

evidence.⁶⁻⁸ The high number of surgical strategies that try to hide, wrap, or cap an injured nerve point to the vagaries of surgical management.^{9,10}

Targeted muscle reinnervation is a surgical strategy for both prevention and treatment of neuroma pain, and it can be performed by any surgeon with comfort dissecting nerves. The targeted muscle reinnervation technique can be performed in any anatomical location where there is muscle under cortical control with an identifiable motor nerve. Part of its utility lies in its simplicity, because it does not involve any implantable hardware, nor does it require a microscope. Our aim is to provide an overview of targeted muscle reinnervation so that the reader will be able to use this surgical strategy in his or her own practice.

WHAT IS TARGETED MUSCLE REINNERVATION?

Targeted muscle reinnervation is a surgical technique by which the cut, distal end of a mixed motor and sensory nerve or a pure sensory nerve is transferred to the motor nerve of a nearby muscle target. Targeted muscle reinnervation was conceived, developed, and first implemented at Northwestern University to enable intuitive control of a multiple-joint advanced myoelectric prosthesis.¹¹⁻¹³ After a decade of performing targeted muscle reinnervation for prosthetic control, it became apparent that targeted muscle reinnervation showed promise in the treatment (and prevention) of amputation-related pain.¹⁴ Targeted muscle reinnervation involves three core steps (Fig. 1):

1. Nerve preparation: Identification of the injured nerve(s) to be treated and cutting back to healthy fascicles.
2. Motor point identification: Identification and dissection of a motor nerve to a nearby muscle target, which is divided to create a denervated muscle segment.
3. Coaptation: Transfer of the nerve of interest to the newly divided motor nerve. Commonly transferred peripheral nerves are displayed in Table 1.

HOW DOES TARGETED MUSCLE REINNERVATION WORK?

Transfer of the symptomatic peripheral nerve to a proximal motor branch results in regeneration of axons with connections to the recipient

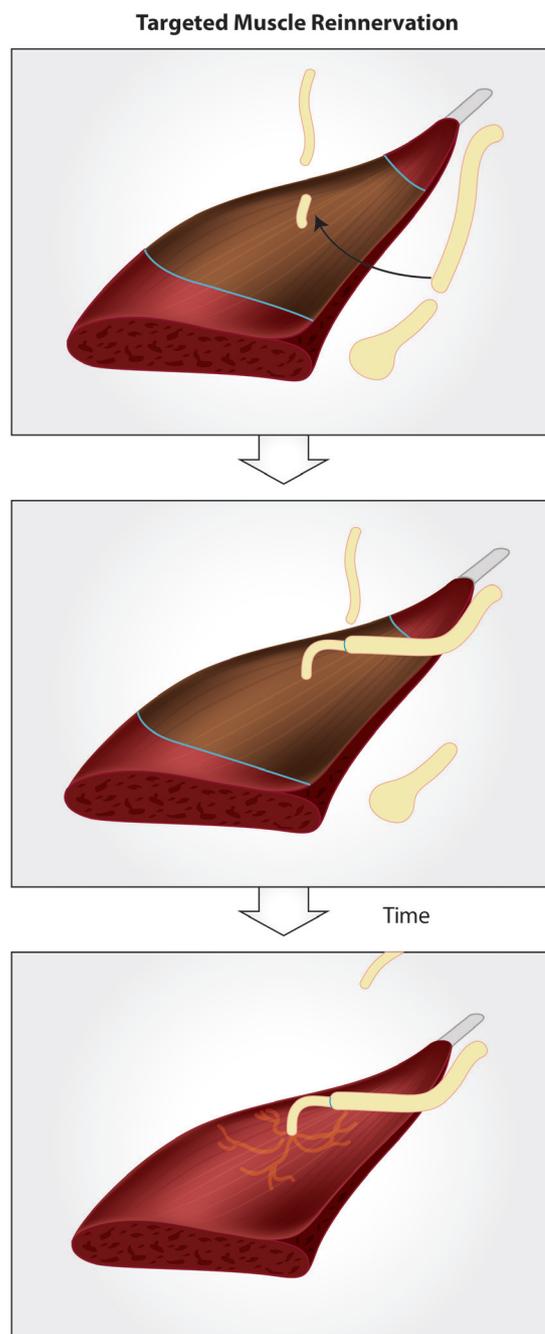


Fig. 1. Targeted muscle reinnervation schematic. (Redrawn from Dumanian GA, Potter BK, Mioton LM, et al. Targeted muscle reinnervation treats neuroma and phantom pain in major limb amputees: A randomized clinical trial. *Ann Surg.* 2019;270:238–246, licensed under CCBY-NC-ND. DOI: 10.1097/SLA.0000000000003088.)

motor end plates and sensory organelles. The act of cutting the recipient motor branch in preparation for the coaptation denervates a segment of the target muscle, thus rendering it a receptive “sink” for new neural ingrowth (i.e., reinnervation). The sprouting, regenerating axons of the

Table 1. Commonly Transferred Nerves for Targeted Muscle Reinnervation

| |
|--------------------------------|
| Upper extremity |
| Median |
| Ulnar |
| Radial sensory |
| Medial antebrachial cutaneous |
| Lateral antebrachial cutaneous |
| Lower extremity |
| Tibial |
| Deep peroneal |
| Superficial peroneal |
| Medial sural |
| Lateral sural |
| Saphenous |
| Abdominal |
| Ilioinguinal |
| Genitofemoral |

newly cut, transferred nerve find “somewhere to go and something to do,” rather than reforming a neuroma as a result of frustrated regeneration. Because of the need to create a denervated recipient muscle, targeted muscle reinnervation is performed as an end-to-end transfer to a cut motor nerve rather than as an end-to-side transfer into an intact nerve. Whereas traditional techniques of hiding injured nerve endings within bone, muscle, or an adjacent nerve (centrocentral nerve coaptation of Gorkish) attempt to render the inevitable neuroma asymptomatic with placement in a new, inaccessible location, targeted muscle reinnervation addresses the problem of neuroma pain by trying to heal (rather than hide) the injured nerve.

