Peripheral nerve injuries have been recognized since antiquity. Management of nerve injuries, including nerve repair, have been described in various textbooks and reports from the Classical era, the Medieval era, in pre-Industrial times, and into the early 20th century (see the article by Friedman for a nice review of the topic37). For instance, Paul of Aegina (7th century) described the concepts of nerve repair and regeneration. With the advent and understanding of the nervous system in the mid-19th century, the description of the neuron as a single cell and its peripheral process, which undergoes the process of anterograde myelin degeneration (described beautifully by Waller in 1850), as well as the response of the peripheral versus the central nervous system to injury and regeneration by Cajal in 1905, provided the fundamental biological insights for an improved understanding of nerve injury and repair cases. By the late 20th century, the advent and popularization of interfascicular nerve grafting techniques heralded a major advance in nerve reconstruction and allowed good outcomes to be achieved in a large percentage of nerve injury repair cases. In the past 2 decades, there has been a paradigm shift in surgical nerve repair, wherein surgeons are not only directing the repair at the injury zone, but also are deliberately performing distal-targeted nerve transfers as a preferred alternative in an attempt to restore function. The peripheral rewiring approach allows the surgeon to convert a very proximal injury with long regeneration distances and (often) uncertain outcomes to a distal injury and repair with a greater potential of regenerative success and functional recovery. Nerve transfers, originally performed as a salvage procedure for severe brachial plexus avulsion injuries, are now routinely done for various less severe brachial plexus injuries and many other proximal nerve injuries, with reliably good to even excellent results. The outcomes from nerve transfers for select clinical nerve injury are emphasized in this review. Extension of the rewiring paradigm with nerve transfers for CNS lesions such as spinal cord injury and stroke are showing great potential and promise. Cortical reeducation is required for success, and an emerging field of rehabilitation and restorative neurosciences is evident, which couples a nerve transfer procedure to robotically controlled limbs and mind-machine interfacing. The future for peripheral nerve repair has never been more exciting.

**KEYWORDS** nerve grafting; nerve transfers; neurolysis; peripheral nerve

**ABBREVIATIONS** AIN = anterior interosseous nerve; CN = cranial nerve; PIN = posterior interosseous nerve; SSN = suprascapular nerve.

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the wound, wide debridement, and repair of nerve under tension (sometimes accompanied by limb shortening or splinting the extremities in a flexed posture for months) with relatively poor results and an occasional success. Improved understanding of the pathology of nerve injury and nerve injury in continuity derived from the World War II experience.

With the subsequent use of nerve autograft techniques, we enter the more modern era of nerve repair injury. Pioneering work by Hanno Millesi and colleagues in the 1960s with the use of interfascicular nerve grafting to avoid tension at the repair and good microsurgical technique (aided by magnification) was a major landmark in the nerve repair era. The use of intraoperative nerve monitoring with the use of nerve action potential studies and their utilization to resect an injury neuroma and graft versus neurolysis alone was a fundamental insight provided by David Kline and colleagues to help surgeons manage the majority of nerve injuries in continuity encountered in clinical practice. A combination of the neurophysiological work by Kline and the microsurgical insights of graft repair without tension by Millesi led to significant improvements in the outcomes of nerve repair in the 1960s and the 1970s. With the use of the operating microscope and these aids, the microsurgical era of nerve repair was fully established in the past 2 generations. As these techniques were adopted and used by the large cadre of peripheral nerve surgeons worldwide, the results from peripheral nerve repair quickly plateaued in the 1980s and 1990s. Indeed, an honest appraisal of these results can be found in various excellent textbooks including those from Kline’s extensive experience and from the excellent review by Brushart, and critical reading of these underscores that approximately 50%–75% of patients have modest recoveries from nerve injury repair by grafting.

