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Targeted Muscle Reinnervation for the Upper and Lower Extremity

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Abstract

Myoelectric devices are controlled by electromyographic signals generated by contraction of residual muscles, which thus serve as biological amplifiers of neural control signals. Although nerves severed by amputation continue to carry motor control information intended for the missing limb, loss of muscle effectors due to amputation prevents access to this important control information. Targeted Muscle Reinnervation (TMR) was developed as a novel strategy to improve control of myoelectric upper limb prostheses. Severed motor nerves are surgically transferred to the motor points of denervated *target* muscles, which, after reinnervation, contract in response to neural control signals for the missing limb. TMR creates additional control sites, eliminating the need to switch the prosthesis between different control modes. In addition, contraction of target muscles, and operation of the prosthesis, occurs in response to attempts to move the missing limb, making control easier and more intuitive. TMR has been performed extensively in individuals with high-level upper limb amputations and has been shown to improve functional prosthesis control. The benefits of TMR are being studied in individuals with transradial amputations and lower limb

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Conflicts of Interest

None

amputations. TMR is also being investigated in an ongoing clinical trial as a method to prevent or treat painful amputation neuromas.

1. Introduction

Continued advances in myoelectric prosthesis technology, including the development of multi-function hands and powered legs, have provided users with the potential for unprecedented degrees of aesthetics and function. However, the lack of an intuitive, robust control interface has in many cases hindered clinical adoption of these devices. Targeted Muscle Reinnervation (TMR), developed initially as a novel control interface for individuals with high level upper limb amputations, is now a clinically accepted surgical procedure that has been performed over two hundred times in the US and around the world. By redirecting nerves severed by amputation to new muscle targets, TMR provides access to previously unavailable neural control information. TMR surgery was first performed in an individual with a shoulder disarticulation amputation [1, 2] and later in individuals with transhumeral amputations [3]. TMR is currently being evaluated individuals with transradial amputations and lower limb amputations, to improve control of multi-functional hands and powered leg prostheses, respectively. Pattern recognition technology, which has evolved alongside TMR, enables full use of the extensive neural control information carried within transferred nerves. Additionally, TMR is being evaluated in a clinical trial as a novel method for the treatment or prevention of amputation neuromas.

1.1. Myoelectric Prosthesis Control

Myoelectric upper limb prostheses are controlled by electromyographic (EMG) signals generated by contraction of residual muscles. Unfortunately, individuals with higher levels of amputation have fewer residual muscles but must control more prosthetic functions. Thus the individual must use one or two remaining muscles to control all prosthesis joints; for example, an individual with a transhumeral amputation must use their triceps and biceps to control wrist and hand movements as well as the flexion and extension of the prosthetic elbow. This requires the user to switch the prosthesis sequentially between elbow, wrist, or hand modes to accomplish a typical task, making prosthesis use slow and cumbersome, in sharp contrast to the seamless movements possible with an intact arm. Additionally, using muscles that are physiologically unrelated to the desired prosthesis movement, e.g., using the biceps to open the prosthetic hand, feels unnatural and unintuitive. These factors contribute to high prosthesis rejection rates for individuals with high-level upper limb amputations [4].

1.2. Targeted Muscle Reinnervation for Improved Prosthesis Control

Neural control signals intended for the wrist and hand, even for movement of individual fingers, is carried in the nerves that were severed by amputation. Studies in animal models indicate that nerves continue to transmit this motor control information after amputation for decades, if not indefinitely [5–8]. However, as these nerves no longer have muscle effectors, this important neural information is unavailable for prosthesis control.

In 1917, Elsberg et al. [9] demonstrated that severed nerves can be transferred to, and successfully reinnervate new muscles, and that subsequently, these reinnervated muscles respond to neural signals from the transferred nerve [8, 10, 11]. This observation led to the concept of TMR: nerves severed because of arm amputation could be surgically transferred to spare ‘target’ muscles [12], i.e., muscles rendered biomechanically redundant after loss of the arm. After reinnervation, contraction of target muscles and EMG signal generation occurs in response to neural control information intended for the missing limb. Thus, for example, when the user attempts to close their missing hand, the transferred median nerve causes depolarization of its target muscle, generating EMG signals that are used to close the prosthetic hand. After TMR, prosthesis control becomes faster, easier, and more intuitive, while allowing up to two prosthetic joints to be moved simultaneously. TMR also creates additional control sites, reducing the need for mode switching.