The motor nerve and associated target muscle are chosen so as not to affect function. In amputees, the nearby muscle has no function, as the distal tendon insertion was removed at the time of limb loss. For cases of neuroma treatment in intact limbs, target muscles are chosen that are easily accessible with a well-placed surgical incision and for which there is redundant muscle function.¹⁵ For instance, the lateral gastrocnemius muscle is relatively unimportant for ankle plantarflexion and is a ready recipient for the sural nerve(s). The sartorius is an expendable muscle with multiple small motor nerves to accept the lateral femoral cutaneous nerve.

For the purposes of myoelectric control, targeted muscle reinnervation capitalizes on the fact that cut peripheral nerves in an amputated extremity continue to carry neural information from the motor cortex. Therefore, a contraindication to targeted muscle reinnervation is a higher level complete nerve injury, such as a brachial plexus avulsion in the upper extremity. Newly reinnervated target muscles provide new end effectors for this peripheral nerve

information, amplifying it, and interacting with a myoelectric prosthetic by means of surface electrodes. Tapping into the information allows a patient to volitionally and intuitively control their prosthetic in much the same way as his or her original extremity, activating simultaneous movements of a prosthetic elbow, wrist, thumb, and fingers in multiple degrees of freedom. “Pattern recognition” of electromyographic signals serves to even further improve the quality of prosthetic control.¹⁶ Signal acquisition by means of “beaming” or through externally channeled wires will improve prosthetic function still further, but are not yet clinically available. Sensory feedback from the prosthetic back to the subject through targeted sensory reinnervation is not the subject of this CME article, but acts to further enhance neural-prosthetic interfacing.^{17,18}

INDICATIONS FOR TARGETED MUSCLE REINNERVATION

Targeted muscle reinnervation has three main indications:

- Treatment of unreconstructable neuromas: These are cases in which there is no distal target for a reconstruction of the resected nerve segment with a graft (allograft or autograft).¹⁹ We include in this category prior failed neuroma excision and grafting, in which a neuroma reforms at the graft site or pain persists. At Northwestern, we consider sensory nerve gaps greater than 2 to 3 cm as better candidates for targeted muscle reinnervation as opposed to reconstruction. In addition, the quality of the pain relief with targeted muscle reinnervation may be better than with reconstruction.
- Management of nerves in acute amputations: We routinely perform concurrent targeted muscle reinnervation at the time of primary amputation for oncologic, vascular, or traumatic indications. The benefits are two-fold for the patient: (1) decreased incidence of neuroma and phantom limb pain, and (2) potential for improved control of a myoelectric prosthesis for upper extremity limb loss.
- Treatment of chronic amputee pain: Amputees with stump neuromas that limit prosthetic use and decrease quality of life are candidates for this procedure. In our experience, targeted muscle reinnervation can successfully treat chronic amputee pain years after the initial amputation.

Surgical Technique: A Practical Guide by Anatomical Region

We generally perform nerve dissection and transfer under 2.5× loupe magnification. A smooth Gerald forceps works well for handling the epineurium of larger nerves, and a microsurgical forceps may facilitate handling of small motor branches. A hand-held nerve stimulator (Checkpoint Surgical, Cleveland, Ohio) is used to identify motor points in target muscles. These new-generation nerve stimulators are required to not tire out the motor nerve, rendering it unstimulatable, to locate intramuscular motor points, and to stimulate motor nerves even up to 1 hour of tourniquet time. Small vessel loops and surgical marking pens are very helpful to mark motor points once located and before neurotomy. For coaptation, we use a locking Castro-Viejo needle driver to pass two or three 6-0 or 7-0 polypropylene epineurial sutures with an attached tapered vascular needle. The coaptation should be located close to the muscle target, with neither tension nor excessive redundancy.

Lower Extremity

The vast majority of amputations are for the lower extremity, primarily because of vascular disease, and thus this represents the most impactful area of involvement for the general reconstructive plastic surgeon.^{15,20,21} As of now, the primary rationale for lower extremity targeted muscle reinnervation is neuroma and phantom pain prevention, as the current generation of leg prosthetics lack the motors, sensors, and batteries required for powered ambulation.²²

Above-Knee Amputation

For an above-knee amputation, nerves to address include the peroneal and tibial components of the sciatic nerve, the posterior femoral cutaneous nerve, and the saphenous nerve (Table 2). For delayed targeted muscle reinnervation to treat chronic pain in an existing above-knee amputee, a posterior vertical midline incision provides ideal exposure. The posterior cutaneous nerve of the thigh is located along the thigh fascia, and then the fascia is opened to identify the sciatic nerve. The common peroneal and tibial components of the sciatic nerve are bluntly separated to the junction of the proximal and middle thirds of the thigh, where the motor nerves to the posterior thigh musculature can be seen to separate from the sciatic nerve. Motor nerves 2 to 3 mm in diameter are then identified to the biceps femoris (long head) and semimembranosus, and a smaller

Table 2. Transfers for Above-Knee Amputations

| Nerve | Primary Targeted Muscles |
|-------------------------------|--------------------------------------|
| Peroneal component of sciatic | Biceps femoris |
| Tibial component of sciatic | Semitendinosus or semimembranosus |
| Posterior femoral cutaneous | Biceps femoris (distal motor branch) |
| Saphenous | Vastus medialis |

more distal motor nerve can be found innervating the short head of the biceps femoris. After neurotomy of the motor nerves, the peroneal component of the sciatic nerve is coapted to the larger biceps femoris motor nerve; the tibial component of the sciatic nerve is coapted to the semimembranosus; and the posterior femoral cutaneous nerve can usually reach the smaller and more distal biceps femoris motor nerve (Fig. 2).²³ The saphenous nerve is coapted through a separate incision located over Hunter's canal to a motor nerve of the vastus medialis. We have previously published a detailed guide to the anatomy of motor points of the thigh compartments and surgical technique for the above-knee amputee, which can serve as an additional resource.²³

Concurrent targeted muscle reinnervation with above-knee amputation can be performed in various ways. Simplest conceptually is for the patient to remain supine for the amputation and then be flipped to the prone position for targeted muscle reinnervation, as described above. Attempting to perform acute targeted muscle reinnervation in the supine position with standard anterior and posterior skin flaps creates some difficulty in reaching the motor points of the posterior thigh. Alternatively, we have performed the above-knee amputation and concurrent targeted muscle reinnervation in the lateral position, raising medial and lateral skin flaps to provide improved access to the sciatic nerve and posterior motor nerves.

