC 2.2; $P < .01$). Patients with an SETS transfer had better results that those with an ETE transfer (SETS = 3.2, ETE = 2.6). There were no donor deficits after operation. One patient developed complex regional pain syndrome.

Conclusions: Patients with earlier surgery and an in-continuity nerve (receiving an SETS transfer) showed improved recovery with a higher BMRC grade compared with those who underwent later surgery. Any improvements in intrinsic hand function would be beneficial to patients.

Keywords: cubital tunnel syndrome; diagnosis; nerve; nerve compression; nerve injury; nerve reconstruction; nerve regeneration.

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:45 AM - 09:55 AM

Therapy After Nerve Repair

Cecelia M. Skotak, OT/L, CHT

No relevant conflicts of interest to disclose

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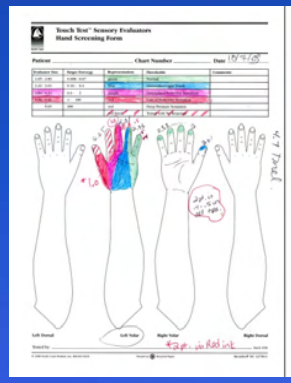
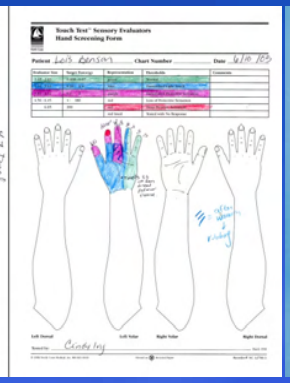
Therapy After Nerve repair: How a Hand Therapist Can Partner With You to Manage Patients with Nerve Injury

Cecelia (Cece) Skotak, OT, CHT
Instructor, Physical Medicine and Rehabilitation
skotak.cecelia@mayo.edu

WAYS THE THERAPIST CAN PARTNER WITH THE SURGEON

- 1. Damage Control (Prevent Complications)
- 2. Assess Status and Track Progress
- 3. Maximize Functional Outcome

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DAMAGE CONTROL

Principles of Complication Prevention

- Avoid Contracture/Instability/Overstretching
- Prevent Tissue Damage Due to Sensory Loss
- Assist with Pain Management
- Maintain Cortical Representation
- Positioning (edema & protection of repair)

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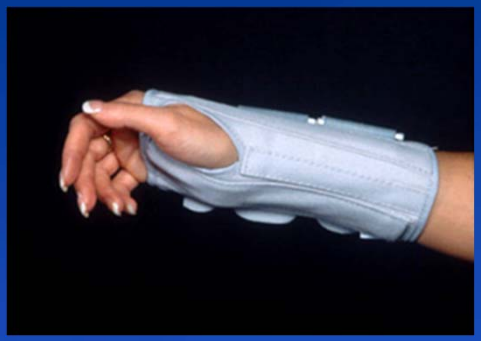
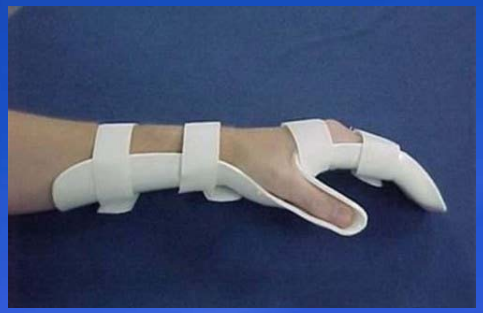
DAMAGE CONTROL
TACTICS TO AVOID CONTRACTURE/ INSTABILITY/ OVERSTRETCHING





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DAMAGE CONTROL
TACTICS TO AVOID CONTRACTURE/ INSTABILITY/ OVERSTRETCHING

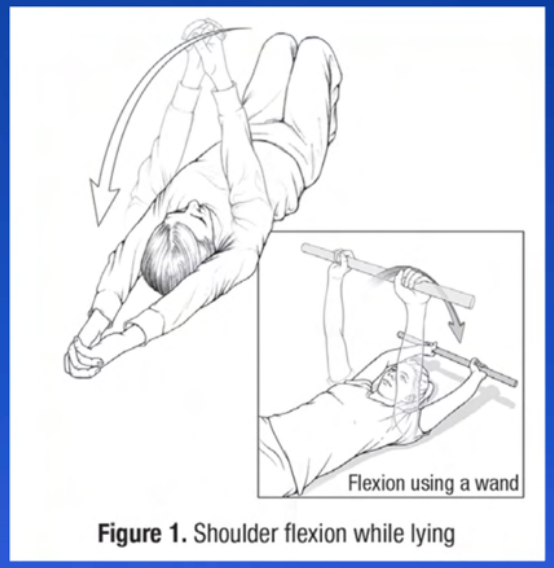


Figure 1. Shoulder flexion while lying

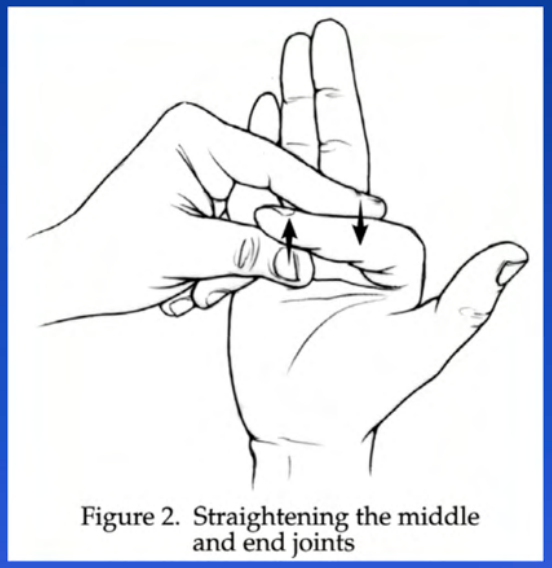


Figure 2. Straightening the middle and end joints

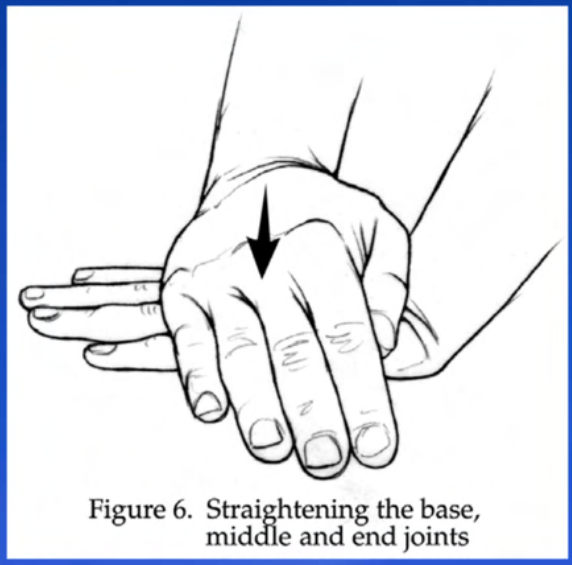
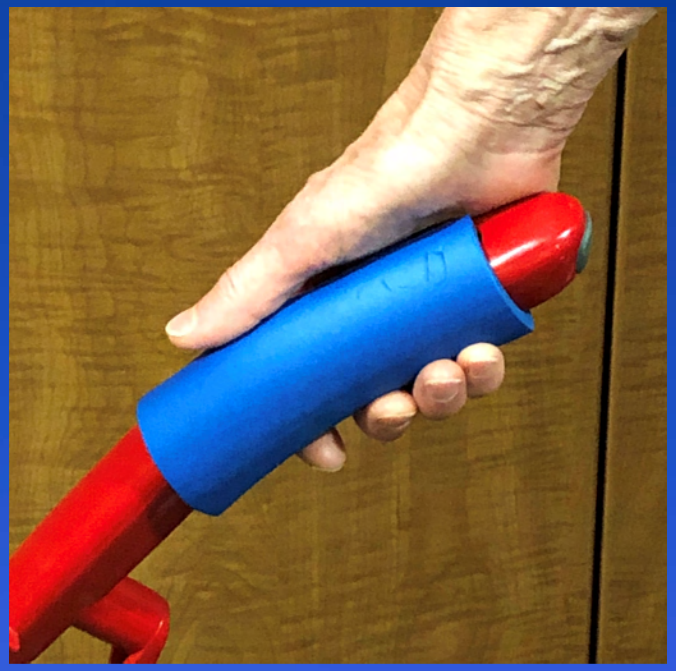
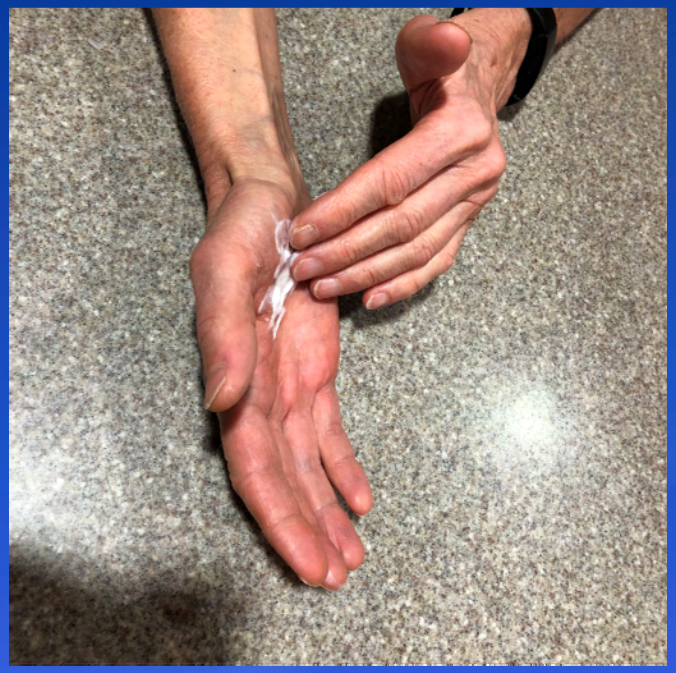


Figure 6. Straightening the base, middle and end joints

Damage Control: Tactics to Prevent Tissue Damage Due to Sensory Loss





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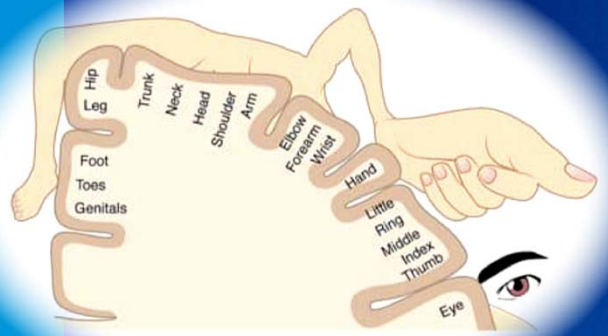
Damage Control: Tactics to Assist With Pain Management

Damage Control
Tactics to Maintain Cortical Representation: Functional Orthotics



Damage Control: Tactics to Maintain Cortical Representation: Discourage Detrimental Compensatory Function

Damage Control
Tactics to Maintain Cortical Representation: Mirror Therapy

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Damage Control
Tactics to Maintain Cortical Representation: Sling

Damage Control
Tactics to Maintain Cortical Representation: Myoelectric Orthosis

https://www.youtube.com/watch?v=ifsvqqdmMDM

Assess Initial Status and Track Progress

- Sympathetic Function
- Sensibility Function
- Motor Function
- Basic and Instrumental Activities of Daily Living Function
- Psychosocial Context
- Help Define Patient Goals

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Assess Initial Status and Track Progress: Sympathetic Function

- Vasomotor
- Sudomotor
- Pilomotor
- Trophic

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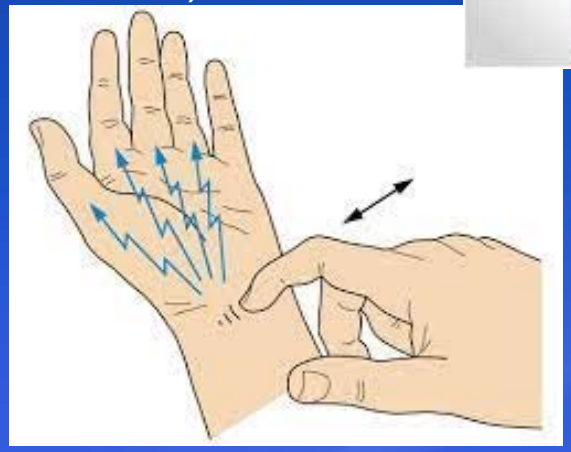
Assess Initial Status and Track Progress: Sensibility Function

- Tinel's
- Mapping of dysfunction
- 10/10 screening
- Light Touch/Monofilament (threshold)
- Two Point (density)
- Stereognosis
- Localization



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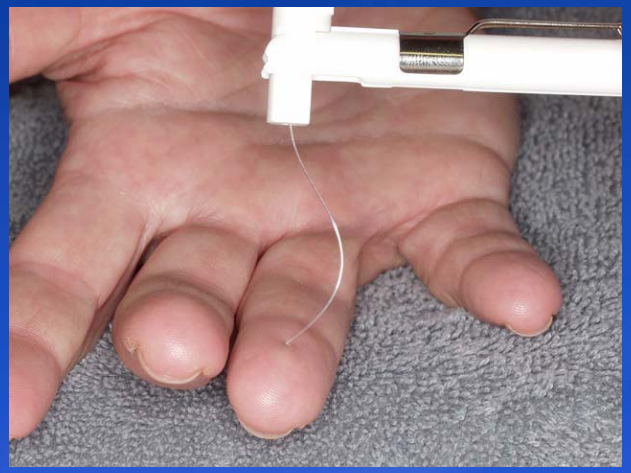
Assess Initial Status and Track Progress: Sensibility Function

Median Nerve Decompression at Wrist:Semmes Weinstein

Date	4/30/2020	8/27/2020	2/25/2021
	right	right	right
Thumb	6.65	4.31	3.61
Index	6.65	4.56	3.61
Long	6.65	4.56	4.31
Radial Ring	6.65	4.31	3.61
Ulnar Ring	2.83	2.83	2.83
Small	2.83	2.83	2.83



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Assess Initial Status and Track Progress: Sensibility Function

Median Nerve Repair at exit of Carpal Tunnel: Two-Point Discrimination

Date	**3/12/2020**	**7/10/2021**	**12/6/2020**
	left	left	left
Thumb	15 mm	10	7
Index	14 mm	12	8
Long	14 mm	14	10
Radial Ring	12 mm	11	9
Ulnar Ring	5 mm	5	5
Small	5 mm	5	5

Assess Initial Status and Track Progress: Motor Function

- Observation of Atrophy
- PROM
- AROM
- MMT
- Grip
- Pinch
- Special Tests and Signs
- Coordination/Dexterity

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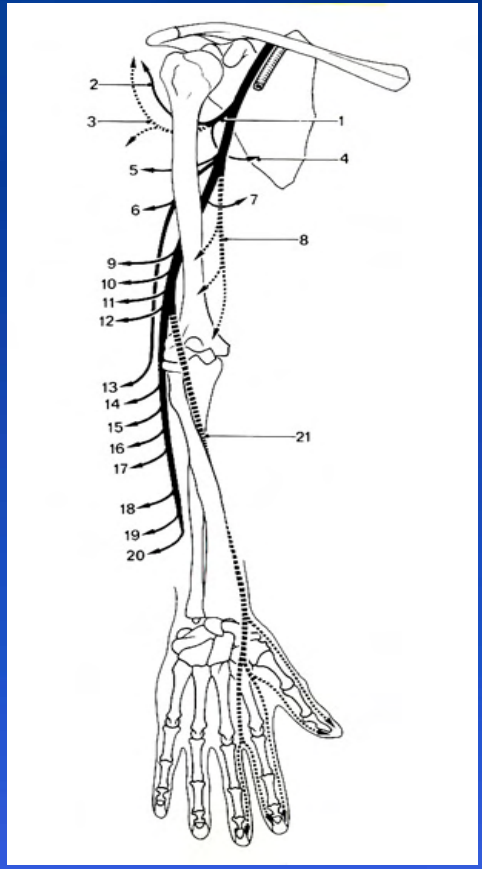
Assess Initial Status and Track Progress: Motor Function



Radial Nerve MMT

Date:	**10/20/2020**	**1/29/2021**
Triceps (C6,**C7,C8**)	5	
Anconeus	Not tested	
Brachialis (Small Part) (**C5,C6**)	Not tested	
Brachioradialis (**C5,C6**)	4+	5
ERCB/L (**C6, C7,** C8)	5/4+	5/5
Supinator (**C6,** C7, C8)	4	5
Extensor Digitorum Communis (**C7,C8**)	2-	3-
Extensor Digiti Minimi (C6,**C7,C8**)	2-	4-
Extensor Carpi Ulnaris (C6, **C7, C8**)	3-	4-
Abductor Pollicis Longus (C6,**C7, C8**)	2-	2-
Extensor Pollicis Brevis (C6, **C7, C8**)	3	3
Extensor Pollicis Longus (**C7, C8**)	1	2-
Extensor Indicis (**C7, C8**)	1	3