**Timing of Nerve Exploration and Repair**

The mechanism and severity of nerve injury determines the possibility of recovery and the need for nerve exploration (Fig. 1). Every peripheral nerve injury in which there is complete nerve damage that will require axonal regeneration and reinnervation is a form of chronic nerve injury. This is because the rate of regeneration in humans is approximately 1 mm/day, and the distance to target end organs from the area of nerve injury is quite lengthy. This renders the distal nerve zone as well as the muscle end organ or the sensory receptor to be chronically denervated. A large body of animal literature as well as circumstantial patient literature with regard to timing of nerve repair and outcomes underscores the fact that outcomes are greatly improved when nerve repair is undertaken earlier. However, if a nerve can regenerate satisfactorily on its own (Sunderland grade 2 injuries and some grade 3 injuries), then the outcome of spontaneous recovery is generally excellent, compared with the modest outcomes of nerve repair. For this reason, most surgeons wait several months before undertaking exploration of nerve injuries in continuity, and appropriately so. In a few (especially European) centers, there has been a shift toward very early exploration and reconstruction. This represents the minority of clinical experience. There has been a gradual and appropriate shift in timing of nerve exploration and possible reconstruction, with an emphasis on intervening earlier, particularly in patients with clinically complete and severe brachial plexus injuries. The dogma of waiting for many months or up to 6–8 months is no longer tenable, and the majority of reconstructive peripheral nerve surgeons now plan to operate on these patients within a few weeks to months from the time of injury.

Imaging revolutionized the diagnosis and management of most aspects of neurosurgery, as well as nerve tumors. Its utility in managing nerve trauma has been less spectacular. The use of improved imaging techniques, especially high-quality ultrasound and MRI, does allow for a better visualization of the area of nerve injury, particularly to image nerve disconnection and/or likely laceration. Indeed, resolution of ultrasound in particular can render the anatomical details of nerve discontinuity at even a fascicular level. A good and practical use of ultrasound is as an adjunct to shape overall management in cases of uncertainty if a nerve is in discontinuity, such as a shrapnel-associated injury or a penetrating nerve injury, such as that associated with gunshot wounds. However, no imaging modality yet allows sufficient spatial resolution to predict whether a sufficient aliquot of nerve fibers is regenerating through the neuroma in continuity, enough to mitigate against surgical evaluation with operating microscope magnification, interfascicular dissection, and use of intraoperative electrophysiology. Hence, the current management of most nerve injuries is the following. For nerves that are clearly lacerated or likely to be lacerated, immediate or very early exploration is recommended. For injuries in which the nerve is likely lacerated in a blunt fashion (for example, a boat propeller injury), delayed exploration and secondary nerve repair with appropriate placement of nerve grafts at approximately 3–4 weeks is warranted. With most nerve injuries, a period of watchful waiting is recommended. For high-velocity severe traction injuries and/or very proximal brachial plexus injuries, earlier exploration after several weeks is recommended, whereas low-velocity injuries such as fracture-associated palsy, a somewhat conservative approach is initially taken with serial clinical and electrophysiological evaluation for recovery. If recovery does not start to manifest after 3–4 months, nerve exploration is undertaken. While some European centers advocate for acute brachial plexus exploration, we remain without any significant level of evidence for operating ultra early versus in a somewhat delayed fashion for the majority of brachial plexus injuries.

**Nerve Repair in the Modern Era: Nerve Transfers**

Improved outcomes from nerve repair essentially required a paradigm shift, which we are now witnessing with the advent and the increased popularity of nerve transfer techniques. A nerve transfer technique essentially involves repair of the distal denervated nerve element by an adjacent foreign donor nerve. These nerve transfers are usually done far distally, beyond the area of original nerve injury and close to the end organ, thereby converting a
proximal nerve injury, with long regeneration distances and uncertain outcomes, to a more distal repair from which recovery is theoretically faster and more robust.

The advent of the modern nerve transfer era began arguably in the early 1990s with a series of papers that began to explore the possibility of neurotization in severe plexus injury using an extraplexal donor nerve such as the intercostals, the spinal accessory nerve, the phrenic nerve, and the medial pectoral nerve. In 1994, Oberlin published his now seminal paper detailing the transfer of an ulnar fascicle to the biceps motor nerve for reanimation of elbow flexion. The success of this relatively simple procedure transformed the collective thinking that had previously regarded nerve transfers as a salvage-only procedure. Several caveats for success include choosing a donor nerve that has redundant function to other preserved nerves so that there is no significant downgrading of function in the patient. Interfascicular dissection so that single fascicles are chosen as donors again decreases the possibility of functional complications. Parenthetically, the popularity of fascicular transfers has offered a renaissance to the surgeon to apply the techniques of internal neurolysis, which historically were used for intraneural dissection for some nerve injuries (Fig. 2). Moreover, the use of nerve transfers also ensures that the specificity of the element being transferred is controlled by the surgeon (using neuroanatomical and neurophysiological knowledge), along with choosing a synergistic donor/recipient combination so that cortical reeducation is possible. The success of nerve transfers is largely facilitated by cortical plasticity, which has been repeatedly demonstrated in the context of nerve transfer rehabilitation. Other factors known to influence success of nerve transfer are donor size matching with the recipient nerve and the robustness of preoperative electromyography-detected activity from the donor nerve/muscle. For example, the optimal donor-to-nerve axon count ratio for elbow flexion seems to be > 0.7:1.