The basic premise of TMR is to create control sites for four essential prosthetic functions: hand open, hand close, elbow flexion, and elbow extension. This is achieved by a combination of novel nerve transfers to create new control sites, together with preservation of existing control sites that can subsequently be used to control only physiologically appropriate prosthetic functions, e.g., using the biceps to flex the elbow.

1.3. Surgical Considerations for successful TMR

For successful myoelectric control after TMR, each reinnervated muscle or muscle segment must generate EMG signals only in response to the transferred nerve. Many muscles are innervated by multiple motor nerve branches (e.g., the pectoralis major muscle is innervated by two separate nerves that branch to form three motor points, and some individuals have additional motor points [13]). All native motor innervation of the target muscle must be cut during TMR surgery or the target muscle will have a combination of natively innervated and re-innervated muscle fibers. The native nerve(s) will generate unwanted EMG signals, confounding prosthesis control. Failure to fully denervate a target muscle may also prevent robust reinnervation because fewer motor end plates are available to the transferred nerve and/or because of competition with remaining native nerves for reinnervation of available sites [14, 15]. Ideally, coaptation is performed directly to the recipient nerve as it enters the muscle (i.e., to the motor point), to minimize the distance (and therefore time) required for nerve regeneration.

Successful TMR requires robust reinnervation of target muscles to obtain strong EMG signals. When a motor neuron is cut, the distal end of the nerve undergoes Wallerian degeneration [16], but proximal fibers send out neural processes that seek new functional connections. Newly divided distal nerve segments guide the propagating nerve growth cone towards muscle synaptic junctions. However, reinnervated muscle typically does not regain previous mass or functional capacity [17–19]. Animal studies have shown that reinnervation of a denervated muscle with an excess of donor nerve fibers (i.e., hyper-reinnervation) results in improved muscle recovery, likely because the probability of any given motor end plate being reinnervated is maximized [20]. In TMR, large brachial plexus nerves (8–10 mm) containing many thousands of motoneurons are transferred to small (~1 mm) distal motor nerves (Figure 1) that innervate relatively small regions of muscle, greatly increasing

the odds of any individual muscle fiber being reinnervated. This so-called hyper-reinnervation leads to robust target muscle reinnervation, even several years after amputation. Hyper-reinnervation may also overcome the age-related reduction in peripheral nerve regeneration [21, 22]—to date TMR has been successfully performed in adults up to 68 years old.

Each brachial plexus nerve controls a discrete set of hand and arm movements, and each nerve is transferred to an independent, separate target muscle (or muscle segment), either on the residual limb or, in the case of shoulder disarticulation amputees, onto adjacent segments of a single muscle, e.g. pectoralis [1]. Conventional control of a myoelectric prosthesis requires EMG signals that are free of cross talk—i.e. not contaminated by EMG signals from adjacent muscles, although this is not as essential for pattern recognition-based control (See section 3.). To prevent nerve fibers from reinnervating adjacent muscle segments, muscle segments are surgically separated to generate a physical barrier of scar tissue [1]. Alternatively, an adipofascial flap can be inserted to physically separate different muscles/muscle segments [3].

The key issues influencing the strength of the EMG signal are muscle size and the thickness of the subcutaneous fat over the muscle [23, 24]. Subcutaneous fat acts as a spatial filter, greatly attenuating the surface EMG signal and reducing the focus of the recording area [25, 26]. Reducing the fat layer depth from 18 mm (typically found over the chest or outer upper arm) to 3 mm dramatically increases the amplitude of the EMG signal [24]. Bone located close to the skin surface can also affect EMG signal magnitude [23], resulting in an increased signal strength on one side of the bone and a reduced signal on the other side. In shoulder disarticulation patients, nerve transfers to the clavicular head of the pectoralis muscle result in very strong EMG signals as this muscle target is adjacent to the clavicle.