Assess Initial Status and Track Progress:
Basic and Instrumental Activities of Daily Living Function

- DASH/QuickDASH
- PROMIS
- Barthel Index
- ADL Checklist/Diary
- Observation and Efficiency Assessment

MAYO CLINIC

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MOTOR

- Motor retraining of re innervated muscles
- Orthotic Fabrication/Fitting
- Therapeutic Activity
- ROM/Strengthening
- Coordination/Dexterity

SENSORY

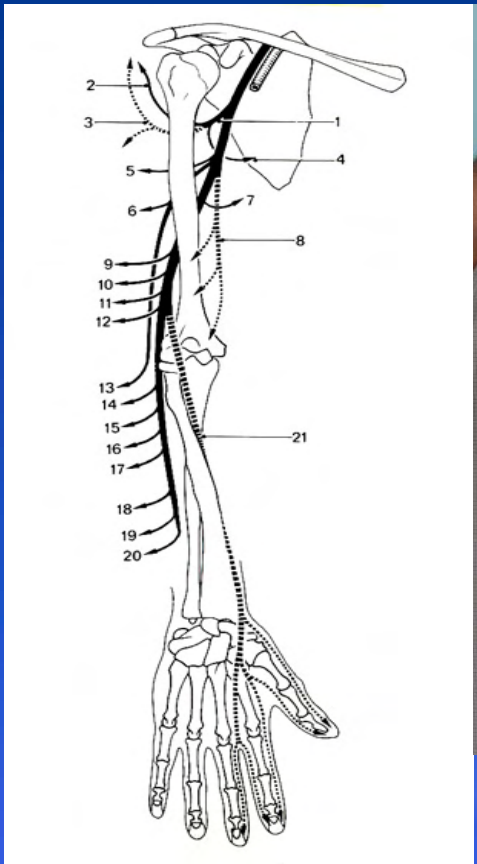
- Sensory Re-education
- Orthotic Fabrication/Fitting
- Protective Tactics while awaiting reinnervation and if incomplete return

ADL ADAPTATIONS

– §Ç‰

34-year-old R hand dominant computer engineer, husband and father of an infant

Neurofibroma of L arm



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- www.htcc.org
- www.handsurgery.org
- www.assh.org
- https://ifsht.org/
- Journals & Education: https://ifsht.org/ht-resources/
- https://nervesurgery.wustl.edu
- United Brachial Plexus Network: https://ubpn.org

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Thank You!

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:55 AM - 10:10 AM

Case Discussion

All Faculty

No relevant conflicts of interest to disclose

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Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:55 AM - 09:58 AM

Case Presentation s

Shelley S. Noland, MD
No relevant conflicts of interest to disclose

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

09:58 AM - 10:10 AM

Case based Debate

Alexander Y. Shin, MD

- TriMed Orthopaedics / Mayo Medical Ventures - Royalties or patent beneficiary
- Aptis Medical – Speaker Bureau

Fraser J. Leversedge, MD

- Axogen – Researcher/Consultant
- Stryker - Consultant
- Bioventus - Consultant
- CoNextions - Consultant
- Wolters Kluwer - Royalties or patent beneficiary

Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:10 AM - 11:00 AM

Part : The painful Nerve

Amber R. Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

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Speaker has not provided a handout for this presentation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:10 AM - 10:20 AM

Non Surgical Management of Neuropathic Pain

Catherine Curtin, MD

- Nine Continents Medical - Consultant

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Non-surgical Management of Neuropathic Pain
Outline

Medications
- Anti-inflammatory
- Gabapentinoids
- Anti-depressants
- Bisphosphonates

Therapy
- Graded motor therapy
- Mirror Therapy
- TENS

Electrical Stimulation
- Gate Therory
- Peripheral Nerve Stimulation

Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:20 AM - 10:30 AM

Conventional Techni ues for Neuroma Management

Ryan W. Schmucker, MD

No relevant conflicts of interest to disclose

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Management of Neuromas of the Upper Extremity

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KEYWORDS

• Neuroma • Management • Surgery

KEY POINTS

- Neuromas of the upper extremity are common, and their treatment can prove challenging. A multitude of operative and nonoperative techniques have been described with varying degrees of efficacy.
- Diagnosis of neuromas is based on physical examination findings and can be aided with the use of selective anesthetic injections.
- Several oral medications have been used in treating neuropathic pain, with anticonvulsants appearing to be the most efficacious.
- The underlying principle of all operative treatment is to remove the nerve or neuroma from any persistent source of mechanical irritation.
- Operative techniques can be divided into 4 categories: resection alone, resection with subsequent nerve grafting or primary repair, containment of the neuroma, or translocation of the nerve.
- The chosen method of treatment depends on the location and type of nerve as well as the injury sustained.

INTRODUCTION

After a nerve sustains a partial or complete injury, it possesses an intrinsic reparative capacity to establish continuity with its distal end. The ensuing proliferation of disorganized axons, myofibroblasts, endothelial cells, and Schwann cells can result in the formation of a neuroma (**Fig. 1**).[1,2] Reports of incidence range from 4% to 25%.[3–5]

Neuromas were first described by Odier in 1811,[1] with patients presenting with disabling pain or loss of motor function. Numerous treatments have been described, with varied success. In this article, the pathophysiology of neuromas, their clinical manifestations, and the role of current nonoperative and operative treatments are reviewed.

CAUSE AND PATHOPHYSIOLOGY OF NEUROMAS

The underlying cause of all neuroma formation is a degree of nerve irritation or injury (**Fig. 2**). Acute injuries are typically iatrogenic or traumatic. Examples of common iatrogenic injuries include damage to the superficial sensory branch of the radial nerve during dorsal exposures of the wrist or distal radius[6,7] or to the palmar cutaneous branch of the median nerve during carpal tunnel surgery.[8] Traumatic injuries generally result from lacerations to digits or the hand, which can result in stump neuromas. Subsequent repair of lacerations or replantation of digits with nerve repair can also result in neuroma formation, particularly if the segmental defect is long, excessive scarring occurs, or a mismatch in size exists between proximal and distal segments.[9]

When transected nerves are not repaired, end neuromas may result from fascicular overgrowth. When a nerve is injured or cut, signals travel retrograde through the proximal axon to the cell body to stimulate a reparative response.[10] There is a milieu of host signaling factors at the site of injury to direct the response, including substance P, calcitonin gene–related peptide, and mast cells,

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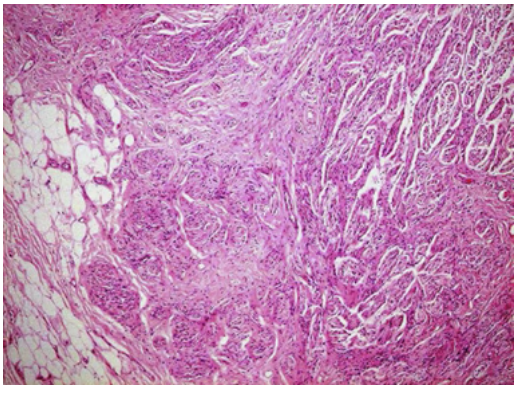

Fig. 1. Sciatic nerve neuroma resulting from above-knee amputation. (*From* Kitcat M, Hunter JE, Malata CM. Sciatic neuroma presenting forty years after above-knee amputation. Open Orthop J 2009;3:126.)

all of which may function to enhance the regenerative process.[11] Various neurotrophic factors, including neuropoietic cytokines, fibroblast growth factors, and neurotrophins, may also be involved. Within the distal segment, Schwann cells and macrophages begin to phagocytose myelin through the process of Wallerian degeneration.[12] The Schwann cells align themselves along the basal lamina of the distal segment to form bands of Bungner, which help to guide the regenerating proximal segment. This is accompanied by an up-regulation of corresponding neurotrophic factors and neurite growth-promoting factors,[12] including neuropoietic cytokines, fibroblast growth factors, and neurotrophins.[13] Within the proximal segment, several sprouts form from the regenerating axon, each with a growth cone on its end that attempts to identify the suitable distal neural tube to guide regeneration.[14] When the regenerating unit cannot identify its corresponding distal segment, elongation cannot occur and an end neuroma forms (**Fig. 3**).[15]

Neuromas may also arise from crush or stretch injuries of the nerve, which remains in continuity. Maintenance of the basal lamina allows for organized regeneration to distal targets,[12] but fascicular escape can still occur through disruption of the perineurium.[13] This subsequent spilling of the fascicles allows disorganized neuroma formation,[16] resulting in a neuroma in continuity.

Inflammation around a nerve can induce scar formation and accounts for a third mechanism of neuroma formation, even in the absence of direct neural injury. Scar tethering of nerves, or traction neuritis, results in activation of the nerve secondary to inflammation, irritation, or mechanical shearing.[17] Nerves of the upper extremity, specifically the digits, are at risk of mechanical irritation, given their proximity to the skin.

Despite their formation, not all neuromas develop painful symptoms.[2] Prediction of pain after partial or complete nerve transection is notoriously difficult, in part because of its multifactorial cause. Neuropathic pain is influenced by the presence of mechanical or chemical irritation, development of local scar tissue (ie, traction neuritis), and dysesthetic sensory symptoms.[1,13] In particular, proximal neuronal activity within the dorsal root ganglion, spawned by the injury, can contribute to the disabling dysesthetic pain. The type and size of nerve that is injured also influence the size and likelihood of neuroma formation. Injuries that occur more proximally lead to larger neuromas as a result of increased axoplasmic flow.[18] Nerves with a higher ratio of fascicles to epineurial tissue are more likely to form neuromas, because it is easier for the fasciculi to escape.[13]

DIAGNOSIS OF NEUROMAS

A history of sharp trauma, crush, or stretch injury along with a thorough physical examination can help diagnose neuromas. Pain related to a single peripheral nerve distribution, with or without accompanying numbness or diminished sensation, may also be useful in localizing the lesion. However, overlapping innervations of adjacent nerve

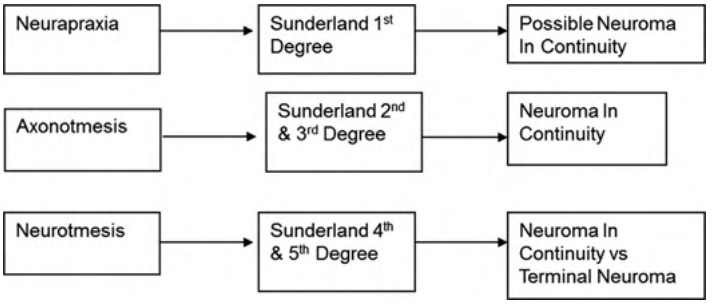

Fig. 2. Comparison of Seddon and Sunderland's classification systems and their relations to neuroma formation.

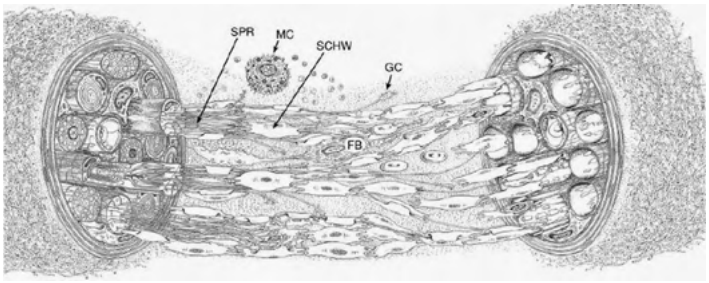

Fig. 3. Response of a nerve to complete transection. Sprouts (SPR) arise from the axons to form a regenerating unit, which has a growth cone (GC) at its leading edge. This growth cone attempts to attach to the bands of Bugner distally and minimize mismatch between axons. The zone of injury is filled with mast cells (MC), Schwann cells (SCHW), and macrophages. (*From* Lundborg G. A 25-year perspective of peripheral nerve surgery: evolving neuroscientific concepts and clinical significance. J Hand Surg Am 2000;25(3):394; with permission.)

territories can lead to some confusion when identifying the specific neuroma. Adjunctive measures, therefore, should be used to aid in the diagnosis.

Adjunctive Measures to Diagnose a Neuroma

- Tinel sign: The sensation of tingling when an injured nerve is stimulated via light percussion. This sign indicates the regeneration of axons and can be present in a nerve that is recovering or can be elicited from a terminal neuroma. An advancing Tinel sign distal to the site of injury is consistent with nerve recovery. A static or nonadvancing Tinel sign is more consistent with a terminal neuroma.[19]
- Anesthetic injection: Local anesthetic injections can help to pinpoint the cause when the diagnosis is questionable.[1] Complete resolution of the symptomatic pain or dysesthesias in the expected anatomic distribution of the injected nerve helps to confirm the diagnosis and show to the patient the expected area of anesthesia after neuroma resection, nerve transposition, or grafting.
- Imaging: Ultrasound guidance can be used to inject suspected neuromas when necessary to target sensory nerves located deep to muscle. Ernberg and colleagues[20] described the use of an ultrasound-guided steroid injection into a painful stump neuroma of the lower extremity, with complete long-term symptom resolution. If the diagnosis continues to remain uncertain or the clinical picture is confusing, advanced imaging such as high-field magnetic resonance imaging may be useful in these circumstances.

NONOPERATIVE TREATMENT OF NEUROMAS

Oral analgesics may have some efficacy in the medical management of neuropathic pain. The roles of antidepressants, anticonvulsants, opioids, and topical agents have all been investigated, at times with mixed results.[21]

- Antidepressants: In a randomized, double-blind, placebo-controlled trial of adults with spinal cord injury, amitriptyline was compared with gabapentin and diphenhydramine with regards to efficacy in controlling neuropathic pain.[22] In patients with high baseline depression scores, amitriptyline showed a significant difference in controlling pain when compared with placebo, but no difference was found in patients with lower baseline depression scores. Otto and colleagues[23] conducted a randomized, double-blind, placebo controlled trial examining the use of escitalopram, a selective serotonin reuptake inhibitor, in the treatment of polyneuropathy. The investigators found only a weak to moderate analgesic effect, with a 1-point reduction in pain on an 11-point scale.
- Opioids: Wilder-Smith and colleagues[24] compared the efficacy of tramadol and amitriptyline in a randomized, placebo-controlled trial of 94 treatment-naive patients with phantom limb pain from posttraumatic amputations. Initial complete relief of limb pain was seen in 67% of patients receiving tramadol, 83% of those receiving amitriptyline and only 3% of placebo patients.

Anticonvulsants

Anticonvulsants are commonly used in the management of neuropathic pain. Pregabalin and gabapentin bind to the α_2-δ subunit of calcium channels on neurons and reduce neurotransmitter release from synapses. A randomized double-blind clinical trial of 254 patients with neuropathic pain after trauma or surgery[25] showed a statistically significant decrease in pain scores for

patients treated with pregabalin compared with placebo after an 8-week period, as well as a decrease in anxiety as measured by the Hospital Anxiety and Depression Scale. However, the overall difference in pain score between the treatment group and placebo was –0.62, on a scale of 0 to 10 ($P = .01$), showing only modest improvement and incomplete pain relief. Gordh and colleagues[26] conducted a multicenter randomized, double-blind, placebo-controlled trial investigating the use of gabapentin for the treatment of pain resulting from traumatic nerve injury. The primary end point for the study was the mean pain intensity score recorded on a visual analogue scale (VAS) from 0 to 100. There was a significant difference between the gabapentin group and placebo group with regards to change in mean pain intensity score from baseline to final week of treatment. However, patients taking gabapentin did note a significant difference in pain relief and improvement in sleep.

Adjuvant Treatment Methods

Before the development of oral pharmacologic interventions, several adjuvant treatment modalities were used for management of neuromas, including injection with phenol, alcohol, formalin and cerebrospinal fluid (of note, the last 2 are no longer practiced).[27,28]

- Phenol injections: Gruber and colleagues[29] injected 82 patients suffering from painful amputation stump neuromas with 0.8 mL of 80% phenol over 1 to 3 treatment sessions, resulting in complete initial eradication of pain in 15% of patients. Patients with lower extremity amputations and those with larger neuromas responded more favorably to phenol injections.
- Alcohol injections: Injections of alcohol into lower extremity stump neuromas has met with variable success. A series of 2 cases was reported in which 100% dehydrated alcohol was injected into the nerve proximal to the neuroma, with complete initial relief, and subsequent slight recurrence.[30]

Others have performed cryoablation, crushing, and cauterizing of nerve endings.[27] Desensitization therapy or splinting of the extremity may also give some symptomatic relief.

