Disclosure: The authors have no financial interest to declare in relation to the content of this article.
motor target. It is possible that the excess axons within the donor nerve may exceed the available recipient axons, potentially allowing for donor axonal escape into the extraendoneurial environment and neuroma formation. TMRpni combines the well-documented benefits of TMR and RPNI, with the theory that the free muscle graft will provide a destination for any escaped donor axons to minimize pain at the coaptation. In essence, we hypothesize that this technique acts as a “biologic nerve wrap” that is similar to other wrap techniques shown to reduce nerve coaptation tenderness and pain.25,26

**TECHNIQUE**

TMRpni begins with traditional TMR nerve transfer, as previously described.20,22,23,27 Briefly, the approach is through the distal amputation exposure if performed at the time of amputation or by proximal incision if performed as a delayed procedure. Under tourniquet, donor sensory or mixed sensory/motor nerves of interest are mobilized. Nearby recipient motor branch targets are identified using a handheld nerve stimulator. The recipient motor nerves are transected close to their muscle insertion, and an end-to-end nerve transfer is performed using an epineural 8-0 suture.

Subsequently, the “RPNI” part of the case ensues. A thin 2–3 × 1 cm² free muscle graft is sharply harvested from the nearby muscle or from an uncontaminated amputated specimen, for each TMRpni coaptation. The free muscle graft is wrapped around the TMR coaptation and secured to itself with an interrupted 6-0 absorbable or nonabsorbable suture. A fibrin glue may be used to hold the construct in place. The incision is closed and a compressive bandage is placed. A postoperative block is administered. Early postoperative range of motion exercises are initiated during the immediate recovery period. Multimodal pharmacotherapy is prescribed consisting of a neuromodulator (eg, gabapentin or pregabalin), NSAIDs, and opioid.

An example patient who underwent TMRpni is shown in Figure 1. A 34-year-old male combat veteran suffered from a dysfunctional limb after sustaining a remote high-energy ballistic injury to the left knee during deployment overseas. He underwent multiple limb preservation procedures but had persistent stiffness and pain. After psychiatry clearance, the patient decided to proceed with elective above-knee amputation. TMRpni was performed at the time of index amputation. In the supine position through the distal amputation approach, the saphenous nerve was coapted to a motor branch to semimembranosus. The coaptation was wrapped in a thin 3 cm × 1 cm free muscle graft harvested from the lateral gastrocnemius of the amputated specimen. The incision was closed and the patient was then placed in a prone position. A separate incision was made in the posterior thigh to expose the sciatic nerve. The common peroneal component of the sciatic nerve was dissected and coapted to a motor branch to biceps femoris and the tibial nerve component of the sciatic nerve coapted to a motor branch to semimembranosus. Each coaptation was wrapped with a thin 3 cm × 1 cm free muscle graft from the discarded specimen. The incision was closed, and a compressive dressings applied. At 4 months follow-up, the patient ambulated with his prosthetic leg and reported no residual limb or phantom pain.

**DISCUSSION**

The efficacy of TMR and RPNI in treating neuropathic pain has been previously reported, with improved pain scores and outcomes compared with those of cohorts undergoing traditional traction neurectomies and cohorts undergoing “burying nerves in the surrounding muscle.”12,16,17 We believe that TMRpni may have advantages compared with TMR or RPNI alone. RPNI is limited by the size of the free muscle graft. If the muscle graft is too small, it will fail to amplify a transcutaneous signal for prosthetic use. If the free muscle graft is too large, it will fail to revascularize and will undergo necrosis. The consequence of a nerve mismatch in TMR is not fully understood but may be a limitation of the technique. It is possible that during distal reinnervation there may be neuronal escape leading to neuroma formation and/or persistent sites of pain. By wrapping the TMR coaptation with a free muscle graft, essentially acting as a biologic nerve wrap, the escape neurons will have a denervated free muscle graft to reinnervate, thereby creating a

---

**Fig. 1.** A 34-year-old man who underwent left above-knee amputation and immediate TMRpni. A, The common peroneal component of the sciatic nerve coapted to the motor branch to biceps femoris. B, Coaptation wrapped with a free muscle graft.
construct akin to an RPNI. Other means of managing nerve mismatch include splitting the donor nerve and coaping to multiple motor recipients and performing a TMR combined with vascularized pedicled RPNI. These 2 options may be limited by the local availability of recipient motor nerves and muscle bulk.

TMRpni can be performed with minimal or no additional risk compared with TMR or RPNI surgery and with minimal additional operative time or cost. Future studies will elucidate the reinnervation distribution between the recipient nerve and autologous, denervated muscle graft. Head-to-head study will be required to compare the ability of TMR, RPNI, and TMRpni to treat residual and phantom limb pain, minimize opiate consumption, and improve prosthetic use.