Below-Knee Amputation: Concurrent Targeted Muscle Reinnervation

For below-knee amputations, the nerves to address include the deep peroneal, superficial peroneal, tibial, tibial and peroneal components of the sural, and saphenous nerves (Table 3).²² Cases in which targeted muscle reinnervation is performed concurrently with an acute amputation are managed differently from cases in which delayed targeted muscle reinnervation is performed to treat chronic neuroma pain. In concurrent targeted muscle reinnervation, the deep posterior compartment of the leg has a wealth of

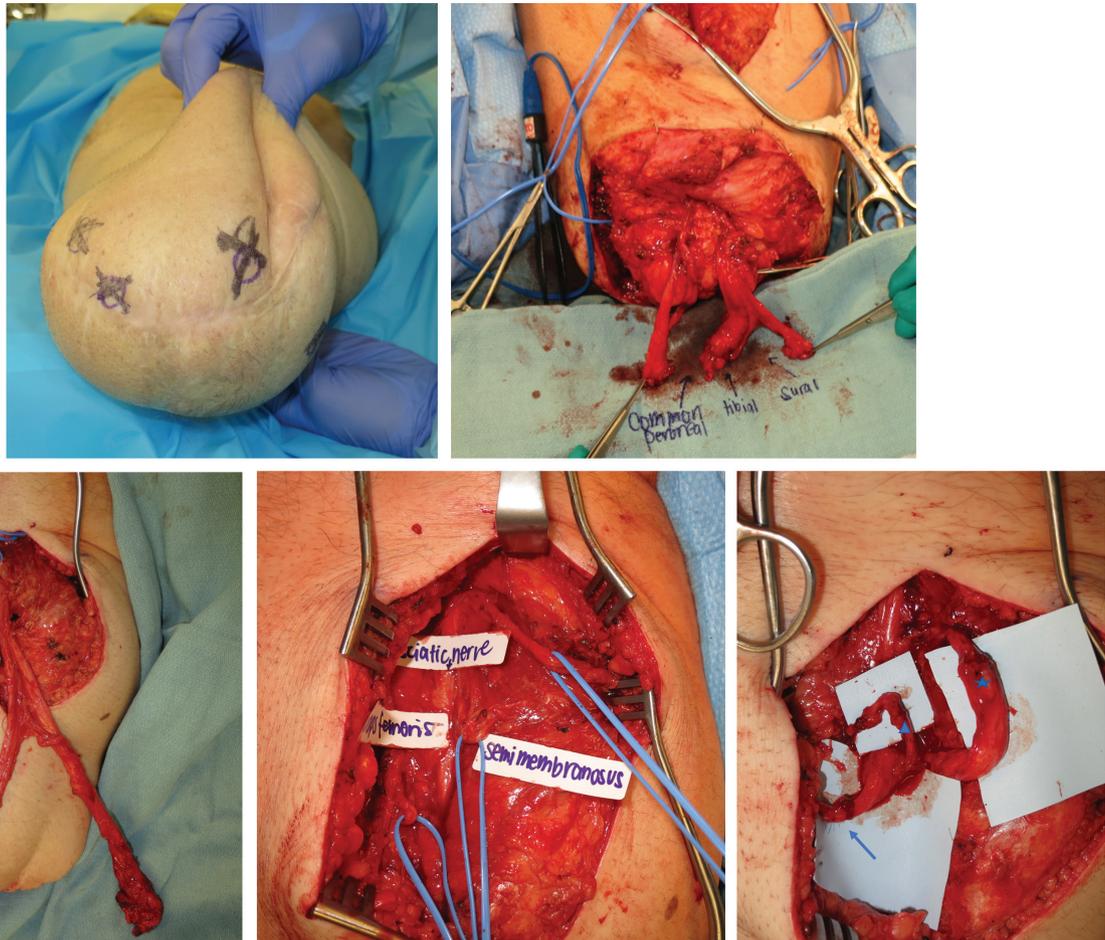


Fig. 2. Delayed targeted muscle reinnervation for chronic above-knee amputation. (Above, left) Areas of neuroma pain are marked preoperatively. From lateral to medial (left to right): sural, common peroneal, tibial, and saphenous nerves. (Above, right) Distal exploration reveals large neuromas of the common peroneal, tibial, and sural nerves. (Below, left) The common peroneal and tibial components of the sciatic nerve have been dissected and bluntly separated to the junction of the proximal and middle thirds of the thigh. (Below, center) Proximally, recipient motor branches to the biceps femoris and semimembranosus are identified with vessel loops. The posterior femoral cutaneous nerve is also identified with a vessel loop at the top right of the image. (Below, right) Coaptations are displayed: tibial component of sciatic to semimembranosus (star), peroneal component of sciatic to biceps femoris (triangle), and posterior femoral cutaneous to biceps femoris (arrow).

Table 3. Concurrent Targeted Muscle Reinnervation Transfers for Below-Knee Amputations

| Nerve | Primary Targeted Muscles | Lower Leg Compartment |
|----------------------------|------------------------------------|-----------------------------------------|
| Deep peroneal | Tibialis anterior | Anterior |
| Superficial peroneal | Peroneus longus | Lateral |
| Tibial | Soleus, or Flexor digitorum longus | Superficial posterior Deep posterior |
| Sural, tibial component* | Medial gastrocnemius | Superficial posterior |
| Sural, peroneal component* | Lateral gastrocnemius | |

*If accessible without overly disruptive dissection into the soft tissue of the posterior flap.

