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Hand/Peripheral Nerve

# Targeted Peripheral Nerve Interface: Case Report with Literature Review

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**Summary:** Nerve transection injuries can result in painful neuromas that adversely affect patient recovery. This is especially significant following amputation surgeries in the setting of prosthetic wear and function. Targeted Muscle Reinnervation and Regenerative Peripheral Nerve Interface (RPNI) are 2 modern surgical techniques that provide neuromuscular targets for these transected nerve endings to reinnervate. These strategies have been previously shown to reduce phantom limb pain, residual limb pain, and neuroma-related pain.[1,2,7,11] Two recent articles described technical adaptations of combining targeted muscle reinnervation and RPNI to create a hybrid procedure.[3,12] In this article, we propose a different modification of targeted muscle reinnervation and RPNI, where the transected nerve stump is coapted to a recipient unit consisting of an intact distal nerve branch with its associated muscle graft. We called this recipient unit a targeted peripheral nerve interface because it contains a distal nerve branch for nerve coaptation and can guide axonal regeneration from the donor nerve to its target muscle graft. We theorize that targeted peripheral nerve interface may lead to more even distribution of regenerating axons with potentially less pain and stronger signals for prosthetic control when compared with standard RPNI. *(Plast Reconstr Surg Glob Open 2021;9:e3532; doi: 10.1097/GOX.0000000000003532; Published online 8 April 2021.)*

## INTRODUCTION

Management of neuroma-related pain, residual limb pain, and phantom limb pain after amputation is challenging. Physiologically, a neuroma forms when a transected peripheral nerve regenerates. However, nerve regeneration in the absence of a receptive target can lead to disorganized axonal sprouting. This results in painful sensations and neuroma-related pain partly due to ectopic firing of transected nerve endings, coupled with a lack of afferent feedback from a distal target.[1–4]

Symptomatic neuromas can be managed nonoperatively with pain medication, neuromodulation, or desensitization.[5] Surgical techniques for neuroma management can be broadly classified as "passive" or "active."[5] Passive techniques include excision combined with burying or implantation of nerve endings.[5] Active techniques, like targeted muscle reinnervation (TMR) and regenerative peripheral nerve interface (RPNI), provide a physiologic distal target for a transected nerve ending: "somewhere to go and something to do."[3–6] TMR involves transferring and coapting the transected nerve stump to a nearby recipient motor nerve branch. This allows regenerating axons from the transected nerve stump to grow through existing endoneurial tubes of the motor nerve branch to reinnervate the denervated but vascularized muscle.[1] In contrast, RPNI involves wrapping the transected nerve stump with a piece of denervated and desvascularized muscle graft, which does not contain specific endoneurial tubes to guide the nerve regeneration. RPNI relies on spontaneous axonal sprouting within the muscle graft for reinnervation, following these steps: (1) initial devascularization and denervation of the muscle graft, (2) early muscle graft atrophy and degeneration, (3) delayed muscle graft revascularization via vascular ingrowth, and (4) reneurotization of the revascularized muscle graft.[5–7]

Both TMR and RPNI have demonstrated efficacy when used independently. In a recent article, Valerio et al described a hybrid technique combining the optimal components of TMR and RPNI.[3] Their technique uses TMR to provide a distal nerve target for direct nerve coaptation, while also using a denervated but vascularized muscle cuff to wrap the nerve coaptation site. This vascularized

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muscle cuff is called vascularized RPNI, and serves to capture escaping axons arising from donor-recipient nerve size mismatch.

We propose a different hybrid of TMR and RPNI, where the transected nerve stump is coapted to a recipient unit consisting of an intact distal nerve branch with its associated muscle graft. We called this recipient unit a targeted peripheral nerve interface (TPNI) because it contains a distal nerve stump for nerve coaptation and can guide axonal regeneration from the transected nerve stump to its target muscle graft. Unlike TMR, where donor-recipient nerve size mismatch can be a challenge, TPNI can be created with minimal donor-recipient nerve size mismatch, since a large caliber donor nerve stump can be split via internal neurolysis into smaller fascicles to match the size of the TPNI nerve branch. In this article, we present our utilization of this technique in 2 patients and provide a concise literature review.