Joseph S. Khouri, MD
University Hospitals Cleveland Medical Center
11100 Euclid Avenue
Cleveland, OH 44106
E-mail: Joe.Khouri@uhhospitals.org

REFERENCES

1. Burgoyne LL, Billups CA, Jirón JL Jr, et al. Phantom limb pain in young cancer-related amputees: recent experience at St. Jude children’s research hospital. *Clin J Pain*. 2012;28:222–225.
2. Clark RL, Bowling FL, Jepson F, et al. Phantom limb pain after amputation in diabetic patients does not differ from that after amputation in nondiabetic patients. *Pain*. 2013;154:729–732.
3. Ephraim PL, Wegener ST, MacKenzie EJ, et al. Phantom pain, residual limb pain, and back pain in amputees: results of a national survey. *Arch Phys Med Rehabil*. 2005;86:1910–1919.
4. Hanley MA, Ehde DM, Jensen M, et al. Chronic pain associated with upper-limb loss. *Am J Phys Med Rehabil*. 2009;88:742–751; quiz 752, 779.
5. Reiber GE, McFarland LV, Hubbard S, et al. Servicemembers and veterans with major traumatic limb loss from Vietnam war and OIF/OEF conflicts: survey methods, participants, and summary findings. *J Rehabil Res Dev*. 2010;47:275–297.
6. Richardson C, Glenn S, Nurmiikko T, et al. Incidence of phantom phenomena including phantom limb pain 6 months after major lower limb amputation in patients with peripheral vascular disease. *Clin J Pain*. 2006;22:353–358.
7. Cheesborough JE, Smith LH, Kuiken TA, et al. Targeted muscle reinnervation and advanced prosthetic arms. *Semin Plast Surg*. 2015;29:62–72.
8. Kuiken TA, Dumanian GA, Lipschutz RD, et al. The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee. *Prosthet Orthot Int*. 2004;28:245–253.
9. Frost CM, Ursu DC, Flattery SM, et al. Regenerative peripheral nerve interfaces for real-time, proportional control of a Neuroprosthetic hand. *J Neuroeng Rehabil*. 2018;15:108.
10. Urbanchek MG, Kung TA, Frost CM, et al. Development of a regenerative peripheral nerve interface for control of a Neuroprosthetic limb. *Biomed Res Int*. 2016;2016:5726730.
11. Cheesborough JE, Souza JM, Dumanian GA, et al. Targeted muscle reinnervation in the initial management of traumatic upper extremity amputation injury. *Hand (N Y)*. 2014;9:253–257.
12. 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.
13. Michno DA, Woollard ACS, Kang NV. Clinical outcomes of delayed targeted muscle reinnervation for neuroma pain reduction in longstanding amputees. *J Plast Reconstr Aesthet Surg*. 2019;72:1576–1606.
14. Souza JM, Cheesborough JE, Ko JH, et al. Targeted muscle reinnervation: a novel approach to postamputation neuroma pain. *Clin Orthop Relat Res*. 2014;472:2984–2990.
15. Valério IL, Dumanian GA, Jordan SW, et al. Preemptive treatment of phantom and residual limb pain with targeted muscle reinnervation at the time of major limb amputation. *J Am Coll Surg*. 2019;228:217–226.
16. Kubiak CA, Kemp SWP, Cederna PS, et al. Prophylactic regenerative peripheral nerve interfaces to prevent postamputation pain. *Plast Reconstr Surg*. 2019;144:421e–430e.
17. Alexander JH, Jordan SW, West JM, et al. Targeted muscle reinnervation in oncologic amputees: early experience of a novel institutional protocol. *J Surg Oncol*. 2019;120:348–358.
18. Zuo RJ, Willand MP, Ho ES, et al. Targeted muscle reinnervation: considerations for future implementation in adolescents and younger children. *Plast Reconstr Surg*. 2018;141:1447–1458.
19. Agnew SP, Schultz AE, Dumanian GA, et al. Targeted reinnervation in the transfemoral amputee: a preliminary study of surgical technique. *Plast Reconstr Surg*. 2012;129:187–194.
20. Bowen JB, Ruter D, Wee C, et al. Targeted muscle reinnervation technique in below-knee amputation. *Plast Reconstr Surg*. 2019;143:309–312.
21. Fracol ME, Janes LE, Ko JH, et al. Targeted muscle reinnervation in the lower leg: an anatomical study. *Plast Reconstr Surg*. 2018;142:541e–550e.
22. Gart MS, Souza JM, Dumanian GA. Targeted muscle reinnervation in the upper extremity amputee: a technical roadmap. *J Hand Surg Am*. 2015;40:1877–1888.
23. Morgan EN, Kyle Potter B, Souza JM, et al. Targeted muscle reinnervation for transradial amputation: description of operative technique. *Tech Hand Up Extrem Surg*. 2016;20:166–171.
24. Pierrie SN, Gaston RG, Loeblf BJ. Targeted muscle reinnervation for prosthesis optimization and neuroma management in the setting of transradial amputation. *J Hand Surg Am*. 2019;44:525.e1–525.e8.
25. Economides JM, DeFazio MV, Attinger CE, et al. Prevention of painful neuroma and phantom limb pain after transfemoral amputations through concomitant nerve coaptation and collagen nerve wrapping. *Neurosurgery*. 2016;79:508–513.
26. Zhu X, Wei H, Zhu H. Nerve wrap after end-to-end and tension-free neurorrhaphy attenuates neuropathic pain: a prospective study based on cohorts of digit replantation. *Sci Rep*. 2018;8:620.
27. Kuiken TA, Barlow AK, Hargrove L, et al. Targeted muscle reinnervation for the upper and lower extremity. *Tech Orthop*. 2017;32:109–116.
28. Valério I, Schulz SA, West J, et al. Targeted muscle reinnervation combined with a vascularized pedicled regenerative peripheral nerve interface. *Plast Reconstr Surg Glob Open*. 2020;8:e2689.