2. TMR for the Upper Extremity

The indication for TMR in the upper limb is poor function with a standard prosthetic device despite adequate rehabilitation and training. Patient evaluation begins with a thorough history and physical examination. Prior operative reports should be reviewed, and X-rays should be obtained to screen for heterotopic ossification and, where appropriate, to determine residual bone length and soft tissue envelope. A long residual limb is optimal, as this typically means that the nerves will be long enough for transfer. As TMR requires functional, cortically connected median, radial, ulnar and/or musculocutaneous nerves, individuals with brachial plexus injuries are not candidates for the procedure. Patients with avulsive injuries should be screened to rule out brachial plexopathy or proximal nerve injury, which can be difficult to diagnose after amputation of the forearm and hand. Photographs taken at the time of these amputations are often obtainable from the referring surgeon, and can reveal a long nerve still visibly attached to the severed limb. A history of a limb avulsion may also mean that nerve endings are too proximal to reach muscle targets. Tinel's sign distal to the mid-humeral level in a residual limb indicates that residual nerves are long enough to be coapted without tension. Voluntary contractions of any muscles present on the residual limb, as well as the pectoralis, serratus, and latissimus muscles must also be verified by physical examination to demonstrate intact innervation and identify potential nerve

transfer targets. Supple soft tissues facilitate the tissue elevation and wide dissection necessary during TMR; this procedure is difficult to perform in a limb with excessive scarring, skin grafts, or with heterotopic ossification. Surgery is also precluded in individuals who are unable to tolerate a 3–4 hour surgical procedure.

Surgical options depend on the level of the amputation and availability of suitable target muscles. Individuals with transhumeral amputations (possibly with an intact elbow joint) retain native innervation of the biceps and triceps, allowing elbow extension and flexion, but have lost median, ulnar, or distal radial innervation. Individuals with a shoulder disarticulation amputation (including those with a residual humeral head) have lost innervation from all brachial plexus nerves (except possibly innervation of a triceps remnant by the proximal radial nerve), thus nerves are transferred to segments of the pectoralis major muscle. For patients with a surgically removed or damaged pectoralis major, a free muscle transfer may also be performed to create a target [27]. Shoulder disarticulation TMR procedures typically result in four new control signals and the loss of the native pectoralis and latissimus innervations. Transhumeral TMR patients maintain their biceps and triceps signals, while regaining their median, distal radial nerve, and sometimes even the ulnar nerve information for prosthetic control. A surgical training video demonstrating key steps in the procedure is available at <http://www.ric.org/research/centers/cbm/index.aspx>

2.1. Transhumeral level TMR

Young patients with adequate biceps and triceps contraction, no plexopathy, a long residual limb, and supple soft tissues are the best candidates for TMR. For bilateral amputees, unilateral or bilateral TMR can be performed. Separate procedures are performed on the ventral (volar) and dorsal sides of the arm. It is also possible to combine a humeral angulation osteotomy at the same time as TMR surgery, typically while the patient is prone and with the aid of cutting guides.

Pre-operatively, the patient is asked to contract the biceps and triceps muscles, and the midline of both of the muscles is marked, dividing the short and long heads of the biceps and the long and lateral heads of the triceps, respectively. Tinel's signs signifying the ends of the median, ulnar, and radial nerve are also marked. The typical nerve transfers for a transhumeral level amputee are shown in Table 1 and Figure 2.

For both ventral and dorsal dissections, it is important to cleanly open the space between the muscle bellies and identify and divide all motor nerve branches to each target muscle. The soft tissues on top of the muscles are thinned by creation of adipofascial flaps. This improves subsequent signal detection by reducing the distance between the target muscles and skin-surface electrodes.

The goal of the ventral incision is to transfer the median nerve to the motor point of the medial head of the biceps (to provide a 'hand close' signal), while preserving the innervation of the musculocutaneous nerve to the lateral head of the biceps (to retain the innate 'elbow flexion' signal). For persons with a long residual limb, the ulnar nerve can also be transferred to an available motor point on the brachialis to provide a wrist control signal. Using an anterior incision, thin skin flaps are developed, leaving a layer of fat on the deep