What follows is a commentary on the state of the art for nerve transfers and restoration of function of the upper extremity, including current controversies. It should be noted that the efficacy of nerve transfers has been reviewed several times in detailed systematic analysis. In general, it has been well accepted that in the context of upper plexus injury involving multiple roots, nerve transfers are superior and more reliable to grafting techniques for the recovery of both elbow flexion and shoulder abduction. Direct end-to-end neurotizations perform better than transfers requiring interposition grafts. In addition, the more extensive the plexus injury, the poorer the recovery.

Shoulder Function

Early work on nerve transfers for shoulder function focused on neurotization of the suprascapular nerve (SSN) and axillary nerve, primarily with accessory and phrenic nerve donors. There has been progressive proof that double neurotization of the SSN and axillary nerve provides best results (Table 1). This is in the context of the commonly utilized triple nerve transfer (accessory nerve to SSN, triceps motor nerve to axillary nerve, ulnar nerve fascicle to biceps motor nerve), which is becoming the standard choice for nerve reconstruction for upper plexus injury.

When compared directly with plexus graft repair, nerve transfers have fared either equal to or better than grafting for restoration of shoulder function. Recovery of shoulder abduction is often greater than 90° with a significant proportion of patients regaining a Medical Research
Council grade ≥ M4 deltoid strength. External rotation outcomes are less impressive.46 Although it is often not quantified in the literature, a major goal for shoulder reinnervation surgery is the restoration of shoulder stability, which happens in the majority of cases where the suprascapular nerve is neurotized.

There is still a strong argument to be made for primary graft repair of the injured nerve element. An example is the relatively common axillary nerve injury that occurs from shoulder dislocation, with pathology typically starting at the level of the posterior cord in the axilla at the emergence of the axillary nerve and then for a variable distance into the quadrangular space as the nerve traverses from an anterior to a posterior location before entering into the deltoid muscle. Many of these injuries do recover spontaneously. For the ones that do not, the traditional management has been to explore the nerve, usually with resection of the intervening neuroma and long graft repairs. The outcomes from such repairs are relatively good for deltoid recovery. Yet many of these injuries are now being repaired surgically with the seemingly more simple technique of doing a posterior exploration of the axillary nerve and then transferring one of the triceps branches to one of the divisions of the axillary nerve. This transfer has a highly reliable recovery of function, but one could argue that this is not better than, and perhaps not even as good as, the traditional reconstructive approach.4 Unfortunately, there is no level 1 or even level 2 evidence to guide us as to what is the appropriate approach between these 2 very alternative reconstructive strategies for pure axillary nerve injuries.

In isolated axillary injury, grafting has recently been found to be superior to nerve transfer for optimal recovery.5 In plexus-level injuries, Bertelli and Ghizoni found...
grafting and nerve transfer superior for shoulder recovery compared with nerve transfer alone.8 This was the preferred technique of Kline, the “belt and suspenders” approach intended to maximize axonal reinnervation of target musculature.45

Elbow Flexion and Extension

Restoration of elbow flexion, along with shoulder stabilization, is a primary goal of any plexus repair or nerve transfer surgery for upper or total plexus injury. Many donors have been used to neurotize the musculocutaneous (or biceps motor) nerve, including the phrenic nerve,40,58,68 intercostal nerves,28,29,58,68 medial pectoral nerve,21 accessory nerve,26 thoracodorsal nerve,43 and contralateral C7 nerve.81 These procedures are effective and seem to provide a reasonable chance for the patient to regain grade ≥ M3 biceps strength (Table 2).19,59,68 They remain invaluable additions to the toolbox for reconstruction of total plexus injury; however, in cases of upper plexus injury, the Oberlin transfer has become standard of care. The procedure, which involves the transfer of an ulnar nerve fascicle to the biceps motor nerve, reliably produces grade ≥ M4 elbow flexion in a large proportion of patients.48,63 Young patients with isolated upper plexus injury and an intact hand fare best.32 Short regeneration distance means that this procedure can be effective, even after delayed presentation (> 6 months from injury).71 Alternatively, nonessential median nerve branches to wrist and finger flexors