motor nerves. At the time of tibial osteotomy, the posterior flap should be dissected cleanly off of the bone with the tibial nerve and vascular bundle divided at the end of the posterior flap (Fig. 3, left and center). The tibial nerve is transferred to any large motor nerve noted to emanate off of its substance. The deep peroneal nerve is transferred to the tibialis anterior and the superficial peroneal nerve is transferred to the peroneus longus—all motor points identified with a hand-held stimulator (Fig. 3, right). These muscles are ideal for targeted reinnervation, as they have a large number of motor points, with many clustered proximally in the middle third of the leg.¹⁵ With this approach

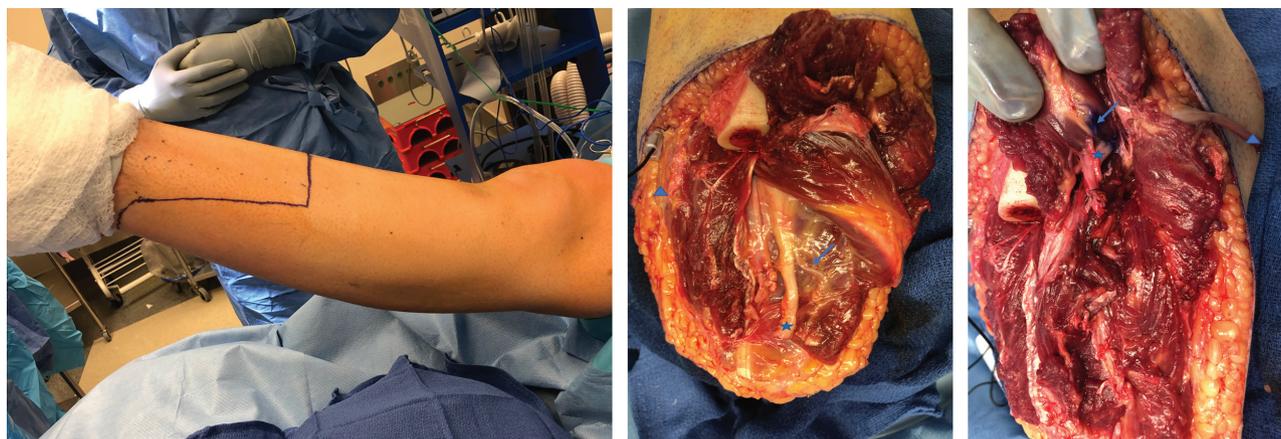


Fig. 3. Concurrent targeted muscle reinnervation and below-knee amputation. (Left) Incision design for below-knee amputation with a posterior flap. (Center) Exposure of the deep posterior compartment with a posterior flap. Star, tibial nerve; arrow, tibial nerve motor branch to soleus; triangle, saphenous nerve. (Right) Exposure of anterior and lateral compartments. Star, deep peroneal nerve; arrow, deep peroneal motor branch to tibialis anterior; triangle, superficial peroneal nerve.

Table 4. Delayed Targeted Muscle Reinnervation Transfers for Chronic Pain in a Below-Knee Amputee: Two-Incision Approach

| Nerve | Primary Targeted Muscles | Lower Leg Compartment |
|----------------------|---------------------------------|-----------------------------------------------------------------------|
| Deep peroneal | Tibialis anterior | Anterior (accessed through an anterolateral incision) |
| Superficial peroneal | Extensor digitorum longus | |
| Tibial | Soleus | Superficial posterior (accessed through a posterior midline incision) |
| Medial sural | Soleus, or medial gastrocnemius | |
| Lateral sural | Lateral gastrocnemius | |

Table 5. Delayed Targeted Muscle Reinnervation Transfers for Chronic Pain in a Below-Knee Amputee: Single-Incision Approach

| Nerve | Primary Targeted Muscles | Lower Leg Compartment |
|--------------------------------------------------------------------------|--------------------------------|-----------------------------------------------------------------------|
| Common peroneal, possible sparing of motor fascicle to anterior tibialis | Lateral gastrocnemius | Superficial posterior (accessed through a posterior midline incision) |
| Tibial | Soleus or medial gastrocnemius | |
| Lateral sural | Lateral gastrocnemius | |
| Medial sural | FHL | Deep posterior |

FHL, flexor hallucis longus.

for concurrent targeted muscle reinnervation, the sural nerves are the most difficult to handle. If identified emerging from the end of the posterior flap, they are dissected a bit proximally and then either tunneled through the posterior flap musculature for coaptation to an additional motor point or wrapped with a free muscle graft and treated as

a regenerative peripheral nerve interface.²⁴ [See [Video 1 \(online\)](#), which demonstrates concurrent targeted muscle reinnervation for an acute below-knee amputation.]

Below-Knee Amputation: Delayed Targeted Muscle Reinnervation

Delayed targeted muscle reinnervation for the established below-knee amputee is a straightforward procedure performed with a tourniquet with the patient in the prone position. A straight posterior midline incision is made approximately 8 to 10 cm long and just lateral to the midline (to more easily reach the peroneal nerve). The tibial component of the sural nerve is identified and divided distally. Typically, on the lateral side of the tibial nerve exists the motor nerve of the soleus muscle and the motor nerve to the flexor hallucis longus ([Fig. 4, above, left](#)). The tibial component of the sural nerve is transferred to the motor nerve of the flexor hallucis longus, and the tibial nerve proper is coapted to the motor nerve of the soleus ([Fig. 4, above, right](#) and [below, left](#)). More superficially, the lateral skin flap is elevated to identify the common peroneal nerve and the motor nerve of the lateral gastrocnemius. The peroneal component of the sural nerve, which can be quite large, is often encountered and should not be confused for the common peroneal nerve. The common peroneal nerve and peroneal component of the sural nerve can both be coapted to separate motor nerves of the lateral gastrocnemius ([Fig. 4, below, right](#)). The medial gastrocnemius muscle is left alone for bulk of the lower limb and knee flexion, but it too can be a muscle target if needed. On occasion, the motor nerve to the anterior tibialis is dissected