fascia. An adipofascial flap is then elevated proximally to reveal the raphe between the short and long heads of the biceps brachii. The musculocutaneous nerve in this space is divided into three branches: the motor nerves to the short and long heads of the biceps and the distal nerve continuing to innervate the brachialis and to continue finally as the lateral antebrachial cutaneous nerve. Dissection on the medial aspect of the arm reveals the median nerve next to the brachial artery and often the smaller, slightly posterior medial antebrachial cutaneous nerve. The median nerve is cut back to healthy fascicles and mobilized to the short head of the biceps. If the nerve is too long, additional length can then be trimmed. The musculocutaneous motor nerve to the biceps short head is divided one cm from its entry into the muscle (the site where a motor nerve enters the muscle is termed a “motor point”), and a nerve coaptation is performed, bringing the small motor nerve into the center of the large median nerve with 6-0 polypropylene suture and loop magnification. To prevent post-operative separation, the epineurium is sewn to the epimysium with polypropylene sutures. If the brachialis is available, the ulnar nerve is identified posterior to the median nerve and medial antebrachial cutaneous nerve and mobilized to the motor nerve of the brachialis, which is most easily identified using a portable nerve stimulator. The ulnar nerve is coapted to this motor point as described for the median nerve. Following placement of the adipofascial flap between the long and short heads of the biceps, a drain and a mildly compressing dressing are applied.

The goal of the posterior incision is to transfer the distal radial nerve to the lateral head of the triceps (to provide a ‘hand open’ signal), while preserving the innervation of the long head of the triceps by the proximal radial nerve (to retain the innate ‘elbow extension’ signal). While possible to do in the supine position with shoulder hyperextension, it is easier to re-prepare and drape the patient in a prone position. The skin incision is made between the long and lateral heads of the triceps, and a proximally-based adipofascial flap is elevated. It is helpful to begin cephalad where the deltoid overlies the triceps, to locate the interspace before the muscle bellies fuse. Elevation of the long head typically reveals the major trunk of the radial nerve, with one or two motor branches leaving to supply the lateral head of the triceps—as seen in radial nerve transfers to restore axillary nerve function for a C5 motor nerve injury. The more proximal motor innervation of the long head of the triceps is not typically visible. The distal radial nerve typically enlarges in size after amputation, feels relatively firm, and electrical stimulation does not generate any muscle contractions. The distal radial nerve is cut back to healthy fascicles, and the motor nerve(s) to the lateral head of the triceps are divided one cm from their entry point into the muscle. The distal radial nerve is then coapted to this motor point, as described previously. The adipofascial flap is placed between the lateral and long heads, and a drain and a mildly compressing dressing are applied.

2.2. TMR for Shoulder Disarticulation Amputation

TMR at the shoulder level requires significant knowledge of upper chest and axillary anatomy. An infraclavicular approach to the plexus and proximal nerve branches is performed by incising the skin two fingerbreadths below the clavicle and carefully opening the interspace between the sternal and clavicular heads of the pectoralis major. All motor nerve branches to the pectoralis must be identified and divided so that the muscle is

completely denervated; however, as the origin of the motor nerves is unimportant, a supraclavicular approach to the plexus is not necessary. Thin skin flaps are raised and subcutaneous adipose is thinned over an approximately 100cm² area over the pectoralis, from the medial chest to the anterior axillary line and from the clavicle inferiorly toward the nipple. An adipofascial flap is then elevated (Figure 3). If the latissimus or serratus anterior are used as target muscles, overlying adipose tissue can be removed by liposuction. The septum between the clavicular and sternal heads of the pectoralis major is identified—the clavicular head overlaps the sternal head by 1 cm—and carefully opened to separate these muscle bellies as well as to find the motor nerves to the pectoralis. The motor nerves to the clavicular head approach the muscle in almost a vertical vector and are often accompanied by a blood vessel. Occasionally, a second small motor nerve innervates this muscle more laterally. The sternal head generally has several motor nerves: a medial branch, a middle branch medial to the pectoralis minor tendon, a lateral branch that travels through the pectoralis minor muscle, and, occasionally, an even more lateral branch that innervates the most lateral muscle fibers. Motor points chosen for nerve transfers must be close enough to the mobilized brachial plexus nerves to allow for coaptation without tension. The radial nerve is stimulated to determine whether there is residual innervation of any triceps remnant, which should be left intact to provide a signal for prosthetic elbow extension.

The brachial plexus and nerves are identified, either medial or lateral to the pectoralis minor tendon. The subclavian artery typically has some thrombosis, as it no longer supplies tissues, and so does not cause difficulty during the dissection. The proximal thoracodorsal nerve, seen deep to the plexus, is a potential recipient for nerve transfer (to reinnervate the latissimus).