PRINCIPLES OF OPERATIVE TREATMENT OF NEUROMAS

When conservative measures fail and a suitable surgical candidate has been identified, selection of the appropriate operative technique centers around 4 therapeutic options: (1) resection of the neuroma; (2) use of nerve grafts to reconnect severed proximal and distal stumps; (3) containment of the neuroma; and (4) translocation of the nerve.

OPERATIVE TECHNIQUES

Resection of Neuromas

Neuroma excision is one of the earliest methods practiced. Tupper[31] reported the results of simple neurectomy in patients with painful postamputation neuromas in the hand and found that 65% had an excellent or satisfactory result. More recently, Guse and Moran[32] evaluated the outcomes of several surgical interventions in the treatment of hand and forearm neuromas in 56 patients, including nerve transposition into bone or muscle, simple excision, and nerve repair. Eleven patients underwent transposition of the neuroma into muscle or bone, 17 neuromas were excised without any additional procedure, and nerve repair was undertaken in the remaining 28 patients. Reoperation rates and mean Disabilities of the Arm, Shoulder and Hand (DASH) score were reported for each treatment group: nerve transposition, 36% (22.4); simple excision, 47% (31.9); nerve repair, 11% (11.4). Given the high rate of reoperation and poor resultant DASH scores, the investigators recommended against simple excision of upper extremity neuromas.

Despite these poor results, excision of a neuroma can be considered when certain criteria are met. These criteria include a palpable tender neuroma in the line of the damaged nerve, an inability to resect a neuroma and graft the nerve ends, persistent pain refractory to nonoperative treatment, and a neuroma adherent to neighboring muscle or tendons.[33]

Repair of Nerves

For digital neuromas in continuity, resection of the neuroma and use of a nerve graft or vein conduit to bridge the resultant gap may be used. Nunley and colleagues[34] reported on the use of a branch of the medial antebrachial cutaneous (MABC) nerve as an autologous graft for digital nerve repair, with modest success. Similarly, Malizos and colleagues[35] reported excellent relief of neuroma pain using vein conduits in the treatment of 23 patients presenting with 27 neglected lacerations or failed primary repairs of sensory nerves in the hand. Relief of the neuroma symptoms was achieved in 94% of patients, with return of good sensory function in 26% of patients and fair sensation in 43%.[35] These results were similar to a

control group of 20 digital and 5 common digital nerves that underwent direct repair of nerve gaps within 1 week of injury.

Collagen tubes are gaining popularity to diminish postamputation neuroma formation. Thomsen and colleagues[36] reported on the use of collagen conduits in 10 patients with 11 digital posttraumatic neuromas in continuity. After an average of 11.8 months follow-up, none of the patients reported neuromalike symptoms, 5 of the 11 digits had good (6 - 10 mm) or excellent (<6 mm) return of 2-point discrimination, and the average Quick-DASH score was 19.3.

Containment of Neuromas

One of the most challenging problems with direct nerve repair or postamputation care is containment of fascicles from cut nerves, which may sprout into surrounding tissue, contributing to dysesthesias. Several techniques have been described to address this issue.

- Silicone caps: Tupper[31] described the use of silicone caps in 32 patients who had little relief with a simple neurectomy. Only 41% of patients obtained an excellent or satisfactory result. Swanson[37] reported a series of 18 patients with 38 upper extremity neuromas who underwent silicone capping as a revision procedure after previous failed neuroma surgeries. Fourteen neuromas (9 patients) had a residual Tinel sign postoperatively, but only 3 patients were dissatisfied with their postoperative results.
- Epineurial grafts: Epineurial grafts have been found to be more effective in minimizing postoperative pain as measured by VAS compared with epineurial ligature or epineurial flaps.[16] Results showed that the mean pain scores at 6 months were significantly lower for the stumps with epineurial grafts compared with epineurial ligature and epineurial flaps (2.06 vs 5.18 vs 4.25, respectively, $P<.05$).[16]
- Nerve capping; An autologous nerve graft is harvested and sewn to the distal end of the affected nerve after neuroma resection.[38] The distal portion of the graft is then left open, or alternatively, for fingers with both digital nerves amputated, a centrocentral nerve union is performed using a nerve graft.[39] Kon and Bloem noted an improvement in symptoms of 18 patients treated with this technique.[40] However, 7 patients continued to have tenderness to percussion at the site of the nerve union and 1 required reexploration at 6 months for recurrent neuroma formation.

Vein grafts may also be harvested and wrapped around nerves to minimize epineurial scarring in revision surgery or after neurolysis. Rat models have shown decreased scar formation after chronic nerve decompression with venous wrapping of nerves.[41] Clinical series using venous wrapping after revision nerve decompression procedures have shown clinical and electrophysiologic improvement[42] with minimal scar formation around the venous wrapped nerve.[43,44]

Nerve Translocation

Relocation of painful neuromas from the digits and palm into more proximal locations is a technique that has gained popularity.[27] The use of nerve relocation or muscle flaps to prevent or treat neuromas is based, in part, on studies that have shown that cut nerves form a cellular end cap when wrapped in innervated muscle, therefore decreasing neuroma formation.[45] In a primate model, Mackinnon and colleagues[45] showed that sensory nerves translocated proximally into muscle had less scar tissue than those left exposed near a wound or those retracted proximal to the wound.

For purposes of preoperative planning when considering nerve translocation, the hand and distal forearm can be divided into 3 zones,[46] each with their own preferred treatment strategy (**Fig. 4**, **Table 1**).

Zone I

Management options for neuromas in zone I include dorsal translocation and intraosseous implantation. Laborde[47] noted that dorsal translocation of symptomatic digital neuromas provided the most predictable relief in a series comparing patients who had undergone excision of the neuroma, ray amputation, neurorrhaphy, or translocation.

Boldrey[28] described intraosseous implantation in 1943. With this technique (**Fig. 5**), an end neuroma is mobilized and a drill hole placed through 1 of the phalangeal or metacarpal bones. Sutures are passed through the end of the nerve stump and passed through the drill hole to dock the nerve within the intraosseous space. Mass[48] described a series of 20 neuromas in 15 patients treated with this technique, with 14 neuromas in 11 patients showing good or excellent results.

Zone II

Zone II of the upper extremity encompasses the palm of the hand and includes, among others, the common digital nerves and the palmar cutaneous branch of the median nerve. Knowledge of these 2 neuromas is salient to the hand surgeon,

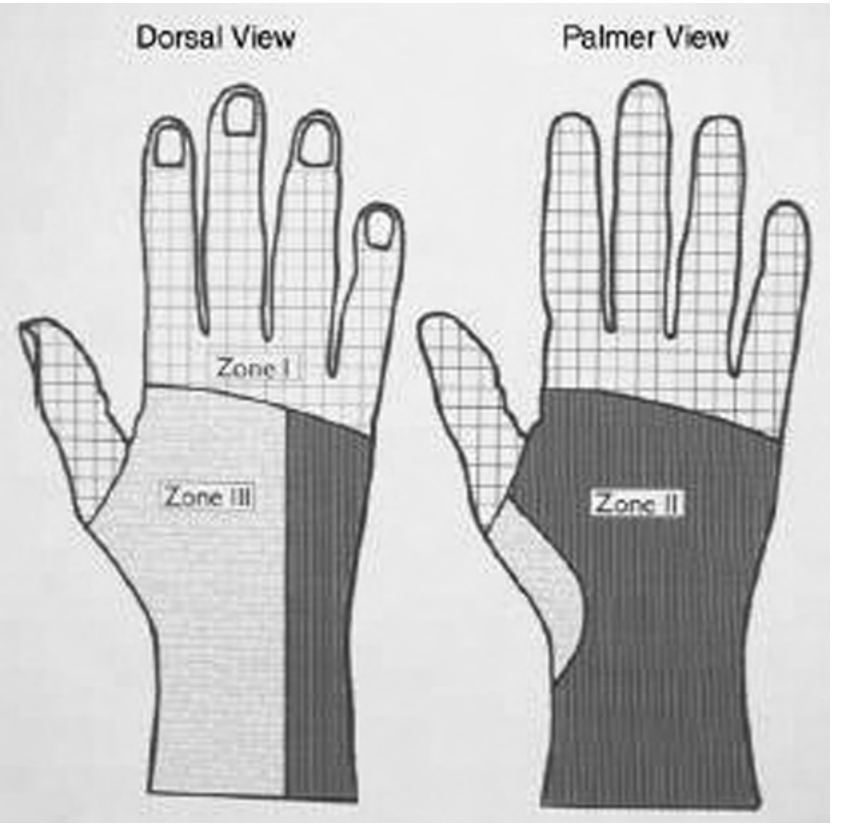

Fig. 4. Division of the hand and forearm into zones for planning of neuroma relocation. (*From* Atherton DD, Leong JC, Anand P, et al. Relocation of painful end neuromas and scarred nerves from the zone II territory of the hand. J Hand Surg Eur Vol 2007;32(1):39; with permission.)

Table 1
Neuromas of the hand and wrist and treatment options based on location

Zone	Nerves Involved	Relocation Options
I	Digital nerves	Proximal phalanx or metacarpal
II	Common digital nerves Palmer cutaneous branches of median and ulnar nerves Dorsal sensory branch of ulnar nerve	Pronator quadratus
III	Superficial branch of the radial nerve Lateral antebrachial cutaneous nerve Medial and posterior cutaneous nerves	Brachioradialis or other muscles of forearm

Adapted from Atherton DD, Leong JC, Anand P, et al. Relocation of painful end neuromas and scarred nerves from the zone II territory of the hand. J Hand Surg Eur Vol 2007;32(1):39; with permission.

because both of these may be injured during a carpal tunnel release, including the common digital branch to the third webspace.[49] If there is injury to the common digital nerve, Vernadakis and colleagues recommend neurolysis and transposition of the nerve between the superficial and deep flexor muscles.

Similarly, an approach to recalcitrant neuromas in continuity of the sensory branches of the median nerve of the palm is resection and grafting.[50] In this technique, the neuroma in continuity is visualized and the motor fascicles dissected out proximal and distal to the neuroma. The motor fascicles are preserved as a unit and the nonfunctioning sensory fascicles are resected and replaced with autologous graft (**Fig. 6**).

Atherton and colleagues[51] reported the results of 33 patients with 46 neuromas undergoing nerve relocation from zone II into pronator quadratus. Of the 46 nerves included in this study, 35 were relocated from the volar and dorsal palm of the hand (zone II) into the pronator quadratus. In cases of common digital nerve neuromas, internal neurolysis off the median or ulnar nerve was necessary to provide length for nerve transposition. The

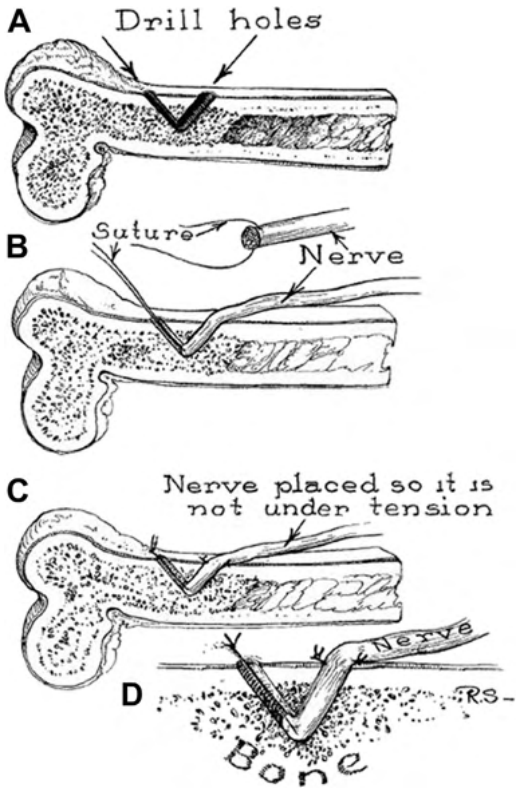

Fig. 5. Original technique described by Boldrey for intraosseous implantation. (*From* Boldrey E. Amputation neuroma in nerves implanted in bone. Ann Surg 1943;118(6):1053; with permission.)

investigators noted that there was near-complete resolution of spontaneous pain and hypersensitivity at the primary site. However, approximately one-third of patients continued to experience persistent pressure and pain associated with movement at the relocation site.

For neuromas in continuity in the palm, Karev and Stahl[52] advocated mobilization of the lumbrical to serve as a volar pad and block to mechanical pressure. In a report of 2 cases with neuromas in continuity of the proximal digital nerve within the palm, the investigators describe a neurolysis, tenotomy of the adjacent lumbrical with palmar transposition over the nerve, and subsequent repair of the lumbrical. Both patients had excellent pain relief postoperatively, without any evidence of a Tinel sign.

Zone III

Historically, successful relocation of neuromas from zone III into forearm muscles has proved challenging in obtaining complete symptom relief, with patients often requiring multiple procedures. This situation may be in part because of overlapping innervation of 2 of the most commonly involved nerves, the lateral antebrachial cutaneous (LABC) nerve and superficial branch of the radial nerve (SBRN)[53] and may require addressing both nerves at the same time. Elliott[17] recommends routine transfer of the LABC and SBRN together into the brachioradialis as the index procedure for neuropathic pain within this distribution, whereas Atherton and colleagues[53] advocate relocation of the SBRN into the brachioradialis, the LABC into the brachialis, and the MABC into the biceps.

Although these methods have shown promise when applied appropriately, success is not universal. Dellon and Mackinnon[54] analyzed a heterogeneous series of 78 neuromas of the distal forearm and hand treated with neuroma resection and muscle implantation. Overall, 42% had excellent relief of pain, 39% reported good pain relief, and 19% had little or no pain relief. Although the overall group of nerves encompassed neuromas from the brachial plexus distally, a total of 7 digital nerves were treated, with none achieving excellent results and only 14% achieving good results. Predictors of poor outcome after neuroma resection and muscle implantation included: (1) presence of a digital neuroma, (2) workmen's compensation; (3) 3 or more previous operations for neurogenic pain. In addition, patients who had nerve transfers into small or superficial recipient muscles, or muscles with large excursion, tended to have worse outcomes.

SPECIFIC NEUROMAS AND TREATMENT STRATEGIES

Pacinian Corpuscle Neuromas

Pacinian corpuscle neuromas, arising in the distal tips of fingers, can result after minor, repetitive trauma, such as sewing,[55] or from a singular traumatic event. Although the cause remains unclear, trauma to the digit has been implicated in 55% of reported cases.[56] Pacinian corpuscle neuromas are generally divided into 3 categories based on pathology: a single hypertrophied corpuscle, an increased number of normal-sized corpuscles, and an increased number of enlarged corpuscles.[56] Excision of the painful corpuscle is often successful, with confirmation of the diagnosis made histologically.