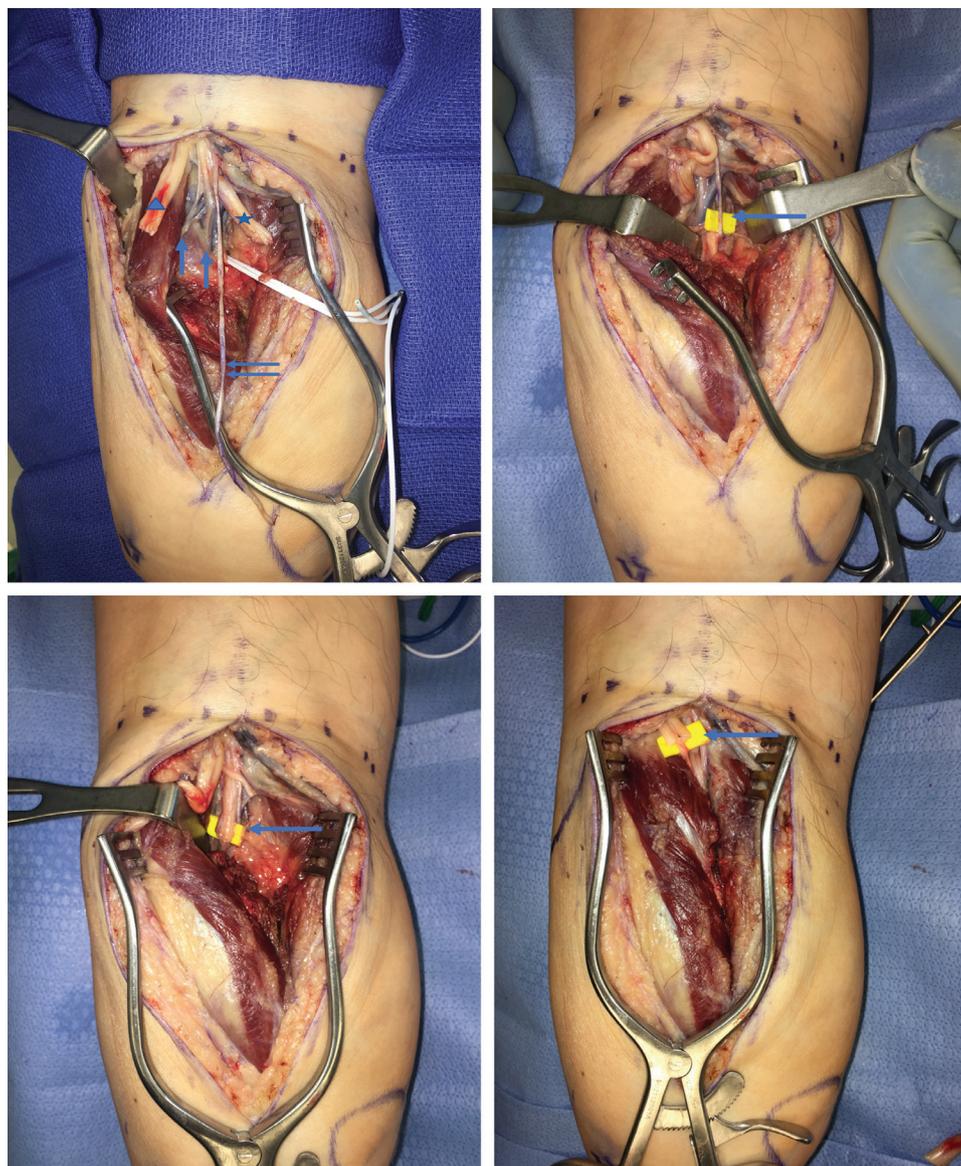


Fig. 4. Delayed targeted muscle reinnervation for chronic below-knee amputation. (*Above, left*) Exposure of nerves to be transferred by means of an 8- to 10-cm longitudinal incision just lateral to the midline. *Star*, tibial nerve; *triangle*, common peroneal nerve; *single arrows*, tibial motor branches to soleus (*left*) and flexor hallucis longus (*right*); *double arrow*, tibial component of the sural nerve. (*Above, right*) The tibial component of the sural nerve is transferred to the motor nerve to the flexor hallucis longus (*blue arrow*). (*Below, left*) The tibial nerve proper is coapted to the motor nerve of the soleus (*blue arrow*). (*Below, right*) The common peroneal nerve is transferred to a motor nerve to the lateral gastrocnemius (*blue arrow*).

off of the common peroneal, again to maintain limb bulk. [See **Video 2 (online)**, which demonstrates delayed targeted muscle reinnervation for chronic neuroma pain in a previous below-knee amputation, single-incision approach.] Despite our concern to maintain soft-tissue bulk, in our many years of performing this procedure, we have not seen a case of significant tissue atrophy leading to difficulties with prosthesis fitting.

A single-incision targeted muscle reinnervation is our most common below-knee amputation targeted muscle reinnervation approach, performed for short residual limbs, for patients with a history of vascular disease to maximize the chances for incisional healing, and most definitely for patients in extreme pain so that the length of excised nerve is maximized. However, we recognize that other nerve transfer patterns are possible and may prove

to be superior to what we have described. On occasion, we perform a two-incision (anterolateral and midline posterior) procedure, transferring the deep peroneal and superficial peroneal nerves independently, which preserves proximal peroneal innervation of the remaining anterior and lateral compartment muscles. This could avoid muscular atrophy that can predispose to bony prominence and poor prosthetic fit. We have also performed the two-incision below-knee amputation targeted muscle reinnervation operation in the lateral position to avoid the position change.

Treatment of Lower Extremity Neuromas in the Intact Limb

Targeted muscle reinnervation for painful unreconstructable nerves because of nerve gaps or for failed prior nerve reconstruction in patients with an intact limb is designed to preserve maximal function. Incisions are made over the area of the neuroma, which is identified in three ways: (1) asking the patient to point with a single finger to the spot of their pain, (2) Tinel sign on examination, and (3) transient resolution of pain with a diagnostic injection of local anesthetic. The incision is extended from the point of the neuroma to maximize exposure to motor points in the compartment of interest for nerve transfer. Our targeted muscle reinnervation outcomes data support our contention that the neuroma does not need to be excised for resolution of symptoms, provided that the upstream neurotomy is performed. However, dissection and excision of the distal neuroma definitively ensures that the upstream neurotomy is of the symptomatic nerve.