TABLE 1. Nerve transfers for shoulder reanimation: selected studies

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>LOE</th>
<th>No. of Pts</th>
<th>Indication</th>
<th>Procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baltzer et al., 2016</td>
<td>III</td>
<td>29</td>
<td>Isolated axillary nerve injury</td>
<td>Triceps motor nerve → axillary nerve vs grafting</td>
<td>Grafting better than TX for MRC ≥3</td>
</tr>
<tr>
<td>Yang et al., 2012</td>
<td>II</td>
<td>615</td>
<td>Upper plexus injury</td>
<td>Various neurotization of SSN &amp; axillary nerve vs graft</td>
<td>Transfers equal to grafting for MRC ≥3 Sabd</td>
</tr>
<tr>
<td>Garg et al., 2011</td>
<td>II</td>
<td>56</td>
<td>Upper plexus injury</td>
<td>Various neurotization of SSN &amp; axillary nerve vs graft</td>
<td>Dual TX for Sabd better than single TX or grafting</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2010</td>
<td>III</td>
<td>37</td>
<td>C5–6 palsy</td>
<td>3 TX vs C5 graft + 3 TX vs C5–6 graft + CN II → SSN + Oberlin</td>
<td>Best results w/ 3 TX + graft</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2007</td>
<td>IV</td>
<td>30</td>
<td>Various severity</td>
<td>CN XI → SSN +/- triceps motor nerve → axillary nerve</td>
<td>45° Sabd for total palsy; 105°–122° for upper BPI</td>
</tr>
<tr>
<td>Terzis et al., 2006</td>
<td>IV</td>
<td>92</td>
<td>Upper &amp; total BPI</td>
<td>Various neurotization of SSN &amp; axillary nerve</td>
<td>Combined SSN &amp; axillary nerve TX superior, 79% good outcome</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2004</td>
<td>IV</td>
<td>10</td>
<td>C5–6 palsy</td>
<td>CN XI → SSN, triceps motor nerve → axillary nerve, Oberlin</td>
<td>100% Sabd recovery, 3/10 grade M4, 7/10 grade M3</td>
</tr>
<tr>
<td>Leechavengvongs et al., 2003</td>
<td>IV</td>
<td>7</td>
<td>Upper plexus injury</td>
<td>Triceps motor nerve → axillary nerve, CN XI → SSN</td>
<td>All pts ≥M4 recovery of deltoid</td>
</tr>
<tr>
<td>Merrell et al., 2001</td>
<td>I</td>
<td>123</td>
<td>Various BPI</td>
<td>Neurotization of SSN vs axillary nerve</td>
<td>SSN better than axillary nerve for return of Sabd</td>
</tr>
<tr>
<td>Merrell et al., 2001</td>
<td>IV</td>
<td>15</td>
<td>Various BPI</td>
<td>CN XI or intercostal nerves → SSN or axillary nerve</td>
<td>Double TX more effective for recovery of Sabd</td>
</tr>
</tbody>
</table>

BPI = brachial plexus injury; LOE = level of evidence; MRC = Medical Research Council; pts = patients; Sabd = shoulder abduction; TX = transfer; +/- = with or without.