Bowler's Thumb

Initially described by Siegel,[57] bowler's thumb is a pathologic condition associated with repeated minor trauma to the ulnar digital nerve of the thumb.[58,59] This trauma leads to swelling and fibrosis of the nerve, resulting in a neuroma with altered sensation, a positive Tinel sign, and changes in 2-point discrimination on the ulnar side of the thumb. It is associated with bowlers

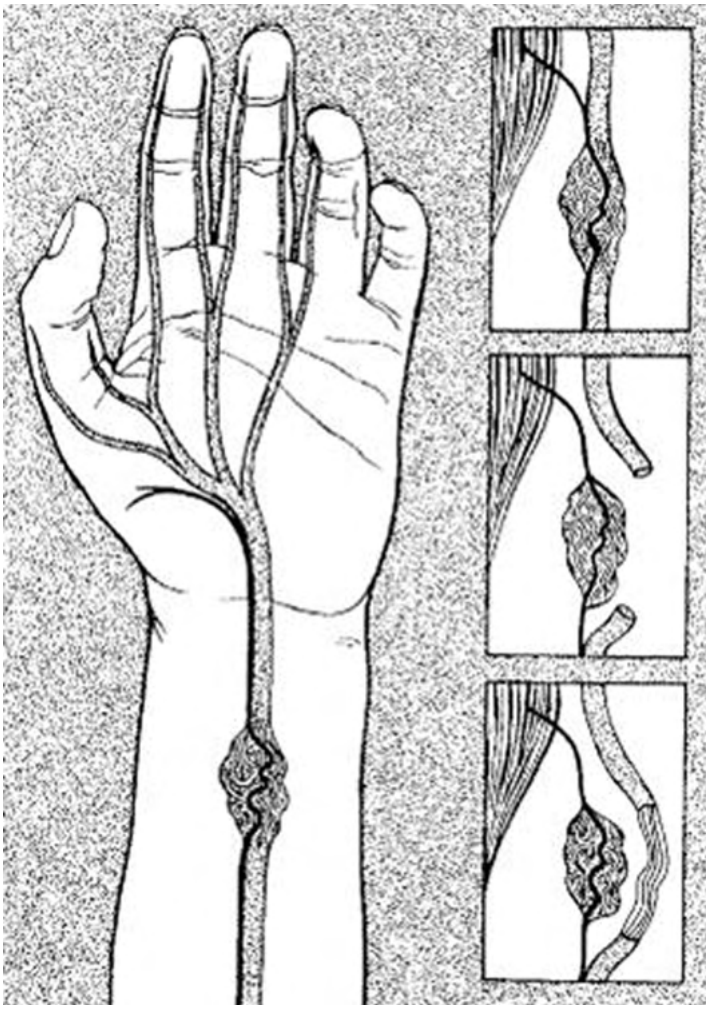

Fig. 6. A neuroma in continuity of the sensory branches of the median nerve with: (1) dissection of the sensory fascicles; (2) resection of the neuroma and preservation of the motor branches; and (3) grafting of the subsequent defect. (*From* Mackinnon SE, Glickman LT, Dagum A. A technique for the treatment of neuroma in-continuity. J Reconstr Microsurg 1992;8(5):380; with permission.)

because of the impingement of the bowling ball on the thumb and presents with a tender mass on the volar surface of the thumb. It can be treated conservatively with activity modification or equipment modification. Neurolysis, nerve transposition, and even neuroma resection have been used with varying degrees of success in several small case series and case reports (**Fig. 7**).[60,61]

Linscheid and Dobyns[61] described their experience in the management of 17 patients with bowler's thumb. Eight patients were treated successfully with nonoperative measures including the use of a plastic thumb guard or cessation of the aggravating activity, whereas 7 proceeded with surgery. Of these 7, 3 were treated by neurolysis alone, 1 underwent neurolysis and translocation of the nerve, 2 neuromas were resected and buried in more proximal tissue and 1 neuroma was resected and the nerve primarily repaired. Six returned to bowling within 2 years, and the seventh was lost to follow-up. Swanson et al described a technique of translocating the ulnar digital nerve beneath the adductor pollicis. This required transection of the adductor pollicis and subsequent reattachment utilizing a suture anchor.[62]

Median Nerve Neuroma in Continuity

Median nerve neuromas in continuity can result from trauma or iatrogenic injury during carpal tunnel surgery. Dellon and Mackinnon[63] described the use of a pronator quadratus flap in the management of this condition. The pronator is approached from the radial and ulnar side and the

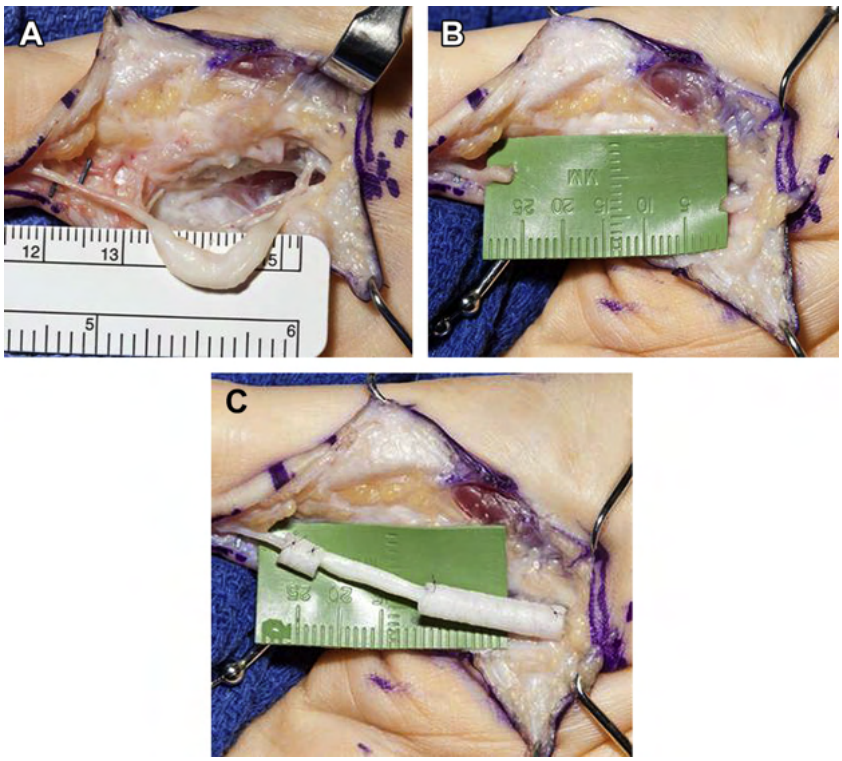

Fig. 7. Bowler's thumb. Examples of (*A*) neuroma in continuity; (*B*) resection; and (*C*) autologous nerve grafting and interposition of collagen conduit.

muscle detached from distal to proximal until the anterior interosseous artery is encountered. The muscle is then elevated with the pedicle and mobilized superficially. Given its limited excursion on the pedicle, it is best suited for median nerve lesions at the level of the wrist. In their series of 7 patients with 6 painful median nerves and 1 painful ulnar nerve, Dellon and Mackinnon[63] reported promising results in regards to symptom resolution. Six of the 7 patients had good or excellent results at 22 months after surgery, and the seventh patient's poor result was attributed to an injury to the forearm 6 months after surgery. De Smet[64] described a series of 4 patients with median nerve neuromas treated with pronator quadratus flaps; all were satisfied with their outcome and had improvement of pain, but mobility restrictions improved in only 2 of the 4 patients. Adani and colleagues[65] examined outcomes from a series of 9 patients over 5 years who underwent placement of pronator quadratus flaps over median nerve neuromas. Five of these patients had previous complete transections; the other 4 experienced partial transections, with all 8 undergoing primary repair and 1 receiving a sural nerve graft. All patients subsequently presented with wrist pain and a positive Tinel sign over the median nerve and were treated with elevation of a pronator quadratus muscle flap to cover the median nerve. Of the 9 patients, 8 had pain relief and 6 had regression of their Tinel sign. None of the patients reported weakness with pronation.

Posterior Interosseous Nerve Neuroma

Neuroma of the posterior interosseous nerve (PIN)[66] is characterized by radiating, burning pain on the dorsal aspect of the wrist and hand. The diagnosis is confirmed with a local anesthetic injection into the PIN distribution. It may be associated with iatrogenic injury during ganglion excision and can be treated with PIN excision via a dorsal approach to the wrist.

In addition to the PIN, the superficial branch of the radial nerve can also contribute to burning paresthesias and pain in the dorsoradial distribution of the hand when injured. Neuromas in this area have historically been difficult to treat, and it is thought that the local anatomy may predispose the nerve to injury. Dellon describes how the nerve is tethered proximal to the wrist by adherence to structures underneath the brachioradialis. Any subsequent distal injury may tether the nerve at

the wrist, predisposing it to mechanical irritation or shearing during normal wrist flexion and extension.[6,13] When treating these neuromas, relocation of the SBRN should be performed into the brachioradialis for optimal pain relief, because it has a small excursion compared with other local muscle options.[54] Attention should be paid to the possible contribution of the LABC nerve to dysesthesias in this region, potentially requiring further intervention for complete relief of pain.

MABC Neuroma

Neuromas of the MABC nerve[67] can be associated with iatrogenic injuries during cubital tunnel surgery. Treatment options for dealing with the resultant neuroma include conservative measures, as well as 2 possible surgical techniques, as described by Stahl and Rosenberg.[68] In their series, 3 of 12 patients underwent proximal resection, and 9 were treated by neurolysis, neuroma resection, and transposition of the nerve deep into the triceps muscle. Mixed results were noted in the former group, whereas in the latter cohort, good to excellent results were achieved in 8 of the 9 as defined by a postoperative VAS score of 3 and an increase in average grip strength from 55% to 87%.

INVESTIGATIONAL TREATMENTS AND FUTURE DIRECTIONS

Given that the formation of a neuroma results from an attempt by the nerve to heal the injured segment, some investigators have explored mechanisms to diminish the healing response. Bipolar and monopolar diathermy have been applied to the cut ends of sharply transected nerves in a rat model in an effort to minimize neuroma formation. This study showed a significant decrease in neuroma formation with the use of monopolar cautery for 4 or 10 seconds compared with the contralateral sharply transected peroneal nerve.[69] Bipolar cautery showed diminished rates of neuroma formation when applied for 10 seconds, but not when applied for 4 seconds. The investigators concluded that although diathermy appeared to lessen the rate of neuroma formation, the mechanism by which it is accomplished remained unclear.

Cryosurgery using a cryoprobe has shown promising results in a series of 6 patients who had failed conservative treatment.[70] Neuromas were explored at the time of surgery and left in continuity, with a 2 mm cryoprobe applied proximal to the neuroma or site of injury. The probe was applied for 2 minutes to freeze the tissue to −60°C, withdrawn for 30 seconds to allow the tissue to thaw and then placed again for 2 minutes. All achieved good or excellent results postoperatively.

Investigations in animal models continue to look for mechanisms to diminish neuroma formation or mediate neuropathic pain. Crotoxin, a neurotoxin derived from rattlesnake venom, has shown efficacy in blocking pain transmission in a rat sciatic nerve model when the transected nerve stumps are immersed in the toxin.[71] However, the mechanism of this antinociceptive effect is still under investigation.

SUMMARY

Neuromas primarily arise from iatrogenic injury, trauma, or chronic irritation. Given their disabling symptoms, an array of treatment strategies exist, with varied results. Successful treatment relies on accurate identification of the offending nerve, containment of the regenerating fascicles, and cessation of mechanical or other noxious stimuli over the regenerating nerve end. The choice of treatment depends in part on the nerve affected, whether it involves critical or noncritical sensation, and its location.[49]

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SPECIAL TOPIC

Surgical Algorithm for Neuroma Management: A Changing Treatment Paradigm

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Ivica Ducic, MD, PhD†

Abstract: Successful treatment of the painful neuroma is a particular challenge to the nerve surgeon. Historically, symptomatic neuromas have primarily been treated with excision and implantation techniques, which are inherently passive and do not address the terminal end of the nerve. Over the past decade, the surgical management of neuromas has undergone a paradigm shift synchronous with the development of contemporary techniques aiming to satisfy the nerve end. In this article, we describe the important features of surgical treatment, including the approach to diagnosis with consideration of neuroma type and the decision of partial versus complete neuroma excision. A comprehensive list of the available surgical techniques for management following neuroma excision is presented, the choice of which is often predicated upon the availability of the terminal nerve end for reconstruction. Techniques for neuroma reconstruction in the presence of an intact terminal nerve end include hollow tube reconstruction and auto- or allograft nerve reconstruction. Techniques for neuroma management in the absence of an intact or identifiable terminal nerve end include submuscular or interosseous implantation, centro-central neurorrhaphy, relocation nerve grafting, nerve cap placement, use of regenerative peripheral nerve interface, "end-to-side" neurorrhaphy, and targeted muscle reinnervation. These techniques can be further categorized into passive/ablative and active/reconstructive modalities. The nerve surgeon must be aware of available treatment options and should carefully choose the most appropriate intervention for each patient. Comparative studies are lacking and will be necessary in the future to determine the relative effectiveness of each technique. *(Plast Reconstr Surg Glob Open 2018;6:e1952; doi: 10.1097/GOX.0000000000001952; Published online 16 October 2018.)*

BACKGROUND

The physiologic response to nerve injury varies depending on the degree and type of neuronal damage, surrounding micro- and macro-environment, patient physiology, and other factors.[1] Following injury to a peripheral nerve, the proximal nerve stump invariably attempts to regenerate toward its distal target. If this process is disorganized or incomplete, it may result in the formation of a neuroma, a growth or tumor of nerve tissue that may become painful.[2–4] Pain resulting from symptomatic neuroma can be debilitating and cause significant morbidity with an associated socioeconomic impact. Symptoms of a neuroma include pain (usually sharp or burning), paresthesias, numbness, cold intolerance, and electrical sensitivity, among others.[5,6]

Many interventions for traumatic neuroma have been described.[7] A number of nonsurgical treatments have been advocated including pain medications, radiofrequency ablation, neuromodulation, and desensitization.[8–10] Unfortunately, pharmacotherapy alone or other symptomatic treatments are often unsatisfactory in the treatment of neuropathic pain.[11] Initial surgical treatment of neuroma focused on excision of the injured segment, or alternatively addressing the autonomic nervous system with sympathectomy.[12]

In the 1980s, Dellon and Mackinnon[13] described the results of neuroma excision and implantation of the nerve end within muscle, demonstrating good to excellent results in 82% of patients. Additional authors described the techniques of neuroma excision and implantation within bone[14] or veins.[15] Despite a modicum of reported success, these

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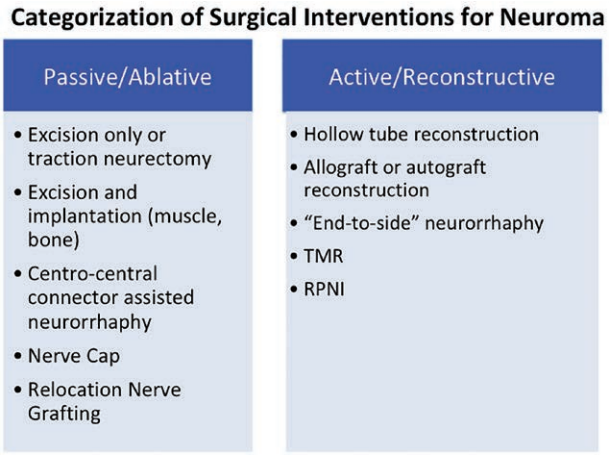

Fig. 1. Categorization of surgical interventions for neuroma into passive/ablative and active/reconstructive techniques.

techniques have not been found to be universally successful in improving symptoms and simple excision alone seems to be inferior to other surgical techniques.[16] The technique of excision and implantation is relatively "passive" in the treatment of neuroma: it involves excision of the diseased nerve segment but does not fundamentally address the regenerative desire of the nerve stump nor does it provide a pathway for neuroma-free regeneration. This can result in recurrence of symptoms and failure to improve pain.

Recent advances in the treatment of symptomatic neuroma have focused on more "active" treatment of the nerve end following neuroma excision, with the goal of satisfying the nerve end and allowing for more physiologic neuronal regeneration.[17] There are increasing numbers of contemporary interventions that aim to improve the outcomes for symptomatic neuroma (Fig. 1). This article provides a list of surgical options for the painful neuroma and discusses an algorithm to consider when deciding on the optimal treatment.

DIAGNOSIS AND INITIAL APPROACH

The diagnosis of symptomatic neuroma is often straightforward but may be challenging, depending on the clinical presentation. A careful history must be taken and include the mechanism of injury, temporal sequence of pain development, degree of impact and level of dysfunction, and goals of treatment. Most symptomatic neuromas involve pain, dysesthesia, hypesthesia, paresthesia, cold intolerance, and most commonly have a Tinel sign at the neuroma site.[5,6]

One must first consider the location and type of neuroma, that is, whether it is a stump (end) neuroma or a neuroma in continuity. Stump neuromas are inherently more straightforward from the standpoint of decision-making: there is, by definition, no distal function of the nerve and therefore less chance for potential functional impairment with surgical intervention. Excision of a neuroma in continuity, on the other hand, may have a significant impact on the function of the nerve (potential downside), which necessarily factors into the decision making.

It is imperative to consider both (1) the function of the involved nerve (sensory, motor, mixed) and (2) the degree of residual nerve function and the amount of pain when deciding about surgical intervention. A patient with mild pain and largely preserved neural function may not be the ideal candidate for neuroma excision as intervention could impact the residual nerve function. Conversely, a patient with incapacitating pain resulting from a neuroma of a noncritical sensory nerve may be a more ideal candidate for neuroma excision and reconstruction, as there is less potential functional downside of intervention. Not all patients with even symptomatic neuromas require surgery, and careful consideration should be undertaken of all options.

At the time of surgery, the neuroma is evaluated and a decision about full versus partial excision is made. For stump neuromas, complete excision is almost always performed, but for neuromas in continuity an intraneural neurolysis with selective neuroma excision may be performed to spare residual function,[18] or the neuroma may be maintained in part and a bypass nerve graft of the injured (usually sensory) component performed.[19]

Depending on the clinical scenario, complete excision of the stump neuroma or selective neurectomy of the neuroma in continuity is first performed. Once the neuroma has been excised, the next step is to determine the optimal reconstructive treatment of the nerve stump.

RECONSTRUCTIVE OPTIONS

There are many possible options to address the nerve end following neuroma excision. In general, the surgical options are divided into 2 major categories based on the presence or absence of the distal nerve end (Fig. 2).

If the Distal Nerve End Is Available

If the terminal nerve end is available, it is intuitive and often preferable to attempt nerve reconstruction to reconstitute the original function of the nerve. Following neuroma excision with the presence of healthy and intact proximal and distal nerve ends, the size of the gap will commonly dictate available options. Smaller nerve gaps have more options for reconstruction and most likely a higher probability of success (Fig. 3).