The deep peroneal nerve is transferred to the extensor digitorum longus, which avoids any possibility of weakening the tibialis anterior and causing foot drop. The superficial peroneal nerve is transferred to the peroneus longus, and the medial and lateral sural nerves are transferred to the gastrocnemius motor points. The saphenous nerve can be treated in the thigh, in which case it can be transferred to the vastus medialis, or below the knee, in which case it is transferred to the soleus. The lateral femoral cutaneous nerve can be transferred to the sartorius or vastus lateralis (Tables 6 and 7).

Figure 5 shows a 49-year-old female patient treated with targeted muscle reinnervation for a superficial peroneal nerve neuroma. She underwent a peroneus longus tendon repair and subsequently developed diffuse lateral leg pain that was relieved by a lidocaine injection around the area of maximal tenderness. On exploration, she was noted to have a superficial peroneal nerve

Table 6. Lower Extremity Targeted Muscle Reinnervation for the Intact Limb

| Nerve | Primary Targeted Muscles |
|----------------------|---------------------------|
| Deep peroneal | Extensor digitorum longus |
| Superficial peroneal | Peroneus longus |
| Medial sural | Lateral gastrocnemius |
| Lateral sural | Lateral gastrocnemius |

Table 7. CPT Coding for Targeted Muscle Reinnervation

| CPT Code | Description |
|----------|-------------------------------------|
| 64905 | Nerve pedicle transfer; first stage |

neuroma in continuity and a long segment, greater than 4 cm, of the superficial peroneal nerve that was red, inflamed, and firm (Fig. 6, above, right). Because of the length of segment involved and severity of her pain, the decision was made to perform targeted muscle reinnervation to a motor branch of the peroneus longus, rather than attempting an allograft reconstruction of the nerve (Fig. 6, below). [See Video 3 (online), which demonstrates treatment of a superficial peroneal neuroma-in-continuity with targeted muscle reinnervation.]

Upper Extremity

Detailed discussion of the anatomy, transfers, technique, and rationale of targeted muscle reinnervation for shoulder disarticulation and transhumeral and transradial amputation has been previously published.^{25–29} The only difference in surgical technique between upper and lower extremity surgery is that the upper extremity skin flaps are defatted surgically to improve signal acquisition for prosthetic limb control.

Digital Amputation

Traction neurectomy is the most common technique to address digital nerves in a digital amputation or revision amputation. In the majority of cases, this is successful, with a recent large retrospective review of revision traumatic amputations reporting only 6.6 percent developing symptomatic neuromas.³⁰ However, for the subset of patients that do develop neuromas, the chance of recurrence with a repeated traction neurectomy was relatively high at 15 percent. Furthermore, of patients that underwent a second operation for digital neuroma, nearly a quarter recurred.

We recently treated a patient with a 3-year history of a painful neuroma at the site of a prior index finger revision amputation on her

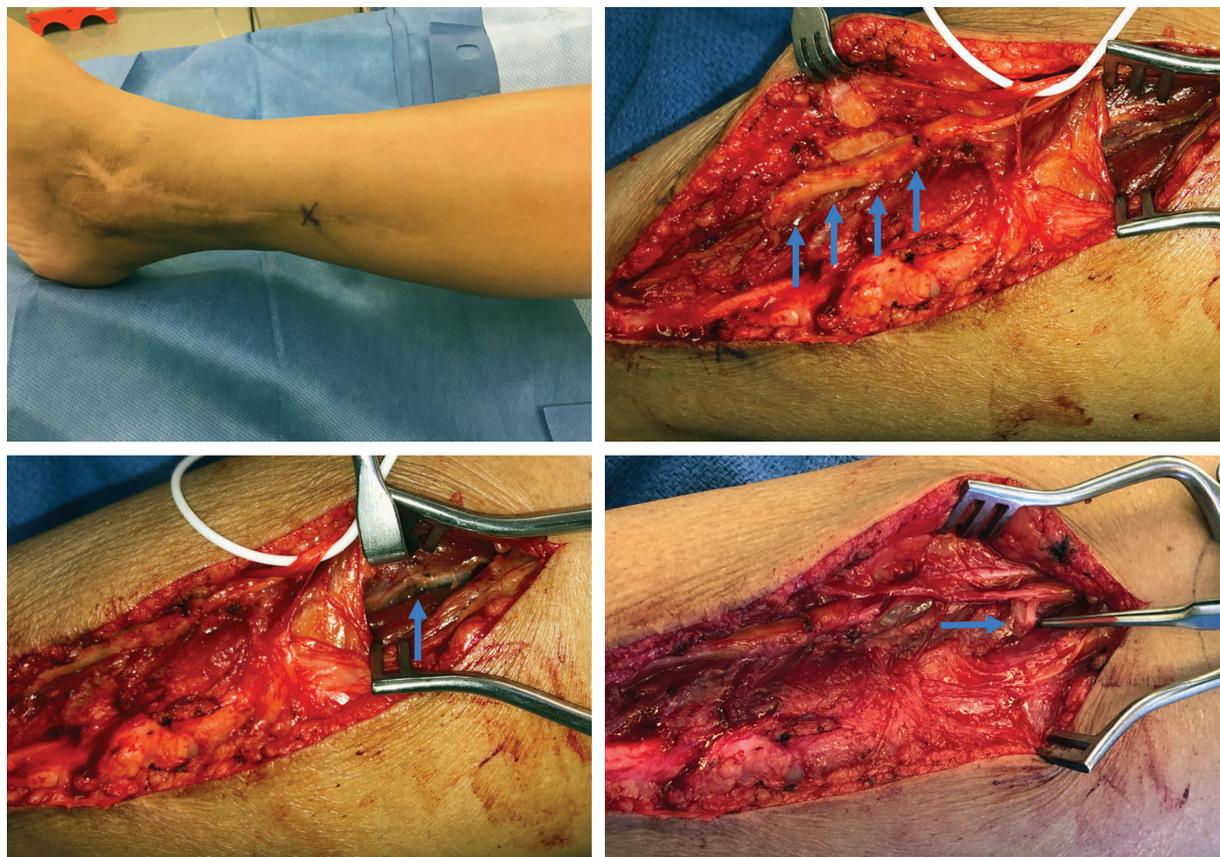


Fig. 5. Targeted muscle reinnervation for a superficial peroneal neuroma-in-continuity. (Above, left) The area of maximum Tinel sign and pain is marked along the patient's prior incision line. (Above, right) Superficial peroneal neuroma-in-continuity with long segment of nerve damage. (Below, left) A motor nerve branch to the peroneus longus muscle is identified. (Below, right) Transfer of the superficial peroneal nerve to the peroneus longus motor nerve is completed.