Brachial plexus nerves are identified by their branching pattern just distal to their emanation off of the cord, and are cut back proximally as far as possible (often 2–3 cm) to reach normal fascicular architecture, while keeping enough length to avoid tension at the coaptation site. Appropriate sites for nerve transfer are identified, and the large mixed nerves are coapted to the pectoralis motor nerves with 6-0 permanent monofilament suture from epineurium to epineurium. Again, a tacking stitch into the nearby muscle epimysium helps to stabilize and reduce tension on the coaptation site.

Typically, four nerves can be transferred, requiring four recipient motor points or nerves (Figure 4). The sternal and clavicular heads of the pectoralis are routinely separated to provide two target muscles; the sternal head can be split, based on its neurovascular anatomy, to create an additional target. Target muscle segments should be at least 4-5 cm in diameter for adequate EMG signal generation. The most common transfers are:

- Musculocutaneous nerve to the motor point of the clavicular head of the pectoralis
- Median nerve to the largest motor point innervating the sternal head of the pectoralis
- Radial nerve to the thoracodorsal nerve (to reinnervate latissimus)

- Ulnar nerve to the motor point on the lateral and deep aspect of the pectoralis minor or long thoracic nerve (to reinnervate serratus anterior)

Alternatively, the radial nerve can be coapted to the long thoracic nerve, or to a nerve serving the lateral inferior aspect of the pectoralis major. End-to-end nerve coaptations are performed as close as possible to the muscle to reduce reinnervation time. Given the location of the thoracodorsal nerve, there is a greater distance from the coaptation site to the latissimus muscle, and as such there may be a longer time period before reinnervation. When available, the best target motor point for the radial nerve is one of the lateral motor nerves to the pectoralis major because they are closer to the target muscle than either the long thoracic or the thoracodorsal nerves are to the serratus and latissimus, respectively. Alternative transfer sites for the ulnar nerve include the most lateral motor nerve serving the pectoralis major. If used, the pectoralis minor must be mobilized laterally and superficially away from the overlying pectoralis major to enable EMG signal detection.

The humeral head is left intact if present, even if the humerus remnant is too short to act as a lever arm for prosthesis control, as attachment to the humeral head maintains the position of the pectoralis major. Excision of the humerus causes the pectoralis and all associated motor nerves to retract medially towards the sternum, rendering the initial dissection more difficult. Additionally, an intact humeral head provides a better aesthetic appearance for the patient.

The adipofascial flap is then divided and placed in between the pectoralis major muscle segments to physically separate the muscle bellies from each other, preventing cross-reinnervation of adjacent segments. The skin is closed over drains after placement of quilting sutures to reduce the likelihood of seroma formation, and quilting sutures are used to bring the skin down to the chest and pectoralis muscle.

Patient may resume wearing their original prosthesis when there is adequate wound healing and after postoperative swelling subsides, typically after 6 weeks. Prosthetic fitting and training to utilize new control sites will take place once EMG signals from reinnervated muscles have become robust, in approximately 3–6 months [28].

2.3. TMR for Transradial Amputations

Transradial amputation is by far the most common major upper limb amputation [29]. Despite significant residual musculature, only two suitable control sites are typically available to control a myoelectric prosthesis. Individuals with transradial amputations can control wrist flexion/extension and wrist rotation—using residual muscles, and can myoelectrically control hand open/close, but cannot perform different hand grasps, as neural control information for intrinsic hand muscles is lost. Interestingly, individuals with more proximal amputations who have had TMR surgery are better able to control multifunctional hands (using pattern recognition control, see Section 3) than are transradial amputees without TMR, likely because nerves transferred by TMR carry control information for the intrinsic hand, finger, and thumb muscles. Providing access to this information would be an important advance for transradial amputees, as new hands that support multiple hand grasps are now available.

Cadaver studies have been conducted to investigate the potential for TMR to both improve prosthesis control in transradial amputees, and nerve transfers have been done to treat neuromas (See section 4). Based on this research and clinical experience, a preferred method for performing distal median and ulnar nerve transfers for transradial TMR involves transfer of the median nerve to the flexor digitorum superficialis (FDS) muscle (Figure 5) and transfer of the ulnar nerve to the flexor carpi ulnaris (FCU) muscle. Both target muscles are superficial and therefore enabling recording of EMG data. Other muscles in the forearm perform similar functions to both target muscles, so no important function or EMG information content is lost as a result of the transfers. The median and ulnar nerves lie beside the target muscles, so are easy to transfer. Finally, both transfers can be done through a single ventral incision. Alternative target muscles can be used if trauma precludes use of the FDS and/or FCU. A clinical trial (number NCT02349035) is currently underway to evaluate the functional benefits of TMR in individuals with transradial amputation.