Nerve Reconstruction with Hollow Tube Construct

Very small resulting nerve gaps are rare following neuroma excision but, if present, may allow for use of a hollow tube construct (conduit, connector, or similar). Hollow tube assisted nerve reconstruction appears to be most effective for short gaps < 6 mm and small diameter nerves; this technique may provide sufficient nerve regeneration to allow for return of nerve function and obviate development of pain.[20,21] However, this technique is not typically possible for neuroma treatment because most gaps following excision are sufficiently large to preclude use. If intervention is performed primarily for pain relief, hollow tube constructs may be considered for longer defects although functional restoration becomes less likely with increasing gap length.

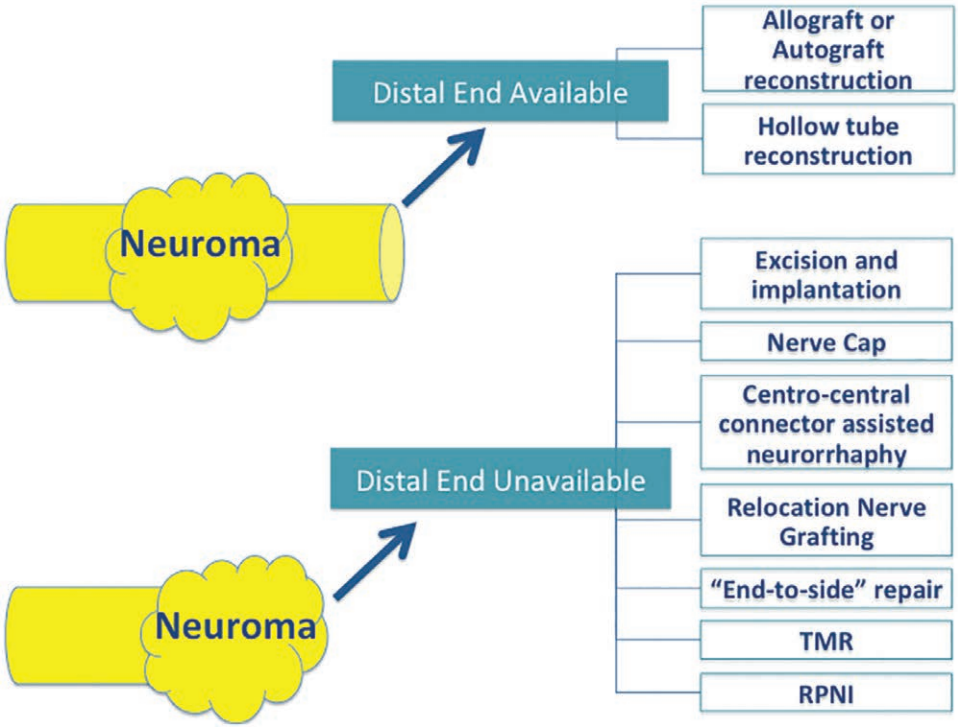

Fig. 2. Surgical options for neuroma treatment based upon availability of distal nerve ending.

Nerve Reconstruction with Autograft or Allograft

More commonly, neuroma excision with identifiable proximal and distal nerve ends will result in a nerve gap warranting reconstruction with a nerve graft. Both nerve autograft and nerve allograft can be used for this purpose.[22] In our experience, most patients with a painful neuroma for which they are undergoing surgical intervention prefer not to have autograft harvested, given the small, but possible, risk of neuropathic pain or symptomatic neuroma at the donor site. Nerve autograft used for reconstruction following excision of a sensory nerve neuroma will inherently trade numbness and pain at 1 site for, at minimum, numbness at the donor site and the potential for additional morbidity.[23,24]

Nerve allograft may be ideally suited for cases of painful, symptomatic neuroma in which excision of the lesion results in a reconstructable nerve gap. This provides the nerve a biologic pathway through which to grow, and avoids a second surgical site. This technique has been successfully reported in a series of patients with lower extremity neuromas.[25] In this study, the authors reviewed 22 patients who underwent allograft reconstruction of lower extremity neuromas with a mean 15 month follow-up, and demonstrated a decrease in ordinal pain score of 2.6 and a 24 and 31 percentage-point decreases in the PROMIS Pain Behavior and Pain interference measures.

If the Distal Nerve End Is Not Available

In many cases of terminal neuromas, the distal nerve is not available for reconstruction. This may occur in cases where the neuroma is extremely distal and the terminal branches are not identifiable, given their small size, and in all cases of amputations where the terminal nerve ends are no longer present. In these situations, it is not possible to perform reconstruction of the native nerve in the absence of a distal target, and one must decide the appropriate technique to address the proximal nerve stump (Fig. 4).

Implantation of Proximal Nerve Stump into Adjacent Tissues

Implantation of the proximal nerve stump into nearby tissues remains the most commonly performed technique for terminal neuromas. In principle, this technique buries the end of the nerve deeper within the tissues, increasing the distance between the site of axonal sprouting and the cutaneous surface thereby providing additional cushioning and protection for the nerve. The nerve can be implanted within many types of tissue, but is commonly placed within a muscle,[13,26] bone,[14,27] or inside veins.[15] This technique has been shown to be effective for both upper and lower extremity neuromas,[28] although it is not universally successful for all patients. Invariably, the end of the nerve will attempt to regrow (albeit in its new position), and may then form a recurrent symptomatic neuroma.

Although this is the surgical technique with the longest track record, it is somewhat simplistic and does not satisfy the nerve end. It is a passive method of treating the nerve end following neuroma excision. There are no randomized trials comparing this technique to others, but there is rationale to believe that it may be inferior to more active methods of neuroma treatment. Traction neurectomy alone appears to have a high rate of symptomatic recurrence.[29]

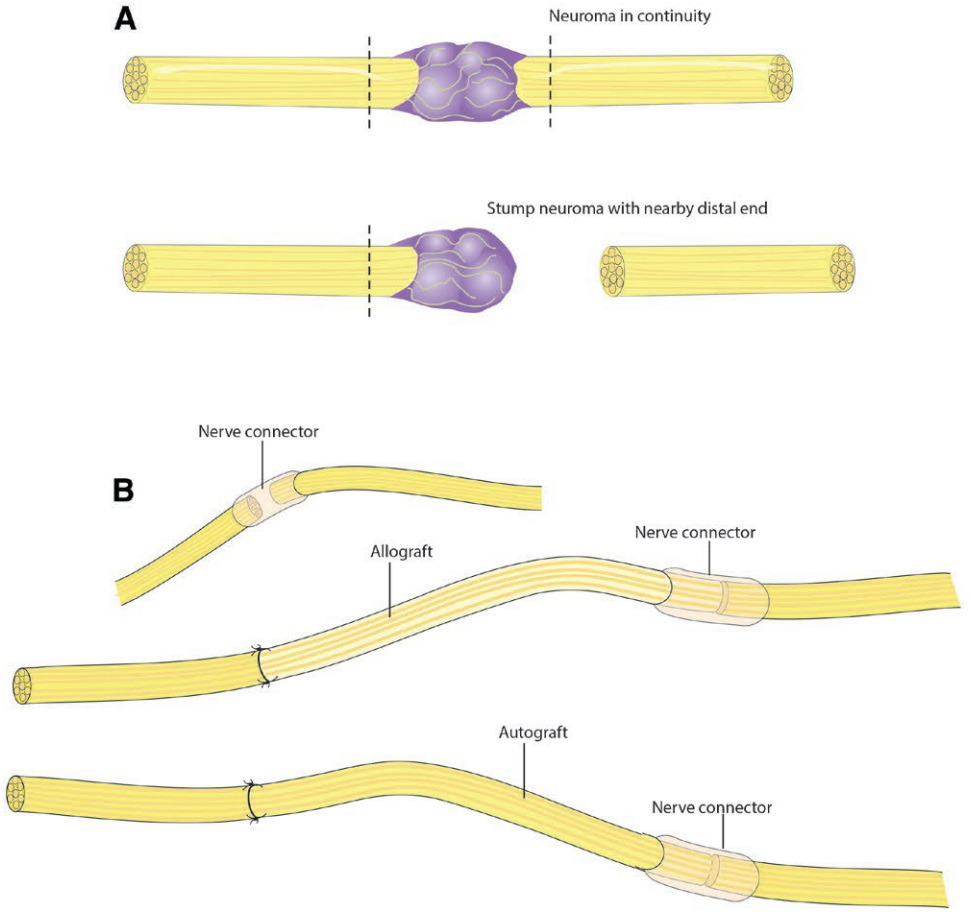

Fig. 3. Surgical options if distal nerve end is available. A, Neuroma excised (either in-continuity, or terminal neuroma with nearby stump available) B, Options for reconstruction.

Centro-central Neurorrhaphy

Controlling the growth of the terminal nerve end by performing an intraneural fascicular coaptation or neurorrhaphy between adjacent nerves is called a centro-central neurorrhaphy. Technically, this involves a fascicular dissection (for large nerves) or a coaptation (for smaller, ie, digital nerves), often with the use of a hollow tube or nerve graft construct. This technique has been studied experimentally,[30] and clinically in the hand[31] and lower extremity.[32,33] Centro-central neurorrhaphy is currently an uncommonly used technique for neuroma management, and is a passive technique that attempts to facilitate pain relief without directly reconstructing the nerve end.

Relocation Nerve Grafting

Relocation nerve grafting is a technique designed to provide a neural runway for the regenerating nerve, allowing axons to grow through the structure of the endoneurial tubes in the direction of an intentionally less painful destination. This is commonly performed with the use of nerve allograft, which can be size-matched and of sufficient length to allow for dissipated nerve growth through the long graft. A microsurgical coaptation is performed, and the terminal end of the nerve graft is directed away from the painful area or surface. As the nerve regenerates, axons grow through the allograft in an organized, structured way toward the end of the graft. This too is a passive technique, as it is redirects axonal regeneration but does not result in restoration of intended function.

Nerve Cap

Placing a cap on the terminal end of the nerve has been attempted to ameliorate painful regrowth of the nerve end. Many different techniques have been utilized to cap the nerve including the use of synthetic materials and vein,[34,35] although this does not seem to be commonly successful with existing materials and unicameral structural capping.[36,37] Other studies have presented more promising results, with capping of the nerve end resulting in lower expression of pain markers in a rat model.[38] Nerve capping is another passive technique as it is designed to reign in the terminal end of the nerve, but does not provide for reconstruction.

RPNI

The regenerative peripheral nerve interface (RPNI) was designed as an internal signal transduction pathway to optimize prosthetic function. In this system, a free muscle graft is wrapped around the terminal nerve stump, which ultimately becomes innervated by the regenerating nerve

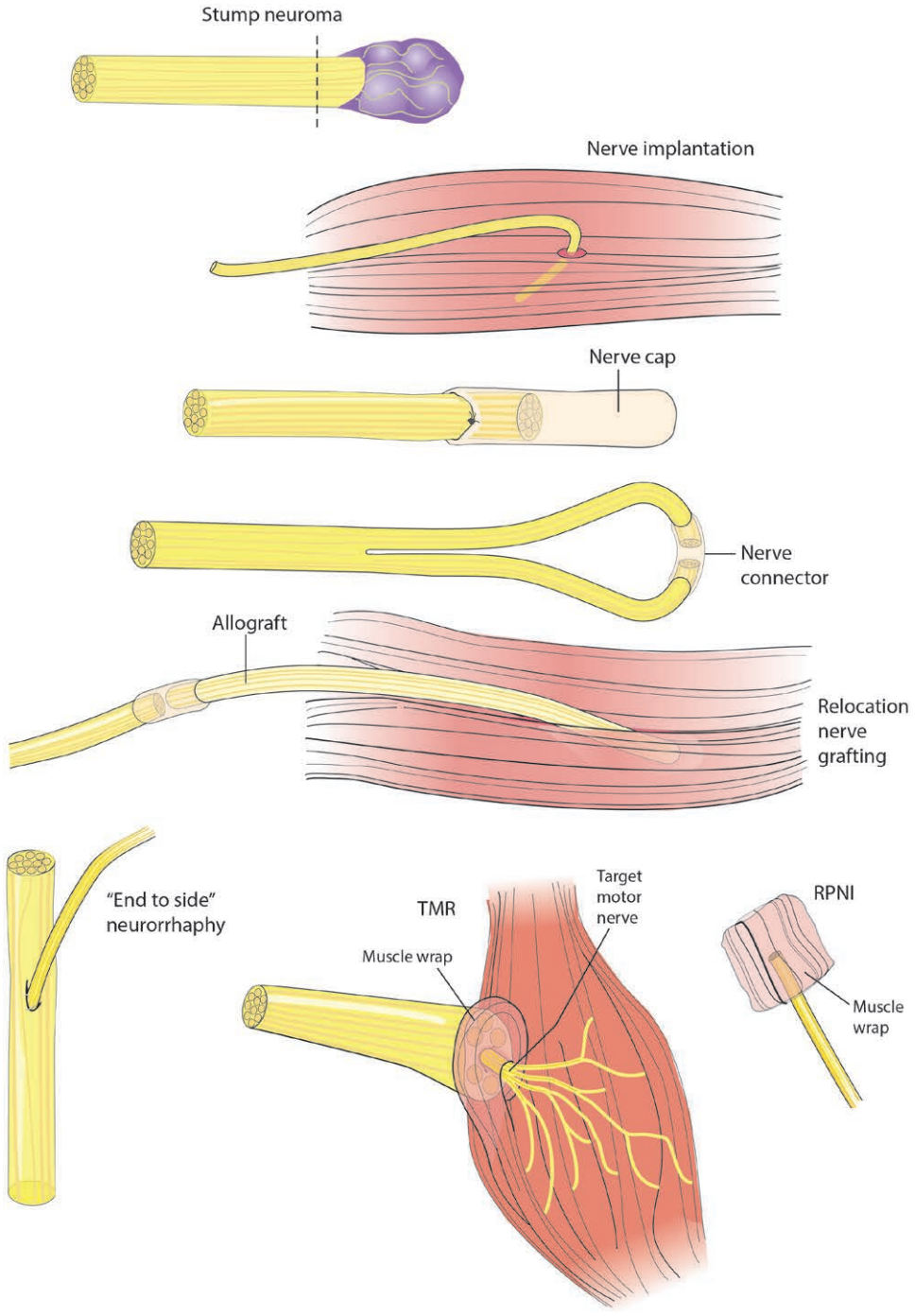

Fig. 4. Surgical options if distal nerve end unavailable. Following neuroma excision, options include implantation in muscle, nerve cap, centro-central neurorrhaphy, relocation nerve grafting, "end-to-side" neurorrhaphy, TMR, or use of RPNI.

and therefore has return of function with less pain.[39] This has been studied in the laboratory[40–42] and appears to have clinical promise based on a pilot study of 16 amputees, which demonstrated a reduction in both neuroma pain and phantom limb pain.[43]

This technique also has potential for the treatment of amputees, as the muscle grafts may provide a pathway (through inclusion of denervated muscle and their related neuromuscular junctions) to allow for more focused neural regeneration and potential reduction of associated pain. This is an active technique, as it directs the terminal nerve end into the empty motor endplates of the denervated muscle.

"End-to-side" Neurorrhaphy

Following neuroma excision, the end of the nerve stump may be coapted to the side of an adjacent intact

nerve. This may involve the creation of an epineural window or alternatively perineural disruption of the recipient nerve. This was first described as "reverse end-to-side neurotization"[44,45] but has also been called "end-to-side nerve repair"[46] and "end-to-side neurorrhaphy."[47] This technique is designed to provide a pathway for regenerating axons down the existing runway of an adjacent nerve. It has been shown experimentally to assist with axonal regeneration and may prevent painful neuroma recurrence,[46,47] but a number of questions remain about the technical execution and the expectations for destination of the axons. This is considered an active technique, as the neural end is coapted directly to an adjacent nerve.

Targeted Muscle Reinnervation

Targeted Muscle Reinnervation (TMR) was initially described by Kuiken et al.[48] as a technique to improve the function of myoelectric prostheses for amputees. In this technique, the blind ends of major peripheral nerves are mobilized and coapted to smaller adjacent motor nerve branches to allow for reinnervation of the newly denervated muscle. This nerve transfer provides a demonstrable function for the mobilized nerves. Fortuitously, this technique appears to have a significant effect on the development of neuroma following nerve transection. This has been studied experimentally[49] and has been shown clinically to be an effective treatment for the treatment of postamputation and neuroma pain.[50]

There are many reasons why TMR holds great promise for the prevention and treatment of neuroma pain.[51] Unlike other described techniques, TMR provides a clear purpose for the otherwise undirected nerve ending; it imbues an ultimate function to the nerve and may obviate the disorganized growth typical of undirected nerve endings. It is another active technique to manage the nerve end as it directly restores function to the transected nerve.