nondominant hand (Fig. 6). She initially experienced an avulsion injury requiring revision amputation at the level of the midproximal phalanx. She frequently experienced sharp, electric shock-type pain from both movement and light touch that limited the use of her hand. During surgery, large terminal neuromas of both the radial and ulnar digital nerves to the index finger were identified at the level of the metacarpophalangeal joint. After resecting the neuromas to healthy fascicles, these nerves were transferred to motor branches to the residual index lumbrical and first dorsal interosseous identified with a stimulator. At 4-month follow-up, the patient had significant relief of her neuroma pain and noted that she was using her hand without thinking about it for the first time in years.

As targeted muscle reinnervation requires exposure of intrinsic muscles in the palm, extending incisions and dissection proximally is likely not warranted for a primary revision amputation at the middle phalanx level or distal given the relatively high success rate of traction neurectomy

for these patients. However, for patients in whom a digital neuroma forms after primary revision amputation, and especially those with a second or third recurrence, targeted muscle reinnervation provides a surgical treatment that allows digital nerve healing into a newly denervated bed.

WHY SHOULD TARGETED MUSCLE REINNERVATION BE USED FOR NEUROMA TREATMENT RATHER THAN MORE ESTABLISHED SURGICAL PROCEDURES?

Historically, the most commonly performed treatment of a neuroma is excision and burying the healthy, freshened end of the cut nerve into a nearby muscle, bone, fat, or vein. Both the efficacy and underlying conceptual rationale for this approach have been brought under increasing scrutiny.³¹ Two recent studies comparing various surgical treatments for painful neuromas of the extremities, including excision alone, excision and cap, excision and transposition, excision and

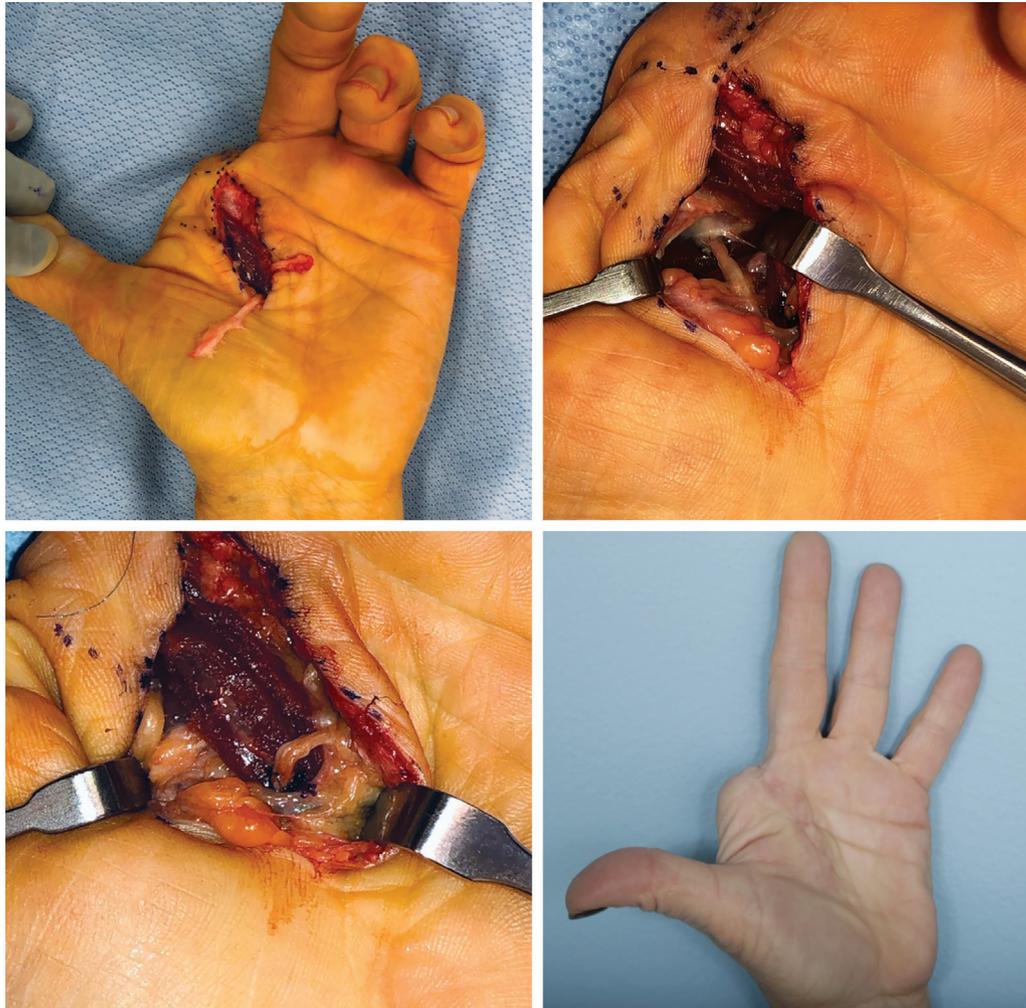


Fig. 6. Targeted muscle reinnervation for digital neuroma. (Above, left) Stump neuromas of both the radial and ulnar digital nerves to the index are identified on exploration. (Above, right) The radial digital nerve is transferred to a motor nerve to the first dorsal interosseous muscle. (Below, left) The ulnar digital nerve is transferred to the residual index lumbrical muscle. (Below, right) Appearance of the palmar incision 3 weeks postoperatively.

repair, and neurolysis and coverage found variable outcomes and no difference in efficacy.^{9,32}