TABLE 2. Nerve transfers for restoration of elbow flexion: selected studies

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>LOE</th>
<th>No. of Pts</th>
<th>Indication</th>
<th>Procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al., 2014</td>
<td>III</td>
<td>24</td>
<td>Upper plexus injury</td>
<td>Ulnar vs median nerve</td>
<td>Equal outcomes</td>
</tr>
<tr>
<td>Martins et al., 2013</td>
<td>III</td>
<td>40</td>
<td>Upper plexus injury</td>
<td>Reinnervation of biceps vs biceps &amp; brachialis</td>
<td>No difference in clinical outcome</td>
</tr>
<tr>
<td>Socolovsky et al., 2012</td>
<td>III</td>
<td>35</td>
<td>Upper plexus injury</td>
<td>Graft vs Oberlin</td>
<td>Oberlin was superior for EF</td>
</tr>
<tr>
<td>Coulet et al., 2010</td>
<td>III</td>
<td>40</td>
<td>C5–6 +/- C7 palsy</td>
<td>Ulnar fascicle vs intercostal nerves → MCN</td>
<td>Ulnar fascicle TX superior for EF</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2010</td>
<td>III</td>
<td>37</td>
<td>C5–6 palsy</td>
<td>3 TX vs C5 graft + 3 TX vs C5–6 graft + CN II → SSN + Oberlin</td>
<td>Best results w/ C5–6 graft + Oberlin</td>
</tr>
<tr>
<td>Mackinnon et al., 2005</td>
<td>IV</td>
<td>6</td>
<td>Upper plexus injury</td>
<td>Ulnar nerve → biceps motor nerve; median nerve → brachialis nerve</td>
<td>Average ≥M4 recovery EF</td>
</tr>
<tr>
<td>Ferraresi et al., 2004</td>
<td>IV</td>
<td>43</td>
<td>C5–7 avulsion</td>
<td>Ulnar or median nerve → biceps motor nerve</td>
<td>M2–M4 recovery</td>
</tr>
<tr>
<td>Leechavengvongs et al., 1998</td>
<td>IV</td>
<td>32</td>
<td>Upper plexus injury</td>
<td>Ulnar fascicle → biceps motor nerve</td>
<td>30/32 w/ M4 EF</td>
</tr>
<tr>
<td>Nagano et al., 1995</td>
<td>IV</td>
<td>112</td>
<td>Upper &amp; total BPI</td>
<td>Intercostal nerves → MCN</td>
<td>87% regained ≥M3 EF</td>
</tr>
<tr>
<td>Oberlin et al., 1994</td>
<td>IV</td>
<td>4</td>
<td>C5–6 avulsion</td>
<td>Ulnar fascicle → biceps motor nerve</td>
<td>100% ≥M3; 75% M4 EF</td>
</tr>
</tbody>
</table>

EF = elbow flexion; MCN = musculocutaneous nerve.
have been used as donors for the biceps or brachialis motor nerve.78 Median to biceps motor nerve transfer produces near equivalent elbow flexion recovery compared to the Oberlin procedure.26 Many authors have purported the use of a double fascicular transfer in elbow flexion restoration, a procedure that involves both a classic Oberlin transfer (ulnar fascicle to biceps motor) as well as median nerve transfer to the nerve innervating the brachialis. Proponents of this technique, such as Mackinnon et al., point to the excellent outcomes it very often achieves, as well as the lack of functional median nerve deficit postoperatively.52,66 However, a recent prospective study found no clinical difference in recovery of elbow flexion between patients who received a single nerve transfer to the biceps motor nerve and those who received a double transfer that also included reinnervation of the brachialis.54 Therefore, the double fascicular transfer for restoration of elbow flexion remains a topic of controversy among experts in the field.

Restoration of elbow extension is often a secondary goal to provide greater elbow control via antagonistic feedback to the elbow flexors.35 In avulsions, phrenic or intercostal nerves are suitable donors to the radial triceps motor nerve.36,39 In isolated lower plexus injury, intact radial fascicles, thoracodorsal nerve, or nerve to brachialis have all recently demonstrated efficacy in restoring functional elbow extension.16,34,75

Hand and Wrist Reanimation

In situations in which hand and wrist function have been affected by lower plexus injury, spinal cord injury, or proximal nerve injury, nerve transfers are increasingly indicated, thanks to much recent work in this field.

In high ulnar injury, and likewise in cubital tunnel syndrome with severe end-stage axonopathy, the distal anterior interosseous nerve (AIN) branch to pronator quadratus has become a popular donor for reinnervation of the distal ulnar motor branch (Fig. 2).60 The outcomes for this procedure may be superior to proximal ulnar grafting for both motor and functional hand outcomes.33,67 Of note, some authors have suggested the use of the end-to-side or “supercharge” repair, in which the distal AIN is grafted onto the side of the ulnar motor branch while maintaining the continuity of the proximal ulnar nerve (Fig. 2).30 Nerve transfers in spinal cord injury are an exciting advancement and a relatively new territory, though sporadic efforts have been previously attempted.43 Nerve transfers for treatment of lower plexus injury overlap significantly with those used in spinal cord injury patients, particularly in midcervical spinal cord injury. The concept is to use intact donor nerves to give the patient function in myotomes distal to the level of injury. The donors and recipients for these transfers are variable and individualized to the patient, and depend on the presence or absence of viable donors as well as functional goals. An emerging theme is the use of nerves to the supinator and the extensor carpi radialis brevis to innervate the posterior interosseous nerve (PIN) and AIN, respectively (Fig. 3).10,14 Procedures of this type are listed in Table 3; of note is the pioneering work of Bertelli and colleagues in this field.5,9,17