DISCUSSION

Pain resulting from a symptomatic neuroma can have a devastating effect on patients, with significant associated dysfunction and disability. Many surgical techniques are available to the nerve surgeon who must decide if surgery is indicated and, if so, what technique to employ. In a recent meta-analysis, Poppler et al.[52] reviewed 54 studies and found that surgical treatment was effective in 77% of patients. Historically, surgeons have traditionally performed passive techniques to treat the nerve end, with neuroma excision and implantation or burying of the stump. Contemporary surgical innovations have resulted in more active and reconstructive modalities of treatment, to better satisfy the nerve ending.

The determination about whether to pursue surgical intervention for neuroma is complex and is based upon multiple factors. First, the patient should have an anatomic distribution of pain, with symptoms referable to the specific involved nerve. Second, it is often prudent to confirm that a local anesthetic block is successful in ameliorating symptoms.[53] This is performed in an effort to mimic the effect of surgery, and to ensure that there is not overwhelming centralization of pain, which may result in the failure of surgical intervention.

The precise timing and impact of pain centralization is not known, but it is evident that patients with long-standing neuropathic pain—often related to neuroma—are more challenging to treat and may have worse outcomes than those addressed sooner in their clinical course. This is likely the result of significant reorganization of the somatosensory cortex, which occurs after nerve injury and neuroma formation.[54,55] Additionally, there appears to be ongoing, progressive cortical reorganization that continues to change over time.[56]

Once a decision is made for surgery, the preferred surgical technique should be chosen based on the particular clinical scenario. Operative techniques have evolved significantly over time, from initial excision-only and simple burying/implantation techniques to more active management of the nerve end. Although true comparative studies are lacking between techniques, there is rationale to pursue a more dynamic management strategy of the nerve end. Doing this may inherently satisfy the nerve and provide greater impetus for functional regeneration.

There has been an ongoing paradigm shift in the treatment of neuroma, and the nerve surgeon now has a plethora of contemporary tools available to more actively address this problem. Each technique has its own applicability in different clinical scenarios, and the surgeon should carefully consider the patient, anatomic, and surgical factors related to surgical decision making. This conceptual change has been made possible due to new techniques (RPNI and TMR) and new technology (processed nerve allograft, connectors, and conduits), which has provided the nerve surgeon additional options in the armamentarium.

Although new techniques are likely to improve outcomes for patients with symptomatic neuroma, high-level studies comparing techniques are lacking, and there is little objective data to assist surgeons. At this time, scientific rationale, experience, and clinical judgment should facilitate decision-making. Rigorous studies are needed to compare efficacy of given techniques, and to parse the different treatment options and their outcomes. It is possible that a combination of techniques will ultimately be employed to provide the best outcomes for this challenging problem.

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Neuromas of the Hand and Upper Extremity

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The painful neuroma is an often debilitating sequela of nerve injury about the hand. The exact pathophysiology of this condition is poorly understood. After sharp trauma to a peripheral nerve, as nerve ends try to connect with their end organs and "find" the distal nerve stump, fascicular escape and scarring can lead to the development of a painful neuroma. Painful neuromas can even be associated with blunt trauma or retraction of a nerve when the nerve is not actually divided. Green's definition of a neuroma is "the inevitable, unavoidable, and biologic response of the proximal stump after it has been divided in situations where regenerating axons are impeded from re-entering the distal stump."[1] A number of unknown factors make certain patients more susceptible to neuroma formation. In addition, certain nerves such as the superficial radial nerve are more prone to the development of a painful neuroma. Treatment of neuromas of the hand is important because they can be quite debilitating and painful, often preventing patients from continuing with their normal daily activities. There are a number of approaches to the painful neuroma, and the treatment plan must be tailored to the individual patient. *(J Hand Surg 2010;35A:499–510. © 2010 Published by Elsevier Inc. on behalf of the American Society for Surgery of the Hand.)*

Key words Hand surgery, neuroma, nerve, nerve injury, nerve repair.

ETIOLOGY

Formation of a neuroma results from abnormal nerve regeneration following a peripheral nerve lesion. Many neuromas can form from cutaneous nerves as a result of chronic irritation, pressure, stretch, poor repair of nerve lesions or previous neuromas, laceration, crush injury, or blunt trauma. The common requirement for the formation of a neuroma is nerve injury. There are 2 common classification systems for nerve injury that will be discussed later.

Another hallmark of neuroma formation is fascicular escape. Yuksel[2] and colleagues hypothesized that the undamaged perineurium is an impenetrable barrier for regenerating axons, but when it is damaged, fascicular escape can occur. Fascicular escape occurs when regenerating axons escape into the surrounding epineurial tissue in a disorganized fashion, accompanied by proliferating fibroblasts, Schwann cells, and blood vessels. These events result in the irregular branching of axons forming whorls, spirals, and convolutions (a neuroma).

Stretch is 1 cause of neuroma formation. Sunderland[3,4] provides a description of the nerve's response to stretch. When a nerve is gradually stretched, the undulations in the nerve and the fascicle are first eliminated, but not those of the nerve fibers, which remain tension free inside the fascicle. With continued stretching, the fibers progress from straightening to stretching to rupture. The rupture of the perineurium eliminates the barrier for the axons within. The breaks in the perineurium allow the contents inside to escape, leading to neuroma formation.

When a nerve's normal response to pressure is disrupted, neuroma formation can result. When pressure is applied to a nerve, the epineurium functions as a shock absorber that dissipates the stresses set up in the nerve, thereby cushioning the fascicles and their contained nerve fibers and protecting them from damage.[4] Nerves that are composed of smaller fascicles that are more widely separated by epineurial tissue are more susceptible to fascicular escape and, therefore, neuroma formation. This occurs because the fascicles are more

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easily displaced within the nerve and have a greater tendency to escape into the surrounding tissues.

The incorrect repair of a peripheral nerve lesion can lead to the formation of a neuroma, according to several different steps, including internal neurolysis by dissection, mobilization of the nerve, preparation of the nerve ends, and apposition of the ends.[3] Internal neurolysis involves freeing of individual fascicles within the nerve trunk. Severance of interfunicular communications or damage to the vascular supply can lead to scarring and neuroma formation. Scarring can also occur during mobilization of the nerve caused by postoperative bleeding from nutrient vessels that were sacrificed. Increasing the length of nerve destroyed can lead to less localization of the fibers representing individual branches, which increase the chances of the regenerating axons of entering foreign tubes. Apposition of nerve ends is also important because the growing axons need to enter the distal stump of the severed nerve if they are to reach the fascicles and endoneurial tubes (bands of Bungner).

Trauma is the main cause of neuroma formation about the hand, but an iatrogenic etiology, such as injury of the palmar cutaneous nerve after carpal tunnel surgery, is not infrequent. Traumatic causes of neuroma formation can be either acute or chronic. Acute injury of the nerve can damage it and prevent the regenerating axons from reaching the distal stump, leading to disorganized nerve fiber growth and the formation of a neuroma. Transection of the ulnar nerve forming a neuroma is shown in Figure 1. Infection, ischemia, and scarring can further advance the process of neuroma formation. Chronic trauma involves chronic irritation or pressure of the involved nerve and can lead to perineural scarring, another hallmark of neuroma formation. This phenomenon, involving fibrosis and hypertrophy of the underlying tissue, occurs in neuromas such as Bowler's thumb and Morton's neuroma.

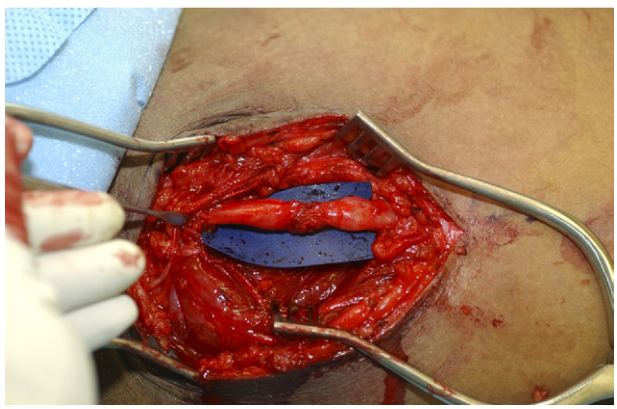

FIGURE 1: Traumatic cut to ulnar nerve forming a neuroma.

As described earlier, nerve injury can be caused by several different means. The level of that injury can be further classified to offer insight into the severity, prognosis, and discussion of the injury. Two classification systems are commonly used in the literature. In the first method of classification, according to Seddon,[5] nerve injuries fall into 3 groups: neurapraxia, axonotmesis, and neurotmesis. *Neurapraxia* is characterized by local myelin damage that can be secondary to compression. In this type of injury, axon continuity is preserved, and no distal nerve degeneration occurs, but the fibers can become demyelinated. *Axonotmesis* is a loss of continuity of axons due to crush injury. *Neurotmesis*, with varying degrees of connective tissue preservation, is equivalent to physiologic disruption of the nerve and might or might not include actual transection of the whole nerve.

The second method of nerve injury classification is according to Sunderland.[4] His grouping separates the injury into 5 grades, based on histologic structure. *First-degree injury* is a temporary, conduction block lesion in which axonal continuity is preserved. In *second-degree injury*, the continuity of the endoneurial sheath of nerve fibers is preserved. However, axonal continuity is lost, with Wallerian degeneration occurring distal to the lesion. Each regenerating axon is directed back to its original end organ, restoring the previous pattern of innervation, because its growth is confined to the endoneurial tube that originally contained it. *Third-degree injury* is a concealed, intrafascicular lesion in which the fascicles are left in continuity but continuity of nerve fibers is lost. There is disintegration of axons and Wallerian degeneration, loss of continuity of the endoneurial sheath and hemorrhage, edema, an inflammatory response, and fibrosis. This complicates axon regeneration because (1) the fibrosis blocks or diverts axons from their proper course, adversely affecting growth, development, and function; and (2) loss of continuity of nerve fibers can be misdirected into foreign endoneurial tubes. In *fourth-degree injury*, the fascicular structure of the nerve has been destroyed, and nerve trunk continuity is preserved by a strand of disorganized tissue. This allows the regenerating axons to escape from the fasciculi. A barrier of fibrous tissue arrests axon growth. *Fifth-degree injury* involves loss of continuity of the nerve trunk. Therefore, neuropraxia and axonotmesis by Seddon's classification and first- and second-degree injury by Sunderland's classification are less likely to result in neuroma formation, whereas neurotmesis and third-, fourth-, and fifth-degree injury are more susceptible.

PATHOLOGY

Some common histopathologic findings of a classic neuroma are nerve fibers and regenerating fascicles in various stages of maturation, with varying amounts of scar tissue, disorganization of nerve fibers, varying orientation of nerve fibers, and possible regeneration into the overlying skin or soft tissue.[6] A terminal neuroma results from transection of a peripheral nerve if the nerve ends are not reunited.[7] The size of a neuroma depends on factors such as the extent of axonal ingrowth and the number of fibroblasts, Schwann cells, and blood vessels present. They are usually larger close to the cell body because axoplasmic flow is more intense in this region.[8] Size also depends on a response to movement, presence of infection or foreign bodies, and general nutritional status.[8] As discussed, complete transection is not required for neuroma formation. A *neuroma-in-continuity* results from peripheral nerve lesions with preserved continuity of the nerve trunk but loss of distal function to varying extents.[1,9] In this type of neuroma, some bundles of nerve remain intact.

NERVE REGENERATION

In order to understand the pathological cause of a neuroma, one must consider the normal processes of nerve regeneration. Lundborg[10] presents a detailed explanation of nerve regeneration, from which the following excerpts were taken. Following axotomy, the nerve cell bodies must survive in order for the nerve to regenerate properly. Following axonal transection, distal parts of the axon disintegrate and experience Wallerian degeneration. Then, neurofilaments and microtubules of the axoplasm disintegrate. The remnants of axons are digested by macrophages, and Schwann cell activity increases, forming columns of cells (bands of Bungner). Some neurotrophic factors involved are the neurotrophins, neuropoietic cytokines (ciliary neurotrophic factor), interleukin 6), and fibroblast growth factors (acid fibroblast growth factor and basic fibroblast growth factor). These growth factors exert their effects by binding to thyrosinkinase receptors and a low-affinity nerve growth factor (NGF) receptor called *p75*, followed by intracellular signaling and gene activation. The NGF is important in the survival of sensory neurons and outgrowth of their neurites, but it has little or no influence on motor neurons. Its mRNA levels are normally low, but they are upregulated in the distal segment of a nerve following injury. The NGF regulates the excitability of nociceptor fibers by altering their expression of key sodium channels, receptors, and neuropeptides involved in transmission of painful stimuli.[11] Normally, the survival of uninjured nerve cells depends on a trophic influence from peripheral target cells. These trophic factors are transported by retrograde axonal transport along the axon and are used to sustain essential activities and survival. The NGF mRNA levels that increase following nerve transection are believed to be triggered by interleukin-1β released by macrophages that engulf myelin debris and degrade axons. Following nerve transection, NGF receptors on the surfaces of the Schwann cells that form bands of Bungner are activated. The regenerating axons them advance along the Schwann cell surface, picking up factors bound to NGF receptors and transferring them into the growth cones and transporting them retrogradely to the nerve cell body. The axons continue to grow along the bands of Bungner, sending out microspikes to explore the microenvironment and assist in determining the growth direction. The glycoproteins laminin and fibronectin are also important in promoting axonal elongation. Finally, some factors that influence the guidance of axonal growth specificity are (1) *tissue specificity*—the guidance of axons as a group to the distal nerve stump rather than other tissues, (2) *fascicular or nerve trunk specificity*—guidance of axons to a fascicular origin, (3) *sensory versus motor specificity*—separating sensory and motor nerve fibers, (4) *topographic specificity*—return of axons to the topographic area that they previously served, and (5) *end organ specificity*—reinnervation of each type of end organ by axons that previously served it.

WHY NEUROMAS CAUSE PAIN

Severe and persisting pain from a neuroma is unusual; however, 2 processes usually provoke such pain. They are (1) persistent mechanical or chemical irritation of the axons within the neuroma and (2) the development of spontaneous and disturbing sensory symptoms, caused by persistent stimulation of the axons within the neuroma and accompanied by the development of spontaneous activity of neurons within the dorsal root ganglion, dorsal horn of the spinal cord, and at even more proximal levels in the central nervous system.[1] Other theories include the Melzack and Wall gate theory of pain and chronic pain related to central or spinal mechanisms.

Stimulus-evoked pain in neuromas can result from activation of nervi nervorum present in connective tissue surrounding nerves, whereas stimulus-independent neuropathic pain can result from damage to afferent sensory fibers in the peripheral or central nervous system.[12] The tissue damage from neuromas results in a local inflammatory response with sensitization of the nociceptors, resulting in altered transduction and increased conduction of the nociceptive impulses toward

the central nervous system.[13] Nicholson[14] suggested that the afferent fiber types are divided into faster conducting, lightly myelinated A δ fibers and slower conducting, unmyelinated C fibers, which are primarily involved in the peripheral aspect of neuropathic pain. Inflammatory cells in the area release intracellular contents to increase the sensitivity of nociceptors to further stimulation. Vasodilation and extravasation of plasma proteins are accompanied by the release of serotonin, bradykinin, histamine, substance P, and products of arachidonic acid metabolism. The end result of these events is chemical sensitization of high-threshold nociceptors to transmit low-intensity, painful stimuli. On neuroma formation, cell constituents that are conveyed via anterograde axoplasmic transport to the cell periphery accumulate in the neuroma, including increased receptors and chemical mediators. Peripheral nerve injury also results in changes in the sympathetic nervous system, leading to an abnormal tissue response in primary nociceptive fibers. Secondary hyperalgesia also develops. *Secondary hyperalgesia* is an area of uninjured tissue around the injury with increased sensitivity to light touch that can produce pain.

Another proposed mechanism for the etiology of pain caused by neuromas was the gate control theory of pain by Melzack and Wall.[15] Their theory proposed that pain is determined by interactions among 3 different systems. These systems are (1) the substantia gelatinosa, which functions as a gate control system that modulates the afferent patterns before influencing T cells in the dorsal horn; (2) the afferent patterns in the dorsal column, which act as a central control trigger that activates selective brain processes that influence the modulating properties of the gate control system; and (3) the T cells, which activate neural mechanisms that comprise the action system responsible for response and perception. The authors believed that the concept of interacting gate control and action systems could explain the hyperalgesia, spontaneous pain, and long delays after stimulation that are characteristic of pathological pain syndromes.