3. TMR for Improved Control of Lower Extremity Prostheses

Powered lower limb prostheses have recently become commercially available [30, 31], and various research groups are working on others [32]. Control of these devices relies either on mechanical sensors in the prosthesis, an instrumented orthosis, or external remote control. However, different ambulation modes—such as level-ground walking, or ascending/descending ramps or stairs, require very different control sequences. Transitioning between these different modes currently requires use of a key fob or performance of unrelated body movements (such as exaggerated hip extension), which is unintuitive and can be unsafe for the user.

EMG signals have been explored as a method for improving control of powered lower limb prostheses. EMG signals from residual thigh muscles contain useful control information that can be combined with mechanical sensor data to create an accurate and responsive control system that enables intuitive, seamless transitions between ambulation modes [33]. Interestingly, EMG alone provides accurate control of a powered prosthesis during non-weight-bearing activities [34].

TMR has also been investigated as a method to access more neural control information to further improve control systems. Cadaver studies have identified several potential target muscles that would be suitable for nerve transfer [35], and TMR is possible for both above and below knee amputees, although to date, nerve transfers in the lower limb have been performed primarily as a treatment for neuroma pain [36] (see section 5). Compared to individuals who had not had nerve transfers [34, 37], one individual with a transfemoral amputation who had TMR surgery had increased control accuracy for ankle movements [38]. TMR may enable control of multiple degrees of freedom in a prosthetic ankle; however, as currently available robotic ankles only provide one degree of freedom, this potential advantage cannot yet be realized.

4. TMR and Pattern Recognition Control

Brachial plexus nerves innervate many small muscles of the hand, wrist, and arm and thus carry a vast number of separate control signals. High-density EMG studies in human TMR subjects demonstrate unique activation patterns corresponding to 16 intended movements of the missing hand, thumb, and fingers in reinnervated target muscles [39]. Reinnervated muscles thus provide a rich source of EMG control information for functions of the missing arm and hand; however, conventional myoelectric control systems do not utilize this valuable control information.

EMG-based pattern recognition systems work by identifying the different EMG signal patterns produced by several muscles, which are unique to each attempted movement. EMG signals are first recorded from multiple muscles as the user performs specific movements. This data is analyzed, and distinguishing feature patterns for each movement are identified [40, 41] and used to train a computer algorithm (or classifier). The classifier can then decode subsequent EMG data to determine which movement the user is trying to perform, and then send the appropriate command to the prosthesis. Thus pattern recognition allows the user to control the prosthesis simply by attempting a desired movement, providing the user with intuitive control of multiple prosthesis functions and eliminating the need for burdensome switching techniques.

Pattern recognition control is synergistic with TMR, in that it allows more of the neural control information contained within transferred nerves to be utilized for prosthesis control. Individuals with high level amputations who have had TMR surgery can perform multiple hand grasps, likely because transferred nerves include motor neurons that previously innervated the amputated intrinsic hand muscles. Pattern recognition makes intuitive sense when considering the muscle activation patterns a person may generate when using their hand. For example, a fine pinch grip may be done with digits 3–5 extended and a three-jaw chuck grip with digits 3–5 flexed (Figure 8)—thus the ulnar nerve signals intended for intrinsic muscles controlling digits 3–5 would contribute much to differentiating these two grasps. Similarly, lateral pinch may be formed with exaggerated thumb adduction, requiring activation of intrinsic muscles normally innervated by the median nerve. Accessing such neural information through TMR and decoding it through pattern recognition techniques enables unprecedented control of upper limb prostheses, including multiple hand grasps. Pattern recognition technology has recently become commercially available for clinical use.