Flail Arm

Reconstruction of total plexus avulsion remains a significant challenge and was the original indication for nerve transfer surgery.99 Available extraplexal donors include cranial nerves (CNs) XI55,76 and XII, the contralateral CN XI,18 intercostal nerves,26,64 the phrenic nerve,40,51 and the contralateral C7 (Table 4).82 Primary goals include restora-
tion of shoulder stability and abduction, as well as elbow flexion. Secondary goals are the recovery of elbow extension, along with wrist and hand function. Of note, intercostal donors may give better elbow flexion outcomes if grafted directly on to the biceps motor branch, and only 2 intercostal nerves may be sufficient for restoration of elbow flexion, although most authors use 3. The use of the contralateral C7 root has yielded inconsistent results, and classically the procedure requires the use of a long interpositional graft. Recent technique advances do show promise to improve these outcomes, by both using a prespinal route to tunnel the C7 donor across midline, and in extreme circumstances, to achieve a tension-free primary repair with the lower trunk by shortening the humerus of the affected side. These procedures are not without complications, in particular up to a 5.4% incidence of vertebral artery laceration.

Evolution of Nerve Surgery Repair: Transfers and Beyond

The evolution of peripheral nerve surgery from one of exploration, neuroanatomical dissection, and reconstruction of the nerve injury site itself to one where essentially a peripheral rewiring procedure is carried out represents a fundamental shift in the repair of peripheral nerve injury that continues to evolve rapidly in the past 2 decades. While there had been some interest in managing nerve
table 3. Nerve transfers for restoration of hand and wrist function: selected studies

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>LOE</th>
<th>No. of Pts</th>
<th>Indication</th>
<th>Procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sallam et al., 2017</td>
<td>III</td>
<td>52</td>
<td>Proximal ulnar injury</td>
<td>Grafting vs AIN → ulnar motor nerve</td>
<td>Improved strength &amp; grip in TX group</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2017</td>
<td>IV</td>
<td>9</td>
<td>Midcervical SCI</td>
<td>Various donors to AIN or finger flexor motor nerve</td>
<td>All work, nerve to ECRB is superior donor to AIN</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2016</td>
<td>IV</td>
<td>28</td>
<td>C5–8 root lesions</td>
<td>AIN (PQ) → ECRB</td>
<td>25/28 M4 WE</td>
</tr>
<tr>
<td>Davidge et al., 2015</td>
<td>IV</td>
<td>55</td>
<td>Proximal ulnar injury</td>
<td>AIN (PQ) → ETS ulnar motor nerve</td>
<td>Improved grip, pinch, 1st DI strength, &amp; self-report scores</td>
</tr>
<tr>
<td>Flores, 2015</td>
<td>III</td>
<td>35</td>
<td>Proximal ulnar injury</td>
<td>AIN (PQ) → ETE ulnar motor nerve vs grafting</td>
<td>Improved motor &amp; functional outcomes in TX group</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2015</td>
<td>IV</td>
<td>20</td>
<td>SCI</td>
<td>Deltoid branch → triceps nerve; supinator nerve → PIN</td>
<td>High proportion of M4 recovery of EE, ThE, FE</td>
</tr>
<tr>
<td>Bertelli et al., 2010</td>
<td>IV</td>
<td>1</td>
<td>SCI, WE intact</td>
<td>Supinator nerve → PIN</td>
<td>M4 + FE, ThE</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2010</td>
<td>IV</td>
<td>4</td>
<td>C7–T1 palsy</td>
<td>Supinator nerve → PIN</td>
<td>Restoration of FE, ThE</td>
</tr>
<tr>
<td>Novak &amp; Mackinnon, 2002</td>
<td>IV</td>
<td>8</td>
<td>High ulnar injury</td>
<td>AIN (PQ) → ulnar motor nerve</td>
<td>8/8 improved pinch, grip, EMG-determined reinnervation</td>
</tr>
</tbody>
</table>