Some central nervous system changes involved with neuroma formation are expansion of receptive field size, an increase in magnitude and duration of response to stimuli, and reduction in threshold so that normally nonpainful mechanical stimuli activate neurons that transmit nociceptive information. Pruimboom et al.[16] postulated the following mechanisms of disease involving the central nervous system and spinal cord for developing chronic pain: (1) neuroanatomical reorganization in the spinal cord and brain, (2) neurophysiological changes in the spinal cord and brain, and (3) activation of glia cells forming an immune reaction in the central nervous system. The activation of the glial cells produces inflammatory cytokines such as interleukin 1, interleukin 6, and tumor necrosis factor α, which activate excitatory neurons in the spinal cord responsible for afferent pain transmission. Chronic activation of these cells can produce long-term changes in neuronal activity that is responsible for pain transmission and could be responsible for the development of chronic pain.

CLINICAL ASPECTS OF NEUROMAS

Substantial pain associated with a scar and altered sensibility in the distribution of the involved nerve are the clinical hallmarks of a neuroma.[17] The diagnosis of pain in a neuroma is based on palpation of a discrete area of tenderness resulting in a distally radiating pain in the distribution of the peripheral nerve plus the identification of an area distal to the site of the positive Tinel's sign that had altered sensation (hypoesthesia, hyperalgesia or anesthesia).[18] Sood, et al.[19] described 4 types of pain associated with neuromas that were identified: spontaneous pain, pain on pressure over the neuroma, pain on movement of adjacent joints, and painful hyperesthesia on light skin touch in the vicinity of the neuroma. One way of evaluating pain associated with neuromas is to use a modified Hendler's back pain rating scale.[8] This consists of 3 components: a body diagram pain drawing, a numerical scale, and a list of pain descriptors. Pain that has a great impact on the patient's life consists of scores of 20 or more points, 3 or more adjectives to describe the pain, and a pain drawing not corresponding to the anatomic distribution of a peripheral nerve. Patients falling in 1 of these categories will likely have a good result; patients falling in 2 of 3 categories are relative contraindications to surgery; and patients in all 3 categories are not surgical candidates.

Another type of pain that might or might not be associated with neuromas is phantom limb pain, which is defined as the sensation that a deafferented body part is still present following amputation. It has been reported to occur in 50% to 80% of amputees.[20] The pain can be related to certain position or movement, can be elicited or exacerbated by a range of physical or psychological factors, and seems to be more intense in the distal portions of the phantom limb. Common descriptions of the pain include a stabbing, throbbing, burning, or cramping feeling. Phantom limb pain is sometimes confused with residual limb or stump pain. Ectopic discharge from a stump neuroma has been postulated as an important peripheral mechanism of phantom limb pain.[20]

These ectopic discharges are related to stimulation of the stump by pressure or cold, but they can also occur spontaneously as a consequence of nerve injury.

COMMON NEUROMAS

Bowler's thumb

Bowler's thumb is a term often applied to perineural fibrosis of the palmar digital nerve supplying the medial aspect of the thumb. It infrequently is a traumatic neuroma caused by proliferation of fibrous tissues both around and within the ulnar digital nerve as a result of adaptive changes in the thumb in response to frequent insertion and compression in the holes of the bowling ball.[21,22] Although named Bowler's thumb, the injury is not simply limited to the sport of bowling, as it can also occur in baseball and following surgery. The clinical presentation of this injury is characterized by pain and sensitivity over the nerve, hyperesthesia in the region of distribution of the nerve, atrophy of the overlying skin or callous formation, subcutaneous scarring, a positive Tinel's sign, frequent paresthesias and hypesthesias, changes in 2-point discrimination on the web aspect, involved nerve thickening, and firmness to palpation.[22,23]

Superficial radial nerve

A neuroma of the superficial radial nerve has often been described as one of the more painful and difficult neuromas to manage. Dellon[24] has suggested that it might even have a predisposition to develop a neuroma. Because of its anatomic location in a common area for wrist exploration, it is prone to iatrogenic injury and neuroma formation. In addition, the nerve is adherent to structures beneath the brachioradialis muscle, and it exits between the crossed tendons of the brachioradialis and extensor carpi radialis longus. However, in 3% to 10% of the general population, the nerve becomes subcutaneous by exiting through the brachioradialis tendon. This anatomic relationship tethers the nerve proximal to the wrist. If the nerve is subsequently injured, the resultant scar tissue will also lead to tethering of the nerve distal to the wrist (against skin, subcutaneous tissue, fascia, tendon, or bone). This, in turn, leads to the nerve being fixed both proximal and distal to the wrist. Dellon et al. demonstrated that the nerve is at maximal stretch in extension and ulnar deviation. This leads to tension and shearing trauma through normal ranges of motion.[24] They argued that because the dorsal cutaneous branch of the ulnar nerve and palmar cutaneous branch of the median nerve do not become tethered in this way and have less excursion through normal wrist motion, they do not observe the same stretch trauma.

There is also shown to be an association between the superficial radial nerve and the lateral antebrachial cutaneous nerve in neuroma development in the forearm. Painful nerves on the wrist and forearm are mainly considered to be related to the superficial radial nerve; however, this area of the forearm also includes the lateral antebrachial cutaneous nerve of the forearm, which can also be a potential source of pain. These nerves can have overlapping territories or have the ability to "invade" empty nerve territories resulting from previous injury or relocation. In a study by Atherton et al.,[25] the authors relocated neuromas located in zone III of the forearm. They relocated neuromas of the superficial radial nerve, lateral antebrachial cutaneous nerve, posterior cutaneous nerve of the forearm, and medial antebrachial cutaneous nerve into the brachioradialis, brachialis, biceps, and muscle bellies slightly proximal to the injuries, respectively. They concluded that the lateral antebrachial cutaneous nerve might need to be relocated after relocation of the superficial radial nerve to avoid leaving any cut branches. This was supported by Dellon and Mackinnon,[24] who showed a partial or complete overlap of the innervated territories of the superficial radial nerve and the lateral antebrachial cutaneous nerve in 75% (63 patients out of 84) of 53 cadaveric and 41 clinical dissections. Dellon and Mackinnon relocated neuromas with combined lateral antebrachial cutaneous nerve and superficial radial nerve innervations into the brachioradialis for 15 patients and showed improved pain relief compared to primary relocation of the superficial radial nerve alone.[24]

Palmar cutaneous nerve: The palmar cutaneous branch of the median nerve is another nerve commonly involved in the formation of a neuroma. A neuroma of this nerve usually results from iatrogenic injury during a carpal tunnel release; however, it can also result from excision of a palmar wrist ganglion or flexor tendon synovectomy.[26] The palmar cutaneous nerve originates from the radial side of the median nerve, 5 to 7 cm proximal to the wrist crease, and provides sensory innervation to the skin over the base of the thenar eminence and proximal palm. The nerve runs parallel to the median nerve, deep to the antebrachial fascia, and then moves toward the radial side next to the flexor carpi radialis synovial sheath. However, variations in this branching pattern are well established, including branching through the palmaris longus tendon or through the antebrachial fascia proximal to the wrist. The site where the nerve is frequently injured is where it lies between the tendons of the flexor carpi radialis and the palmaris longus muscles. A more radially placed incision during surgery is more likely to cross the distribution of

the palmar cutaneous nerve, with subsequent injury and neuroma formation.[27] The surgical incisions should, therefore, be placed on the ulnar side of the axis of the ray of the ring finger, at the level of the heel of the hand, in order to prevent subsequent injury and neuroma formation.[28] Microscopic magnification is also helpful in preventing nerve ligation and neuroma formation.[29]

Amputation stump neuromas: Neuromas can also occur in amputation stumps, and are often a missed diagnosis in amputee patients. The multitude of causes for stump pain in an amputee can result in neuromas being overlooked as the etiology of the pain. The most common etiologies of postamputation neuromas are due to a painful phantom or local stump problem. It is thought that between 10% and 25% of all patients having surgical amputation have a neuroma as the cause of their chronic pain.[30] The pain caused by amputation stump neuromas can be due to scar tissue, intervention of soft tissue or bony structures, pressure or irritation on the neuroma, or irritation by the prosthesis. The signs and symptoms remain the same for this type of neuroma, which include a positive Tinel's sign, paresthesias, and pain.

Neuromas resulting from poor surgical repair: Neuromas can form after poor surgical repair of peripheral nerve lesions. In a study done by Meek et al.,[31] the most frequent complication occurring after nerve grafting in patients with peripheral nerve injury in the upper extremities was neuroma formation. They postulated that this was most likely due to misdirection of regenerating axons that gave an inappropriate restoration that did not function as the original innervations pattern did. This can occur even if perfect growth of regenerating axons to their target organ occurs. Axons can grow out of the suture line, as well, leading to the formation of a neuroma. Scar tissue formation at the suture line can also inhibit advancement of axonal sprouts. Another adverse outcome that can occur with poor nerve grafting is neuroma-in-continuity formation due to a mismatch in diameter between the severed nerve and the graft. The clinical aspects of pain and morbidity related to these neuromas are similar to those mentioned earlier.

TREATMENT OF NEUROMAS

A multitude of techniques are used to treat peripheral neuromas, some of them dating back more than 50 years. The fact that there is such a wide range of treatment methods suggests that there is no 1 way that is completely effective in the management of these peripheral neuromas. Some initial methods of treatment include physical therapy, desensitization, and pain medication. Oral pharmacological treatment with drugs such as gabapentin or pregabalin is sometimes used. If there has not been a useful response in 6 months, it is unlikely to occur, and surgical treatments must be considered.[8] Green further describes indications for resection of a terminal neuroma as follows: "(1) there is persistent pain and dysesthesia; (2) there is no hope of reuniting the damaged nerve; (3) there is palpable, tender neuroma in the line of the damaged nerve; (4) the neuroma is, or may be, irritated within by adherence to moving muscle or tendon; (5) there is no suggestion of distortion of symptoms or signs by the patient; and (6) there has been no previous excision of a neuroma."

Some of the treatments used are transposition into muscle or vein, burying in bone, centro-centralization, coverage with flaps or vascularized tissue, nerve stripping, silicone rubber capping, re-resection of amputation stump neuromas, and re-repair of poorly performed surgical peripheral nerve repair. They are described in more detail later. In addition to the general methods of treatment discussed earlier, treatments specific to neuromas of the palmar cutaneous nerve, superficial radial nerve, and lateral antebrachial cutaneous nerve will be discussed. Successful treatment of a neuroma requires the following: careful analysis of the extent of disability, membrane stabilizing drugs or other agents from time to time, surgery that includes postoperative infusion of local anesthetic, and an urgent program of postoperative rehabilitation for the part and the patient. Prevention is the best; far too many are caused by surgeons.[1]

The surgical management of patients with painful neuromas follows 3 principles: (1) If appropriate distal nerve and sensory receptors are available, a nerve graft can be used to direct fibers from the proximal stump distally into the nerve; (2) if a distal nerve is not available and restoration of function is critical, innervated free tissue transfers can be used to accept the regenerating nerves from the injured sensory nerve; and (3) if the local tissue environment is not suitable for a nerve graft, or if the patient has had multiple previous unsuccessful operations for pain control, the neuroma is resected and the proximal stump of the nerve is managed in 1 of the following manners.

Transposition into muscle: One of the more widely used techniques for treatment of peripheral neuromas is transposition of the neuroma into muscle tissue. The goals of this treatment are to place the transected end of the sensory nerve well away from an area that is subject to repeated trauma, movement, and mechanical stimulation; to place no tension on the nerve itself; and to place the neuroma in an area so as to prevent regeneration of the nerve into the skin and minimize the for-

mation of scar tissue about the transected nerve end.[18] Translocation removes the neuroma from its bed of scar tissue, often in an area of inadequate soft tissue cover, and it is placed in an area that is not repeatedly traumatized or involved in power grip.[26] In a study by Dellon,[18] 82% of the study group achieved good to excellent relief of their painful neuromas by implantation of the nerve after neuroma resection into an appropriate muscle. Histological evaluation showed that the nerve implanted into muscle formed a nonclassic neuroma: no interaction with muscle fibers, small regenerating units of clusters of immature nerve fibers in a connective tissue–poor environment, and no random disorganized whorling of large and small fascicles with well-myelinated fibers in dense connective tissue stroma that characterize the classic neuroma. The factors contributing to less satisfactory results or failure in their study were digital neuromas, workers compensation injuries, 3 or more previous surgeries for pain, radial sensory neuroma treatment, and implantation into small superficial muscles with substantial excursion. MacKinnon[6] demonstrated that biopsies of nerves implanted into muscle showed no evidence of nerve regeneration through muscle into the overlying tissue. Other findings were that a cap of connective tissue fibroblasts separated the neural elements from muscle tissue, the nerves had fewer and smaller fibers in fascicles, no myofibroblasts, and a greater amount of neural tissue in neuromas that were transposed into muscle.

One of the most commonly used muscles for transposition is the pronator quadratus muscle. In general, the procedure for relocation into the pronator quadratus involves dissection and resection of the neuroma proximally, leaving sufficient length of nerve to allow comfortable and loose passage of the nerve through the flexor tendons, and then the neuroma is implanted into the muscle, with care taken to avoid tension on the nerve in any position of the wrist or forearm. The nerve end is buried in the pronator quadratus muscle at a depth of approximately 0.5 cm.[18,19] In addition, Sood[19] recommended separating nerve fiber bundles ending in the neuroma from the parent nerve by intraneural dissection in order to maintain maximum sensory nerve function distally. Atherton et al.[32] successfully relocated neuromas from zone II of the hand into the pronator quadratus muscle. This procedure had excellent results, with these procedures achieving complete control of spontaneous baseline pain.[32] The advantages of implantation into the pronator quadratus muscle as opposed to others are as follows: (1) division of the nerves in the proximal part of the hand and wrist usually leaves insufficient length of nerve in the palm or dorsum to reach the dorsolateral part of metacarpal bones, (2) relocation into the intrinsic muscles of the hand leaves the neuroma susceptible to trauma during hand use, and (3) proximal relocation deep to the long finger flexor muscles in the mid-forearm is unsatisfactory because the excursions of the flexor muscles stimulate the neuroma.[19]

Transposition into vein: In addition to being transposed into muscle tissue, neuromas have also been transposed into the lumen of veins. In theory, there is an interaction between regenerating axons and the vessel endothelium, with an adverse effect of blood on nerve regeneration.[7] In this technique, the affected nerve is identified proximal to the neuroma and dissected distally to free the neuroma from surrounding scar tissue, resected back to the healthy nerve, and mobilized sufficiently to allow implantation into an adjacent vein without tension.[7,33] The nerve is then inserted into the vein and held with an epineural suture through the venous wall.[7,33] Results from a study done by Herbert[33] showed that 13 of 14 patients reported dramatic, immediate pain relief, with 86% successful after the initial surgery and 100% successful after revision. Herbert also showed histologically that nerve stumps transposed into a vein lumen showed more organized endoneural architecture, small fascicles oriented in the same direction, and a high rate of myelinated axons.[34] Advantages of this technique are that subcutaneous veins are readily available throughout the body; suitable veins are usually in close proximity, making substantial nerve mobilization unnecessary; and the nerve end is situated well within the vein lumen, preventing regenerating axons from accessing the tissue outside the vein.[7]

Burying in bone: Burying neuromas in bone is 1 of the oldest techniques available, having been practiced for more than 50 years. Boldrey first conducted experiments by burying acutely lacerated ulnar nerves of dogs into bone. He found that, histologically, neuroma formation of those buried was smaller than outside. In 1984, Mass showed 90% acceptable results for transfer of the neuroma into the proximal phalanx or the metacarpal.[35] Hazari and Eliott[36] experimented with relocating digital nerves into the phalanx bones. In their study, they buried the nerve ends 1 phalanx back from the site of amputation or nerve injury, but it proved ineffective because the relocated nerve end was still close to the end of the digit and continued to be traumatized regularly. In addition, the digital tip or stump remained innervated and painful, as the small nerve branches innervating the skin of the palmar or dorsal surface of each phalangeal segment left the main digital nerve proximal to that segment. They changed to moving the

main digital nerve ends 2 phalangeal segments proximally and received better results, but some relocations remained uncomfortable on closing the fingers together at the site where the nerve turned across the edge of the drill hole into bone. Some possible reasons for failure for this technique are that the nerve is not sutured into or through the bone or an incomplete preoperative evaluation missed branches of the nerve that needed transferring individually or by more proximal transfer of the main nerve.[35]