## CASE REPORT AND TECHNIQUE

We describe the use of TPNI as performed by the senior author in the setting of below knee amputation. Amputation was indicated due to the sequelae pilon fractures in both patients: (1) a 65-year-old woman with 25 years of post-traumatic right ankle pain refractory to nonsurgical and surgical management, and (2) a 42-year-old man with recurrent osteomyelitis of the left ankle. A similar technique may be utilized for other upper or lower extremity amputation sites.

### Surgical Technique

In each patient, to create a TPNI, we identify the tibial nerve (adjacent to the posterior tibial artery) in the amputated leg (Fig. 1) and trace it distally as it arborizes into the muscles within the deep posterior compartment (Fig. 2). We then excise a 3 cm × 1 cm × 0.5 cm muscle graft centered on the location where the nerve branch penetrates into the muscle, with the long axis of the muscle graft parallel to the direction of the muscle fibers. This yields a TPNI consisting of a standard RPNI with an intact nerve branch penetrating the muscle graft in the central portion (Fig. 3).

Next, we identify the proximal transected ends of the tibial, deep peroneal, superficial peroneal, sural, and saphenous nerves in the below knee amputation stump wound. Tibial and superficial peroneal nerves are usually of larger caliber, and internal neurolysis is performed to split each large caliber nerve into 2–4 smaller fascicles for better size match to the TPNI nerve branches (Fig. 4). Nerve coaptation is performed using two 8-0 nylon sutures, followed by application of fibrin glue. Lateral edges of the muscle graft are then sutured together using 5-0 Vicryl sutures, similar to the standard RPNI technique previously described.[7–9] Typically, 3–6 TPNI can be harvested from the amputated portion of the leg. If there are insufficient TPNI units to be used, we then manage the remaining transected nerve stumps using standard RPNI.

**Fig. 1.** Clinical picture of a TPNI harvested from the amputated portion of the leg.

### Outcome

At 3 months follow-up, both patients had been fitted with prosthetic limbs and were ambulating independently. Both patients reported infrequent minimal residual limb or phantom pain that did not interfere with their activities and neither patient required narcotic pain medication at this follow-up timepoint.

## DISCUSSION

Prevention and treatment of neuropathic pain from potentially symptomatic neuromas is increasingly important in the treatment of patients undergoing amputation.[5] In this article, we propose a modified RPNI technique, where the transected nerve stump is coapted to a nerve branch associated with a piece of denervated, devascularized muscle graft to help guide nerve regeneration (TPNI). With this construct, nerve regeneration can occur along an intact nerve branch associated with the neuromuscular unit, potentially leading to better intramuscular distribution of reinnervation pattern and less neuroma-related pain. Furthermore, we theorize that with more even distribution of axonal sprouting along existing endoneurial tubes, TPNI may have the potential to produce stronger signals for prosthetic control. For example, a recent study by Nassif and Chia demonstrated reanimation of eyelid function using neurotized platysma grafts that functioned as “mini neuromuscular units.” Such units could act as a source of contraction signals for prosthetic control.[10] Histological and animal studies may be helpful