DI = dorsal interosseous; ECRB = extensor carpi radialis brevis; EE = elbow extension; EMG = electromyography; ETE = end-to-end; ETS = end-to-side; FE = finger extension; PQ = pronator quadratus; SCI = spinal cord injury; ThE = thumb extension; WE = wrist extension.

table 4. Nerve transfers for flail arm: selected studies

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>LOE</th>
<th>No. of Pts</th>
<th>Indication</th>
<th>Procedure</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhatia et al., 2017</td>
<td>IV</td>
<td>22</td>
<td>Severe BPI</td>
<td>Contralat C7 nerve direct repair vs interposition graft</td>
<td>Better grade (M3) WF w/ direct repair</td>
</tr>
<tr>
<td>Xiao et al., 2014</td>
<td>III</td>
<td>30</td>
<td>Total BPI</td>
<td>2 vs 3 vs 4 intercostal nerves → MCN</td>
<td>2 intercostals are sufficient</td>
</tr>
<tr>
<td>Wang et al., 2013</td>
<td>IV</td>
<td>75</td>
<td>Severe BPI</td>
<td>Contralat C7 nerve → lower trunk (arm shortening)</td>
<td>≥M3 FF (64%), ThF (53%), WF (72%)</td>
</tr>
<tr>
<td>Lin et al., 2012</td>
<td>IV</td>
<td>6</td>
<td>Plexus avulsion</td>
<td>Full-length phrenic nerve → radial nerve</td>
<td>5/6 w/ ≥M3 WE, 4/6 w/ ≥M3 FE</td>
</tr>
<tr>
<td>Terzis &amp; Kokkalis, 2009</td>
<td>IV</td>
<td>56</td>
<td>Severe avulsion BPI</td>
<td>Contralat C7 nerve → MCN or axillary, radial, or median nerve</td>
<td>≥M3 Sabd 20%, EF 52%, ThE 24%, WE/FE 20%, WF/FF 34%</td>
</tr>
<tr>
<td>Bertelli &amp; Ghizoni, 2004</td>
<td>IV</td>
<td>24</td>
<td>Avulsion BPI, various</td>
<td>Ulnar nerve vs CN XI vs phrenic nerve → biceps motor nerve</td>
<td>Good EF recovery for all donors, mainly M4</td>
</tr>
<tr>
<td>Songcharoen et al., 1996</td>
<td>IV</td>
<td>216</td>
<td>Avulsion BPI, various</td>
<td>CN XI → MCN</td>
<td>72.5% w/ ≥M3 EF</td>
</tr>
<tr>
<td>Chuang et al., 1995</td>
<td>III</td>
<td>99</td>
<td>Upper &amp; total BPI</td>
<td>Various donor &amp; recipient nerves</td>
<td>Phrenic nerve &amp; CN XI → Axillary nerve &amp; SSN most reliable</td>
</tr>
<tr>
<td>Ogino &amp; Naito, 1995</td>
<td>IV</td>
<td>10</td>
<td>Avulsion BPI</td>
<td>Intercostals → MCN &amp; median</td>
<td>60% w/ M3 WF, 40% w/ M3 FF</td>
</tr>
<tr>
<td>Gu et al., 1990</td>
<td>IV</td>
<td>65</td>
<td>Avulsion BPI</td>
<td>Phrenic nerve → MCN, various other</td>
<td>84.6% functional recovery, no effect on respiration</td>
</tr>
</tbody>
</table>

FF = finger flexion; ThF = thumb flexion; WF = wrist flexion.
root avulsions by reconstructing the spinal cord–nerve interface led by Carlstedt et al.,24 using nerve root implantation or even nerve graft augmentation,6 the recovery results from these heroic attempts were meager compared with those of nerve transfers. Initially, nerve transfers were done for so-called irreversible brachial plexus injuries involving proximal nerve root avulsion from the spinal cord. More recently, many surgeons have turned to offering distal fascicular transfer as a preferred approach to manage more proximal brachial plexus injuries with a higher likelihood of functional recovery. Unfortunately, with the increasing utilization of distal nerve transfer techniques, there are many missed opportunities to evaluate and appropriately treat the area of the nerve injury zone itself. Indeed, the pooled analysis literature on brachial plexus repairs65 still underscores the fact that a nerve reconfiguration at the level of the injury with grafting, along with the combination of targeted distal fascicular transfers, may offer the best possibility for recovery.