Gorkisch pinch, centro-centralization: Another method used for the treatment of peripheral neuromas is the Gorkisch pinch, or centro-centralization. This technique was described by Gorkisch[37] for the prevention of amputation neuromas in the hand. Centro-central nerve repair involves the coaptation of 2 nerve cords of central origin. The technique can also be applied for 1 nerve if it is split into 2 fascicles of equal size. The 2 nerves or fascicles have simple end-to-end repair. Subsequently one of the nerves or fascicles of central origin is severed again in its proximal segment, producing a transplant of 5 to 10 mm. The transplant functions to prevent the axons coming from both fascicles of nerves from meeting in the suture area. If several fascicles are coapted, they are positioned so that they lie stepwise in the area of repair to keep the interfascicular connective tissue proliferation within bounds and reduce the possibility of axonal compression. Microscopically, they showed that in the intact autologous transplant, single axonal proliferations from both parts of the nerve were visible, lying parallel, and interdigitating. They also showed that, after an axonal overlap of 2 to 5 mm has developed, further growth ceases. The anastomosis is able to withstand the forces resulting from nerve growth, and it guides the growing axonal ends toward each other. A theory for the cessation of axonal growth is that there must be a continuous flow of axoplasm in both directions and that protein synthesis of the cell is regulated by intraperineural pressure with the aid of axoplasm flow. If these newly formed axons are under pressure in the transplantation area, it results in a reduction of protein production and axoplasm flow in the neuron, acting to inhibit neuroma development. Their study had promising results, with only 1 of 30 patients going on to develop a neuroma. A study by Belcher[38] also showed successful inhibition of axon migration and reinnervation of skin and scar by centro-central nerve union. They theorized that if a graft is not used, axon sprouts of fascicles cannot penetrate into each other because endoneurial tubes are full and axons will penetrate into neighboring connective and scar tissue forming a neuroma. Barbera and Albert-Pamplo showed good clinical results after performing centro-centralization on painful neuromas in patients with lower extremity amputations. They had 21 of 22 patients who were free of their neuroma pain at an average of 15 months of follow-up.[39]

Coverage with flaps or tissue: One of the newer methods for treatment of peripheral neuromas is coverage with vascularized soft tissue or flaps. It is speculated that providing the injured nerve with a vascularized and nourished milieu through flap coverage might offer mechanical support and aid in favorable optimization of neurochemical and electrical activity of the nerve and reduce irritability.[40] Some types of flaps used are hypothenar fat pad flaps, fasciosubcutaneous Becker-type flaps, synovial flaps, muscle flaps, and fascial flaps.[41] The fascial flaps allow wrapping with well-vascularized tissue and provide a gliding surface for the nerve. Yuksel[2] used epineural flaps to prevent neuroma formation. Results of the study showed no pain at rest for any of the subjects. Adani used the pronator quadratus to create a flap that can then be used to cover the neuroma-in-continuity. Krishnan et al.[40] used multiple vascularized soft tissue to cover painful neuromas. They concluded that the technically difficult procedure should be considered only when there is repeated failure of simpler surgeries, pain resistant to medical therapy, poor soft tissue healing, and absence of microvascular risk factors. One technique applicable to neuromas embedded in heavy scar tissue close to the flexion crease of the distal interphalangeal joint when there is an intact distal nerve end is the Lasso island flap.[42] This technique is mainly used on the radial border of the index finger and consists of a nerve suture beneath a sensitive vascularized skin island. This technique is described in Foucher.[42] The advantages of using this kind of flap are that a nerve graft is not required, nerve repair is formed without tension because all of the strain is taken by the distal skin suture, the advanced nerve remains well vascularized, and the island places the area of nerve regeneration in a well-vascularized bed that resolves without a recurrent scar. Good to excellent results were obtained in 19 of 23 patients.

Nerve stripping: Another technique used for neuroma treatment is nerve stripping. This technique was described by Lanzetta[26] for the treatment of palmar cutaneous nerve neuromas. First, the neuroma is freed from the surrounding tissue and a 1.5-cm long segment of nerve is dissected and rolled over straight mosquito forceps. Longitudinal traction along the direction of the nerve is then applied, using a gentle but steady pull,

until the nerve is disconnected and slid away from the main trunk. The nerve is then removed from the incision. In the study, all patients reported complete relief from pain 4 days after surgery. The injured sensory branch of the nerve can be stripped away from the main trunk without causing harm to the parent nerve. The study also showed that removing the injured nerve as far as its traceable intraneural origin showed no adverse effect on the median nerve, and it did not cause the neuroma to recur proximally.

Silicone rubber capping: Silicone rubber capping of the nerve stump was another method used to treat painful neuromas. The following procedure was described in Tupper.[43] In this study, silicone rubber caps were placed over the resected proximal nerve stump to contain the neuroma and decrease the amount of fibrous tissue reaction between it and the surrounding tissue. Two different types of caps were used: the Ducker-Hayes cuff, which had a looser fit, and the Frackelton cap, which had a more snug fit. The results of the study demonstrated no improvement with the silicone capping, and several of the caps became dislodged. Today, the procedure is rarely performed due to poor results.

Re-resection of amputation stump neuromas: Neuromas that form in the stump of a limb or digit following amputation must be resected. Some surgical methods used for treatment of amputation stump neuromas are silicone capping, centro-central anastomosis, and burying techniques. Many methods have been used in order to prevent these neuromas from forming, but there is not 1 accepted method of treatment. Some techniques described are using scalpel, electrocautery, or laser to dissect the nerve and placing gentle traction on the nerve, cutting it sharply and then allowing it to retract into the proximal region of the limb, allowing the stump to heal without painfully entrapping the nerve in scar tissue.[30] In Ducic et al.,[30] the authors used a technique of neuroma excision with muscle implantation previously described by Dellon.[18] They discovered that by avoiding the surgical scar and using an approach proximal to the most distal part of the stump, a faster recovery and quicker return to use of a prosthesis was possible. Depending on the amputation level, patients in the study had the option of using a stump shrinker for edema control for 3 weeks after surgery and resuming use of their prosthesis about 6 weeks after surgery. The authors had no intraoperative or perioperative complications, and no recurrences of neuromas were reported. Herndon et al.[44] treated amputation stump neuromas by keeping the neuroma intact with its mature encapsulating scar and transporting it *en bloc* to an adjacent area free of scar and not subjected to trauma. Their theory was that by using an atraumatic transfer method and transferring the neuroma to a well-nourished, well-padded, and minimally traumatized area, they eliminated the recurrence rate of neuromas. They found that 82% of patients with amputation stump neuromas had excellent results, which they defined as at most mild pain that did not influence daily activity, mild Tinel's sign, and functional interference with only heavy or delicate work secondary to the location of the neuroma. Geraghty et al.[45] studied 8 patients with neuromas following upper limb amputation. The surgical methods used in this study were burying in soft tissue, excision, and burying in vein. They found that, after surgical intervention, all patients had a reduction in pain and 6 of 8 patients had increased use of their prostheses.

Re-repair of poorly performed surgical peripheral nerve repair: Recurrence of neuroma formation can be a frustrating and sometimes frequent occurrence. In a study done by Laborde et al.,[46] the authors examined different surgical methods and their rates of neuroma recurrence. In this study, they separated their patients into 5 groups: those requiring simple excision and implantation into muscle, those who required more than 1 excision of recurrent neuromas, patients with ray amputations, patients with translocations of their neuromas, and patients who had excision and secondary neurorrhaphy or nerve grafting. Of the 38 patients in the study, 25 required a second excision and 11 were subject to 3 or more excisions. They found that the patients who were subjected to ray amputations had the highest recurrence rate and those subjected to translocation had the best results.

Treatment of neuromas of the palmar cutaneous nerve: Neuromas of the palmar cutaneous nerve are often a result of iatrogenic injury during carpal tunnel release, as shown in Figure 2. Evans et al.[28] treated these neuromas by implantation into the pronator quadratus muscle in the forearm. They divided the palmar cutaneous nerve at

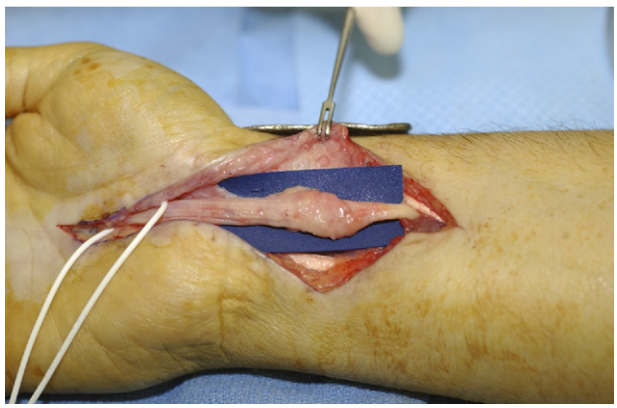

FIGURE 2: Cut median nerve after endoscopic carpal tunnel release.

the tubercle of the scaphoid and implanted into the center of the muscle. They ensured that enough length was left in the nerve so that no tension was placed on it during wrist range of motion. The authors achieved subjective improvement in pain scores for 12 of 13 patients in the study. Atherton et al.[32] used the same method of transposition and achieved complete control of spontaneous basal pain in their patients after resection. They hypothesized that their success was due to the depth of the relocation—because the nerve was buried deep, it was not subjected to trauma or other types of stimulation and, therefore, was not painful to the patient.

Treatment of neuromas of the superficial radial nerve: A neuroma of the superficial radial nerve is 1 of the most common and most difficult neuromas to treat. Dellon and MacKinnon[18] treated 26 patients with dorsal radial nerve neuromas by implantation into the brachioradialis muscle and achieved good to excellent pain relief in 88% of the population. The authors had previous failures when implanting the nerves into small superficial muscles with substantial excursion, such as the abductor pollicis longus and extensor pollicis brevis group. When the nerves were relocated into the brachioradialis, they achieved pain relief and an increase in motion. They hypothesized that this occurred because the neuroma was subject to less trauma, movement, mechanical stimulation, and tension on the nerve when implanted into the brachioradialis as compared to the previously mentioned muscles. Other failures were due to concurrent neuromas in the lateral antebrachial cutaneous nerve for reasons described earlier. Vernadakis et al.[17] also suggested preliminary success with end-to-side repair, but long-term results are yet to be seen. Nerve grafting has also been attempted, with evidence of regeneration across the grafts and restoration of sensation, but it showed persistence of pain over the dorsum of the hand.[17] The large range of motion across the wrist puts tension on the graft, leading to scar formation between the skin, nerve graft, and underlying tendons. Therefore, this technique is not indicated except in cases of acute trauma when tension-free repair is not possible.

Treatment of neuromas of the lateral antebrachial cutaneous nerve: The lateral antebrachial cutaneous nerve is another common site for neuroma formation. The overlap of the lateral antebrachial cutaneous nerve and the superficial radial nerve make treatment of these types of neuromas more complex than others. Dellon and Mackinnon treated 15 patients with neuromas innervated by both the superficial radial nerve and the lateral antebrachial cutaneous nerve by implantation into the brachioradialis muscle. They achieved 88% good to excellent pain relief results.[18] Atherton et al.[25] also studied the treatment of lateral antebrachial cutaneous nerve neuromas. In the case of isolated neuromas, the nerve can be relocated into the brachialis muscle above the elbow. When there was a concurrent superficial radial nerve neuroma, the nerves were relocated into the brachioradialis muscle. The authors achieved total resolution of pain and hypersensitivity at the primary site in 47 of 51 nerves relocated. Preoperative anesthetic blocks can be used to assist in determining the nerves that are responsible for neuroma formation and to help direct treatment options.

Pharmacological treatment: Pharmacological treatment presents an alternative treatment for those who either do not want to have more invasive procedures or cannot tolerate such procedures. The 2 main drugs that are used for treatment of neuropathic pain related to peripheral neuromas are pregabalin and gabapentin. These drugs are classified as anticonvulsant drugs and are also used for the treatment of epilepsy, diabetic neuropathy, and postherpetic neuralgia. The mechanisms of both drugs are the same. Pregabalin and gabapentin exert their effect by binding to the $\alpha_2\delta$ subunit of voltage-gated calcium channels, reducing influx of calcium into nerve terminals.[14,47–49] This reduced influx of calcium leads to a decrease in neurotransmitter release, including glutamate, noradrenaline, and substance P.[49,50] Both drugs are structural analogs of gamma-aminobutyric acid (GABA), but there is conflicting evidence on its role in the mechanisms of the drugs. One suggestion is that the drugs enhance GABA uptake in the brain by increasing the number of brain GABA transporters in the plasma membrane, reducing the number intracellularly, and also increasing neuronal GABA concentrations.[51] Others suggest that they have no effect on the uptake or breakdown of GABA.[47] The absorption and metabolism of pregabalin and gabapentin are similar. Both drugs are rapidly absorbed after oral administration, are not bound to plasma proteins, are eliminated by the kidneys, and do not interact with hepatic enzymes.[47,49,51] The lack of metabolism of both drugs eliminates potential problems associated with active metabolites that have unfavorable pharmacodynamic profiles and may decrease risk for clinically important pharmacokinetic interactions.[49] Renal impairment substantially affects the pharmacokinetics of both drugs, and the dosage must be adjusted accordingly.[12,47,51] Gabapentin and pregabalin also share the most common adverse effects. The effects that have been reported are dizziness, somnolence,

peripheral edema, nausea, gastrointestinal upset, and infection.[13,47,50,51] Guay[51] also reported pregabalin to cause withdrawal symptoms such as insomnia, nausea, headache, and diarrhea with abrupt or rapid discontinuation of pregabalin. The difference between the 2 drugs is their pharmacokinetic profile. Pregabalin, unlike gabapentin, has a pharmacological profile that is linear and dose-proportional at doses up to 900 mg/day. The pharmacokinetic profile advantage over gabapentin is that the linear pharmacokinetics result in predictable changes in plasma concentrations when the dosage changes, which is not the case for gabapentin, which has decreased absorption at high doses.[49] The decreased absorption of gabapentin is the result of its transport mechanism. The transport mechanism becomes saturated at high doses, which reduces the bioavailability as dosage is increased.[49] Therefore, this results in the failure of systemic exposure to increase proportion to dose, with a need to use lower doses more frequently to maximize the amount of drug that is absorbed. In summary, pregabalin has an advantage over gabapentin because of its linear pharmacokinetics, narrow dosing range, and lack of need for dose titration.[51]

Rehabilitation: Rehabilitation is another aspect of treatment for neuromas of the hand. Rehabilitation involves the gradual withdrawal of supportive measures while patients accustoms themselves back into normal daily activities. The goals of rehabilitation are as follows: an objective assessment of disability and accurate measurement of outcome; reduction of the degree of disability by physical and other therapies; to patients' original work, to that work modified, or to suitable other work; and restoration of the patient's ability to live in their homes, to enjoy recreation and social activities, and to be independently mobile.[1] Specific treatment might be indicated in those with a fixed deformity, weakness, loss of endurance, loss of balance, loss of confidence, and neuropathic pain.[1] Padded finger stalls can help to alleviate the pain, and serial splinting along with physiotherapy has been used for rehabilitation. Some additional methods used in rehabilitation are desensitization, massage, transcutaneous nerve stimulation, and vibration. Vibration is useful for desensitizing painful areas and is used at the periphery of painful areas with gradual movement toward the center.[17] When the affected area has been desensitized, sensory reeducation can be instituted.

The treatment of neuromas remains an important issue in orthopedics. There is a wide variety of causes of neuroma formation, as discussed earlier. Likewise, a large number of treatment options have been described in the literature. Although there is no 1 good treatment option, certain principles will offer better clinical outcomes. First, patient selection is critical. Patients should have signs and symptoms consistent with a specific nerve injury or anatomic distribution, and the physician should be able to confidently identify the nerve in question. It is important to maximize nonsurgical management, including pain management and physiotherapy. At the time of surgery, definitive neuroma resection and tension-free coverage (in muscle, bone, vein, flaps, or anastomosed with other nerves), or repair when possible, will provide the least amount of subsequent nerve irritation. A thorough postoperative rehabilitation program to help patients return to their normal daily activities is equally important.

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:30 AM - 10:40 AM

Targeted Muscle Reinnervation

Jason H. Ko, MD, MBA
No relevant conflicts of interest to disclose

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SEPTEMBER 30 - OCTOBER 2, 2021

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:40 AM - 10:50 AM

Regenerative Peripheral Nerve Interfaces

Kyle R. Eberlin, MD

- Axogen - Consultant
- Integra - Consultant
- Checkpoint - Consultant
- Tissium - Consultant

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:50 AM - 11:00 AM

Case Discussion

All Faculty

No relevant conflicts of interest to disclose

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:50 AM - 10:52 AM

Case Presentation

Amber R. Leis, MD

- Checkpoint – Speaker
- Axogen - Speaker

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Live Pre03: Current Treatment of Nerve Injuries, Gaps, and Neuromas

10:52 AM - 11:00 AM

Case based Debate

Jason H. Ko, MD, MBA |

Speaker has no financial relationships to disclose.

Kyle R. Eberlin, MD

- Axogen - Consultant
- Integra - Consultant
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Speaker has not provided a handout for this presentation

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