5. TMR as a Prevention or Treatment for Neuromas

Amputation neuromas arise at the end of nerves severed by amputation and comprise disorganized, chaotic axons encased in scar tissue. Neuromas can cause focal pain that is often difficult to treat medically or surgically and are responsible for much of the residual limb pain experienced after a traumatic amputation. Over 150 various treatments for end-neuromas that have been described in the literature [42]. The simplest method—neuroma excision and traction neurectomy has excellent or satisfactory results in 65% of patients [43]. Neuroma excision followed by burying the nerve end in muscle [44], translocating the neuroma away from areas of pressure [45], and centro-centralization techniques [46] have all

shown high levels of patient satisfaction with low recurrence rates, albeit in small-scale studies.

By providing a distal target for the transected axons to grow into, TMR represents a novel technique for the prevention and treatment of neuromas and their painful sequelae. Despite the mismatch in sizes between the donor mixed nerve and recipient motor nerve, only one patient out of the hundred who have undergone TMR at Northwestern Memorial Hospital (NMH) had been re-explored for a symptomatic neuroma at the nerve coaptation site. In contrast, symptomatic neuromas in three transhumeral patients were identified after TMR in the musculocutaneous or lateral antebrachial cutaneous nerves, which had not been transferred to target muscles [47]. No symptomatic neuromas were identified after TMR in individuals with shoulder disarticulation amputations—where all severed nerves are transferred to target muscles. Similar results were obtained for the lower limb when nerve transfers were performed with the purpose of preventing or treating neuroma pain, either in the acute phase (within days of the amputation) or in the non-acute setting (months to years after amputation) [47]. We are currently conducting a clinical trial (number NCT02205385) to determine the efficacy of TMR compared to surgical burial of the nerve endings in treatment of amputation neuromas.

At NMH, we use TMR techniques routinely for symptomatic neuromas in both the forearm and the leg, and for neuroma prevention at the time of a planned major amputation. In a transradial amputation, for example, the median nerve can be transferred to the anterior interosseous nerve through a proximal incision, the ulnar nerve can be transferred to the flexor carpi ulnaris, and the radial nerve can be transferred to the pronator quadratus. In below knee and above knee amputees, neuromas can be excised and nerves transferred to a more proximal motor points of the soleus and gastrocnemius muscles. The superficial peroneal nerve is transferred to the deep peroneal nerve after the motor nerve to the anterior tibialis muscle has split off. For above knee amputations, the sciatic nerve is split into its component tibial and common peroneal divisions [48] and coapted to motor points of the semimembranosus, the long head of the biceps femoris, and/or the semitendinosus. The motor nerve that is divided to create the motor point is mobilized proximally or buried; our clinical observation is that motor nerves (despite having sensory fibers) do not form symptomatic neuromas when cut.

Nerve transfers using TMR concepts can be used to treat a symptomatic mixed nerve or sensory nerve neuromas throughout the body and in non-amputees. Sensory nerves can be mobilized proximally and coapted to a redundant motor point, for example, on the soleus muscle, which has been effective in the repair of symptomatic sural nerve neuromas with long nerve gaps where the nerve could not otherwise be repaired.

Summary/Conclusion

TMR provides a superior neural interface for the control of myoelectric prostheses, with demonstrated functional benefits for individuals with high level upper limb amputations. Ongoing research suggests that similar benefits may be provided to individuals with transradial and lower limb amputations. Advances in robotic technology, direct skeletal

attachment, signal processing, together with TMR will usher in improved quality of life and functional outcomes for individuals with upper and lower extremity amputations.

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Figure 1.
Coaptation of large donor nerve (blue arrow) to small motor point (green arrow)

Figure 2. Diagram of residual limb (ventral view) after transhumeral amputation showing muscles innervated by transferred nerves (blue) and intact native nerves (green) and, in parentheses, prosthetic function controlled by each muscle

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Figure 4.
Typical nerve transfers in shoulder disarticulation patient.

Figure 5.
Median nerve transfer to motor branch (Br) of FDS for transradial TMR.

Table 1

Nerve transfers and prosthetic function, transhumeral TMR

Nerve	Target Muscle	Prosthetic Function
Musculocutaneous	Biceps, long head (native innervation)	Elbow flexion
Median	Biceps, short head (nerve transfer)	Hand close
Radial (distal)	Triceps, lateral head (nerve transfer)	Hand open
Radial (proximal)	Triceps, long head (native innervation)	Elbow extension
Ulnar	Brachialis (if available)	Wrist function