In a recent *Plastic and Reconstructive Surgery* Special Topics article, Eberlin and Ducic argued for surgical strategies that aim to satisfy the regenerating nerve ends by promoting regeneration and neuroma prevention.³¹ A growing body of literature supports this conceptual shift to attempt to heal rather than hide injured nerves.³³ Retrospective data from the Mayo Clinic experience with treatment of hand and forearm neuromas with an average 20-year follow-up showed that patients who underwent nerve excision and repair had significantly lower Disabilities of the Arm, Shoulder, and Hand scores than patients who underwent simple excision or nerve transposition to bone or muscle.³⁴ Our own experience with use

of processed nerve allograft to reconstruct painful neuromas in the foot and ankle, predominantly of the sural and superficial peroneal nerves, showed a significant decrease in Patient-Reported Outcomes Measurement Information System pain scores from before to after intervention.¹⁹ We have also had success using processed nerve allograft to treat painful abdominal wall neuromas.³⁵ Targeted muscle reinnervation is a natural extension of these concepts, where the amputated nerves by definition are not reconstructible.

WHAT ARE THE DATA FOR TARGETED MUSCLE REINNERVATION?

A series of case studies initially proved the feasibility, reproducibility, and efficacy of

targeted muscle reinnervation for prosthetic control.^{11,13,27,36,37} As we accumulated an increasing patient experience with targeted muscle reinnervation, an overwhelming trend became apparent: many amputee patients who underwent targeted muscle reinnervation reported either a complete resolution or substantial reduction in their pre-existing residual limb neuroma pain. We subsequently performed a retrospective review of 26 patients with greater than 6-month follow-up treated with targeted muscle reinnervation at Northwestern and San Antonio Military Medical Center. Fifteen of 26 patients (57 percent) experienced postamputation neuroma pain before undergoing targeted muscle reinnervation. Following targeted muscle reinnervation, 14 of the 15 patients with preoperative neuroma pain reported complete resolution of their pain, with the remaining patient experiencing improvement but not complete resolution.¹⁴ Close to 90 percent of patients went on to successful surgery for a targeted muscle reinnervation–controlled prosthesis. Our group recently published results of a prospective, single-blind, randomized, controlled trial that compared targeted muscle reinnervation to standard treatment of muscle burying for amputees with chronic neuroma-related residual limb pain and phantom pain.³⁸ At a follow-up of nearly 1.5 years, targeted muscle reinnervation showed a clinically meaningful decrease in numeric pain scores of 3.0 points for worst residual limb pain and 3.5 points for worst phantom pain, compared to a 1.2-point decrease in local pain and a 0.5-point increase in phantoms for muscle burying. For residual limb pain, 67 percent of the targeted muscle reinnervation group versus 27 percent of the standard treatment arm reported being totally pain free or having only mild pain at 1.5-year follow-up. A companion article to this study demonstrated an even more dramatic reduction in neuroma and phantom pain when targeted muscle reinnervation was performed at the time of amputation.³⁹ Together, these two articles demonstrate the effectiveness of targeted muscle reinnervation in patients blinded to treatment, and improved outcomes with the prevention (rather than the treatment) of pain and phantoms. Although some element of pain centralization can occur, especially with longstanding nerve injury, the vast majority of patients can have improvement in their symptoms with these nerve transfers. Improvement in pain can lead to improved function, and our group has recently published data showing improved functional outcomes with

targeted muscle reinnervation of both the upper and lower extremities in a series of 33 patients as measured with patient-reported outcomes.⁴⁰

WHAT ARE THE ALTERNATIVES TO TARGETED MUSCLE REINNERVATION?

Regenerative peripheral nerve interfaces are the primary surgical alternative to targeted muscle reinnervation that attempt to heal, rather than to hide, an injured nerve ending.²⁴ Initially designed for control of myoelectric prostheses, a regenerative peripheral nerve interface involves implantation of the cut end of a peripheral nerve into a free muscle graft. With revascularization, a free muscle graft is shown to sprout nerve receptors and to act as a denervated bed to attract the sprouting axons. A retrospective case series of 16 amputees treated with a regenerative peripheral nerve interface for neuroma pain relief showed a 71 percent reduction in average neuroma pain score (from 8.7 to 2.5) and a 53 percent reduction in average phantom pain score (from 8.0 to 3.8). Notable were very high reported *average* preoperative pain scores of 8.5 for neuroma pain and 8.0 for phantom pain, which could be explained by recall bias given that preoperative pain scores were collected by means of a phone survey performed at a mean of 7.5 months after surgery. Nonetheless, the data suggest promise for use of regenerative peripheral nerve interfaces as a technique to treat neuroma pain, and the results of future studies will be informative.

An advantage of regenerative peripheral nerve interfaces is the surgical simplicity of simply wrapping identified nerves in a free muscle graft, allowing the procedure to be performed without more proximal incisions and by surgeons not specifically trained to handle peripheral nerves. However, a technical caveat is that the surgeon must appropriately size the free muscle graft to prevent graft necrosis, leading to failed innervation.³² A comparative advantage of targeted muscle reinnervation is that it eliminates this variable from the decision-making process and does not involve a risk of failure of the procedure because of the lack of graft survival. The potential denervated bed is far larger for targeted muscle reinnervation than for the regenerative peripheral nerve interface, as the former maintains its vascularity, whereas the latter is limited by the engraftment process. For the upper extremity for prosthetic control, regenerative peripheral nerve interfaces require electrodes with transcutaneous wires or through an osseointegrated implant, whereas the

signal from a targeted muscle reinnervation nerve transfer is strong enough to be detected on the skin surface without transcutaneous wires. Future studies are needed to elucidate the comparative effectiveness of these complementary procedures for treatment of injured and nonreconstructible nerves.

CONCLUSIONS

Targeted muscle reinnervation is a surgical technique for the management of injured or cut nerves by which the cut, distal end of a peripheral nerve is transferred to and reinnervates a muscle target. Targeted muscle reinnervation represents a paradigm shift from neuroma management from hiding to healing. Concurrent targeted muscle reinnervation represents the next frontier by preventing the development of neuromas at the time of nerve injury.

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