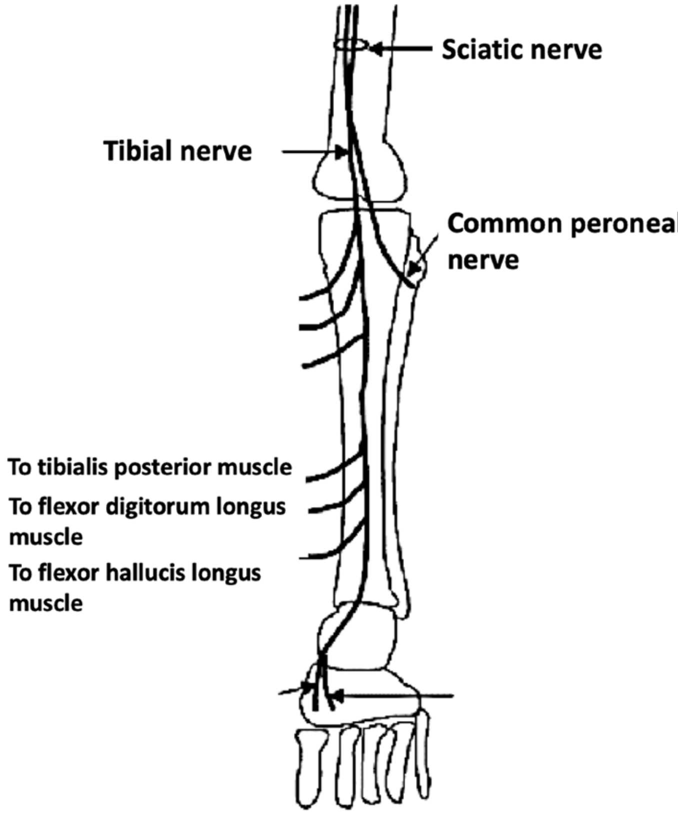


**Fig. 2.** Anatomy of tibial nerve branches entering the muscles of the deep posterior compartment.

**Fig. 3.** Clinical picture of the tracing of the distal nerve branch as it arborizes into the muscle. This segment of the tibial nerve has 2 branches. Two separate TPNI units can be harvested from this segment (each measuring 3 cm × 1 cm × 0.5 cm, with the muscle graft centered on the nerve branch insertion point).

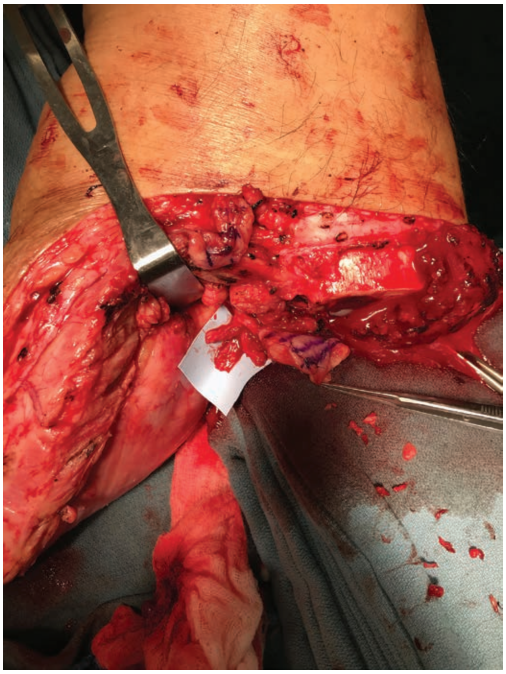

**Fig. 4.** Clinical picture of the splitting of the proximal tibial nerve stump into multiple fascicles for better size match at donor-recipient nerve coaptation site.

to delineate the nerve branching pattern within the muscle graft, to determine if a larger TPNI unit (longer and wider, but not thicker, to ensure graft survival) would potentially offer stronger signals for prosthetic control.

TPNI utilizes the muscle graft harvested from the amputated body part, with no donor site morbidity. Furthermore, it has the added benefit of having an associated nerve branch to allow primary nerve-to-nerve coaptation with good donor-recipient nerve size match, since the donor nerve size can be surgically modified via internal neurolysis. Nerve coaptation using 8-0 nylon sutures can easily be done under loupe magnification, and branching points of the tibial nerve are easily visible on the amputated part of the leg traveling with the posterior tibial artery, requiring minimal additional dissection. This modified technique may offer improvement in outcome with regard to the management of amputation stump neuroma pain and prosthetic control.

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