A further evolution of nerve transfer techniques involves the increasingly greater use of distal transfers to treat more proximal nerve injury such as injuries involving the ulnar, radial, and median nerves (see case examples in Fig. 2).13,60,65 Combinations of fascicular transfer distally from preserved branches of one of the aforementioned nerves to peripheral branches of the damaged nerve proximally are now being increasingly offered as an alternative to the classic tendon transfer techniques. In addition, many surgeons, led by Bertelli,32 are now recommending the combination of proximal nerve repairs (such as for high radial nerve injuries), with the augmentation of distal transfers from branches of the median nerve to the radial nerve to more reliably and quickly recover function such as finger extension. In the modern era, the peripheral nerve surgeon therefore has the exciting prospect of using existing microsurgical techniques, aided by intraoperative electrophysiology along with the creative use of a wide combination or permutations of nerve transfer options.

Nerve Transfers to Treat CNS Pathology

A further extension of these transfer techniques has been to use them to augment and reanimate function in patients with spinal cord injuries as noted above. These entail transfers of nerve fascicles from preserved nerves above the level of the spinal cord lesion (so-called supraspinal) to nerves at or below the level of the spinal cord injury (sublesional) in patients with complete quadruplegia. For example, in a complete C6 quadriplegia, a combination of transfer of the fascicle of the axillary nerve to triceps nerve can restore elbow extension and a fascicle from the radial nerve branch to the supinator to the PIN can reanimate finger extension, while finger flexion can be achieved by transferring a median nerve branch to the pronator teres to the AIN for thumb and finger flexion (Fig. 3). This example represents a complete paradigm shift in that the surgeon uses a deliberate peripheral nerve rewiring procedure to overcome the neurological deficit imposed by a structural lesion in the CNS, in this case, the spinal cord. Recent attempts of similar procedures to reanimate the extremity in patients with central pathology such as hemispheric stroke have emerged. In a paper reported in the New England Journal of Medicine, pioneering work from China involved the transfer of the C7 spinal nerve root from the normal arm to the contralateral C7 of the paralyzed arm in an attempt to restore motor function and decrease spasticity in the paralyzed upper extremity from the stroke.85 The results were modest, and on editorial speculation, Spinner et al. noted that the results on the basis of the temporal kinetics of recovery were likely more on the basis of decreased inhibition and spasticity from neurotomy alone (of C7) rather than recovery on the basis of nerve regeneration.77 Whatever the mechanism, this clinical experience from the Chinese group nevertheless represents a bold direction in peripheral nerve surgery for the repair of CNS trauma.

Future Perspectives

The above review hopefully underscores the vast majority of choices available to reconstructive nerve surgeons to repair peripheral nerve injuries. Exploration, assessment, and nerve reconstruction of the original nerve injury remain the mainstay of surgical management. However, the increasing and appropriate use of distal targeted transfers along with central reeducation are becoming much more popular, even for injuries that were once considered for primary nerve repair.

The shift toward peripheral rewiring and central reeducation in our opinion will continue to evolve. We are already starting to see the next step in this revolution with the pioneering work of Aszmann et al.,3 where a deliberate amputation of the paralyzed arm is done in a patient with intractable and nonrecovering severe brachial plexus injury with flail limb despite prior attempted nerve reconstruction. In patients exposed to prior intensive and systematic training, 2 reliable myoelectrical signals from the forearm are used to create movements in a prosthetic hand, specifically between the thumb and the other fingers. The patients were able to conduct new tasks (including bimanual performance) with the new prosthesis after amputation. Not only is it possible for these patients to gain some functional recovery of the limb but intriguingly there is a significant decrease in neuropathic pain in these patients, the mechanisms of which is not yet understood. Undoubtedly some degree of cortical plasticity and central rewiring is involved, and further research into the neuroanatomical, physiological, and mechanistic substrate is required to decipher this process. In the near future, with the further advent of robotic technology and with the improving understanding and incorporation of the brain-machine interface, we will undoubtedly see further evolution of peripheral rewiring procedures along with central reeducation to improve outcomes further.

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Midha. Analysis and interpretation of data: Grochmal. Drafting the article: both authors. Critically revising the article: Midha. Reviewed submitted version of manuscript: Midha. Approved the final version of the manuscript on behalf of both authors: Midha.

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